



HAL
open science

Modélisation de la dynamique des populations naturelles d'*Aedes albopictus* et réponse à la lutte antivectorielle

Marion Haramboure

► To cite this version:

Marion Haramboure. Modélisation de la dynamique des populations naturelles d'*Aedes albopictus* et réponse à la lutte antivectorielle. Zoologie des invertébrés. Université Montpellier, 2020. Français. NNT : 2020MONTG071 . tel-03340551

HAL Id: tel-03340551

<https://theses.hal.science/tel-03340551>

Submitted on 10 Sep 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

THÈSE POUR OBTENIR LE GRADE DE DOCTEUR DE L'UNIVERSITÉ DE MONTPELLIER

En Biologie des Interactions

École doctorale GAIA

Cirad

Modélisation de la dynamique des populations naturelles d'*Aedes albopictus* et réponse à la lutte antivectorielle

Présentée par Marion Haramboure
Le 16 décembre 2020

Sous la direction de Pierrick Labbé
et Annelise Tran

Devant le jury composé de

Elisabeta Vergu, Directrice de recherche, INRAE Paris

Patrick Mavingui, Directeur de recherche, CNRS

Célestine Atyame-Nten, Maître de Conférence, Université de la Réunion

Didier Fontenille, Directeur de Recherche, IRD Montpellier

Hélène Thebault, Gestionnaire de la lutte anti-vectorielle, ARS Réunion

Pierrick Labbé, Professeur des Universités, Université de Montpellier

Annelise Tran, Directrice de Recherche, Cirad La Réunion

Thierry Baldet, Chargé de Recherche, Cirad La Réunion

Rapporteuse

Rapporteur

Examinatrice

Examineur

Invitée

Directeur

Co-directrice

Encadrant



UNIVERSITÉ
DE MONTPELLIER

MARION HARAMBOURE

**MODÉLISATION DE LA DYNAMIQUE DES
POPULATIONS NATURELLES
D'*Aedes albopictus*
ET RÉPONSE À LA LUTTE ANTI-VECTORIELLE**

16 décembre 2020



Cirad et Université de Montpellier

"On ne voit bien qu'avec le coeur. L'essentiel est invisible pour les yeux." Antoine de Saint-Exupéry (Le petit prince, 1943).



Merci Anne-Sophie Toutain pour cette très jolie illustration.

Remerciements

Il y a trois ans, j'ai imaginé ce que serait selon moi la thèse idéale. J'étais bien loin d'imaginer que ma thèse serait bien plus merveilleuse encore. C'est grâce à l'ensemble des personnes que j'ai eu l'occasion de rencontrer lors de ces trois années que ma thèse a été MAGIQUE.

Mes premiers remerciements iront à mes directeurs Annelise Tran et Pierrick Labbé ainsi qu'à mon encadrant de thèse, Thierry Baldet qui sont tous trois des personnes positives qui manient très bien la technique du "sandwich" (on commence par les points positifs, on poursuit avec les points négatifs et on finit par féliciter l'étudiant pour son travail).

Mille mercis à [Annelise Tran](#), qui a cru en moi durant ces trois années. Merci d'avoir su me laisser autonome et prendre mes propres décisions tout en me guidant lorsque j'en avais besoin. Merci également pour ton calme et ta patience, et ça même lorsque j'arrivais tard au travail ou encore lorsque j'ai rayé ta voiture (encore désolée). Merci également pour m'avoir préservé des personnes malveillantes et merci d'être une scientifique intègre. Je pense avoir réussi à "tuer la mère" au bout de trois ans, mais tu resteras à jamais une source d'inspiration !

Un immense merci à [Pierrick Labbé](#), qui malgré les 8910 km qui nous séparent, a toujours été présent lorsque j'en avais besoin, avec des conseils à chaque fois très pertinents. Il se cache derrière ton imposante carrure et ta puissante voix (peuvent impressionner au premier abord) un homme au grand cœur, qui a toujours eu les mots pour m'encourager et me rassurer.

Un grand merci à [Thierry Baldet](#), qui a toujours la référence bibliographique qu'il me faut ! Tu as réussi à partager avec moi tes connaissances en entomologie et à me fournir des connaissances capitales pour l'avancement de ma thèse. Tes petites blagues et ta bonne humeur

"matinal" me manqueront.

Ce travail de thèse s'inscrit dans le projet ERC Revolinc. Je tiens donc à exprimer toute ma gratitude à **Jérémy Bouyer** qui m'a fait confiance pour mener à bien cette thèse.

Je remercie également **Léa Douchet**, que j'ai eu l'occasion d'encadrer lors de son stage de Master 2. Ta rigueur, ta motivation et tes compétences indiscutables en modélisation ont été précieuses pour ma thèse. Ta bonne humeur au quotidien a rendu cette première expérience d'encadrement forte enrichissante. Je ne pouvais pas rêver meilleure stagiaire.

Je n'aurai pas réussi seul à déterminer la formule analytique du R_0 du modèle épidémiologique. Je remercie donc **David Pleydell** qui est un excellent modélisateur du Cirad et qui m'a fortement aidé à travailler sur la modélisation de la boosted TIS et sur le modèle épidémiologique.

Ce travail n'aurait pu se faire sans l'ARS de La Réunion et l'EID Méditerranée qui contribuent chaque jour à la surveillance et au contrôle du moustique tigre en France et sans qui ce travail n'aurait été possible.

Je remercie les membres de mon comité de suivi, **Frédéric Simard**, **David Pleydell**, **Pauline Ezanno** et **Célestine Atyame Nten** pour leurs échanges constructifs autour de la modélisation et de la lutte anti-vectorielle, mais aussi pour leurs conseils précieux relatifs à la gestion de thèse. Merci à **Yves Dumont** pour avoir participé à mon premier comité de suivi.

Je remercie le jury, **Elisabeta Vergu**, **Patrick Mavingui**, **Célestine Atyame Nten** et **Didier Fontenille**, pour avoir accepté d'évaluer mon travail, pour la relecture de mon manuscrit et pour votre présence à la soutenance.

L'équipe Astre du Cirad :

Je tiens à adresser un mot pour **Catherine Cetre**, **Claire Garros**, **Cécile Squarzoni** et **Eric Cardinale** pour avoir contribué à une ambiance d'équipe aussi joyeuse et bienveillante.

Merci à **Hélène Guis** pour m'avoir si bien accueillie lors de ma venue à Madagascar et merci également à **Daouda Kassie** pour son extrême gentillesse.

Merci à **Anne-Sophie Toutain**, qui est pour moi bien plus qu'une collègue. Tu es une personne incroyable, qui sème le bonheur autour d'elle! Ta créativité, ta prise d'initiative, ton humour et ton énergie font de toi une personne inspirante, qui ne laisse personne indifférent. Ma dernière année de thèse n'aurait pas été aussi fun sans toi.

Merci à Anaïs Etheves qui a toujours été là durant ces 3 années de thèse et qui a toujours fait preuve d'une grande patience lorsque je massacrais le patrimoine réunionnais avec mon créole approximatif.

Merci à tout les doctorants de l'équipe et à Noellie Gay, pour tout ses moments de folies qui m'ont fait rire aux éclats.

Merci aux VSC de qui l'équipe ne peut se passer : A Renouille (ou Renaud Levantidis pour les autres), qui a été mon confident, parfois même ma source de motivation ; A Miguy Patchea-pin, notre petit soleil de l'open space, dont le sourire illumine les locaux ; A Denis Josse qui sait faire preuve d'une grande écoute lorsque j'avais besoin de parler de tout et de rien (ce qui arrive très souvent) ; A Floriane Boucher et ses délicieux gâteaux à jamais inégalés ; A Marlène Dupraz pour ses paroles pleines de sagesses.

J'envoie tout mon amour à l'ensemble des stagiaires qui redonnent un coup de "peps" à l'équipe. J'ai une pensée particulière pour mes amours, Samuel Benkimoun, Yemna Abbade et Amaïas Avalos, sans qui mon adaptation à La Réunion n'aurait pas été aussi joyeuse. Vos rires résonnent encore dans l'open space et dans mon cœur. Je pense également à Violette Silve, notre "Grammar-Nazie" qui a bien voulu prendre de son temps personnel pour corriger mes fautes d'orthographe.

Je remercie les personnes de l'administration pour la gestion de mes missions, qui n'a pas toujours été simple et toutes les personnes du Cirad de Montpellier pour m'avoir accueillie lors de mes missions.

L'unité Aïda du Cirad :

Je remercie l'équipe de m'avoir fait confiance pour prendre le poste de chercheuse en écologie des populations pour la gestion territoriale des ravageurs des cultures. Je remercie en particulier Mathias Christina et Louise Leroux pour m'avoir aidée pour l'oral ainsi que Thierry Brévault, Krishna Naudin, Jean-Paul Laclau mais également Cyril Piou (UMR CBGP) et Karine Berthier (de l'Inrae) pour mon recrutement.

Les équipes scientifiques qui travaillent au sein de la plateforme du Cyroi :

Je remercie l'équipe de Symbiotic pour leurs échanges constructifs autour de la lutte antivectorielle, avec une spéciale dédicace pour Benjo (Benjamin Gaudillat) avec qui j'ai partagé à la fois des fous rires et d'inoubliables randonnées autour de l'île.

Je remercie l'équipe TIS de l'IRD qui a collaboré au développement de modèles sur la lutte anti-vectorielle. Merci à [Lucie Maquereau](#) et [David Damiens](#) pour les repas du midi marqués par des éclats de rire et nos soirées jeux de société.

A l'équipe "Evolution, Vecteurs, Adaptation et Symbioses" de l'ISEM

Merci à [Mylène Weill](#), [Mathieu Sicard](#), [Christophe Boete](#), [Sandra Unal](#), [Manon Bonneau](#), [Patrick Makoundou](#) et toutes les personnes de l'équipe pour m'avoir accueillie comme l'une des leurs lors de mes missions à Montpellier.

A l'unité "Infectious Disease Modelling" du Swiss TpH Institute

Lors de ma thèse, j'ai eu l'occasion de réaliser un échange au sein du Swiss TpH Institute. Je remercie [Nakul Chitnis](#) et l'équipe de modélisation qui m'a accueillie et intégrée au sein de leur laboratoire afin de travailler sur un modèle de résistance aux insecticides et qui ont partagé avec moi leurs connaissances en modélisation mathématique et statistique.

Aux enseignants :

Merci à [Audrey Jeager](#) qui m'a accordé sa confiance pour reprendre ses cours de SIG et qui, grâce à son organisation, m'a permis d'exercer à l'université sans difficulté malgré la pandémie actuelle qui rend difficile le travail des enseignants.

Merci également à [Jean-Charles Sicard](#) pour sa gentillesse et pour avoir partagé avec moi sa passion pour l'enseignement.

A ma famille et mes amis :

A ma mère, qui m'a toujours soutenue dans les décisions que j'ai pris. Qui a été une mère courageuse et qui a donné son maximum pour que je ne manque de rien. Merci pour avoir été la meilleure des mères.

A toi mon tout mon coco de l'amour, mon papangue agressif, mon anguille frétilante. Je suis tellement heureuse que tu fasses partie de ma vie. Tu m'as soutenue et aidée lorsque le moral n'était pas au beau fixe, tu as même veillé à me confectionner de bon petits plats lorsque je travaillais tard le soir. Parce que je sais que ton amour n'a pas de frontière et que peu importe où la vie nous mènera, tu me suivras, je t'aime.

A mes copines **Mathilde** et **Jessica**. Voilà plus de 10 ans que l'on se connaît et vous êtes toujours présentes à chaque fois que je suis de passage à Mont de Marsan. Nous sommes rentrées ensemble dans le "monde des adultes" et même si un jour nos chemins devaient se séparer, vous aurez toujours une place importante dans mon cœur.

A **Sergio**, pour ses merveilleux carris et son aide précieuse lorsque j'en avais besoin.

A toutes les personnes que j'ai rencontré lors de mes études et que je ne pourrais oublier : **Elise verrier**, **Maeva Hucy**, **Laurie Araspin**, **Manon Poisson**, **Léa Baudin**, **Maeva Répelin** et tellement d'autre encore.

A mes copines **Alex** et **Adeline** que j'ai rencontrées à l'APLAMEDOM et avec qui j'ai partagé des moments inoubliables à La Réunion qui resteront gravés à jamais.

Articles et Poster

Articles

[1] Hafsia, S., Atyame-Nten, C., **Haramboure, M.**, Tran, A., Baldet, T., and Mavingui, P. (2020) Updating history of dengue virus circulation in Reunion Island. In : *Being drafted*.

[2] **Haramboure, M.**, Labbé, P., Baldet, T., Damiens, D., Gouagna, L.C., Bouyer, J., and Tran, A. (2020). Modelling the dengue outbreak from La Réunion Island in 2018. In : *Being drafted*

[3] Douchet, L., **Haramboure, M.**, Baldet, T., L'Ambert, G., Damiens, D., Gouagna, L. C., Bouyer, J., Labbé, P., Tran, A. (2020). What is(are) the most effective method(s) to control the tiger mosquito? Comparing sterile male releases and other methods in temperate and tropical climates. *Submitted in : Scientific Report*.

[4] Benkimoun, S., Atyame-Nten, C., **Haramboure, M.**, Degenne, P., Thébault, H., Dehecq, J.S., Tran, A. (2020). The basic reproduction number (R_0) proves its efficiency to develop an operational dynamic mapping tool for dengue surveillance and control in Reunion Island. *Under Reviewing*.

[5] **Haramboure, M.**, Labbé, P., Baldet, T., Damiens, D., Gouagna, L. C., Bouyer, J., Tran, A. (2020). Modelling the control of *Aedes albopictus* mosquitoes based on sterile males release techniques in a tropical environment. In : *Ecological Modelling*, 424, 109002.

[6] Tran, A., Mangeas, M., Demarchi, M., Roux, E., Degenne, P., **Haramboure, M.**, Le Goff, G., Damiens, D., Gouagna, L. C., Herbreteau, V., and Dehecq, J.S. (2020). “Complementarity of empirical and process-based approaches to modelling mosquito population dynamics with *Aedes albopictus* as an example—Application to the development of an operational mapping tool of vector populations”. In : PLOS ONE 15.1. doi :10.1371/journal.pone.0227407.

Posters

[1] **Haramboure, M.**, Labbé, P., Baldet, T., Bouyer, J., Tran, A. (2018). Modelling the effect of the sterile insect technique alone or combined with the auto-dissemination method on the *Aedes albopictus* mosquitoes. *Poster presented at E-Sove*. Palermo, Sicily.

[2] **Haramboure, M.**, Labbé, P., Baldet, T., Bouyer, J., Tran, A. (2018). Modelling *Aedes albopictus* response to control methods based on sterilized males release. *Poster presented at Evolutionary Biology*, Montpellier, France.

EIR-A

Dans le cadre de la participation à l'École internationale de recherche d'Agreenium (EIR-A), un échange de 2 mois a été réalisé au sein du laboratoire Swiss Tropical and Public Health (Swiss TPH) ainsi que la participation à un séminaire en 2018 et 2019 sur "GlobalHealth – Biodiversité, santé des écosystèmes, santé humaine" et "Transitions agricoles et alimentaires : produire, transformer, distribuer et consommer autrement" respectivement (<https://www.agreenium.fr/page/parcours-doctoral-eir-a>).

Notations

Alizés	Actions de lutte intégrées sur zone et d'éducation sanitaire
ANSES	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail
ARS	Agence Régionale de Santé
bti	<i>Bacillus thuringiensis subsp. israelensis</i>
BTIS	Technique de l'insecte stérile boostée
EDO	Équations Différentielles Ordinaires
EID méditerranée	Entente interdépartementale pour la démoustication du littoral méditerranéen
IC	Incompatibilité cytoplasmique
IRIS	Ilots Regroupés pour l'Information Statistique
LAV	Lutte Anti-Vectorielle
OMS	Organisation Mondiale de la Santé
Piège BG-sentinel	Piège Biogent sentinel
REVOLINC	Révolutionner la lutte contre les insectes
TIS	Technique de l'Insecte Stérile
TII	Technique de l'Insecte Incompatible
RIDL	Release of Insects carrying a Dominant Lethal
R_0	Taux de reproduction de base
UBV	Ultra Bas Volume

Glossaire

Agent entomopathogène	Organismes tels que des champignons, des virus ou encore des bactéries utilisés pour la lutte contre les insectes nuisibles.
Arbovirus	Virus ayant pour vecteur les arthropodes hématophages.
Capacité vectorielle	mesure l'efficacité de transmission d'un vecteur dans les conditions naturelles. Elle tient compte de la compétence vectorielle, la bio-écologie du vecteur et, plus particulièrement, tout ce qui influe sur les chances de contact entre le vecteur et l'hôte vertébré (durée de vie, densité, préférences trophiques, etc.).
Compétence vectorielle	Aptitude intrinsèque d'un arthropode à transmettre un agent pathogène modulée par des facteurs extrinsèques tels que la température, l'humidité et le contact avec l'homme.
Cycle gonotrophique	Succession des phénomènes physiologiques qui se produisent chez les femelles moustiques entre l'oviposition et le repas de sang.
Morbidité	Nombre des malades dans un groupe donné et pendant un temps déterminé.

Nullipare	Femelles qui n'ont jamais pondu d'œuf
Oviposition	Acte pour une femelle de pondre et de placer ses œufs dans un endroit particulier pour favoriser l'éclosion.
Pare	Femelles qui ont pondu au moins une fois des œufs
Résilience	Capacité d'un système vivant (ex : population) à retrouver les structures et les fonctions de son état de référence après une perturbation
Sérotype	Nom donné à une variété sérologique d'une espèce ou sous-espèce de micro-organisme (bactérie, virus) basée sur des caractéristiques de leurs antigènes de surface ou de leurs protéines reconnues par des méthodes sérologiques.
Système déterministe	Système pour lequel les mêmes entrées produisent toujours exactement les mêmes sorties.
Système stochastique	Synonyme d'aléatoire, en référence au hasard et s'oppose par définition au système déterminisme.
Tétracycline	Antibiotique bactériostatique de la classe des cyclines (ou tétracyclines)
Thermonébulisation	Génération d'un brouillard dense de très fines particules chargées d'insecticides
Transgène	Séquence isolée d'un gène, transférée d'un organisme à un autre, lors de la mise en œuvre de la transgénèse.
Transgénèse	Incorporer un ou plusieurs gènes dans le génome d'un organisme vivant.
Transinfection	Infection d'un hôte par une bactérie ou un virus prélevé sur un autre hôte, souvent par micro-injection.
Vitellogenèse	Formation des matières de réserve (vitellus) de l'œuf

Table des matières

I	Introduction générale	Page 1
1	<i>Aedes albopictus</i> , l'œil du tigre	1
1.1	Les maladies vectorielles	1
1.2	Le moustique tigre : les contrastes géographiques	2
1.2.1	Une espèce vectrice en milieu tropical et sub-tropical	3
1.2.2	L'invasion du moustique tigre en Europe	3
2	Le contrôle du moustique tigre	4
2.1	Les méthodes de contrôle conventionnelles d' <i>Ae. albopictus</i> en France	4
2.1.1	Les actions de lutte antivectorielle en période inter-épidémique	6
2.1.2	Les actions de lutte anti-vectorielle en période épidémique	6
2.2	Les méthodes de contrôles alternatives	7
2.2.1	Le Piégeage de Masse	7
2.2.2	L'autodissémination	9
2.2.3	Les méthodes basées sur des lâchers de mâles stériles	9
i	<i>La Technique de l'Insecte Stérile</i>	9
ii	<i>La technique de l'Insecte Incompatible</i>	10
iii	<i>Release of Insects carrying a Dominant Lethal</i>	12
2.2.4	Les produits répulsifs	12
2.2.5	La lutte biologique	12
2.3	La boosted TIS : une méthode de lutte intégrée	13
3	La modélisation : un outil de choix pour comprendre et optimiser la LAV	15
3.1	Modélisation quantitative, statistique ou mécaniste	15
3.2	Le choix du modèle mathématique	16
3.2.1	Représentation des populations ou des individus	16

TABLE DES MATIÈRES

3.2.2	Les phénomènes aléatoires	16
3.3	Le développement d'un modèle mathématique.....	17
3.4	Modélisation de la dynamique des populations d' <i>Aedes albopictus</i>	17
3.5	Modélisation de la TIS et boosted TIS pour lutter contre les moustiques	18
3.6	Modélisation de la transmission d'agents pathogènes par les moustiques	18
4	Objectifs et méthodologie	19
4.0.1	Contexte et objectif général.....	19
4.0.2	Démarche scientifique.....	21

II Modélisation de la TIS et BTIS à La Réunion _____ Page 23

III Impact de la TIS/BTIS dans un contexte de lutte intégrée en milieu tropical et tempéré _____ Page 40

IV Modélisation de la dynamique de transmission de la dengue à La Réunion _____ Page 58

V Discussion générale _____ Page 72

1	Retour sur les résultats majeurs	73
1.1	Des résultats en accord avec la littérature.....	73
1.2	Des avancées significatives	73
2	L'approche choisie.....	74
2.1	Le modèle entomologique	75
2.2	La modélisation de la lutte anti-vectorielle	76
2.3	Le modèle épidémiologique.....	76
2.4	L'impact de la LAV sur la transmission de la dengue.....	76
3	Vers un modèle prenant en compte les déplacements des populations d'hôtes et de vecteurs.....	77
3.1	La dispersion des moustiques	77
3.2	Les déplacements humains	78
4	Perspectives de l'étude	79
4.1	L'économie	79
4.2	La modélisation de la résistance au pyriproxyfène	80
4.3	D'autres méthodes de LAV	81
4.4	D'autres espèces cibles.....	82
5	Conclusion	82

A Annexe _____ Page 114

TABLE DES MATIÈRES

Annexes	Page 114
1 Determination of the basic reproduction number (R_0)	114
2 Poster	116
3 Annexes de l'article 1	117
4 Annexes de l'article 2	124
5 Annexes de l'article 3	134

Table des figures

I.1	Carte de la distribution prédite d' <i>Aedes albopictus</i>	2
I.2	Pulvérisations d'aldulticide autour des cas de dengue confirmés	5
I.3	Illustrations des techniques de luttes alternatives	8
I.4	Les méthodes de lutte contre <i>Aedes albopictus</i>	11
I.5	Présentation du concept de la "Boosted TIS".	14
I.6	Objectifs et démarche scientifique de la thèse	22

Introduction générale

La mondialisation a été profitable au moustique tigre, *Aedes albopictus* (Skuse 1834). Originaire d'Asie, cette espèce invasive a pu coloniser l'Europe, l'Afrique et l'Amérique lors de ces quatre dernières décennies en raison de l'intensification du commerce international. Il constitue aujourd'hui une menace pour la santé humaine en tant que qu'insecte vecteur du virus de la dengue, auquel 3,9 milliards de personnes, dans 128 pays, seraient exposées, et contre lequel, en l'absence de vaccin ou de traitement spécifique, le contrôle des populations vectrices est la seule mesure de lutte. Heureusement, à cœur vaillant rien n'est impossible et de nouvelles méthodes de lutte anti-vectorielle voient le jour. Mais quelles stratégies de lutte sont les plus efficaces ? A quel moment doit débiter une action de contrôle ? Pour combien de temps ? Nombreuses sont les questions auxquelles il est difficile de répondre. Mais à chaque question sa réponse et les modèles sont des outils précieux pour nous aider. Mon travail de thèse s'est attelé durant trois ans à apporter des réponses à ces questions à travers des approches de modélisation mathématique. J'ai développé des modèles afin de mieux comprendre l'impact de la lutte anti-vectorielle sur les populations d'*Ae. albopictus*. Mes travaux se sont focalisés en particulier sur les nouvelles méthodes de lutte basées sur les lâchers de mâles stériles.

1

Aedes albopictus, l'œil du tigre

1.1 Les maladies vectorielles

Les maladies à transmission vectorielle sont des maladies infectieuses transmises principalement par des arthropodes hématophages, en majorité des insectes. Elles seraient responsables de plus de 17 % des maladies infectieuses et provoqueraient plus d'un million de décès chaque an-

née dans le monde [187]. Le paludisme est la maladie vectorielle qui présente la plus forte morbidité et de mortalité. Au niveau mondial, on estime en 2018 le nombre de cas et de décès dus au paludisme à 228 millions et 405 000 respectivement [181]. C'est pourquoi 2,7 milliards US\$

CHAPITRE I. INTRODUCTION GÉNÉRALE

ont été investis en 2018 pour son contrôle et son élimination [181].

Il existe de nombreuses autres maladies à transmission vectorielle, mais elles ne constituent pas une priorité de santé publique, notamment parce qu'elles n'affectent essentiellement que des populations à faible revenu dans les régions en développement d'Afrique, d'Asie et d'Amérique. Elles sont donc classées comme "maladies tropicales négligées" [188]. Le fardeau de ces maladies tropicales négligées est mal compris, et jusqu'à ces 5 à 10 dernières années, ces maladies ont manqué d'investissement pour leur étude [260].

Parmi ces maladies, l'Organisation Mondiale de la Santé (OMS) met l'accent sur une maladie virale transmise par le moustique : la dengue [188]. Transmise par les moustiques du genre *Aedes*, on estime à 390 millions le nombre de cas de dengue par an [32]. Si de nombreuses infections de dengue n'entraînent que des manifestations bénignes, et donc une mortalité inférieure à celle du paludisme, des complications potentiellement mortelles peuvent survenir [182]. Par ailleurs, la morbidité de la dengue n'a cessé d'augmenter, passant de 2,2 millions en 2010 à 3,2 millions en 2015 [182].

1.2 Le moustique tigre : les contrastes géographiques

Aedes albopictus, appelé également "moustique tigre", représente un risque sanitaire important puisqu'il s'agit, avec l'espèce *Ae. aegypti*, de l'un des principaux vecteurs responsables du maintien, de la dispersion et de la transmission de la dengue en zone urbaine. Originaire d'Asie du Sud-Est, ce moustique vecteur a colonisé les îles de l'océan Indien et de l'océan Paci-

fique [147, 65]. Au cours des années 80, il a étendu son aire de répartition en Europe, aux États-Unis et au Brésil [159] (Figure I.1). L'expansion de son aire de répartition a été facilitée par l'intensification du commerce international durant le 20^e siècle. A titre d'exemple, le commerce des pneus a été responsable de l'introduction du moustique tigre aux États-Unis [202] et en Italie [61].

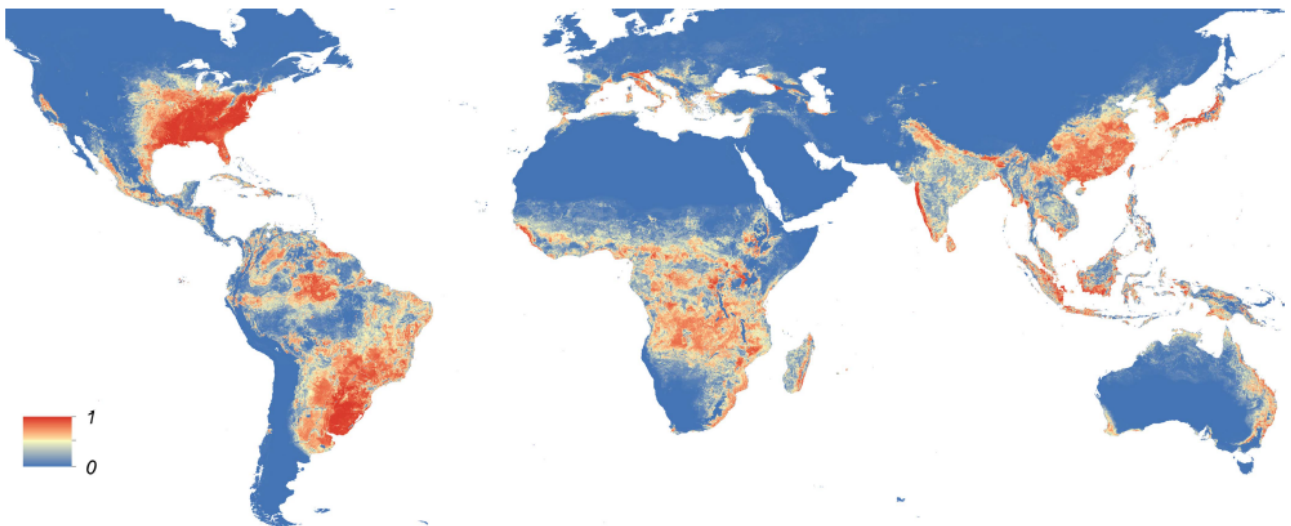


FIGURE I.1 – Carte de la distribution prédite d'*Ae. albopictus* en 2015 issue de Kraemer et al. [125]. La carte représente la probabilité d'occurrence (de 0 en bleu à 1 en rouge) à une résolution de 5km × 5km.

CHAPITRE I. INTRODUCTION GÉNÉRALE

1.2.1 Une espèce vectrice en milieu tropical et sub-tropical

Aedes aegypti (Linnaeus 1762) a longtemps été considéré comme un vecteur plus efficace qu'*Ae. albopictus* pour la propagation de nombreux agents pathogènes comme le virus de la dengue. Hautement anthropophile, sa forme pantropicale urbaine, *Ae. aegypti aegypti* a évolué pour vivre tout son cycle de vie, des larves à l'adulte, à proximité des humains, préférant se nourrir de ces derniers même en présence d'autres mammifères [205, 191]. A l'inverse, *Ae. albopictus* est zoophile et anthropophile, et n'a pas cette coexistence préférentielle avec les humains. Cette espèce serait en outre un moins bon vecteur parce que les femelles *Ae. albopictus* prennent des repas sanguins sur d'autres hôtes, qualifiés de "culs-de-sacs épidémiques",¹ ou encore parce que leurs compétence vectorielle² est moindre en comparaison de celle d'*Ae. aegypti* [205, 191]. Cependant, *Ae. albopictus* fut le seul ou principal vecteur des épidémies de dengue à Hawaï [11], à La Réunion [249], en Afrique centrale [174] et dans le sud de la Chine [174]. Le contrôle d'*Ae. albopictus* occupe donc une place centrale dans les régions où l'espèce est présente pour prévenir et contrôler les maladies vectorielles comme la dengue.

Comme toutes les espèces de moustiques, le cycle de vie d'*Ae. albopictus* est scindé en deux phases : une phase aquatique et une phase aérienne. Durant la phase aquatique quatre stades larvaires se succèdent puis, survient la formation de nymphes d'où émergeront par la suite les moustiques adultes aériens. La durée de la phase larvaire est de 8.8 (à 30°C) à 35 jours (à 15°C) [65]. L'espérance de vie des femelles et des mâles adultes est respectivement de 20 et 15 jours (à 30°C) à 39 et 31 jours (à 15°C)[65]. Les mâles

1.2.2 L'invasion du moustique tigre en Europe

En Europe, *Ae. albopictus* s'est installé d'abord en Albanie en 1979, puis en Italie en 1990 [221, 219]. En 2015, l'espèce est signalée dans 20 pays d'Europe, principalement autour du bassin méditerranéen [77]. En France, *Ae. albopictus* a été détecté pour la première fois en 2004 dans le Sud-Est de la France. En 2018, il était présent dans 42 départements de France métropolitaine [196].

Les populations d'*Ae. albopictus* présentes dans le bassin méditerranéen sont capables de transmettre la dengue [43]. Par ailleurs, des cas de transmissions autochtones de maladies virales sont régulièrement signalés suite à l'introduction de voyageurs infectés en Europe laissant redouter l'émergence d'épidémie [257, 101] comme par exemple l'épidémie de chikungunya de 2007 et 2017 en Italie [206, 248, 144]. On note également en 2019 la première détection de cas locaux de Zika sur le continent européen, transmis par *Ae. albopictus* dans le sud de la France [99]. De même, si le risque lié au transport de moustiques infectés par la dengue est faible [162], la littérature a déjà rapporté des cas causés par ce mode de transmission [253].

émergent avant les femelles, les fécondant ainsi dès leur émergence [54]. Des inséminations multiples peuvent avoir lieu à condition qu'elles se fassent dans les 40 minutes suivant l'émergence des femelles [41]. Les mâles et les femelles adultes se nourrissent de nectar [54, 24]. De plus, les femelles sont hématophages, le sang étant nécessaire à la vitellogenèse et la maturation des œufs [54, 24] qui seront pondus juste après la prise du repas de sang [54, 24]. Les femelles pondent généralement les œufs d'un même lot par petites

1. individu hôte d'un agent pathogène mais ne permettant pas sa transmission dans les conditions habituelles (ex : chats, écureuils).

2. aptitude intrinsèque d'un arthropode à transmettre un agent pathogène.

CHAPITRE I. INTRODUCTION GÉNÉRALE

quantités et distribuent ainsi leurs œufs dans différents gîtes [203]. Ce comportement de ponte est dénommé "skip-oviposition behavior" en anglais. La succession de phénomènes physiologiques et comportementaux ayant lieu de la prise de sang jusqu'à l'oviposition est appelée "cycle gonotrophique". Sachant qu'un cycle gonotrophique est réalisé entre 2 et 3,5 jours selon les conditions de température, une femelle peut réaliser ainsi jusqu'à 6 cycles gonotrophiques au cours de sa vie [65].

Aedes albopictus se disperse essentiellement de proche en proche, en raison de son comportement d'oviposition par distribution des œufs dans différents gîtes larvaires. Ainsi, en matière de dispersion active, *Ae. albopictus* parcourt en général moins de 100 m par jour [172]. La colonisation de nouvelles aires est le résultat d'une dispersion passive via les activités de l'Homme et notamment par les moyens de transports maritimes, aériens et terrestre [193, 34]. Entre continents, la voie de dispersion majeure se fait à l'état d'œuf ou de larve [193, 34]. A l'intérieur d'un conti-

nant ou d'un pays, le moustique tigre conquiert de nouveaux territoire à l'état adulte en empruntant les voies de communication terrestre (routes, autoroutes, train, ...) [85].

Aedes albopictus était à l'origine une espèce forestière d'Asie. Par la suite, l'espèce a étendu son aire de répartition aux zones urbaines et péri-urbaines [63, 199] où il colonise essentiellement des gîtes créés par l'Homme (ex : coupelles, pots de fleurs, pneus, boîtes de conserve, ...) [15], *i.e.* des gîtes pour la plupart cryptiques [50]. *Aedes albopictus* est exophile et exophage, la majorité de ses gîtes larvaires et des gîtes de repos, de même que son activité de piqûre, sont en extérieur. .

En s'adaptant à des milieux plus tempérés, *Ae. albopictus* a développé une sensibilité photopériodique. Lorsque la durée de l'éclairement journalier diminue, les femelles photosensibles vivant en milieu tempéré pondent des œufs dits "dormants". Ils sont résistants à la dessiccation et n'écloront qu'à la saison suivante, assurant la survie de l'espèce au cours de l'hiver [54, 24].

2

Le contrôle du moustique tigre

2.1 Les méthodes de contrôle conventionnelles d'*Ae. albopictus* en France

Il n'existe aucun traitement antiviral spécifique de la dengue [263]. Si un vaccin contre la maladie est actuellement homologué, l'OMS préconise son utilisation uniquement dans les pays où les données épidémiologiques indiquent une forte morbidité [186]. Ce vaccin, le Dengvaxia ne confère pas une protection complète et son usage est limité aux personnes ayant déjà été infectées par la dengue, du fait d'un risque accru après la première dose de vaccination d'hospitalisation et de dengue grave chez les personnes n'ayant ja-

mais été infectées par la dengue [256]. D'autres vaccins contre la dengue mais aussi contre le chikungunya et Zika sont en cours de développement. Par conséquent, en l'absence de vaccins pour la prévention et de thérapies pour le traitement de la dengue et des autres arboviroses transmises par les *Aedes*, les programmes de santé publique favorisent actuellement la Lutte Anti-Vectorielle (LAV) (cf. encadré ci-dessous) pour prévenir ou limiter la transmission autochtone de ces maladies.



FIGURE I.2 – Pulvérisations d'aldulticide autour des cas de dengue confirmés réalisées par l'ARS à La Réunion. Photographie ©A. Tran, Cirad

La lutte anti-vectorielle (LAV) - définition et objectifs

"La LAV inclut la lutte contre les arthropodes hématophages quand ces derniers sont des vecteurs potentiels d'agents pathogènes pour l'homme ou les animaux, ou lorsque la nuisance qu'ils provoquent devient un problème de santé publique ou vétérinaire.

Elle s'appuie sur des méthodes qui diffèrent selon les vecteurs et selon les contextes épidémiologiques et socio-économiques. Elle inclut la lutte biocide, la lutte biologique, la lutte génétique, la protection individuelle, l'action sur l'environnement, l'éducation sanitaire, la mobilisation sociale et l'évaluation permanente de toutes ces méthodes" [95].

"Elle a pour objectif de contribuer, au côté d'autres actions de santé publique, à minimiser les risques d'endémisation ou d'épidémisation, à diminuer la transmission d'agents pathogènes par des vecteurs, à gérer les épidémies de maladies vectorielles, le tout dans un cadre stratégique formalisé" [95].

L'OMS préconise une stratégie de LAV intégrée [180, 183] qui s'articule autour de quatre piliers :

- *la surveillance intégrée (vectorielle et épidémiologique) ;*
- *les traitements de LAV ;*
- *la mobilisation sociale ou participation communautaire ;*
- *la coordination inter et intra sectorielle (ou prise en compte de toutes les possibilités de collaboration au sein des secteurs public et privé).*

Le contrôle vectoriel peut être développé comme une activité de routine en période inter-épidémique ou comme une activité durant une épidémie. Pour bien optimiser les ressources, les

actions doivent cibler en priorité les aires où les risques de transmission sont les plus élevés. Dans le cadre de la LAV, la question de l'efficacité des types de traitements vectoriels doit toujours être envisagée dans la perspective d'une stratégie intégrée, qui doit cibler simultanément les différents stades de vie du vecteur en question et combiner des méthodes pour réduire la densité, la longévité des adultes et la transmission d'agents pathogènes. L'efficacité de la LAV s'évalue in fine en termes de réduction de l'incidence de l'infection virale et de ce fait s'inscrit dans des actions et des évaluations conceptuellement pluridisciplinaires. [20]

2.1.1 Les actions de lutte antivectorielle en période inter-épidémique

En période inter-épidémique, la LAV a pour but de prévenir l'apparition ou l'expansion d'un cycle de circulation autochtone des virus transmis. Elle permet également de réduire la nuisance en période d'abondance des populations de moustique. Pour *Ae. albopictus*, les actions de LAV consistent principalement en la suppression des gîtes larvaires [180]. *Ae. albopictus* étant exophile, la recherche des gîtes larvaires est réalisée à l'extérieur des habitations. Bien que la réduction des gîtes ait été déclarée comme la méthode la plus efficace pour le contrôle d'*Ae. albopictus* [86, 180], elle est difficile à mettre en œuvre et à maintenir, car elle nécessite une forte collaboration communautaire [90]. De plus, les larves d'*Ae. albopictus* peuvent se développer dans des gîtes difficilement accessibles ou localisables par des inspections visuelles [90].

Pour ce qui est des gîtes identifiés, mais difficiles d'accès ou impossible à supprimer, il est possible d'utiliser des larvicides chimiques à faible toxicité comme le temephos, des régulateurs de croissance comme le pyriproxyfène, des inhibiteurs de synthèse de la chitine comme le diflubenzuron ou un insecticide larvicide d'origine biologique : le *Bacillus thuringiensis subsp. israelensis* (*Bti*) [95, 17, 195, 260]. Le *Bti* est une bactérie à Gram positif qui, grâce à la production de toxines, détruit la muqueuse intestinale des organismes cibles sensibles [252, 129]. Les lé-

sions intestinales qui en découlent empêchent les larves de moustiques de s'alimenter et meurent [252]. Différentes formulations anti-larvaires de *Bti* se sont montrées efficaces en Europe contre les larves d'*Ae. albopictus* [4, 18, 220]. En Italie, elles sont distribuées aux citoyens et recommandées pour les milieux résidentiels en raison de leur absence de toxicité, appropriée pour une utilisation par le public [210]. Cependant, le problème des gîtes difficilement localisables ou traitables persiste.

En période interépidémique, l'appropriation par les populations de ces actions de suppression des gîtes larvaires passe également par la sensibilisation et la diffusion de recommandations précises en matière de réduction du contact homme-moustique tels que l'usage de répulsifs corporels (section 2.2.4), de vêtements protecteurs, de pose d'écrans anti-moustiques sur les ouvertures d'habitations, d'aménagement de l'habitat et des espaces verts.

2.1.2 Les actions de lutte anti-vectorielle en période épidémique

Lors des situations d'urgence, pour supprimer une épidémie en cours ou pour prévenir une épidémie naissante, les actions de LAV pratiquées en période interépidémique (suppression des gîtes larvaires, mobilisation sociale) sont renforcées par des traitements résiduels d'adulticides pour réduire la densité de femelles moustiques hématophages, seules responsables de la trans-

mission d'agents pathogènes (Figure I.2). Actuellement, les pyréthrinoïdes sont la seule famille d'adulticides autorisée en Europe [1]. Parmi les pyréthrinoïdes, la deltaméthrine est l'insecticide le plus utilisé en France [19]. Il s'agit d'un insecticide à large spectre, qui agit par contact et par ingestion. Il cible les canaux sodium et bloque la transmission de l'influx nerveux des insectes (c.-à-d. un effet neurotoxique), les insectes décèdent alors de paralysie [252, 129]. Ces adulticides sont dispersés dans un périmètre de 100 à 150 m autour des cas isolés [20], correspondant à la surface de dispersion active du moustique

2.2 Les méthodes de contrôles alternatives

L'utilisation conventionnelle des insecticides présentent de nombreuses externalités négatives comme l'apparition de résistance, les rendant moins efficaces, et leur impact sur l'environnement, notamment leur toxicité pour les insectes non cibles [76]. Par ailleurs, l'utilisation des traitements de lutte conventionnelle est contrainte par la difficulté à accéder à des jardins privés,

2.2.1 Le Piégeage de Masse

Les pièges à moustiques furent initialement conçus comme outils de surveillance, et n'ont été envisagés que récemment comme stratégie de lutte [244, 90, 5]. Les techniques de piégeage massif reposent sur l'utilisation de deux types de pièges : les ovitraps et les BG-sentinels (Figure I.4). Un ovitrap est un petit récipient d'eau et fournit un substrat sur lequel les femelles gravides peuvent pondre [91]. Les ovitraps exploitent la propension comportementale d'*Ae. albopictus* à pondre dans des gîtes artificiels de taille réduite [241]. Quant au piège BG-sentinel (Biogent sentinel), il s'agit d'un piège qui libère du CO_2 afin d'attirer les femelles en recherche

[172]. Par ailleurs, des pulvérisations spatiales de pyrethroides adulticides sont réalisées autour des foyers de transmission établie [180, 20]. Ces pulvérisations génèrent un brouillard de gouttelettes très fines qui tuent les moustiques adultes par contact de manière quasi-instantanée [14]. Les pulvérisations sont réalisées à l'échelle d'un quartier [20]. Il existe trois types de pulvérisations spatiales : des pulvérisations à UBV (Ultra Bas Volume), des traitements autoportés par thermonebulisation à chaud ou par traitement à froid [180, 20].

qui ne permet pas un traitement exhaustif des zones où le virus circule [64]. De tout cela résulte un rapport coût/efficacité incertain. Comme l'a souligné l'avis de l'Anses de janvier 2013 [132], il existe donc un besoin de méthodes alternatives aux insecticides pour limiter la transmission d'agents pathogènes par les moustiques, et plus particulièrement *Ae. albopictus*.

d'hôte [126]. Ce piège exploite donc le comportement des femelles moustiques lors de la recherche du repas de sang nécessaire pour la ponte. Les pièges peuvent capturer également des mâles à la recherche de partenaires pour l'accouplement [130, 230]. Ces pièges sont rendus létaux car ils intègrent soit des insecticides pour augmenter le taux de mortalité des moustiques, soit des surfaces adhésives qui empêchent les moustiques de s'envoler [194, 207, 208, 209, 258, 150, 80, 23] (Figure I.3).

La technique du piégeage de masse a permis une réduction significative des populations d'*Ae. aegypti* au Brésil aussi bien avec des ovitraps [160] qu'avec des pièges BG-sentinel [62], de même qu'en Italie pour contrôler les popula-

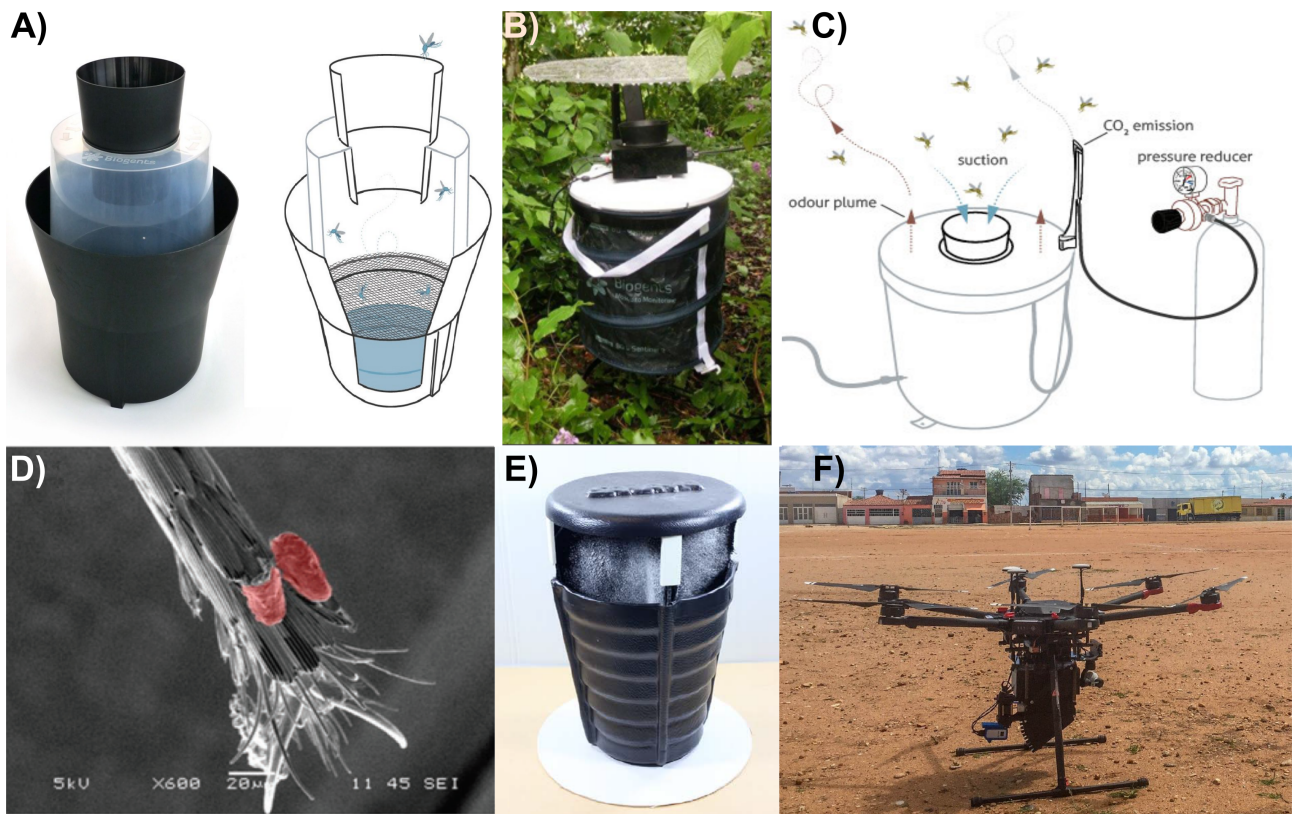


FIGURE I.3 – Illustrations des A) pièges à ovitrap; B) et C) des pièges BG-sentinel; D) et E) de la technique d'autodissémination; F) de la TIS. Les photos et schémas des ovitraps et pièges BG-sentinel sont issus de <https://eu.biogents.com/> et <https://www.bg-sentinel.com/en/>, respectivement. Les parois des pièges sont entourées de surfaces adhésives qui empêchent les moustiques de sortir. D) Les écailles d'un tarse de moustique forment une surface idéale pour ramasser les particules de poussière de pyriproxyfène (représentées en rouge) [66]. E) Une station d'autodissémination entourée d'un large filet pour empêcher les femelles de pondre [48]; F) Drone utilisé pour des lâchers de moustiques stériles au Brésil [123]

tions d'*Ae. albopictus* avec des pièges BG-sentinel [81]. Cependant, le piégeage massif n'a d'effet significatif que si une réduction au préalable des populations de moustiques a été réalisée et s'il y a une forte mobilisation communautaire [118]. De plus, la différence d'attractivité entre les pièges et les gîtes naturels nécessite encore des études sur le terrain pour optimiser le nombre de pièges à l'hectare [118].

2.2.2 L'autodissémination

Une approche pour contourner la difficulté de localiser et de traiter les habitats larvaires est la technique de l'autodissémination [66, 90, 18, 93, 5]. Cette méthode repose sur le postulat qu'un biocide peut être disséminé par les femelles elles-mêmes, lors de l'oviposition dans les différents gîtes larvaires au cours d'un même cycle gonotrophique [66] (Figure I.3). Le pyriproxifène fait partie des biocides pouvant être autodisséminé [224]. Il s'agit d'un régulateur de croissance, analogue de l'hormone juvénile, qui empêche la métamorphose de la larve vers l'adulte [66]. Le pyriproxifène est déposé sous forme de poudre dans des pièges de repos ou des pièges pondoirs (appelés stations de dissémination). Les femelles adultes ayant visité la station de dissémination et s'étant imprégnées de pyriproxifène le dispersent ensuite dans les gîtes larvaires naturels, réduisant l'émergence des nymphes en adultes au sein de la population locale de moustiques [116, 66] (Figure I.4).

L'autodissémination s'est avérée efficace pour traiter les gîtes cryptiques qui ne sont pas affectés par les méthodes de lutte conventionnelles [152]. Sur le terrain, cette technique a permis une augmentation de la mortalité des nymphales des populations d'*Ae. albopictus* en Espagne [48] et aux États-Unis [245, 246]. Cependant, comme les techniques de piégeage massif, la différence d'attractivité entre les stations de dissémination et

les gîtes naturels nécessite encore des études sur le terrain pour optimiser le nombre de pièges à l'hectare et leur efficacité avant d'envisager une utilisation à grande échelle [152].

2.2.3 Les méthodes basées sur des lâchers de mâles stériles

i La Technique de l'Insecte Stérile

La technique de l'insecte stérile (TIS) est basée sur la libération d'un grand nombre d'insectes mâles stérilisés, par irradiation ou traitement chimique, pour supprimer les populations de moustiques vecteurs [79, 90, 18, 74, 93, 5] (Figure I.3). La TIS cible le système reproductif de l'espèce afin de réduire les stades juvéniles. En effet, l'irradiation ou traitement chimique induit des mutations dominantes létales aléatoires dans les cellules germinales, qui agissent sur les œufs de la femelle pour empêcher leur fécondation [200]. Le concept est que les mâles stériles s'accoupleront avec les femelles sauvages qui ne pourront plus alors produire de progéniture le reste de leur existence [5]. Seuls les mâles sont relâchés car un lâcher de femelles risquerait d'accroître la nuisance et la transmission d'agents pathogènes et de diminuer l'efficacité de l'intervention en détournant certains mâles stériles de l'accouplement avec les femelles sauvages ciblées [90, 5] (Figure I.4).

La TIS s'est montrée efficace pour lutter contre des insectes d'intérêt médical, vétérinaire et agricole comme les glossines [250], les lucilies [264] et les mouches du fruit [82]. La TIS a également été utilisée pour réduire les populations d'*Ae. albopictus* en Italie [27]. Cependant, les essais contre les moustiques ont rencontré moins de succès [28, 124] en raison notamment du fort taux d'accroissement naturel et de la forte densité des populations [14]. En effet, la suppression d'une espèce cible avec la TIS n'est possible que

si 1) les mâles stériles rivalisent avec succès avec leurs concurrents sauvages; 2) le taux de libération des mâles stériles est suffisamment élevé pour surpasser le taux naturel d'accroissement de la population, afin de conférer aux mâles relâchés un rapport numérique suffisamment avantageux pour induire une stérilité de la population; et 3) la population cible est fermée (absence d'immigration) [79, 74, 100]. En outre, la plupart des programmes qui ont permis la suppression d'une population d'insectes ont démarré les contrôles lorsque les populations sur le terrain étaient de faible densité, soit du fait d'une installation récente de l'insecte-cible dans un nouveau territoire, de la bio-écologie de l'insecte-cible (ex : faible taux de reproduction, dynamique saisonnière marquée) ou encore de l'action conjuguée d'autres méthodes de lutte [79]. Aujourd'hui si aucun cadre législatif ou réglementaire européen n'existe pour encadrer les lâchers de moustiques mâles stérilisés [14, 40], des essais pilotes contre *Ae. albopictus* ont déjà eu lieu en Italie [27] et à La Réunion [2]. J'ai porté une attention particulière à cette méthode de contrôle lors de ma thèse.

ii La technique de l'Insecte Incompatible

Une version modifiée de la TIS, appelée la technique de l'Insecte Incompatible (TII), utilise les endosymbiotes *Wolbachia* afin d'in-

duire une stérilité dans les populations cibles [90, 18, 93, 5]. Les *Wolbachia* sont des protéobactéries endocellulaires trouvées dans au moins 60 % des insectes connus [109], incluant *Ae. albopictus*. Des moustiques mâles transinfectés par *Wolbachia* sont relâchés dans l'environnement pour s'accoupler avec des femelles de type sauvage. *Wolbachia* induit la mort prématurée des embryons en raison de l'incompatibilité cytoplasmique (IC) [266] après des croisements entre mâles infectés et femelles sauvages non infectées. Si les mâles infectés sont relâchés en nombre suffisant, des accouplements incompatibles se produiront et, finalement, la population de moustiques s'effondrera [93] (Figure I.4).

Cette stratégie a été déployée pour la première fois contre les moustiques en 1967 en Birmanie où des *Culex quinquefasciatus* infectés par *Wolbachia* ont été relâchés dans les populations sauvages, démontrant la capacité de ces mâles infectés à éliminer les populations locales de moustiques [135]. La TII permettrait de surmonter la réduction des performances des mâles stériles due à l'irradiation de la TIS [79, 106, 107], bien que cette perte de performances soit moindre dans le genre *Aedes* [13]. Cependant, la question du statut réglementaire des insectes transinfectés par *Wolbachia* dans l'Union européenne et donc de l'utilisation de la TII contre les moustiques n'est pas encore déterminée [14].

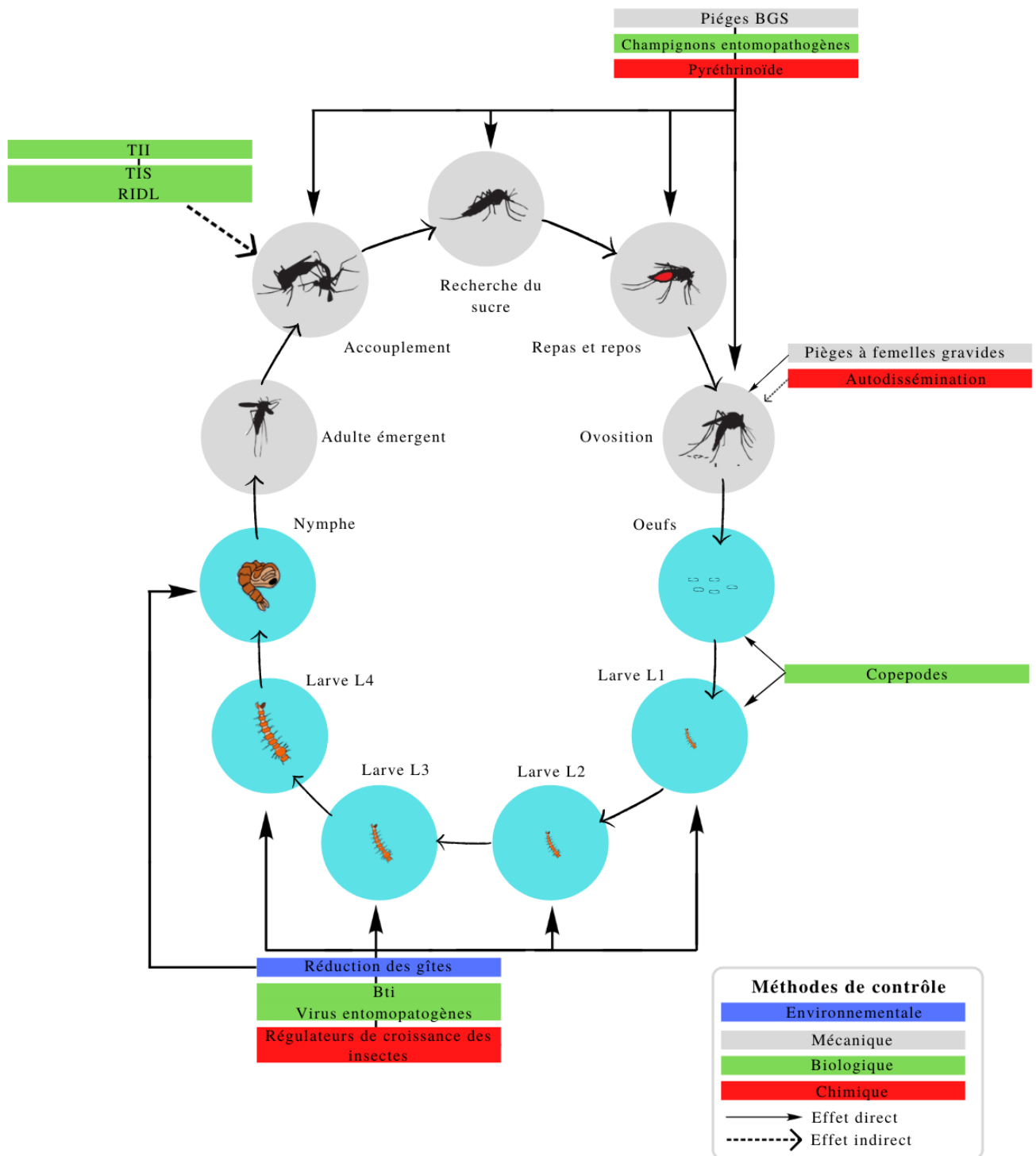


FIGURE I.4 – Les stratégies de contrôles alternatives contre *Aedes albopictus*, figure inspirée de l'article de Baldacchino et al. [17]. *Bti* : *Bacillus thuringiensis* var. *Israelensis* ; *TIS* : Technique de l'Insecte Stérile ; *TII* : Technique de l'Insecte Incompatible ; *RIDL* : Release of Insects carrying a Dominant Lethal.

iii *Release of Insects carrying a Dominant Lethal*

La TIS a été déclinée en une nouvelle méthode, la RIDL, ou "Release of Insects carrying a Dominant Lethal" [14]. Les moustiques sont génétiquement modifiés au laboratoire, ce sont donc des OGMs (Organisme Génétiquement Modifié), pour leur conférer un transgène responsable d'une létalité dominante, et la RIDL consiste ensuite à relâcher ces mâles transgéniques ; cette létalité est répressible, la progéniture ayant besoin pour se développer d'un composant qui n'existe pas dans la nature, comme la tétracycline [90, 18, 93, 5]. Contrairement à la suppression de la population basée sur les TIS et TII, la RIDL n'agit pas sur la ponte des œufs, mais sur les stades larvaires, puisqu'elle empêche la croissance des larves en adultes [14]. Cette létalité tardive pourrait être avantageuse pour le contrôle des populations de moustiques [255, 197]. En effet, les densités larvaires dépendent de ressources limitées (nutriments et espace dans les gîtes larvaires), ce qui se traduit par une compétition entre larves. A l'inverse, la létalité embryonnaire générée par la TIS classique réduit cette compétition, pouvant même conduire à des phénomènes de surcompensation, tels qu'une réduction importante du potentiel de reproductivité des femelles n'engendrerait pas nécessairement une réduction de la taille de la population cible [197] (Figure I.4).

La RIDL d'Oxitec est la seule technique de lutte contre les moustiques développée aujourd'hui à un niveau opérationnel en lutte antivectorielle [197, 100]. Cependant, la mortalité des descendants de mâles transgéniques n'est pas de 100%, ce qui peut se traduire par une dissémination des transgènes dans l'environnement [87]. Pour le moment, les lâchers de mâles transgéniques de moustiques ne sont pas autorisés en

Europe [14].

2.2.4 Les produits répulsifs

Une autre alternative est celle des produits répulsifs naturels (ex. huiles essentielles de plantes) ou synthétiques (ex. DEET) induisant une modification du comportement des insectes pour réduire le contact vecteur-humain [5]. Mais les études rigoureuses utilisant des protocoles pertinents et standardisés sont encore trop rares, si bien que leur utilisation demeure aujourd'hui encore largement empirique [56] (Figure I.4). Ils restent néanmoins préconisés pour la protection individuelle en cas d'épidémie d'arboviroses, en respectant les conditions d'utilisation notamment pour les femmes enceintes et les jeunes enfants.

2.2.5 La lutte biologique

Le terme de lutte biologique désigne l'ensemble des ennemis naturels des insectes qui regroupent les organismes prédateurs ainsi que l'ensemble des parasites et pathogènes des insectes [95, 180] (Figure I.4). Il existe de nombreux agents entomopathogènes naturels :

- les champignons entomopathogènes sont une alternative très prometteuse aux méthodes conventionnelles de contrôle des moustiques du genre *Aedes*. Par exemple, le champignon *Beauveria bassiana* a entraîné en laboratoire et en semi-field une réduction de la fécondité et de la survie des femelles moustiques *Ae. aegypti* en recherche d'un repas de sang [259].
- les copépodes sont également des ennemis naturels des moustiques puisque ce sont des prédateurs de larves [180]. À la Nouvelle-Orléans, les populations d'*Ae. albopictus* vivant dans des piles de pneus ont été éliminées 3 ans après l'introduction de *Macrocyclus albidus* [157]. Au Vietnam,

l'utilisation de *Mesocyclops spp.* dans la lutte à grande échelle, via une forte mobilisation communautaire, a permis d'éliminer localement *Ae. aegypti* dans de nombreux villages [119, 122, 169].

- les densovirus, des virus spécifiques des moustiques, peuvent augmenter la mortalité larvaire [49]. Toutefois, peu d'études ont été réalisées sur le terrain en raison notamment de la grande difficulté à produire ces agents pathogènes en masse [95].
- les poissons larvivores tels que *Gambusia affinis* sont des prédateurs des larves d'*Ae. albopictus* [145]. Cependant, il existe peu de bibliographie quant à leur efficacité en utilisation opérationnelle, et leur dissémination à proximité ou dans des milieux humides naturels pose question en termes écologiques.

2.3 La boosted TIS : une méthode de lutte intégrée

Une méthode de contrôle ne peut se suffire à elle-seule ni être efficace à long terme. De ce fait, la lutte doit être intégrée en combinant différentes méthodes de lutte afin de cibler les différents stades de vie du moustique pour réduire durablement la densité et la longévité des moustiques, réduire le contact homme-vecteur, et ainsi limiter la transmission d'agents pathogènes [90]. Par exemple, les méthodes de contrôle alternatives précédemment citées (section 2.2) sont plus efficaces lorsqu'une réduction au préalable des populations de moustiques est réalisée via des pulvérisations d'insecticides ou des campagnes de destruction des gîtes [79, 152, 74, 118, 100]. Cependant, la lutte intégrée des moustiques ne consiste pas simplement à ajouter différentes méthodes : si certaines pourraient agir en synergie, d'autres pourraient en effet avoir des effets antagonistes, ou être simplement redondantes et en-

Bien que l'utilisation de ces agents de lutte biologique essentiellement antilarvaires constitue une alternative intéressante aux insecticides chimiques, leur utilisation opérationnelle dans un programme de LAV se heurte à de nombreuses contraintes. La biodisponibilité de ces agents entomopathogènes dans les gîtes larvaires multiples et variées parfois cryptiques, difficilement traitables ou atteignables, constitue un obstacle important à leur utilisation [90]. De plus, *Ae. albopictus* pouvant utiliser comme gîte larvaire des petits récipients remplis d'eau de façon éphémère, il peut être difficile de maintenir durablement les populations d'agents de lutte biologique sur le terrain [90]. Des contraintes financières peuvent également se poser en raison des coûts élevés de production et de déploiement ces agents de lutte. [5].

traîner un gaspillage économique [185]. La stratégie de LAV basée sur l'utilisation d'une combinaison de méthodes de LAV doit être définie en tenant compte des critères d'efficacité, d'acceptabilité, de faisabilité et de durabilité. Lors de ma thèse, je me suis attachée à étudier l'optimisation de la LAV dans un contexte de lutte intégrée.

Une nouvelle approche de lutte intégrée qui semble être prometteuse est la combinaison de la TIS et de la TII. L'exigence d'une séparation parfaite des mâles et des femelles avant le lâcher des mâles infectés est importante pour la TII. La libération accidentelle des femelles peut entraîner la perte d'efficacité de la TII et transformer un programme de suppression des populations de moustiques en remplacement de la population [14]. Lorsque la TII est couplée à la TIS, les moustiques transinfectés par *Wolbachia* sont irradiés à faible dose. Si cela n'a pas ou peu d'effet

CHAPITRE I. INTRODUCTION GÉNÉRALE

sur la survie ou la compétitivité des mâles infectés [13], une faible dose est suffisante pour garantir la stérilité des femelles infectées si certaines se trouveraient libérées [35, 36, 137]. De plus, la présence des *Wolbachia* (TII) pourrait réduire la capacité des femelles moustiques à transmettre le pathogène [167, 110]. La combinaison TII-TIS a permis l'élimination durant 2 ans d'une population d'*Ae. albopictus* dans une zone résidentielle isolée au sein de la ville de Guangzhou en Chine [267].

En parallèle, la "boosted TIS" (BTIS), est une autre méthode de lutte intégrée, combinant l'autodissémination et la TIS. Les mâles stériles sont imprégnés d'un biocide transmis aux femelles pendant l'accouplement (Figure I.5). Les biocides peuvent ensuite être spécifiquement dispersés vers les gîtes larvaires par les femelles imprégnées [37, 38]. Ce concept est étudié dans le cadre du projet REVOLINC (ERC Consolidator grant no. 682387) dans lequel s'inscrit ma thèse (<https://revolinc.cirad.fr/>).

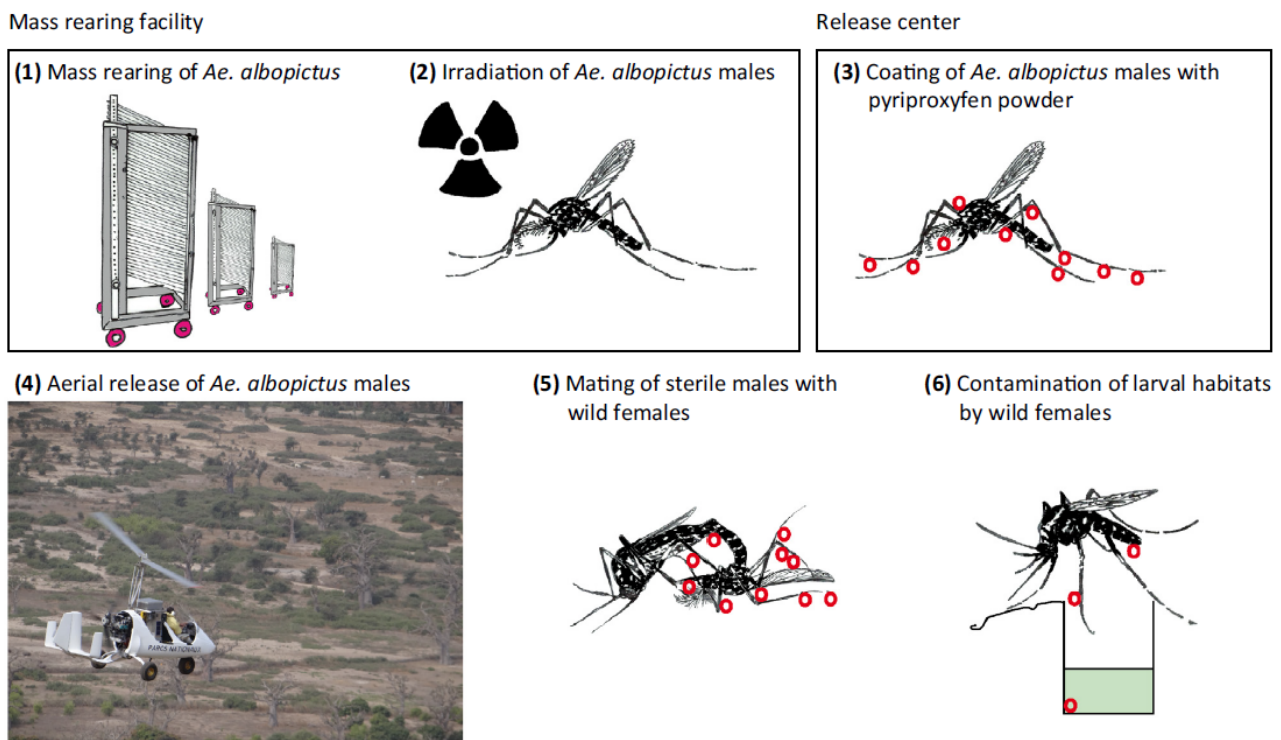


FIGURE I.5 – Présentation du concept "Boosted TIS". Les mâles *Aedes albopictus* sont élevés en masse en laboratoire. Ils sont imprégnés de pyriproxyfène (cercles rouges) puis libérés par voie aérienne. Une fois dans l'environnement, ils s'accoupleront avec des femelles sauvages qui à leur tour contamineront les habitats larvaires.

Afin d'atteindre une meilleure efficacité³ et efficacité⁴ possible de la LAV, la recherche en lutte antivectorielle nécessite un ensemble de disciplines scientifiques complémentaires. Si les approches observationnelles et expérimentales sont indispensables, l'expérimentation de nouvelles méthodes de LAV et de stratégies de lutte intégrée sur de large échelles spatiales et temporelles reste coûteuse et longue à réaliser. De même, la diversité des interactions entre organismes et avec l'environnement, leurs hétérogénéités spatiales et temporelles, ou simplement le caractère cryptique de la plupart de ces interactions, affectent nos capacités d'observation sur le terrain, qui ne révèlent que la partie émergée d'un système complexe. Enfin, la faisabilité elle-même, les risques associés, et donc l'acceptabilité, des expérimentations peuvent poser problème.

En complément de ces approches observation-

nelles et expérimentales, la modélisation est une approche cruciale pour améliorer la compréhension de phénomènes complexes et optimiser les options de gestion [94]. Si les modèles sont une simplification de la réalité, ils doivent permettre d'étudier des hypothèses qui sont difficiles à tester par le terrain ou l'expérimentation, et de tirer des conclusions généralisables [158]. En particulier, les modèles permettent de comparer l'impact de différents scénarios de LAV sur la dynamique prédite des populations de moustiques, voire *in fine* sur la dynamique d'une maladie vectorielle. Ils permettent ainsi de tester des hypothèses, des stratégies, et d'anticiper les risques associés. La suite de l'introduction du manuscrit présentera le développement de différents modèles qui visent à étudier l'impact de la LAV et en particulier des TIS et BTIS, sur les populations d'*Ae. albopictus*.

3.1 Modélisation quantitative, statistique ou mécaniste

Il existe une infinité de façons de simplifier la réalité, et la meilleure dépend essentiellement de la question posée [104]. Si tous les modèles permettent de faire des projections et des prédictions, il a souvent été suggéré qu'une distinction peut être faite entre les modèles qualitatifs (conceptuels) et les modèles quantitatifs dont font partie les **modèles statistiques** et les **modèles mécanistes** [111, 251]. Les modèles statistiques tentent de trouver la fonction prédictive d'une variable-réponse à partir de données observées [240]. Basés sur des relations corrélatives, les modèles statistiques sont simples, mais

nécessitent des données pour la construction et la validation du modèle.

Les modèles mécanistes décrivent les connaissances biologiques, formalisées à l'aide de formules mathématiques ou à l'aide de simulations [240]. Si, à l'inverse des modèles statistiques, les modèles mécanistes ne nécessitent pas de données d'observation pour leur construction, ils nécessitent une quantité importante de connaissances sur les processus biologiques. De tels modèles sont adaptés pour tester *in silico* des stratégies de contrôle ciblant des stades particuliers, et ainsi aider à la prise de décision pour la surveillance et

3. Efficacité décrit la réalisation des objectifs. C'est la comparaison entre les objectifs fixés au départ et les résultats atteints (d'où l'importance d'avoir des objectifs clairs au départ).

4. Utilisation rationnelle des moyens à disposition et vise à analyser si les objectifs ont été atteints à moindre coût (financier, humain et organisationnel).

le contrôle des populations vectorielles [201, 240]. Pour cette raison, je me suis concentrée lors de

ma thèse sur des modèles mécanistes.

3.2 Le choix du modèle mathématique

Il existe une diversité de modèles qui considèrent des processus différents et sont liés à des hypothèses différentes (sous-jacentes à la structure du modèle). Le modèle choisi doit être adapté à l'échelle spatiale, l'existence de données et au modèle biologique.

3.2.1 Représentation des populations ou des individus

Selon l'échelle à laquelle on se situe, on distingue deux types de modèles : les modèles de type **individu-centré** et les modèles de type **masse-interaction** [60].

Les **modèles individu-centré** représentent explicitement les individus et les interactions entre individus et avec leur environnement. Ces modèles peuvent être très réalistes, mais ils peuvent être complexes à définir et coûteux en temps de calcul [30]. C'est pourquoi les modèles individu-centré sont adaptés pour des **petites échelles** spatio-temporelles et des populations de petite taille [236, 60, 102, 30].

Les modèles de **masse-interaction** représentent une population dans son ensemble dans le but d'étudier les interactions dans et entre les populations [236, 60]. Ce sont des modèles analytiques (équations différentielles ou matrice) qui ne tiennent pas compte de la possible variabilité individuelle. Ces modèles sont moins réalistes que les modèles individu-centré car ils admettent des hypothèses concernant la biologie individuelle qui sont peu probables dans les systèmes naturels (ex : tous les individus sont semblables) [30]. Ce type de modèles est néanmoins plus adapté pour représenter une population d'organismes abondants, tels que les moustiques, ou pour des

grandes échelles spatio-temporelles pour lesquels il peut être fastidieux de suivre chaque individu au sein d'une grande population [75].

3.2.2 Les phénomènes aléatoires

Comme l'écrit Stephen King, "La vie est sœur du hasard." (The Green Mile). Intuitivement, l'on comprend facilement que tous les individus d'une population ne peuvent avoir exactement les mêmes taux de survie et de reproduction. Au contraire, chaque individu a une singularité et des traits d'histoire de vie différents. Pour cette raison, il existe une dichotomie entre les modèles mathématiques, avec les **modèles déterministes** d'une part, et les **modèles stochastiques** d'une autre. Les **modèles déterministes** sont ceux où les individus (ou populations) ont un comportement moyen. Il n'y a pas de variabilité des paramètres et des fonctions du modèle [47]. A l'opposé, les **modèles stochastiques** considèrent qu'il existe de la variabilité dans le fonctionnement des individus (ou populations) [47]. Les modèles stochastiques ont le meilleur potentiel pour simuler les variations des processus observés, mais cette variation peut masquer les effets d'un mécanisme particulier. De plus, les modèles stochastiques contrairement aux modèles déterministes permettent de représenter les phénomènes d'extinction et les phénomènes rares. En revanche, ils sont coûteux en temps de calcul. Ainsi, les modèles stochastiques sont adaptés pour de petites populations ou des études à petite échelle, où le hasard a un fort impact sur l'avenir des populations. A l'inverse, un modèle déterministe est adapté pour de grandes populations ou des études à grande

échelle, comme dans le cas des moustiques [234].

3.3 Le développement d'un modèle mathématique

La modélisation consiste à traduire un phénomène observé en formalisation mathématique ou en code informatique après l'élaboration d'un modèle conceptuel (par exemple, sous la forme d'un diagramme). Lorsqu'il n'est pas possible de déterminer les solutions mathématiques de forme fermée d'un modèle, ce dernier repose sur des simulations numériques pour approximer leurs solutions. Le modèle est alors qualifié de **simulationnel** et fait opposition au modèle **analytique** [243, 242].

Lorsque l'on développe un modèle, il est important de vérifier que le comportement de celui-ci est en accord avec ce que l'on connaît du système observé. Dans un second temps, il est possible de passer à l'étape de validation du modèle si des données d'observation qui n'ont pas été utilisées pour le construire sont disponibles [225]. Les variables simulées par le modèle sont alors confrontées aux données [218]. Un modèle

est par essence faux puisqu'il s'agit d'une simplification de la réalité. Toutefois, un modèle validé est considéré comme acceptable dans le cadre de l'utilisation initialement prévue, car la validation répond à des exigences spécifiques de performance [215]. Par ailleurs, cette étape n'est pas une étape obligatoire car elle ne permet pas de tester une théorie scientifique ou d'attester d'une « vérité » scientifique [47]. Elle est néanmoins désirable pour évaluer la qualité du modèle.

Les sorties des modèles produisent des connaissances sur le phénomène observé et peuvent être utilisées dans les processus de prises de décision. L'analyse du modèle peut également aboutir à une amélioration de la communication entre modélisateurs et spécialistes des autres disciplines (par exemple en formulant des recommandations sur les expérimentations à réaliser pour mieux comprendre le phénomène étudié) [242].

3.4 Modélisation de la dynamique des populations d'*Aedes albopictus*

La prise en compte de la dynamique de population de l'insecte-cible dans les modèles est cruciale pour comprendre et optimiser l'impact de la LAV. L'étude de la dynamique de populations de moustiques renseigne sur l'abondance des moustiques au cours du temps en un lieu donné. Développer des modèles de dynamique de population structurés en classes d'âge peut s'avérer crucial pour plusieurs raisons. Premièrement, les méthodes de lutte vont cibler un stade en particulier. Deuxièmement, l'OMS recommande, comme nous l'avons déjà souligné, de développer des stratégies de lutte intégrée [185]. Pour cette raison, le détail des différents stades de vie

permettra de modéliser avec plus de précision les différentes options possibles, c.-à-d. les combinaisons de différentes méthodes de lutte, afin de définir la meilleure stratégie de lutte intégrée. Enfin, la différenciation des stades adultes est importante au niveau épidémiologique (nullipares/pares), puisque ce sont les femelles pares qui ont déjà pris un repas de sang qui peuvent potentiellement transmettre l'agent pathogène [46].

Cailly et al. [46] ont développé un modèle générique d'abondance des populations de moustiques lié aux conditions météorologiques (température et précipitations). Il s'agit d'un modèle mécaniste basé sur des Équations Diffé-

rentielles Ordinaires (EDO) dont chaque équation décrit un stade du cycle de vie du moustique. Après confrontation à des données entomologiques, le modèle permet de prédire les populations d'*Anopheles hyrcanus*, *Anopheles maculipennis s.l.*, *Culex pipiens*, *Aedes caspius* et *Ae. albopictus* [46, 239, 89]. Ce modèle a notam-

ment été adapté aux populations d'*Ae. albopictus* à La Réunion par Tran et al. [240]. Ce modèle présente l'avantage d'être très robuste. De plus, la modélisation de chaque stade de vie des moustiques et l'impact du climat sur chacun des stades sont de véritables atouts pour tester l'impact de la LAV [46].

3.5 Modélisation de la TIS et boosted TIS pour lutter contre les moustiques

Des modèles sur l'utilisation de la TIS pour lutter contre les moustiques ont été développés afin de 1) optimiser les stratégies des lâchers de mâles stériles [255, 45, 88, 140, 112, 6, 168] 2) étudier l'impact de l'environnement sur l'efficacité de la TIS [72, 153, 164], 3) évaluer l'effet de la TIS couplée à l'utilisation conventionnelle d'insecticides [92, 108] et 4) évaluer le bénéfice économique en cas d'épidémie de dengue [9]. Par ailleurs, un modèle a été développé pour explorer l'impact de la BTIS sur les populations d'*Ae. albopictus* [198] : ce modèle avait pour objectif d'évaluer l'impact de la BTIS par rapport à l'action de la TIS classique et de l'autodissémination.

L'ensemble de ces modèles sont des modèles de masse-interaction, formalisés à l'aide d'EDO, pour la plupart déterministes et en temps continu

[79]. Toutefois, aucun de ces modèles n'intègre de données environnementales réelles, et ils n'ont pas été validés sur des données entomologiques. Or, la capacité vectorielle (abondance, durée de vie, contact avec l'homme, fréquence des repas de sang...) des moustiques, conditionnant la dynamique de transmission d'un pathogène comme le virus de la dengue, est dépendante de l'environnement dans lequel ils vivent. Les relations de l'insecte avec son milieu doivent donc être étudiées avec plus de précision et à l'aide de nouveaux outils afin d'optimiser la LAV [94]. Ma thèse a donc porté sur le développement de modèles implémentant des lâchers de mâles stériles, imprégnés ou non d'un biocide (mais aussi d'autres techniques de LAV), appliqués à différents contextes environnementaux et validés sur des données entomologiques.

3.6 Modélisation de la transmission d'agents pathogènes par les moustiques

Le but du contrôle des vecteurs étant au final celui des maladies vectorielles, et afin de prédire l'efficacité des méthodes de contrôle des vecteurs sur la transmission d'agents pathogènes, des modèles épidémiologiques doivent être construits et couplés aux modèles entomologiques [94]. Les modèles épidémiologiques étudient la transmission des pathogènes d'un individu à un autre afin de prédire les épidémies et leur ampleur dans le temps et l'espace [104].

Pour ce faire, la très grande majorité des modèles épidémiologiques compartimentent la population d'hôtes selon leurs états cliniques et étudient les flux d'hôtes entre les différents compartiments [121, 16, 10]. Le modèle le plus classique est le modèle SIR, qui divise la population de taille N en trois compartiments avec les individus Susceptibles (S), Infectieux (I) et Guéris (R, pour

"Recovered" en anglais) [104, 120] :

$$\begin{cases} \frac{dS}{dt} = -\beta S \\ \frac{dI}{dt} = \beta S - \gamma I \\ \frac{dR}{dt} = \gamma I \end{cases} \quad (\text{I.1})$$

avec β la force d'infection qui est la vitesse à laquelle les individus sensibles sont infectés et qui est fonction du nombre d'individus infectieux ; ce paramètre contient des informations sur les interactions entre les individus qui conduisent à la transmission de l'infection. γ correspond au taux de guérison de l'infection [104, 120].

Dans le cas de maladies à transmission vectorielle, deux systèmes de transmission couplés sont utilisés pour décrire les processus de transmission entre le vecteur et l'hôte (cf. modèle chapitre IV). De plus, des compartiments supplémentaires peuvent être rajoutés selon les ma-

ladies étudiées. Bien souvent, un compartiment pour des hôtes infectés, mais non encore infectants (E, pour "Exposed" en anglais) est ajouté dans le cas de la modélisation de la transmission de la dengue [171, 231, 114, 231, 52, 141, 51].

Les modèles semblent se concentrer sur la compréhension de la dynamique de transmission et seulement 37% des modèles incluraient une mesure de contrôle, en particulier dans le cas des modèles de dengue [201]. Les vaccins quand ils existent, les lâchers de moustiques adultes, l'utilisation de larvicides et des moustiquaires imprégnées sont les méthodes de contrôle les plus modélisées [201]. Si la plupart des modèles n'ont considéré qu'un seul type de méthode de LAV, il existe des modèles couplant plusieurs méthodes de contrôles conventionnelles [44, 265, 73]. Étudier l'impact de la TIS et de la BTIS sur la transmission de la dengue dans un contexte de lutte intégrée se révèle ainsi être un nouveau challenge.

4 Objectifs et méthodologie

4.0.1 Contexte et objectif général

La Réunion est un département français situé au sud-ouest de l'océan Indien. Elle couvre une superficie de 2512km^2 pour une population de 850727 habitants et une densité de population de 339,8 habitants par km^2 . La topographie est montagneuse et le littoral concentre la moitié de la population [31]. L'île est traversée par un gradient de précipitations Est / Ouest, allant d'une pluviométrie annuelle maximale de 15931 mm enregistrée dans l'Est (un des records mondiaux), à une pluviométrie annuelle minimale de 183 mm dans l'ouest [161].

Aedes albopictus est le vecteur impliqué dans les épidémies de dengue à La Réunion. En 1977-1978, l'île fut touchée par une épidémie de dengue affectant près de 30 à 35 % de la

population réunionnaise [166, 59]. Postérieurement, une deuxième épidémie de plus faible intensité eut lieu en 2004 avec 228 cas cliniquement compatibles avec une dengue [70]. Par la suite, entre 2004 et 2017, l'île a été en situation inter-épidémique avec des cas de dengue sporadiques fréquemment identifiés et des foyers de transmission dans l'ouest et le sud de l'île [70]. Depuis 2017, une nouvelle épidémie de dengue affecte l'île. Seuls 100 cas ont été déclarés en 2017, mais par la suite la circulation virale s'est intensifiée et 25139 cas de dengue ont été déclarés de janvier 2018 à février 2020. Au départ, seul le sérotype 2 a été détecté en 2017 et 2018, puis une circulation indigène du sérotype 1 a été relevé en 2019, et en 2020 le sérotype 3 a également été identifié dans l'Est et le Nord de l'île [217]. Cette circu-

CHAPITRE I. INTRODUCTION GÉNÉRALE

lation séquentielle sur un même territoire de différentes sérotypes aggrave le tableau clinique de la dengue avec un risque accru de dengue sévère chez des individus en infection secondaire et tertiaire. On note également l'émergence du virus du chikungunya dans l'Océan Indien en 2004 et l'épidémie majeure qui a frappé La Réunion en 2005 et 2006 avec là-encore *Ae. albopictus* pour vecteur [204]. Au cours de cette épidémie, un tiers de la population Réunionnaise a été infectée. Depuis, un certain nombre souffre de complications neurologiques et de douleurs articulaires chroniques [179, 78].

Jusqu'en 1979, les actions de LAV à la Réunion ne ciblaient que l'espèce vectrice du paludisme, *Anopheles arabiensis* [59, 216, 192]. Subséquentement, la maladie fut éliminée avec une notification officielle prononcée en 1979 [165], et elle ne sévissait plus que sous forme de cas importés. C'est pourquoi l'objectif principal de la LAV a été alors de lutter contre la réintroduction du paludisme, à cause de la persistance du vecteur local (*An. arabiensis*) et d'un flux important de parasites à partir des pays voisins. La prévention de la réintroduction a reposé sur le dépistage passif et le traitement précoce des cas importés, associés à une lutte antilarvaire guidée par une surveillance entomologique méticuleuse. Ce n'est qu'en réaction aux épidémies de dengue en 2004 que les actions d'éducation sanitaire, de surveillance et de démoustication furent étendues à *Ae. albopictus* [64]. De 2006 à aujourd'hui, l'ARS (Agence Régionale de Santé) est en charge de la surveillance entomologique d'*Ae. albopictus* et des actions de LAV conventionnelles en période inter-épidémique et épidémique (section 2.1.1). *Aedes albopictus* est omniprésent dans les zones urbaines jusqu'à 1200 m d'altitude et reste actif en hiver austral malgré des températures moyennes pouvant descendre à 13 °C [63]. L'ARS focalise donc les actions de

lutte dans les zones urbaines où l'espèce colonise essentiellement des gîtes larvaires anthropiques [213]. En 2018, un plan ORSEC (Organisation de la Réponse de la Sécurité Civile) a été déclenché afin de mettre en œuvre rapidement tous les moyens de lutte nécessaires pour faire face à l'épidémie de dengue [20]. Pourtant, l'épidémie persiste toujours, soulignant l'importance de coupler les méthodes de LAV utilisées en routine avec d'autres méthodes alternatives afin d'optimiser et améliorer l'efficacité de la lutte.

Les échanges entre La Réunion et la France métropolitaine sont intenses, en particulier l'été, en juillet–août. Le risque de transporter des passagers infectés est important [33], notamment dans le sud de la France, où les populations d'*Ae. albopictus* sont très abondantes à cette période de l'année. Quand cela arrive, des insecticides sont pulvérisés autour des cas confirmés (section 2.2). Mais l'utilisation de méthodes alternatives aux insecticides, dans un programme de lutte intégrée, pourrait être utile pour réduire l'utilisation des insecticides, en particulier en période inter-épidémique.

La TIS est une méthode alternative prometteuse mais sa mise en place suppose que le nombre de mâles stériles dépasse celui des mâles sauvages et demande donc des moyens de production très importants [8, 17, 137, 74, 93]. La BTIS pourrait potentiellement limiter ce problème. Toutefois, il s'agit d'un concept émergent encore peu étudié. Comme l'expérimentation de nouvelles stratégies de LAV reste très coûteuse, les modèles mathématiques sont des outils de choix pour les évaluer et les optimiser à priori.

L'**objectif général** de la thèse a donc été d'évaluer et d'optimiser l'impact de méthodes de lutte basées sur des lâchers de mâles stériles dans le cadre de la LAV intégrée sur les populations d'*Ae. albopictus* et sur la circulation de la dengue, à La Réunion principalement, mais aussi dans le climat tempéré du Sud de la France métropolitaine.

4.0.2 Démarche scientifique

L'objectif général a été décliné en quatre questions de recherche (Figure I.6). La **première question** était d'évaluer les effets de la TIS et de la BTIS sur les populations de moustiques *Ae. albopictus* à la Réunion. Pour ce faire, les effets des deux méthodes de lutte ont été introduits dans un modèle de dynamique des populations naturelles d'*Ae. albopictus* à La Réunion. Le modèle est basé sur le modèle de Tran et al. [240]. Selon la classification de Turner et al. [243], ce modèle peut-être décrit comme :

- mécaniste car il incorpore des processus d'intérêt à travers une description des éléments sous-jacents et de leurs interactions ;
- spatialement explicite, car il localise les quantités simulées dans un espace dimensionnalisé ;
- déterministe, car il n'introduit aucune source d'aléatoire dans les calculs (les mêmes entrées provoqueront toujours les mêmes sorties) ;

- simulationnel, car les solutions reposent sur des simulations numériques.

Après confrontation du modèle aux données entomologiques récoltées par l'ARS, une analyse de sensibilité a été réalisée pour identifier les paramètres-clés de la TIS et BTIS, et des simulations ont été effectuées afin d'optimiser les paramètres concernant les lâchers de mâles stériles (chapitre II).

La **seconde question** de recherche était de mesurer l'apport de la TIS et BTIS dans un contexte de lutte intégrée. Pour cela, nous avons intégré au modèle la modélisation d'autres méthodes de LAV : piégeage massif des moustiques adultes, destruction mécanique des gîtes, auto-dissémination. Le modèle a été adapté en milieu tempéré (Montpellier) afin de comparer, à l'aide de simulations, l'impact des stratégies de lutte intégrée entre milieu tropical et tempéré. Pour mener à bien ce projet, j'ai encadré au cours de ma deuxième année de thèse une stagiaire de Master 2, Léa Douchet, qui a participé à l'adaptation du modèle en milieu tempéré (chapitre III).

La **troisième question** de recherche était d'évaluer les effets de la LAV sur la transmission du virus de la dengue à La Réunion. Le modèle de dynamique des populations de moustiques a été couplé avec un modèle épidémiologique SEI-SEIR. Le modèle a été confronté aux données épidémiologiques de 2018 récoltées par l'ARS. Puis, des analyses statistiques ont été réalisées afin d'évaluer l'impact de l'échelle des données et des actions de LAV sur les sorties du modèle (chapitre IV).

Comprendre et optimiser l'impact des méthodes de contrôle sur les populations d'*Aedes albopictus*

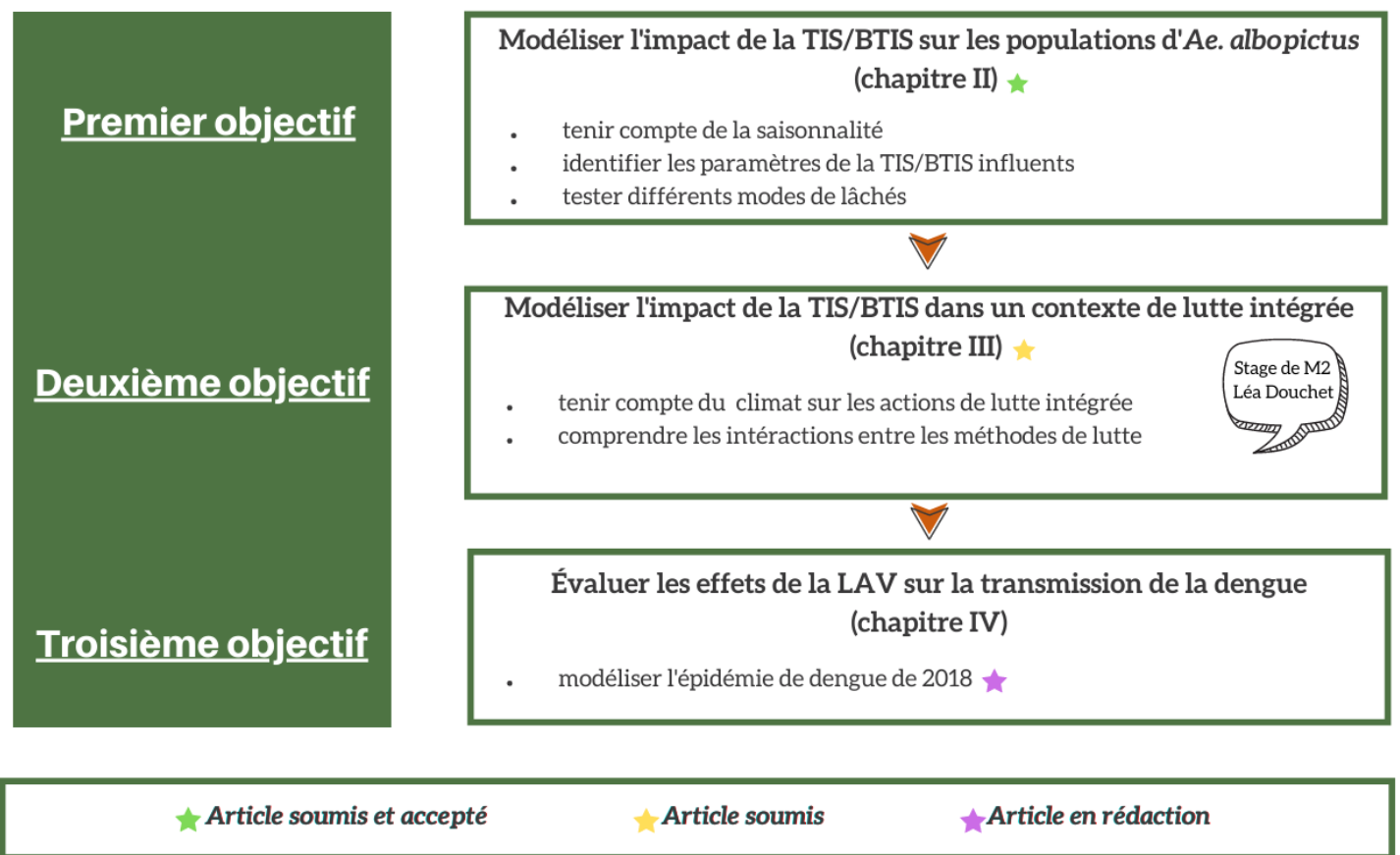


FIGURE I.6 – Objectif et démarche scientifique de la thèse

La modélisation de la TIS et BTIS à La Réunion

Parce qu'*Aedes albopictus* est le vecteur impliqué dans la transmission des virus de la dengue et du chikungunya à la Réunion, il constitue une priorité de santé publique sur l'île. A cause de perspectives toujours lointaines d'un vaccin capable de conférer une immunité protectrice contre l'ensemble des sérotypes de la dengue et des limites des méthodes de lutte anti-vectorielle (LAV) conventionnelles présentées en introduction (chapitre I section 2.1.1 et 2.1.2), les acteurs politiques de la Réunion encouragent la recherche et l'expérimentation de nouvelles techniques de lutte contre les vecteurs, notamment à partir de lâchés de moustiques mâles stériles, telles que la Technique de l'Insecte Stérile (TIS) et la Technique de l'Insecte Stérile renforcée (BTIS) [83]. Cependant, il est nécessaire de procéder à une évaluation de chacune de ces techniques, avant d'envisager leur utilisation à grande échelle [83].

Ce constat a conduit au développement d'un modèle mathématique, indispensable pour tester *in silico* l'impact de la TIS et BTIS sur les populations d'*Ae. albopictus*. Un premier modèle de dynamique des populations d'*Ae. albopictus* avait été développé par Tran et al. (2020). Ce modèle présente sous forme de cartographie numérique la densité des moustiques à l'échelle des zones de surveillance entomologique (appelées "ALIZE"). Il est actuellement utilisé en routine par l'Agence Régionale de Santé de la Réunion (ARS). En développant un modèle de dynamique des populations basé sur cet outil, et en intégrant les effets théoriques de la TIS et BTIS, l'étude présentée dans ce chapitre avait pour objectif de répondre aux interrogations suivantes :

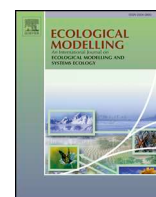
- Quel est l'impact de la TIS sur les populations d'*Ae. albopictus* ?
- Quel est la valeur ajoutée de la BTIS par rapport à la TIS ?
- Comment optimiser ces deux méthodes de lutte à la Réunion ?

Article 1 : Modelling the control of *Aedes albopictus* mosquitoes based on sterile males release techniques in a tropical environment

Cette étude a fait l'objet d'un article publié dans le journal "Ecological modelling" :

Haramboure, M., Labbé, P., Baldet, T., Damiens, D., Gouagna, L. C., Bouyer, J., Tran, A. (2020). Modelling the control of *Aedes albopictus* mosquitoes based on sterile males release techniques in a tropical environment. *Ecological Modelling*, 424, 109002.

Les annexes de l'article sont en annexe du manuscrit (Annexe 3).



Modelling the control of *Aedes albopictus* mosquitoes based on sterile males release techniques in a tropical environment



Marion Haramboure^{*,a,b,c,d,e}, Pierrick Labbé^c, Thierry Baldet^{a,b}, David Damiens^{f,g},
Louis Clément Gouagna^{f,g}, Jérémy Bouyer^{b,h,i}, Annelise Tran^{a,b,d,e}

^a CIRAD, UMR ASTRE, Sainte-Clotilde F-97490, Reunion, France

^b ASTRE, Univ Montpellier, CIRAD, INRAE, Montpellier, France

^c ISEM, UMR 5554, CNRS-UM-IRD-EPHE, Université de Montpellier, Montpellier, France

^d CIRAD, UMR TETIS, Sainte-Clotilde F-97490, Reunion, France

^e TETIS, Univ Montpellier, AgroParisTech, CIRAD, CNRS, INRAE, Montpellier, France

^f IRD, UMR MIVEGEC, IRD224-CNRS5290-UM, Reunion, France

^g IRD / GIP CYROI, Sainte-Clotilde, Reunion, France

^h CIRAD, UMR ASTRE, F-34398 Montpellier, France

ⁱ Insect Pest Control Laboratory, Joint FAO/IAEA Programme of Nuclear Techniques in Food and Agriculture, Vienna A-1400, Austria

ARTICLE INFO

Keywords:

SIT
Boosted SIT
Vector control
Pyriproxyfen
Population dynamics
Mosquito

ABSTRACT

The Sterile Insect Technique (SIT), used to control insect populations, consists of releasing males sterilized by ionizing radiations. Wild females that mate with these males can no longer produce viable offspring, which may drive the population decline. Although this method has proved its efficiency, its effect may be more limited for fast-reproducing large-population species, such as *Aedes albopictus*. A novel approach, named "boosted SIT" has been designed to strengthen the SIT technique: It consists of coating sterile males with a biocide that will be transferred to the mated females, which will then contaminate the oviposition sites. This study is aimed at exploring demographic effects of both techniques (SIT and boosted SIT) through their inclusion in a weather-driven abundance model of the *Aedes albopictus* population dynamics in the geographical context of La Reunion Island. Sensitivity analysis showed that the date to start the release, as well as the quantity of sterile males released and their competitiveness, are of key importance for both control methods. According to our results, boosted SIT allows 1) Increasing the effectiveness of the SIT when the sterile males released are of medium quality in terms of competitiveness, and 2) extending the optimal window to start the control period.

1. Introduction

Vector-borne diseases account for about 17% of the estimated global burden of infectious diseases and are responsible for more than 700,000 deaths every year (World Health Organization and UNICEF, 2017). Dengue is the most common and widespread arbovirus. The number of dengue infections is estimated at 390 millions every year, of which 96 million induce clinical symptoms (of various severities) (Bhatt et al., 2013). Dengue virus is transmitted by mosquitoes of the genus *Aedes*, in particular *Ae. albopictus* and *Ae. aegypti*. These species are also vectors of other arboviruses, including Zika and Chikungunya. The global distributions of these three arboviruses have recently expanded, causing many severe disease outbreaks in urban human populations (Patterson et al., 2016). Different vaccines have been developed for

dengue and Zika, but their efficacy remains to be studied (Musso and Gubler, 2016; WHO, 2018). Moreover, no disease-specific treatment for these arboviruses exists (Caglioti et al., 2013). In this context, mosquito control remains the cornerstone of disease prevention.

The "Tiger mosquito", *Aedes (Stegomyia) albopictus* (Skuse) (Diptera: Culicidae), a species native to the forests of Southeast Asia (Smith, 1956), has expanded its distribution by adapting to new sources of blood and environments. Its proximity with humans has enabled it to colonize new territories through international trade (e.g. tire trade (Reiter, 1998)). Although being less competent than its sister species *Ae. aegypti* to transmit dengue viruses (Paupy et al., 2009), *Ae. albopictus* was the only vector involved in some recent dengue outbreaks (Gasperi et al., 2012; Paupy et al., 2009; Rezza, 2012; Wu et al., 2010).

For many mosquito-borne diseases, larvicides have demonstrated

* Corresponding author.

E-mail addresses: marion.haramboure@cirad.fr (M. Haramboure), pierrick.labbe@umontpellier.fr (P. Labbé), thierry.baldet@cirad.fr (T. Baldet), david.damiens@ird.fr (D. Damiens), louis-clement.gouagna@ird.fr (L.C. Gouagna), jeremy.bouyer@cirad.fr (J. Bouyer), annelise.tran@cirad.fr (A. Tran).

<https://doi.org/10.1016/j.ecolmodel.2020.109002>

Received 24 October 2019; Received in revised form 18 February 2020; Accepted 19 February 2020

Available online 19 March 2020

0304-3800/© 2020 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

their efficiency to reduce transmission during outbreaks (World Health Organization, 2009). However, *Ae. albopictus* uses multiple cryptic and dispersed breeding sites of all sorts (tires, beverage cans, plastic items, etc.). They are difficult to locate and treat, which significantly hinders larvicides control of this vector (Connelly and Carlson, 2009). Mobilization of the local communities to eliminate these diverse containers used by peridomestic *Ae. albopictus* could be an effective solution, but changing attitudes and behaviors can take many years (Gubler and Clark, 1996; Tapia-Conyer et al., 2012; Winch et al., 1992). An integrated and sustainable control of *Ae. albopictus* is therefore necessary, which cannot rely solely on the usual insecticide usage or the goodwill of local communities, but must be supplemented by alternative treatment methods (Achee et al., 2019).

A promising alternative for such a cryptic-breeding insect is the Sterile Insect Technique (SIT). It relies on the mass-release of males sterilized by ionizing radiation. Since female mosquitoes are inseminated by only one male during their life (with very rare exceptions), mating with such males negates their reproductive success, hence causing the target population to decline (Dunn and Follett, 2017; Flores and O'Neill, 2018). SIT has been shown to be effective in eradicating tsetse flies (Vreysen et al., 2014), screwworms (Wyss, 2000) and medflies (Enkerlin et al., 2017). In the case of mosquito control, success has been more variable, although particularly good results have been obtained in Italy (Bellini et al., 2013) and more recently in China, in combination with the Incompatible Insect Technique (IIT) Zheng et al. (2019). Indeed, mosquito populations are generally very large, and a significant reduction in their population therefore requires the release of a large number of sterile males, whom breeding, sorting from females and irradiating are costly.

An efficacy-improving upgrade, named boosted SIT, has recently been proposed (Bouyer et al., 2016; Bouyer and Lefrançois, 2014): Its rationale is that the released males are the best available vectors to contaminate females with toxic agents that could be further disseminated to other compartments of the target population by self-dissemination. It has been proposed to coat the sterilized males with pyriproxyfen, an insect growth regulator that prevents the emergence of adult mosquito from the aquatic pupae (Invest and Lucas, 2008; Maoz et al., 2017): the insecticide could be transferred to females by mating, which in turn could specifically contaminate their breeding sites. By using females themselves as insecticide vectors, boosted SIT could therefore drastically improve control of species with cryptic breeding habits such as *Ae. albopictus*. However, many questions remain, such as the number of males to be released for efficient control, or the magnitude of the potential "boosting" effect. Both depend on the duration of contamination of breeding sites (no consensus appears in the bibliography (Invest and Lucas, 2008)) and on the effectiveness of pyriproxyfen transfers from males to females and from females to breeding sites, parameters for which empirical data are not available yet.

In cases empirical data are lacking, mathematical models are often useful for planning mosquito population management strategies. They can be used to understand and predict population density in relation to environmental variations (Ewing et al., 2016; Ezanno et al., 2015; Roche et al., 2015; Tran et al., 2013), and to anticipate the effects of population management measures under various scenarios (Cailly et al., 2012). In the case of SIT, such theoretical models have been developed in order to 1) optimize the strategies of sterile males releases (Almeida et al., 2019; Cai et al., 2014; Evans and Bishop, 2014; Huang et al., 2017; Li and Yuan, 2015; Multerer et al., 2019; White et al., 2010), 2) study the impact of the environment on SIT (Dufourd and Dumont, 2013; Maiti et al., 2006; Mishra et al., 2018), and 3) evaluate the effect of SIT coupled with standard use of insecticides (Fister et al., 2013; Hendron and Bonsall, 2016). A recently-published model by Pleydell and Bouyer (2019) specifically studied the efficacy gain of boosted versus standard SIT in a theoretical population. Their results suggest that boosted SIT could drastically reduce the required number of males released. However, to our knowledge, none of these models

have studied the effects of SIT or boosted SIT on *Ae. albopictus* populations under realistic environmental conditions.

The objectives of the present study were thus 1) to evaluate the efficacy gain of boosted SIT in real geographical and climatic conditions, with the example of La Reunion Island a tropical island where *Ae. albopictus* is the main chikungunya and dengue vector (Delatte et al., 2008), and 2) to optimize SIT and boosted SIT strategies in this context. Between 2005 and 2006, Reunion Island was affected by a large chikungunya epidemic, with more than 38% of the population infected (ARS and IVS, 2010). An epidemic of dengue is currently spreading, with more than 24,300 indigenous cases as of July 01, 2019 (ARS and Préfecture Réunion, 2019). Located in the Indian Ocean, between Madagascar and Mauritius, La Reunion Island is a small volcanic island (2512 km²) with a mountainous topography. *Aedes albopictus* mosquitoes are mainly found at low elevations in urban and peri-urban areas (Boyer et al., 2014). Moreover, the island is characterized by an East/West precipitation gradient, ranging from a maximal annual rainfall of 15,931 mm recorded in the eastern part, to a minimal annual rainfall of 183 mm in the West (Météo France, 2019). The island is characterized by two seasons, with a hot and wet austral summer (from November to March), and a rather mild and dry winter. La Reunion Island, with its diverse landscapes and contrasting climate, is thus an excellent place to study the impact of control methods against *Ae. albopictus* in a realistic, variable, environment. Moreover, since the severe 2005–2006 chikungunya epidemic, *Ae. albopictus* populations have been regularly monitored by the Regional Health Agency. A deterministic model of *Ae. albopictus* population dynamics has been recently developed by Tran et al. (2020) and validated using these extensive entomological data. This model realistically integrates the climatic variations of La Reunion Island on the *Ae. albopictus* population dynamics (Tran et al., 2013): i) Temperature impacts the development time of aquatic stages and the mortality of larvae, pupae and adults, ii) rainfalls positively impact the number of available breeding sites and the environmental carrying capacity, iii) heavy rainfalls impact the mortality rates of aquatic stages by flooding the breeding habitats (Dieng et al., 2012). This model is currently used by the Regional Health Agency as a tool for decision support, called "ALBORUN" (Tran et al., 2020).

In the present study, we modified this ALBORUN population dynamic model to integrate the potential effects of SIT and boosted SIT on the *Ae. albopictus* populations in La Reunion Island. After controlling its accuracy on the same entomological data used in Tran et al. (2020), we first performed a global sensitivity analysis to identify the key parameters affecting the efficacy of SIT and boosted SIT. We then assessed the optimal timing for both control methods under a tropical environment, taking into account the spatial heterogeneity of micro-climates in La Reunion Island to produce a detailed map of the locally-optimal starting months of the control period. Finally, we studied the effects of two different sterile males release strategies, constant or density-dependent, on *Ae. albopictus* populations.

2. Materials and methods

2.1. Study area

The study area is delimited by 1203 operational urban sectors defined by the vector control service of the Regional Health Agency. 31 weather stations of the French Meteorological Service at La Reunion Island provide the daily average temperature and rainfall intensity records from 2011 to 2016. Each operational urban sector is associated with the nearest weather station (Fig. 1).

2.2. Weather-driven abundance model

To simulate *Ae. albopictus* population dynamics, we modified the ALBORUN mechanistic model (Tran et al., 2020). ALBORUN computes the densities of the different stages of *Ae. albopictus* life cycle, aquatic

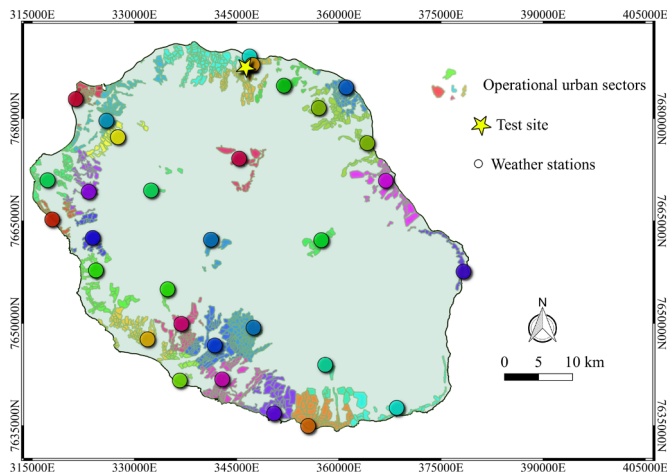


Fig. 1. Map of La Reunion Island with the localization of operational urban sectors (defined by the Regional Health Agency) and their associated weather stations (from the French meteorological service), in matching colors. The star is the location of the Duparc sector, where sterile male release trials started in July 2019..

(eggs: E , larvae: L , pupae: P) and aerial (emerging females: F_{em} , nulliparous females: F_n , parous females: F_p), using a system of ordinary differential equations (ODE). Parous females are females that have taken a blood meal and oviposited at least once, whereas nulliparous females did not yet lay eggs. Nulliparous and parous females are both again divided into three compartments according to the gonotrophic cycle, distinguishing between host-seeking females, engorged females and females seeking a breeding site. In total, the model is composed of 10 compartments. It thus makes it possible to compute independently and simultaneously the population dynamics in each operational urban sector. The ALBORUN outputs have been validated using entomological field data from La Reunion Island (Tran et al., 2020).

In the present study, ALBORUN was modified to assess effects of SIT and boosted-SIT control strategies (Fig. 2):

1. As these strategies are based on the release of sterile males, a specific male compartment M was explicitly included; it computes the number of wild males available for mating with females;
2. The number of compartments was reduced to avoid over-parametrization. The sub-compartments for nulliparous and parous females were thus aggregated into a single compartment each (nulliparous females: F_n , parous females: F_p).

The modified model, called "mALBORUN", is therefore:

$$\begin{cases}
 \frac{dE}{dt} = f_F(\beta_1 F_n + \beta_2 F_p) - (m_E + f_E)E \\
 \frac{dL}{dt} = f_E E - (m_L(1 + \frac{L}{K_L}) + f_L)L \\
 \frac{dP}{dt} = f_L L - (m_P + f_P)P \\
 \frac{dF_{em}}{dt} = \sigma f_P P \exp\left(-\mu_{em}\left(1 + \frac{P}{K_P}\right)\right) - (m_{F_{em}} + \gamma_{F_{em}})F_{em} \\
 \frac{dF_n}{dt} = \gamma_{F_{em}} F_{em} - (m_F + \mu_{F_r} + f_F)F_n \\
 \frac{dF_p}{dt} = f_F F_n - (m_F + \mu_{F_r})F_p \\
 \frac{dM}{dt} = (1 - \sigma)f_P P \exp\left(-\mu_{em}\left(1 + \frac{P}{K_P}\right)\right) - \mu_M M
 \end{cases}
 \tag{1}$$

The Greek letters represent parameters that are not influenced by weather: β_1 and β_2 respectively represent the egg laying rate of

nulliparous and parous females, σ is the sex-ratio, $\gamma_{F_{em}}$ is the rate of emerging females that succeed in blood feeding (thus becoming gravid but still nulliparous females, as they have not completed a full gonotrophic cycle). f_F correspond to the transition rate from nulliparous to parous females. μ_{em} is the pupae mortality rate at emergence, i.e. the transition from pupae to emerging adults, and μ_{F_r} corresponds to the additional mortality rate during breeding-site seeking behavior. The Arabic letters are weather-driven functions: f_x is the transition rate from stage x to the next, m_x is the mortality rate at stage x , and K_L and K_P are the breeding-sites carrying capacity for larvae and pupae, respectively. In the aquatic stage, larval and pupal competition are modeled by two density-dependant functions modifying their mortality rate. The pupal competition occurs at emergence: As the emergence time is short (Clements, 2000), the classic formula of density-dependent survival rate $\left(1 - \mu_{em}\left(1 + \frac{P}{K_P}\right)\right)$, meaning that the competition induces a higher death rate at emergence when pupae density P increases, can be expressed as a probability rate using the formula $\exp\left(-\mu_{em}\left(1 + \frac{P}{K_P}\right)\right)$ (Cailly et al., 2012). Larval mortality (m_L) is similarly increased when their density L increases. Parameters and functions are similar to the ALBORUN model by Tran et al. (2020) (Table: 1).

Due to the aggregation of female sub-compartments, the value of the parameter μ_{F_r} and the function f_F had to be reevaluated to ensure consistency between the original and modified models. The value of μ_{F_r} was estimated using a maximum likelihood method ("Multi-Level Single-Linkage" or MSL algorithm, nloptr package, R software, <https://cran.r-project.org/web/packages/nloptr/index.html>) to adjust mALBORUN to the outputs of ALBORUN (i.e. the density of mosquitoes for each compartment). In addition, the mALBORUN f_F value was obtained by summing the times spent by the nulliparous and parous females in the host-seeking, blood-feeding and breeding site-seeking compartments in ALBORUN.

For each time step, mALBORUN predicts the abundance of *Ae. albopictus* for the seven stages and for each operational urban sectors. The model was further validated using the entomological data from Tran et al. (2020), i.e. a longitudinal study on the larval stages of *Ae. albopictus* at five northern sites in 2012 and 2013. A Spearman test was performed to assess the correlation coefficient between the observed larvae abundances and those predicted by the model.

2.3. Modelling the effects of control methods

2.3.1. SIT model

mALBORUN (Eq. 1, Fig. 2) was then extended to include the effects of sterile male releases for the SIT control method (mALBORUN-SIT model, Fig. 3). The ODE thus becomes:

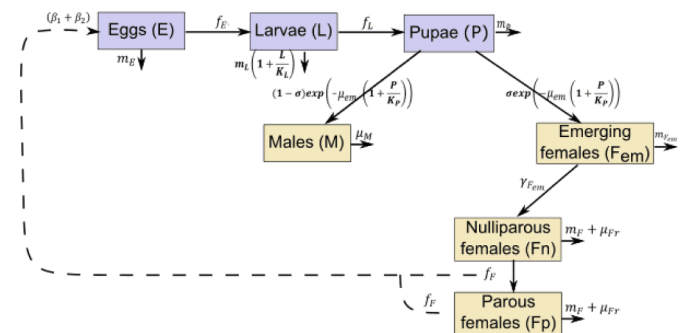


Fig. 2. Diagram of the modified weather-driven abundance model. The compartments in blue correspond to the aquatic stages, those in yellow correspond to the aerial stages. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

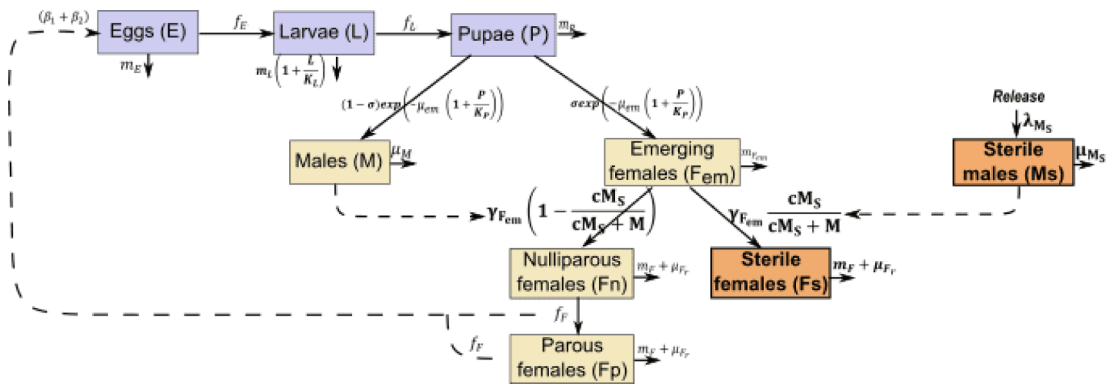


Fig. 3. Diagram of the mALBORUN-SIT model. The bolded and orange compartments are the compartments that have been added to mALBORUN (Fig. 2).

$$\begin{cases}
 \frac{dE}{dt} = f_F(\beta_1 F_n + \beta_2 F_p) - (m_E + f_E)E \\
 \frac{dL}{dt} = f_E E - \left(m_L \left(1 + \frac{L}{K_L}\right) + f_L\right)L \\
 \frac{dP}{dt} = f_L L - (m_P + f_P)P \\
 \frac{dF_{em}}{dt} = \sigma f_P P \exp\left(-\mu_{em} \left(1 + \frac{P}{K_P}\right)\right) - (m_{F_{em}} + \gamma_{F_{em}})F_{em} \\
 \frac{dF_n}{dt} = \gamma_{F_{em}} F_{em} \left(1 - \frac{cM_s}{cM_s + M}\right) - (m_F + \mu_{F_r} + f_F)F_n \\
 \frac{dF_p}{dt} = f_F F_n - (m_F + \mu_{F_r})F_p \\
 \frac{dF_s}{dt} = \gamma_{F_{em}} F_{em} \frac{cM_s}{cM_s + M} - (m_F + \mu_{F_r})F_s \\
 \frac{dM}{dt} = (1 - \sigma) f_P P \exp\left(-\mu_{em} \left(1 + \frac{P}{K_P}\right)\right) - \mu_M M \\
 \frac{dM_s}{dt} = -\mu_{M_s} M_s \\
 M_s(T_{start} + n\tau^+) = M_s(T_{start} + n\tau) + \lambda_{M_s}, \quad n = 1, 2, 3.
 \end{cases} \quad (2)$$

where the equations that are different from mALBORUN (Eq. 1) are bolded. M_s is the abundance of sterile males in the population. The simulated SIT control period starts at date T_{start} , and a number λ_{M_s} of

males sterilized by radiation is released periodically (which increases M_s); τ and n are the periodicity and number of releases, respectively, $n\tau^+$ is the moment immediately after the n^{th} release. The irradiation affects the mortality μ_{M_s} of the sterile males (Balestrino et al., 2010; Oliva et al., 2013). It also has an impact on their competitiveness c , which summarizes the ability of sterile males to find females, mate and transfer semen, as well as the number of females with whom they are able to copulate with Oliva et al. (2012); c is expressed relatively to wild males, i.e. $0 \leq c < 1$ when sterile males M_s are less competitive than their wild counterparts M , $c = 1$ when they are similar. In the case where encountering leads to mating, and since females can only be fertilized once, their spermatheca are filled with sterile sperm. Thus, $F_{em} \frac{cM_s}{cM_s + M}$ females become sterilized females F_s (i.e. they cannot produce viable offspring; (Anguelov et al., 2012; Esteva and Mo Yang, 2005; Mishra et al., 2018; Thome et al., 2010)

For emerging females F_{em} , $p = \frac{cM_s}{cM_s + M}$ is the probability to mate a sterile male and $(1-p)$ is the probability to mate with a wild male. Females that mate with sterile or wild males become either sterile or nulliparous, with a transition rate .

2.3.2. Boosted SIT model

mALBORUN-SIT model (Eq. 2, Fig. 3) was then extended to incorporate the boosted SIT effects (mALBORUN-BSIT model, Fig. 4) and

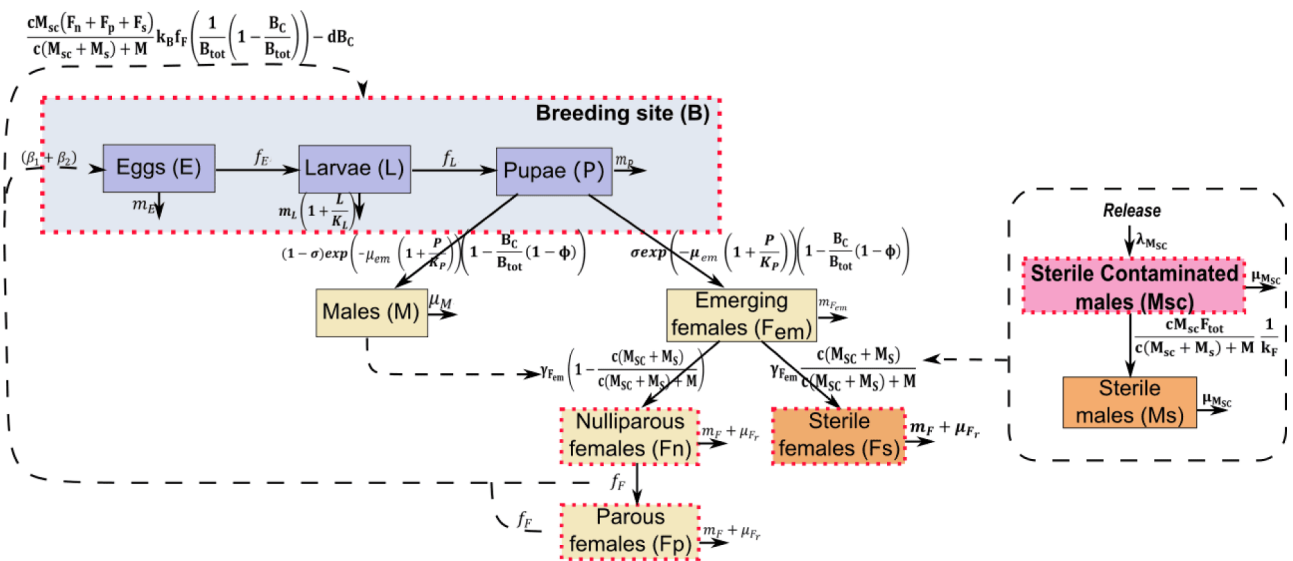


Fig. 4. Diagram of the mALBORUN-BSIT model. The bolded compartments have been added to mALBORUN-SIT. The red-dashed compartments are those that can be contaminated by the pyriproxyfen.

the ODE becomes:

$$\left\{ \begin{aligned}
 \frac{dE}{dt} &= f_E (\beta_1 F_n + \beta_2 F_p) - (m_E + f_E) E \\
 \frac{dL}{dt} &= f_E E - \left(m_L \left(1 + \frac{L}{K_L} \right) + f_L \right) L \\
 \frac{dP}{dt} &= f_L L - (m_P + f_P) P \\
 \frac{dF_{em}}{dt} &= \sigma f_P P \exp \left(-\mu_{em} \left(1 + \frac{P}{K_P} \right) \right) \left(1 - \frac{B_c}{B_{tot}} (1 - \phi) \right) - (m_{F_{em}} + \gamma_{F_{em}}) F_{em} \\
 \frac{dF_n}{dt} &= \gamma_{F_{em}} F_{em} \left(1 - \frac{c(M_{sc} + M_s)}{c(M_{sc} + M_s) + M} \right) - (m_F + \mu_{F_r} + f_F) F_n \\
 \frac{dF_p}{dt} &= f_F F_n - (m_F + \mu_{F_r}) F_p \\
 \frac{dF_s}{dt} &= \gamma_{F_{em}} F_{em} \frac{c(M_{sc} + M_s)}{c(M_{sc} + M_s) + M} - (m_F + \mu_{F_r}) F_s \\
 \frac{dM}{dt} &= (1 - \sigma) f_P P \exp \left(-\mu_{em} \left(1 + \frac{P}{K_P} \right) \right) \left(1 - \frac{B_c}{B_{tot}} (1 - \phi) \right) - \mu_M M \\
 \frac{dM_{sc}}{dt} &= -\frac{M_{sc} F_{tot}}{c(M_{sc} + M_s) + M} \frac{1}{k_F} - \mu_{M_{sc}} M_{sc} \\
 \frac{dM_s}{dt} &= \frac{M_{sc} F_{tot}}{c(M_{sc} + M_s) + M} \frac{1}{k_F} - \mu_{M_s} M_s \\
 \frac{dB_c}{dt} &= \frac{c M_{sc} (F_n + F_p + F_s)}{c(M_{sc} + M_s) + M} k_B f_F \left(1 - \frac{B_c}{B_{tot}} \right) - dB_c \\
 M_{sc} (T_{start} + n\tau) &= M_{sc} (T_{start} + n\tau) + \lambda_{M_{sc}}, \quad n = 1, 2, 3.
 \end{aligned} \right. \quad (3)$$

where the equations that are different from mALBORUN-SIT (Eq. 2) appear in bold.

The objective of the boosted SIT is to impact the emergence of *Ae. albopictus* via the pyriproxyfen through the contamination of breeding sites. We therefore introduced B_{tot} the total number of breeding sites, and B_c , the number of contaminated breeding sites. In uncontaminated breeding sites (probability $1 - \frac{B_c}{B_{tot}}$) F_{em} females and M males would emerge from pupae at the same rate as in the mALBORUN-SIT model. However, this rate may be lower in contaminated breeding sites (probability $\frac{B_c}{B_{tot}}$), as emergence is inhibited by pyriproxyfen. Let ϕ be the proportion of adults emerging from pupae in pyriproxyfen-contaminated sites, the overall emergence rate would therefore be modified by the factor $1 - \frac{B_c}{B_{tot}} (1 - \phi)$. When $\phi = 0$ the effect of pyriproxyfen is maximal: no pupae can emerge from a contaminated breeding site; conversely, when $\phi = 1$, all pupae can emerge despite the presence of pyriproxyfen (e.g. resistance of *Aedes albopictus* to pyriproxyfen), which is equivalent to SIT alone (Fig. G1).

For this strategy, the released males are always sterile, but they are also coated with pyriproxyfen; their abundance is noted M_{sc} . During the control period with the boosted SIT, a number $\lambda_{M_{sc}}$ of these males is periodically released in the population (the periodicity τ and the number of releases n can be modified, see mALBORUN-SIT model). When mating with females, M_{sc} males transfer part of their pyriproxyfen coating to the females, thus contaminate them, the "boosting" effect being that these females would in turn contaminate the breeding sites B_c . This transfer results in these males losing their coating, thus becoming "sterile-uncontaminated males" M_s . Since M_{sc} males can mate with any females in the population, the number of contacts is $\frac{c M_{sc} F_{tot}}{c(M_{sc} + M_s) + M}$, where $F_{tot} = F_{em} + F_n + F_p + F_s$ (i.e. the total number of adult females), and c the competitiveness of irradiated males (whether M_{sc} or M_s , see mALBORUN-SIT model). The number of M_{sc} becoming sterile-uncontaminated males M_s is therefore $\frac{c M_{sc} F_{tot}}{c(M_{sc} + M_s) + M} \frac{1}{k_F}$, where k_F allows to adjust the number of mates necessary for the M_{sc} males to lose their coating. However, all released males, whether still coated with pyriproxyfen (M_{sc}) or having lost their

coating (M_s), are sterile, and can therefore sterilize females.

As in mALBORUN-SIT, the reproductive status of emerging females F_{em} in mALBORUN-BSIT will be determined by their first mating: if they mate with a sterile male (probability $p = \frac{c(M_{sc} + M_s)}{c(M_{sc} + M_s) + M}$), they become sterile females F_s , if they mate with a wild male (probability $1 - p$), they become nulliparous gravid females F_n .

In order to limit the number of compartments, we did not make an explicit distinction between contaminated and uncontaminated females. Any female can be contaminated by M_{sc} males: emerging F_{em} , nulliparous F_n , parous F_p or sterile F_s , even if the last three categories cannot be fecundated. As F_{em} females become F_s after such mating, $\frac{c M_{sc} (F_n + F_p + F_s)}{c(M_{sc} + M_s) + M}$ is the number of females contaminated with pyriproxyfen after contact with M_{sc} males. We thus considered that any mated females (sterile or not) oviposit in larval breeding sites after a time f_F . If they were contaminated, they would then transfer some of their pyriproxyfen to breeding sites, thus reducing their level of contamination until complete decontamination. This imperfect transfer of pyriproxyfen transfer is modelled by the factor k_B , the number of females required to contaminate a breeding site. When $0 \leq k_B < 1$, several females are required to contaminate a single breeding site (imperfect transfer of pyriproxyfen from M_{sc} males to females, rapid decontamination of females, insufficient transfer of pyriproxyfen to the breeding site, ...). When $k_B > 1$, a single female can contaminate several breeding sites. Overall, $\frac{c M_{sc} (F_n + F_p + F_s)}{c(M_{sc} + M_s) + M} k_B f_F$ is therefore the "effective" number of contaminated breeding sites.

To compute the number of new contaminated breeding site, we also considered the probability that a breeding site was not yet contaminated, i.e. $1 - \frac{B_c}{B_{tot}}$. Finally, we took into account the possibility that a breeding site B_c may remain contaminated for only a limited period of time d .

2.3.3. Models outputs

At each time-step, the models predict the abundance of *Ae. albopictus* for each stage and for each operational urban sector. Moreover, four synthetic model outputs were computed to assess the impact of both SIT and boosted SIT methods on the mosquito population (Fig. A1):

1. the *reduction rate* was calculated as the size of females ($F_n + F_p$) during the control period divided by i) the size of females without control, to evaluate the effect of the SIT, and ii) the size of females during the SIT control, to evaluate the added effect of the boosted SIT.
2. the *sterility rate* was defined as the number of sterile females F_s divided by the total number of fertilized females ($F_n + F_p + F_s$) during the control period.
3. the *resilience* corresponds to the time required to return to the natural dynamics. It was calculated as the number of days required after a treatment period for the controlled population to reach the same abundance as a uncontrolled population.
4. the *reduction of emergence* was estimated as the ratio between the number of pupae present in contaminated breeding sites that became adults during the boosted SIT control and the number of pupae that became adults in a similar but uncontrolled population

2.3.4. Sensitivity analysis

A Sensitivity Analysis (SA) was performed on the four synthetic outputs using the variance-based method of Fourier Amplitude Sensitivity Test Saltelli et al. (2000) with the Sensitivity R package (<https://cran.r-project.org/web/packages/sensitivity/index.html>). The parameters of mALBORUN-SIT (μ_{M_s} , c), mALBORUN-BSIT ($\mu_{M_{sc}}$, d , k_B , k_B) and the parameters relative to the release (τ , n , T_{start} , λ_{M_s} , $\lambda_{M_{sc}}$) were

varied simultaneously using a uniform distribution. The boundaries of the parameters were chosen according to knowledge from bibliography, results of experiments and observational studies (Table: 2). The parameters contributing to more than 20% of the variance of a given model output were considered to have a strong influence on the output. The SA was replicated on four urban sectors selected randomly in the North, South, East and West of the island to account for environmental variability. Model sensitivity was analyzed over 256,000 simulations. Only outputs with normally distributed variations were analyzed.

2.3.5. Release strategies

Release starting month:

We produced a map of the optimal release starting month for each output of mALBORUN-SIT and mALBORUN-BSIT model. The release starting date (T_{start}) varied from January to December. The optimal release starting month corresponds to the month for which the output values is maximum. Due to the inter-annual weather variations, the simulations were replicated for three years (2013, 2014, 2015), and since several operational urban sectors are connected to the same weather station, the simulations were computed for only one sector per weather station, selected randomly.

We have also performed an optimization in order to find the month that gives the best value for all model outputs to summarize information in only one map. For this purpose, we defined the function:

$$f(T_{start}, s) = -\sum_y (\text{Reduction rate}_y + \text{Sterility rate}_y + \frac{\text{Resilience}_y}{365} + \text{Emergence reduction}_y)$$

with $\begin{cases} s \in \text{urban sectors} \\ y \in [2013; 2015] \end{cases}$ (4)

The higher the values of all outputs of the models (i.e. in terms of *Ae. albopictus* populations control) for a given starting date (T_{start}) and urban sector (s), the lower the value of the function $f(T_{start}, s)$. It should be noted that the resilience was divided by 365 days, so that any effect lasting more than one year had a strong influence. A global and local optimization algorithm from the nloptr R package (<https://cran.r-project.org/web/packages/nloptr/index.html>) was then used to minimize the function $f(T_{start}, s)$.

Number of sterile male released:

Two strategies differing in the number of sterile male released each time (mALBORUN-SIT: λ_{Ms} , mALBORUN-BSIT: λ_{Msc}) were compared:

1. In the first strategy, both λ_{Ms} , λ_{Msc} and τ were constant during the control period. Ten λ_{Ms} and λ_{Msc} values were tested from 1, to 10 times the sum of nulliparous and parous females at the beginning of the control period; six τ were tested, from 15 days down to 5. A total of 60 simulations were performed for an extended release control period of three or six month.
2. In the second strategy, λ_{Ms} and λ_{Msc} values were proportional to the number of nulliparous and parous females at the release dates. The values of λ_{Ms} , λ_{Msc} , τ , and the total number of simulations were similar to the first strategy.

The SIT program has chosen one site for the their future sterile male release trials corresponding to one of the operational urban sectors in Reunion Island called "Duparc Sector" (Fig. 1). We therefore selected this site to predict the impact of the two different release strategies on the control of the local population of *Ae. albopictus*, for both SIT and boosted-SIT methods.

2.4. Initialization and simulations

Models were implemented in R (<http://www.rproject.org/>). At $t = 0$, the population consisted in 1000 eggs for each operational urban sectors. Simulations ran over 6 years. We used the weather data from

2011 to 2016 as the input of the models. The first year was not retained for outputs computation. No sterile male has been released during the last year, which allowed computing the time required for the *Ae. albopictus* population to recover its natural dynamics, i.e. the resilience time (in days).

3. Results

The ALBORUN model has been modified and simplified, in order to model the effects of control methods (mALBORUN). As in the original model, mALBORUN predicts the abundances of *Ae. albopictus* by stage (eggs, larvae, pupae, adults: females and males) over time for each operational urban sector, using daily rainfall and temperature data over 6 consecutive years as entries. The effects of the SIT (mALBORUN-SIT) and boosted SIT (mALBORUN-BSIT) were then introduced to predict and compare the impact of the two control strategies under different scenarios (Fig. 5).

3.1. mALBORUN is consistent with the entomological data

Simulated mosquito abundances of the modified mALBORUN model, based on weather conditions, are consistent with the entomological data collected at five locations in 2012 and 2013 in La Reunion Island (Fig. 6). As in the original ALBORUN model (Tran et al., 2020), the predictions were strongly correlated with the observed abundances (P-value < 0.001) at sites with higher larval densities and high seasonal variations (correlation coefficients for Saint-Paul: 0.86; La Possession: 0.70; Sainte-Marie: 0.68; Sainte-Suzanne: 0.75). The correlation coefficient was lower (0.61, P-value=0.06) for the eastern site (St-Benoit), where the observed abundances of *Ae. albopictus* was lower (< 20 larvae/trap) with few seasonal variations. Nevertheless, the model reproduced the major trends in the intra-annual population fluctuations for all sites: abundances indeed show a peak occurring in March-April, at the end of the austral summer, and a minimum at the end of the austral winter (Fig. 5).

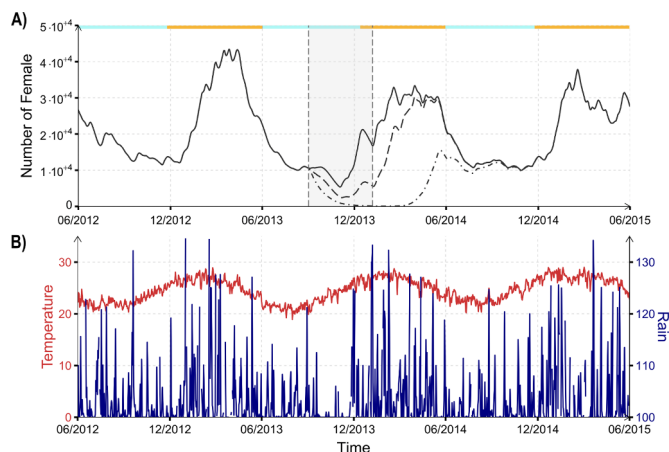


Fig. 5. Predicted adult females of *Aedes albopictus* population in La Reunion Island A) Simulated number of adult females (nulliparous (F_n) + parous (F_p)) and B) Daily rainfall (blue) and mean temperature (red) in the Duparc Sector. Population dynamics without control (mALBORUN) is represented in solid line and the population dynamics controlled with SIT (mALBORUN-SIT) and boosted SIT (mALBORUN-BSIT) are represented in long dashed line and in dotted line respectively. The grey background indicates the control period and the colored bars symbolize in orange the austral summer (November-March) and in light blue the austral winter on the top panel. Parameter values and functions of the models are in Tables 1 and 2. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Parameters value and functions for ALBORUN (Tran et al., 2020) The letter *R* and *T* correspond to the daily rainfall and temperature respectively.

Parameters	Definition	Value	Ref
β_1	Number of eggs laid/ovipositing nulliparous female	60	(Delatte et al., 2009)
β_2	Number of eggs laid/ovipositing parous female	80	(Delatte et al., 2009)
σ	Sex-ratio at emergence	0.5	(Delatte et al., 2009)
μ_E	Minimum egg mortality rate (day ⁻¹)	0.05	(Tran et al., 2013)
μ_{em}	Mortality rate during emergence (day ⁻¹)	0.1	(Tran et al., 2013)
μ_{Fr}	Mortality rate related to seeking behaviour (day ⁻¹)	0.06	(Optimization)
μ_M	Mortality rate of males (day ⁻¹)	0.0735	(Oliva et al., 2013)
T_E	Minimal temperature needed for egg development (°C)	10	(Delatte et al., 2009)
TDD_E	Total number of degree-day necessary for egg development (°C)	110	(Tran et al., 2013)
γ_{Fem}	Development rate of emerging females (day ⁻¹)	0.4	(Tran et al., 2013)
γ_{Fo}	Transition rate from ovipositing to host-seeking females (day ⁻¹)	0.2	(Tran et al., 2013)
γ_{Fh}	Transition rate from host-seeking to engorged females (day ⁻¹)	0.2	(Tran et al., 2013)
T_{Fg}	Minimal temperature needed for egg maturation in females (°C)	10	(Delatte et al., 2009)
TDD_{Fg}	Total number of degree-day necessary for egg maturation (°C)	77	(Delatte et al., 2009)
κ_{Lfix}	Standard rainfall-independent environment carrying capacity for larvae		Field observations
κ_{Lvar}	Standard rainfall-dependent environment carrying capacity for larvae		Field observations
κ_{Pfix}	Standard rainfall-independent environment carrying capacity for pupae		Field observations
κ_{Pvar}	Standard rainfall-dependent environment carrying capacity for pupae		Field observations
Functions	Definition	Expression	Ref
f_E	Transition function from egg to larva	$\begin{cases} \frac{T(t) - T_E}{TDD_E}, & \text{if } (t) > T_E. \\ 0, & \text{otherwise.} \end{cases}$	(Tran et al., 2013)
f_L	Transition function from larva to pupa	$-0.0007T^2 + 0.0392T - 0.3911$	(Tran et al., 2013)
f_P	Transition function from pupa to emerging adult	$0.0008T^2 - 0.0051T + 0.0319$	(Tran et al., 2013)
m_E	Egg mortality	$\mu_E + \begin{cases} 0.1, & \text{if } R < 80. \\ 0, & \text{otherwise.} \end{cases}$	(Dieng et al., 2012; Tran et al., 2013)
m_L	Larva mortality	$0.02 + 0.0007e^{(0.1838(T-10))} + \begin{cases} 0.5, & \text{if } R < 80. \\ 0, & \text{otherwise.} \end{cases}$	(Delatte et al., 2009; Dieng et al., 2012)
m_P	Pupa mortality	$0.02 + 0.0003e^{(0.2228(T-10))} + \begin{cases} 0.5, & \text{if } R < 80. \\ 0, & \text{otherwise.} \end{cases}$	(Delatte et al., 2009; Dieng et al., 2012)
m_f	Female mortality	$0.025 + 0.0003e^{(0.1745(T-10))}$	(Delatte et al., 2009)
f_{Fg}	Transition function from engorged to oviposition site-seeking female	$\begin{cases} \frac{T(t) - T_{Fg}}{TDD_{Fg}}, & \text{if } (t) > T_{Fg}. \\ 0, & \text{otherwise.} \end{cases}$	(Tran et al., 2013)
f_{Fo}	Transition function from ovipositing to host-seeking female	$\frac{\gamma_{Fo}(1 + P_{norm})}{1}$	(Pachka et al., 2016)
f_F	Transition rate from nulliparous to parous females	$\frac{1}{1/f_{Fo} + 1/\gamma_{Fh} + 1/f_{Fg}}$	
K_L	Environment carrying capacity for larvae	$K_L(t) = \kappa_{Lfix} + \kappa_{Lvar} R_{norm}(t)$	(Tran et al., 2013)
K_P	Environment carrying capacity for pupae	$K_P(t) = \kappa_{Pfix} + \kappa_{Pvar} R_{norm}(t)$	(Tran et al., 2013)

Table 2
mALBORUN-SIT and mALBORUN-BSIT parameter values.

Parameters	Definition	Value and bounds	Ref
<i>c</i>	Sterile males competitiveness	0.23 [0.01 – 0.9]	(Bellini et al., 2007; 2013; Madakacherry et al., 2014; Oliva et al., 2012)
μ_{Ms}^a, μ_{Msc}^b	Mortality rate of sterile males (day ⁻¹)	0.087 [0.18 – 0.065]	(Balestrino et al., 2010; Oliva et al., 2013)
<i>k_F</i>	Expected number of contaminating mating	1 [1 – 8]	Current work
<i>k_B</i>	Expected number of breeding sites that a female contaminates	1 [1 – 8]	Current work
<i>d</i>	Expected decontamination rate at breeding sites (day ⁻¹)	0.048 [0.08 – 0.0065]	(Caputo et al., 2012; Darriet and Corbel, 2006; Devine et al., 2009; Sihuinchu et al., 2005; Snetselaar et al., 2014; Suman et al., 2014)
ϕ	Proportion of pupae surviving to pyriproxyfen	0.3 [0.02, 0.5]	(Caputo et al., 2012; Chang Moh et al., 2008; Darriet and Corbel, 2006; Devine et al., 2009; Snetselaar et al., 2014)
$\lambda_{Ms}^a, \lambda_{Msc}^b$	Number of sterile males released /ha	1000 [600 – 6000]	(Bellini et al., 2013; Carvalho et al., 2015; Harris et al., 2011; Romeo et al., 2020)
τ	Periodicity of the releases (day)	7 [5 – 10]	(Bellini et al., 2013; Romeo et al., 2020)
<i>n</i>	Number of releases	18 [13 – 20]	(Bellini et al., 2013; Romeo et al., 2020)
<i>T_{Start}</i>	Starting date of the control period	01 sept. [1 Jan. - 31 Dec.]	

^a mALBORUN-SIT

^b mALBORUN-BSIT

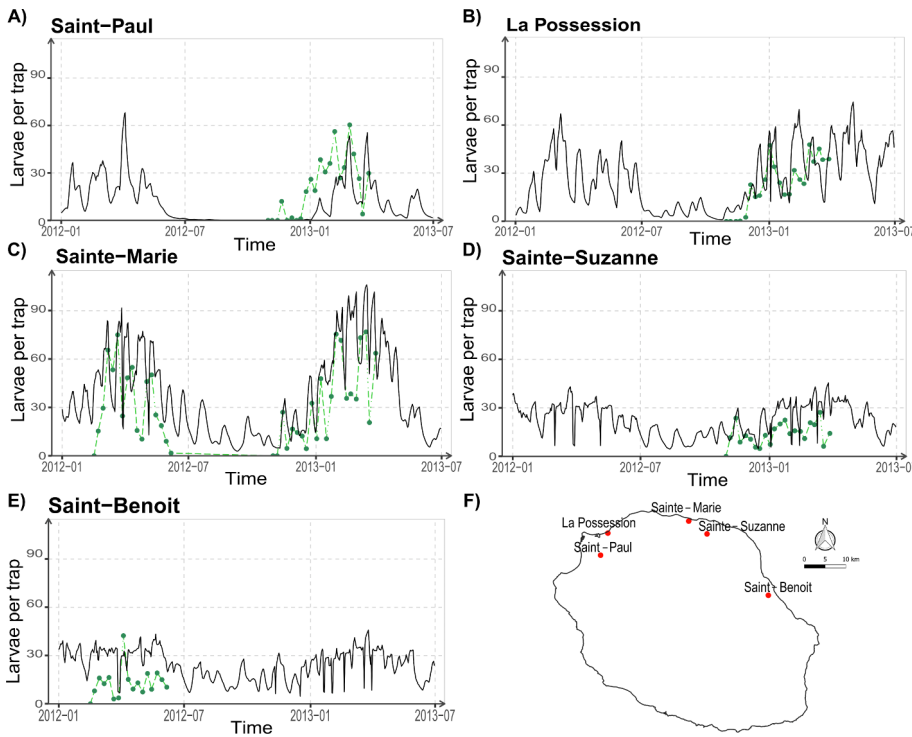


Fig. 6. mALBORUN model validation. The simulated dynamics of larvae (black lines) was compared to field data (green points) collected in 2012 and 2013 at A) Saint-Paul, B) La Possession, C) Sainte-Marie, D) Sainte-Suzanne and E) Saint-Benoit sites. F) The sites are located in the North of La Reunion Island. Parameter values and functions of the model are in Table 1.

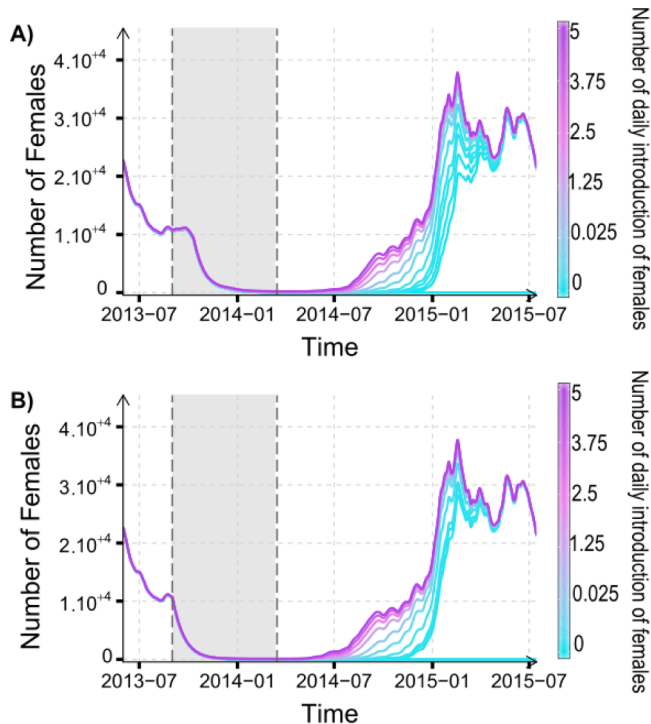


Fig. 7. Effect of migration on resilience in mALBORUN-SIT A) and mALBORUN-BSIT B). From one female every 40 days (introduction = 1/40) to five females per day (introduction = 5) were allowed to enter the target population during and after sterile male release. Weather data at the Duparc Sector from La Reunion Island were used as example. Parameter values and functions of the models are in Tables 1 and 2.

3.2. The number of sterile males released, their competitiveness and the timing of release are the key parameters of the control

To assess the most influential parameters, a SA was performed for the mALBORUN-SIT and mALBORUN-BSIT models. We analyzed four model outputs: the reduction rate, the sterility rate, the resilience time and the reduction of emergence (see Methods). Surprisingly, it was shown that the resilience time (*i.e.* the time required after the treatment stopped for a treated population to reach a size similar to a untreated population) was not normally distributed. This was due to the complete elimination of the population that was predicted for some parameters sets: As the model was run on an isolated population, without migration, no resilience was possible. To verify whether these elimination events were maintained in the presence of a limited migration or rather a no-migration artifact, we simulated the introduction of adult females into the population, from one female every 40 days to five females per day. A total of 12 simulations were performed (Fig. 7). The results showed that even very low immigration was sufficient enough for the population to eventually return to its natural dynamics, in sharp contrast with the elimination predicted in the no-migration case: it thus suggested that the local eliminations were indeed artifacts. Consequently, we decided to perform another SA with the introduction of a few females (one every 40 days as shown in Fig. 7).

For both models, the reduction rate relative to the number of females ($F_h + F_p$) without control was not normally distributed and could therefore not be analyzed.

Considering mALBORUN-SIT model (Fig. 8A), the competitiveness of the sterile males (c) was identified as the most influential parameter for both sterility rate and resilience (> 50%). The number of sterile males released (λ_{M_s}) and the starting date of the control period (T_{start}) were the second most influential parameters (*ca.* 25% each), for both outputs. Finally, a strong effect of the number of releases (n) was

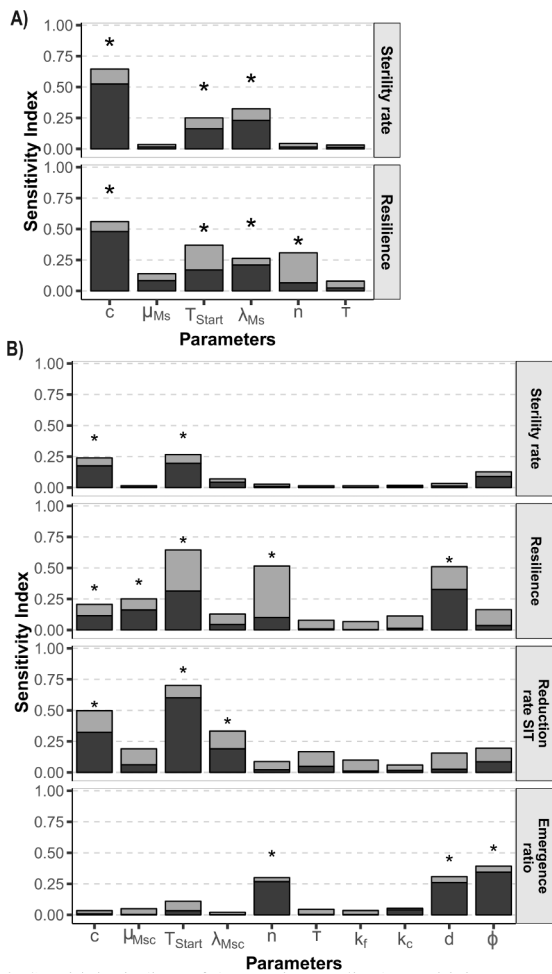


Fig. 8. Sensitivity indices of the Fourier amplitude sensitivity test (FAST) for mALBORUN-SIT A) and mALBORUN-BSIT B) outputs. In dark grey, main effects; in light grey, interactions. 256,000 simulations with 6400 points per parameter and four replicates. Parameters contributing to more than 20% of the output variance were considered to be influential parameters (identified by a star for each output). See Table 2 for parameter definitions. To prevent the eradication artifacts due to the absence of migration (see 3.2), one female was introduced every 40 days in each operational urban sector. Parameter values and functions of the models are in Tables 1 and 2.

detected on resilience, mainly through interactive effects.

For the mALBORUN-BSIT model (Fig. 8B), the results of the SA were slightly different: while both the starting date of the control period (T_{Start}) and the competitiveness of the sterile males (c) were the determinants of the sterility rate and remained influential on resilience, c appeared less determinant than in mALBORUN-SIT (ca. 25%). Similarly, the number of sterile males released (λ_{Ms}) no longer had any influence. However, the number of releases (n) remained influential on resilience, as well as two additional parameter, the mortality rate of sterile males (μ_{Msc}) and the expected duration of contamination at larval sites (d).

We also assessed the main parameters influencing the observed differences in reduction rates between SIT and boosted SIT applications. They were again explained mainly by T_{Start} , c and λ_{Msc} , rather (which is surprising) than by parameters specific to mALBORUN-BSIT (k_f , k_b , d ,

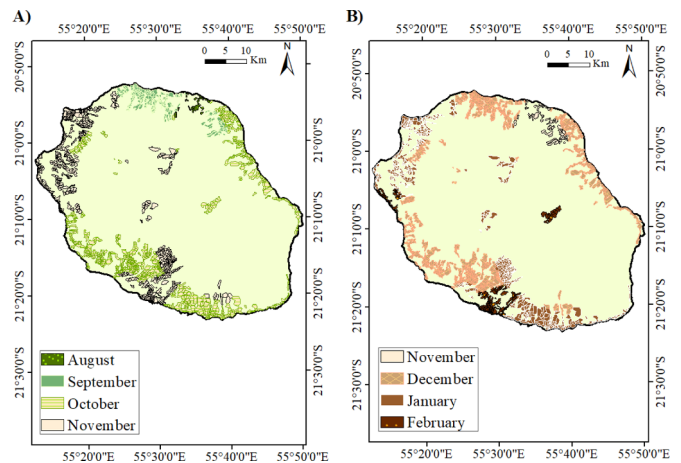


Fig. 9. Map of the optimal starting months for the sterile males releases at La Reunion Island. The optimal date was estimated by optimizing the outputs for A) mALBORUN-SIT and B) mALBORUN-BSIT over three years. The optimal date is the same for all the sectors connected to the same weather station.

ϕ). Finally, two of these specific parameters had, as expected, a strong influence on the emergence ratio: the proportion of pupae surviving pyriproxyfen ϕ and the expected duration of contamination at larval sites $\frac{1}{d}$.

For both models, the SA showed that there was a high impact of first-order parameter interactions on the outputs. For example, during the control period, an *Ae. albopictus* population reduction rate of 0.8 can be achieved either with $c = 0.6$ and $\lambda_{Ms} = 2800$ sterile males/ha, or with a competitiveness of $c = 0.4$ and $\lambda_{Ms} = 4000$ sterile males/ha with the SIT (Fig. 10A). Similarly for boosted SIT, $c = 0.6$ and $\lambda_{Msc} = 1200$, or $c = 0.4$ and $\lambda_{Msc} = 1800$, achieve the same population reduction of 0.8; note that fewer males need to be released compared to SIT (Fig. 10B).

3.3. Boosted SIT control should start later than SIT

As shown by the SA, the starting date of the release of sterile males (T_{Start}) was a key parameter for both SIT and boosted SIT. A map was produced for each control method that shows the specific optimal T_{Start} for each operational urban sectors (that depends on local climatic conditions). For SIT (Fig. 9A and Fig. B1), the date to begin the release was optimal when the density of *Ae. albopictus* population was low, thus on average, in October, at the end of the austral winter (May - October). For boosted SIT (Fig. 9B and Fig. C1), the optimal date was postponed by several months, on average in December, when the population density of *Ae. albopictus* has already increased Fig. C1.

3.4. Boosted SIT carries higher benefits when sterile males are poor competitors

The other important parameters identified by the SA were competitiveness (c) and the number of sterile males released (mALBORUN-SIT: λ_{Ms} , mALBORUN-BSIT: λ_{Msc}). However these two parameters are in direct interaction: The more competitive the sterile males are, the fewer released males are needed to obtain similar results in terms of relative reduction rate or resilience. Although we plotted the impact of parameter c alone on *Ae. albopictus* population control with SIT and

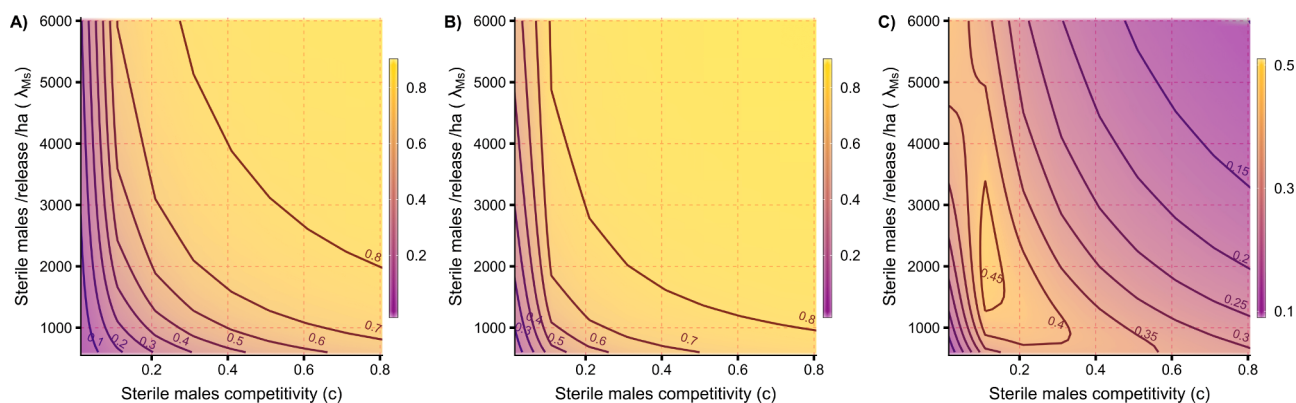


Fig. 10. Impact of the number of sterile males released and of their competitiveness on the female numbers ($F_n + F_p$) reduction. The reduction of the abundance of adult females is indicated A) for SIT (mALBORUN-SIT) relatively to a non-controlled population (mALBORUN); B) for boosted SIT (mALBORUN-BSIT) relatively to a non-controlled population (mALBORUN); and C) for boosted SIT (mALBORUN-BSIT) relatively to a population controlled with SIT (mALBORUN-SIT). The reduction proportion is represented by a color gradient from purple (low reduction) to yellow (large reduction), with isoclines represented with a contour plot (from 0.1 to 0.8 reduction). The weather conditions of a single sector were used for the simulations (i.e. Duparc Sector at La Reunion Island). To prevent the eradication artifacts due to the absence of migration (see text), one female was introduced every 40 days in each the operational urban sectors.

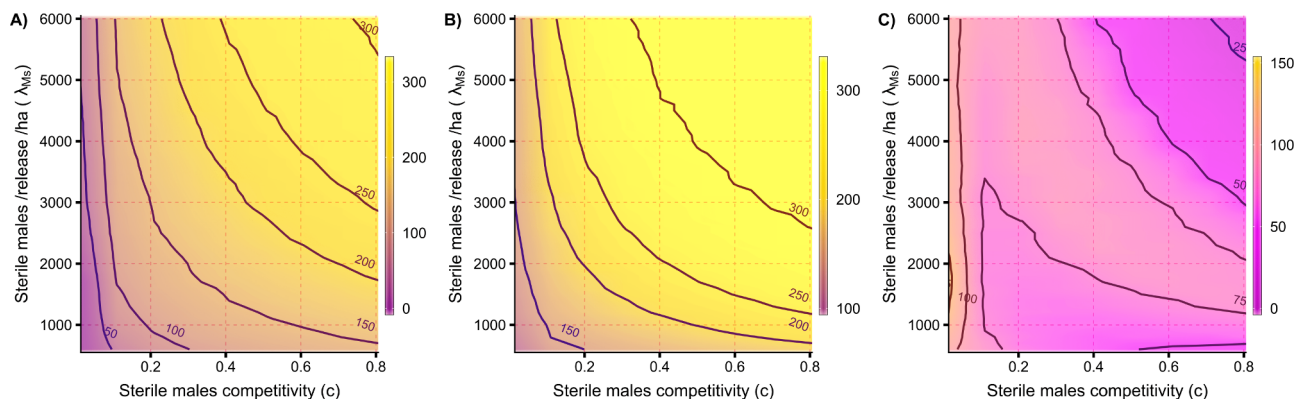


Fig. 11. Impact of the number of sterile males released and of their competitiveness on the population resilience time. The time required for a treated population to reach the population size it would have had without treatment (mALBORUN) is indicated A) for SIT (mALBORUN-SIT); B) for boosted SIT (mALBORUN-BSIT). The resilience time difference between the two control methods is indicated in C). The resilience time is represented by a color gradient from purple (fast resilience) to yellow (slow resilience), with isoclines represented with a contour plot (every 50 days required for resilience). The weather conditions of a single sector (Duparc Sector at La Reunion Island) were used for the simulations. To prevent the eradication artifacts due to the absence of migration (see text), one female was introduced every 40 days in each the operational urban sectors.

boosted SIT, (Fig. F1 and Fig. F2), it is more relevant to analyse the combined effect of c and $\lambda_{Msc}/\lambda_{Ms}$.

We first analyzed how this interaction impacts the reduction rate in female numbers ($F_n + F_p$), for each control method independently (Fig. 10A: SIT, Fig. 10B: Boosted SIT). For both methods, the reduction rate increased with c , λ_{Ms} and λ_{Msc} , but the competitiveness was clearly the main determinant. In order to assess the added benefits of the boosted SIT method, we also calculated the difference in the reduction rate between mALBORUN-SIT and mALBORUN-BSIT for various combinations (Fig. 10C): It appeared that the boosted SIT was mostly beneficial when the sterile males were poor competitors, but not too poor ($0.17 < c < 0.4$).

We then analyzed how the interaction between the number of sterile males released and their competitiveness impacted the resilience time, for each control method independently (Fig. 11A: SIT, Fig. 11B: Boosted

SIT). As for reduction rate, and for both methods, the resilience time increased with c , λ_{Ms} and λ_{Msc} , but the competitiveness was again clearly the main determinant. In order to assess the added benefits of the boosted SIT method, we also calculated the difference in resilience time between mALBORUN-SIT and mALBORUN-BSIT for various combinations (Fig. 11C): It appeared that boosted SIT was again mostly beneficial when sterile males were poor competitors.

3.5. Constant releases are better than density-dependent releases

We compared the impact on reduction rates and resilience times for two control strategies differing in the number of sterile males released (mALBORUN-SIT: λ_{Ms} , mALBORUN-BSIT: λ_{Msc}): i) A constant number during the control period and ii) a number proportional to the number of adult females at the time of release. The second release strategy has

been proposed to reduce the rearing cost of the sterile males.

For both models, the first strategy appeared more efficient: the population was reduced to a greater extent and returned to its initial dynamics more slowly after the control period (Fig. D1). However, while the difference between the two release strategies was relatively small in terms of reduction rates, the resilience time was much more affected, since it was reduced by about 3 times with the second strategy. For example for SIT, with $n=7$ days and $\lambda_{M_s}=10$ times the number of females, the population was reduced by 95% and required 335 days to return to natural dynamics with constant releases, while for proportional releases the population was decreased by 82% and only needed 92 days to return to natural dynamics. Similar results were obtained for boosted SIT (Fig. E1).

4. Discussion

We developed a weather-driven abundance model of *Ae. albopictus* at La Reunion island (mALBORUN) based on the ALBORUN mechanistic model Tran et al. (2020), and integrated the effects of SIT (mALBORUN-SIT) and boosted SIT (mALBORUN-BSIT) on population dynamics. These non-autonomous models include the impact of temperature and rainfall, which are two important drivers of the mosquito dynamics (Agusto et al., 2015; Delatte et al., 2009; Dieng et al., 2012; Kruijff et al., 1973; Roiz et al., 2010; Tran et al., 2020). The predicted abundance of mosquito populations follows environmental fluctuations (Fig. 5) and was consistent with entomological field collections (Fig. 6). Thus, our models are adapted to areas with a high climatic spatial heterogeneity, as it is the case in La Reunion island. To our knowledge, these are the first models that integrate real weather data in order to analyze the effects of SIT and boosted SIT on mosquito populations. Non-autonomous models were chosen because, as White et al. (2010) pointed out, environmental data are of major importance to optimize these control strategies, particularly to determine the optimal period for effective releases of sterile males (Fig. H1). Our results have indeed shown that the multitude of microclimates in La Reunion island lead to different optimal starting months depending on the areas concerned by the release of sterile males (Fig. 9).

4.1. Migration should be considered in future models

According to our results, both SIT and boosted SIT could lead to virtual elimination of *Ae. albopictus* populations: in both models, as the populations are modeled independently, some sets of parameters induced a density equilibrium close to zero after treatment (Fig. 7). Nevertheless, we have shown that this result is probably an artifact due to the non inclusion of mosquito dispersal in the models. Although Lacroix et al. (2009) has shown a relatively low dispersal ability for *Ae. albopictus*, simulations showed that the introduction of even a tiny number of females would result in a rapid recovery of the mosquito population after the treatments (Fig. 7). It is still possible that some Allee effect (not modelled here) may be induced by the reduction in the number of successful mating when males densities become low (this would increase the difficulty of finding a mate), which would delay the population's regrowth and increase the probability of sustainable elimination after treatment (Li et al., 2007; Li and Yuan, 2015; Strugarek et al., 2019). Nevertheless, our results are consistent with a recent pilot trial of transgenic *Ae. aegypti* males releases in Brazil, which showed that the population had not been eliminated despite a significant decrease in wild mosquito populations during the control period (Garziera et al., 2017). The future integration of adult mosquito

migration into our model, taking into account the heterogeneity of environment and its impact on migration rates, would therefore be a crucial development to provide more accurate quantitative predictions (Dunning et al., 1995).

4.2. Competitiveness vs. number of released males equilibrium, and control timing are crucial for SIT efficiency

According to the SA results for the mALBORUN-SIT model, the competitiveness and the quantity of sterile males released are the two most important parameters that determine the effective control of *Ae. albopictus* populations (Fig. 8A). Similarly to previous findings by Pleydell and Bouyer (2019), appropriate combinations of these two parameters values could indeed lead to important population reductions (Fig. 10). However, other studies have shown that this competitiveness is highly variable depending on local conditions at the sterile-males release sites (e.g. Bellini et al., 2007; Bellini et al., 2013; Madakacherry et al., 2014; Oliva et al., 2012). Thus, an accurate estimate of this competitiveness, in the environment where releases occur, is necessary to improve the predictive capacity of the model and to assess the efficiency of this strategy in a particular field context. As underlined by White et al. (2010), reduced competitiveness of sterile males can be offset by larger releases (Fig. 8), and our model allows an accurate estimate of this balance. It should be noted that increasing the number of released males would entail additional, and potentially high, economic costs.

The starting month for the sterile males releases is also a crucial parameter for the SIT control method (Fig. 9). According to our results, the best date corresponds to the end of the austral winter, when the wild mosquito populations are at the lowest density: As there are fewer wild competitors, sterile males have a higher probability of mating with females (Dufourd and Dumont, 2012; Huang et al., 2017; White et al., 2010), which may partly compensate their lower competitiveness. However, and despite the additional cost, we have shown here that the full benefit of these early releases requires a significant and consistent number of sterile males from the start (Fig. D1), rather than a number of males released proportionally to the number of wild adult females (Cai et al., 2014; Li and Yuan, 2015). Again our model allows for accurate forecasts under various scenarios, and can therefore help control agencies in making informed operational decisions.

4.3. Boosted SIT could be an interesting improvement, but some parameters need to be evaluated before implementation

The mALBORUN-BSIT model analyses showed that coating sterile males with pyriproxyfen could potentially improve the efficiency of the SIT control. The additional population reduction due to this "boost" is particularly strong (up to 45% more than SIT alone) for sterile males with intermediate competitiveness (i.e. $0.2 < c < 0.5$, Fig. 10C); it cannot compensate too poor males ($c < 0.2$), and provide lower improvements when they are already good competitors ($c > 0.5$). Similarly, boosted SIT could significantly increase the population resilience time, up to 75 more days again for males with intermediate competitiveness and for reasonable number released (Fig. 11C). This strategy would thus be most interesting in contexts where increasing the quality of the males released is difficult, due to the direct effects of the sterilizing radiations and/or the effects of mass-rearing in production facilities. However, an estimation of the relative costs of the coating boost or of producing more males should be considered too, and our model provides a reliable framework for such analyzes.

As for SIT alone, the timing of boosted SIT implementation appears crucial: the boost effects are more visible in early austral summer (Fig. 9). This confirms the work of Pleydell and Bouyer (2019) who have shown that the boosted-SIT must be applied when the population begins to increase: when the population is too low, only a small amount of pyriproxyfen is transferred to females and therefore to breeding sites, so that the boosting effect is lost. It should be noted that, in choosing conservative hypotheses for our study, we did not consider direct contamination of breeding sites by males. Yet, this contamination may occur as some *Ae. aegypti* males were found in sticky ovitraps (Ritchie et al., 2003). Direct contact of contaminated males with breeding sites could slightly increase the effectiveness of the pyriproxyfen transfer from females under these conditions (Mains et al., 2015). However, the obvious advantage of the boosted approach is that the starting date of releases is delayed: consequently, fewer releases are needed for a similar effect.

Two other parameters appeared to be significant (although much less important than the previous ones) in the success of the boosted SIT control method: the duration of pyriproxyfen contamination of breeding sites, confirming (Pleydell and Bouyer, 2019), and the proportion of pupae surviving pyriproxyfen, both related to the dose of the contaminants. Crucially, the relative importance of these two parameters actually highlights the limitations of our predictions: although qualitatively robust, our results should be taken with caution for quantitative predictions. For several key parameters of the model, there is indeed little or no empirical data, mainly because the concept of boosted SIT is recent. Several studies are currently in progress to improve the coating technique. Similarly, the efficiency of the male/female and female/breeding sites contamination remains to be determined experimentally, both in the laboratory and under natural conditions. Finally, we did not consider the potential direct impacts of pyriproxyfen on female fecundity and/or on the hatching rate, which could modify the boosting effect: some have been described, but they appear to vary depending on the formulation of pyriproxyfen used (Dell Chism and Apperson, 2003; Itoh et al., 1994; Mbare et al., 2013; Unlu et al., 2017). Again, additional experimental studies are needed to adjust the BSIT model to more realistic conditions and provide quantitatively accurate predictions.

4.4. SIT and boosted SIT should be part of integrated management strategies against *Aedes albopictus*

Our study clearly shows that for realistic sets of key parameters, SIT could provide effective control of mosquito populations, and that boosted SIT could even improve this efficiency. Compared to the classical use of chemical insecticides, boosted SIT based on pyriproxyfen would be used in a very targeted way, at very low doses. Moreover, the contaminated mosquitoes are expected to specifically contaminate their small and mostly artificial breeding sites, created and maintained by humans, which should limit any risk of environmental contamination. However, as with any use of chemical insecticides, the autodissemination of pyriproxyfen to boost the SIT can lead to the development of mosquito resistance (Tantely et al., 2010; Vontas et al., 2012; Zaim and Guillet, 2002). mALBORUN-BSIT model provides a solid framework for studying the potential evolution of insecticide resistance in mosquito populations in order to prevent its occurrence or control its spread by optimizing the use of the boosted SIT under various scenarios (Barbosa et al., 2018). Moreover, if the coating with the pyriproxyfen is more advanced, other candidates have been proposed, like the use of natural biocides such as densovirus (Carlson et al., 2006). Again, our

model provides the appropriate framework for evaluating this method *in silico*.

SIT and boosted-SIT are not the only alternative control methods available in the literature or in the field: they are and should be considered as alternative tools in a broader set, with complementary actions. Mass trapping of adult mosquitoes, for example, have shown promising results (Barrera et al., 2017; Degener et al., 2014). While our study focused on sterile males release techniques, Pleydell and Bouyer (2019) studied, for example, the effects of SIT and boosted SIT coupled with the disposition in the environment of artificial oviposition sites contaminated with pyriproxyfen (autodissemination station). Interactions between different method controls used simultaneously or sequentially could be positive or negative (Barclay, 1987; Knippling, 1979) and should be considered to optimize mosquito population control. Our mechanistic model that takes into account the different stages of the mosquito life cycle provides an appropriate framework for implementing and testing alternative mosquito control methods compared to, or in combination with, SIT and boosted SIT, and would be a valuable tool to guide vector control policies. It could also be coupled with an epidemic model to study the impact of control methods on the basic reproduction rate (R_0) of diseases (e.g. Danbaba and Garba, 2018a; Danbaba and Garba, 2018b; Dumont and Chiroleu, 2010; Hendron and Bonsall, 2016; Mishra et al., 2018).

5. Conclusion

The control of *Ae. albopictus* based on sterile males release techniques in La Reunion Island was modelled for the first time with a weather-driven model validated by entomological field data. The results show that sustainable control of *Ae. albopictus* populations is possible with SIT, but depends strongly on an equilibrium between the relative competitiveness of the sterile males compared to wild ones and the number of males released, as well as on the starting month of the control. It also showed that even low migration can affect population dynamics and should be taken into account, and that it is preferable to carry out pulsed releases with a constant number of males released during the control period. Our study also showed promising results for boosted SIT: it can significantly improve the efficiency of SIT when the sterile males released have a moderate competitiveness, and allows for later (and shorter) control implementation. Our model provides a solid framework for the future development of operational tools to enable control agencies to make informed decisions, particularly for the implementation of integrated management strategies to control arbovirus transmission.

CRediT authorship contribution statement

Marion Haramboure: Methodology, Software, Formal analysis, Writing - original draft, Visualization. **Pierrick Labbé:** Methodology, Validation, Formal analysis, Writing - review & editing, Supervision. **Thierry Baldet:** Validation, Writing - review & editing, Project administration. **David Damiens:** Writing - review & editing, Data curation. **Louis Clément Gouagna:** Writing - review & editing, Data curation. **Jérémy Bouyer:** Conceptualization, Resources, Writing - review & editing, Project administration, Funding acquisition, Data curation. **Annelise Tran:** Methodology, Validation, Formal analysis, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Acknowledgements

The authors would like to thank Pauline Ezanno (Ecole nationale vétérinaire, agroalimentaire et de l'alimentation de Nantes -

Atlantique - ONIRIS) for her help on the sensitivity analysis, J.S. Dehecq (Agence Régionale de Santé - ARS) for the entomological data and David Pleydell (CIRAD-INRA of Montpellier) for fruitful discussions on the boosted SIT.

This work has been funded by the European Research Council under the European Union's Horizon 2020 research and innovation program (grant agreement no. 682387-REVOLINC), in the framework of the One Health Indian Ocean network (www.onehealth-oi.org). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

- Achee, N.L., Grieco, J.P., Vatandoost, H., Seixas, G., Pinto, J., Ching-NG, L., Martins, A.J., Juntarajumnong, W., Corbel, V., Gouagna, C., David, J.-P., Logan, J.G., Orsborne, J., Marois, E., Devine, G.J., Vontas, J., 2019. Alternative strategies for mosquito-borne arbovirus control. *PLOS Neglected Tropical Diseases* 13 (1), e0006822. <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0006822>
- Agusto, F., Gumel, A., Parham, P., 2015. Qualitative assessment of the role of temperature variations on malaria transmission dynamics. *J. Biol. Syst.* 23 (4), 1550030.
- Almeida, L., Duprez, M., Privat, Y., Vauchelet, N. Control strategies on mosquitos population for the fight against arboviruses. [arXiv:1901.05688 \[math\]](https://arxiv.org/abs/1901.05688).
- Anguelov, R., Dumont, Y., Lubuma, J., 2012. Mathematical modeling of sterile insect technology for control of anopheles mosquito. *Computers & Mathematics with Applications* 64 (3), 374–389. <http://www.sciencedirect.com/science/article/pii/S0898122112001939>
- ARS, IVS, 2010. Dengue et chikungunya à la réunion et à mayotte. *Bulletin de veille sanitaire*.
- ARS, Préfecture Réunion, 2019. Epidémie de dengue à la réunion: toutes les communes de l'île sont touchées. Communiqué de presse.
- Balestrino, F., Medici, A., Candini, G., Carrieri, M., MacCagnani, B., Calvitti, M., Maini, S., Bellini, R., 2010. γ Ray Dosimetry and Mating Capacity Studies in the Laboratory on *Aedes albopictus* Males. *Journal of medical entomology*. <http://agris.fao.org/agris-search/search.do?recordID=US201301863383>
- Barbosa, S., Kay, K., Chitnis, N., Hastings, I.M., 2018. Modelling the impact of insecticide-based control interventions on the evolution of insecticide resistance and disease transmission. *Parasites Vectors* 11 (1), 482. <https://doi.org/10.1186/s13071-018-3025-z>.
- Barclay, H.J., 1987. Combining methods of pest control: complementarity of methods and a guiding principle. *Nat. Resour. Model.* 2 (2), 299–323. <https://doi.org/10.1111/j.1939-7445.1987.tb00040.x>.
- Barrera, R., Acevedo, V., Felix, G.E., Hemme, R.R., Vazquez, J., Munoz, J.L., Amador, M., 2017. Impact of Autocidal Gravid Ovitrap on Chikungunya Virus Incidence in *Aedes aegypti* (Diptera: Culicidae) in Areas With and Without Traps. *Journal of Medical Entomology* 54 (2), 387–395. <https://academic.oup.com/jme/article/54/2/387/2952745>
- Bellini, R., Calvitti, M., Medici, A., Carrieri, M., Celli, G., Maini, S., 2007. *Aedes albopictus* in Italy: first results of a pilot trial. *Area-Wide Control of Insect Pests* 505–515.
- Bellini, R., Medici, A., Puggioli, A., Balestrino, F., Carrieri, M., 2013. Pilot field trials with *Aedes albopictus* irradiated sterile males in Italian urban areas. *J. Med. Entomol.* 50

- (2), 317–325.
- Bhatt, S., Gething, P.W., Brady, O.J., Messina, J.P., Farlow, A.W., Moyes, C.L., Drake, J.M., Brownstein, J.S., Hoen, A.G., Sankoh, O., Myers, M.F., George, D.B., Jaenisch, T., Wint, G.R.W., Simmons, C.P., Scott, T.W., Farrar, J.J., Hay, S.I., 2013. The global distribution and burden of dengue. *Nature* 496 (7446), 504–507. <https://www.nature.com/articles/nature12060>
- Bouyer, J., Chandre, F., Gilles, J., Baldet, T., 2016. Alternative vector control methods to manage the Zika virus outbreak: more haste, less speed. *The Lancet Global Health* 4 (6). [http://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(16\)00082-6/abstract](http://www.thelancet.com/journals/langlo/article/PIIS2214-109X(16)00082-6/abstract)
- Bouyer, J., Lefrançois, T., 2014. Boosting the sterile insect technique to control mosquitoes. *Trends in Parasitology* 30 (6), 271–273. <http://www.sciencedirect.com/science/article/pii/S1471492214000567>
- Boyer, S., Foray, C., Dehecq, J.-S., 2014. Spatial and Temporal Heterogeneities of *Aedes albopictus* Density in La Reunion Island: Rise and Weakness of Entomological Indices. *PLOS ONE* 9 (3), e91170. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0091170>
- Caglioti, C., Lalle, E., Carletti, C., Capobianchi, M.R., Bordini, L., 2013. Chikungunya virus infection: an overview. *N. Microbiol.* 36 (3).
- Cai, L., Ai, S., Li, J., 2014. Dynamics of Mosquitoes Populations with Different Strategies for Releasing Sterile Mosquitoes. *Siam Journal on Applied Mathematics* 74 (6), 1786–1809. WOS:000346845900004
- Cailly, P., Tran, A., Balenghien, T., L'Ambert, G., Toty, C., Ezanno, P., 2012. Climate-driven abundance model to assess mosquito control strategies. *Ecological Modelling - ECOL MODEL* 227, 7–17.
- Caputo, B., Ienco, A., Cianci, D., Pombi, M., Petrarca, V., Baseggio, A., Devine, G.J., Torre, A.D., 2012. The "Auto-Dissemination" Approach: A Novel Concept to Fight *Aedes albopictus* in Urban Areas. *PLOS Neglected Tropical Diseases* 6 (8), e1793. <http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0001793>
- Carlson, J., Suchman, E., Buchatsky, L., 2006. Dengoviruses for Control and Genetic Manipulation of Mosquitoes. *Advances in Virus Research*. 68. Elsevier, pp. 361–392. <http://linkinghub.elsevier.com/retrieve/pii/S006535270668010X>
- Carvalho, D.O., McKemey, A.R., Garziera, L., Lacroix, R., Donnelly, C.A., Alphey, L., Malavasi, A., Capurro, M.L., 2015. Suppression of a field population of *Aedes aegypti* in Brazil by sustained release of transgenic male mosquitoes. *PLoS Negl. Trop. Dis.* 9 (7), e0003864.
- Chang Moh, S., To, S., Joshua, N., Duong, S., Michael B., N., 2008. SIX months of *Aedes aegypti* control with a novel controlled-release formulation of pyriproxyfen in domestic water storage containers in CAMBODIA - ProQuest. *Southeast Asian Journal of Tropical Medicine and Public Health* 39 (5), 822. <https://search.proquest.com/openview/541deccd381e3432cb22ad8faffce73f/1?pq-origsite=gscholar&cbl=34824>
- Clements, A., 2000. The biology of mosquitoes volume 1: development. *Nutr. Reprod.* 231–234.
- Connelly, C., Carlson, 2009. *Florida Mosquito Control 2009: The State of the Mission as Defined by Mosquito Controllers, Regulators, and Environmental Managers*. Vero Beach, FL: University of Florida.
- Danbaba, U.A., Garba, S.M., 2018. Analysis of model for the transmission dynamics of zika with sterile insect technique. *Texts Biomath.* 1, 81–99.
- Danbaba, U.A., Garba, S.M., 2018. Modeling the transmission dynamics of zika with sterile insect technique. *Math. Methods Appl. Sci.* 41 (18), 8871–8896.
- Darriet, F., Corbel, V., 2006. Laboratory evaluation of pyriproxyfen and spinosad, alone and in combination, against *Aedes aegypti* larvae. *J. Med. Entomol.* 43 (6), 1190–1194.
- Degener, C.M., Eiras, E., Ázara, T.M.F., Roque, R.A., Rösner, S., Codeço, C.T., Nobre, A.A., Rocha, E.S.O., Kroon, E.G., Ohly, J.J., Geier, M., 2014. Evaluation of the Effectiveness of Mass Trapping With BG-Sentinel Traps for Dengue Vector Control: A Cluster Randomized Controlled Trial in Manaus, Brazil. *Journal of Medical Entomology* 51 (2), 408–420. <https://academic.oup.com/jme/article/51/2/408/882690>
- Delatte, H., Gimonneau, G., Triboire, A., Fontenille, D., 2009. Influence of temperature on immature development, survival, longevity, fecundity, and gonotrophic cycles of *Aedes albopictus*, vector of chikungunya and dengue in the indian ocean. *J. Med. Entomol.* 46 (1), 33–41.
- Delatte, H., Paupy, C., Dehecq, J.S., Thiria, J., Failloux, A.-B., Fontenille, D., 2008. *Aedes albopictus*, vecteur des virus du chikungunya et de la dengue à la Réunion : biologie et contrôle. *Parasite* 15 (1), 3–13. <https://hal-pasteur.archives-ouvertes.fr/pasteur-01696240/document>
- Dell Chism, B., Apperson, C.S., 2003. Horizontal transfer of the insect growth regulator pyriproxyfen to larval microcosms by gravid *Aedes albopictus* and *Ochlerotatus triseriatus* mosquitoes in the laboratory. *Medical and Veterinary Entomology* 17 (2), 211–220. <http://onlinelibrary.wiley.com/doi/10.1046/j.1365-2915.2003.00433.x/abstract>
- Devine, G.J., Perea, E.Z., Killeen, G.F., Stancil, J.D., Clark, S.J., Morrison, A.C., 2009. Using adult mosquitoes to transfer insecticides to *Aedes aegypti* larval habitats., using adult mosquitoes to transfer insecticides to *Aedes aegypti* larval habitats. *Proc. Natl. Acad. Sci. U.S.A.* 106 (28), 11530–11534.
- Dieng, H., Rahman, G.M.S., Abu Hassan, A., Che Salmah, M.R., Satho, T., Miale, F., Boots, M., Sazaly, A., 2012. The effects of simulated rainfall on immature population dynamics of *Aedes albopictus* and female oviposition. *Int. J. Biometeorol.* 56 (1), 113–120.
- Dufourd, C., Dumont, Y., 2012. Modeling and Simulations of Mosquito Dispersal. The Case of *Aedes albopictus*. *BIOMATH* 1 (2), 1209262. <http://biomathforum.org/biomath/index.php/biomath/article/view/j.biomath.2012.09.262>
- Dufourd, C., Dumont, Y., 2013. Impact of environmental factors on mosquito dispersal in the prospect of sterile insect technique control. *Computers & Mathematics with Applications* 66 (9), 1695–1715. <http://www.sciencedirect.com/science/article/pii/S0898122113002307>
- Dumont, Y., Chiroleu, F., 2010. Vector control for the chikungunya disease. *Math. Biosci. Eng.: MBE* 7 (2), 313–345.
- Dunn, D.W., Follett, P.A., 2017. The Sterile Insect Technique (SIT) - an introduction. *Entomologia Experimentalis et Applicata* 164 (3), 151–154. <http://onlinelibrary.wiley.com/doi/10.1111/eea.12619/abstract>
- Dunning, J.B., Stewart, D.J., Danielson, B.J., Noon, B.R., Root, T.L., Lamberson, R.H., Stevens, E.E., 1995. Spatially Explicit Population Models: Current Forms and Future Uses. *Ecological Applications* 5 (1), 3–11. <http://onlinelibrary.wiley.com/doi/10.2307/1942045/abstract>
- Enkerlin, W.R., Ruelas, J.M.G., Pantaleon, R., Litera, C.S., Cortés, A.V., López, J.L.Z., Dávila, D.O., Gerardo, P.M., Villarreal, L.S., Roldán, E.C., López, F.H., Castillo, A.A., Dominguez, D.C., Mora, A.V., Arana, P.R., Barrios, C.C., Midgård, D., Villatoro, C.V., Prera, E.L., Estradé, O.Z., Aldana, R.C., Culajay, J.L., Ramírez, F.R.y., Fernández, P.L., Moreno, G.O., Flores, J.R., Hendrichs, J., 2017. The Moscamed Regional Programme: review of a success story of area-wide sterile insect technique application. *Entomologia Experimentalis et Applicata* 164 (3), 188–203. <https://onlinelibrary.wiley.com/doi/abs/10.1111/eea.12611>
- Esteva, L., Mo Yang, H., 2005. Mathematical model to assess the control of *Aedes aegypti* mosquitoes by the sterile insect technique. *Mathematical Biosciences* 198 (2), 132–147. <http://www.sciencedirect.com/science/article/pii/S0025556405001045>
- Evans, T.P., Bishop, S.R., 2014. A spatial model with pulsed releases to compare strategies for the sterile insect technique applied to the mosquito *Aedes aegypti*. *Mathematical Biosciences* 254 (Supplement C), 6–27. <http://www.sciencedirect.com/science/article/pii/S0025556414001072>
- Ewing, D.A., Cobbold, C.A., Purse, B.V., Nunn, M.A., White, S.M., 2016. Modelling the effect of temperature on the seasonal population dynamics of temperate mosquitoes. *Journal of Theoretical Biology* 400 (Supplement C), 65–79. <http://www.sciencedirect.com/science/article/pii/S0022519316300285>
- Ezanno, P., Aubry-Kientz, M., Arnoux, S., Cailly, P., L'Ambert, G., Belenghien, T., Tran, A., 2015. PREVET. 120. A generic weather-driven model to predict mosquito population dynamics applied to species of Anopheles, Culex and Aedes genera of southern France
- Fister, K.R., McCarthy, M.L., Oppenheimer, S.F., Collins, C., 2013. Optimal control of insects through sterile insect release and habitat modification. *Math. Biosci.* 244 (2), 201–212.
- Flores, H.A., O'Neill, S.L., 2018. Controlling vector-borne diseases by releasing modified mosquitoes. *Nature Reviews Microbiology*. <http://www.nature.com/articles/s41579-018-0025-0>
- Garziera, L., Pedrosa, M.C., de Souza, F.A., Gomez, M., Moreira, M.B., Virginio, J.F., Capurro, M.L., Carvalho, D.O., 2017. Effect of interruption of over-flooding releases of transgenic mosquitoes over wild population of *Aedes aegypti*: two case studies in Brazil. *Entomologia Experimentalis Et Applicata* 164 (3), 327–339. WOS:000413403700015
- Gasper, G., Bellini, R., Malacrida, A.R., Crisanti, A., Dottori, M., Aksoy, S., 2012. A New Threat Looming over the Mediterranean Basin: Emergence of Viral Diseases Transmitted by *Aedes albopictus* Mosquitoes. *PLOS Neglected Tropical Diseases* 6 (9), e1836. <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0001836>
- Gubler, D.J., Clark, G.G., 1996. Community involvement in the control of *Aedes aegypti*. *Acta Tropica* 61 (2), 169–179. <http://www.sciencedirect.com/science/article/pii/S001706X9500103L>
- Harris, A.F., Nimmo, D., McKemey, A.R., Kelly, N., Scaife, S., Donnelly, C.A., Beech, C., Petrie, W.D., Alphey, L., 2011. Field performance of engineered male mosquitoes. *Nature Biotechnology* 29 (11), 1034. <https://doi.org/10.1038/nbt0911>
- Hendron, R.-W.S., Bonsall, M.B., 2016. The interplay of vaccination and vector control on small dengue networks. *Journal of Theoretical Biology* 407, 349–361. <http://linkinghub.elsevier.com/retrieve/pii/S0022519316302181>
- Huang, M., Song, X., Li, J., 2017. Modelling and analysis of impulsive releases of sterile mosquitoes. *Journal of Biological Dynamics* 11 (1), 147–171. WOS:000389042600004
- Invest, J., Lucas, J., 2008. Pyriproxyfen as a mosquito larvicide. *Proc. Sixth Int. Conf. Urban Pests* 239–245.
- Itoh, T., Kawada, H., Abe, A., Eshita, Y., Rongsriyam, Y., Igarashi, A., 1994. Utilization of bloodfed females of *Aedes aegypti* as a vehicle for the transfer of the insect growth regulator pyriproxyfen to larval habitats. *J. Am. Mosq. Control Assoc.* 10 (3), 344–347.
- Knipling, E.F., 1979. The basic principles of insect population suppression and management. The basic principles of insect population suppression and management.(No. 512).
- Kruijff, H.A.M.d., Woodall, J.P., Tang, A.T., 1973. The influence of accumulated rainfall and its pattern on mosquito (Diptera) populations in Brazil. *Bulletin of Entomological Research* 63 (2), 327–333. <https://www.cambridge.org/core/journals/bulletin-of-entomological-research/article/influence-of-accumulated-rainfall-and-its-pattern-on-mosquito-diptera-populations-in-brazil/FC59F425732C586A35BF8CF8CBEBA1C2>
- Lacroix, R., Delatte, H., Hue, T., Reiter, P., 2009. Dispersal and Survival of Male and Female *Aedes albopictus* (Diptera: Culicidae) on Réunion Island. *Journal of Medical Entomology* 46 (5), 1117–1124. <https://bioone.org/journals/Journal-of-Medical-Entomology/volume-46/issue-5/033.046.0519/Dispersal-and-Survival-of-Male-and-Female-Aedes-albopictus-i/10.1603/033.046.0519.full>
- Li, J., Song, B., Wang, X., 2007. An extended discrete Ricker population model with Allee effects. *J. Diff. Equ. Appl.* 13 (4), 309–321. <https://doi.org/10.1080/10236190601079191>
- Li, J., Yuan, Z., 2015. Modelling releases of sterile mosquitoes with different strategies. *J. Biol. Dyn.* 9 (1), 1–14. <https://doi.org/10.1080/17513758.2014.977971>
- Madakacherry, O., Lees, R.S., Gilles, J.R.L., 2014. *Aedes albopictus* (Skuse) males in laboratory and semi-field cages: release ratios and mating competitiveness. *Acta Trop.*

- 132 Suppl, S124–129.
- Mains, J.W., Brelsfoard, C.L., Dobson, S.L., 2015. Male mosquitoes as vehicles for insecticide. *PLoS Negl. Trop. Dis.* 9 (1), e0003406. <https://doi.org/10.1371/journal.pntd.0003406>.
- Maiti, A., Patra, B., Samanta, G.P., 2006. Sterile insect release method as a control measure of insect pests: A mathematical model. *Journal of Applied Mathematics and Computing* 22 (3), 71–86. <https://link.springer.com/article/10.1007/BF02832038>
- Maoz, D., Ward, T., Samuel, M., Müller, P., Runge-Ranzinger, S., Toledo, J., Boyce, R., Velayudhan, R., Horstick, O., 2017. Community effectiveness of pyriproxyfen as a dengue vector control method: A systematic review. *PLOS Neglected Tropical Diseases* 11 (7), e0005651. <http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0005651>
- Mbare, O., Lindsay, S.W., Fillinger, U., 2013. Dose-response tests and semi-field evaluation of lethal and sub-lethal effects of slow release pyriproxyfen granules (sumilarv® 0.5g) for the control of the malaria vectors *Anopheles gambiae sensu lato*. *Malar. J.* 12, 94. <https://doi.org/10.1186/1475-2875-12-94>.
- Mishra, A., Ambrosio, B., Gakkhar, S., Aziz-Alaoui, M.A., 2018. A Network Model for Control of Dengue Epidemic Using Sterile Insect Technique. *Mathematical Biosciences and Engineering* 15 (2), 441–460. WOS:000412001800006
- Multerer, L., Smith, T., Chitnis, N., 2019. Modeling the impact of sterile males on an *Aedes aegypti* population with optimal control. *Mathematical Biosciences* 311, 91–102. <http://www.sciencedirect.com/science/article/pii/S0025556418302505>
- Musso, D., Gubler, D.J., 2016. Zika virus. *Clin. Microbiol. Rev.* 29 (3).
- Météo France, 2019. Pluies annuelles à la réunion. <http://www.meteofrance.re/climat/pluies-annuelles>.
- Oliva, C.F., Jacquet, M., Gilles, J., Lemperiere, G., Maquart, P.-O., Quilici, S., Schooneman, F., Vreysen, M.J.B., Boyer, S., 2012. The Sterile Insect Technique for Controlling Populations of *Aedes albopictus* (Diptera: Culicidae) on Reunion Island: Mating Vigour of Sterilized Males. *PLOS ONE* 7 (11), e49414. <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0049414>
- Oliva, C.F., Maier, M.J., Gilles, J., Jacquet, M., Lemperiere, G., Quilici, S., Vreysen, M.J.B., Schooneman, F., Chadee, D.D., Boyer, S., 2013. Effects of irradiation, presence of females, and sugar supply on the longevity of sterile males *Aedes albopictus* (Skuse) under semi-field conditions on Reunion Island. *Acta Trop.* 125.
- Pachka, H., Annelise, T., Alan, K., Power, T., Patrick, K., Véronique, C., Janusz, P., Ferran, J., 2016. Rift valley fever vector diversity and impact of meteorological and environmental factors on culex pipiens dynamics in the okavango delta, botswana. *Parasites Vectors* 9 (1), 434.
- Patterson, J., Sammon, M., Garg, M., 2016. Dengue, Zika and Chikungunya: Emerging Arboviruses in the New World. *Western Journal of Emergency Medicine* 17 (6), 671–679. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5102589/>
- Paupy, C., Delatte, H., Bagny, L., Corbel, V., Fontenille, D., 2009. *Aedes albopictus*, an arbovirus vector: From the darkness to the light. *Microbes and Infection* 11 (14), 1177–1185. <http://www.sciencedirect.com/science/article/pii/S1286457909001051>
- Pleydell, D.R.J., Bouyer, J., 2019. Biopesticides improve efficiency of the sterile insect technique for controlling mosquito-driven dengue epidemics. *Communications Biology* 2 (1), 201. <https://www.nature.com/articles/s42003-019-0451-1>
- Reiter, P., 1998. *Aedes albopictus* and the world trade in used tires, 1988-1995: the shape of things to come?. *Journal of the American Mosquito Control Association* 14 (1), 83–94. http://archive.org/details/cbarchive_103653_aedesalbopictusandtheworldtrad1998
- Rezza, G., 2012. *Aedes albopictus* and the reemergence of dengue. *BMC Public Health* 12 (1), 72. <https://doi.org/10.1186/1471-2458-12-72>.
- Ritchie, S.A., Long, S., Hart, A., Webb, C.E., Russell, R.C., 2003. An aductalid sticky ovitrap for sampling container-breeding mosquitoes. *J. Am. Mosq. Control Assoc.* 19 (3), 235–242.
- Roche, B., Léger, L., L'Ambert, G., Lacour, G., Foussadier, R., Besnard, G., Barré-Cardi, H., Simard, F., Fontenille, D., 2015. The Spread of *Aedes albopictus* in Metropolitan France: Contribution of Environmental Drivers and Human Activities and Predictions for a Near Future. *PLOS ONE* 10 (5), e0125600. <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0125600>
- Roiz, D., Rosà, R., Arnoldi, D., Rizzoli, A., 2010. Effects of Temperature and Rainfall on the Activity and Dynamics of Host-Seeking *Aedes albopictus* Females in Northern Italy. *Vector-Borne and Zoonotic Diseases* 10 (8), 811–816. <https://www.liebertpub.com/doi/full/10.1089/vbz.2009.0098>
- Romeo, B., Marco, C., Fabrizio, B., Arianna, P., Jeremy, B., 2020. Field performance of irradiated male mosquitoes during release trials in northern Italy. in submission.
- Saltelli, A., Chan, K., Scott, M., 2000. Sensitivity Analysis. Probability and Statistics Series. John and Wiley & Sons, New York.
- Sihuíncha, M., Zamora-Perea, E., Orellana-Ríos, W., Stancil, J.D., Lopez-Sifuentes, V., Vidal-Ore, C., Devine, G.J., 2005. Potential use of pyriproxyfen for control of *Aedes aegypti* (Diptera: Culicidae) in iquitos, Perú | journal of medical entomology. *Vector Control Pest Manage. Resistance Repellents* 42 (4), 620–630.
- Smith, C.E.G., 1956. The history of dengue in tropical Asia and its probable relationship to the mosquito *Aedes aegypti*. *J. Trop. Med. Hygiene* 59 (10), 243–251.
- Snetselaar, J., Andriessen, R., Suer, R.A., Osinga, A.J., Knols, B.G., Farenhorst, M., 2014. Development and evaluation of a novel contamination device that targets multiple life-stages of *Aedes aegypti*. *Parasites Vectors* 7 (1), 200. <https://doi.org/10.1186/1756-3305-7-200>.
- Strugarek, M., Bossin, H., Dumont, Y., 2019. On the use of the sterile insect release technique to reduce or eliminate mosquito populations. *Applied Mathematical Modelling* 68, 443–470. <http://www.sciencedirect.com/science/article/pii/S0307904X18305638>
- Suman, D.S., Farajollahi, A., Healy, S., Williams, G.M., Wang, Y., Schoeler, G., Gaugler, R., 2014. Point-source and area-wide field studies of pyriproxyfen auto-dissemination against urban container-inhabiting mosquitoes. *Acta Tropica* 135, 96–103. <http://www.sciencedirect.com/science/article/pii/S0001706X14001090>
- Tantely, M.L., Tortosa, P., Alout, H., Berticat, C., Berthomieu, A., Rutee, A., Dehecq, J.-S., Makoundou, P., Labbé, P., Pasteur, N., Weill, M., 2010. Insecticide resistance in *Culex pipiens quinquefasciatus* and *Aedes albopictus* mosquitoes from La Réunion Island. *Insect Biochemistry and Molecular Biology* 40 (4), 317–324. <http://www.sciencedirect.com/science/article/pii/S0965174810000342>
- Tapia-Conyer, R., Méndez-Galván, J., Burciaga-Zúñiga, P., 2012. Community participation in the prevention and control of dengue: the patio limpio strategy in Mexico. *Paediatrics and International Child Health* 32 (s1), 10–13. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3381439/>
- Thome, R.C.A., Yang, H.M., Esteve, L., 2010. Optimal control of *Aedes aegypti* mosquitoes by the sterile insect technique and insecticide. *Mathematical Biosciences* 223 (1), 12–23. WOS:000273896400002
- Tran, A., L'Ambert, G., Lacour, G., Benoît, R., Demarchi, M., Cros, M., Cailly, P., Aubry-Kientz, M., Balenghien, T., Ezanno, P., 2013. A Rainfall- and Temperature-Driven Abundance Model for *Aedes albopictus* Populations. *International Journal of Environmental Research and Public Health* 10 (5), 1698–1719. <http://www.mdpi.com/1660-4601/10/5/1698>
- Tran, A., Mangeas, M., Demarchi, M., Roux, E., Degenne, P., Haramboure, M., Le Goff, G., Damiens, D., Gouagna, L.-C., Herbretaveu, V., et al., 2020. Complementarity of empirical and process-based approaches to modelling mosquito population dynamics with *Aedes albopictus* as an example—application to the development of an operational mapping tool of vector populations. *PLoS ONE* 15 (1), e0227407.
- Unlu, I., Suman, D.S., Wang, Y., Klingler, K., Faraji, A., Gaugler, R., 2017. Effectiveness of auto-dissemination stations containing pyriproxyfen in reducing immature *Aedes albopictus* populations. *Parasites & Vectors* 10 (1). <http://parasitesandvectors.biomedcentral.com/articles/10.1186/s13071-017-2034-7>
- Vontas, J., Kiousoulis, E., Pavlidi, N., Morou, E., della Torre, A., Ranson, H., 2012. Insecticide resistance in the major dengue vectors *Aedes albopictus* and *Aedes aegypti*. *Pesticide Biochemistry and Physiology* 104 (2), 126–131. <http://www.sciencedirect.com/science/article/pii/S0048357512000818>
- Vreysen, M.J.B., Saleh, K., Mramba, F., Parker, A., Feldmann, U., Dyck, V.A., Msangi, A., Bouyer, J., 2014. Sterile Insects to Enhance Agricultural Development: The Case of Sustainable Tsetse Eradication on Unguja Island, Zanzibar, Using an Area-Wide Integrated Pest Management Approach. *PLOS Neglected Tropical Diseases* 8 (5), e2857. <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0002857>
- White, S.M., Rohani, P., Sait, S.M., 2010. Modelling pulsed releases for sterile insect techniques: fitness costs of sterile and transgenic males and the effects on mosquito dynamics. *Journal of Applied Ecology* 47 (6), 1329–1339. WOS:000283983200020
- WHO, 2018. Dengue vaccine: WHO position paper - september 2018. *Weekly epidemiological record* (93), 457–476.
- Winch, P., Kendall, C., Gubler, D., 1992. Effectiveness of community participation in vector-borne disease control. *Health Policy and Planning* 7 (4), 342–351. <https://academic.oup.com/heapol/article/7/4/342/632764>
- World Health Organization, 2009. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. WHO. Google-Books-ID: dlc0YSlyGYwC
- World Health Organization, UNICEF, 2017. Global vector control response 2017–2030. <https://apps.who.int/iris/handle/10665/259205>
- Wu, J.-Y., Lun, Z.-R., James, A.A., Chen, X.-G., 2010. Dengue fever in Mainland China. *Am. J. Trop. Med. Hyg.* 83 (3), 664–671. <https://doi.org/10.4269/ajtmh.2010.09-0755>
- Wyss, J.H., 2000. Screw worm eradication in the Americas. *Ann. N. Y. Acad. Sci.* 916 (1), 186–193. <https://doi.org/10.1111/j.1749-6632.2000.tb05289.x>
- Zaim, M., Guillet, P., 2002. Alternative insecticides: an urgent need. *Trends in Parasitology* 18 (4), 161–163. <http://www.sciencedirect.com/science/article/pii/S1471492201022206>
- Zheng, X., Zhang, D., Li, Y., Yang, C., Wu, Y., Liang, X., Liang, Y., Pan, X., Hu, L., Sun, Q., Wang, X., Wei, Y., Zhu, J., Qian, W., Yan, Z., Parker, A.G., Gilles, J.R.L., Bourtzis, K., Bouyer, J., Tang, M., Zheng, B., Yu, J., Liu, J., Zhuang, J., Hu, Z., Zhang, M., Gong, J.-T., Hong, X.-Y., Zhang, Z., Lin, L., Liu, Q., Hu, Z., Wu, Z., Baton, L.A., Hoffmann, A.A., Xi, Z., 2019. Incompatible and sterile insect techniques combined eliminate mosquitoes. *Nature* 572 (7767), 56–61. <https://www.nature.com/articles/s41586-019-1407-9>

Impact de la TIS/BTIS dans un contexte de lutte intégrée en milieu tropical et tempéré

J'ai étudié dans le chapitre II l'impact des deux méthodes de lutte basées sur les lâchers de mâles stériles, la TIS et BTIS sur les populations de moustiques tigres à la Réunion. Dans ce chapitre, j'aborde la généralité du modèle de dynamique des populations ainsi que la modélisation de différentes stratégies de lutttes intégrées dans divers contextes géographiques.

En effet, la dynamique des populations d'*Ae. albopictus* dépend des conditions climatiques. Alors qu'en milieu tropical, elle est continue tout au long de l'année (chapitre II), en milieu tempéré, les oeufs entrent en dormance lors de l'hiver et résistent à la dessiccation jusqu'au printemps. Ce mécanisme aboutit à une dynamique différente des populations de moustiques entre les milieux tropical (ex : La Réunion) et tempéré (ex : France métropolitaine). Aussi, l'enjeu en matière de santé publique en France métropolitaine est de prévenir et de circonscrire le risque de développement de foyers autochtones de cas de dengue suite à l'importation de voyageurs virémiques au cours de la saison favorables aux moustiques vecteurs. C'est pourquoi j'ai choisi d'étendre le modèle développé au chapitre 2 à la ville de Montpellier où *Ae. albopictus* est présent depuis 2011 et où des actions de LAV sont menées par l'EID Méditerranée (Entente Interdépartementale pour la Démoustication). J'ai ainsi pu comparer par la modélisation la dynamique des populations d'*Ae. albopictus* et l'impact de la LAV sur celle-ci dans des climats différents.

Parmi les différentes méthodes de LAV présentées dans l'introduction (sections 2.1 et 2.2), j'ai introduit au modèle de dynamique de population d'*Ae. albopictus* les effets de la destruction mécanique des gîtes sur les populations d'*Ae. albopictus* ainsi que l'impact de méthodes de LAV innovantes (techniques de piégeage massif et d'auto-dissémination). Mon choix s'est basé sur des méthodes actuellement mises en place (destruction mécanique des gîtes) ou sujettes à des essais pilotes à la Réunion ou Montpellier en alternatives aux adulticides.

Cette étude avait pour objectif de répondre aux questions suivantes :

CHAPITRE III. IMPACT DE LA TIS/BTIS DANS UN CONTEXTE DE LUTTE INTÉGRÉE EN MILIEU TROPICAL ET TEMPÉRÉ

- Quel est l'apport de la TIS et BTIS dans des stratégies de lutte intégrée ?
- Quelles sont les méthodes de LAV qui pourraient agir en synergie avec la TIS et BTIS ? Ou à l'inverse celles qui auraient des effets antagonistes, ou qui seraient redondantes lorsqu'elles sont couplées à la TIS et BTIS ?
- Quelles sont les stratégies de lutte les plus adaptées aux milieux tropical et tempéré ?

Article 2 : What is(are) the most effective method(s) to control the tiger mosquito ? Comparing sterile male releases and other methods in temperate and tropical climates

Cette étude a fait l'objet d'un article co-écrit avec une stagiaire de Master 2 que j'ai encadrée (Léa Douchet). Celui-ci a été soumis au journal "Scientific report" :

Douchet, L., Haramboure, M., Baldet, T., L'Ambert, G., Damiens, D., Gouagna, L. C., Bouyer, J., Labbé, P., Tran, A. (2020). What is(are) the most effective method(s) to control the tiger mosquito ? Comparing sterile male releases and other methods in temperate and tropical climates. *Soumis dans Scientific Report.*

Les annexes de l'article sont en annexe du manuscrit (Annexe 4).

What is(are) the most effective method(s) to control the tiger mosquito? Comparing sterile male releases and other methods in temperate and tropical climates

Léa Douchet^{1,2,+}, Marion Haramboure^{1,2,3,4,5,+,*}, Thierry Baldet^{1,2}, Gregory L'Ambert⁶, David Damiens^{7,8}, Louis Clément Gouagna^{7,8}, Jeremy Bouyer^{2,9,10,11}, Pierrick Labbé³, and Annelise Tran^{1,2,4,5}

¹CIRAD, UMR ASTRE, F-97491 Sainte-Clotilde, Reunion, France

²ASTRE, Univ Montpellier, CIRAD, INRAE, Montpellier, France

³ISEM, UMR 5554, CNRS-UM-IRD-EPHE, Université de Montpellier, Montpellier, France

⁴CIRAD, UMR TETIS, F-97491 Sainte-Clotilde, Reunion, France

⁵TETIS, Univ Montpellier, AgroParisTech, CIRAD, CNRS, INRAE, Montpellier, France

⁶Department of Research and Development, EID Méditerranée, Montpellier, France

⁷IRD, UMR MIVEGEC, CNRS-UM-IRD, Reunion, France

⁸IRD / GIP CYROI, Sainte-Clotilde, Reunion, France

⁹CIRAD, UMR ASTRE, F-34398 Montpellier, France

¹⁰Insect Pest Control Laboratory, Joint FAO/IAEA Programme of Nuclear Techniques in Food and Agriculture, A-1400 Vienna, Austria

¹¹CIRAD, UMR ASTRE, F97410, Saint-Pierre, Reunion, France

*marion.haramboure@cirad.fr

+these authors contributed equally to this work

ABSTRACT

Background: The expansion of mosquito species worldwide is creating a powerful network for the spread of arboviruses. In addition to the destruction of breeding sites (prevention) and mass trapping, methods based on the sterile insect technique (SIT), the autodissemination of pyriproxyfen (ADT), and a fusion of elements from both of these known as boosted SIT (BSIT), are being developed to meet the urgent need for effective vector control. However, the comparative potential of these methods has yet to be explored in different environments. This is needed to propose and integrate informed guidelines into sustainable mosquito management plans.

Methods: We extended a weather-dependent model of *Aedes albopictus* population dynamics to assess the effectiveness of these different vector control methods, alone or in combination, in a tropical (Reunion island, southwest Indian Ocean) and a temperate (Montpellier area, southern France) climate.

Results: Our results confirm the potential of SIT in temperate climates when performed early in the year (mid-March). In such a climate, the timing of the vector control action was the key factor in its success. In tropical climates, the potential of the combination of methods becomes interesting. BSIT and the combination of ADT with SIT were twice as effective compared to the use of SIT alone.

Keywords: vector control, mass trapping, breeding site reduction, SIT, boosted SIT, autodissemination, *Aedes albopictus*, dengue, modelling

1 Introduction

Native to Asia¹, the tiger mosquito *Aedes albopictus* (Skuse, 1894) has colonized America, Africa and Europe along with the intensification of globalization²⁻⁴. Its great ecological plasticity, due to specific traits such as its ability to colonize a wide range of larval sites and to feed on a wide variety of hosts, its diapause capacity, and the tolerance of its eggs to desiccation^{5,6}, has enabled this spectacular worldwide migration. The species has become established on every continent, from tropical to temperate regions⁷. A vector of dengue, Chikungunya and Zika viruses, *Ae. albopictus* represents a major threat to human

health^{8–11} and has been involved in numerous epidemics due to these viruses in tropical areas^{12–15}. Although these viruses are not yet established in Europe, their frequent introduction by infected travellers (e.g., Chikungunya in Italy, 2007¹⁶ and 2017¹⁷) increases the risk of outbreaks in regions where *Ae. albopictus* is abundant^{17–20}. As there are no effective vaccines against these vector-borne diseases^{21,22}, vector control remains the cornerstone of disease prevention.

Insecticide spraying and the mechanical destruction of potential breeding sites constitute the classic solutions to control outbreaks²³. However, the behaviour of *Ae. albopictus*, which breeds in multiple cryptic and dispersed sites (tires, beverage cans, plastic items, etc...), hampers the effectiveness of these methods²⁴. They therefore need to be supplemented to achieve sustainable control²⁵.

Mass trapping and the autodissemination technique (ADT) are alternative control methods that are based on the behaviour of female mosquitoes^{25,26}. Mass trapping consists of capturing females with artificial ovipositing sites (or ovitraps)^{27–29} or traps that mimic the presence of a blood-feeding source (Biogents Sentinel, BGS)^{30,31}; the traps also capture males in search of a mate^{32,33}. To overcome the difficulties of conventional insecticide-based methods to reach cryptic habitats, ADT uses the ovipositing behaviour of females to deliver the lethal agent: female mosquitoes are attracted to artificial breeding sites (stations) impregnated with a biocide, which they then transfer to natural breeding sites³⁴. Both methods have shown promising reductions in mosquito populations^{35–37}, but their efficiency relies heavily on the attractiveness and the density of traps and ADT stations^{26,37,38}.

Another alternative for the control of *Aedes* populations is the sterile insect technique (SIT), which relies on the mass-release of males sterilized by ionizing radiation²⁵. As females generally mate only once at the beginning of their lives, those that mate with sterilized males produce non-viable eggs, causing the target population to decline^{25,39,40}. Significant reductions have been achieved in Italy⁴¹ and in China⁴². However, since the processes involved in producing large numbers of sterile males (mass rearing, handling and irradiation) may reduce their sexual performance⁴³, the number of sterile males must be much higher than that of wild males for SIT to be effective, constituting a significant hindrance for large-scale application^{39,40,44–46}. A modified version of SIT known as boosted SIT (BSIT), which combines elements of SIT and ADT, has recently been proposed^{47,48}. Released sterile males are coated with pyriproxyfen (PP), a biocide that inhibits the emergence of pupae^{49,50}. PP can be transferred during mating to females which then, in turn, contaminate their breeding sites. However, BSIT remains in the experimental phase for the time being.

Due to the diversity of approaches, target species ecological contexts and logistical constraints, it is difficult to directly assess in the field the effect of each of these different techniques used alone, and even more so in combination. In such situations, mathematical models are useful tools that can provide insight into the ecological response to different mosquito population management strategies, and can help plan field trials (eg^{51–58}). Several models have been developed to predict and understand the potential effects of SIT on mosquito populations^{56,59–69}, and two recent studies have assessed the potential impact of BSIT. Pleydell *et al.* compared BSIT, SIT, and ADT in a constant environment⁷⁰, while Haramboure *et al.* compared BSIT and SIT in realistic tropical ecological settings using a weather-driven mosquito population dynamics model⁷¹. Both studies concluded that BSIT would require fewer released sterile males, or could tolerate irradiated males with lower competitiveness, compared to SIT. However, to our knowledge, neither study used such models to compare all of the different control methods available, including conventional insecticide-based methods and their combinations.

The objective of the present study was therefore to take advantage of the weather-driven abundance model developed by Haramboure *et al.*⁷¹ to combine and compare different control methods against *Ae. albopictus* in realistic tropical and temperate climates. We extended this model, originally developed for a tropical area (Reunion Island, Indian Ocean), to the specificities (e.g., winter diapause) of a temperate area, Montpellier (France), where *Ae. albopictus* has been established since 2010⁷². It should be noted that cases of Chikungunya transmitted locally by *Ae. albopictus* occurred in this city in 2014⁷³. After controlling the model accuracy on entomological data from an *Ae. albopictus* population without vector control, we performed a global sensitivity analysis to identify the key parameters affecting the impact of SIT and BSIT in temperate versus tropical climates. We also integrated the effect of prevention (i.e., mechanical destruction of potential breeding sites), mass trapping (ovitraps or BGS-traps) and ADT stations on *Ae. albopictus* populations. Simulations were used to assess the effects of these different control methods, independently or in synergy with SIT and BSIT. This model thus provides a comprehensive evaluation of current vector control methods against the tiger mosquito, and can help control agencies plan their mosquito management strategies in different environments.

2 Results

Sterile male releases are the most efficient control methods

The weather-driven abundance model developed by Haramboure *et al.*⁷¹ in the context of the tropical climate of Reunion Island (Indian Ocean), and which already implements SIT and BSIT, was modified to i) adapt it to a temperate climate by taking into account the winter season in Europe, with a diapause phase, and by modifying the values of the parameters to those observed in

a temperate climate⁷⁴, and ii) implement other vector control methods (Figure 1): a) prevention, through the destruction of breeding sites (triangles), b) ovitrap (hollow circles) which capture only females, c) BGS-traps (full circles) which capture all adults, and d) ADT (diamonds) which contaminate the breeding sites (for more details see Methods). We then assessed the effects of the different control methods and their combinations by measuring the induced reduction rate, *i.e.*, the maximum reduction of fertilized females compared to an untreated population, and the resilience, *i.e.*, the time required for the population to recover similar dynamics to that of the untreated one.

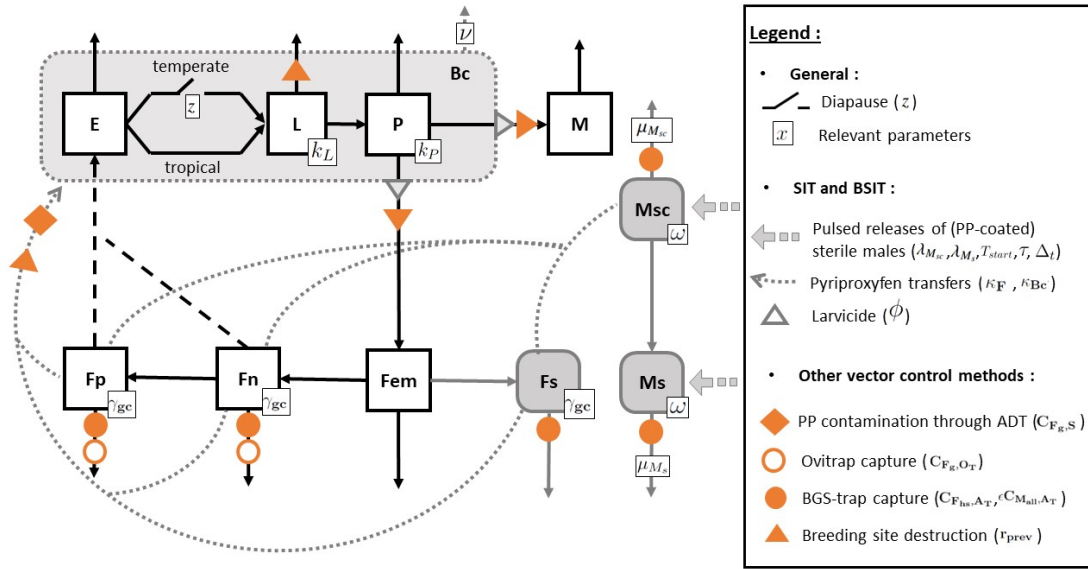


Figure 1. Simplified diagram of the model. The *Aedes albopictus* life cycle is computed in 7 stages: 3 are aquatic stages present in the breeding sites, eggs (E), larvae (L) and pupae (P), 4 are adult aerial stages, males (M), emerging females (F_{em}), nulliparous females (F_n) and parous females (F_p). Black arrows indicate transitions between stages. Diapause only occurs in the temperate climate and depends on the z parameter. Changes resulting from SIT and BSIT are indicated by grey lines and boxes representing sterile males, whether PP-coated (M_{sc}) or not (M_s), sterile females (F_s) and contaminated breeding sites (B_c). The key parameters, in particular those affected by vector control actions, are: k_L and k_P respectively the larval and pupae carrying capacities, γ_{gc} the duration of the gonotrophic cycle, ω the relative competitiveness of sterile males, $\mu_{M_{sc}}$ and μ_{M_s} the mortality of sterile males, respectively PP-coated or not, v the breeding site PP decontamination rate, and ϕ the probability for PP-exposed larvae to survive and pupate. Additional vector control actions were added to the model (orange): mass trapping (full circles for BGS-traps and hollow circles for ovitrap) according to the probability of capture (respectively $C_{F_{hs},BGS}$, $\epsilon C_{M_{all},BGS}$ and C_{F_g,O_T}), prevention (triangles) by reduction of breeding sites (r_{prev}), and PP autodissemination (diamonds for ADT) which depends on females contamination ($C_{F_g,S}$).

Of all the vector control actions tested alone, SIT and BSIT were by far the most effective when used at an optimal time (Figure 2). In the temperate climate (Figure 2, A), SIT provided effective control of the mosquito population with a reduction rate close to 1 and a resilience of up to 3 years when used early in the year (around March). The PP-boost delivered by BSIT provided no additional benefit, except when control started later in the year. The efficacy of both methods was strongly reduced in the tropical climate, although BSIT proved to be more effective than SIT, with a reduction rate of 0.77 vs 0.41, respectively; resilience was also doubled with the use of BSIT compared to SIT (Figure 2, B).

The other vector control methods, *i.e.*, prevention, ovitrap, BGS-traps and ADT, showed very low resilience compared to SIT and BSIT (less than one year in both climates). In the temperate climate, the reduction rate provided by these methods was also much lower than SIT (< 0.35). In the tropical climate, a high reduction rate (0.69), 1.7 times higher than that of SIT, potentially could be achieved by using ADT.

Finally, for both climates, the efficiency of prevention was directly correlated to the effort put into the method, represented by the rate of breeding sites destroyed (Figure 3 and Figure 4). In contrast, the reduction rate obtained using ADT, ovitrap and BGS-traps reached a plateau after which increasing the effort, *i.e.*, adding devices, did not improve the effect. As shown in Figures 3 and 4, the optimal number of devices were 1 ovitrap for 4 houses in a temperate climate and 1 per house in a tropical climate, and more than 2 BGS-traps per house or 1 ADT station for 4 houses in both climates.

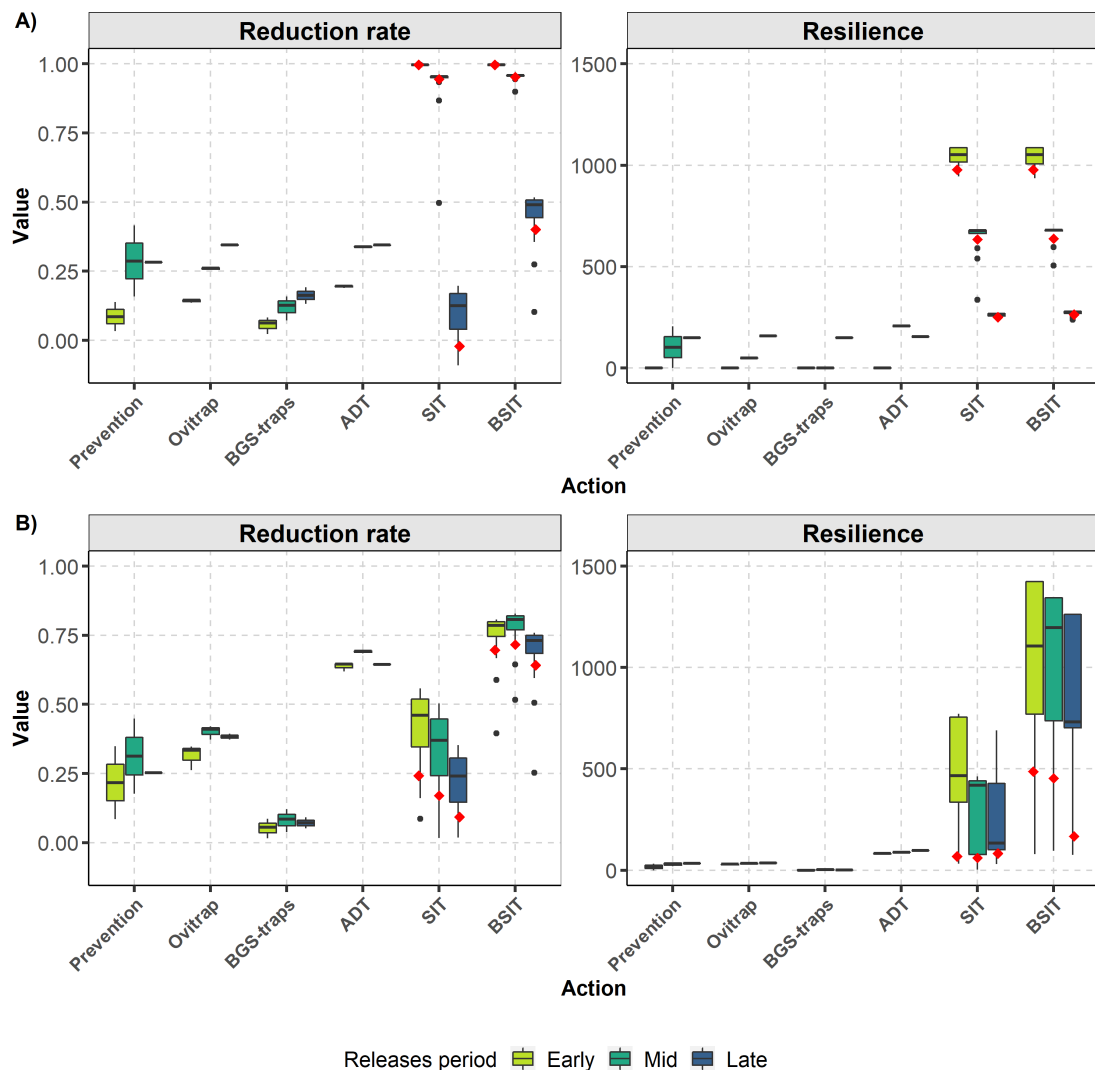


Figure 2. Reduction rate and resilience of vector control actions against *Aedes albopictus* in (A) a temperate climate and (B) a tropical climate. Three periods of actions were tested: early in the year (Early) when the mosquito population is low, midway in the year (Mid) when the population is increasing, and later in the year (Late) when the population reaches its maximum. Resilience is given in number of days. Red diamonds indicate the results of simulations for SIT and BSIT with a reference number of released males (1,000 males/ha).

While other control methods are more efficient in large mosquito populations, sterile male releases should start early in the season

As indicated above, SIT was generally more efficient (higher reduction rates and greater resilience) when it began early in the year (Figure 2), when mosquito abundance is low (supporting results in Appendix A). For subsequent releases, the reduction rate is reduced by a maximum of 10-fold in the temperate climate and by a maximum of 2-fold in the tropical climate (Figure 2). While the effect of BSIT was similar in the temperate climate, the optimal release period for BSIT was later in the tropical climate, when the population starts to increase (Mid), favouring PP transfer between males and females; however, the longest resilience for BSIT was obtained when mosquito abundance was low, *i.e.*, early in the year.

Surprisingly, SIT can cause a temporary increase in the female population when performed during peak abundance in a temperate climate (see Appendix B). This increase is specific to releases of less than 1,100 males per hectare and is not observed in the tropical climate (Figure 2 and Figure 3), where the population is more stable throughout the year and does not show such a high growth rate (Figure 4). This undesirable effect on the population is probably due to a reduction in larval

competition, since it disappears when the density-dependent terms of the model are removed (see Appendix B).

The efficiency of the other vector control actions also depends on their timing (Figure 2). Breeding site destruction and traps/stations were more effective for intermediate to large populations in both climates (reduction rate, Figure 2). The longest resilience was also observed for actions performed later in the year (about five months in the temperate climate), although resilience was much lower (about three weeks) in the tropical climate (resilience, Figure 2).

Vector control actions can be advantageously combined

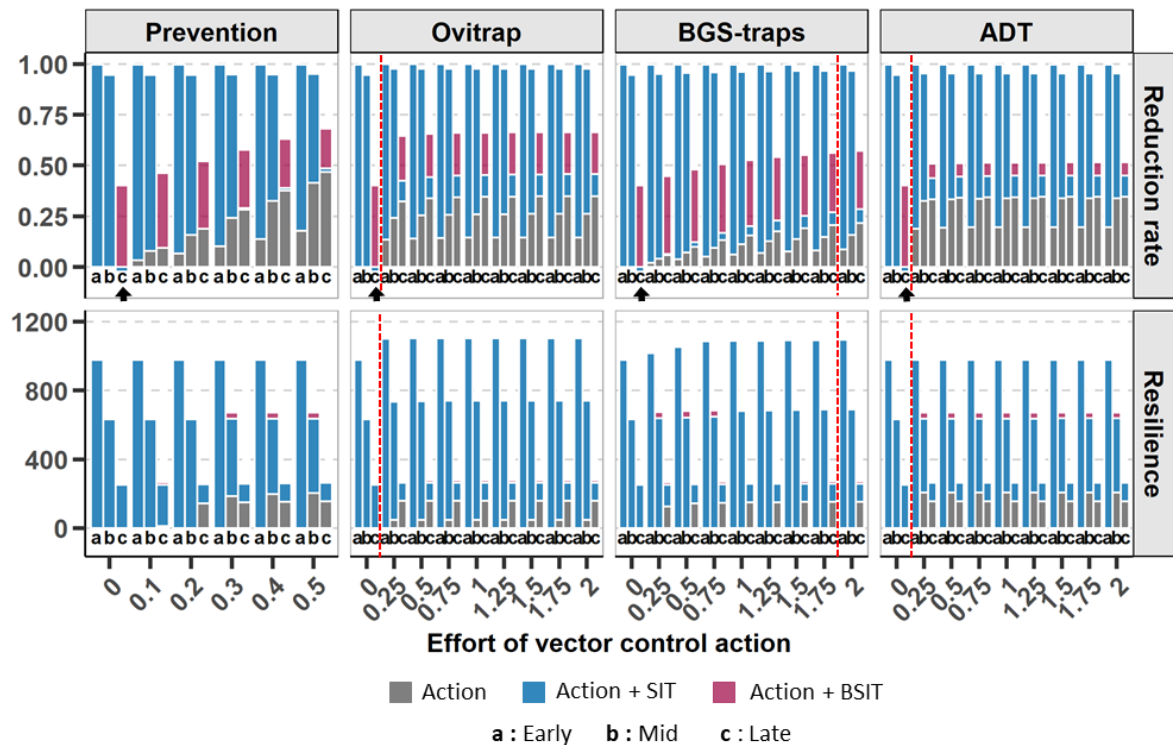


Figure 3. Reduction rate and resilience in the temperate climate for an increasing effort in vector control actions against *Aedes albopictus*. Vector control actions (ovitrap, BGS-traps, ADT and prevention) are represented by grey bars. The benefits added by combining them with 1) SIT (releases of 1,000 males/ha) and 2) BSIT (releases of 1,000 males/ha) are represented by pink and blue bars, respectively. The effort devoted to each control action is indicated, either as a rate of breeding sites destroyed for prevention, or as the number of traps/stations per house for ovitrap, BGS-traps and ADT. Three control periods were tested: early in the year (Early) when the mosquito population is low, midway in the year (Mid) when the population is increasing, and later in the year (Late) when the population reaches its maximum. The red dashed line indicates the number of ovitrap, BGS-traps and ADT stations required to reach the plateau of maximum effect for the action performed alone. The black arrows show the very specific case of the negative reduction rate caused by late releases of SIT without any other vector control action.

By combining SIT or BSIT (releases of 1,000 males/ha, see Methods) with other vector control methods, the observed responses were different and depended on the climate (Figures 3 and 4).

In the temperate climate, the combination of SIT with any other vector control action did not improve the reduction rate produced by SIT alone in the optimal period (*i.e.*, early treatment; Figure 3), although resilience could be extended (+123 days) with the use of traps (BGS-traps, ovitrap) at low density. When the mosquito population was high (late releases), BSIT with prevention or traps (ovitrap, BGS-traps) appeared to be the best combinations: the reduction rate could be increased by 26% with the destruction of 50% of the breeding sites, or with the use of ovitrap (any effort). BSIT and ADT are redundant for breeding site contamination, so that their combination appeared unnecessary. Finally, combining actions prevented the population increase due to the late use of SIT (see above).

In the tropical climate, BSIT was more efficient than SIT alone (Figure 4). The combination of BSIT with prevention or ovitrap could slightly increase the reduction rate (up to 14% with the destruction of 50% of the breeding sites and up to 7%

for 1 ovitrap per house), but BGS-traps did not improve it, and the combination of BSIT and ADT was again of no interest. However, combining BSIT with prevention, ovitrap or BGS-traps early in the season could greatly improve resilience (+270 days) without a significant decrease in the reduction rate. Moreover, this increase in resilience was observed for a small effort on vector control actions: 10% of prevention (i.e., destruction of 10% of the breeding sites), 1 ovitrap, BGS-trap or ADT station for 4 houses. Finally, and interestingly, simulations showed that the combination of SIT with ADT stations produced a higher reduction rate (0.79 ± 0.003) than BSIT used alone (0.71) or in combination (0.76 ± 0.01), with an effort of 1 station per 2 houses (Figure 4).

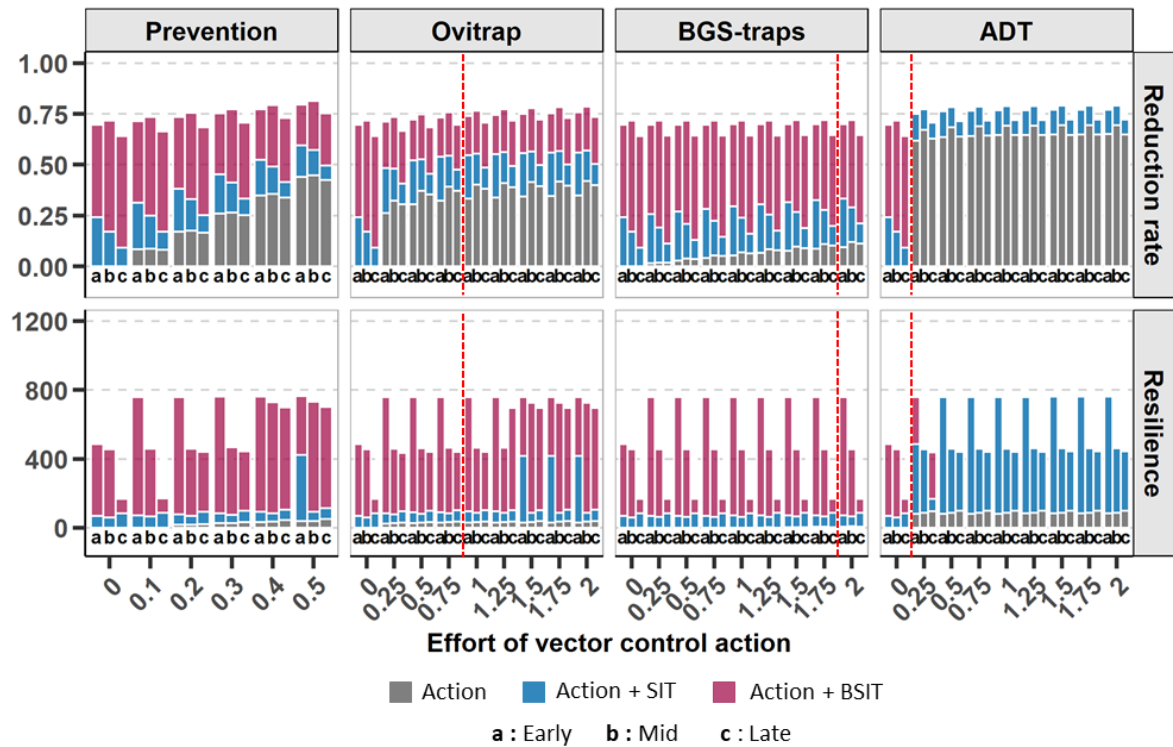


Figure 4. Reduction rate and resilience in the tropical climate for an increasing effort in vector control actions against *Aedes albopictus*. Vector control actions (ovitrap, BGS-traps, ADT and prevention) are represented by grey bars. The benefits added by combining them with 1) SIT (releases of 1,100 males/ha) and 2) BSIT (releases of 1,100 males/ha) are represented by pink and blue bars, respectively. The effort devoted to each control action is indicated, either as a rate of breeding sites destroyed for prevention, or as the number of traps/stations per house for ovitrap, BGS-traps and ADT. Three control periods were tested: early in the year (Early) when the mosquito population is low, midway in the year (Mid) when the population is increasing, or later in the year (Late) when the population reaches its maximum. The red dashed lines indicate the number of ovitrap, BGS-traps or ADT stations required to reach the plateau of maximum effect for the action performed alone.

3 Discussion

Vector control measures are most effective and sustainable when they are fully integrated into a broader mosquito management approach⁷⁵. Integrated mosquito management is not simply a matter of adding together different methods because while some may act synergistically, others may have antagonist effects, or may simply be redundant, wasting money and effort⁷⁵. Moreover, the environment is a critical factor to consider when optimizing mosquito control methods⁶⁰. Our weather-driven mechanistic model, validated on entomological data in a temperate (Appendix C) and a tropical environment⁷¹, thus provides the first estimates of the combined effect of different control methods against the tiger mosquito. The model is based on the release of sterile males (SIT or BSIT) and preventive mechanical destruction of breeding sites, mass trapping (ovitrap or BGS-traps) and autodissemination of biocides (ADT) under different environmental conditions.

Mechanical control methods have similar effects against *Aedes albopictus* in temperate and tropical environments

According to the simulations, mass trapping (using ovitraps or BGS-traps) and prevention are the least effective control methods against *Ae. albopictus* populations, with broadly similar magnitudes in tropical and temperate environments. However, mass trapping and prevention are more efficient in a temperate environment when the population size is high, around mid-summer (*i.e.*, July-August). This is probably due to the fact that adult mosquito densities are reduced to zero during winter (whereas there are always adults in tropical environments); early in the season, the density of the adult population therefore is too low to capture a significant amount of females (Figure 2). A field study nevertheless suggests that mass trapping methods show a significant population reduction only after a prior reduction in mosquito populations⁷⁶. However, no matter when the starting date falls, a critical element in the control of mosquito populations with traps is the involvement of local communities⁷⁶. This is even more important for prevention, because vector control can be constrained when private gardens are difficult to access, hindering the exhaustive treatment of areas⁷⁷.

SIT is the most effective method to control *Aedes albopictus* in a temperate climate

In a temperate climate, SIT is much more effective at the beginning of the season, *i.e.*, just after the end of the diapause of *Ae. albopictus* eggs at the close of winter (Figure 5). As sterile males must compete with their wild competitors, starting the releases when the population is at its lowest increases their probability of mating with a female for a given release rate^{60,67,78}.

However, even later in the season, but before the peak of abundance, the potential efficiency of SIT far exceeds that of other traditional vector control methods, so coupling vector control methods with SIT seems unnecessary in temperate environments when the releases start early enough (Figures 2 and 3). The seasonal reduction in density due to climatic conditions therefore suggests that a large investment in SIT would be more effective than investing in a combination of control methods⁷⁹.

Counter intuitively, however, and as shown in other studies^{60,80,81}, the application of SIT during peak abundance could increase population sizes at the start of the control effort by reducing larval competition (Appendix B). In this worst-case scenario, the integration of another control method with SIT could then be a back-up solution; any method that reduces the mosquito population prior to the application of SIT would indeed increase the effectiveness of SIT^{44,79}.

SIT must be supported with other control methods against *Aedes albopictus* in a tropical environment

In contrast with temperate climate conditions, where only diapausing eggs survive the winter, a tropical climate offers favourable temperatures throughout the year and facilitates the continuous dynamics of all stages of *Ae. albopictus* populations⁷¹. The seasonal reduction in mosquito density is therefore too limited to allow effective population control by SIT alone (Figure 2). In this context, boosting SIT with pyriproxyfen (BSIT) and the combination of SIT with ADT have been shown to be the two most effective combined control methods. The action of pyriproxyfen lasts longer in tropical climates due to the continuous dynamics and more abundant populations of *Ae. albopictus* throughout the year. Moreover, the transmission mechanisms of pyriproxyfen and the skip-oviposition behaviour of females for both methods are more effective with slightly larger mosquito populations (*i.e.*, mid release period, Figure 4), leading to more effective control^{70,71,82}. They therefore also make it possible to delay when control actions are implemented.

Coupling BSIT with prevention or ovitraps does not significantly increase the rate of reduction, but it does double the resilience of control if implemented at an early stage. BGS-traps do not appear to have a significant effect on control, probably because they also capture sterile males, but they also do not interfere with the effectiveness of SIT or BSIT (Figure 4).

Finally, the best combination in tropical environments seems to be SIT + ADT, with the highest reduction rates and the longest resilience time obtained from only 1 station every 4 houses, with the increased effort reaching a plateau of efficiency (Figure 4). However, this plateau is likely to depend on variables such as the density of local populations of *Ae. albopictus* or the type of housing in the intervention area.

Further developments: towards an integrated operational tool

The weather-driven model presented in this study accurately describes the population dynamics of *Ae. albopictus* in different environments. However, the parameters used were chosen from bibliographical and experimental knowledge, and several parameters and processes, in particular for BSIT, remain unquantified. For those cases, we chose conservative assumptions. For example, we neglected the potential direct transmission of pyriproxyfen from males to breeding sites⁸³, as the number of males caught in ovitraps is low compared to females⁸⁴. Such conservative assumptions could lead to an underestimation of the BSIT effect. However, the model could be easily adjusted if more precise measurements are published in the future.

Another potential limitation is that populations are modelled independently, effectively as isolated populations. As the dimensions of the parcels in Montpellier and Reunion Island (more than 5 and 4 ha respectively) are larger than the active flight distance of *Ae. albopictus* (less than 100 m^{85,86}), it seems reasonable to neglect the dispersion of mosquitoes (arrival or departure of individuals). However, a recent pilot trial of transgenic male releases in Brazil showed that it is very difficult to eliminate non-isolated mosquito populations⁸⁷. Indeed, due to their high fertility, a few *Ae. albopictus* females could have a

significant impact when population numbers are low, which could significantly reduce the expected resilience⁷¹. The integration of limited adult migration would therefore be a crucial development to provide more robust predictions.

Despite these limitations, our model can nevertheless be easily used as an operational tool for decision-making, allowing the *in silico* experimentation of various vector control strategies. By computing the life cycle of *Ae. albopictus* in detail, the modelling framework developed is flexible in design, so that any control protocol or integrated strategy, including the sequential implementation of different methods, can be tested easily. A previous version (without any control action implemented) is in fact already routinely used by the services in charge of vector control on Reunion Island to predict *Ae. albopictus* densities over the entire island and identify priority intervention sites⁸⁸. The current version of the model allows early planning, so that vector control stakeholders can test their own control scenarios. This model could easily be set up to run in an area where *Ae. aegypti* is the main vector since the latter shares similar traits with *Ae. albopictus*.

Our model also could be used to test additional vector control strategies. Indeed, in this study, we focused on innovative control methods which are currently in the testing phase on Reunion Island and/or in Montpellier, but other control methods exist^{25,89}. These methods include the Incompatible Insect Technique (IIT) and the Release of Insects carrying a Dominant Lethal (RIDL), which are strategies based on the release of modified males inducing a reduction in the descendants⁴⁰. For example, a combination of SIT + IIT made it possible to suppress *Ae. albopictus* populations from an island in China⁴². Likewise, we focused on the autodissemination of pyriproxyfen, but other biocides could be considered such as densoviruses⁹⁰. The advantage of our mechanistic model is that it details the life cycle of *Ae. albopictus* and thus it is possible to introduce the effects of many strategies.

Furthermore, this model could help public health services as its structure allows it to be coupled with an epidemiological model. Such a combined model would allow one to study not only the impact of vector control methods^{66,68,91-93}, but also the effect of vaccination⁹⁴ or patient isolation⁹⁵ on the basic reproduction rate (R_0) of vector-borne diseases, in particular for dengue. The ensuing dengue propagation modelled could then be compared to observed field data^{96,97}. Finally, thanks to its relatively simple visual displays and its versatility, our model could be used to increase community awareness and involvement. By implementing different actions and visually comparing their impacts, it could help in mobilizing the public, which could have a significant impact on the control of mosquito populations^{98,99}. For example, it could help to increase the use of traps and limit the number of human breeding sites⁷⁶, which would contribute to better management and long-term sustainability of mosquito populations^{100,101}.

4 Methods

Modelling the effects of SIT and BSIT

To model the effects of SIT and BSIT on *Ae. albopictus* populations in a temperate climate, we adapted the model developed for Reunion, a French island with a tropical climate⁷¹. It is a stage-structured continuous model of differential equations composed of 11 compartments (Figure 1; the complete model is given in Appendix D) :

i) Seven compartments describe the mosquito's life cycle: eggs (E), larvae (L), pupae (P), emerging females (F_{em}), nulliparous females (F_n), parous females (F_p) and males (M). The only difference between the tropical and the temperate climate (apart from the parameters values) is that the z parameter has been added in the latter to take into account the winter season. This allows the inclusion of a diapause period during which the transition from eggs to larvae is stopped, similar to the model proposed by Tran *et al.*⁷⁴ (supplementary information is in Appendix D).

ii) The last four compartments model SIT and BSIT control methods: released males, either sterile-only in the case of SIT (M_s), or sterile and pyriproxyfen-coated (PP-coated) in the case of BSIT (M_{sc}), sterile females (F_s) and contaminated breeding sites B_c (Figure 1). Vector control begins at T_{start} and ends after τ days. During this period, λ_X sterile males, with $X = M_{sc}$ or M_s respectively PP-coated or not, are released every Δ_t days (pulsed releases). They die at a rate of μ_{M_s} (or $\mu_{M_{sc}}$ for PP-coated males). The probability that these sterile males, PP-coated or not, mate with emerging females (F_{em}) depends on their relative competitiveness ω and abundance (M_{sc} and M_s respectively) compared to wild males (M), and determines the proportion of F_{em} females that become sterile females (F_s). Moreover, for BSIT specifically:

1. PP-coated sterile males (M_{sc}) transfer some PP to all females they mate with, until their coating disappears after κ_F matings, at which time they become M_s males;
2. PP-contaminated females disseminate the contaminant (PP) in κ_{B_c} breeding sites while laying eggs at each gonotrophic cycle (γ_{gc});
3. in these κ_{B_c} PP-contaminated breeding sites, the larvae have a probability ϕ to survive and pupate, which affects the total pupae emergence rate;
4. PP degrades in these breeding sites, which therefore decontaminate at a rate v .

Environmental conditions have an impact on the population dynamics of *Ae. albopictus* in different parts of the model: *i*) temperature has an impact on the development time of aquatic stages and the mortality of larvae (L), pupae (P) and adult females (F_{em} , F_n , F_p), *ii*) rainfall affects the number of available breeding sites and their carrying capacities (k_L , k_P), and *iii*) heavy rainfall has an impact on the mortality rates of aquatic stages by washing out breeding habitats. Larval and pupal competition was modelled by density-dependent functions⁷⁴. The study area is divided into independent parcels that take into account the spatial heterogeneity of the distribution of breeding sites.

Parameter estimates were based both on expert knowledge and the literature. Parameters values for SIT and BSIT are presented in Table 1; the values of the model life cycle parameters in temperate conditions are presented in Appendix E; see⁷¹ for the life cycle parameters values in tropical conditions. The modelled population dynamics for temperate conditions without any vector control actions have been validated on entomological data (Appendix C).

Modelling the effects of the other control methods

We then extended the model to simulate the effect of several alternative control methods, based on mechanical prevention, ovitraps, adult traps and larvicide autodissemination stations (ADT). For these methods, we assumed that they were applied for a specific period of time at a constant intensity and uniformly throughout the area. After this period, the system returned to its initial state. They were computed independently or in combination with SIT or BSIT (the complete model is given in Appendix D). Parameter estimations were based on both expert knowledge and the literature (Table 1)

Table 1. Parameters values of vector control methods

Parameter	Definition	Value	Range	Reference
T_{start}	Releases starting time	-	1 Jan.- 31 Dec.	current work
τ	Release period length (<i>days</i>)	126	[30 – 180]	41
Δ_t	Time between two releases (<i>days</i>)	7	[5 – 10]	41
$\lambda_{M_s}, \lambda_{M_{sc}}$	Number of sterile males released	1000	[600 – 6000]	41
ω	Sterile male competitiveness	0.23	[0.01 – 0.9]	102, 103
$\mu_{M_s}, \mu_{M_{sc}}$	Sterile male mortality	0.086	[0.065 – 0.18]	70
κ_F	Number of contaminating matings	1	[1 – 8]	current work
κ_{Bc}	Number of contaminating ovipositions	1	[1 – 8]	current work
ν	Duration of larval sites contamination (<i>day</i> ⁻¹)	1/33	[1/100 – 1/5]	70
ϕ	Proportion of larvae surviving PP exposure	0.3	[0.02 – 0.5]	70, 83
r_{prev}	Rate of breeding sites destruction	-	[0 – 0.5]	current work
S_T	ADT stations density (/house)	-	[0 – 2]	104, 105
O_T	Ovitraps density (/house)	-	[0 – 2]	76
BGS	BGS-traps density (/house)	-	[0 – 2]	31, 106
α_g	Trap or station attraction for gravid females	6.984	-	107
α_{hs}	BGS-trap attraction for host -seeking females	0.52	-	108
$\alpha_{M_{all}}$	BGS-trap attraction for males	0.24	-	108
ϵ	Proportion of males landing on feeding sources	0.0244	-	108

Prevention

Prevention, *i.e.*, the mechanical destruction of potential breeding sites, was mathematically implemented in the form of a reduction of the number of available breeding sites, expressed as a percentage of the initial values ($B_{tot}(1 - r_{prev})$), and thus of the carrying capacities ($k_x(1 - r_{prev})$ with $x \in \{L, P\}$) for larvae and pupae, respectively.

BGS-traps

Commonly used BGS-traps capture both females (F_{hs}) and males (M_{all}). Mass trapping control was implemented in the form of an additional mortality rate due to capture, $c_{x,BGS}$, with $x \in \{F_{hs}; M_{all}\}$. We assumed that any adult mosquito entering the trap would die:

1. Females (F_{hs}) are caught when seeking a host, *i.e.*, parous (F) or nulliparous females; their capture rate was thus $\gamma_{gc} c_{F_{hs}, BGS}$ per day. The probability of capture of females ($c_{F_{hs}, BGS}$) was estimated by the relative availability of traps, weighted by their attractiveness for females ($\alpha_{F_{hs}}$), compared to other blood-feeding sources, *i.e.*, the number of humans living in the area N_{tot} (Eq. 1).
2. Males, wild or sterile ($M_{all} = M + M_s + M_{sc}$), are captured while searching for a mate; their daily capture rate depends on the probability that a male will land on the female's blood-feeding source (ϵ) and that this feeding source is in fact a trap ($c_{M_{all}, BGS}$), and is therefore expressed by $\epsilon c_{M_{all}, BGS}$. We conservatively neglected the fact that males could also be trapped when flying near the trap. The probability of males being caught was therefore estimated by the relative

availability of traps, weighted by their attractiveness to males ($\alpha_{M_{all}}$), compared to the number of females on other potential blood-feeding sources, again N_{tot} (Eq. 1).

$$c_{x,BGS} = \frac{\alpha_x BGS}{\alpha_x BGS + N_{tot}} \quad \text{with } x \in \{F_{hs}; M_{all}\} \quad (1)$$

Ovitrap

Gravid females are attracted to ovitraps when they are looking for an ovipositing site. We assumed that only females were caught by the ovitraps (no males) and that any female entering the trap would die with her offspring. This was implemented by adding a specific mortality parameter (c_{F_g, O_T}), equal to the probability of being caught, for nulliparous (F_n) and parous (F_p) females. The probability of females being captured by ovitraps is therefore the ovitraps density (O_T) weighted by the relative attractiveness of ovitraps (α_{F_g, O_T}) among all the available breeding sites, *i.e.*, breeding sites (B_{tot}) or ovitraps (Eq. 2).

$$c_{F_g, O_T} = \frac{\alpha_{F_g} O_T}{B_{tot} + \alpha_{F_g} O_T} \quad (2)$$

As a female can be captured only once per gonotrophic cycle, the ovitrap capture rate is thus $\gamma_{gc} c_{F_g, O_T}$.

Autodissemination (ADT)

Similarly, gravid females may be attracted to ADT stations when looking for an ovipositing site. The main difference is that females entering ADT stations do not die, instead they are coated with PP and contaminate the breeding sites which they visit later. Contamination of gravid females (c_{F_g, S_T}) was described by their probability of entering ADT stations instead of a breeding site: we used the same approach as for ovitraps (Eq. 2), replacing the density of ovitraps O_T by the density of ADT stations S_T . We assumed similar attractiveness for ovitraps and ADT stations, and again that no males were caught.

We modelled the contamination of the breeding sites visited later as for BSIT (see above): at each gonotrophic cycle (γ_{gc}), contaminated females ($c_{F_g, S_T}(F_n + F_p + F_s)$) laying in an uncontaminated laying site (in proportion $\frac{B_{tot} - B_c}{B_{tot}}$) transfer part of their PP-coating to it (κ_{Bc}). The number of newly-contaminated breeding sites thanks to ADT stations is therefore $c_{F_g, S_T}(F_n + F_p + F_s) \kappa_{Bc} \gamma_{gc} \left(\frac{B_{tot} - B_c}{B_{tot}} \right)$.

Initial conditions and simulations

The model was implemented in R (<http://www.rproject.org/>). The numerical solutions were estimated using the implicit Runge–Kutta method from the `DeSolve` package.

At t_0 , the population in each parcel consisted of 10^6 eggs (stage E).

To assess the effect of vector control actions in a tropical climate, simulations using tropical parameter values were performed on four parcels from the North, South, East and West of Reunion Island. Each parcel was associated with the nearest meteorological station to drive the population dynamics. Due to inter-annual weather variations, we worked with the average daily temperature and rainfall recorded from 2012 to 2016 on the island.

The model was also used to identify key parameters affecting the efficiency of SIT and BSIT in a temperate climate (Appendix F), and to assess the effect of vector control actions in a temperate climate. Five years of weather records (2014–2018), daily temperatures and rainfalls, provided by the French meteorological organization, Météo France, were used as inputs. The model was run for *i*) parcels corresponding to five residential areas for which entomological data were available to validate the model (Appendix C), and *ii*) four parcels with the same characteristics (size and carrying capacities) as the parcels on Reunion Island to compare the results in temperate and tropical climates.

Numerical analysis of vector control efficiency

Model outputs

We focused our analyses on two outputs from the model of Haramboure *et al.*⁷¹:

- the **reduction rate** was computed by dividing the abundance of fertilized females during the vector control period by the abundance they would reach at the same time in an untreated population, minus 1 (reduction);
- the **resilience**, *i.e.*, the number of days after the end of the control required for the population abundance to reach a similar level (less than 10% difference) to that of a population without vector control. Resilience was computed on eggs and adult females.

Effectiveness of vector control methods

The effects of ovitraps, ADT stations, BGS-traps and mechanical prevention have been assessed in different scenarios, alone and in combination with either SIT or BSIT. In combination, it was assumed that the two vector control methods were applied simultaneously, during the same time period. To provide realistic scenarios⁴¹ and to reveal potential interactions between the methods, the number of males released in SIT and BSIT was set at 1,000 males per hectare. The resilience and reduction rate were compared to determine whether SIT conferred a net benefit over the other control method alone, and whether BSIT could increase this benefit. The outputs of these two models were computed for different levels of effort in prevention (r_{prev}), and for different densities of trapping devices (BGS, O_T) or ADT stations (S_T) (Table 1).

Finally, three periods of vector control were defined according to the abundance of mosquitoes: *i*) the end of the winter, when the population is lowest; *ii*) the beginning of the summer, when the population begins to increase; and *iii*) the end of the summer, when the population has reached its peak (Table 2). They were tested in independent scenarios, respectively named "Early release", "Mid release" and "Late release". The date of releases for the "Early release" scenario was defined based on the basis of the best release date for SIT and BSIT, computed by an optimization process (see Appendix A).

Table 2. Typical starting date for vector control defined when the mosquito population a) is at its lowest (Early release), b) begins to increase (Mid release) and c) has reached its maximum (Late release).

	Tropical climate				Temperate climate
	North	East	South	West	All
a) Early	6 Aug	5 Aug	4 Sep	23 Oct	24 Mar
b) Mid	8 Dec	1 Nov	9 Dec	24 Dec	20 May
c) Late	21 Jan	29 Jan	13 Feb	5 Feb	17 Jun

Given the wide climatic variations within Reunion Island, the three vector control periods were specific to each zone, North, East, West and South in tropical climates, whereas in temperate climate, a single configuration for each period was applied on all parcels (Tab. 2).

References

- Smith, C. E. G. The History of Dengue in Tropical Asia and its Probable Relationship to the Mosquito *Aedes aegypti*. *J. Trop. Medicine Hyg.* **59**, 243–51 (1956).
- Reiter, P. *Aedes albopictus* and the world trade in used tires, 1988-1995: the shape of things to come?. *J. Am. Mosquito Control. Assoc.* **14**, 83–94 (1998).
- Lounibos, L. P. Invasions by Insect Vectors of Human Disease. *Annu. Rev. Entomol.* **47**, 233–266, DOI: [10.1146/annurev.ento.47.091201.145206](https://doi.org/10.1146/annurev.ento.47.091201.145206) (2002).
- Medley, K. A., Jenkins, D. G. & Hoffman, E. A. Human-aided and natural dispersal drive gene flow across the range of an invasive mosquito. *Mol. Ecol.* **24**, 284–295, DOI: [10.1111/mec.12925](https://doi.org/10.1111/mec.12925) (2015).
- Sota, T. & Mogi, M. Survival time and resistance to desiccation of diapause and non-diapause eggs of temperate *Aedes* (*Stegomyia*) mosquitoes. *Entomol. Exp. et Appl.* **63**, 155–161, DOI: [10.1111/j.1570-7458.1992.tb01570.x](https://doi.org/10.1111/j.1570-7458.1992.tb01570.x) (1992). [_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1570-7458.1992.tb01570.x](https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1570-7458.1992.tb01570.x).
- Poelchau, M. F., Reynolds, J. A., Denlinger, D. L., Elsik, C. G. & Armbruster, P. A. A de novo transcriptome of the Asian tiger mosquito, *Aedes albopictus*, to identify candidate transcripts for diapause preparation. *BMC Genomics* **12**, 619, DOI: [10.1186/1471-2164-12-619](https://doi.org/10.1186/1471-2164-12-619) (2011).
- Bonizzoni, M., Gasperi, G., Chen, X. & James, A. A. The invasive mosquito species *Aedes albopictus*: current knowledge and future perspectives. *Trends Parasitol.* **29**, 460–468, DOI: [10.1016/j.pt.2013.07.003](https://doi.org/10.1016/j.pt.2013.07.003) (2013).
- Paupy, C., Delatte, H., Bagny, L., Corbel, V. & Fontenille, D. *Aedes albopictus*, an arbovirus vector: From the darkness to the light. *Microbes Infect.* **11**, 1177–1185, DOI: [10.1016/j.micinf.2009.05.005](https://doi.org/10.1016/j.micinf.2009.05.005) (2009).
- Wu, J.-Y., Lun, Z.-R., James, A. A. & Chen, X.-G. Dengue Fever in Mainland China. *The Am. J. Trop. Medicine Hyg.* **83**, 664–671, DOI: [10.4269/ajtmh.2010.09-0755](https://doi.org/10.4269/ajtmh.2010.09-0755) (2010).
- Gasperi, G. *et al.* A New Threat Looming over the Mediterranean Basin: Emergence of Viral Diseases Transmitted by *Aedes albopictus* Mosquitoes. *PLOS Neglected Trop. Dis.* **6**, e1836, DOI: [10.1371/journal.pntd.0001836](https://doi.org/10.1371/journal.pntd.0001836) (2012).
- Rezza, G. *Aedes albopictus* and the reemergence of Dengue. *BMC Public Heal.* **12**, 72, DOI: [10.1186/1471-2458-12-72](https://doi.org/10.1186/1471-2458-12-72) (2012).

12. Higgs, S. The 2005-2006 Chikungunya Epidemic in the Indian Ocean. *Vector-Borne Zoonotic Dis.* **6**, 115–116, DOI: [10.1089/vbz.2006.6.115](https://doi.org/10.1089/vbz.2006.6.115) (2006).
13. Ratsitorahina, M. *et al.* Outbreak of Dengue and Chikungunya Fevers, Toamasina, Madagascar, 2006. *Emerg Infect Dis* **14**, 1135–1137, DOI: [10.3201/eid1407.071521](https://doi.org/10.3201/eid1407.071521) (2008).
14. Grard, G. *et al.* Zika Virus in Gabon (Central Africa) – 2007: A New Threat from *Aedes albopictus*? *PLOS Neglected Trop. Dis.* **8**, e2681, DOI: [10.1371/journal.pntd.0002681](https://doi.org/10.1371/journal.pntd.0002681) (2014).
15. Vincent, M. *et al.* From the threat to the large outbreak: dengue on Reunion Island, 2015 to 2018. *Euro Surveill* **24**, DOI: [10.2807/1560-7917.ES.2019.24.47.1900346](https://doi.org/10.2807/1560-7917.ES.2019.24.47.1900346) (2019).
16. Rezza, G. *et al.* Infection with chikungunya virus in Italy: an outbreak in a temperate region. *The Lancet* **370**, 1840–1846, DOI: [10.1016/S0140-6736\(07\)61779-6](https://doi.org/10.1016/S0140-6736(07)61779-6) (2007).
17. Lindh, E. *et al.* The Italian 2017 Outbreak Chikungunya Virus Belongs to an Emerging *Aedes albopictus*-Adapted Virus Cluster Introduced From the Indian Subcontinent. *Open Forum Infect Dis* **6**, DOI: [10.1093/ofid/ofy321](https://doi.org/10.1093/ofid/ofy321) (2018).
18. Ruche, G. L. *et al.* First two autochthonous dengue virus infections in metropolitan France, September 2010. *Eurosurveillance* **15**, 19676, DOI: [10.2807/ese.15.39.19676-en](https://doi.org/10.2807/ese.15.39.19676-en) (2010).
19. Gjenero-Margan, I. *et al.* Autochthonous dengue fever in Croatia, August–September 2010. *Eurosurveillance* **16**, 19805, DOI: [10.2807/ese.16.09.19805-en](https://doi.org/10.2807/ese.16.09.19805-en) (2011).
20. Rovida, F. *et al.* Viremic Dengue virus infections in travellers: Potential for local outbreak in Northern Italy. *J. Clin. Virol.* **50**, 76–79, DOI: [10.1016/j.jcv.2010.09.015](https://doi.org/10.1016/j.jcv.2010.09.015) (2011).
21. WHO. Dengue vaccine: WHO position paper – September 2018. *Wkly. epidemiological record* 457–476 (2018).
22. World Health Organization and others. Dengue and severe dengue. Tech. Rep., World Health Organization. Regional Office for the Eastern Mediterranean (2019).
23. Organization, W. H. *Dengue : Guidelines for Diagnosis, Treatment, Prevention and Control* (WHO, 2009). Google-Books-ID: dlc0YSIyGYwC.
24. Connelly, C. & Carlson. Florida Mosquito Control 2009: The State of the Mission as Defined by Mosquito Controllers, Regulators, and Environmental Managers. *Vero Beach, FL: Univ. Florida.* (2009).
25. Achee, N. L. *et al.* Alternative strategies for mosquito-borne arbovirus control. *PLOS Neglected Trop. Dis.* **13**, e0006822, DOI: [10.1371/journal.pntd.0006822](https://doi.org/10.1371/journal.pntd.0006822) (2019).
26. Faraji, A. & Unlu, I. The Eye of the Tiger, the Thrill of the Fight: Effective Larval and Adult Control Measures Against the Asian Tiger Mosquito, *Aedes albopictus* (Diptera: Culicidae), in North America. *J Med Entomol* **53**, 1029–1047, DOI: [10.1093/jme/tjw096](https://doi.org/10.1093/jme/tjw096) (2016).
27. Mackay, A. J., Amador, M. & Barrera, R. An improved autocidal gravid ovitrap for the control and surveillance of *Aedes aegypti*. *Parasites & Vectors* **6**, 225, DOI: [10.1186/1756-3305-6-225](https://doi.org/10.1186/1756-3305-6-225) (2013).
28. Barrera, R. *et al.* Impact of Autocidal Gravid Ovitrap on Chikungunya Virus Incidence in *Aedes aegypti* (Diptera: Culicidae) in Areas With and Without Traps. *J Med Entomol* **54**, 387–395, DOI: [10.1093/jme/tjw187](https://doi.org/10.1093/jme/tjw187) (2017).
29. Barrera, R., Amador, M., Munoz, J. & Acevedo, V. Integrated vector control of *Aedes aegypti* mosquitoes around target houses. *Parasites & Vectors* **11**, 88, DOI: [10.1186/s13071-017-2596-4](https://doi.org/10.1186/s13071-017-2596-4) (2018).
30. Jawara, M. *et al.* Optimizing Odor-Baited Trap Methods for Collecting Mosquitoes during the Malaria Season in The Gambia. *PLOS ONE* **4**, e8167, DOI: [10.1371/journal.pone.0008167](https://doi.org/10.1371/journal.pone.0008167) (2009).
31. Englbrecht, C., Gordon, S., Venturelli, C., Rose, A. & Geier, M. Evaluation of BG-Sentinel Trap as a Management Tool to Reduce *Aedes albopictus* Nuisance in an Urban Environment in Italy. *moco* **31**, 16–25, DOI: [10.2987/14-6444.1](https://doi.org/10.2987/14-6444.1) (2015).
32. Lacroix, R., Delatte, H., Hue, T., Dehecq, J. S. & Reiter, P. Adaptation of the BG-Sentinel trap to capture male and female *Aedes albopictus* mosquitoes. *Med. Vet. Entomol.* **23**, 160–162, DOI: [10.1111/j.1365-2915.2009.00806.x](https://doi.org/10.1111/j.1365-2915.2009.00806.x) (2009).
33. Suman, D. S. *et al.* Point-source and area-wide field studies of pyriproxyfen autodissemination against urban container-inhabiting mosquitoes. *Acta Trop.* **135**, 96–103, DOI: [10.1016/j.actatropica.2014.03.026](https://doi.org/10.1016/j.actatropica.2014.03.026) (2014).
34. Devine, G. Auto-Dissemination of Pyriproxyfen for the Control of Container-inhabiting Mosquitoes – a Progress Review. *Outlooks on Pest Manag.* **27**, 164–167 (2016).
35. Devine, G. J. *et al.* Using adult mosquitoes to transfer insecticides to *Aedes aegypti* larval habitats., Using adult mosquitoes to transfer insecticides to *Aedes aegypti* larval habitats. *Proc Natl Acad Sci U S A* **106**, 11530, 11530–11534, DOI: [10.1073/pnas.0901369106](https://doi.org/10.1073/pnas.0901369106), [10.1073/pnas.0901369106](https://doi.org/10.1073/pnas.0901369106) (2009).

36. Caputo, B. *et al.* The “Auto-Dissemination” Approach: A Novel Concept to Fight *Aedes albopictus* in Urban Areas. *PLOS Neglected Trop. Dis.* **6**, e1793, DOI: [10.1371/journal.pntd.0001793](https://doi.org/10.1371/journal.pntd.0001793) (2012).
37. Gaugler, R., Suman, D. & Wang, Y. An autodissemination station for the transfer of an insect growth regulator to mosquito oviposition sites. *Med. Vet. Entomol.* **26**, 37–45, DOI: [10.1111/j.1365-2915.2011.00970.x](https://doi.org/10.1111/j.1365-2915.2011.00970.x) (2012).
38. El-Sayed, A. M., Suckling, D. M., Wearing, C. H. & Byers, J. A. Potential of Mass Trapping for Long-Term Pest Management and Eradication of Invasive Species. *J Econ Entomol* **99**, 1550–1564, DOI: [10.1093/jee/99.5.1550](https://doi.org/10.1093/jee/99.5.1550) (2006). Publisher: Oxford Academic.
39. Dunn, D. W. & Follett, P. A. The Sterile Insect Technique (SIT) – an introduction. *Entomol Exp Appl* **164**, 151–154, DOI: [10.1111/eea.12619](https://doi.org/10.1111/eea.12619) (2017).
40. Flores, H. A. & O’Neill, S. L. Controlling vector-borne diseases by releasing modified mosquitoes. *Nat. Rev. Microbiol.* DOI: [10.1038/s41579-018-0025-0](https://doi.org/10.1038/s41579-018-0025-0) (2018).
41. Bellini, R., Medici, A., Puggioli, A., Balestrino, F. & Carrieri, M. Pilot field trials with *Aedes albopictus* irradiated sterile males in Italian urban areas. *J. Med. Entomol.* **50**, 317–325 (2013).
42. Zheng, X. *et al.* Incompatible and sterile insect techniques combined eliminate mosquitoes. *Nature* **572**, 56–61, DOI: [10.1038/s41586-019-1407-9](https://doi.org/10.1038/s41586-019-1407-9) (2019).
43. Bouyer, J. & Vreysen, M. Yes, irradiated sterile male mosquitoes can be sexually competitive! *Trends Parasitol.* (2020). In press.
44. Alphey, L. *et al.* Sterile-Insect Methods for Control of Mosquito-Borne Diseases: An Analysis. *Vector Borne Zoonotic Dis* **10**, 295–311, DOI: [10.1089/vbz.2009.0014](https://doi.org/10.1089/vbz.2009.0014) (2010).
45. Baldacchino, F. *et al.* Control methods against invasive *Aedes* mosquitoes in Europe: a review - Baldacchino - 2015 - Pest Management Science - Wiley Online Library. DOI: [10.1002/ps.4044](https://doi.org/10.1002/ps.4044) (2015).
46. Lees, R., Gilles, J., Hendrichs, J., Vreysen, M. & Bourtzis, K. Back to the future: the sterile insect technique against mosquito disease vectors. *Curr. Opin. Insect Sci.* **10**, 156–162, DOI: [10.1016/j.cois.2015.05.011](https://doi.org/10.1016/j.cois.2015.05.011) (2015).
47. Bouyer, J. & Lefrançois, T. Boosting the sterile insect technique to control mosquitoes. *Trends Parasitol.* **30**, 271–273, DOI: [10.1016/j.pt.2014.04.002](https://doi.org/10.1016/j.pt.2014.04.002) (2014).
48. Bouyer, J., Chandre, F., Gilles, J. & Baldet, T. Alternative vector control methods to manage the Zika virus outbreak: more haste, less speed. *The Lancet Glob. Heal.* **4**, e364, DOI: [10.1016/S2214-109X\(16\)00082-6](https://doi.org/10.1016/S2214-109X(16)00082-6) (2016).
49. Invest, J. & Lucas, J. Pyriproxyfen as a mosquito larvicide. *Proc. Sixth Int. Conf. on Urban Pests* 239–245 (2008).
50. Maoz, D. *et al.* Community effectiveness of pyriproxyfen as a dengue vector control method: A systematic review. *PLOS Neglected Trop. Dis.* **11**, e0005651, DOI: [10.1371/journal.pntd.0005651](https://doi.org/10.1371/journal.pntd.0005651) (2017).
51. White, M. T. *et al.* Modelling the impact of vector control interventions on *Anopheles gambiae* population dynamics. *Parasites Vectors* **4**, 153, DOI: [10.1186/1756-3305-4-153](https://doi.org/10.1186/1756-3305-4-153) (2011).
52. Cailly, P. *et al.* Climate-driven abundance model to assess mosquito control strategies. *Ecol. Model. - ECOL MODEL* **227**, 7–17, DOI: [10.1016/j.ecolmodel.2011.10.027](https://doi.org/10.1016/j.ecolmodel.2011.10.027) (2012).
53. Arifin, S. N., Madey, G. R. & Collins, F. H. Examining the impact of larval source management and insecticide-treated nets using a spatial agent-based model of *Anopheles gambiae* and a landscape generator tool. *Malar J* **12**, 290, DOI: [10.1186/1475-2875-12-290](https://doi.org/10.1186/1475-2875-12-290) (2013).
54. Lee, S. S., Baker, R. E., Gaffney, E. A. & White, S. M. Optimal barrier zones for stopping the invasion of *Aedes aegypti* mosquitoes via transgenic or sterile insect techniques. *Theor Ecol* **6**, 427–442, DOI: [10.1007/s12080-013-0178-4](https://doi.org/10.1007/s12080-013-0178-4) (2013).
55. Jakob, L. & Yan, G. Modeling the Effects of Integrating Larval Habitat Source Reduction and Insecticide Treated Nets for Malaria Control. *PLOS ONE* **4**, e6921, DOI: [10.1371/journal.pone.0006921](https://doi.org/10.1371/journal.pone.0006921) (2009).
56. Almeida, L., Duprez, M., Privat, Y. & Vauchelet, N. Control strategies on mosquitos population for the fight against arboviruses. *arXiv:1901.05688 [math]* (2019). ArXiv: 1901.05688.
57. North, A. R., Burt, A. & Godfray, H. C. J. Modelling the potential of genetic control of malaria mosquitoes at national scale. *BMC Biol.* **17**, 26, DOI: [10.1186/s12915-019-0645-5](https://doi.org/10.1186/s12915-019-0645-5) (2019).
58. Strugarek, M., Bossin, H. & Dumont, Y. On the use of the sterile insect release technique to reduce or eliminate mosquito populations. *Appl. Math. Model.* **68**, 443–470, DOI: [10.1016/j.apm.2018.11.026](https://doi.org/10.1016/j.apm.2018.11.026) (2019).

59. Maiti, A., Patra, B. & Samanta, G. P. Sterile insect release method as a control measure of insect pests: A mathematical model. *J. Appl. Math. Comput.* **22**, 71–86, DOI: [10.1007/BF02832038](https://doi.org/10.1007/BF02832038) (2006).
60. White, S. M., Rohani, P. & Sait, S. M. Modelling pulsed releases for sterile insect techniques: fitness costs of sterile and transgenic males and the effects on mosquito dynamics. *J. Appl. Ecol.* **47**, 1329–1339, DOI: [10.1111/j.1365-2664.2010.01880.x](https://doi.org/10.1111/j.1365-2664.2010.01880.x) (2010). WOS:000283983200020.
61. Dufourd, C. & Dumont, Y. Impact of environmental factors on mosquito dispersal in the prospect of sterile insect technique control. *Comput. & Math. with Appl.* **66**, 1695–1715, DOI: [10.1016/j.camwa.2013.03.024](https://doi.org/10.1016/j.camwa.2013.03.024) (2013).
62. Fister, K. R., McCarthy, M. L., Oppenheimer, S. F. & Collins, C. Optimal control of insects through sterile insect release and habitat modification. *Math. Biosci.* **244**, 201–212, DOI: [10.1016/j.mbs.2013.05.008](https://doi.org/10.1016/j.mbs.2013.05.008) (2013). WOS:000322805400014.
63. Cai, L., Ai, S. & Li, J. Dynamics of Mosquitoes Populations with Different Strategies for Releasing Sterile Mosquitoes. *SIAM J. Appl. Math.* **74**, 1786–1809, DOI: [10.1137/13094102X](https://doi.org/10.1137/13094102X) (2014). WOS:000346845900004.
64. Evans, T. P. & Bishop, S. R. A spatial model with pulsed releases to compare strategies for the sterile insect technique applied to the mosquito *Aedes aegypti*. *Math. Biosci.* **254**, 6–27, DOI: [10.1016/j.mbs.2014.06.001](https://doi.org/10.1016/j.mbs.2014.06.001) (2014).
65. Li, J. & Yuan, Z. Modelling releases of sterile mosquitoes with different strategies. *J. Biol. Dyn.* **9**, 1–14, DOI: [10.1080/17513758.2014.977971](https://doi.org/10.1080/17513758.2014.977971) (2015).
66. Hendron, R.-W. S. & Bonsall, M. B. The interplay of vaccination and vector control on small dengue networks. *J. Theor. Biol.* **407**, 349–361, DOI: [10.1016/j.jtbi.2016.07.034](https://doi.org/10.1016/j.jtbi.2016.07.034) (2016).
67. Huang, M., Song, X. & Li, J. Modelling and analysis of impulsive releases of sterile mosquitoes. *J. Biol. Dyn.* **11**, 147–171, DOI: [10.1080/17513758.2016.1254286](https://doi.org/10.1080/17513758.2016.1254286) (2017). WOS:000389042600004.
68. Mishra, A., Ambrosio, B., Gakkhar, S. & Aziz-Alaoui, M. A. A Network Model for Control of Dengue Epidemic Using Sterile Insect Technique. *Math. Biosci. Eng.* **15**, 441–460, DOI: [10.3934/mbe.2018020](https://doi.org/10.3934/mbe.2018020) (2018). WOS:000412001800006.
69. Multerer, L., Smith, T. & Chitnis, N. Modeling the impact of sterile males on an *Aedes aegypti* population with optimal control. *Math. Biosci.* **311**, 91–102, DOI: [10.1016/j.mbs.2019.03.003](https://doi.org/10.1016/j.mbs.2019.03.003) (2019).
70. Pleydell, D. R. J. & Bouyer, J. Biopesticides improve efficiency of the sterile insect technique for controlling mosquito-driven dengue epidemics. *Commun. Biol.* **2**, 201, DOI: [10.1038/s42003-019-0451-1](https://doi.org/10.1038/s42003-019-0451-1) (2019).
71. Haramboure, M. *et al.* Modelling the control of *Aedes albopictus* mosquitoes based on sterile males release techniques in a tropical environment. *Ecol. Model.* **424**, 109002, DOI: [10.1016/j.ecolmodel.2020.109002](https://doi.org/10.1016/j.ecolmodel.2020.109002) (2020).
72. ANSES. Portail de signalement du moustique tigre.
73. Delisle, E. *et al.* Chikungunya outbreak in Montpellier, France, September to October 2014. *Eurosurveillance* **20**, 21108, DOI: [10.2807/1560-7917.ES2015.20.17.21108](https://doi.org/10.2807/1560-7917.ES2015.20.17.21108) (2015). Publisher: European Centre for Disease Prevention and Control.
74. Tran, A. *et al.* A Rainfall- and Temperature-Driven Abundance Model for *Aedes albopictus* Populations. *Int. J. Environ. Res. Public Heal.* **10**, 1698–1719, DOI: [10.3390/ijerph10051698](https://doi.org/10.3390/ijerph10051698) (2013).
75. Organization, W. H. & others. WHO position statement on integrated vector management. *Wkly. Epidemiol. Rec. Relev. épidémiologique hebdomadaire* **83**, 177–181 (2008).
76. Johnson, B. J., Ritchie, S. A. & Fonseca, D. M. The State of the Art of Lethal Oviposition Trap-Based Mass Interventions for Arboviral Control. *Insects* **8**, 5, DOI: [10.3390/insects8010005](https://doi.org/10.3390/insects8010005) (2017).
77. Delatte, H. *et al.* *Aedes albopictus*, vecteur des virus du chikungunya et de la dengue à la Réunion : biologie et contrôle. *Parasite* **15**, 3 – 13, DOI: [10.1051/parasite/2008151003](https://doi.org/10.1051/parasite/2008151003) (2008).
78. Dufourd, C. & Dumont, Y. Modeling and Simulations of Mosquito Dispersal. The Case of *Aedes albopictus*. *BIOMATH* **1**, 1209262, DOI: [10.11145/j.biomath.2012.09.262](https://doi.org/10.11145/j.biomath.2012.09.262) (2012).
79. Bouyer, J., Yamada, H., Pereira, R., Bourtzis, K. & Vreysen, M. J. B. Phased Conditional Approach for Mosquito Management Using Sterile Insect Technique. *Trends Parasitol.* **36**, 325–336, DOI: [10.1016/j.pt.2020.01.004](https://doi.org/10.1016/j.pt.2020.01.004) (2020). Publisher: Elsevier.
80. McIntire, K. M. & Juliano, S. A. How can mortality increase population size? A test of two mechanistic hypotheses. *Ecology* **99**, 1660–1670, DOI: [10.1002/ecy.2375](https://doi.org/10.1002/ecy.2375) (2018). [_eprint: https://esajournals.onlinelibrary.wiley.com/doi/pdf/10.1002/ecy.2375](https://esajournals.onlinelibrary.wiley.com/doi/pdf/10.1002/ecy.2375).
81. Neale, J. T. & Juliano, S. A. Finding the sweet spot: What levels of larval mortality lead to compensation or overcompensation in adult production? *Ecosphere* **10**, e02855, DOI: [10.1002/ecs2.2855](https://doi.org/10.1002/ecs2.2855) (2019). [_eprint: https://esajournals.onlinelibrary.wiley.com/doi/pdf/10.1002/ecs2.2855](https://esajournals.onlinelibrary.wiley.com/doi/pdf/10.1002/ecs2.2855).

82. Seixas, G. *et al.* An evaluation of efficacy of the auto-dissemination technique as a tool for *Aedes aegypti* control in Madeira, Portugal. *Parasites Vectors* **12**, 202, DOI: [10.1186/s13071-019-3454-3](https://doi.org/10.1186/s13071-019-3454-3) (2019).
83. Mains, J. W., Brelsfoard, C. L. & Dobson, S. L. Male Mosquitoes as Vehicles for Insecticide. *PLOS Neglected Trop. Dis.* **9**, e0003406, DOI: [10.1371/journal.pntd.0003406](https://doi.org/10.1371/journal.pntd.0003406) (2015).
84. Ritchie, S. A., Long, S., Hart, A., Webb, C. E. & Russell, R. C. An adulticidal sticky ovitrap for sampling container-breeding mosquitoes. *J. Am. Mosq. Control. Assoc.* **19**, 235–242 (2003).
85. Lacroix, R., Delatte, H., Hue, T. & Reiter, P. Dispersal and Survival of Male and Female *Aedes albopictus* (Diptera: Culicidae) on Réunion Island. *ment* **46**, 1117–1124, DOI: [10.1603/033.046.0519](https://doi.org/10.1603/033.046.0519) (2009).
86. Marini, F., Caputo, B., Pombi, M., Tarsitani, G. & Torre, A. D. Study of *Aedes albopictus* dispersal in Rome, Italy, using sticky traps in mark–release–recapture experiments. *Med. Vet. Entomol.* **24**, 361–368, DOI: [10.1111/j.1365-2915.2010.00898.x](https://doi.org/10.1111/j.1365-2915.2010.00898.x) (2010).
87. Garziera, L. *et al.* Effect of interruption of over-flooding releases of transgenic mosquitoes over wild population of *Aedes aegypti*: two case studies in Brazil. *Entomol. Exp. Appl.* **164**, 327–339, DOI: [10.1111/eea.12618](https://doi.org/10.1111/eea.12618) (2017). WOS:000413403700015.
88. Tran, A. *et al.* Complementarity of empirical and process-based approaches to modelling mosquito population dynamics with *Aedes albopictus* as an example—Application to the development of an operational mapping tool of vector populations. *PLOS ONE* **15**, e0227407, DOI: [10.1371/journal.pone.0227407](https://doi.org/10.1371/journal.pone.0227407) (2020).
89. Baldacchino, F. *et al.* An integrated pest control strategy against the Asian tiger mosquito in northern Italy: a case study. *Pest Manag. Sci.* **73**, 87–93, DOI: [10.1002/ps.4417](https://doi.org/10.1002/ps.4417) (2017). [_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1002/ps.4417](https://onlinelibrary.wiley.com/doi/pdf/10.1002/ps.4417).
90. Perrin, A. *et al.* Mosquito densovirus: the revival of a biological control agent against urban *Aedes* vectors of arboviruses. *bioRxiv* 2020.04.23.055830, DOI: [10.1101/2020.04.23.055830](https://doi.org/10.1101/2020.04.23.055830) (2020). Publisher: Cold Spring Harbor Laboratory Section: New Results.
91. BURATTINI, M. N. *et al.* Modelling the control strategies against dengue in Singapore. *Epidemiol Infect* **136**, 309–319, DOI: [10.1017/S0950268807008667](https://doi.org/10.1017/S0950268807008667) (2008).
92. Yang, H. M. & Ferreira, C. P. Assessing the effects of vector control on dengue transmission. *Appl. Math. Comput.* **198**, 401–413, DOI: [10.1016/j.amc.2007.08.046](https://doi.org/10.1016/j.amc.2007.08.046) (2008).
93. Dumont, Y. & Chiroleu, F. Vector control for the Chikungunya disease. *Math Biosci Eng* **7**, 313–345 (2010).
94. Hladish, T. J. *et al.* Designing effective control of dengue with combined interventions. *Proc. Natl. Acad. Sci.* **117**, 3319–3325 (2020). Publisher: National Acad Sciences.
95. Tang, B. *et al.* The effectiveness of quarantine and isolation determine the trend of the COVID-19 epidemics in the final phase of the current outbreak in China. *Int. J. Infect. Dis.* **95**, 288–293, DOI: [10.1016/j.ijid.2020.03.018](https://doi.org/10.1016/j.ijid.2020.03.018) (2020).
96. Jr, R. C. R. *et al.* Estimating the impact of city-wide *Aedes aegypti* population control: An observational study in Iquitos, Peru. *PLOS Neglected Trop. Dis.* **13**, e0007255, DOI: [10.1371/journal.pntd.0007255](https://doi.org/10.1371/journal.pntd.0007255) (2019). Publisher: Public Library of Science.
97. Wahid, I. *et al.* Integrated vector management with additional pre-transmission season thermal fogging is associated with a reduction in dengue incidence in Makassar, Indonesia: Results of an 8-year observational study. *PLOS Neglected Trop. Dis.* **13**, e0007606, DOI: [10.1371/journal.pntd.0007606](https://doi.org/10.1371/journal.pntd.0007606) (2019). Publisher: Public Library of Science.
98. Castro, M. *et al.* A community empowerment strategy embedded in a routine dengue vector control programme: A cluster randomised controlled trial. *Trans R Soc Trop Med Hyg* **106**, 315–321, DOI: [10.1016/j.trstmh.2012.01.013](https://doi.org/10.1016/j.trstmh.2012.01.013) (2012).
99. Andersson, N. *et al.* Evidence based community mobilization for dengue prevention in Nicaragua and Mexico (Camino Verde, the Green Way): cluster randomized controlled trial. *BMJ* **351**, h3267, DOI: [10.1136/bmj.h3267](https://doi.org/10.1136/bmj.h3267) (2015).
100. Gubler, D. J. & Clark, G. G. Community involvement in the control of *Aedes aegypti*. *Acta Trop.* **61**, 169–179, DOI: [10.1016/0001-706X\(95\)00103-L](https://doi.org/10.1016/0001-706X(95)00103-L) (1996).
101. Baly, A. *et al.* Cost effectiveness of *Aedes aegypti* control programmes: participatory versus vertical. *Trans R Soc Trop Med Hyg* **101**, 578–586, DOI: [10.1016/j.trstmh.2007.01.002](https://doi.org/10.1016/j.trstmh.2007.01.002) (2007). Publisher: Oxford Academic.
102. Oliva, C. F. *et al.* The Sterile Insect Technique for Controlling Populations of *Aedes albopictus* (Diptera: Culicidae) on Reunion Island: Mating Vigour of Sterilized Males. *PLOS ONE* **7**, e49414, DOI: [10.1371/journal.pone.0049414](https://doi.org/10.1371/journal.pone.0049414) (2012).

103. Madakacherry, O., Lees, R. S. & Gilles, J. R. L. *Aedes albopictus* (Skuse) males in laboratory and semi-field cages: release ratios and mating competitiveness. *Acta Trop.* **132 Suppl**, S124–129, DOI: [10.1016/j.actatropica.2013.11.020](https://doi.org/10.1016/j.actatropica.2013.11.020) (2014).
104. Abad-Franch, F., Zamora-Perea, E., Ferraz, G., Padilla-Torres, S. D. & Luz, S. L. B. Mosquito-Disseminated Pyriproxyfen Yields High Breeding-Site Coverage and Boosts Juvenile Mosquito Mortality at the Neighborhood Scale. *PLoS Negl Trop Dis* **9**, DOI: [10.1371/journal.pntd.0003702](https://doi.org/10.1371/journal.pntd.0003702) (2015).
105. Unlu, I. *et al.* Large-Scale Operational Pyriproxyfen Autodissemination Deployment to Suppress the Immature Asian Tiger Mosquito (Diptera: Culicidae) Populations. *J Med Entomol* 1–11, DOI: [10.1093/jme/tjaa011](https://doi.org/10.1093/jme/tjaa011) (2020).
106. Degener, C. M. *et al.* Mass trapping with MosquiTRAPs does not reduce *Aedes aegypti* abundance. *Memórias do Instituto Oswaldo Cruz* **110**, 517–527, DOI: [10.1590/0074-02760140374](https://doi.org/10.1590/0074-02760140374) (2015). Publisher: Fundação Oswaldo Cruz.
107. Boubidi, S. C. Surveillance et contrôle du moustique tigre, *Aedes albopictus* (Skuse, 1894) à Nice, sud de la France. (2016).
108. Kröckel, U., Rose, A., Eiras, Á. E. & Geier, M. NEW TOOLS FOR SURVEILLANCE OF ADULT YELLOW FEVER MOSQUITOES: COMPARISON OF TRAP CATCHES WITH HUMAN LANDING RATES IN AN URBAN ENVIRONMENT. *moco* **22**, 229–238, DOI: [10.2987/8756-971X\(2006\)22\[229:NTFSOA\]2.0.CO;2](https://doi.org/10.2987/8756-971X(2006)22[229:NTFSOA]2.0.CO;2) (2006).
109. Bossard, M., Feranec, J., Otahel, J. & others. CORINE land cover technical guide: Addendum 2000. (2000). Publisher: European Environment Agency Copenhagen.
110. Delatte, H., Gimonneau, G., Triboire, A. & Fontenille, D. Influence of temperature on immature development, survival, longevity, fecundity, and gonotrophic cycles of *Aedes albopictus*, vector of chikungunya and dengue in the Indian Ocean. *J. Med. Entomol.* **46**, 33–41 (2009).
111. Lacour, G. *et al.* *Aedes albopictus* (Skuse, 1894)(Diptera: Culicidae) in France: gonotrophic cycle, fecundity and longevity. In *Proceedings of the International Conference “Emerging Vector-borne Diseases in a Changing European Environment”, Montpellier, France*, 10–12 (2010).
112. Lacour, G. *et al.* Winter is coming: diapause phenology, wing shape and size seasonality of a temperate population of *Aedes albopictus* (Diptera: Culicidae). In *Proceedings of the 18th European Society of Vector Ecology Conference, Montpellier, France*, 8–11 (2012).
113. Morris, M. D. Factorial Sampling Plans for Preliminary Computational Experiments. *Technometrics* **33**, 161–174, DOI: [10.1080/00401706.1991.10484804](https://doi.org/10.1080/00401706.1991.10484804) (1991).

Acknowledgements

This work was funded by the European Research Council under the European Union’s Horizon 2020 research and innovation program (grant agreement no. 682387—REVOLINC), in the framework of the One Health Indian Ocean network (www.onehealth-oi.org). Entomological data from Montpellier were collected in the framework of AUTODIS project (research collaboration agreement no. 18C07). The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Author contributions statement

L.D. and M.H. developed the models and analyzed the results, supervised by T.B., P.L. and A.T. G.L. provided the entomological data from Montpellier. All authors reviewed the manuscript.

Modélisation de l'épidémie de dengue de 2018 à La Réunion

Les chapitres II et III mettent en évidence l'impact de la LAV basée sur des techniques alternatives aux adulticides. Ces études se sont focalisées sur le développement d'un modèle de dynamique des populations d'*Ae. albopictus* à la Réunion. Or, l'objectif initial de ces méthodes de LAV est de prévenir l'émergence de nouvelles épidémies (chapitre I section 2.1).

Dans ce chapitre, l'objectif principal était donc de modéliser l'épidémie de dengue à La Réunion. Pour cela, le modèle de dynamique des population de moustiques a été couplé à un modèle de transmission de la dengue. J'ai choisi de modéliser la transmission du virus dengue à une échelle plus large que le modèle de dynamique des populations, en lien avec les données que j'avais pour construire et valider le modèle. En effet, le modèle épidémiologique a été développé à l'échelle de zones infra-communales assez larges définies par l'INSEE (appelées "IRIS" dans l'article IV), alors que le modèle de dynamique des populations avait été développé à une échelle plus fine, celle des zones ALIZES (chapitre II).

Un second objectif fut d'identifier par une approche statistique les facteurs explicatifs des différences entre les prédictions du modèle et le nombre de cas confirmés de dengue. En effet, le modèle de transmission ne s'ajustait pas aux données sur l'ensemble des zones IRIS de l'île. En définitive, l'étude met en évidence l'impact des actions de LAV menées par l'ARS sur l'épidémie de dengue en 2018.

L'étude présentée dans ce chapitre est une étude préliminaire. Des analyses supplémentaires doivent être réalisées. En particulier, une analyse de sensibilité devrait être réalisée pour identifier les paramètres qui influencent le plus la transmission de la dengue et pour lesquels il est important d'avoir une estimation précise. A terme, l'objectif sera de modéliser l'impact des différentes méthodes de LAV sur la transmission de la dengue à la Réunion.

Article 3 : Modelling the dengue outbreak from La Réunion Island in 2018

Cette partie fait l'objet d'un article en cours de rédaction. Comme explicité dans le paragraphe précédent, des simulations supplémentaires doivent être réalisées afin de rendre cet article publiable. Les annexes de l'article sont en annexe du manuscrit (Annexe 5).

Modelling the dengue outbreak from La Réunion Island in 2018

Marion Haramboure^{1,2,3,4,5,+,*}, Pierrick Labbé³, Thierry Baldet^{1,2}, Hélène Thébault¹⁰, Louis Clément Gouagna^{6,7}, Jeremy Bouyer^{8,2,9}, and Annelise Tran^{1,2,4,5}

¹CIRAD, UMR ASTRE, F-97491 Sainte-Clotilde, Reunion, France

²ASTRE, Univ Montpellier, CIRAD, INRA, Montpellier, France

³ISEM, UMR 5554, CNRS-UM-IRD-EPHE, Université de Montpellier, Montpellier, France

⁴CIRAD, UMR TETIS, F-97491 Sainte-Clotilde, Reunion, France

⁵TETIS, Univ Montpellier, AgroParisTech, CIRAD, CNRS, IRSTEA, Montpellier, France

⁶IRD, UMR MIVEGEC, CNRS-UM-IRD, Reunion, France

⁷IRD / GIP CYROI, Sainte-Clotilde, Reunion, France

⁸CIRAD, UMR ASTRE, F-34398 Montpellier, France

⁹Insect Pest Control Laboratory, Joint FAO/IAEA Programme of Nuclear Techniques in Food and Agriculture, A-1400 Vienna, Austria

¹⁰Agence Régionale de Santé, Sainte-Clotilde, Reunion, France

*marion.haramboure@cirad.fr

+these authors contributed equally to this work

ABSTRACT

Dengue is the most prevalent arboviral infection transmitted by mosquitoes of the genus *Aedes*. Mosquito populations are driven by temperature and precipitation which gives them a seasonal dynamic. Understanding how environmental conditions affect epidemic dynamics is critical to understand the dengue transmission. Here, we developed a virus transmission model applied at La Reunion Island where an unprecedented dengue outbreak occur since 2018. A weather-dependent model of *Aedes albopictus* was coupled with a Susceptible-Exposed-Infected-Recovered (SEIR) compartmental model. The model of *Aedes albopictus* was spatialized at the scale of operational mosquitoes control sectors while the epidemiological model was spatialized at a larger scale, according to our data. We used the cumulative numbers of dengue cases in 2018 to evaluate the model goodness-of-fit. The model correctly predicted the number of dengue cases in 58% of the island, but it overestimates the number of cases in rest of La Reunion. Statistical analysis indicate an impact of vector control methods on the transmission of dengue. Thus, the heterogeneous control strategies and the microclimate in at La Reunion lead to important fluctuations in mosquito density and modify the transmission dynamics of dengue. In addition, the results highlight an impact of modelling scale. The proposed model can be easily extend to understand the impact of different control method to prevent the transmission of dengue fever in La Reunion.

Keywords: dengue, epidemiological model, Aedes albopictus, control vector, spatial scale

1 Introduction

Vector-borne diseases account for 17% of infectious diseases¹. Among these, dengue is the most prevalent viral infection, affecting around 390 million people per year² and which morbidity increased from 2.2 million in 2010 to 3.2 million in 2015³. Dengue is caused by a virus of the Flaviviridae family and there are four serotypes of the virus that cause dengue (DENV-1, DENV-2, DENV-3 and DENV-4) and transmitted by mosquitoes of the genus *Aedes*⁴. Recovery from infection is believed to provide lifelong immunity against that serotype. However, cross-immunity to the other serotypes after recovery is only partial, and temporary. Subsequent infections (secondary infection) by other serotypes increase the risk of developing severe dengue³. Dengue outbreaks occur when the virus is circulating among a human population with a large fraction of susceptible individuals, and are usually preceded by a localized growth of vector abundance⁵. To date, no specific antiviral treatment exist against the disease⁴. A vaccine is currently licensed, but the World Health Organization (WHO) recommends its utilization only in countries where epidemiological data indicate a high burden of disease⁶. Thus, mosquito control remains the main tool to prevent and limit dengue transmission⁴.

Aedes aegypti has long been considered the most efficient vector for dengue viruses. Although less competent, *Ae. albopictus*

was however the sole or main vector of dengue epidemics in Hawaii⁷, in the Indian Ocean⁸, in central Africa⁹ and southern China⁹. The control of urban *Aedes* relies essentially on the mechanical or chemical suppression of breeding sites and on adulticide sprays around reported dengue cases¹⁰. In particular, it was demonstrated that the reduction of breeding sites is the most efficient method for controlling *Ae. albopictus*^{11,12}. However, as *Ae. albopictus* breeds in multiple cryptic and dispersed sites (tires, beverage cans, plastic items, etc...), these methods are difficult to implement and maintain, because they require a strong community involvement¹³. Moreover, the difficulty of accessing private gardens does not allow an exhaustive treatment of the target areas¹⁴. For these reasons, dengue transmission can persist in highly-populated places, despite significant efforts in vector control¹⁵.

In La Reunion, an island in the Western Indian Ocean, a major dengue outbreak occurred in 2004¹⁶, followed by a larger chikungunya (another arbovirus) outbreak in 2005-2006¹⁷. Since then, health education, surveillance and *Ae. albopictus* control strategies have become a major public health priority. Despite an active vector control program, a new dengue outbreak started in 2018 in the island⁸. The measures adopted to stop the transmission have been further strengthened, but the outbreak persisted in 2019 and 2020. Understanding the factors impacting the transmission of dengue in La Reunion Island is therefore needed to optimize vector control accordingly.

Mathematical models are crucial tools to understand and to predict the dynamics of disease transmission¹⁸⁻²⁰, and to *a priori* predict²¹ or to *a posteriori* evaluate^{2,22} the impacts of vector control on disease spread. The model of malaria transmission developed by Ross-Macdonald provided the classical theoretical framework for many modelling mosquito-borne diseases²³. One major compartment is however usually neglected, if not forgotten, in these models, *i.e.* the vector dynamics, which largely depends on the weather conditions. Mosquito populations are driven by both temperature and rainfall. It is important to take into account these two factors to better understand the dynamics of dengue transmission. Moreover, its models are applied to a global scales. But at local scale, both the seasonality of the mosquito population and the role of control strategies can induce a large variation in mosquito abundance. Specifically, seasonal dynamics of mosquito density follow the fluctuation of local climate conditions, with peak abundance in the summer¹⁹. We propose to study the transmission dynamics of dengue on a local scale integrating the impact of temperatures and precipitation on the dynamics of mosquito populations.

In the last couple of years, we have developed weather-driven abundance models for La Reunion Island, to predict the abundance of mosquito populations²⁴ and to assess the impact of the control methods on *Ae. albopictus* dynamics²⁵. The aim of the present study was to couple these *Ae. albopictus* dynamics models with an epidemiological model of dengue virus transmission between hosts and vectors, to predict its seasonal spread in La Reunion Island. We then compared the model outputs with dengue cases data reported in 2018, using statistical analyses to assess its performances and to understand the discrepancies between model predictions and observations, considering factors related to seasonality, spatial scale and vector control.

2 Methods

2.1 Study area

La Reunion Island is a French department in the South-West of the Indian Ocean. The island covers an area of 2,500 km² for a population of about 860,000 inhabitants, and a mean population density of 340 inhabitants per km². The population is located mostly (>50%) on the coast, where the density can triple to more than 1,000 inhabitants per km²²⁶. La Reunion Island is characterized by a humid sub-tropical climate with two seasons: the "austral summer" with hot temperature and heavy precipitations (November–April) and the "austral winter" with mild temperatures, lower precipitations (May–October). The temperature decreases progressively from the coast to the central mountains. However, the imposing relief of the island (the maximum altitude is 3,700 metres) creates a wide range of microclimates.

In 1977-1978, the island was affected by an outbreak of dengue fever, caused by dengue virus serotype 2 (DENV-2)²⁷, which affected 30 to 35% of the population²⁸. Subsequently, autochthonous dengue cases were regularly identified, with foci of transmission of limited size, in the West and the South of the island (REFS: Vincent 2019). But since 2017, a new dengue outbreak affects the island: only 97 cases were declared in 2017, but the viral circulation intensified to 25,139 cases of dengue fever reported from January 2018 to February 2020. While only DENV-2 was detected in 2017 and 2018, serotype 1 was also detected in 2019, and an indigenous circulation of serotype 3 in the East and North of the island was identified in 2020²⁹.

Ae. albopictus is the only vector involved in dengue epidemics in Reunion Island. It is omnipresent in urban areas up to an altitude of 1200m³⁰.

2.2 Environmental Data

We used entomological, epidemiological and weather data organized on different spatial scales (Fig. 1):

1. the ALIZES areas ("Actions de Lutte Intégrée sur Zone et d'Education Sanitaire"; $n = 1203$) are operational sectors defined by the vector control service of the Regional Health Agency (ARS). They correspond to units of inhabited areas

at the scale of which prevention, surveillance and control interventions are co-organized. Their surfaces vary from 3 to 340 ha, to include on average 238 households. Specifically, information on the number of breeding sites is collected on a regular basis by the vector control services for each ALIZES area²⁴.

2. The IRIS areas ("Ilots Regroupés pour l'Information Statistique"; $n = 293$) are defined by the French Institute for Statistics and Economics Surveys (INSEE: "Institut National de la Statistique et des Etudes Economiques") and correspond to the most detailed population census areas in Reunion Island in 2016. Their surfaces vary from 9 to 8312 ha, so that an IRIS area can cover several ALIZES areas (Fig. 1). For each IRIS area, the following information was collected: the size of the human population (INSEE, <https://www.data.gouv.fr/fr/>), the number of confirmed cases of dengue fever reported from January to December 2018 and their date of occurrence (source: Regional Health Agency), and the dates of the vector control interventions performed by the vector control service (*i.e.* suppression of breeding sites, peri-residential adulticide treatment during day and space spraying during night, around isolated confirmed cases and in emerging sources of contamination) during the year 2018.
3. Daily temperature (minimum and maximum) and rainfall were recorded from 2017 to 2018 by the meteorological service "Meteo France" via a network of weather stations covering all urban areas of Reunion Island (Fig. 1).

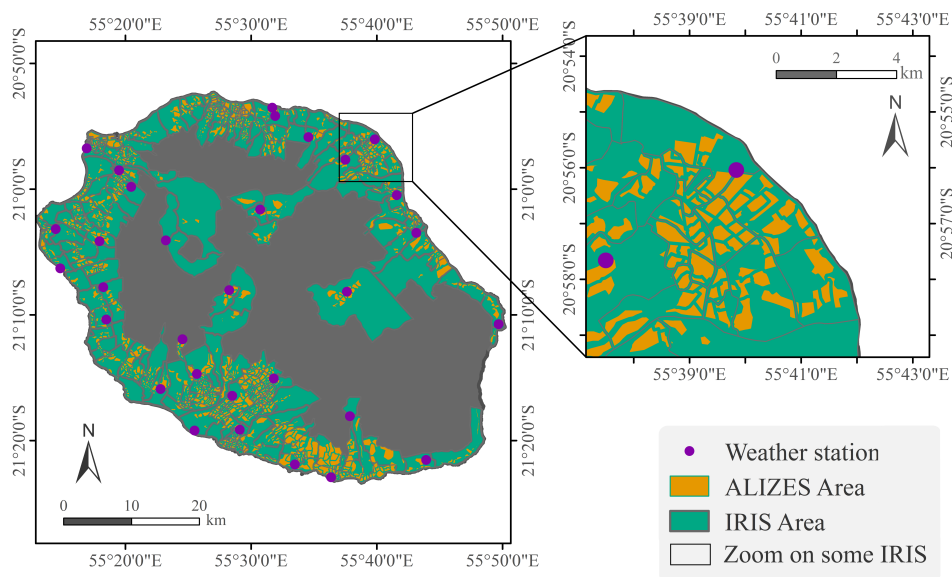


Figure 1. Study area. On the left, map of La Réunion Island with the delineation of the IRIS (green) and ALIZES (orange) areas, weather stations being represented by purple dots. A zoom on the right shows that IRIS areas can encompass and overlap several ALIZES areas.

2.3 Dengue transmission model

We developed a model of dengue virus transmission in Reunion Island associating two sub-models: an entomological model running at ALIZES level, and an epidemiological model running at IRIS level. The abundance of *Ae. albopictus* female mosquitoes simulated by the entomological model at ALIZES level is aggregated at IRIS level to be used as input in the epidemiological model (Fig. 2).

2.3.1 Entomological model

Ae. albopictus abundance is computed using a mechanistic model developed for La Reunion Island by Haramboure *et al.*²⁵. It consists in three aquatic stages (eggs E , larvae L and pupae P), and four aerial stages (males M , emerging females F_{em} , nulliparous F_n and parous F_p females). Larvae and pupae compete for food and space in breeding sites. These competitions are modeled using density-dependant functions.

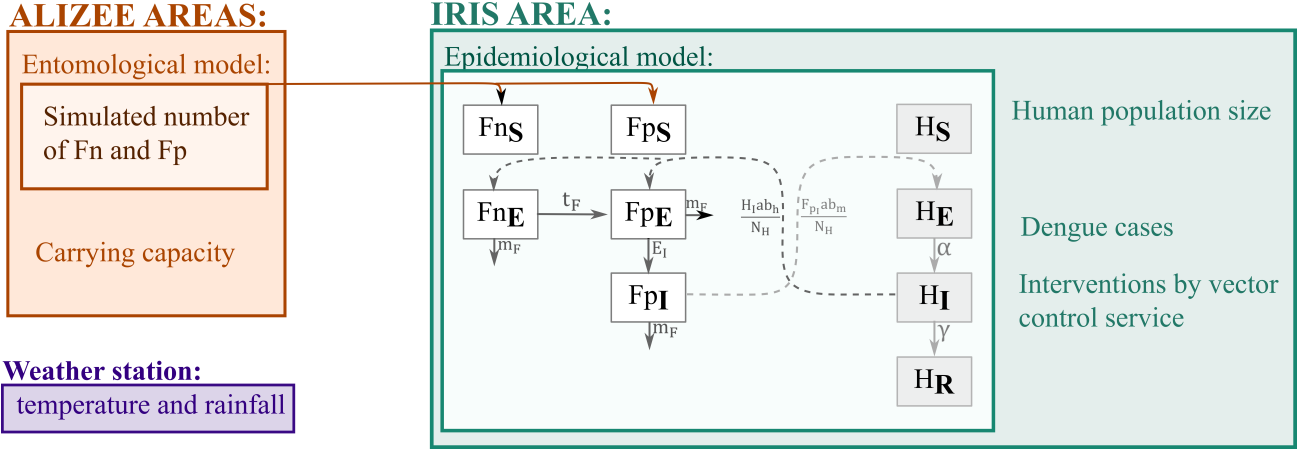


Figure 2. Data and sub-models organization according to ALIZES and IRIS scales. The green and orange squares correspond to the data and sub-models organized at IRIS and ALIZES scales, respectively. The diagram represents the epidemiological model, the corresponding diagram for the entomological model can be found in Haramboure *et al.*²⁵. The orange arrows correspond to the sums of females predicted by the entomological model in all ALIZES areas included into one IRIS area, which will be then computed in the epidemiological model.

The model includes the impact of temperature and rainfall on the mosquitoes' life cycle. Temperature impacts the development time of aquatic stages and the mortality of larvae, pupae and adults. The rainfall affects the carrying-capacities, estimated for each ALIZES area from field observations²⁴. Moreover, heavy rainfalls increase the mortality rates of aquatic stages by flooding the breeding sites.

Full details of the model and its validation against entomological field data can be found in Haramboure *et al.*²⁵.

2.3.2 Epidemiological model

We used a classical SEI-SEIR epidemiological model. The vector population is represented by SEI equations (eq. 1). The nulliparous females (F_n) were divided into two epidemiological stages for dengue transmission, Susceptible (S) and Exposed (E), while parous females (F_p) could also become Infectious (I) (see below). The host population is represented by SEIR equations (eq. 2): human hosts (H) are subdivided into four compartments, Susceptible (S), Exposed (E), Infectious (I), and the additional Recovered (R) compartment, due to potential immunity acquisition (Appendix 2). The SEI-SEIR systems of equations thus are:

$$\begin{cases} \frac{dF_{nS}}{dt} = \sum_{A \cap I} F_n - F_{nS} \frac{H_I a b_h}{N_H} \\ \frac{dF_{nE}}{dt} = F_{nS} \frac{H_I a b_h}{N_H} - F_{nE} (m_F + f_F) \\ \frac{dF_{pS}}{dt} = \sum_{A \cap I} F_p - F_{pS} \frac{H_I a b_h}{N_H} \\ \frac{dF_{pE}}{dt} = F_{pS} \frac{H_I a b_h}{N_H} + f_F F_{nE} - F_{pE} (m_F + e_i) \\ \frac{dF_{pI}}{dt} = e_i F_{pE} - F_{pI} m_F \end{cases} \quad (1)$$

$$\begin{cases} \frac{dH_S}{dt} = -H_S \frac{F_{pI} a b_m}{N_H} \\ \frac{dH_E}{dt} = H_S \frac{F_{pI} a b_m}{N_H} - \alpha H_E \\ \frac{dH_I}{dt} = \alpha H_E - \gamma H_I \\ \frac{dH_R}{dt} = \gamma H_I \end{cases} \quad (2)$$

Latin letters denote weather-driven functions, the Greek letters are constant parameters. Epidemiological parameters and functions were estimated from literature (Table 1).

On the vector side (eq. 1), we make the assumption that the quantity of susceptible females (F_{n_S} and F_{p_S}) at the IRIS scale is much larger than that of exposed (F_{n_E} and F_{p_E}) and infectious females (F_{p_I}) (Appendix A). Thus, the quantity of susceptible nulliparous (F_{n_S}) and parous (F_{p_S}) mosquito females in a given IRIS area (I) is approximated, respectively, to the sum of nulliparous (F_n) and parous (F_p) females estimated by the entomological model in the ALIZES areas (A) overlapping that IRIS area (I): $\sum_{A \cap I} F_n$ and $\sum_{A \cap I} F_p$. The dynamics of exposed (F_{n_E} and F_{p_E}) and infectious (F_{p_I}) mosquito females is modeled as follows: nulliparous females become parous at a transition rate noted (f_F). Nulliparous and parous females die at a natural death rate m_F . Susceptible females (F_{n_S} and F_{p_S}) become infected at a rate $\frac{H_I a b_h}{N_H}$, with a the daily mosquito biting rate, b_h the probability of virus transmission from host to vector, and $\frac{H_I}{N_H}$ the probability for susceptible females (F_{n_S}) to meet infected humans (H_I) among the entire human population ($N_H = H_S + H_E + H_I + H_R$). Then, infected but not infectious mosquito females (F_{n_E} and F_{p_E}) become parous infectious females (F_{p_I}) after a latent period, defined by the temperature-dependent function (ei_p). The model does not include an infectious stage for nulliparous females, as we considered that the extrinsic incubation period ($1/ei_p$) is longer than the duration of the nulliparous stage ($1/f_F$): the fastest extrinsic incubation period is 8 days at $36^\circ C$ (REF), while the transition from nulliparous to parous lasts from 2 days to 3.5 days³¹.

On the host side (eq. 2), the number of susceptible humans (H_S) becoming infected (H_E) by infectious mosquito females (F_{p_I}) is expressed as $\frac{H_S F_{p_I} a b_m}{N_H}$, where a is the daily mosquito biting rate, b_m is the probability of transmission from vector to host, and $\frac{F_{p_I} H_S}{N_H}$ is the probability for parous infectious females (F_{p_I}) to meet susceptible humans (H_S) in the entire human population (N_H). After a latency, defined by the parameter α , exposed humans (H_E) become infectious (H_I). They recover (H_R), at a rate γ . The human population was supposed constant, thus human birth and mortality were ignored in this model.

Table 1. Parameters values and functions of the epidemiological model. *The letter T corresponds to the daily temperature.*

Notation	Definition	Value	Ref
$1/\alpha$	Intrinsic incubation period of dengue (day)	7	32
γ	Recovery rate (day^{-1})	$1/7$	32
a	Average daily biting rate	$\begin{cases} 0.0043T + 0.0943, & \text{if } 21^\circ C \leq T \leq 32^\circ C. \\ 0, & \text{otherwise.} \end{cases}$	33
b_m	Probability of transmission from vector to host	$\begin{cases} 0.001044T(T - 12.286)\sqrt{32.461 - T}, & \text{if } 12.3^\circ C \leq T \leq 32.5^\circ C. \\ 0, & \text{otherwise.} \end{cases}$	34
b_h	Probability of transmission from hosts to vectors	$\begin{cases} 0.0729T - 0.9037, & \text{if } 12.4^\circ C \leq T \leq 26^\circ C. \\ 1, & \text{if } 26.6^\circ C \leq T \leq 32.5^\circ C. \\ 0, & \text{otherwise.} \end{cases}$	34
$1/ei_p$	Extrinsic incubation period of dengue (day)	$\begin{cases} 4e^{5.15 - 0.123T}, & \text{if } 12^\circ C \leq T \leq 36^\circ C. \\ 0, & \text{otherwise.} \end{cases}$	33
m_F	Mosquito female natural mortality rate (day^{-1})	$0.025 + 0.0003e^{(0.1745(T-10))}$	31
f_F	Transition rate from nulliparous to parous females (day^{-1})	$\begin{cases} 0.2 + \frac{(T-10)}{77}, & \text{if } T > 10^\circ C. \\ 0, & \text{otherwise.} \end{cases}$	25

2.4 Initialization and simulations

The entomological and epidemiological models were implemented in R (<http://www.rproject.org/>). Numerical solutions were estimated using the explicit Runge–Kutta numerical scheme. They were run over one year, corresponding to the year 2018, after a starting period of one year, corresponding to the year 2017. At $t = 0$, the *Ae. albopictus* population in each ALIZES area was composed of 1000 eggs (E) and the human population in each IRIS area was assumed to be fully susceptible to the virus. An infected human (H_I) was introduced in each IRIS at the respective date of the first case reported in 2018.

The temperatures recorded from 2017 to 2018 were an input common to both models, while precipitation data were used only in the entomological model (Fig. 2). Each ALIZES and IRIS area was associated with the nearest weather station. Due to the large size of the IRIS areas, it was possible that there were several weather stations within a unique IRIS area. In such cases,

we took the daily average of the temperatures and of the precipitations recorded by all the corresponding weather stations.

2.5 Statistical analysis

For each IRIS area, the total numbers of infected (H_I) and recovered (H_R) hosts predicted by the model were compared with the corresponding cumulative numbers of observed dengue cases in 2018. The model goodness-of-fit was evaluated as the sum of the differences between the simulated and the observed data (DifSimObs).

We defined 5 explanatory variables in order to understand differences between model predictions and observed data at IRIS level. Two variables related to the data scales were considered: i) the size of the IRIS area (in ha) (ISize) and ii) the variance in the sizes of the mosquito populations in the ALIZES areas comprised in the IRIS area (VarMosquito). Two variables were related to vector control interventions with i) the response time after the appearance of the first dengue case (in days) (TimeAction), and ii) the ratio of the number of dengue cases over the number of interventions (RatioAction). The fifth variable corresponded to the month of appearance of the first dengue case in each IRIS (values ranging from 1 to 12) (MonthCase).

The structures of the 293 IRIS areas were compared using a principal component analysis (PCA) on differences between the simulated and the observed data, with the package “ade4”³⁵. We excluded from the following analyses 24 IRIS where no dengue case was reported in 2018.

We then used a Generalized Linear Model (GLM) to explore the effects of the 5 explanatory variables on differences between the simulated and the observed data (DifSimObs). The GLM was thus:

$$DifSimObs = ISize + VarMosquito + TimeAction + RatioAction + MonthCase + \varepsilon \quad (3)$$

Due to data over-dispersion, we assumed a negative binomial distribution for the residuals ε ³⁶. Moreover, correlations between explanatory variables were first assessed using Spearman test, and interactions between significantly correlated variables were included in the GLM. The model was simplified as follows: significance of the different terms was tested, starting from the interaction terms, using likelihood ratio tests (LRT) corrected for overdispersion^{37,38}, as described by³⁹; non-significant terms ($P > 0.05$) were removed.

3 Results

3.1 The model accurately predicts the number of dengue cases in a majority of IRIS areas

The outputs of the epidemiological model were compared to the number of dengue cases reported in 2018 (Fig.4) for the 269 infected IRIS areas (Appendix 3). In 55% of them (n=148), the model correctly predicted the number of dengue cases (e.g. Fig.4 A and B), *i.e.* with a difference on average $10 (\pm 3)$ cases between the number of predicted and observed cases (from 0 to 36 additional cases). Conversely, the model overestimated this number in 40% of the IRIS areas (n=107), with on average 61 (± 3) more cases predicted (max 100 additional cases), and underestimated it in only 5% of the areas (n=13), with on average 17 (± 4) less cases predicted (max 53 cases not predicted) (e.g. Fig.4 C and D). The large majority (85%) of the areas where the model overestimated the number of dengue cases were located in the South or in the West of the island. Moreover, all the areas where the model underestimated the number of dengue cases were located in the Western part of the island.

3.2 No clear characteristics of the IRIS areas unequivocally explain the discrepancies, although they are probably linked to vector control interventions

To better understand the causes of the discrepancies between predictions and observations, we first performed a Principal Component Analysis (PCA) to identify groups of IRIS areas and links between explanatory variables (Figure 5). The PCA explains 48.8% the total inertia with 27.5% on axis 1 and 21.3% of axis 2. Axis 1 is linked to the variance between mosquito population sizes within an ALIZES area (VarMosquito), the date of appearance of the first dengue case and (MonthCase) and the ratio of the number of dengue cases over the number of interventions (RatioAction). Axis 2 is linked to the size of the IRIS area (ISize) and the response time after the appearance of the first dengue case (TimeAction). However, most variability was found between IRIS areas, whether the model accurately predicted the number of dengue cases or not, so that no particular characteristics unequivocally explain the discrepancies.

Using a GLM (model AIC= 271.3, parameter of dispersion = 0.85), we found that the differences between simulated and observed data (DifSimObs) resulted from vector control interventions, as they significantly decreased in IRIS areas where the first dengue case appeared later in the year (MonthCase, -1.14 ± 0.08 , $Z = -14.2$, $p < 2e^{-16}$) or where the number of interventions remained limited relatively to the number of cases observed (RatioAction, $b = 2.7 \pm 0.1$, $Z = 2.2$, $p = 0.02$). Similarly the differences between simulated and observed data significantly increased with the variable VarMosquito ($1.5e^{-06} \pm 2e^{-07}$, $Z = 8.5$, $p < 2e^{-16}$), suggesting an effect of the technical discrepancies between IRIS and ALIZES scales. Although significant correlations were found between the ISize and VarMosquito variables ($R_s(267) = 0.15$, $p < 0.02$) and between MonthCase and RatioAction

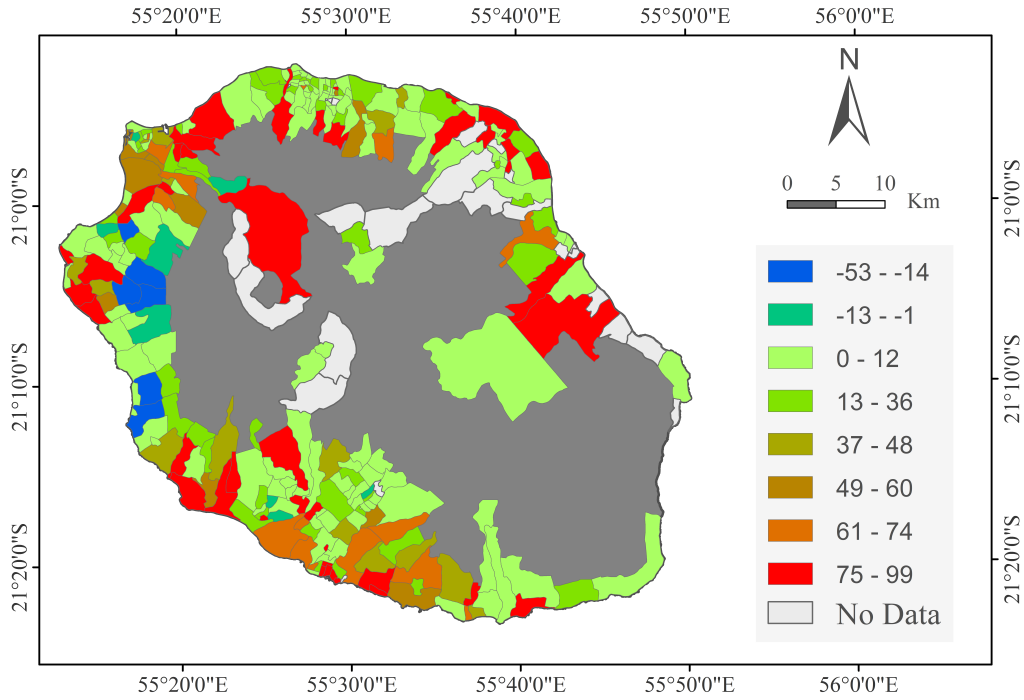


Figure 3. Geographical distribution of the accuracy of the model predictions compared to observed data. A color gradient going from blue to red via green represents the variable *DifSimObs* weighted by the number of observations. The green IRIS are the IRIS with a difference from 0 to 36 additional cases between simulated number of infected (H_I) and recovered (H_R) and the cumulative number of observed dengue cases. The IRIS in red and blue are the IRIS for which the model respectively overestimates and underestimates the number of dengue cases. The IRIS in white are the IRIS where there was no dengue case in 2018.

variables ($R_s(267) = -0.3, p < 0.001$) using Spearman tests, none of these interactions remained significant in the GLM (Table 2).

Table 2. Z_{Value} and P_{Value} for the various variables and interactions tested using the General Linear Model (GLM). For the meaning of the different variables, see text.

Variable	Average	Standard deviation	Z_{Value}	P_{Value}
ISize	0.014	$4.3e^{-04}$	3.2	0.4
VarMosquito	$1.5e^{-06}$	$2e^{-07}$	8.5	$<2e^{-16}$
TimeAction	-0.005	0.04	-1.4	0.07
RatioAction	2.7	0.1	2.2	0.02
MonthCase	-1.14	0.08	-14.2	$<2e^{-16}$
VarMosquito:ISize	$2.6e^{-10}$	$1.4e^{-10}$	1.7	0.2
MonthCase:RatioAction	0.08	0.07	1.4	0.3

To take into account a possible effect of the vector control interventions in the model, we added an adult mortality parameter, x , representing the effect of adulticide pulverizations following the detection of dengue cases. Adulticide pulverization is usually restricted to the closest proximity of dengue cases^{8,10,14,40}, so that mosquitoes within an IRIS are not all exposed to the insecticide: we thus assumed that all of exposed and contaminated females were sprayed, because they are most likely around the dengue cases, but weighted the x parameter by the IRIS size for males and susceptible females. We selected a small IRIS comprising a single ALIZES in order to eliminate as much as possible the modeling scale effect (zero variance). x varied from 0 to 1 and we retained the value for which the difference between the model and the observed data is minimum: a realistic additional mortality of 0.14 during vector control interventions dramatically reduces the difference between the predictions and the observed data (Appendix B). These simulations should be repeated on other IRIS to ensure that the addition of this

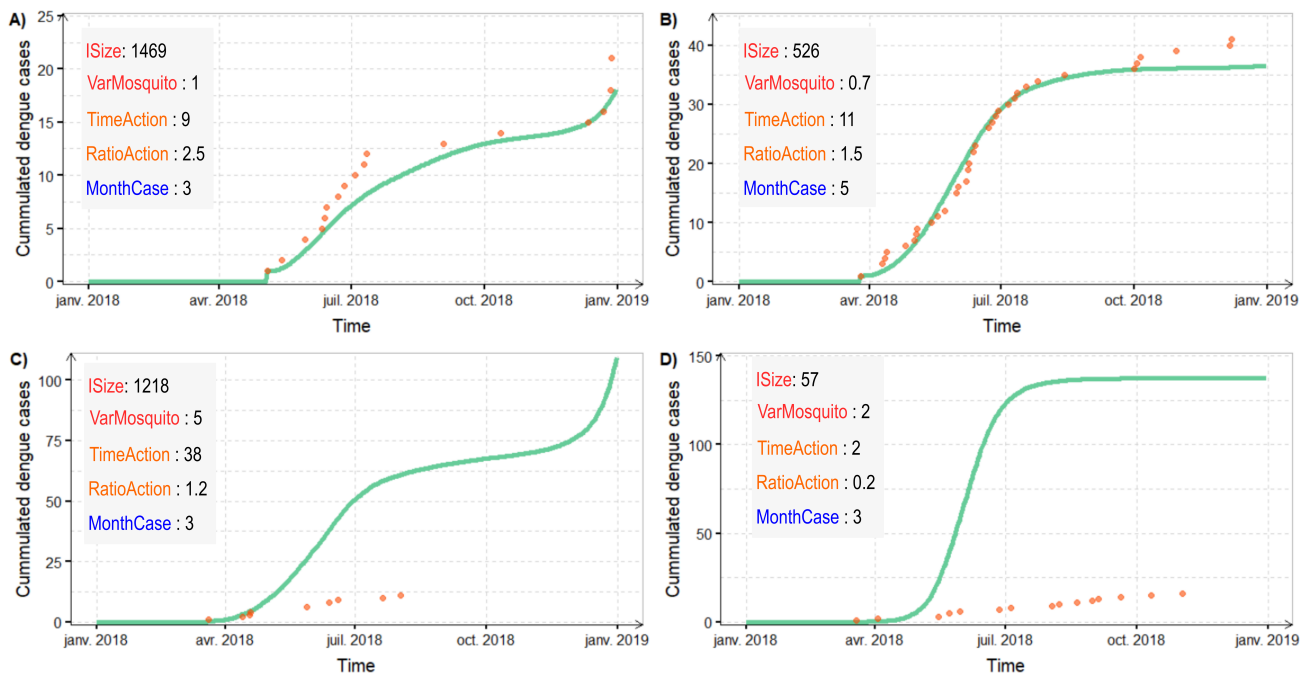


Figure 4. Comparison of the simulated results with the observed dengue cases. *The orange dots correspond to the cumulative number of observed cases, the green line represents the cumulative sum of infected (H_I) and removed (H_R) cases simulated by the model. We selected two IRIS where the model outputs fit the data and two others where the model and the outputs are different.*

parameter is crucial to model the epidemic dynamics. But due to the variable profile of IRIS, it is difficult to identify IRIS with a low effect of data scales (ISize and VarMosquito).

4 Discussion

In this study we used a weather-driven abundance model of the *Aedes albopictus* population dynamics²⁵ coupled with a SEI-SEIR epidemiological model to simulate dengue outbreaks on La Reunion Island. The predicted numbers of dengue cases were compared with the actual 2018 dengue outbreak data. The results show that the model capture most of the dengue dynamics in the island, and can thus be used to anticipate transmission patterns and test the potential impacts of various anti-vectorial management strategies.

4.1 The Many cases of dengue in the West and South of the island

The South and the West of La Reunion island regions were the regions where the outbreak started and where the number of recorded cases was the highest⁸. The populations of *Ae. albopictus* are driven by temperature and rainfall^{2,31,41-43}. The west of the island is the region where the climate is hotter and drier. Paradoxically, this is the region where the number of breeding site is the most important because the human store more water in small containers such as saucers or flowerpots, which are favorable breeding sites for the development of *Ae. albopictus* larvae²⁴. The populations of *Ae. albopictus* are therefore more abundant in the west of the island and the risk of transmission is therefore higher⁴⁴. If the model overestimated the number of dengue cases in the South or in the West of La Reunion island (Appendix 3), the conclusion of a high risk of outbreak in its regions is not completely wrong. On the other hand, there is in the west a group of IRIS located in the heights of the island where the model underestimates the number of dengue cases. Additional field studies, including studies to update estimates of number breeding sites, are needed to understand why this underestimation of dengue cases.

4.2 Control methods had an impact on the dengue outbreak in 2018

Vector control had an impact on the dengue outbreak in 2018. *Ae. albopictus* populations are more abundant during the austral summer, from November to April because the temperatures are warm and the rainfall is more numerous. There is also a peak in the abundance of *Ae. albopictus* populations in March^{24,25}. This is why, when the first dengue case appears on an IRIS at the beginning of the year, the model could overestimate the number of dengue cases due to the high abundance of *Ae. albopictus*

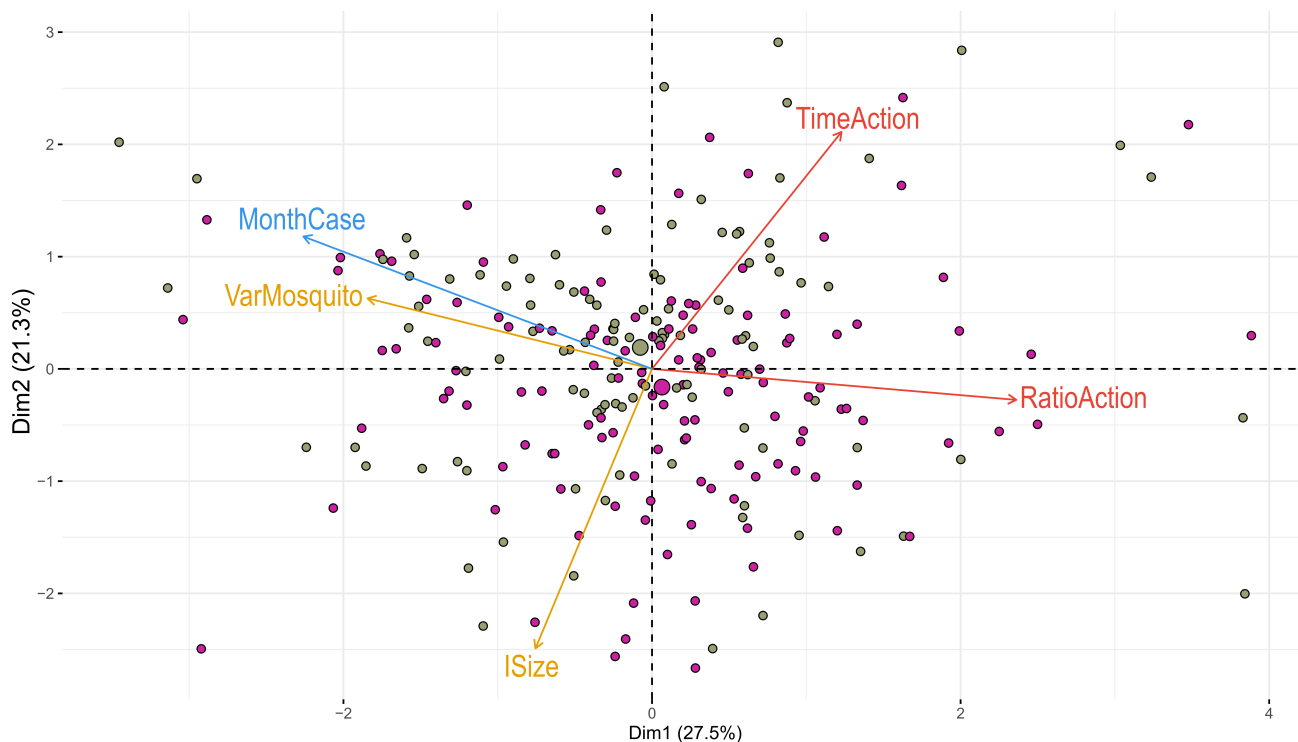


Figure 5. PCA of 5 variables and 269 IRIS areas. The red variables are related to vector control interventions (*TimeAction* and *RatioAction*), the orange ones are related to data scales (*ISize* and *VarMosquito*), and the blue variable to the dengue outbreak (*MonthCase*). The green dots represent IRIS areas with accurate model predictions, the purple dots those where predictions did not match the observed data.

populations⁴⁵. We can thus conclude this is at this moment that the impact of vector control is most visible²². In addition, the model overestimates the number of cases predicted in IRIS where interventions are high compared to the number of dengue cases observed. These results confirm the study of⁴⁶, which suggested that control measures had contributed to reducing the transmission of chikungunya during the 2005-2006 outbreak from La Reunion. The proportion of immune human required to stop the transmission of the chikungunya should have been around 75% (In Comoros and Kenya, respectively 60% and 70% of the population developed antibodies to stop the outbreak^{47,48}), but only 38% of populations was contaminated and the lack of resurgence in 2007 may well have been due to collective and individual vector control measures. A simple test consisting to modeling with parsimony the mortality of adult mosquitoes in a small IRIS allow a better fit of outbreak model to observations (Appendix B). More studies on the control methods currently used in La Reunion is important to modelling with more precision the vector control and optimize them.

4.3 The choice of the spatial scale impacts the modeling of the outbreak

There is a dissociation between the epidemiological model, spatialized at the IRIS scale, and the entomological model, spatialized at the ALIZES scale. The epidemiological model integrates both the densities of human populations, estimated by INSEE at the IRIS scale, and all the abundances of *Ae. albopictus* populations predicted by the entomological model in the ALIZES within the an IRIS area. We have made the choice of a double spatial scale in order to conserve these information, which are indeed important for representing the transmission of dengue⁴⁹. In addition, the *Ae. albopictus* abundances predicted by the model were validated on entomological data in the study of²⁵.

The epidemiological model assumes a homogeneous transmission of dengue virus within each IRIS, as it is conventional in epidemiological models⁵⁰. However, this assumption was in conflict with real epidemic dynamic, which are heterogeneous at the spatial and individual levels⁵¹. Indeed, the diversity of biotopes within the island due to the mountainous topography and the anthropogenic land-use modifications can influence the appearance of breeding sites⁵². Thus, the abundance of *Ae. albopictus* and the transmission of the dengue virus may vary within an IRIS. Thus the hypothesis of homogeneous transmission could overestimate the dengue cases in the IRIS where *Ae. albopictus* abundances vary greatly between the ALIZES zones. However, this homogeneous transmission hypothesis does not seem completely aberrant because human can easily move at the IRIS scale

(eg. to do their shopping, go to school/work, etc...). In addition, this scale seems to be the best trade-off between the scale of the island (larger scale) and the scale of the ALIZE (smaller scale). A larger scale would only have increased the transmission bias linked to the hypothesis of homogeneous transmission. Moreover, this scale is not relevant to test the impact of control methods in different geographic and climatic within the island. Conversely, the hypothesis of a homogeneous transmission would have been completely valid on the scale of the ALIZES area, but a modeling on a finer scale would have led to too much stochasticity and it would have been very difficult, if not impossible, to test the validity of the model throughout the country.

4.4 Towards tool for dengue surveillance and control

For now, the epidemiological model was not developed to be a tool for the surveillance and control of dengue. The model does not include mosquito dispersal and human mobility. If in the case of the *Ae. albopictus*, this is not a problem because its dispersal distance (100m⁵³) is less than the size of the IRIS (at least 9 ha), human mobility can participate in the expansion of the dengue virus^{54,55}. Moreover, the model only represents the transmission dynamics of serotype 2 in La Reunion island⁸ and the outbreak appeared in a largely non-immune population⁵⁶. Then we considered that the population was completely naive. In fact, 97 dengue cases were reported in 2017⁸. In addition, since 2019 and 2020, serotype 1 and 3 circulate on the island. Thus, if we wish to prevent the emergence of a dengue outbreak, we should model the other dengue serotypes. But once again, in the absence of available data, such model applied to La Reunion seems to be difficult.

4.5 Perspective: Modelling alternative vector control methods

No one can remain impassive to the fact that, despite all the efforts undertaken by the vector control agencies and despite all the resources deployed, more than 6,000 cases were reported in 2018⁸. Avoid the outbreak was perhaps not possible. This is why it is essential to optimize the current control methods but also to establish other control methods in order to prevent a new outbreak⁵⁷. The weather-driven abundance model was originally developed to test the impact of different vector control methods on *Ae. albopictus* populations. Thus, the impact of the different control methods should be integrated into the model in order to assess the impact of the control methods on the transmission of dengue.

References

1. Organization, W. H. & others. Vector control. Tech. Rep., World Health Organization. Regional Office for South-East Asia (2017).
2. Bhatt, S. *et al.* The global distribution and burden of dengue. *Nature* **496**, 504–507, DOI: [10.1038/nature12060](https://doi.org/10.1038/nature12060) (2013).
3. Organization, W. H. Dengue and severe dengue. Tech. Rep., World Health Organization (2020).
4. World Health Organization and others. Dengue and severe dengue. Tech. Rep., World Health Organization. Regional Office for the Eastern Mediterranean (2019).
5. Gubler, D. J., Ooi, E. E., Vasudevan, S. & Farrar, J. *Dengue and Dengue Hemorrhagic Fever, 2nd Edition* (CABI, 2014). Google-Books-ID: TI_YBAAAQBAJ.
6. Organization, W. H. & others. Dengue vaccine: WHO position paper, July 2016–recommendations. *Vaccine* **35**, 1200–1201 (2017). Publisher: Elsevier.
7. Añez, G. & Rios, M. Dengue in the United States of America: A Worsening Scenario?, DOI: <https://doi.org/10.1155/2013/678645> (2013). ISSN: 2314-6133 Library Catalog: www.hindawi.com Pages: e678645 Publisher: Hindawi Volume: 2013.
8. Vincent, M. *et al.* From the threat to the large outbreak: dengue on Reunion Island, 2015 to 2018. *Euro Surveill* **24**, DOI: [10.2807/1560-7917.ES.2019.24.47.1900346](https://doi.org/10.2807/1560-7917.ES.2019.24.47.1900346) (2019).
9. Norman, Gratz. Critical review of the vector status of *Aedes albopictus*. *Med. Vet. Entomol.* (2004).
10. Baldet, T. *et al.* Avis du 31/07/2018 révisé le 23/10/2018 de l'Agence Nationale de Sécurité Sanitaire et de l'Alimentation, de l'Environnement et du Travail (ANSES) relatif à "l'analyse de la stratégie de lutte anti-vectorielle (LAV) mise en œuvre à La Réunion depuis 2017". *ANSES* 1–86 (2018).
11. Estrada-Franco, J. G. & Craig, G. B. Biology, disease relationships, and control of *Aedes albopictus*. *Biol. disease relationships, control Aedes albopictus* (1995). ISBN: 9789275130421 Publisher: Pan American Health Organization.
12. Organization, W. H. *Dengue : Guidelines for Diagnosis, Treatment, Prevention and Control* (WHO, 2009). Google-Books-ID: dlc0YSIyGYwC.
13. Faraji, A. & Unlu, I. The Eye of the Tiger, the Thrill of the Fight: Effective Larval and Adult Control Measures Against the Asian Tiger Mosquito, *Aedes albopictus* (Diptera: Culicidae), in North America. *J Med Entomol* **53**, 1029–1047, DOI: [10.1093/jme/tjw096](https://doi.org/10.1093/jme/tjw096) (2016).

14. Delatte, H. *et al.* *Aedes albopictus*, vecteur des virus du chikungunya et de la dengue à la Réunion : biologie et contrôle. *Parasite* **15**, 3 – 13, DOI: [10.1051/parasite/2008151003](https://doi.org/10.1051/parasite/2008151003) (2008).
15. Ministry of Health of Singapore. Final Report of the Expert Panel on Dengue. (2005).
16. D’Ortenzio, E., Balleydier, E., Bavielle, M., Filleul, L. & Renault, P. Dengue à la Réunion et dans les îles du sud-ouest de l’océan Indien. *Médecine et Maladies Infect.* **41**, 475–479, DOI: [10.1016/j.medmal.2010.11.021](https://doi.org/10.1016/j.medmal.2010.11.021) (2011).
17. Renault, P. *et al.* A Major Epidemic of Chikungunya Virus Infection on Réunion Island, France, 2005–2006. *The Am. J. Trop. Medicine Hyg.* **77**, 727–731, DOI: [10.4269/ajtmh.2007.77.727](https://doi.org/10.4269/ajtmh.2007.77.727) (2007). Publisher: The American Society of Tropical Medicine and Hygiene.
18. Mordecai, E. A. *et al.* Detecting the impact of temperature on transmission of Zika, dengue, and chikungunya using mechanistic models. *PLOS Neglected Trop. Dis.* **11**, e0005568, DOI: [10.1371/journal.pntd.0005568](https://doi.org/10.1371/journal.pntd.0005568) (2017).
19. Li, R. *et al.* Climate-driven variation in mosquito density predicts the spatiotemporal dynamics of dengue. *PNAS* **116**, 3624–3629, DOI: [10.1073/pnas.1806094116](https://doi.org/10.1073/pnas.1806094116) (2019).
20. Zhou, S. *et al.* Examining the Effect of the Environment and Commuting Flow from/to Epidemic Areas on the Spread of Dengue Fever. *Int J Environ Res Public Heal.* **16**, DOI: [10.3390/ijerph16245013](https://doi.org/10.3390/ijerph16245013) (2019).
21. Dumont, Y. & Chiroleu, F. Vector control for the Chikungunya disease. *Math Biosci Eng* **7**, 313–345 (2010).
22. Li, M.-T. *et al.* The Driving Force for 2014 Dengue Outbreak in Guangdong, China. *PLOS ONE* **11**, e0166211, DOI: [10.1371/journal.pone.0166211](https://doi.org/10.1371/journal.pone.0166211) (2016).
23. Perkins, T. A. *et al.* A review of transmission models of dengue: a quantitative and qualitative analysis of model features. *Dengue dengue hemorrhagic fever* 99 (2014). Publisher: CABI International Boston.
24. Tran, A. *et al.* Complementarity of empirical and process-based approaches to modelling mosquito population dynamics with *Aedes albopictus* as an example—Application to the development of an operational mapping tool of vector populations. *PLOS ONE* **15**, e0227407, DOI: [10.1371/journal.pone.0227407](https://doi.org/10.1371/journal.pone.0227407) (2020).
25. Haramboure, M. *et al.* Modelling the control of *Aedes albopictus* mosquitoes based on sterile males release techniques in a tropical environment. *Ecol. Model.* **424**, 109002, DOI: [10.1016/j.ecolmodel.2020.109002](https://doi.org/10.1016/j.ecolmodel.2020.109002) (2020).
26. Besson, L. Un Réunionnais sur quatre vit dans les Hauts. (2017). Publisher: Insee La Réunion-Mayotte.
27. Mora, B. *L’épidémie de DENGUE à l’Ile de la Réunion en 1977-1978*. PhD Thesis (1979).
28. Coulanges, P., Clerc, Y., Jousset, F. X., Rodhain, F. & Hannoun, C. Dengue on Réunion. Isolation of a strain at the Pasteur Institute of Madagascar. *Bull. de la Soc. de Pathol. Exot. et de ses Fil.* **72**, 205–209 (1979). Publisher: Societe de Pathologie Exotique/Masson.
29. Santé publique France. Dengue à la Réunion Augmentation du nombre de cas hebdomadaire. *Point de situation au 26 janvier 2020* (2010).
30. Delatte, H. *et al.* Geographic Distribution and Developmental Sites of *Aedes albopictus* (Diptera: Culicidae) During a Chikungunya Epidemic Event. *Vector-Borne Zoonotic Dis.* **8**, 25–34, DOI: [10.1089/vbz.2007.0649](https://doi.org/10.1089/vbz.2007.0649) (2008).
31. Delatte, H., Gimonneau, G., Triboire, A. & Fontenille, D. Influence of temperature on immature development, survival, longevity, fecundity, and gonotrophic cycles of *Aedes albopictus*, vector of chikungunya and dengue in the Indian Ocean. *J. Med. Entomol.* **46**, 33–41 (2009).
32. Andraud, M., Hens, N., Marais, C. & Beutels, P. Dynamic Epidemiological Models for Dengue Transmission: A Systematic Review of Structural Approaches. *PLOS ONE* **7**, e49085, DOI: [10.1371/journal.pone.0049085](https://doi.org/10.1371/journal.pone.0049085) (2012).
33. Liu-Helmersson, J., Stenlund, H., Wilder-Smith, A. & Rocklöv, J. Vectorial Capacity of *Aedes aegypti*: Effects of Temperature and Implications for Global Dengue Epidemic Potential. *PLOS ONE* **9**, e89783, DOI: [10.1371/journal.pone.0089783](https://doi.org/10.1371/journal.pone.0089783) (2014).
34. Lambrechts, L. *et al.* Impact of daily temperature fluctuations on dengue virus transmission by *Aedes aegypti*. *PNAS* **108**, 7460–7465, DOI: [10.1073/pnas.1101377108](https://doi.org/10.1073/pnas.1101377108) (2011).
35. Dray, S., Dufour, A.-B. & Chessel, D. The ade4 Package – II: Two-Table and K-Table Methods. *R News* **7**, 47–52 (2007).
36. Zuur, A. F., Ieno, E. N., Walker, N. J., Saveliev, A. A. & Smith, G. M. GLM and GAM for count data. In *Mixed effects models and extensions in ecology with R*, 209–243 (Springer, 2009).
37. Lebreton, J.-D., Burnham, K. P., Clobert, J. & Anderson, D. R. Modeling survival and testing biological hypotheses using marked animals: a unified approach with case studies. *Ecol. monographs* **62**, 67–118 (1992). Publisher: Wiley Online Library.

38. Anderson, D., Burnham, K. & White, G. AIC model selection in overdispersed capture-recapture data. *Ecology* **75**, 1780–1793 (1994). Publisher: Wiley Online Library.
39. Crawley, M. The R book chichester. UK: Wiley [Google Scholar] (2007).
40. Fontenille, D. *et al.* *La lutte antivectorielle en France*. IRD Éditions (2009).
41. Kruijff, H. A. M. d., Woodall, J. P. & Tang, A. T. The influence of accumulated rainfall and its pattern on mosquito (Diptera) populations in Brazil. *Bull. Entomol. Res.* **63**, 327–333, DOI: [10.1017/S0007485300039092](https://doi.org/10.1017/S0007485300039092) (1973).
42. Roiz, D., Rosà, R., Arnoldi, D. & Rizzoli, A. Effects of Temperature and Rainfall on the Activity and Dynamics of Host-Seeking *Aedes albopictus* Females in Northern Italy. *Vector-Borne Zoonotic Dis.* **10**, 811–816, DOI: [10.1089/vbz.2009.0098](https://doi.org/10.1089/vbz.2009.0098) (2010).
43. Dieng, H. *et al.* The effects of simulated rainfall on immature population dynamics of *Aedes albopictus* and female oviposition. *Int J Biometeorol* **56**, 113–120, DOI: [10.1007/s00484-011-0402-0](https://doi.org/10.1007/s00484-011-0402-0) (2012).
44. Benkimoun, S. *et al.* The basic reproduction number (R0) proves its efficiency to develop an operational dynamic mapping tool for dengue surveillance and control in Reunion Island. *Under reviewing* (2020).
45. Erickson, R. A., Presley, S. M., Allen, L. J. S., Long, K. R. & Cox, S. B. A dengue model with a dynamic *Aedes albopictus* vector population. *Ecol. Model.* **221**, 2899–2908, DOI: [10.1016/j.ecolmodel.2010.08.036](https://doi.org/10.1016/j.ecolmodel.2010.08.036) (2010).
46. Boëlle, P.-Y. *et al.* Investigating Transmission in a Two-Wave Epidemic of Chikungunya Fever, Réunion Island. *Vector-Borne Zoonotic Dis.* **8**, 207–218, DOI: [10.1089/vbz.2006.0620](https://doi.org/10.1089/vbz.2006.0620) (2008). Publisher: Mary Ann Liebert, Inc., publishers.
47. Sergon, K. *et al.* SEROPREVALENCE OF CHIKUNGUNYA VIRUS INFECTION ON GRANDE COMORE ISLAND, UNION OF THE COMOROS, 2005. *The Am. J. Trop. Medicine Hyg.* **76**, 1189–1193, DOI: [10.4269/ajtmh.2007.76.1189](https://doi.org/10.4269/ajtmh.2007.76.1189) (2007). Publisher: The American Society of Tropical Medicine and Hygiene.
48. World Health Organization. OMS | Chikungunya – Kenya (2016). Publisher: World Health Organization.
49. Lord, C. C., Woolhouse, M. E. J., Heesterbeek, J. a. P. & Mellor, P. S. Vector-borne diseases and the basic reproduction number: a case study of African horse sickness. *Med. Vet. Entomol.* **10**, 19–28, DOI: [10.1111/j.1365-2915.1996.tb00077.x](https://doi.org/10.1111/j.1365-2915.1996.tb00077.x) (1996). [_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1365-2915.1996.tb00077.x](https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1365-2915.1996.tb00077.x).
50. Reiner, R. C. *et al.* A systematic review of mathematical models of mosquito-borne pathogen transmission: 1970–2010. *J. The Royal Soc. Interface* **10**, 20120921, DOI: [10.1098/rsif.2012.0921](https://doi.org/10.1098/rsif.2012.0921) (2013). Publisher: Royal Society.
51. Favier, C. *et al.* Influence of spatial heterogeneity on an emerging infectious disease: the case of dengue epidemics. *Proc. Royal Soc. B: Biol. Sci.* **272**, 1171–1177, DOI: [10.1098/rspb.2004.3020](https://doi.org/10.1098/rspb.2004.3020) (2005). Publisher: Royal Society.
52. Wilke, A. B. B. *et al.* Urbanization creates diverse aquatic habitats for immature mosquitoes in urban areas. *Sci Rep* **9**, 1–11, DOI: [10.1038/s41598-019-51787-5](https://doi.org/10.1038/s41598-019-51787-5) (2019). Number: 1 Publisher: Nature Publishing Group.
53. Lacroix, R., Delatte, H., Hue, T. & Reiter, P. Dispersal and Survival of Male and Female *Aedes albopictus* (Diptera: Culicidae) on Réunion Island. *ment* **46**, 1117–1124, DOI: [10.1603/033.046.0519](https://doi.org/10.1603/033.046.0519) (2009).
54. Stoddard, S. T. *et al.* The Role of Human Movement in the Transmission of Vector-Borne Pathogens. *PLOS Neglected Trop. Dis.* **3**, e481, DOI: [10.1371/journal.pntd.0000481](https://doi.org/10.1371/journal.pntd.0000481) (2009). Publisher: Public Library of Science.
55. Stoddard, S. T. *et al.* House-to-house human movement drives dengue virus transmission. *Proc. Natl. Acad. Sci.* **110**, 994–999 (2013). Publisher: National Acad Sciences.
56. Larrieu, S. *et al.* Dengue outbreaks: a constant risk for Reunion Island. Results from a seroprevalence study among blood donors. *Trans R Soc Trop Med Hyg* **108**, 57–59, DOI: [10.1093/trstmh/trt110](https://doi.org/10.1093/trstmh/trt110) (2014). Publisher: Oxford Academic.
57. Luz, P. M., Struchiner, C. J. & Galvani, A. P. Modeling Transmission Dynamics and Control of Vector-Borne Neglected Tropical Diseases. *PLOS Neglected Trop. Dis.* **4**, e761, DOI: [10.1371/journal.pntd.0000761](https://doi.org/10.1371/journal.pntd.0000761) (2010).

Acknowledgements

Author contributions statement

Discussion générale

A l'aide d'outils mathématiques, cette thèse a eu pour objectif de mieux comprendre et d'optimiser l'impact de différentes méthodes de LAV et de leurs combinaisons sur les populations d'*Ae. albopictus* et sur la transmission de la dengue. Nous nous sommes en particulier focalisés sur la TIS et BTIS, des techniques basées sur des lâchers de mâles stériles qui sont actuellement en phase d'évaluation à La Réunion. Un premier modèle de dynamique des populations, intégrant les effets du climat a été développé afin d'explorer l'impact de ces deux techniques de contrôle sur les populations d'*Ae. albopictus* à La Réunion. Par la suite, d'autres méthodes de LAV ont été introduites au modèle afin d'évaluer leur potentielles synergies, positives ou négatives, ou leur redondances avec la TIS et BTIS. Ce modèle a été ensuite étendu à la ville de Montpellier pour comparer l'impact des méthodes de lutte dans différents contextes climatiques. Enfin, le modèle entomologique a été couplé avec un modèle épidémiologique dans le but d'évaluer l'impact de la LAV sur la transmission de la dengue à la Réunion. Dans cette section, nous mettrons en perspective nos principaux résultats au regard d'autres travaux scientifiques et discuterons notamment les choix de modélisation. Ce manuscrit s'achèvera par des perspectives de recherche suite à nos travaux pour développer les connaissances dans le domaine du contrôle des moustiques *Aedes* urbains, principaux vecteurs d'arboviroses humaines.

1.1 Des résultats en accord avec la littérature

De nombreuses études évaluant l'impact de lâchers de mâles stériles sur les populations naturelles de moustiques par la modélisation sont disponibles dans la bibliographie. Les principaux résultats présentés dans les chapitres II et III sont en accord avec les enseignements issus de ces études visant à évaluer l'impact de la TIS sur des populations de moustiques :

- les lâchers de mâles stériles doivent démarquer au moment où la population de moustiques est faible [255, 72, 113] ;
- les lâchers périodiques avec une quantité de mâles stériles constante au cours du temps sont plus efficaces car elles permettent une pression croissante au cours de la période de contrôle [255, 72, 88, 113] ;
- la compétitivité et la quantité des mâles relâchés sont deux paramètres importants et dépendants [255, 198].

Le développement de ces modèles avait une finalité de recherche théorique, avec généralement des hypothèses simplificatrices fortes (environnement constant et/ou simplification des stades de vie aquatiques et/ou adultes en une équation), mais leurs auteurs, essentiellement des théoriciens modélisateurs, ont souligné l'importance de réaliser des analyses adaptées à partir des données entomologiques, épidémiologiques et économiques spécifiques à une région pour évaluer l'ef-

1.2 Des avancées significatives

Les variations de la taille des populations de moustiques sont difficiles à quantifier, et les effets des interventions humaines comme la lutte antivectorielle sont difficiles à distinguer des

efficacité et l'efficacité des différentes stratégies de LAV, et les optimiser [9, 88].

Ma thèse est la première tentative pour adresser cette limite, en présentant des modèles intégrant les effets de la TIS et BTIS dans un milieu spatialement explicite (c.-à-d. tenant compte de la distribution des gîtes larvaires et de l'hétérogénéité climatique). Pour cela, une collaboration entre plusieurs disciplines, notamment des entomologistes et des épidémiologistes a été nécessaire, ainsi que le recommandent plusieurs auteurs pour le développement de modèles utiles et performants [95]. Grâce aux travaux de recherche réalisés au laboratoire ou sur le terrain, nous disposons de nombreuses données sur *Ae. albopictus*, comme ses traits de vie (durée de développement, longévité, ...) et son écologie (typologie et productivité des gîtes larvaires, ...) [54, 55, 65, 131, 178], ainsi que sur certaines méthodes de LAV dirigées contre ses populations naturelles [25, 175, 176, 177, 27, 26, 48, 97, 118]. Ainsi, des scénarios appropriés ont pu être simulés et fournir des estimations détaillées à l'échelle de La Réunion (milieu tropical) et de Montpellier (milieu tempéré). Cependant, il faut rester prudent car seule la dynamique des populations d'*Ae. albopictus* a été validée à partir des données d'observations récoltées par l'ARS à La Réunion et l'EID méditerranée à Montpellier.

autres facteurs naturels qui modulent la présence et l'abondance d'une espèce d'insecte dans un environnement donné [255]. C'est pourquoi l'évaluation de l'impact des méthodes de LAV sur

CHAPITRE V. DISCUSSION GÉNÉRALE

les populations de moustiques cibles dans des contextes opérationnels bien définis faisaient encore défaut [96]. Par ailleurs, des questions demeuraient quant à la faisabilité et à la capacité des actions de LAV à s'intégrer efficacement dans la gestion intégrée de la lutte contre les moustiques [96]. Le développement et l'analyse de modèles spatiaux et temporels se présentait donc comme une pierre angulaire de l'évaluation des méthodes de LAV contre les maladies arbovirales. Les modèles développés dans cette thèse ont ainsi permis d'explorer l'impact de la TIS et BTIS couplées à d'autres méthodes de LAV alternatives aux adulticides dans un contexte opérationnel, et constituent une première avancée qui doit bien sûr être prolongée.

Le modèle épidémiologique met aussi en avant l'impact des actions de LAV menées par l'ARS en 2018 pour freiner la transmission de la dengue à La Réunion. Un modèle avait déjà été développé couplant un modèle de la dynamique des populations de moustiques tigres [240] avec le taux de reproduction de base (R_0 ¹) de Ross-Macdonald pour produire des cartes dynamiques du R_0 de la dengue à partir de variables environnementales à La Réunion ???. Ici, nous avons présenté le premier modèle épidémiologique étudiant la transmission de la dengue entre les hôtes et vecteurs à l'échelle infra-communale. Cependant, ce dernier n'a pu être validé que partiellement.

2

L'approche choisie

Notre choix s'est porté sur le développement de modèles mécanistes pour étudier l'impact de différentes méthodes de LAV, seules ou en combinaison, sur les populations d'*Ae. albopictus*. Les modèles mécanistes fournissent un cadre approprié pour l'évaluation préliminaire

En effet, les modèles de transmission sont généralement validés en les confrontant à des données épidémiologiques de dengue à des échelles plus larges [44, 142, 29]. A une échelle locale, des processus non pris en compte par le modèle peuvent entrer en jeu (ex : mouvements humains, lutte anti-vectorielle, ...).

Les modèles développés lors de cette thèse pourraient être utilisés pour générer des outils opérationnels d'aide à la décision, mais ils peuvent être également utilisés comme des outils de communication et de sensibilisation. Nul ne peut rester indifférent au fait que, malgré tous les efforts de LAV déployés, 25, 139 cas de dengue ont été confirmés de janvier à février 2020 [249]. Cette épidémie persiste encore lors de la rédaction de ce manuscrit. Par ailleurs, la population comme les autorités politiques sont dans l'attente de la mise en place de méthodes de LAV alternatives aux pulvérisations d'insecticides chimiques, de moins en moins bien tolérés pour des raisons écologiques et de santé, tout en améliorant l'efficacité de ce contrôle. Les enseignements issus de cette thèse pourraient contribuer à la mise en place d'essais pilotes de ces nouvelles méthodes dans le contexte réunionnais, inciter à la mise en place de nouvelles stratégies de LAV intégrées, et encourager l'engagement communautaire qui est indispensable à la réussite d'un programme de lutte contre ces vecteurs [103, 21, 118].

1. nombre de cas directement générés par un cas infecté dans une population d'individus sensibles

CHAPITRE V. DISCUSSION GÉNÉRALE

leurs prévues, en raison des variations de production, de la gestion opérationnelle, de la faisabilité et de la capacité en main-d'œuvre et équipement, mais aussi des conditions météorologiques. Les gestionnaires seront donc intéressés par les risques de perte d'efficacité, voire d'échec, dûs à de telles fluctuations, et les adaptations à réaliser en conséquence afin d'atteindre un objectif particulier (par exemple la non-transmission locale de la dengue). Ceci sous-entend une certaine flexibilité de toute stratégie intégrée de LAV pour lui permettre de s'adapter dans le temps aux évolutions internes ou externes, de manière relative

2.1 Le modèle entomologique

Cette thèse est basée sur l'adaptation d'un modèle générique de dynamique des populations initialement appliqué aux espèces *An. hyrcanus* et *An. maculipennis*, 2 espèces de moustiques vecteurs potentiels du paludisme, en Camargue [46]. Ce même modèle a par la suite été appliqué à deux autres espèces de moustiques d'intérêt médical dans la même région : *Culex pipiens* et *Ae. caspius* [89]. Il a enfin été adapté aux populations d'*Ae. albopictus* à Nice [239], à La Réunion [240] et chapitre II) et à Montpellier (chapitre III). Pour ces différentes espèces et ces différentes régions, ce modèle de dynamique des populations a été à chaque fois validé à partir de données de suivis de stades aquatiques (oeufs, larves) ou adultes dans les différentes zones géographiques. C'est ce qui nous apporte ainsi une confiance raisonnablement élevée quant à sa robustesse et à son caractère générique pour les populations de moustiques.

Un modèle est dit simple lorsque sa formulation (analytique ou non) comporte peu de paramètres, et qu'il est possible d'en prévoir le comportement sans avoir recours à des simulations [53, 151]. Ces modèles font opposition aux mo-

ou dans la durée, de façon à garantir sa pertinence, son efficacité et sa durabilité. Mais à quel moment et de quelle manière peut-on envisager d'utiliser un modèle dans la prise de décision ? Il importe de disposer d'une évaluation poussée du modèle par confrontation avec des données d'observation. Il est important de réaliser une analyse critique de la structure du modèle, de ses hypothèses, des conditions d'application, et des valeurs et distribution des paramètres à l'aide d'analyses de sensibilité. C'est ce dont nous allons discuter dans les parties suivantes.

dèles complexes. Il paraît évident après la lecture du manuscrit, que notre modèle entomologique tombe dans la catégorie complexe, car il prend en compte un ensemble de mécanismes biologiques tels que la compétition entre les stades aquatiques, la distinction entre les femelles pares et nullipares, ainsi que l'impact de l'environnement *etc.* En effet, il semblait important de modéliser l'ensemble du cycle de vie d'*Ae. albopictus* dans un milieu explicite afin de pouvoir répondre à l'objectif de ma thèse, et en particulier de pouvoir modéliser l'impact d'une méthode de LAV ciblant un stade particulier. Une trop grande simplification du modèle l'aurait rendu inadapté à nos questions, peut-être trop artificiel et irréaliste, et peu transférable au système réel correspondant (pour la confrontation/validation) [47]. Cependant, nous avons pris le parti d'en réduire partiellement la complexité, par exemple en synthétisant le nombre de compartiments pour les femelles adultes (femelles pares *vs* nullipares). Ceci nous a permis d'avoir un modèle plus parcimonieux et de faciliter par la suite à la fois l'introduction des effets de la LAV dans le modèle et le couplage avec un modèle épidémiologique.

CHAPITRE V. DISCUSSION GÉNÉRALE

2.2 La modélisation de la lutte anti-vectorielle

À l'exception de la TIS pour laquelle nombreux modèles ont déjà été développés, nous avons fait le choix de modéliser les autres méthodes de LAV à partir d'un ensemble d'hypothèses conservatrices. Une représentation simple de ces techniques permettait dans un premier temps d'évaluer la significativité de leur impact sur la suppression des populations d'*Ae. albopictus*. Néanmoins, comme nous l'avons déjà souligné, les résultats présentés doivent être considérés avec précaution car l'impact des méthodes de LAV sur les populations d'*Ae. albopictus* n'a pas pu être validé à l'aide de données terrain, que ce soit dans le contexte réunionnais ou dans le contexte montpelliérain. Actuellement, des essais préliminaires de la TIS contre *Ae. albopictus*, me-

nés par l'IRD, ont été réalisés à la Réunion afin d'estimer la survie, la dispersion et la compétitivité des mâles stériles lâchés dans l'environnement [136]. De plus, des essais semi-field et des essais pilotes de terrain de BTIS sont prévus à La Réunion pour l'hiver 2021. Ces données permettront d'évaluer l'impact de la TIS et de la BTIS en situation terrain, et ainsi d'affiner notre modèle. De même, des essais pilotes de la TIS contre *Ae. albopictus* ont déjà été réalisés à l'île Maurice [117]. En adaptant notre modèle à l'île Maurice, il pourrait être possible de confronter les sorties du modèle avec des données terrains dans un contexte insulaire comparable à La Réunion afin de valider les effets prédits de cette méthode de LAV.

2.3 Le modèle épidémiologique

L'évaluation du modèle épidémiologique a nécessité l'acquisition de données relatives à la répartition des cas de dengue en 2018 à la Réunion. Ces données sont sensibles parce que susceptibles d'aboutir à l'identification de personnes (J.-G. Ganascia, CNRS). C'est pourquoi il a fallu réfléchir à une échelle spatiale qui 1) ne permette pas de localiser exactement les individus infectés sur l'île, 2) n'engendre pas trop de stochasticité, et 3) permette tout de même de représenter la transmission de la dengue à différents endroits de l'île. Notre approche a été validée par l'ARS Réunion qui nous a permis d'utiliser ces données et nous les a transmises à l'échelle des IRIS. Par la suite, il sera crucial de réaliser une analyse de sensibilité pour identifier les paramètres épidémiologiques influençant le plus la dynamique du modèle, paramètres dont les va-

leurs doivent être estimées le plus précisément possible.

Si le modèle entomologique est complexe, la structure du modèle épidémiologique reste relativement simple. En repartant de l'approche proposée par [67] et [247] basée sur une matrice de prochaine génération, il est possible d'obtenir la formule analytique du R_0 du modèle (Annexe 1). Le R_0 est une mesure du succès de l'invasion d'un agent pathogène dans une population : si $R_0 > 1$, une épidémie est possible si l'agent pathogène est introduit ; tandis que si $R_0 < 1$, l'introduction échouera [104]. À terme, des simulations devront être réalisées pour étudier l'impact de la LAV sur le R_0 du modèle afin de déterminer la quantité et les caractéristiques de contrôles nécessaires pour prévenir l'émergence d'une nouvelle épidémie à la Réunion.

2.4 L'impact de la LAV sur la transmission de la dengue

D'après le Haut Conseil des Biotechnologies, "l'objectif visé par la LAV est la réduction de la population d'*Ae. albopictus* sous le seuil requis pour la transmission des pathogènes" [14]. Afin de répondre pleinement au dernier objectif fixé par la thèse, il faudrait :

- **évaluer les paramètres de la LAV qui ont un impact sur la transmission de la dengue.** Une analyse de sensibilité globale du R_0 doit être réalisée, pour identifier les paramètres de la TIS et de la BTIS (par ex. nombre de lâchers, récurrence, etc.) ayant un impact *in fine* sur la transmission, en définissant une gamme de valeurs pour chaque paramètre de la LAV à l'aide d'estimations issues de la littérature, et de données de laboratoire et de terrain.
- **estimer le pourcentage de femelles stériles relâchées qui pourraient être susceptibles d'entraîner une transmission locale de la dengue.** La TIS ou la BTIS nécessitent une étape de sexage

pour séparer les mâles des femelles, afin d'éliminer ces dernières avant d'effectuer les lâchers, pour éviter des piqûres supplémentaires et une éventuelle transmission [149]. Toutefois, les méthodes de sexage ne sont pas optimales et 1 à 2% de femelles stériles peuvent être relâchées avec les mâles [39]. En considérant par exemple qu'il peut y avoir jusqu'à 6000 mâles irradiés lâchés par hectare chaque semaine l'hiver à la Réunion, cela reviendrait donc à lâcher environ 60 à 120 femelles irradiées à chaque fois. Grâce à notre modèle, il est possible de réaliser des simulations tenant compte de pourcentages variables de femelles stériles introduites périodiquement dans le système et d'évaluer leur impact épidémique. Ceci permettrait de déterminer les pourcentages induisant un basculement du R_0 au dessus du seuil épidémique (> 1), et ainsi d'évaluer la tolérance acceptable en terme d'erreurs de sexage.

3

Vers un modèle prenant en compte les déplacements des populations d'hôtes et de vecteurs

3.1 La dispersion des moustiques

La dynamique d'une population de moustiques est régulée par quatre processus : mort, naissance, immigration et émigration, qui dépendent en grande partie de l'environnement. Or nous avons fait le choix de négliger la dispersion des moustiques dans le modèle, car l'échelle spatiale de modélisation choisie, correspondant aux zones de surveillance entomologique, était supérieure à la distance rapportée dans la littérature pour la dispersion active des moustiques en milieu urbain (de l'ordre de quelques centaines de mètres aussi bien tropical que tempéré [156, 136]). Or nous savons que la suppression des

populations après l'arrêt des contrôles ne peut persister que si les populations sont isolées [105], ce qui n'est pas le cas pour *Ae. albopictus* dans un contexte insulaire "hyper connecté" comme La Réunion, avec une absence de structuration des populations et d'isolement par la distance [134]. Cependant, modéliser à une échelle plus locale la dynamique des populations de moustiques, incluant les migrations aussi bien actives (vol des femelles) que passive (via les moyens de transports humains [85]), permettrait de répondre à d'autres questions telles que :

- Quelle est la zone tampon à réaliser autour

CHAPITRE V. DISCUSSION GÉNÉRALE

d'une zone de traitement afin de limiter la ré-augmentation des populations de moustiques via des phénomènes de dispersion ?

- Quel est l'impact du paysage (ex : occupation du sol, fragmentation du paysage, présence de corridors écologiques) sur l'efficacité des lâchers de mâles stériles ?

L'intégration au modèle de la dispersion des moustiques peut être envisagée par de nombreuses approches telles que : les modèles basés sur des équations de diffusion-réaction [71, 212], les modèles de méta-populations [148, 155], les automates cellulaires [143], ou encore les modèles

basés agents [115, 68, 98]. Dans la grande majorité des cas, même si le paysage est explicite, ce sont des paysages théoriques qui sont utilisés [189, 222], car l'on sait peu de choses de l'impact de l'occupation du sol et la structure du paysage sur la dispersion des moustiques. Leurs effets n'ont été que rarement intégrés dans les modèles [238, 143, 47]. Si Lacroix et al. [131] ont étudié la dispersion d'*Ae. albopictus* en milieu urbain et rural à La Réunion, des études sur l'impact de l'occupation du sol et la structure du paysage restent essentielles à mener pour réaliser un modèle appliqué tenant mieux compte de cette dimension spatiale.

3.2 Les déplacements humains

La transmission de la dengue présente des variations géographiques évidentes à La Réunion. Cette hétérogénéité est causée par divers facteurs, parmi lesquels les mouvements humains [154, 226, 69], puisque les sujets humains asymptomatiques, et donc en pleine santé et libres de tout mouvement, constituent le réservoir viral le plus important contribuant à l'infection des moustiques vecteurs [233]. Ces déplacements humains peuvent être simulés à l'aide de modèles basés agents [143] ou encore à l'aide de modèles de méta-populations [269, 268]. Pour le moment, nous disposons seulement de données relatives aux déplacements professionnels à la Réunion, à l'échelle des communes (INSEE). Une première approche modélisant ces déplacements entre les communes de l'île permettrait d'étudier leurs impacts sur la dynamique de transmission de la dengue et de cibler des zones de

LAV prioritaires pour enrayer la propagation de la maladie sur l'ensemble du territoire lors des périodes épidémiques. Néanmoins, ce type de mobilité professionnelle ne couvre qu'une partie des déplacements susceptibles d'engendrer des contaminations loin du lieu de domicile : le week-end est aussi une période durant laquelle les gens se déplacent et restent en extérieur, augmentant leur risque d'exposition [57]. L'acquisition de données téléphoniques mobiles offrirait une source unique d'informations sur l'agrégation et les mouvements humains : de telles données ont été utilisées pour répondre à l'épidémie d'Ebola de 2014-2015 en Afrique de l'Ouest [237] et pour la prévention de la dengue au Nord-Est du Brésil [3]. Cependant, il s'agit de données à la fois coûteuses en temps de traitement (et en argent), mais également sensibles au niveau éthique.

4 Perspectives de l'étude

Le but initial de ce doctorat était de modéliser l'impact de la TIS et de la BTIS, méthodes de LAV basés sur des lâchers de mâles stériles, contre les populations d'*Ae. albopictus*. En exposant la réflexion et les arguments qui ont justifié les choix de modélisation réalisés, ainsi que

les résultats qui ont été obtenus, nous espérons avoir montré que cet objectif a été en très grande partie atteint. Néanmoins ces travaux ouvrent de nombreuses perspectives de recherche, dont une partie sera présentée ci-après.

4.1 L'économie

L'impact économique des maladies vectorielles est considérable, et les pays affectés par des maladies à transmission vectorielle connaissent une croissance plus faible que les autres [262]. On estime par exemple à 8,9 milliards de dollars US le coût économique de la dengue à l'échelle mondiale en 2013 [223]. Un vaccin contre la dengue a été commercialisé récemment [256], qui a été jugé très rentable dans les pays où la transmission du virus est élevée [58]. Cependant, il ne confère pas une protection complète et son usage est limité aux personnes ayant déjà été infectées, du fait d'un risque d'hospitalisation et de forme de dengue grave accru après la première dose de vaccination chez les personnes n'ayant jamais été infectées par ce virus. D'autres vaccins contre la dengue sont en cours de développement, certains en phase 3 clinique, mais ils ne sont pas encore disponibles opérationnellement.

Au niveau des méthodes de LAV, Alphey et al. [9] prévoit que la RIDL pourrait éliminer rapidement la dengue au sein d'une communauté humaine, et à un coût moindre (environ 2,30\$ US par cas évité) que les coûts directs et indirects dus à la maladie (en moyenne 86–190 US\$ par cas de dengue). Récemment, Brady et al. [42] estiment que les stratégies de remplacement de populations par des moustiques transinfectés par *Wolbachia* engendreraient un rapport coût-efficacité

brut inférieur à 1500\$ US par DALY ("disability-adjusted life years"; c.-à-d. les années de vie en parfaite santé qui ont été perdues) évité dans les aires urbaines densément peuplées.

Modéliser l'impact économique de la LAV est donc crucial pour comparer *in silico* différentes stratégies possibles. Si cette thèse n'intègre pas la dimension économique, il serait cependant possible d'utiliser le modèle épidémiologique développé dans le chapitre IV, et des estimations des coûts des différentes méthodes de la LAV, pour comparer les coûts simulés par cas évité grâce aux actions de LAV avec des estimations du coût moyen de la dengue, et la prise en compte d'autres dépenses, comme celles engendrées au niveau des foyers pour la protection contre les moustiques [235].

Bien qu'une évaluation économique doivent être réalisée pour comparer les différentes techniques de LAV, il convient également d'étudier les avantages potentiels plus larges pour la société, tels que la préservation de la biodiversité et de la santé résultant d'une utilisation réduite des insecticides, ou au contraire les problèmes potentiels pour l'environnement liés aux techniques de LAV, par exemple les piégeages d'espèces non-cibles dans les ovitraps, ou la diffusion incontrôlée de transgènes dans les populations sauvages pour la RIDL [95].

CHAPITRE V. DISCUSSION GÉNÉRALE

4.2 La modélisation de la résistance au pyriproxyfène

Le contrôle des vecteurs s'est compliqué avec l'apparition et la diffusion des résistances aux insecticides (cf. définition dans l'encadré ci-dessous). Dans le cas des moustiques, un grand nombre de résistances à différents insecticides chimiques [184, 190, 211, 146] et d'origine biologique [173] ont été rapportés. Chez les popula-

tions d'*Ae. albopictus* à la Réunion, seul une résistance à la dieldrine (*Rdl*) a été détectée pour le moment [232]. Des baisses de sensibilité notable aux pyréthrinoïdes utilisés en LAV (deltaméthrine) ont néanmoins été récemment relevées au sein des populations d'*Ae. albopictus* à La Réunion (ARS, communication personnelle).

La résistance aux insecticides - définition

La résistance d'une espèce cible peut être définie comme une diminution héréditaire de la sensibilité à un insecticide chez certains individus [170]. Il s'agit d'individus porteurs d'un ou plusieurs allèles de résistance leur permettant de survivre et de se reproduire en présence d'insecticide. L'exposition répétée des populations d'insectes aux insecticides entraîne une sélection de ces individus résistants, et donc une augmentation de la fréquence des allèles de résistance dans les générations suivantes.

Ce processus de sélection dépend de plusieurs facteurs :

- **Facteurs biologiques** : les insectes tel que les moustiques qui ont un temps de développement court, de nombreuses générations par an, et une forte prolificité (stratégie *r*) deviennent plus rapidement résistants, puisque la probabilité d'apparition d'un allèle de résistance par mutation est plus forte et la sélection plus efficace, que pour des insectes au développement long, avec un nombre limité de générations et de descendants (stratégie *k*). Par ailleurs, des flux géniques entre populations plus importants (migration) favorisent la diffusion des gènes de résistance ;
- **Facteurs génétiques** : sa fréquence, son degré de dominance, l'avantage sélectif qu'il confère en présence de traitements et le coût génétique (réduction de valeur sélective) qui lui est associé en l'absence des traitements, et l'interaction (épistasie) entre différents gènes de résistance, peuvent aussi impacter la dynamique évolutive d'un allèle de résistance [138, 7] ;
- **Facteurs opérationnels** : cette dynamique évolutive dépend aussi de facteurs tels que l'historique des traitements insecticides dans une zone géographique, la dose et le rythme des applications, la rémanence du biocide, la nature des traitements, l'existence d'autres sources de pressions sélectives [84, 127, 128, 163, 12].

Lors de cette thèse, j'ai porté une attention particulière au pyriproxyfène dans le cas de la BTIS et de l'autodissémination. Le pyriproxyfène n'a aucun effet mutagène ou toxique sur les mammifères aux doses recommandées par l'OMS, car il cible une voie métabolique spécifique de l'in-

secte [261]. Il est utilisé contre les nuisibles d'intérêt en santé publique (ex : mouches domestiques, cafards), les ravageurs agricoles (ex : pucerons, aleurodes) et les insectes vecteurs d'agents pathogènes (ex : moustiques) [229], contre lesquels il est autorisé comme larvicide y compris dans

CHAPITRE V. DISCUSSION GÉNÉRALE

les containers domestiques utilisés pour l'eau de boisson [261]. Pour le moment, la résistance au pyriproxifène reste peu documentée, et seuls des niveaux modestes de résistance ont été signalés en Californie [228]. Cependant, il est nécessaire d'anticiper les effets des mécanismes de résistance aux insecticides utilisés en LAV pour ne pas reproduire les erreurs du passé.

Barbosa et al. [22] ont modélisé l'évolution de la résistance aux insecticides dans une population de *Culex pipiens* à l'aide d'un modèle de dynamique des populations. Le modèle est scindé en trois sous-populations de moustiques avec : les moustiques sensibles (SS), les moustiques résistants (RR) et les moustiques au génotype intermédiaire (SR). En l'absence de coût génétique et de traitement insecticide, les sous-populations tendent inévitablement vers un équilibre stable avec une fréquence des allèles de résistance de 0.5 dans l'ensemble de la population. C'est pourquoi les simulations du modèle développé par Barbosa et al. [22] ne montraient que les dernières étapes de propagation de la résistance après les inter-

4.3 D'autres méthodes de LAV

Lors de cette thèse, j'ai porté une attention particulière à la TIS et BTIS, mais il existe de nombreuses autres méthodes qui pourraient être utilisées pour contrôler les populations d'*Ae. albopictus*. L'avantage du modèle est que le cycle de vie du moustique est simulé avec suffisamment de détails pour permettre d'inclure facilement l'impact de différentes méthodes de LAV.

Outre la TIS, il existe d'autres méthodes basées sur des lâchers de mâles stériles tel que la TII et la RIDL (cf. 2.2.3). L'action de la TII sur les populations de moustiques est similaire à la TIS. Ainsi, les hypothèses de la TII sont les mêmes que celles de la TIS dans les modèles [71, 72, 140, 227]. A l'inverse, pour la RIDL,

en partant du postulat que les sous-populations de moustiques résistants étaient déjà présentes. En l'absence d'information sur le coût génétique associé aux gènes de résistance au pyriproxifène, la modélisation de leur évolution dans une population d'*Ae. albopictus* presque entièrement sensible à La Réunion ne peut actuellement pas donner de résultats solides.

Par ailleurs, le pyriproxifène est très efficace contre de nombreux insectes, à très faibles doses, ce qui pourrait entraîner des problèmes d'ordre écologique s'il était répandu largement dans les environnements naturels. Il serait donc important d'évaluer cet effet dans le cadre de techniques telles que la BTIS, pour laquelle les femelles sont sensées en transporter dans leur gîtes larvaires dispersés dans l'environnement. Une telle dispersion pourrait en effet aussi affecter de nombreuses espèces d'insectes non-cibles (alors que les populations d'insectes sont déjà en fort déclin, avec des réductions très alarmantes de leur abondance dans de nombreuses régions du globe).

il faudrait modifier certaines hypothèses, car ces techniques entraînent une augmentation des mortalités larvaires et n'agissent pas sur la viabilité des œufs. Des modèles ont par ailleurs déjà été développés pour étudier l'impact de la RIDL sur la dynamique des populations de moustiques [254, 9, 98].

La BTIS est un concept émergent et les premières études ont porté sur le développement d'une formulation de pyriproxifène capable de se transmettre des mâles aux moustiques femelles lors de l'accouplement ou des tentatives de copulation, puis des femelles aux gîtes larvaires. Mais un champignon ou un virus pourrait être utilisé à la place du pyriproxifène, avec une spé-

CHAPITRE V. DISCUSSION GÉNÉRALE

cificité plus forte qui permettrait d'éviter les problèmes écologiques évoqués plus haut. Les densovirus [38], qui sont très spécifiques à l'espèce cible ou aux espèces étroitement apparentées, sont un exemple de candidats biocides [49] proposé en association avec des mâles stériles. Dans le cas du virus AeDENV isolé d'*Ae. albopictus*, seules les

4.4 D'autres espèces cibles

Durant ma thèse, je me suis focalisée sur la modélisation des populations d'*Ae. albopictus*. Avec une démarche similaire à celle présentée dans ce manuscrit et en modifiant les paramètres ou en adaptant certaines hypothèses du modèle, il est possible de modéliser l'impact de la LAV sur d'autres espèces nuisibles.

Actuellement, la TIS est une technique largement utilisée pour lutter contre les mouches des fruits [79]. De surcroît, la mouche orientale des fruits, *Bactrocera dorsalis*, a été détectée pour la première fois en 2017 à la Réunion et a aussitôt causé des dégâts considérables sur les cultures locales de mangues. Des mesures de surveillance ont été renforcées et des traitements hebdomadaires avec un insecticide homologué sont réalisés dans un rayon de 500 mètres autour des foyers de forte densité de *Bactrocera dorsalis*. Les services de l'Etat à La Réunion [139]. En se basant sur l'approche de modélisation utilisée dans cette thèse, une étude de la faisabilité de la TIS pourrait être réalisée.

Il existe pour le moment peu d'informations concernant le contrôle des populations de mous-

autres espèces d'*Aedes* ou de *Culex* sont sensibles au virus. Pour le moment, la modélisation de la BTIS avec un densovirus à l'aide du modèle de population développé dans cette thèse me semble néanmoins difficile, car il existe trop peu d'informations sur les interactions entre les vecteurs et les densovirus.

tiques avec la BTIS. En revanche, des expérimentations réalisées en laboratoire sur la mouche tsé-tsé vectrice de trypanosomes humaines et animales en Afrique subsaharienne [214] réalisées dans le cadre du même projet ERC Revolinc, ont été récemment publiées par Laroche et al. [133]. Cette publication fournit des informations à propos de 1) la persistance du pyriproxifène sur les mâles stériles de glossines (*Glossina palpalis palpalis*), 2) l'impact du pyriproxifène sur la survie des mâles, 3) la dynamique du transfert du pyriproxifène d'un mâle stérile à une femelle pendant l'accouplement, 4) ainsi que l'impact du pyriproxifène sur la production de pupes et 5) l'émergence des adultes. Par ailleurs au Sénégal, les programmes opérationnels de contrôle de la mouche tsé-tsé avec la TIS sont remplacés depuis février 2020 par la BTIS en raison de la résurgence de cette espèce au sein de sites résiduels (J. Bouyer, communication personnelle). Une réadaptation complète du modèle permettrait d'avoir une modélisation plus précise pour prédire l'impact de la BTIS sur les populations de ce vecteur d'intérêt médical et vétérinaire.

5

Conclusion

L'objectif général de ma thèse était de comprendre et d'optimiser l'impact de la LAV basée sur des lâchers de mâles stériles (TIS et

BTIS) sur les populations d'*Ae. albopictus*. Nous avons développé un modèle mécaniste qui représente l'ensemble du cycle de vie d'*Ae. albopictus*

CHAPITRE V. DISCUSSION GÉNÉRALE

pilotés par des variables environnementales, en milieu tropical et tempéré, et, comme une méthode de LAV ne peut se suffire à elle seule ni être efficace à long terme, nous y avons intégré les effets d'autres méthodes de LAV. Pour la première fois, ce modèle permet donc d'évaluer l'impact de différentes méthodes de LAV dans des conditions géographiques et climatiques réelles, et de les optimiser en conséquence. Enfin, une première étape d'association de ce modèle populationnel avec un modèle épidémiologique de la dengue à l'échelle infra-communale à la Réunion a été réalisée pour tester l'impact des stratégies de LAV sur la dynamique du virus.

Cette thèse a mis en évidence que la modélisation est une discipline à cheval avec plusieurs autres disciplines. En effet, le développement de

modèles intégrés ne peut être l'apanage des seuls modélisateurs et biomathématiciens, mais doit impliquer une approche et des équipes multidisciplinaires. Les résultats présentés dans ce manuscrit sont le fruit d'un dialogue continu entre les gestionnaires de la LAV et la communauté scientifique, qui a permis de développer nos modèles mathématiques d'une part et de les valider d'autre part à l'aide de données collectées dans les laboratoires ou sur le terrain. Sans ces interactions, il n'aurait pas été lors de cette thèse, et il ne sera pas dans le futur, possible d'explorer et de comprendre les changements provoqués par les méthodes de LAV sur la dynamique des populations de vecteurs et celle des maladies qu'ils transmettent.

Bibliographie

- [1] European Centre for Disease Prevention and Control. Vector control with a focus on *Aedes aegypti* and *Aedes albopictus* mosquitoes : literature review and analysis of information. *ECDC TECHNICAL REPORT*, 2017.
- [2] Début de la phase pilote pour la Technique de l’Insecte Stérile (TIS) à la Réunion | Site Web IRD, Feb. 2020. URL <https://www.ird.fr/debut-de-la-phase-pilote-pour-la-technique-de-linsecte-sterile-tis-la-reunion>.
Library Catalog : www.ird.fr.
- [3] F. F. Abel Manguera, R. Smania-Marques, I. Dutra Fernandes, V. Alves Albino, R. Olinda, T. Acácia Santos-Silva, J. Traxler, D. Matheson, and S. Santos. The prevention of arboviral diseases using mobile devices : a preliminary study of the attitudes and behaviour change produced by educational interventions. *Trop. Med. Int. Health*, 24(12) :1411–1426, 2019. ISSN 1365-3156. doi: 10.1111/tmi.13316.
- [4] G. C. Abramides, D. Roiz, R. Guitart, S. Quintana, I. Guerrero, and N. Giménez. Effectiveness of a multiple intervention strategy for the control of the tiger mosquito (*Aedes albopictus*) in Spain. *Trans R Soc Trop Med Hyg*, 105(5) :281–288, May 2011. ISSN 0035-9203. doi: 10.1016/j.trstmh.2011.01.003. URL <https://academic.oup.com/trstmh/article/105/5/281/1884536>.
Publisher : Oxford Academic.
- [5] N. L. Achee, J. P. Grieco, H. Vatandoost, G. Seixas, J. Pinto, L. Ching-NG, A. J. Martins, W. Juntarajumnong, V. Corbel, C. Gouagna, J.-P. David, J. G. Logan, J. Orsborne, E. Marois, G. J. Devine, and J. Vontas. Alternative strategies for mosquito-borne arbovirus control. *PLoS Neglected Tropical Diseases*, 13(1) :e0006822, Jan. 2019. ISSN 1935-2735. doi: 10.1371/journal.pntd.0006822. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0006822>.
- [6] L. Almeida, M. Duprez, Y. Privat, and N. Vauchelet. Control strategies on mosquitos population

BIBLIOGRAPHIE

- for the fight against arboviruses. *arXiv :1901.05688 [math]*, Jan. 2019. URL <http://arxiv.org/abs/1901.05688>. arXiv : 1901.05688.
- [7] H. Alout, P. Labbé, A. Berthomieu, P. Makoundou, P. Fort, N. Pasteur, and M. Weill. High chlorpyrifos resistance in *Culex pipiens* mosquitoes : strong synergy between resistance genes. *Heredity*, 116(2) :224–231, 2016. Publisher : Nature Publishing Group.
- [8] L. Alphey, M. Benedict, R. Bellini, G. G. Clark, D. A. Dame, M. W. Service, and S. L. Dobson. Sterile-Insect Methods for Control of Mosquito-Borne Diseases : An Analysis. *Vector Borne Zoonotic Dis*, 10(3) :295–311, Apr. 2010. ISSN 1530-3667. doi: 10.1089/vbz.2009.0014. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2946175/>.
- [9] N. Alphey, L. Alphey, and M. B. Bonsall. A Model Framework to Estimate Impact and Cost of Genetics-Based Sterile Insect Methods for Dengue Vector Control. *PLoS One*, 6(10) :e25384, Oct. 2011. ISSN 1932-6203. doi: 10.1371/journal.pone.0025384. WOS :000295966900023.
- [10] R. M. Anderson, B. Anderson, and R. M. May. *Infectious diseases of humans : dynamics and control*. Oxford university press, 1992.
- [11] G. Añez and M. Rios. Dengue in the United States of America : A Worsening Scenario?, June 2013. URL <https://www.hindawi.com/journals/bmri/2013/678645/>. ISSN : 2314-6133 Library Catalog : www.hindawi.com Pages : e678645 Publisher : Hindawi Volume : 2013.
- [12] B. S. Assogba, H. Alout, A. Koffi, C. Penetier, L. S. Djogbénou, P. Makoundou, M. Weill, and P. Labbé. Adaptive deletion in resistance gene duplications in the malaria vector *Anopheles gambiae*. *Evolutionary Applications*, 11(8) :1245–1256, 2018. ISSN 1752-4571. doi: 10.1111/eva.12619. URL <https://onlinelibrary.wiley.com/doi/abs/10.1111/eva.12619>. _eprint : <https://onlinelibrary.wiley.com/doi/pdf/10.1111/eva.12619>.
- [13] C. M. Atyame, P. Labbé, C. Lebon, M. Weill, R. Moretti, F. Marini, L. C. Gouagna, M. Calvitti, and P. Tortosa. Comparison of Irradiation and Wolbachia Based Approaches for Sterile-Male Strategies Targeting *Aedes albopictus*. *PLOS ONE*, 11(1) :e0146834, Jan. 2016. ISSN 1932-6203. doi: 10.1371/journal.pone.0146834. URL <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0146834>. Publisher : Public Library of Science.
- [14] C. Bagnis, M.-A. Barny, P. Boireau, T. Brévault, B. Chauvel, C. Collonnier, D. Couvet, and others. Avis en réponse à la saisine HCB du 12 octobre 2015 concernant l’utilisation de moustiques génétiquement modifiés dans le cadre de la lutte antivectorielle. Paris, le 31 mai 2017. *Comité Scientifique Du Haut Conseil Des Biotechnologies*, 2017.
- [15] L. Bagny, H. Delatte, N. Elissa, S. Quilici, and D. Fontenille. *Aedes* (Diptera : Culicidae) Vectors of Arboviruses in Mayotte (Indian Ocean) : Distribution Area and Larval Habitats. *J Med Entomol*, 46(2) :198–207, Mar. 2009. ISSN 0022-2585. doi: 10.1603/033.046.0204. URL <https://academic.oup.com/jme/article/46/2/198/873943>. Publisher : Oxford Academic.
- [16] N. T. Bailey. The mathematical theory of epidemics. Technical report, 1957.

BIBLIOGRAPHIE

- [17] F. Baldacchino, B. Caputo, F. Chandre, A. Drago, A. d. Torre, F. Montarsi, and A. Rizzoli. Control methods against invasive *Aedes* mosquitoes in Europe : a review - Baldacchino - 2015 - Pest Management Science - Wiley Online Library. June 2015. doi: 10.1002/ps.4044. URL <http://onlinelibrary.wiley.com/doi/10.1002/ps.4044/full>.
- [18] F. Baldacchino, F. Bussola, D. Arnoldi, M. Marcantonio, F. Montarsi, G. Capelli, R. Rosà, and A. Rizzoli. An integrated pest control strategy against the Asian tiger mosquito in northern Italy : a case study. *Pest Management Science*, 73(1) :87–93, 2017. ISSN 1526-4998. doi: 10.1002/ps.4417. URL <https://onlinelibrary.wiley.com/doi/abs/10.1002/ps.4417>.
_eprint : <https://onlinelibrary.wiley.com/doi/pdf/10.1002/ps.4417>.
- [19] T. Baldet, F. DARRIET, J. David, I. Dusfour, M. Franc, A. Izri, P. Labbe, L. Lagadic, and C. Lagneau. Utilisation Des Insecticides et Gestion de La Résistance. *Centre national d'Expertise sur les Vecteurs.*, Rennes, 2014.
- [20] T. Baldet, P. Carnevale, J. Devillers, S. Dupé, H. Noel, and D. Roiz. Avis du 31/07/2018 révisé le 23/10/2018 de l'Agence Nationale de Sécurité Sanitaire et de l'Alimentation, de l'Environnement et du Travail (ANSES) relatif à "l'analyse de la stratégie de lutte anti-vectorielle (LAV) mise en œuvre à La Réunion depuis 2017". *ANSES*, pages 1–86, 2018.
- [21] A. Baly, M. E. Toledo, M. Boelaert, A. Reyes, V. Vanlerberghe, E. Ceballos, M. Carvajal, R. Maso, M. La Rosa, O. Denis, and P. Van der Stuyft. Cost effectiveness of *Aedes aegypti* control programmes : participatory versus vertical. *Trans R Soc Trop Med Hyg*, 101(6) :578–586, June 2007. ISSN 0035-9203. doi: 10.1016/j.trstmh.2007.01.002. URL <https://academic.oup.com/trstmh/article/101/6/578/1891008>. Publisher : Oxford Academic.
- [22] S. Barbosa, K. Kay, N. Chitnis, and I. M. Hastings. Modelling the impact of insecticide-based control interventions on the evolution of insecticide resistance and disease transmission. *Parasites & Vectors*, 11(1) :482, Aug. 2018. ISSN 1756-3305. doi: 10.1186/s13071-018-3025-z. URL <https://doi.org/10.1186/s13071-018-3025-z>.
- [23] R. Barrera, V. Acevedo, G. E. Felix, R. R. Hemme, J. Vazquez, J. L. Munoz, and M. Amador. Impact of Autocidal Gravid Ovitrap on Chikungunya Virus Incidence in *Aedes aegypti* (Diptera : Culicidae) in Areas With and Without Traps. *J Med Entomol*, 54(2) :387–395, Mar. 2017. ISSN 0022-2585. doi: 10.1093/jme/tjw187. URL <https://academic.oup.com/jme/article/54/2/387/2952745>.
- [24] N. Becker, D. Petric, M. Zgomba, C. Boase, M. Madon, C. Dahl, and A. Kaiser. *Mosquitoes and their control*. Springer Science & Business Media, 2010.
- [25] R. Bellini, M. Calvitti, A. Medici, M. Carrieri, G. Celli, and S. Maini. *Aedes albopictus* in Italy : First Results of a Pilot Trial. *Area-Wide Control of Insect Pests*, pages 505–515, 2007.
- [26] R. Bellini, F. Balestrino, A. Medici, G. Gentile, R. Veronesi, and M. Carrieri. Mating competitiveness of *Aedes albopictus* radio-sterilized males in large enclosures exposed to natural

BIBLIOGRAPHIE

- conditions. *J Med Entomol*, 50(1) :94–102, Jan. 2013. ISSN 0022-2585. doi: 10.1603/ME11058. URL <http://europepmc.org/abstract/med/23427657>.
- [27] R. Bellini, A. Medici, A. Puggioli, F. Balestrino, and M. Carrieri. Pilot field trials with *Aedes albopictus* irradiated sterile males in Italian urban areas. *J. Med. Entomol.*, 50(2) :317–325, Mar. 2013. ISSN 0022-2585.
- [28] M. Q. Benedict and A. S. Robinson. The first releases of transgenic mosquitoes : an argument for the sterile insect technique. *Trends in Parasitology*, 19(8) :349–355, Aug. 2003. ISSN 1471-4922. doi: 10.1016/S1471-4922(03)00144-2. URL <http://www.sciencedirect.com/science/article/pii/S1471492203001442>.
- [29] S. Benkimoun, C. M. Atyame, M. Haramboure, P. Degenne, H. Thébault, J.-S. Dehecq, and A. Tran. The basic reproduction number (R_0) proves its efficiency to develop an operational dynamic mapping tool for dengue surveillance and control in Reunion Island. *Under reviewing*, 2020.
- [30] L. Berec. Techniques of spatially explicit individual-based models : construction, simulation, and mean-field analysis. *Ecological modelling*, 150(1-2) :55–81, 2002. Publisher : Elsevier.
- [31] L. Besson. Un Réunionnais sur quatre vit dans les Hauts. 2017. Publisher : Insee La Réunion-Mayotte.
- [32] S. Bhatt, P. W. Gething, O. J. Brady, J. P. Messina, A. W. Farlow, C. L. Moyes, J. M. Drake, J. S. Brownstein, A. G. Hoen, O. Sankoh, M. F. Myers, D. B. George, T. Jaenisch, G. R. W. Wint, C. P. Simmons, T. W. Scott, J. J. Farrar, and S. I. Hay. The global distribution and burden of dengue. *Nature*, 496(7446) :504–507, Apr. 2013. ISSN 1476-4687. doi: 10.1038/nature12060. URL <https://www.nature.com/articles/nature12060>.
- [33] D. BICOUT, J. Devillers, A.-B. Failloux, C. Paupy, P. Quenel, D. Roiz, and F. Simard. AVIS de l’ANSES relatif au risque d’importation de la dengue en France métropolitaine par des moustiques infectés en provenance de La Réunion. *ANSES*, 2018.
- [34] M. Bonizzoni, G. Gasperi, X. Chen, and A. A. James. The invasive mosquito species *Aedes albopictus* : current knowledge and future perspectives. *Trends in Parasitology*, 29(9) :460–468, Sept. 2013. ISSN 1471-4922. doi: 10.1016/j.pt.2013.07.003. URL <http://www.sciencedirect.com/science/article/pii/S1471492213001086>.
- [35] K. Bourtzis and A. S. Robinson. Insect pest control using *Wolbachia* and/or radiation. In *Insect Symbiosis, Volume 2*, pages 247–268. CRC Press, 2006.
- [36] K. Bourtzis, S. L. Dobson, Z. Xi, J. L. Rasgon, M. Calvitti, L. A. Moreira, H. C. Bossin, R. Moretti, L. A. Baton, G. L. Hughes, P. Mavingui, and J. R. L. Gilles. Harnessing mosquito–*Wolbachia* symbiosis for vector and disease control. *Acta Tropica*, 132 :S150–S163, Apr. 2014. ISSN 0001-706X. doi: 10.1016/j.actatropica.2013.11.004. URL <http://www.sciencedirect.com/science/article/pii/S0001706X13003276>.

BIBLIOGRAPHIE

- [37] J. Bouyer and T. Lefrançois. Boosting the sterile insect technique to control mosquitoes. *Trends in Parasitology*, 30(6) :271–273, June 2014. ISSN 1471-4922. doi: 10.1016/j.pt.2014.04.002. URL <http://www.sciencedirect.com/science/article/pii/S1471492214000567>.
- [38] J. Bouyer, F. Chandre, J. Gilles, and T. Baldet. Alternative vector control methods to manage the Zika virus outbreak : more haste, less speed. *The Lancet Global Health*, 4(6) :e364, June 2016. ISSN 2214-109X. doi: 10.1016/S2214-109X(16)00082-6. URL [http://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(16\)00082-6/abstract](http://www.thelancet.com/journals/langlo/article/PIIS2214-109X(16)00082-6/abstract).
- [39] J. Bouyer, L. C. Gouagna, C. Gourlay-Frances, J.-L. Pujol, J. Raude, E. Schultz, and H. Thebaud. Avis en réponse à la saisine DGPR du 10 octobre 2017 concernant l’élaboration de recommandations pour autoriser le lâcher de moustiques stériles à des fins de lutte anti-vectorielle. *HCSP*, 2018.
- [40] J. Bouyer, H. Yamada, R. Pereira, K. Bourtzis, and M. J. B. Vreysen. Phased Conditional Approach for Mosquito Management Using Sterile Insect Technique. *Trends in Parasitology*, 36(4) :325–336, Apr. 2020. ISSN 1471-4922, 1471-5007. doi: 10.1016/j.pt.2020.01.004. URL [https://www.cell.com/trends/parasitology/abstract/S1471-4922\(20\)30014-3](https://www.cell.com/trends/parasitology/abstract/S1471-4922(20)30014-3). Publisher : Elsevier.
- [41] S. Boyer, C. Toty, M. Jacquet, G. Lempérière, and D. Fontenille. Evidence of Multiple Inseminations in the Field in *Aedes albopictus*. *PLOS ONE*, 7(8) :e42040, Aug. 2012. ISSN 1932-6203. doi: 10.1371/journal.pone.0042040. URL <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0042040>.
- [42] O. J. Brady, D. D. Kharisma, N. N. Wilastonegoro, K. M. O’Reilly, E. Hendrickx, L. S. Bastos, L. Yakob, and D. S. Shepard. The cost-effectiveness of controlling dengue in Indonesia using wMel Wolbachia released at scale : a modelling study. *BMC Medicine*, 18(1) :186, July 2020. ISSN 1741-7015. doi: 10.1186/s12916-020-01638-2. URL <https://doi.org/10.1186/s12916-020-01638-2>.
- [43] M. Brustolin, C. Santamaria, S. Napp, M. Verdún, R. Rivas, N. Pujol, S. Talavera, and N. Busquets. Experimental study of the susceptibility of a European *Aedes albopictus* strain to dengue virus under a simulated Mediterranean temperature regime. *Medical and Veterinary Entomology*, 32(4) :393–398, Dec. 2018. ISSN 1365-2915. doi: 10.1111/mve.12325. URL <https://onlinelibrary.wiley.com/doi/10.1111/mve.12325>. Publisher : John Wiley & Sons, Ltd.
- [44] M. N. BURATTINI, M. CHEN, A. CHOW, F. A. B. COUTINHO, K. T. GOH, L. F. LOPEZ, S. MA, and E. MASSAD. Modelling the control strategies against dengue in Singapore. *Epidemiol Infect*, 136(3) :309–319, Mar. 2008. ISSN 0950-2688. doi: 10.1017/S0950268807008667. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2870819/>.
- [45] L. Cai, S. Ai, and J. Li. Dynamics of Mosquitoes Populations with Different Strategies for Releasing Sterile Mosquitoes. *SIAM J. Appl. Math.*, 74(6) :1786–1809, 2014. ISSN 0036-1399. doi: 10.1137/13094102X. WOS :000346845900004.

BIBLIOGRAPHIE

- [46] P. Cailly, A. Tran, T. Balenghien, G. L'Ambert, C. Toty, and P. Ezanno. Climate-driven abundance model to assess mosquito control strategies. *Ecological Modelling - ECOL MODEL*, 227 : 7–17, Feb. 2012. doi: 10.1016/j.ecolmodel.2011.10.027.
- [47] Cailly, Priscilla. *Modélisation de la dynamique spatio-temporelle d'une population de moustiques, sources de nuisances et vecteurs d'agents pathogènes*. PhD thesis, 502 Biologie Santé Nantes Angers, 2011. URL <https://tel.archives-ouvertes.fr/tel-00766348>.
- [48] B. Caputo, A. Ienco, D. Cianci, M. Pombi, V. Petrarca, A. Baseggio, G. J. Devine, and A. d. Torre. The “Auto-Dissemination” Approach : A Novel Concept to Fight *Aedes albopictus* in Urban Areas. *PLOS Neglected Tropical Diseases*, 6(8) :e1793, Aug. 2012. ISSN 1935-2735. doi: 10.1371/journal.pntd.0001793. URL <http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0001793>.
- [49] J. Carlson, E. Suchman, and L. Buchatsky. Densoviruses for Control and Genetic Manipulation of Mosquitoes. In *Advances in Virus Research*, volume 68, pages 361–392. Elsevier, 2006. ISBN 978-0-12-039868-3. doi: 10.1016/S0065-3527(06)68010-X. URL <http://linkinghub.elsevier.com/retrieve/pii/S006535270668010X>.
- [50] K. Chandel, D. S. Suman, Y. Wang, I. Unlu, E. Williges, G. M. Williams, and R. Gaugler. Targeting a Hidden Enemy : Pyriproxyfen Autodissemination Strategy for the Control of the Container Mosquito *Aedes albopictus* in Cryptic Habitats. *PLOS Neglected Tropical Diseases*, 10(12) :e0005235, Dec. 2016. ISSN 1935-2735. doi: 10.1371/journal.pntd.0005235. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0005235>. Publisher : Public Library of Science.
- [51] P. Chanprasopchai, P. Pongsumpun, and I. M. Tang. Effect of Rainfall for the Dynamical Transmission Model of the Dengue Disease in Thailand, Aug. 2017. URL <https://www.hindawi.com/journals/cmmm/2017/2541862/>. ISSN : 1748-670X Pages : e2541862 Publisher : Hindawi Volume : 2017.
- [52] Q. Cheng, Q. Jing, R. C. Spear, J. M. Marshall, Z. Yang, and P. Gong. Climate and the Timing of Imported Cases as Determinants of the Dengue Outbreak in Guangzhou, 2014 : Evidence from a Mathematical Model. *PLOS Neglected Tropical Diseases*, 10(2) :e0004417, Feb. 2016. ISSN 1935-2735. doi: 10.1371/journal.pntd.0004417. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004417>.
- [53] M. Choisy, J.-F. Guégan, and P. Rohani. Mathematical modeling of infectious diseases dynamics. *Encyclopedia of infectious diseases : modern methodologies*, 379, 2007. Publisher : John Wiley and Sons Inc Hoboken.
- [54] A. N. Clements and others. *The biology of mosquitoes : development, nutrition and reproduction*, volume 1. Chapman & Hall London, 1992.
- [55] A. N. Clements and others. *The biology of mosquitoes. Volume 2 : sensory reception and behaviour*. CABI publishing, 1999.

BIBLIOGRAPHIE

- [56] A. Cohuet and C. Pennetier. L'efficacité des principaux répulsifs contre les moustiques les plus dangereux. 2017.
- [57] A. R. Cook, L. R. Carrasco, V. J. Lee, E. E. Ooi, M. I.-C. Chen, D. C. Lye, and Y. S. Leo. Higher Risk of Infection with Dengue at the Weekend among Male Singaporeans. *The American Journal of Tropical Medicine and Hygiene*, 87(6) :1116–1118, Dec. 2012. ISSN 0002-9637, 1476-1645. doi: 10.4269/ajtmh.2012.11-0648. URL <https://www.ajtmh.org/content/journals/10.4269/ajtmh.2012.11-0648>. Publisher : The American Society of Tropical Medicine and Hygiene.
- [58] L. Coudeville, N. Baurin, and D. S. Shepard. The potential impact of dengue vaccination with, and without, pre-vaccination screening. *Vaccine*, 38(6) :1363–1369, Feb. 2020. ISSN 0264-410X. doi: 10.1016/j.vaccine.2019.12.012. URL <http://www.sciencedirect.com/science/article/pii/S0264410X19316548>.
- [59] P. Coulanges, Y. Clerc, F. X. Jousset, F. Rodhain, and C. Hannoun. Dengue on Réunion. Isolation of a strain at the Pasteur Institute of Madagascar. *Bulletin de la Societe de Pathologie Exotique et de ses Filiales*, 72(3) :205–209, 1979. ISSN 0037-9085. URL <https://www.cabdirect.org/cabdirect/abstract/19802901402>. Publisher : Societe de Pathologie Exotique/Masson.
- [60] T. Czárán. *Spatiotemporal models of population and community dynamics*, volume 21. Springer Science & Business Media, 1998.
- [61] G. L. Dalla Pozza, R. Romi, C. Severini, and others. Source and spread of *Aedes albopictus* in the Veneto region of Italy. *Journal of the American Mosquito Control Association-Mosquito News*, 10(4) :589–592, 1994. Publisher : [Fresno, Calif.] : The Association,[c1985-.
- [62] C. M. Degener, Á. E. Eiras, T. M. F. Ázara, R. A. Roque, S. Rösner, C. T. Codeço, A. A. Nobre, E. S. O. Rocha, E. G. Kroon, J. J. Ohly, and M. Geier. Evaluation of the Effectiveness of Mass Trapping With BG-Sentinel Traps for Dengue Vector Control : A Cluster Randomized Controlled Trial in Manaus, Brazil. *J Med Entomol*, 51(2) :408–420, Mar. 2014. ISSN 0022-2585. doi: 10.1603/ME13107. URL <https://academic.oup.com/jme/article/51/2/408/882690>.
- [63] H. Delatte, J. Dehecq, J. Thiria, C. Domerg, C. Paupy, and D. Fontenille. Geographic Distribution and Developmental Sites of *Aedes albopictus* (Diptera : Culicidae) During a Chikungunya Epidemic Event. *Vector-Borne and Zoonotic Diseases*, 8(1) :25–34, Jan. 2008. ISSN 1530-3667. doi: 10.1089/vbz.2007.0649. URL <https://www.liebertpub.com/doi/abs/10.1089/vbz.2007.0649>.
- [64] H. Delatte, C. Paupy, J. S. Dehecq, J. Thiria, A.-B. Failloux, and D. Fontenille. *Aedes albopictus*, vecteur des virus du chikungunya et de la dengue à la Réunion : biologie et contrôle. *Parasite*, 15(1) :3 – 13, Mar. 2008. doi: 10.1051/parasite/2008151003. URL <https://hal-pasteur.archives-ouvertes.fr/pasteur-01696240/document>.

BIBLIOGRAPHIE

- [65] H. Delatte, G. Gimonneau, A. Triboire, and D. Fontenille. Influence of temperature on immature development, survival, longevity, fecundity, and gonotrophic cycles of *Aedes albopictus*, vector of chikungunya and dengue in the Indian Ocean. *J. Med. Entomol.*, 46(1) :33–41, Jan. 2009. ISSN 0022-2585.
- [66] G. Devine. Auto-Dissemination of Pyriproxyfen for the Control of Container-inhabiting Mosquitoes – a Progress Review. *Outlooks on Pest Management*, 27(4) :164–167, Aug. 2016.
- [67] O. Diekmann and J. Heesterbeek. *Wiley series in mathematical and computational biology. Mathematical epidemiology of infectious diseases : model building, analysis and interpretation.* New York : Wiley, 2000.
- [68] C. J. Dommar, R. Lowe, M. Robinson, and X. Rodó. An agent-based model driven by tropical rainfall to understand the spatio-temporal heterogeneity of a chikungunya outbreak. *Acta Tropica*, 129 :61–73, Jan. 2014. ISSN 0001-706X. doi: 10.1016/j.actatropica.2013.08.004. URL <http://www.sciencedirect.com/science/article/pii/S0001706X1300209X>.
- [69] M. Donnat, B. Gozalvez-Kreuzer, Y. Roca, A. Conde Cosme, J. Choque Rios, J.-P. Hervé, and P. Handschumacher. La dynamique de la dengue à Santa Cruz de la Sierra (Bolivie) entre paysages à risques et mobilités. Appréciation des inégalités et gestion du risque. *Espace populations sociétés. Space populations societies*, (2011/1) :33–46, Mar. 2011. ISSN 0755-7809. doi: 10.4000/eps.4318. URL <http://journals.openedition.org/eps/4318>. Number : 2011/1 Publisher : Université des Sciences et Technologies de Lille.
- [70] E. D’Ortenzio, E. Balleydier, M. Bavielle, L. Filleul, and P. Renault. Dengue à la Réunion et dans les îles du sud-ouest de l’océan Indien. *Médecine et Maladies Infectieuses*, 41(9) :475–479, Sept. 2011. ISSN 0399-077X. doi: 10.1016/j.medmal.2010.11.021. URL <http://www.sciencedirect.com/science/article/pii/S0399077X1100014X>.
- [71] C. Dufourd and Y. Dumont. Modeling and Simulations of Mosquito Dispersal. The Case of *Aedes albopictus*. *BIOMATH*, 1(2) :1209262, Dec. 2012. ISSN 1314-7218. doi: 10.11145/j.biomath.2012.09.262. URL <http://biomathforum.org/biomath/index.php/biomath/article/view/j.biomath.2012.09.262>.
- [72] C. Dufourd and Y. Dumont. Impact of environmental factors on mosquito dispersal in the prospect of sterile insect technique control. *Computers & Mathematics with Applications*, 66(9) :1695–1715, Nov. 2013. ISSN 0898-1221. doi: 10.1016/j.camwa.2013.03.024. URL <http://www.sciencedirect.com/science/article/pii/S0898122113002307>.
- [73] Y. Dumont and F. Chiroleu. Vector control for the Chikungunya disease. *Math Biosci Eng*, 7(2) :313–345, Apr. 2010. ISSN 1551-0018.
- [74] D. W. Dunn and P. A. Follett. The Sterile Insect Technique (SIT) – an introduction. *Entomol Exp Appl*, 164(3) :151–154, Sept. 2017. ISSN 1570-7458. doi: 10.1111/eea.12619. URL <http://onlinelibrary.wiley.com/doi/10.1111/eea.12619/abstract>.

BIBLIOGRAPHIE

- [75] J. B. Dunning, D. J. Stewart, B. J. Danielson, B. R. Noon, T. L. Root, R. H. Lamberson, and E. E. Stevens. Spatially Explicit Population Models : Current Forms and Future Uses. *Ecological Applications*, 5(1) :3–11, Feb. 1995. ISSN 1939-5582. doi: 10.2307/1942045. URL <http://onlinelibrary.wiley.com/doi/10.2307/1942045/abstract>.
- [76] I. Dusfour, J. Vontas, J.-P. David, D. Weetman, D. M. Fonseca, V. Corbel, K. Raghavendra, M. B. Coulibaly, A. J. Martins, S. Kasai, and F. Chandre. Management of insecticide resistance in the major Aedes vectors of arboviruses : Advances and challenges. *PLOS Neglected Tropical Diseases*, 13(10) :e0007615, Oct. 2019. ISSN 1935-2735. doi: 10.1371/journal.pntd.0007615. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0007615>. Publisher : Public Library of Science.
- [77] G. Duvallet, D. Fontenille, V. Robert, and others. *Entomologie médicale et vétérinaire*. Editions Quae, 2017.
- [78] A. Duvignaud, A. Fianu, A. Bertolotti, J. Jaubert, A. Michault, P. Poubeau, A. Fred, M. Méchain, B.-A. Gaüzère, F. Favier, D. Malvy, and P. Gérardin. Rheumatism and chronic fatigue, the two facets of post-chikungunya disease : the TELE-CHIK cohort study on Reunion island. *Epidemiology & Infection*, 146(5) :633–641, Apr. 2018. ISSN 0950-2688, 1469-4409. doi: 10.1017/S0950268818000031. URL <https://www.cambridge.org/core/journals/epidemiology-and-infection/article/rheumatism-and-chronic-fatigue-the-two-facets-of-postchikungunya-disease-the-telechik-co-9219D0C9D7B26C605C9452B0EADA61D6>. Publisher : Cambridge University Press.
- [79] V. A. Dyck, J. Hendrichs, and A. S. Robinson. *Sterile Insect Technique : Principles and Practice in Area-Wide Integrated Pest Management*. Springer Science & Business Media, Feb. 2006. ISBN 978-1-4020-4051-1.
- [80] A. E. Eiras, T. S. Buhagiar, and S. A. Ritchie. Development of the Gravid <I>Aedes</I> Trap for the Capture of Adult Female Container-Exploiting Mosquitoes (Diptera : Culicidae). *jnl. med. entom.*, 51(1) :200–209, Jan. 2014. ISSN 00222585, 00222585. doi: 10.1603/ME13104. URL <https://academic.oup.com/jme/article-lookup/doi/10.1603/ME13104>.
- [81] C. Englbrecht, S. Gordon, C. Venturelli, A. Rose, and M. Geier. Evaluation of BG-Sentinel Trap as a Management Tool to Reduce Aedes albopictus Nuisance in an Urban Environment in Italy. *moco*, 31(1) :16–25, Mar. 2015. ISSN 8756-971X, 1943-6270. doi: 10.2987/14-6444.1. URL <https://bioone.org/journals/Journal-of-the-American-Mosquito-Control-Association/volume-31/issue-1/14-6444.1/Evaluation-of-BG-Sentinel-Trap-as-a-Management-Tool-to/10.2987/14-6444.1.full>.
- [82] W. R. Enkerlin, J. M. G. Ruelas, R. Pantaleon, C. S. Litera, A. V. Cortés, J. L. Z. López, D. O. Dávila, P. M. Gerardo, L. S. Villarreal, E. C. Roldán, F. H. López, A. A. Castillo, D. C. Dominguez, A. V. Mora, P. R. Arana, C. C. Barrios, D. Midgarden, C. V. Villatoro, E. L. Prera, O. Z. Estradé, R. C. Aldana, J. L. Culajay, F. R. y. Ramírez, P. L. Fernández,

BIBLIOGRAPHIE

- G. O. Moreno, J. R. Flores, and J. Hendrichs. The Moscamed Regional Programme : review of a success story of area-wide sterile insect technique application. *Entomologia Experimentalis et Applicata*, 164(3) :188–203, 2017. ISSN 1570-7458. doi: 10.1111/eea.12611. URL <https://onlinelibrary.wiley.com/doi/abs/10.1111/eea.12611>.
- [83] Ericka Bareigts, Philippe Naillet, Ramlati Ali,, Marine Brenier, Paul Christophe, Loïc Dombrevail,, Sereine Mauborgne,, Max Mathiasin, Bérengère Poletti, Valérie Thomas, Élisabeth Toutut-Picard, Stéphanie Atger, Delphine Bagarry, Annie Chapelier, Alain David, Marc Delatte, Jeanine Dubié, Françoise Dumas, Raphaël Gérard, Didier Martin, Jean François Mbaye, Emmanuelle Ménard, Philippe Michel-Kleisbauer, Jean-Philippe Nilor, Jean-Hugues Ratenon, Frédéric Reiss, Cédric Roussel, Benoit Simian, Jean-Louis Touraine, Stéphane Viry, and Martine Wonner. Rapport fait au nom de la commission d’enquête chargée d’évaluer les recherches, la prévention et les politiques publiques à mener contre la propagation des moustiques Aedes et des maladies vectorielles. *Assemblée Nationale*, Tome 1 :1–226, July 2020.
- [84] R. Eritja and C. Chevillon. Interruption of Chemical Mosquito Control and Evolution of Insecticide Resistance Genes in *Culex pipiens* (Diptera : Culicidae). *J Med Entomol*, 36(1) :41–49, Jan. 1999. ISSN 0022-2585. doi: 10.1093/jmedent/36.1.41. URL <https://academic.oup.com/jme/article/36/1/41/876137>. Publisher : Oxford Academic.
- [85] R. Eritja, J. R. B. Palmer, D. Roiz, I. Sanpera-Calbet, and F. Bartumeus. Direct Evidence of Adult *Aedes albopictus* Dispersal by Car. *Scientific Reports*, 7(1) :14399, Oct. 2017. ISSN 2045-2322. doi: 10.1038/s41598-017-12652-5. URL <https://www.nature.com/articles/s41598-017-12652-5>. Number : 1 Publisher : Nature Publishing Group.
- [86] J. G. Estrada-Franco and G. B. Craig. Biology, disease relationships, and control of *Aedes albopictus*. *Biology, disease relationships, and control of Aedes albopictus*, (42), 1995. URL <http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IscisScript=iah/iah.xis&src=google&base=PAH0&lang=p&nextAction=lnk&exprSearch=19601&indexSearch=ID>. ISBN : 9789275130421 Publisher : Pan American Health Organization.
- [87] B. R. Evans, P. Kotsakiozi, A. L. Costa-da Silva, R. S. Ioshino, L. Garziera, M. C. Pedrosa, A. Malavasi, J. F. Virginio, M. L. Capurro, and J. R. Powell. Transgenic *Aedes aegypti* Mosquitoes Transfer Genes into a Natural Population. *Scientific Reports*, 9(1) :13047, Sept. 2019. ISSN 2045-2322. doi: 10.1038/s41598-019-49660-6. URL <https://www.nature.com/articles/s41598-019-49660-6>. Number : 1 Publisher : Nature Publishing Group.
- [88] T. P. Evans and S. R. Bishop. A spatial model with pulsed releases to compare strategies for the sterile insect technique applied to the mosquito *Aedes aegypti*. *Mathematical Biosciences*, 254(Supplement C) :6–27, Aug. 2014. ISSN 0025-5564. doi: 10.1016/j.mbs.2014.06.001. URL <http://www.sciencedirect.com/science/article/pii/S0025556414001072>.
- [89] P. Ezanno, M. Aubry-Kientz, S. Arnoux, P. Cailly, G. L’Ambert, C. Toty, T. Balenghien, and A. Tran. A generic weather-driven model to predict mosquito population dynamics applied

BIBLIOGRAPHIE

- to species of Anopheles, Culex and Aedes genera of southern France. *Preventive veterinary medicine*, 120, Jan. 2015. doi: 10.1016/j.prevetmed.2014.12.018.
- [90] A. Faraji and I. Unlu. The Eye of the Tiger, the Thrill of the Fight : Effective Larval and Adult Control Measures Against the Asian Tiger Mosquito, *Aedes albopictus* (Diptera : Culicidae), in North America. *J Med Entomol*, 53(5) :1029–1047, Sept. 2016. ISSN 0022-2585. doi: 10.1093/jme/tjw096. URL <https://academic.oup.com/jme/article/53/5/1029/2240844>.
- [91] R. Fay, D. A. Eliason, and others. A preferred oviposition site as a surveillance method for *Aedes aegypti*. *Mosq news*, 26(4) :531–5, 1966.
- [92] K. R. Fister, M. L. McCarthy, S. F. Oppenheimer, and C. Collins. Optimal control of insects through sterile insect release and habitat modification. *Math. Biosci.*, 244(2) :201–212, Aug. 2013. ISSN 0025-5564. doi: 10.1016/j.mbs.2013.05.008. WOS :000322805400014.
- [93] H. A. Flores and S. L. O’Neill. Controlling vector-borne diseases by releasing modified mosquitoes. *Nature Reviews Microbiology*, May 2018. ISSN 1740-1526, 1740-1534. doi: 10.1038/s41579-018-0025-0. URL <http://www.nature.com/articles/s41579-018-0025-0>.
- [94] D. Fontenille, T. Balenghien, D. Bley, J. Desenclos, C. Lagneau, E. Malin, and M. Setbon. Comment la recherche contribue-t-elle à l’amélioration de la LAV ? 2009.
- [95] D. Fontenille, C. Lagneau, S. Lecollinet, R. LEFAIT-ROBIN, M. SETBON, B. Tirel, and A. Yebakima. *La lutte antivectorielle en France*. IRD Éditions. 2009.
- [96] C. Fouet and C. Kamdem. Integrated Mosquito Management : Is Precision Control a Luxury or Necessity? *Trends Parasitol*, 35(1) :85–95, Jan. 2019. ISSN 1471-4922. doi: 10.1016/j.pt.2018.10.004. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6503858/>.
- [97] R. Gaugler, D. Suman, and Y. Wang. An autodissemination station for the transfer of an insect growth regulator to mosquito oviposition sites. *Medical and Veterinary Entomology*, 26 (1) :37–45, Mar. 2012. ISSN 1365-2915. doi: 10.1111/j.1365-2915.2011.00970.x. URL <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2915.2011.00970.x/full>.
- [98] J. E. Gentile, S. S. C. Rund, and G. R. Madey. Modelling sterile insect technique to control the population of *Anopheles gambiae*. *Malar. J.*, 14 :92, Feb. 2015. ISSN 1475-2875. doi: 10.1186/s12936-015-0587-5. WOS :000350605300001.
- [99] S. Giron, F. Franke, A. Decoppet, B. Cadiou, T. Travaglini, L. Thirion, G. Durand, C. Jeanin, G. L’Ambert, G. Grard, H. Noël, N. Fournet, M. Auzet-Caillaud, C. Zandotti, S. Aboukaïs, P. Chaud, S. Guedj, L. Hamouda, X. Naudot, A. Ovize, C. Lazarus, H. d. Valk, M.-C. Paty, and I. Leparç-Goffart. Vector-borne transmission of Zika virus in Europe, southern France, August 2019. *Eurosurveillance*, 24(45) :1900655, Nov. 2019. ISSN 1560-7917. doi: 10.2807/1560-7917.ES.2019.24.45.1900655. URL <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2019.24.45.1900655>. Publisher : European Centre for Disease Prevention and Control.

BIBLIOGRAPHIE

- [100] C. Golstein, P. Boireau, and J.-C. Pagès. Benefits and limitations of emerging techniques for mosquito vector control. *Comptes Rendus Biologies*, 342(7) :270–272, Sept. 2019. ISSN 1631-0691. doi: 10.1016/j.crvi.2019.09.024. URL <http://www.sciencedirect.com/science/article/pii/S1631069119301131>.
- [101] C. M. Gossner, E. Ducheyne, and F. Schaffner. Increased risk for autochthonous vector-borne infections transmitted by *Aedes albopictus* in continental Europe. *Eurosurveillance*, 23(24) :1800268, June 2018. ISSN 1560-7917. doi: 10.2807/1560-7917.ES.2018.23.24.1800268. URL <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2018.23.24.1800268>. Publisher : European Centre for Disease Prevention and Control.
- [102] P. Gros. La représentation de l’espace dans les modèles de dynamique des populations. L’exemple des modèles dynamiques déterministes à temps et espace continus. Jan. 2001. URL <https://archimer.ifremer.fr/doc/00013/12409/>.
- [103] D. J. Gubler and G. G. Clark. Community involvement in the control of *Aedes aegypti*. *Acta Tropica*, 61(2) :169–179, Apr. 1996. ISSN 0001-706X. doi: 10.1016/0001-706X(95)00103-L. URL <http://www.sciencedirect.com/science/article/pii/0001706X9500103L>.
- [104] J.-F. Guégan and M. Choisy. *Introduction à l’épidémiologie intégrative*. De Boeck Supérieur, 2008.
- [105] M. Haramboure, P. Labbé, T. Baldet, D. Damiens, L. C. Gouagna, J. Bouyer, and A. Tran. Modelling the control of *Aedes albopictus* mosquitoes based on sterile males release techniques in a tropical environment. *Ecological Modelling*, 424 :109002, May 2020. ISSN 0304-3800. doi: 10.1016/j.ecolmodel.2020.109002. URL <http://www.sciencedirect.com/science/article/pii/S0304380020300740>.
- [106] M. Helinski and B. Knols. Mating competitiveness of male *Anopheles arabiensis* mosquitoes irradiated with a partially or fully sterilizing dose in small and large laboratory cages. *Journal of medical entomology*, 45(4) :698–705, 2008. Publisher : Oxford University Press Oxford, UK.
- [107] M. E. Helinski, A. G. Parker, and B. G. Knols. Radiation biology of mosquitoes. *Malar J*, 8(2) :S6, Nov. 2009. ISSN 1475-2875. doi: 10.1186/1475-2875-8-S2-S6. URL <https://doi.org/10.1186/1475-2875-8-S2-S6>.
- [108] R.-W. S. Hendron and M. B. Bonsall. The interplay of vaccination and vector control on small dengue networks. *Journal of Theoretical Biology*, 407 :349–361, Oct. 2016. ISSN 00225193. doi: 10.1016/j.jtbi.2016.07.034. URL <http://linkinghub.elsevier.com/retrieve/pii/S0022519316302181>.
- [109] K. Hilgenboecker, P. Hammerstein, P. Schlattmann, A. Telschow, and J. H. Werren. How many species are infected with *Wolbachia*? – a statistical analysis of current data. *FEMS Microbiol Lett*, 281(2) :215–220, Apr. 2008. ISSN 0378-1097. doi: 10.1111/j.1574-6968.2008.01110.x. URL <https://academic.oup.com/femsle/article/281/2/215/475300>. Publisher : Oxford Academic.

BIBLIOGRAPHIE

- [110] A. A. Hoffmann, I. Iturbe-Ormaetxe, A. G. Callahan, B. L. Phillips, K. Billington, J. K. Axford, B. Montgomery, A. P. Turley, and S. L. O'Neill. Stability of the wMel Wolbachia Infection following Invasion into *Aedes aegypti* Populations. *PLOS Neglected Tropical Diseases*, 8(9) :e3115, Sept. 2014. ISSN 1935-2735. doi: 10.1371/journal.pntd.0003115. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003115>. Publisher : Public Library of Science.
- [111] C. S. Holling. The strategy of building models of complex ecological systems. *Systems analysis in ecology*, pages 195–214, 1966. Publisher : Academic Press New York.
- [112] M. Huang, X. Song, and J. Li. Modelling and analysis of impulsive releases of sterile mosquitoes. *J. Biol. Dyn.*, 11(1) :147–171, 2017. ISSN 1751-3758. doi: 10.1080/17513758.2016.1254286. WOS :000389042600004.
- [113] Y. Huang, Y. Qin, H. Feng, P. Wan, and Z. Li. Modeling the evolution of insect resistance to one- and two-toxin Bt-crops in spatially heterogeneous environments. *Ecological Modelling*, 347 (Supplement C) :72–84, Mar. 2017. ISSN 0304-3800. doi: 10.1016/j.ecolmodel.2017.01.001. URL <http://www.sciencedirect.com/science/article/pii/S0304380017300066>.
- [114] R. Isea. Analysis of an SEIR-SEI four-strain epidemic dengue model with primary and secondary infections. *arXiv :1406.4155 [q-bio]*, June 2014. URL <http://arxiv.org/abs/1406.4155>. arXiv : 1406.4155.
- [115] C. Isidoro, N. Fachada, F. Barata, and A. Rosa. Agent-Based Model of Dengue Disease Transmission by *Aedes aegypti* Populations. In G. Kampis, I. Karsai, and E. Szathmáry, editors, *Advances in Artificial Life. Darwin Meets von Neumann*, Lecture Notes in Computer Science, pages 345–352, Berlin, Heidelberg, 2011. Springer. ISBN 978-3-642-21283-3. doi: 10.1007/978-3-642-21283-3_43.
- [116] T. Itoh, H. Kawada, A. Abe, Y. Eshita, Y. Rongsriyam, and A. Igarashi. Utilization of bloodfed females of *Aedes aegypti* as a vehicle for the transfer of the insect growth regulator pyriproxyfen to larval habitats. *J. Am. Mosq. Control Assoc.*, 10(3) :344–347, Sept. 1994. ISSN 8756-971X.
- [117] D. P. Iyaloo, J. Bouyer, S. Facknath, and A. Bheecarry. Pilot Suppression trial of *Aedes albopictus* mosquitoes through an Integrated Vector Management strategy including the Sterile Insect Technique in Mauritius. *bioRxiv*, page 2020.09.06.284968, Sept. 2020. doi: 10.1101/2020.09.06.284968. URL <https://www.biorxiv.org/content/10.1101/2020.09.06.284968v1>. Publisher : Cold Spring Harbor Laboratory Section : New Results.
- [118] B. J. Johnson, S. A. Ritchie, and D. M. Fonseca. The State of the Art of Lethal Oviposition Trap-Based Mass Interventions for Arboviral Control. *Insects*, 8(1) :5, Mar. 2017. doi: 10.3390/insects8010005. URL <https://www.mdpi.com/2075-4450/8/1/5>.
- [119] B. Kay and V. S. Nam. New strategy against *Aedes aegypti* in Vietnam. *The Lancet*, 365 (9459) :613–617, Feb. 2005. ISSN 0140-6736. doi: 10.1016/S0140-6736(05)17913-6. URL <http://www.sciencedirect.com/science/article/pii/S0140673605179136>.

BIBLIOGRAPHIE

- [120] M. J. Keeling and K. T. Eames. Networks and epidemic models. *Journal of The Royal Society Interface*, 2(4) :295–307, Sept. 2005. doi: 10.1098/rsif.2005.0051. URL <https://royalsocietypublishing.org/doi/full/10.1098/rsif.2005.0051>. Publisher : Royal Society.
- [121] W. O. Kermack, A. G. McKendrick, and G. T. Walker. A contribution to the mathematical theory of epidemics. *Proceedings of the Royal Society of London. Series A, Containing Papers of a Mathematical and Physical Character*, 115(772) :700–721, Aug. 1927. doi: 10.1098/rspa.1927.0118. URL <https://royalsocietypublishing.org/doi/abs/10.1098/rspa.1927.0118>. Publisher : Royal Society.
- [122] P. Kittayapong, U. Chansang, C. Chansang, and A. Bhumiratana. Community Participation and Appropriate Technologies for Dengue Vector Control at Transmission Foci in Thailand. *moco*, 22(3) :538–546, Sept. 2006. ISSN 8756-971X, 1943-6270. doi: 10.2987/8756-971X(2006)22[538:CPAATF]2.0.CO;2. URL [https://bioone.org/journals/journal-of-the-american-mosquito-control-association/volume-22/issue-3/8756-971X\(2006\)22\[538:CPAATF\]2.0.CO;2/Community-Participation-and-Appropriate-Technologies-for-Dengue-Vector-Control-at-10.2987/8756-971X\(2006\)22\[538:CPAATF\]2.0.CO;2.full](https://bioone.org/journals/journal-of-the-american-mosquito-control-association/volume-22/issue-3/8756-971X(2006)22[538:CPAATF]2.0.CO;2/Community-Participation-and-Appropriate-Technologies-for-Dengue-Vector-Control-at-10.2987/8756-971X(2006)22[538:CPAATF]2.0.CO;2.full). Publisher : The American Mosquito Control Association.
- [123] A. Klaptocz, J. Germann, W. Ponsot, O. Lopez, S. Bothner, P. Meier, J. Bouyer, N. Culbert, T. Wallner, G. Salvador, A. Dicko, R. Argilles-Herrero, J. F. Virginio, M. Gómez, F. Almeida, M. C. Pedrosa, A. T. Pinto, and L. Garziera. Drone-based Aerial Release Mechanism for Mosquitoes. Technical Report v1.0, Apr. 2018.
- [124] W. Klassen and C. F. Curtis. History of the Sterile Insect Technique. In V. A. Dyck, J. Hendrichs, and A. Robinson, editors, *Sterile Insect Technique : Principles and Practice in Area-Wide Integrated Pest Management*, pages 3–36. Springer Netherlands, Dordrecht, 2005. ISBN 978-1-4020-4051-1. doi: 10.1007/1-4020-4051-2_1. URL https://doi.org/10.1007/1-4020-4051-2_1.
- [125] M. U. Kraemer, M. E. Sinka, K. A. Duda, A. Q. Mylne, F. M. Shearer, C. M. Barker, C. G. Moore, R. G. Carvalho, G. E. Coelho, W. Van Bortel, G. Hendrickx, F. Schaffner, I. R. Elyazar, H.-J. Teng, O. J. Brady, J. P. Messina, D. M. Pigott, T. W. Scott, D. L. Smith, G. W. Wint, N. Golding, and S. I. Hay. The global distribution of the arbovirus vectors *Aedes aegypti* and *Ae. albopictus*. *eLife*, 4 :e08347, June 2015. ISSN 2050-084X. doi: 10.7554/eLife.08347. URL <https://doi.org/10.7554/eLife.08347>. Publisher : eLife Sciences Publications, Ltd.
- [126] U. Kröckel, A. Rose, Á. E. Eiras, and M. Geier. NEW TOOLS FOR SURVEILLANCE OF ADULT YELLOW FEVER MOSQUITOES : COMPARISON OF TRAP CATCHES WITH HUMAN LANDING RATES IN AN URBAN ENVIRONMENT. *moco*, 22(2) :229–238, June 2006. ISSN 8756-971X, 1943-6270. doi: 10.2987/8756-971X(2006)22[229:NTFSOA]2.0.CO;2. URL <https://bioone.org/journals/Journal-of-the-American-Mosquito-Control-Association/>

BIBLIOGRAPHIE

volume-22/issue-2/8756-971X(2006)22[229:NTFSOA]2.0.CO;2/
NEW-TOOLS-FOR-SURVEILLANCE-OF-ADULT-YELLOW-FEVER-MOSQUITOES/10.2987/
8756-971X(2006)22[229:NTFSOA]2.0.CO;2.full.

- [127] P. Labbe, T. Lenormand, and M. Raymond. On the worldwide spread of an insecticide resistance gene : a role for local selection. *Journal of Evolutionary Biology*, 18(6) :1471–1484, 2005. ISSN 1420-9101. doi: 10.1111/j.1420-9101.2005.00938.x. URL <https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1420-9101.2005.00938.x>.
_eprint : <https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1420-9101.2005.00938.x>.
- [128] P. Labbé, C. Berticat, A. Berthomieu, S. Unal, C. Bernard, M. Weill, and T. Lenormand. Forty Years of Erratic Insecticide Resistance Evolution in the Mosquito *Culex pipiens*. *PLOS Genetics*, 3(11) :e205, Nov. 2007. ISSN 1553-7404. doi: 10.1371/journal.pgen.0030205. URL <https://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.0030205>. Publisher : Public Library of Science.
- [129] P. Labbé, H. Alout, L. Djogbénou, N. Pasteur, and M. Weill. 14 - Evolution of Resistance to Insecticide in Disease Vectors. In M. Tibayrenc, editor, *Genetics and Evolution of Infectious Disease*, pages 363–409. Elsevier, London, Jan. 2011. ISBN 978-0-12-384890-1. doi: 10.1016/B978-0-12-384890-1.00014-5. URL <http://www.sciencedirect.com/science/article/pii/B9780123848901000145>.
- [130] R. Lacroix, H. Delatte, T. Hue, J. S. Dehecq, and P. Reiter. Adaptation of the BG-Sentinel trap to capture male and female *Aedes albopictus* mosquitoes. *Medical and Veterinary Entomology*, 23(2) :160–162, 2009. ISSN 1365-2915. doi: 10.1111/j.1365-2915.2009.00806.x. URL <https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2915.2009.00806.x>.
- [131] R. Lacroix, H. Delatte, T. Hue, and P. Reiter. Dispersal and Survival of Male and Female *Aedes albopictus* (Diptera : Culicidae) on Réunion Island. *Entomology*, 46(5) : 1117–1124, Sept. 2009. ISSN 0022-2585, 1938-2928. doi: 10.1603/033.046.0519. URL <https://bioone.org/journals/Journal-of-Medical-Entomology/volume-46/issue-5/033.046.0519/Dispersal-and-Survival-of-Male-and-Female-iAedes-albopictus-i/10.1603/033.046.0519.full>.
- [132] B. Lapied, F. Darriet, R. Delorme, J. Devillers, J.-P. Jaeger, C. Lagneau, F. Quiniou, and A. Yébakima. Hiérarchisation des insecticides potentiellement utilisables en lutte anti-vectorielle (LAV). Technical report, anses Agence nationale de sécurité sanitaire, de l'alimentation, de l'agriculture et de la pêche, 2013.
- [133] L. Laroche, S. Ravel, T. Baldet, R. Lancelot, F. Chandre, M. Rossignol, V. Le Goff, M. Duhayon, J.-F. Fafet, A. G. Parker, and J. Bouyer. Boosting the sterile insect technique with pyriproxyfen increases tsetse flies *Glossina palpalis gambiensis* sterilization in controlled conditions. *Scientific Reports*, 10(1) :9947, June 2020. ISSN 2045-2322. doi: 10.1038/s41598-020-66850-9. URL <https://www.nature.com/articles/s41598-020-66850-9>. Number : 1 Publisher : Nature Publishing Group.

BIBLIOGRAPHIE

- [134] A. C. Latreille, P. Milesi, H. Magalon, P. Mavingui, and C. M. Atyame. High genetic diversity but no geographical structure of *Aedes albopictus* populations in Réunion Island. *Parasit Vectors*, 12(1) :597, Dec. 2019. ISSN 1756-3305. doi: 10.1186/s13071-019-3840-x.
- [135] H. Laven. Speciation and evolution in *Culex pipiens*. *Genetics of insect vectors of disease*, pages 251–275, 1967. Publisher : Elsevier.
- [136] G. Le Goff, D. Damiens, A.-H. Ruttee, L. Payet, C. Lebon, J.-S. Dehecq, and L.-C. Gouagna. Field evaluation of seasonal trends in relative population sizes and dispersal pattern of *Aedes albopictus* males in support of the design of a sterile male release strategy. *Parasites & Vectors*, 12(1) :81, Feb. 2019. ISSN 1756-3305. doi: 10.1186/s13071-019-3329-7. URL <https://doi.org/10.1186/s13071-019-3329-7>.
- [137] R. Lees, J. Gilles, J. Hendrichs, M. Vreysen, and K. Bourtzis. Back to the future : the sterile insect technique against mosquito disease vectors. *Current Opinion in Insect Science*, 10 :156–162, Aug. 2015. doi: 10.1016/j.cois.2015.05.011.
- [138] T. Lenormand, D. Bourguet, T. Guillemaud, and M. Raymond. Tracking the evolution of insecticide resistance in the mosquito *Culex pipiens*. *Nature*, 400(6747) :861–864, Aug. 1999. ISSN 1476-4687. doi: 10.1038/23685. URL <https://www.nature.com/articles/23685/>. Number : 6747 Publisher : Nature Publishing Group.
- [139] Les services de l’Etat à La Réunion. Détection d’une nouvelle mouche des fruits à La Réunion (*Bactrocera dorsalis*) - Dispositif de lutte, May 2017. URL <http://www.reunion.gouv.fr/detection-d-une-nouvelle-mouche-des-fruits-a-la-a2844.html>. Last Modified : 2017-05-19.
- [140] J. Li and Z. Yuan. Modelling releases of sterile mosquitoes with different strategies. *Journal of Biological Dynamics*, 9(1) :1–14, Jan. 2015. ISSN 1751-3758. doi: 10.1080/17513758.2014.977971. URL <https://doi.org/10.1080/17513758.2014.977971>.
- [141] M.-T. Li, G.-Q. Sun, L. Yakob, H.-P. Zhu, Z. Jin, and W.-Y. Zhang. The Driving Force for 2014 Dengue Outbreak in Guangdong, China. *PLOS ONE*, 11(11) :e0166211, Nov. 2016. ISSN 1932-6203. doi: 10.1371/journal.pone.0166211. URL <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0166211>.
- [142] R. Li, L. Xu, O. N. Bjørnstad, K. Liu, T. Song, A. Chen, B. Xu, Q. Liu, and N. C. Stenseth. Climate-driven variation in mosquito density predicts the spatiotemporal dynamics of dengue. *PNAS*, 116(9) :3624–3629, Feb. 2019. ISSN 0027-8424, 1091-6490. doi: 10.1073/pnas.1806094116. URL <https://www.pnas.org/content/116/9/3624>.
- [143] C. Linard, N. Ponçon, D. Fontenille, and E. F. Lambin. A multi-agent simulation to assess the risk of malaria re-emergence in southern France. *Ecological Modelling*, 220(2) : 160–174, Jan. 2009. ISSN 0304-3800. doi: 10.1016/j.ecolmodel.2008.09.001. URL <http://www.sciencedirect.com/science/article/pii/S0304380008004304>.

BIBLIOGRAPHIE

- [144] E. Lindh, C. Argentini, M. E. Remoli, C. Fortuna, G. Faggioni, E. Benedetti, A. Amendola, G. Marsili, F. Lista, G. Rezza, and G. Venturi. The Italian 2017 Outbreak Chikungunya Virus Belongs to an Emerging *Aedes albopictus*-Adapted Virus Cluster Introduced From the Indian Subcontinent. *Open Forum Infect Dis*, 6(1), Dec. 2018. ISSN 2328-8957. doi: 10.1093/ofid/ofy321. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6345083/>.
- [145] L.-j. LIU, Y.-j. CAO, G.-q. ZHANG, and X.-l. TONG. Predation of *Gambusia affinis* (Baird et Girard) to *Aedes albopictus* Skuse [J]. *Journal of Pathogen Biology*, 11, 2008.
- [146] X. S. Liu and D. H. Dean. Redesigning *Bacillus thuringiensis* Cry1Aa toxin into a mosquito toxin. *Protein Eng Des Sel*, 19(3) :107–111, Mar. 2006. ISSN 1741-0126. doi: 10.1093/protein/gzj009. URL <https://academic.oup.com/peds/article/19/3/107/1524417>. Publisher : Oxford Academic.
- [147] L. P. Lounibos. Invasions by Insect Vectors of Human Disease. *Annual Review of Entomology*, 47(1) :233–266, 2002. doi: 10.1146/annurev.ento.47.091201.145206. URL <https://doi.org/10.1146/annurev.ento.47.091201.145206>.
- [148] A. M. Lutambi, M. A. Penny, T. Smith, and N. Chitnis. Mathematical modelling of mosquito dispersal in a heterogeneous environment. *Mathematical Biosciences*, 241(2) :198–216, Feb. 2013. ISSN 0025-5564. doi: 10.1016/j.mbs.2012.11.013. URL <http://www.sciencedirect.com/science/article/pii/S0025556412002337>.
- [149] C. Lutrat, D. Giesbrecht, E. Marois, S. Whyard, T. Baldet, and J. Bouyer. Sex Sorting for Pest Control : It’s Raining Men! *Trends in Parasitology*, 35(8) :649–662, Aug. 2019. ISSN 1471-4922. doi: 10.1016/j.pt.2019.06.001. URL <http://www.sciencedirect.com/science/article/pii/S1471492219301321>.
- [150] A. J. Mackay, M. Amador, and R. Barrera. An improved autocidal gravid ovitrap for the control and surveillance of *Aedes aegypti*. *Parasites & Vectors*, 6(1) :225, Aug. 2013. ISSN 1756-3305. doi: 10.1186/1756-3305-6-225. URL <https://doi.org/10.1186/1756-3305-6-225>.
- [151] S. Mahevas. Simulation de la dynamique de pêche : modélisation, complexité et incertitude. June 2009. URL <https://archimer.ifremer.fr/doc/00000/7302/>.
- [152] J. W. Mains, C. L. Brelsfoard, and S. L. Dobson. Male Mosquitoes as Vehicles for Insecticide. *PLOS Neglected Tropical Diseases*, 9(1) :e0003406, Jan. 2015. ISSN 1935-2735. doi: 10.1371/journal.pntd.0003406. URL <http://dx.plos.org/10.1371/journal.pntd.0003406>.
- [153] A. Maiti, B. Patra, and G. P. Samanta. Sterile insect release method as a control measure of insect pests : A mathematical model. *J. Appl. Math. Comput.*, 22(3) :71–86, Oct. 2006. ISSN 1598-5865, 1865-2085. doi: 10.1007/BF02832038. URL <https://link.springer.com/article/10.1007/BF02832038>.
- [154] M. P. Mammen Jr, C. Pingate, C. J. Koenraadt, A. L. Rothman, J. Aldstadt, A. Nisalak, R. G. Jarman, J. W. Jones, A. Srikiatkachorn, C. A. Ypil-Butac, and others. Spatial and temporal

BIBLIOGRAPHIE

- clustering of dengue virus transmission in Thai villages. *PLoS Med*, 5(11) :e205, 2008. Publisher : Public Library of Science.
- [155] M. L. Mann Manyombe, B. Tsanou, J. Mbang, and S. Bowong. A metapopulation model for the population dynamics of anopheles mosquito. *Applied Mathematics and Computation*, 307 (Supplement C) :71–91, Aug. 2017. ISSN 0096-3003. doi: 10.1016/j.amc.2017.02.039. URL <http://www.sciencedirect.com/science/article/pii/S0096300317301509>.
- [156] F. Marini, B. Caputo, M. Pombi, G. Tarsitani, and A. D. Torre. Study of *Aedes albopictus* dispersal in Rome, Italy, using sticky traps in mark–release–recapture experiments. *Medical and Veterinary Entomology*, 24(4) :361–368, 2010. ISSN 1365-2915. doi: 10.1111/j.1365-2915.2010.00898.x. URL <https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2915.2010.00898.x>.
- [157] G. G. Marten and others. Elimination of *Aedes albopictus* from tire piles by introducing *Macrocyclus albidus* (Copepoda, Cyclopidae). *J Am Mosq Control Assoc*, 6 :689–693, 1990.
- [158] H. McCallum. *Population Parameters : Estimation for Ecological Models*. John Wiley & Sons, Apr. 2008. ISBN 978-0-470-75742-0.
- [159] J. M. Medlock, K. M. Hansford, F. Schaffner, V. Versteirt, G. Hendrickx, H. Zeller, and W. V. Bortel. A Review of the Invasive Mosquitoes in Europe : Ecology, Public Health Risks, and Control Options. *Vector-Borne and Zoonotic Diseases*, 12(6) :435–447, Apr. 2012. ISSN 1530-3667. doi: 10.1089/vbz.2011.0814. URL <https://www.liebertpub.com/doi/full/10.1089/VBZ.2011.0814>. Publisher : Mary Ann Liebert, Inc., publishers.
- [160] M. A. V. Melo-Santos, J. J. M. Varjal-Melo, A. P. Araújo, T. C. S. Gomes, M. H. S. Paiva, L. N. Regis, A. F. Furtado, T. Magalhaes, M. L. G. Macoris, M. T. M. Andrighetti, and C. F. J. Ayres. Resistance to the organophosphate temephos : Mechanisms, evolution and reversion in an *Aedes aegypti* laboratory strain from Brazil. *Acta Tropica*, 113(2) :180–189, Feb. 2010. ISSN 0001-706X. doi: 10.1016/j.actatropica.2009.10.015. URL <http://www.sciencedirect.com/science/article/pii/S0001706X09003350>.
- [161] Météo France. Pluies annuelles à la Réunion, 2019. URL <http://www.meteofrance.re/climat/pluies-annuelles>.
- [162] L. Mier-y Teran-Romero, A. J. Tatem, and M. A. Johansson. Mosquitoes on a plane : Disinsection will not stop the spread of vector-borne pathogens, a simulation study. *PLOS Neglected Tropical Diseases*, 11(7) :e0005683, July 2017. ISSN 1935-2735. doi: 10.1371/journal.pntd.0005683. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0005683>. Publisher : Public Library of Science.
- [163] P. Milesi, T. Lenormand, C. Lagneau, M. Weill, and P. Labbé. Relating fitness to long-term environmental variations in natura. *Molecular Ecology*, 25(21) :5483–5499, 2016. ISSN 1365-294X. doi: 10.1111/mec.13855. URL <https://onlinelibrary.wiley.com/doi/abs/10.1111/mec.13855>. _eprint : <https://onlinelibrary.wiley.com/doi/pdf/10.1111/mec.13855>.

BIBLIOGRAPHIE

- [164] A. Mishra, B. Ambrosio, S. Gakkhar, and M. A. Aziz-Alaoui. A Network Model for Control of Dengue Epidemic Using Sterile Insect Technique. *Math. Biosci. Eng.*, 15(2) :441–460, Apr. 2018. ISSN 1547-1063. doi: 10.3934/mbe.2018020. WOS :000412001800006.
- [165] O. mondiale de la Santé. Élimination du paludisme sur l’île de La Réunion : 40 ans plus tard. 2014. Publisher : Organisation mondiale de la Santé.
- [166] B. Mora. *L’épidémie de DENGUE à l’île de la Réunion en 1977-1978*. PhD Thesis, 1979.
- [167] L. A. Moreira, I. Iturbe-Ormaetxe, J. A. Jeffery, G. Lu, A. T. Pyke, L. M. Hedges, B. C. Rocha, S. Hall-Mendelin, A. Day, M. Riegler, L. E. Hugo, K. N. Johnson, B. H. Kay, E. A. McGraw, A. F. van den Hurk, P. A. Ryan, and S. L. O’Neill. A Wolbachia Symbiont in *Aedes aegypti* Limits Infection with Dengue, Chikungunya, and Plasmodium. *Cell*, 139(7) :1268–1278, Dec. 2009. ISSN 0092-8674. doi: 10.1016/j.cell.2009.11.042. URL <http://www.sciencedirect.com/science/article/pii/S0092867409015001>.
- [168] L. Multerer, T. Smith, and N. Chitnis. Modeling the impact of sterile males on an *Aedes aegypti* population with optimal control. *Mathematical Biosciences*, 311 :91–102, May 2019. ISSN 0025-5564. doi: 10.1016/j.mbs.2019.03.003. URL <http://www.sciencedirect.com/science/article/pii/S0025556418302505>.
- [169] V. S. Nam, N. T. Yen, H. M. Duc, T. C. Tu, V. T. Thang, N. H. Le, L. H. San, L. L. Loan, V. T. Q. Huong, L. H. K. Khanh, H. T. T. Trang, L. Z. Y. Lam, S. C. Kutcher, J. G. Aaskov, J. A. L. Jeffery, P. A. Ryan, and B. H. Kay. Community-Based Control of *Aedes aegypti* By Using *Mesocyclops* in Southern Vietnam. *The American Journal of Tropical Medicine and Hygiene*, 86(5) :850–859, May 2012. ISSN 0002-9637, 1476-1645. doi: 10.4269/ajtmh.2012.11-0466. URL <https://www.ajtmh.org/content/journals/10.4269/ajtmh.2012.11-0466>. Publisher : The American Society of Tropical Medicine and Hygiene.
- [170] R. Nauen. Insecticide resistance in disease vectors of public health importance. *Pest Management Science*, 63(7) :628–633, 2007. ISSN 1526-4998. doi: 10.1002/ps.1406. URL <https://onlinelibrary.wiley.com/doi/abs/10.1002/ps.1406>. _eprint : <https://onlinelibrary.wiley.com/doi/pdf/10.1002/ps.1406>.
- [171] E. A. C. Newton and P. Reiter. A Model of the Transmission of Dengue Fever with an Evaluation of the Impact of Ultra-Low Volume (ULV) Insecticide Applications on Dengue Epidemics. *The American Journal of Tropical Medicine and Hygiene*, 47(6) :709–720, Dec. 1992. ISSN 0002-9637, 1476-1645. doi: 10.4269/ajtmh.1992.47.709. URL <https://www.ajtmh.org/content/journals/10.4269/ajtmh.1992.47.709>. Publisher : The American Society of Tropical Medicine and Hygiene.
- [172] M. L. Niebylski and G. B. Craig. Dispersal and survival of *Aedes albopictus* at a scrap tire yard in Missouri. *J. Am. Mosq. Control Assoc.*, 10(3) :339–343, Sept. 1994. ISSN 8756-971X.
- [173] C. Nielsen-Ieroux, N. Pasteur, J. Prêtre, J.-f. Charles, H. Ben Sheikh, and C. Chevillon. High Resistance to *Bacillus sphaericus* Binary Toxin in *Culex pipiens* (Diptera : Culicidae) : The

BIBLIOGRAPHIE

- Complex Situation of West Mediterranean Countries. *J Med Entomol*, 39(5) :729–735, Sept. 2002. ISSN 0022-2585. doi: 10.1603/0022-2585-39.5.729. URL <https://academic.oup.com/jme/article/39/5/729/954483>. Publisher : Oxford Academic.
- [174] Norman, Gratz. Critical review of the vector status of *Aedes albopictus*. *Medical and Veterinary Entomology*, 2004. URL <http://onlinelibrary.wiley.com/doi/10.1111/j.0269-283X.2004.00513.x/full>.
- [175] C. F. Oliva, M. Jacquet, J. Gilles, G. Lemperiere, P.-O. Maquart, S. Quilici, F. Schooneman, M. J. B. Vreysen, and S. Boyer. The Sterile Insect Technique for Controlling Populations of *Aedes albopictus* (Diptera : Culicidae) on Reunion Island : Mating Vigour of Sterilized Males. *PLOS ONE*, 7(11) :e49414, Nov. 2012. ISSN 1932-6203. doi: 10.1371/journal.pone.0049414. URL <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0049414>.
- [176] C. F. Oliva, D. Damiens, M. J. B. Vreysen, G. Lemperière, and J. Gilles. Reproductive Strategies of *Aedes albopictus* (Diptera : Culicidae) and Implications for the Sterile Insect Technique. *PLOS ONE*, 8(11) :e78884, Nov. 2013. ISSN 1932-6203. doi: 10.1371/journal.pone.0078884. URL <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0078884>.
- [177] C. F. Oliva, M. J. Maier, J. Gilles, M. Jacquet, G. Lemperiere, S. Quilici, M. J. B. Vreysen, F. Schooneman, D. D. Chadee, and S. Boyer. Effects of irradiation, presence of females, and sugar supply on the longevity of sterile males *Aedes albopictus* (Skuse) under semi-field conditions on Reunion Island. *Acta Trop.*, 125(3) :287–293, Mar. 2013. ISSN 1873-6254. doi: 10.1016/j.actatropica.2012.11.010.
- [178] C. F. Oliva, D. Damiens, and M. Q. Benedict. Male reproductive biology of *Aedes* mosquitoes. *Acta Tropica*, 132 :S12–S19, Apr. 2014. ISSN 0001-706X. doi: 10.1016/j.actatropica.2013.11.021. URL <http://www.sciencedirect.com/science/article/pii/S0001706X13003446>.
- [179] J. R. M. Oliveira, P. Gérardin, T. Couderc, H. Randrianaivo, X. Fritel, and M. Lecuit. Chikungunya virus-associated encephalitis : A cohort study on La Réunion Island, 2005–2009 Author Response. *Neurology*, 86(21) :2025–2026, May 2016. ISSN 0028-3878, 1526-632X. doi: 10.1212/WNL.0000000000002732. URL <https://n.neurology.org/content/86/21/2025>. Publisher : Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology Section : WriteClick® Editor’s Choice.
- [180] W. H. Organization. *Dengue : Guidelines for Diagnosis, Treatment, Prevention and Control*. WHO, 2009. ISBN 978-92-4-154787-1. Google-Books-ID : dlc0YSIyGYwC.
- [181] W. H. Organization. *World malaria report 2019*. World Health Organization, 2019.
- [182] W. H. Organization. *Dengue and severe dengue*. Technical report, World Health Organization, 2020.
- [183] W. H. Organization and R. O. f. S.-E. Asia. *Comprehensive Guideline for Prevention and Control of Dengue and Dengue Haemorrhagic Fever. Revised and expanded edition*. WHO Regional

BIBLIOGRAPHIE

- Office for South-East Asia, 2011. ISBN 978-92-9022-387-0. URL <https://apps.who.int/iris/handle/10665/204894>. Accepted : 2016-04-06T11 :32 :37Z.
- [184] W. H. Organization and others. Pesticides and their application : for the control of vectors and pests of public health importance. Technical report, World Health Organization, 2006.
- [185] W. H. Organization and others. WHO position statement on integrated vector management. *Weekly Epidemiological Record= Relevé épidémiologique hebdomadaire*, 83(20) :177–181, 2008.
- [186] W. H. Organization and others. Dengue vaccine : WHO position paper, July 2016–recommendations. *Vaccine*, 35(9) :1200–1201, 2017. Publisher : Elsevier.
- [187] W. H. Organization and others. Vector control. Technical report, World Health Organization. Regional Office for South-East Asia, 2017.
- [188] Organization World Health. Agir pour réduire l’impact mondial des maladies tropicales négligées : premier rapport de l’OMS sur les maladies tropicales négligées. In *Agir pour réduire l’impact mondial des maladies tropicales négligées : premier rapport de l’OMS sur les maladies tropicales négligées*, pages 172–172. 2011.
- [189] M. Otero, H. G. Solari, and N. Schweigmann. A Stochastic Population Dynamics Model for *Aedes Aegypti* : Formulation and Application to a City with Temperate Climate. *Bull. Math. Biol.*, 68(8) :1945–1974, Nov. 2006. ISSN 0092-8240, 1522-9602. doi: 10.1007/s11538-006-9067-y. URL <https://link.springer.com/article/10.1007/s11538-006-9067-y>.
- [190] N. Pasteur and G. Sinègre. Esterase polymorphism and sensitivity to dursban organophosphorus insecticide in *Culex pipiens pipiens* populations. *Biochem Genet*, 13(11) :789–803, Dec. 1975. ISSN 1573-4927. doi: 10.1007/BF00484411. URL <https://doi.org/10.1007/BF00484411>.
- [191] J. Patterson, M. Sammon, and M. Garg. Dengue, Zika and Chikungunya : Emerging Arboviruses in the New World. *West J Emerg Med*, 17(6) :671–679, Nov. 2016. ISSN 1936-900X. doi: 10.5811/westjem.2016.9.30904. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5102589/>.
- [192] C. Paupy, R. Girod, M. Salvan, F. Rodhain, and A.-B. Failloux. Population structure of *Aedes albopictus* from La Réunion Island (Indian Ocean) with respect to susceptibility to a dengue virus. *Heredity*, 87(3) :273–283, Sept. 2001. ISSN 1365-2540. doi: 10.1046/j.1365-2540.2001.00866.x. URL <https://www.nature.com/articles/6888660/>. Number : 3 Publisher : Nature Publishing Group.
- [193] C. Paupy, H. Delatte, L. Bagny, V. Corbel, and D. Fontenille. *Aedes albopictus*, an arbovirus vector : From the darkness to the light. *Microbes and Infection*, 11(14) :1177–1185, Dec. 2009. ISSN 1286-4579. doi: 10.1016/j.micinf.2009.05.005. URL <http://www.sciencedirect.com/science/article/pii/S1286457909001051>.

BIBLIOGRAPHIE

- [194] M. Perich, A. Kardec, I. Braga, I. Portal, R. Burge, B. Zeichner, W. Brogdon, and R. Wirtz. Field evaluation of a lethal ovitrap against dengue vectors in Brazil. *Medical and veterinary entomology*, 17(2) :205–210, 2003. Publisher : Wiley Online Library.
- [195] A. Perrin, A.-S. Gosselin-Grenet, M. Rossignol, C. Ginibre, B. Scheid, C. Lagneau, F. Chandre, T. Baldet, M. Ogliastro, and J. Bouyer. Mosquito densoviruses : the revival of a biological control agent against urban Aedes vectors of arboviruses. *bioRxiv*, page 2020.04.23.055830, Apr. 2020. doi: 10.1101/2020.04.23.055830. URL <https://www.biorxiv.org/content/10.1101/2020.04.23.055830v1>. Publisher : Cold Spring Harbor Laboratory Section : New Results.
- [196] L. Peyrebrune. Cartes de présence du moustique tigre (*Aedes albopictus*) en France métropolitaine. *Ministère des solidarités et de la santé*, 2020. URL <https://solidarites-sante.gouv.fr/sante-et-environnement/risques-microbiologiques-physiques-et-chimiques/especes-nuisibles-et-parasites/article/cartes-de-presence-du-moustique-tigre-aedes-albopictus>.
- [197] H. K. Phuc, M. H. Andreasen, R. S. Burton, C. Vass, M. J. Epton, G. Pape, G. Fu, K. C. Condon, S. Scaife, C. A. Donnelly, P. G. Coleman, H. White-Cooper, and L. Alphey. Late-acting dominant lethal genetic systems and mosquito control. *BMC Biol*, 5(1) :11, Mar. 2007. ISSN 1741-7007. doi: 10.1186/1741-7007-5-11. URL <https://doi.org/10.1186/1741-7007-5-11>.
- [198] D. R. J. Pleydell and J. Bouyer. Biopesticides improve efficiency of the sterile insect technique for controlling mosquito-driven dengue epidemics. *Communications Biology*, 2(1) :201, May 2019. ISSN 2399-3642. doi: 10.1038/s42003-019-0451-1. URL <https://www.nature.com/articles/s42003-019-0451-1>.
- [199] A. Ponlawat and L. C. Harrington. Blood Feeding Patterns of *Aedes aegypti* and *Aedes albopictus* in Thailand. *J Med Entomol*, 42(5) :844–849, Sept. 2005. ISSN 0022-2585. doi: 10.1093/jmedent/42.5.844. URL <https://academic.oup.com/jme/article/42/5/844/863877>. Publisher : Oxford Academic.
- [200] M. Proverbs. Induced sterilization and control of insects. *Annual review of entomology*, 14(1) : 81–102, 1969. Publisher : Annual Reviews 4139 El Camino Way, PO Box 10139, Palo Alto, CA 94303-0139, USA.
- [201] R. C. Reiner, T. A. Perkins, C. M. Barker, T. Niu, L. F. Chaves, A. M. Ellis, D. B. George, A. Le Menach, J. R. C. Pulliam, D. Bisanzio, C. Buckee, C. Chiyaka, D. A. T. Cummings, A. J. Garcia, M. L. Gattton, P. W. Gething, D. M. Hartley, G. Johnston, E. Y. Klein, E. Michael, S. W. Lindsay, A. L. Lloyd, D. M. Pigott, W. K. Reisen, N. Ruktanonchai, B. K. Singh, A. J. Tatem, U. Kitron, S. I. Hay, T. W. Scott, and D. L. Smith. A systematic review of mathematical models of mosquito-borne pathogen transmission : 1970–2010. *Journal of The Royal Society Interface*, 10(81) :20120921, Apr. 2013. doi: 10.1098/rsif.2012.0921. URL <https://royalsocietypublishing.org/doi/full/10.1098/rsif.2012.0921>. Publisher : Royal Society.

BIBLIOGRAPHIE

- [202] P. Reiter. *Aedes albopictus* and the world trade in used tires, 1988-1995 : the shape of things to come?. *Journal of the American Mosquito Control Association*, 14(1) :83–94, 1998. URL http://archive.org/details/cbarchive_103653_aedesalbopictusandtheworldtrad1998.
- [203] P. Reiter, M. A. Amador, R. A. Anderson, and G. G. Clark. Short Report : Dispersal of *Aedes aegypti* in an Urban Area after Blood Feeding as Demonstrated by Rubidium-Marked Eggs. *The American Journal of Tropical Medicine and Hygiene*, 52(2) :177–179, Feb. 1995. ISSN 0002-9637, 1476-1645. doi: 10.4269/ajtmh.1995.52.177. URL <https://www.ajtmh.org/content/journals/10.4269/ajtmh.1995.52.177>. Publisher : The American Society of Tropical Medicine and Hygiene.
- [204] P. Renault, J.-L. Solet, D. Sissoko, E. Balleydier, S. Larrieu, L. Filleul, C. Lassalle, J. Thiria, E. Rachou, H. d. Valk, D. Ilef, M. Ledrans, I. Quatresous, P. Quenel, and V. Pierre. A Major Epidemic of Chikungunya Virus Infection on Réunion Island, France, 2005–2006. *The American Journal of Tropical Medicine and Hygiene*, 77(4) :727–731, Oct. 2007. ISSN 0002-9637, 1476-1645. doi: 10.4269/ajtmh.2007.77.727. URL <https://www.ajtmh.org/content/journals/10.4269/ajtmh.2007.77.727>. Publisher : The American Society of Tropical Medicine and Hygiene.
- [205] G. Rezza. *Aedes albopictus* and the reemergence of Dengue. *BMC Public Health*, 12(1) :72, Jan. 2012. ISSN 1471-2458. doi: 10.1186/1471-2458-12-72. URL <https://doi.org/10.1186/1471-2458-12-72>.
- [206] G. Rezza, L. Nicoletti, R. Angelini, R. Romi, A. Finarelli, M. Panning, P. Cordioli, C. Fortuna, S. Boros, F. Magurano, G. Silvi, P. Angelini, M. Dottori, M. Ciufolini, G. Majori, and A. Cassone. Infection with chikungunya virus in Italy : an outbreak in a temperate region. *The Lancet*, 370 (9602) :1840–1846, Dec. 2007. ISSN 0140-6736. doi: 10.1016/S0140-6736(07)61779-6. URL <http://www.sciencedirect.com/science/article/pii/S0140673607617796>.
- [207] S. A. Ritchie, S. Long, A. Hart, C. E. Webb, and R. C. Russell. An adulticidal sticky ovitrap for sampling container-breeding mosquitoes. *J. Am. Mosq. Control Assoc.*, 19(3) :235–242, Sept. 2003. ISSN 8756-971X.
- [208] S. A. Ritchie, L. P. Rapley, C. Williams, P. H. Johnson, M. Larkman, R. M. Silcock, S. A. Long, and R. C. Russell. A lethal ovitrap-based mass trapping scheme for dengue control in Australia : I. Public acceptability and performance of lethal ovitraps. *Medical and Veterinary Entomology*, 23(4) :295–302, 2009. ISSN 1365-2915. doi: 10.1111/j.1365-2915.2009.00833.x. URL <https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2915.2009.00833.x>.
_eprint : <https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1365-2915.2009.00833.x>.
- [209] S. A. Ritchie, T. S. Buhagiar, M. Townsend, A. Hoffmann, A. F. van den Hurk, J. L. McMahon, and A. E. Eiras. Field Validation of the Gravid *Aedes* Trap (GAT) for Collection of *Aedes aegypti* (Diptera : Culicidae). *J Med Entomol*, 51(1) :210–219, Jan. 2014. ISSN 0022-2585. doi: 10.1603/ME13105. URL <https://academic.oup.com/jme/article/51/1/210/865868>. Publisher : Oxford Academic.

BIBLIOGRAPHIE

- [210] S. Rivas Morales. *Economics of vector-borne diseases prevention : The case of the Tiger Mosquito control and Chikungunya and Dengue prevention plan in the Emilia-Romagna region (Northern Italy)*. Tesi di dottorato, alma, June 2016. URL <http://amsdottorato.unibo.it/7683/>.
- [211] D. R. Roberts and R. G. Andre. Insecticide Resistance Issues in Vector-Borne Disease Control. *The American Journal of Tropical Medicine and Hygiene*, 50(6_Suppl) :21–34, Jan. 1994. ISSN 0002-9637, 1476-1645. doi: 10.4269/ajtmh.1994.50.21. URL <https://www.ajtmh.org/content/journals/10.4269/ajtmh.1994.50.21>. Publisher : The American Society of Tropical Medicine and Hygiene.
- [212] B. Roche, L. Léger, G. L’Ambert, G. Lacour, R. Foussadier, G. Besnard, H. Barré-Cardi, F. Simard, and D. Fontenille. The Spread of *Aedes albopictus* in Metropolitan France : Contribution of Environmental Drivers and Human Activities and Predictions for a Near Future. *PLOS ONE*, 10(5) :e0125600, May 2015. ISSN 1932-6203. doi: 10.1371/journal.pone.0125600. URL <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0125600>.
- [213] F. Rodhain. Fièvre jaune, dengue et autres arboviroses exotiques. *Encyclopédie Médico-Chirurgicale*, 2001.
- [214] I. Roditi and M. J. Lehane. Interactions between trypanosomes and tsetse flies. *Current Opinion in Microbiology*, 11(4) :345–351, Aug. 2008. ISSN 1369-5274. doi: 10.1016/j.mib.2008.06.006. URL <http://www.sciencedirect.com/science/article/pii/S1369527408000908>.
- [215] E. J. Rykiel. Testing ecological models : the meaning of validation. *Ecological Modelling*, 90(3) :229–244, Nov. 1996. ISSN 0304-3800. doi: 10.1016/0304-3800(95)00152-2. URL <http://www.sciencedirect.com/science/article/pii/0304380095001522>.
- [216] M. Salvan and J. Mouchet. *Aedes albopictus* et *Aedes aegypti* à l’île de La Réunion. *Ann Soc Belg Med Trop*, 74(4) :323–6, 1994.
- [217] Santé publique France. Dengue à la Réunion Augmentation du nombre de cas hebdomadaire. *Point de situation au 26 janvier 2020*, 2010.
- [218] R. G. Sargent. VERIFICATION AND VALIDATION OF SIMULATION MODELS. *IEEE Press*, page 18, 2007.
- [219] F. Schaffner, J. M. Medlock, and W. V. Bortel. Public health significance of invasive mosquitoes in Europe. *Clinical Microbiology and Infection*, 19(8) :685–692, Aug. 2013. ISSN 1198-743X. doi: 10.1111/1469-0691.12189. URL <http://www.sciencedirect.com/science/article/pii/S1198743X14614130>.
- [220] E. Scholte, M. Dik, A. Ibañez-Justicia, W. Den Hartog, B. Schoelitsz, M. Brooks, M. Braks, and M. Steeghs. Findings and control of two invasive exotic mosquito species, *Aedes albopictus* and *Ae. atropalpus* (Diptera : Culicidae) in the Netherlands, 2011. *Euro Mosq Bull*, 30 :1–14, 2012.

BIBLIOGRAPHIE

- [221] E.-J. Scholte, B. G. Knols, R. A. Samson, and W. Takken. Entomopathogenic fungi for mosquito control : A review. *J Insect Sci*, 4, June 2004. ISSN 1536-2442. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC528879/>.
- [222] J. Shaman. Amplification due to spatial clustering in an individual-based model of mosquito-avian arbovirus transmission. *Trans. Roy. Soc. Trop. Med. Hyg.*, 101(5) :469–483, May 2007. ISSN 0035-9203. doi: 10.1016/j.trstmh.2006.11.007.
- [223] D. S. Shepard, E. A. Undurraga, Y. A. Halasa, and J. D. Stanaway. The global economic burden of dengue : a systematic analysis. *The Lancet Infectious Diseases*, 16(8) :935–941, Aug. 2016. ISSN 1473-3099. doi: 10.1016/S1473-3099(16)00146-8. URL <http://www.sciencedirect.com/science/article/pii/S1473309916001468>.
- [224] M. Sihuinchá, E. Zamora-Perea, W. Orellana-Rios, J. D. Stancil, V. Lopez-Sifuentes, C. Vidal-Ore, and G. J. Devine. Potential Use of Pyriproxyfen for Control of *Aedes aegypti* (Diptera : Culicidae) in Iquitos, Perú | Journal of Medical Entomology. *VECTOR CONTROL, PEST MANAGEMENT, RESISTANCE, REPELLENTS*, 42(4) :620–630, 2005. URL <http://www.bioone.org/doi/abs/10.1603/0022-2585%282005%29042%5B0620%3APUOPFC%5D2.0.CO%3B2?journalCode=ment&>.
- [225] K. Soudani. Introduction à la modélisation en Biologie des Populations et des Ecosystèmes. *Université Paris-Sud*, 2010.
- [226] S. T. Stoddard, A. C. Morrison, G. M. Vazquez-Prokopec, V. P. Soldan, T. J. Kochel, U. Kitron, J. P. Elder, and T. W. Scott. The Role of Human Movement in the Transmission of Vector-Borne Pathogens. *PLOS Neglected Tropical Diseases*, 3(7) :e481, July 2009. ISSN 1935-2735. doi: 10.1371/journal.pntd.0000481. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0000481>. Publisher : Public Library of Science.
- [227] M. Strugarek, H. Bossin, and Y. Dumont. On the use of the sterile insect release technique to reduce or eliminate mosquito populations. *Applied Mathematical Modelling*, 68 :443–470, Apr. 2019. ISSN 0307-904X. doi: 10.1016/j.apm.2018.11.026. URL <http://www.sciencedirect.com/science/article/pii/S0307904X18305638>.
- [228] T. Su, J. Thieme, T. Lura, M.-L. Cheng, and M. Q. Brown. Susceptibility Profile of *Aedes aegypti* L. (Diptera : Culicidae) from Montclair, California, to Commonly Used Pesticides, With Note on Resistance to Pyriproxyfen. *J. Med. Entomol.*, 56(4) :1047–1054, 2019. ISSN 1938-2928. doi: 10.1093/jme/tjz019.
- [229] J. J. Sullivan and K. S. Goh. Environmental fate and properties of pyriproxyfen. *Journal of Pesticide Science*, 33(4) :339–350, 2008. doi: 10.1584/jpestics.R08-02.
- [230] D. S. Suman, A. Farajollahi, S. Healy, G. M. Williams, Y. Wang, G. Schoeler, and R. Gaugler. Point-source and area-wide field studies of pyriproxyfen autodissemination against urban container-inhabiting mosquitoes. *Acta Tropica*, 135 :96–103, July 2014. ISSN 0001-706X. doi:

BIBLIOGRAPHIE

- 10.1016/j.actatropica.2014.03.026. URL <http://www.sciencedirect.com/science/article/pii/S0001706X14001090>.
- [231] S. Syafruddin and M. Noorani. SEIR model for transmission of dengue fever in Selangor Malaysia. *IJMPS*, 9 :380–389, 2012.
- [232] M. L. Tantely, P. Tortosa, H. Alout, C. Berticat, A. Berthomieu, A. Rutee, J.-S. Dehecq, P. Makoundou, P. Labbé, N. Pasteur, and M. Weill. Insecticide resistance in *Culex pipiens quinquefasciatus* and *Aedes albopictus* mosquitoes from La Réunion Island. *Insect Biochemistry and Molecular Biology*, 40(4) :317–324, Apr. 2010. ISSN 0965-1748. doi: 10.1016/j.ibmb.2010.02.005. URL <http://www.sciencedirect.com/science/article/pii/S0965174810000342>.
- [233] Q. A. Ten Bosch, H. E. Clapham, L. Lambrechts, V. Duong, P. Buchy, B. M. Althouse, A. L. Lloyd, L. A. Waller, A. C. Morrison, U. Kitron, G. M. Vazquez-Prokopec, T. W. Scott, and T. A. Perkins. Contributions from the silent majority dominate dengue virus transmission. *PLoS Pathog.*, 14(5) :e1006965, 2018. ISSN 1553-7374. doi: 10.1371/journal.ppat.1006965.
- [234] H. Thieme. *Classic models of density-dependent population growth for single species. Mathematics in population biology*. Princeton, NJ : Princeton University Press, 2003.
- [235] J. Thuilliez, C. Bellia, J.-S. Dehecq, and O. Reilhes. Household-Level Expenditure on Protective Measures Against Mosquitoes on the Island of La Réunion, France. *PLoS Neglected Tropical Diseases*, 8(1) :e2609, Jan. 2014. ISSN 1935-2735. doi: 10.1371/journal.pntd.0002609. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0002609>. Publisher : Public Library of Science.
- [236] D. Tilman, C. L. Lehman, and P. Kareiva. Population dynamics in spatial habitats. *Spatial ecology : The role of space in population dynamics and interspecific interactions*, pages 3–20, 1997. Publisher : Princeton University Press Princeton, New Jersey.
- [237] D. Tom-Aba, P. M. Nguku, C. C. Arinze, and G. Krause. Assessing the Concepts and Designs of 58 Mobile Apps for the Management of the 2014-2015 West Africa Ebola Outbreak : Systematic Review. *JMIR Public Health Surveill*, 4(4) :e68, Oct. 2018. ISSN 2369-2960. doi: 10.2196/publichealth.9015.
- [238] A. Tran and M. Raffy. On the dynamics of dengue epidemics from large-scale information. *Theoretical Population Biology*, 69(1) :3–12, Feb. 2006. ISSN 0040-5809. doi: 10.1016/j.tpb.2005.06.008. URL <http://www.sciencedirect.com/science/article/pii/S0040580905000948>.
- [239] A. Tran, G. L’Ambert, G. Lacour, R. Benoît, M. Demarchi, M. Cros, P. Cailly, M. Aubry-Kientz, T. Balenghien, and P. Ezanno. A Rainfall- and Temperature-Driven Abundance Model for *Aedes albopictus* Populations. *International Journal of Environmental Research and Public Health*, 10(5) :1698–1719, Apr. 2013. doi: 10.3390/ijerph10051698. URL <http://www.mdpi.com/1660-4601/10/5/1698>.

BIBLIOGRAPHIE

- [240] A. Tran, M. Mangeas, M. Demarchi, E. Roux, P. Degenne, M. Haramboure, G. L. Goff, D. Damiens, L.-C. Gouagna, V. Herbreteau, and J.-S. Dehecq. Complementarity of empirical and process-based approaches to modelling mosquito population dynamics with *Aedes albopictus* as an example—Application to the development of an operational mapping tool of vector populations. *PLOS ONE*, 15(1) :e0227407, Jan. 2020. ISSN 1932-6203. doi: 10.1371/journal.pone.0227407. URL <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0227407>.
- [241] J. D. Trexler, C. S. Apperson, and C. Schal. Laboratory and Field Evaluations of Oviposition Responses of *Aedes albopictus* and *Aedes triseriatus* (Diptera : Culicidae) to Oak Leaf Infusions. *J Med Entomol*, 35(6) :967–976, Nov. 1998. ISSN 0022-2585. doi: 10.1093/jmedent/35.6.967. URL <https://academic.oup.com/jme/article/35/6/967/2221751>. Publisher : Oxford Academic.
- [242] M. Turner and S. R. Carpenter. Ecosystem Modeling for the 21st Century. *Ecosystems*, Nov. 2016. doi: 10.1007/s10021-016-0076-x.
- [243] M. G. Turner, R. H. Gardner, R. V. O’neill, and R. V. O’Neill. *Landscape ecology in theory and practice*, volume 401. Springer, 2001.
- [244] I. Unlu, A. Faraji, N. Indelicato, and D. M. Fonseca. The hidden world of Asian tiger mosquitoes : immature *Aedes albopictus* (Skuse) dominate in rainwater corrugated extension spouts. *Trans R Soc Trop Med Hyg*, 108(11) :699–705, Nov. 2014. ISSN 0035-9203. doi: 10.1093/trstmh/tru139. URL <https://academic.oup.com/trstmh/article/108/11/699/2765220>. Publisher : Oxford Academic.
- [245] I. Unlu, K. Klingler, N. Indelicato, A. Faraji, and D. Strickman. Suppression of *Aedes albopictus*, the Asian tiger mosquito, using a ‘hot spot’ approach. *Pest Management Science*, 72(7) :1427–1432, 2016. ISSN 1526-4998. doi: 10.1002/ps.4174. URL <https://onlinelibrary.wiley.com/doi/abs/10.1002/ps.4174>.
- [246] I. Unlu, I. Rochlin, D. S. Suman, Y. Wang, K. Chandel, and R. Gaugler. Large-Scale Operational Pyriproxyfen Autodissemination Deployment to Suppress the Immature Asian Tiger Mosquito (Diptera : Culicidae) Populations. *J Med Entomol*, pages 1–11, 2020. doi: 10.1093/jme/tjaa011. URL <https://academic.oup.com/jme/advance-article/doi/10.1093/jme/tjaa011/5719610>.
- [247] P. van den Driessche and J. Watmough. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180(1) :29–48, Nov. 2002. ISSN 0025-5564. doi: 10.1016/S0025-5564(02)00108-6. URL <http://www.sciencedirect.com/science/article/pii/S0025556402001086>.
- [248] A. Vega-Rua, K. Zouache, V. Caro, L. Diancourt, P. Delaunay, M. Grandadam, and A.-B. Failloux. High Efficiency of Temperate *Aedes albopictus* to Transmit Chikungunya and Dengue Viruses in the Southeast of France. *PLOS ONE*, 8(3) :e59716, Mar. 2013. ISSN 1932-6203. doi:

BIBLIOGRAPHIE

- 10.1371/journal.pone.0059716. URL <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0059716>. Publisher : Public Library of Science.
- [249] M. Vincent, S. Larrieu, P. Vilain, A. Etienne, J.-L. Solet, C. François, B. Roquebert, M.-C. Jaffar Bandjee, L. Filleul, and L. Menudier. From the threat to the large outbreak : dengue on Reunion Island, 2015 to 2018. *Euro Surveill*, 24(47), Nov. 2019. ISSN 1025-496X. doi: 10.2807/1560-7917.ES.2019.24.47.1900346. URL <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6885751/>.
- [250] M. J. B. Vreysen, K. Saleh, F. Mramba, A. Parker, U. Feldmann, V. A. Dyck, A. Msangi, and J. Bouyer. Sterile Insects to Enhance Agricultural Development : The Case of Sustainable Tsetse Eradication on Unguja Island, Zanzibar, Using an Area-Wide Integrated Pest Management Approach. *PLOS Neglected Tropical Diseases*, 8(5) :e2857, May 2014. ISSN 1935-2735. doi: 10.1371/journal.pntd.0002857. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0002857>.
- [251] K. E. F. Watt. *Systems Analysis in Ecology*. Elsevier, Oct. 2013. ISBN 978-1-4832-6901-6. Google-Books-ID : bGYhBQAAQBAJ.
- [252] M. Whalon, D. Mota-Sanchez, and R. Hollingworth. Analysis of global pesticide resistance in arthropods. *Global pesticide resistance in arthropods*, 5 :31, 2008. Publisher : CAB International UK.
- [253] P. Whelan, H. Nguyen, K. Hajkovicz, J. Davis, D. Smith, A. Pyke, V. Krause, and P. Markey. Evidence in Australia for a Case of Airport Dengue. *PLOS Neglected Tropical Diseases*, 6(9) :e1619, Sept. 2012. ISSN 1935-2735. doi: 10.1371/journal.pntd.0001619. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0001619>. Publisher : Public Library of Science.
- [254] M. T. White, J. T. Griffin, T. S. Churcher, N. M. Ferguson, M.-G. Basáñez, and A. C. Ghani. Modelling the impact of vector control interventions on *Anopheles gambiae* population dynamics. *Parasites Vectors*, 4(1) :153, July 2011. ISSN 1756-3305. doi: 10.1186/1756-3305-4-153. URL <https://doi.org/10.1186/1756-3305-4-153>.
- [255] S. M. White, P. Rohani, and S. M. Sait. Modelling pulsed releases for sterile insect techniques : fitness costs of sterile and transgenic males and the effects on mosquito dynamics. *J. Appl. Ecol.*, 47(6) :1329–1339, Dec. 2010. ISSN 0021-8901. doi: 10.1111/j.1365-2664.2010.01880.x. WOS :000283983200020.
- [256] WHO. Dengue vaccine : WHO position paper – September 2018. *Weekly epidemiological record*, (93) :457–476, 2018.
- [257] A. Wilder-Smith and D. J. Gubler. Geographic Expansion of Dengue : The Impact of International Travel. *Medical Clinics of North America*, 92(6) :1377–1390, Nov. 2008. ISSN 0025-7125. doi: 10.1016/j.mcna.2008.07.002. URL <http://www.sciencedirect.com/science/article/pii/S0025712508000989>.

BIBLIOGRAPHIE

- [258] C. R. Williams, S. A. Ritchie, S. A. Long, N. Dennison, and R. C. Russell. Impact of a Bifenthrin-Treated Lethal Ovitrap on *Aedes aegypti* Oviposition and Mortality in North Queensland, Australia. *J Med Entomol*, 44(2) :256–262, Mar. 2007. ISSN 0022-2585. doi: 10.1093/jmedent/44.2.256. URL <https://academic.oup.com/jme/article/44/2/256/863209>. Publisher : Oxford Academic.
- [259] G. M. Williams, A. Faraji, I. Unlu, S. P. Healy, M. Farooq, R. Gaugler, G. Hamilton, and D. M. Fonseca. Area-Wide Ground Applications of *Bacillus thuringiensis* var. *israelensis* for the Control of *Aedes albopictus* in Residential Neighborhoods : From Optimization to Operation. *PLOS ONE*, 9(10) :e110035, Oct. 2014. ISSN 1932-6203. doi: 10.1371/journal.pone.0110035. URL <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0110035>. Publisher : Public Library of Science.
- [260] A. L. Wilson, O. Courtenay, L. A. Kelly-Hope, T. W. Scott, W. Takken, S. J. Torr, and S. W. Lindsay. The importance of vector control for the control and elimination of vector-borne diseases. *PLOS Neglected Tropical Diseases*, 14(1) :e0007831, Jan. 2020. ISSN 1935-2735. doi: 10.1371/journal.pntd.0007831. URL <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0007831>. Publisher : Public Library of Science.
- [261] World Health Organization. Atrazine in drinking-water : background document for development of WHO guidelines for drinking-water quality. Technical report, World Health Organization, 2003.
- [262] World Health Organization. Maladies à transmission vectorielle. 2020. URL <https://www.who.int/fr/news-room/fact-sheets/detail/vector-borne-diseases>.
- [263] World Health Organization and others. Dengue and severe dengue. Technical report, World Health Organization. Regional Office for the Eastern Mediterranean, 2019.
- [264] J. H. Wyss. Screwworm Eradication in the Americas. *Annals of the New York Academy of Sciences*, 916(1) :186–193, 2000. ISSN 1749-6632. doi: 10.1111/j.1749-6632.2000.tb05289.x. URL <https://nyaspubs.onlinelibrary.wiley.com/doi/abs/10.1111/j.1749-6632.2000.tb05289.x>.
- [265] L. Yakob and G. Yan. Modeling the Effects of Integrating Larval Habitat Source Reduction and Insecticide Treated Nets for Malaria Control. *PLOS ONE*, 4(9) :e6921, Sept. 2009. ISSN 1932-6203. doi: 10.1371/journal.pone.0006921. URL <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0006921>.
- [266] J. H. Yen and A. R. Barr. New hypothesis of the cause of cytoplasmic incompatibility in *Culex pipiens* L. *Nature*, 232(5313) :657–658, 1971. Publisher : Springer.
- [267] X. Zheng, D. Zhang, Y. Li, C. Yang, Y. Wu, X. Liang, Y. Liang, X. Pan, L. Hu, Q. Sun, X. Wang, Y. Wei, J. Zhu, W. Qian, Z. Yan, A. G. Parker, J. R. L. Gilles, K. Bourtzis, J. Bouyer, M. Tang, B. Zheng, J. Yu, J. Liu, J. Zhuang, Z. Hu, M. Zhang, J.-T. Gong, X.-Y. Hong, Z. Zhang,

BIBLIOGRAPHIE

- L. Lin, Q. Liu, Z. Hu, Z. Wu, L. A. Baton, A. A. Hoffmann, and Z. Xi. Incompatible and sterile insect techniques combined eliminate mosquitoes. *Nature*, 572(7767) :56–61, Aug. 2019. ISSN 1476-4687. doi: 10.1038/s41586-019-1407-9. URL <https://www.nature.com/articles/s41586-019-1407-9>.
- [268] S. Zhou, S. Zhou, L. Liu, M. Zhang, M. Kang, J. Xiao, and T. Song. Examining the Effect of the Environment and Commuting Flow from/to Epidemic Areas on the Spread of Dengue Fever. *Int J Environ Res Public Health*, 16(24), 2019. ISSN 1660-4601. doi: 10.3390/ijerph16245013.
- [269] G. Zhu, T. Liu, J. Xiao, B. Zhang, T. Song, Y. Zhang, L. Lin, Z. Peng, A. Deng, W. Ma, and Y. Hao. Effects of human mobility, temperature and mosquito control on the spatiotemporal transmission of dengue. *Science of The Total Environment*, 651 :969–978, Feb. 2019. ISSN 0048-9697. doi: 10.1016/j.scitotenv.2018.09.182. URL <http://www.sciencedirect.com/science/article/pii/S004896971833626X>.

Annexes

1

Determination of the basic reproduction number (R0)

The transmission matrix (T) of the epidemic model is :

$$T = \begin{pmatrix} 0 & 0 & 0 & 0 & \frac{ab_h F_{ns}}{N_H} \\ 0 & 0 & 0 & 0 & \frac{ab_h F_{ps}}{N_H} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & ab_m & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and the transition matrix (M) is :

$$M = \begin{pmatrix} -(m_F + \gamma_F) & 0 & 0 & 0 & 0 \\ \gamma_F & -(m_F + \alpha_E) & 0 & 0 & 0 \\ 0 & \alpha_E & -m_F & 0 & 0 \\ 0 & 0 & 0 & -\alpha_I & 0 \\ 0 & 0 & 0 & \alpha_I & -\gamma_H \end{pmatrix}$$

$$-M^{-1} = \begin{pmatrix} \frac{1}{(m_F + \gamma_F)} & 0 & 0 & 0 & 0 \\ \frac{\gamma_F}{(m_F + \gamma_F)} \frac{1}{(m_F + \alpha_E)} & \frac{1}{(m_F + \alpha_E)} & 0 & 0 & 0 \\ \frac{\gamma_F}{(m_F + \gamma_F)} \frac{\alpha_E}{(m_F + \alpha_E)} \frac{1}{m_F} & \frac{\alpha_E}{(m_F + \alpha_E)} \frac{1}{m_F} & \frac{1}{m_F} & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{\alpha_I} & 0 \\ 0 & 0 & 0 & \frac{1}{\gamma_H} & \frac{1}{\gamma_H} \end{pmatrix}$$

ANNEXE A. ANNEXE

$$E = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 0 \end{pmatrix}$$

$$K = -E'TM^{-1}E = \begin{pmatrix} 0 & 0 & \frac{ab_h F_{ns}}{N_H} \frac{1}{\gamma_H} \\ 0 & 0 & \frac{ab_h F_{ps}}{N_H} \frac{1}{\gamma_H} \\ \frac{\alpha_E}{(m_F + \alpha_E)} \frac{\gamma_F}{(m_F + \gamma_F)} \frac{ab_m}{m_F} & \frac{\alpha_E}{(m_F + \alpha_E)} \frac{ab_m}{m_F} & 0 \end{pmatrix}$$

R_0 is equivalent to the dominant eigenvalue of K . Thus,

$$R_0 = \sqrt{\frac{a^2 b_m b_h \alpha_E}{(\alpha_E + m_F) m_F \gamma_H N} \left(F_{ps} + \frac{\gamma_F F_{ns}}{(m_F + \gamma_F)} \right)}$$

2 **Poster**

Modeling *Aedes albopictus* response to control methods based on sterilized males release

Marion Haramboure¹, Pierrick Labbé², Thierry Baldet³, Jeremy Bouyer^{3,4} and Annelise Tran^{1,5}

1 CIRAD, UMR ASTRE, Sainte-Clotilde, Reunion, France; 2 ISEM, UMR 5554, CNRS-UM-IRD-EPHE, Université de Montpellier, Montpellier, France; 3 CIRAD, UMR ASTRE, Montpellier, France; 4 CIRAD, UMR INTERTRYP, Montpellier, France; 5 CIRAD, UMR TETIS, Sainte-Clotilde, Reunion, France.

Insecticide-based mosquito population control is now suboptimal:

- Environment and economic externalities
- Loss of efficiency due to acquired resistance

➔ Need for alternative methods to **control mosquitoes' densities**.

We studied the impact of the **Sterile Insect Technique (SIT)** and **Boosted SIT** on the populations dynamics of *Ae. albopictus* in Réunion island.

SIT (A) ➔ The females that mate with the ionized males **do not produce viable offspring**.

Boosted SIT (B) ➔ The **pyriproxyfen** disrupts the emergence of pupae present in a contaminated breeding site.

A) Ionizing radiation → Large number of sterile males release

B) Ionizing radiation + Pyriproxyfen → Large number of sterile contaminated males release → Females contaminated by pyriproxyfen → Pyriproxyfen contaminates breeding sites

A **mechanistic model** of seasonal mosquito population dynamics has been developed.

Oviposition: Parous females, Nulliparous females, Males, Unfertilized females.

Life cycle: Eggs → Hatching → Larvae → Pupa → Pupation → Pupae → Adults.

Control methods: SIT (sterilizing males), Boosted SIT (sterilizing males + pyriproxyfen).

⚡: natural mortality

The model is **climate-driven** and predict the **abundance of mosquito** in 1,203 areas of Réunion island. **Validated with a previous model** used by a mosquito surveillance manager in Réunion island.

Ste-Marie
Pearson's correlation coef. = 0,49

St-Paul
Pearson's correlation coef. = 0,84

From 08/15/2013 to 12/15/2013, 20000 males are weekly introduced in the population.

Key result:

- SIT control the population for 4.5 months
- Boosted SIT seem to provide a sustained **long-term control**

➔ **The model appears a efficient tool to investigate:**

- release strategies
- effectiveness' threshold
- impact of climate



Tran, A., Mangeas, M., Roux, E., Demarchi, M., Degenne, P., Legoff, G., Damiens, D., Gouagna, C., Herbreteau, V., Dehecq, J.S. (2018). Complementarity of empirical and process-based approaches to modeling mosquito population dynamics with *Aedes albopictus* as an example. (Submitted)

Bouyer, J., & Lefrançois, T. (2014). Boosting the sterile insect technique to control mosquitoes. *Trends in parasitology*, 30(6), 27

Bouyer, J., Chandre, F., Gilles, J., & Baldet, T. (2016). Alternative vector control methods to manage the Zika virus outbreak: more haste, less speed. *The Lancet Global Health*, 4(6), e364.



Appendix A. Model outputs

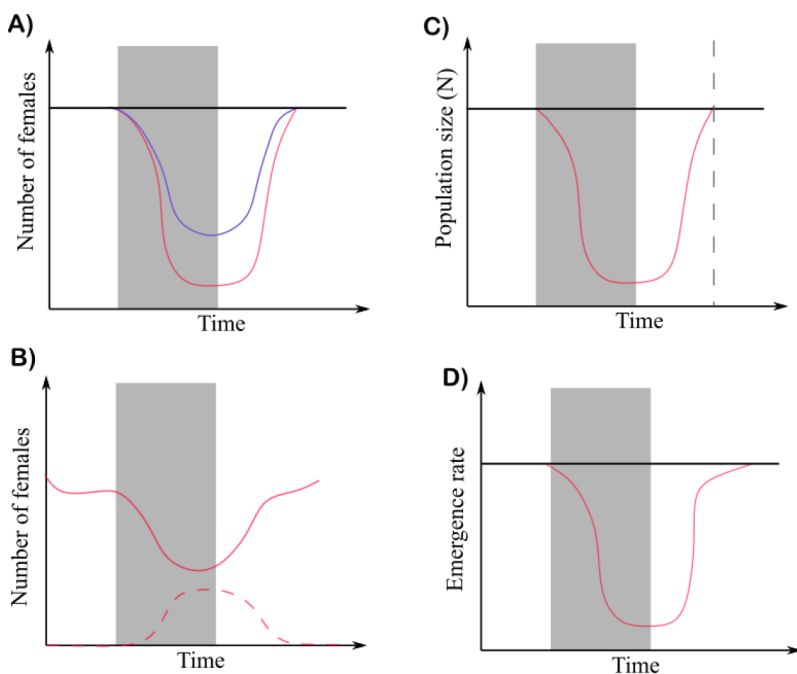


Fig. A1. Schematic representation of the models' outputs. The reduction rate A), the sterility rate B), and the time to return to the natural dynamics C) are the outputs for mALBORUN-SIT and mALBORUN-BSIT models. The reduction of emergence D) is mALBORUN-BSIT output only. The gray square corresponds to the period of control. The black line corresponds to the outputs of the reference mALBORUN model, the blue and red lines correspond to the outputs of mALBORUN-SIT and mALBORUN-BSIT, respectively. In the Figure B), the continuous line corresponds to the total number of fecundated females ($F_n + F_p + F_s$), while the dotted line corresponds to the number of sterile females f_s . In Figure C), the vertical black dotted line corresponds to the time needed to return to the natural dynamics after treatment (resilience). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Appendix B. Map of the optimal starting month for SIT

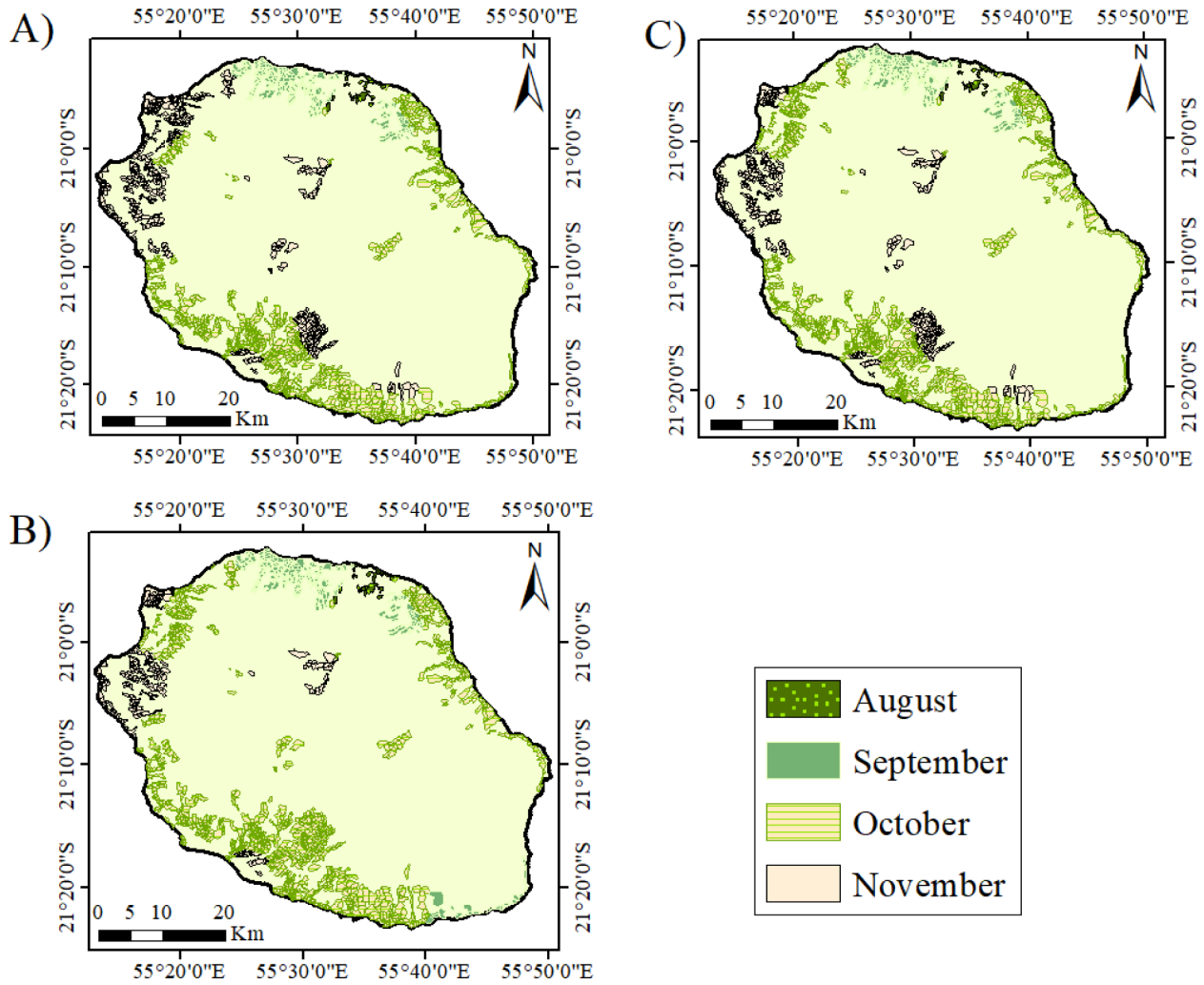


Fig. B1. Optimal starting month for the outputs of the mALBORUN-SIT model at La Reunion Island. Map of the optimal release starting month for the reduction rate A), the sterility rate B), and the time to return to the natural dynamics C) are the outputs for mALBORUN-SIT model over three years. The optimal month is the same for all the sectors connected to the same weather station.

Appendix C. Map of the optimal starting month for boosted SIT

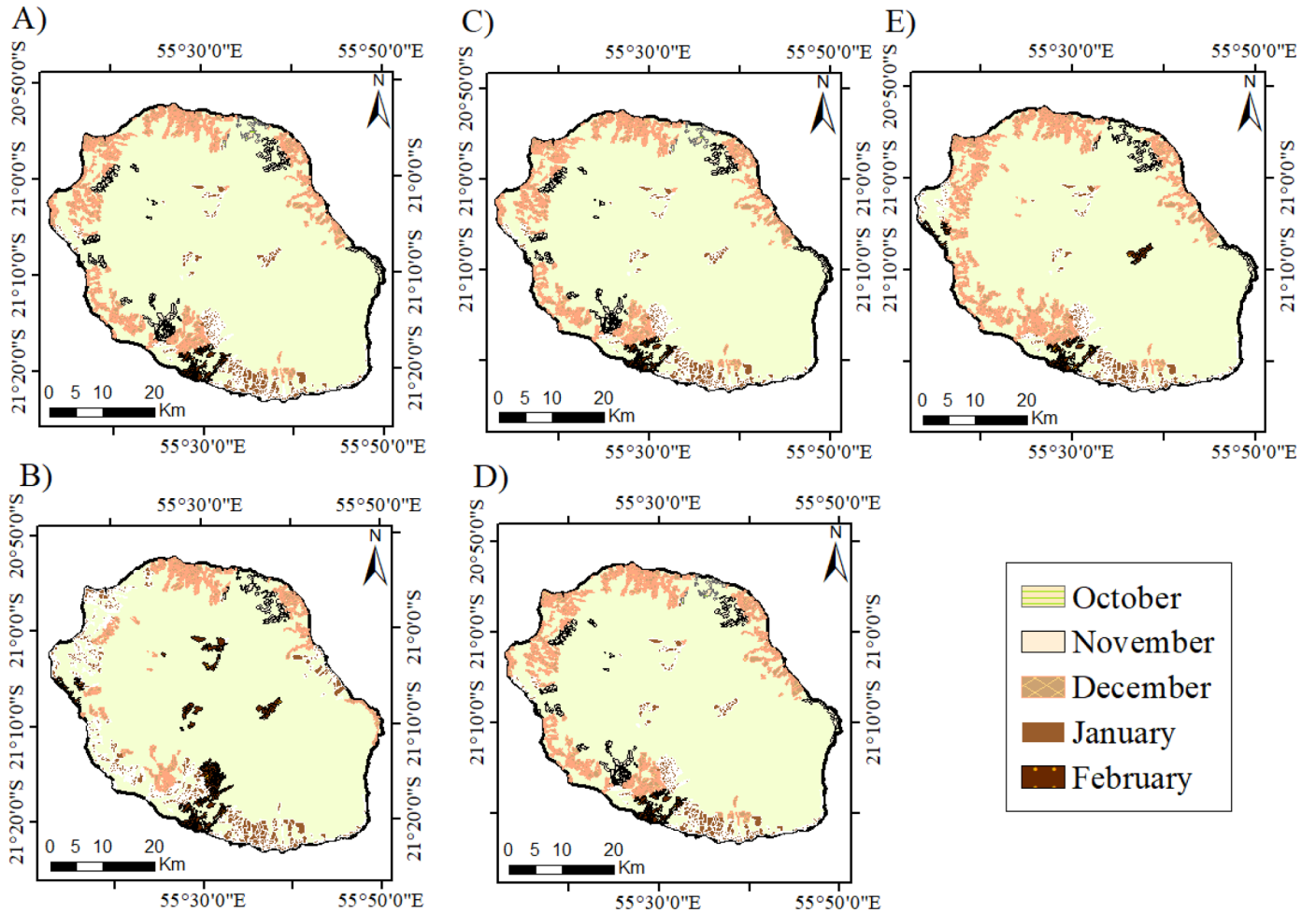


Fig. C1. Optimal starting month for the outputs of the mALBORUN-BSIT model at La Reunion Island. Map of the optimal release starting month for the reduction rate between boosted SIT application and non-controlled population A) or SIT-controlled population B), the sterility rate C), the time to return to the natural dynamics D) and E) are the outputs for mALBORUN-BSIT model over three years. The optimal month is the same for all the sectors connected to the same weather station.

Appendix D. Number of sterile males released for SIT

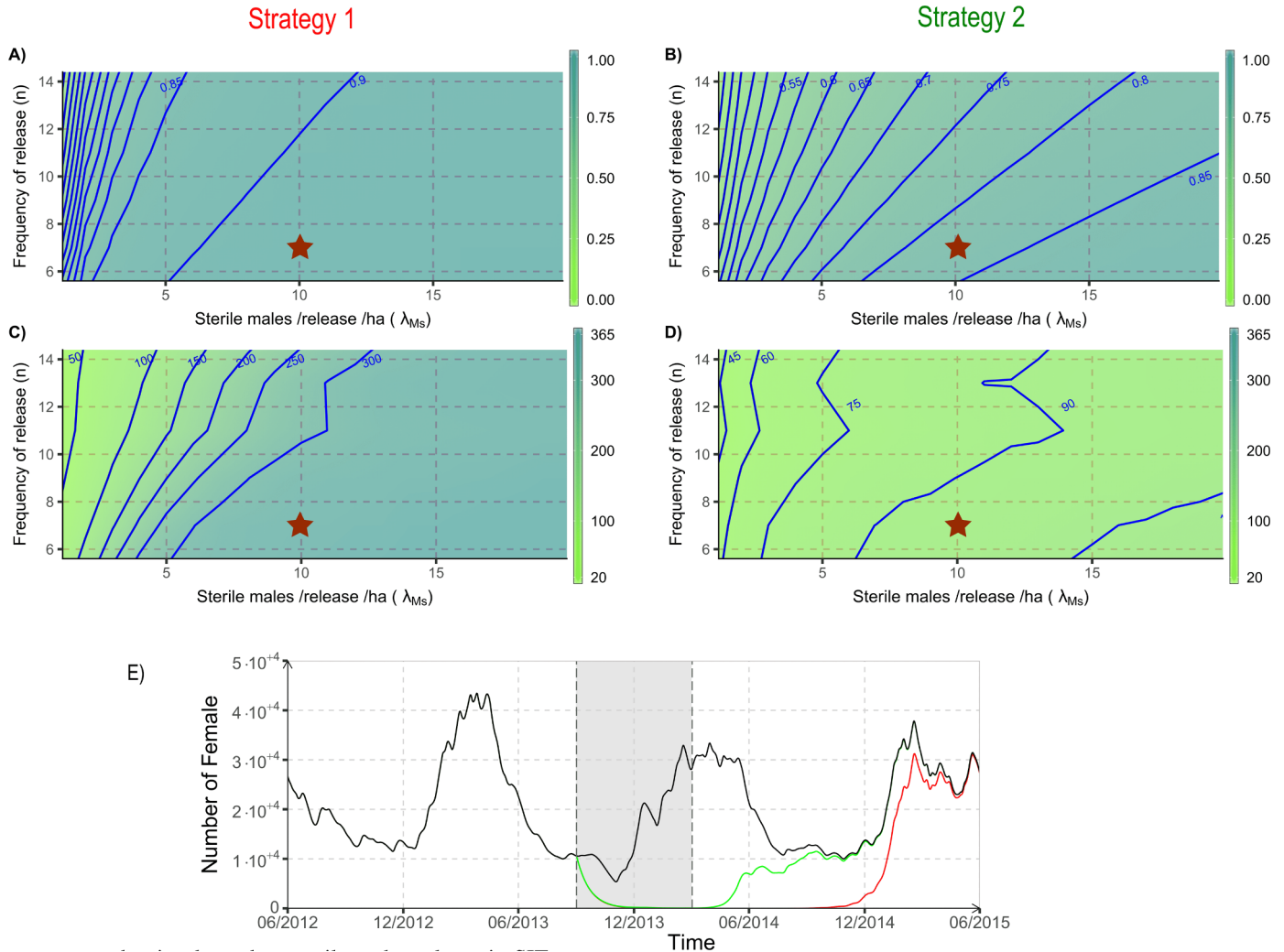


Fig. D1. Constant versus density-dependent sterile males release in SIT The impacts of two release strategies for the number of sterile males, constant (strategy 1) and proportional to the adult females density (strategy 2) are presented (on the left and right, respectively). The proportional reduction of the population size compared to a non-treated population (*mALBORUN-SIT* vs. *mALBORUN*) is represented with a contour plot (ranging from 0.55% to 0.9) for A) constant releases and B) proportional releases. The resilience time is represented with a contour plot (ranging from 45 to 300 days) for C) constant releases and D) proportional releases. Ten values of λ_{Ms} were tested, from 1, to 10 times the number of adult females at the beginning of the control period (strategy 1) or during the release dates (strategy 2). Six τ were tested, from 15 days down to 5 days. (E) Population dynamics without control (in black), with constant releases (in red) and with proportional release (in green), for $\tau = 7$ days and $\lambda_{Ms} = 10$ (star on panels A, B, C and D); the control period is grayed. The weather conditions of a single sector were used for the simulations (i.e. Duparc sector at La Reunion Island). To prevent the eradication artifacts due to the absence of migration (see text), one female was introduced every 40 days in each the operational urban sectors. Parameter values and functions of the model are in Tables 1 and 2. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Appendix E. Number of sterile males released for boosted SIT

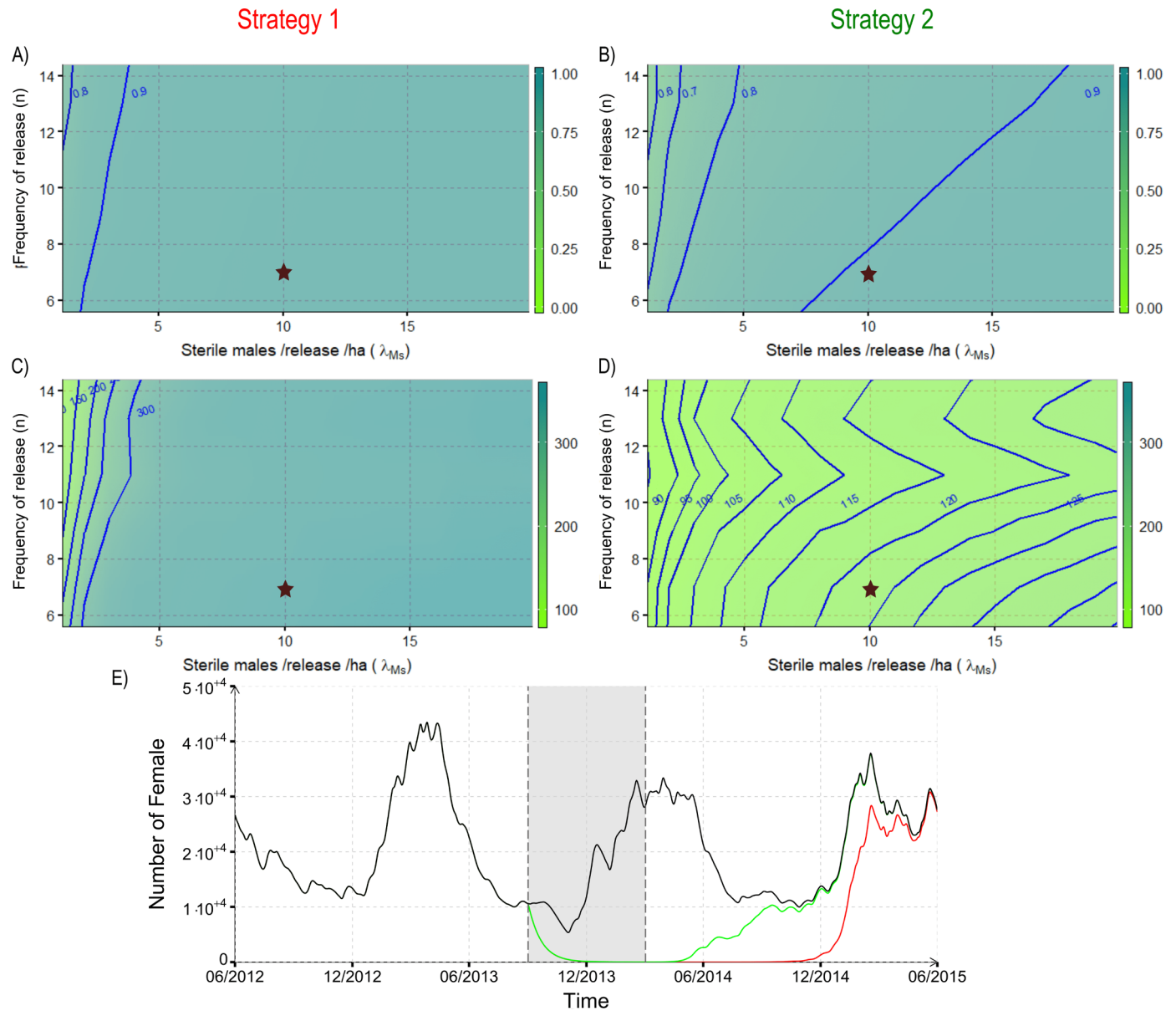


Fig. E1. Constant versus density-dependent sterile males release in the boosted SIT. The impacts of two release strategies for the number of sterile males, constant (strategy 1) and proportional to the adult females density (strategy 2) are presented (on the left and right, respectively). The proportion reduction of the population size compared to a non-treated population is represented with a contour plot (ranging from 0.6% to 0.9) for A) constant releases and B) proportional releases. The resilience time is represented with a contour plot (ranging from 90 to 300 days) for C) constant releases and D) proportional releases. Ten values of λ_{Ms} were tested, from 1, to 10 times the number of adult females at the beginning of the control period (constant releases) or during the release dates (proportional releases). Six τ were tested, from 15 days down to 5 days. (E) Population dynamics without control (in black), with strategy 1 (in red) and with strategy 2 (in green), for $\tau = 7$ days and $\lambda_{Ms} = 10$ (star on panels A, B, C and D); the control period is grayed. The weather conditions of a single sector were used for the simulations (i.e. Duparc sector at La Reunion Island). To prevent the eradication artifacts due to the absence of migration (see text), one female was introduced every 40 days in each of the operational urban sectors. Parameter values and functions of the model are in Tables 1 and 2. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Appendix F. Impacts of variations in sterile male competitiveness (c)

The reduction and sterility rates of the population increases sharply with increasing competitiveness (c) of the sterile males (M_s or M_{sc} , for SIT or BSIT, resp.), until it reaches a plateau. While emerging females sterilization was modeled identically, a higher sterility rate was observed with boosted SIT than with SIT. This difference is due to the fact that the greater population reduction induced by boosted SIT increases the probability of sterile males to encounter emerging females and sterilize them. In terms of population resilience after the control period, no difference was observed for the selected parameter set. Similarly, competitiveness (c) did not have much impact on pupal emergence for boosted SIT.

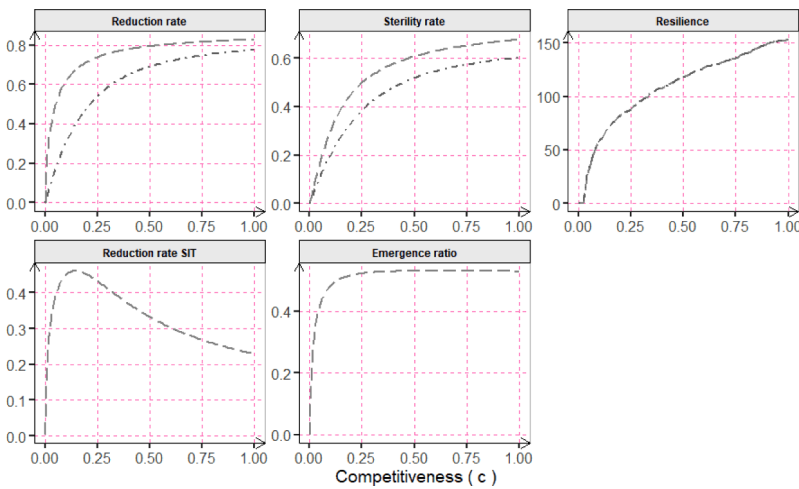


Fig. F1. Impact of the competitiveness parameter (c) variation on mALBORUN-SIT and mALBORUN-BSIT model outputs. The dynamics of a population controlled with SIT (mALBORUN-SIT) and boosted SIT (mALBORUN-BSIT) are represented with dashed line and dotted line, respectively. Parameter values and functions of the models are in Tables 1 and 2.

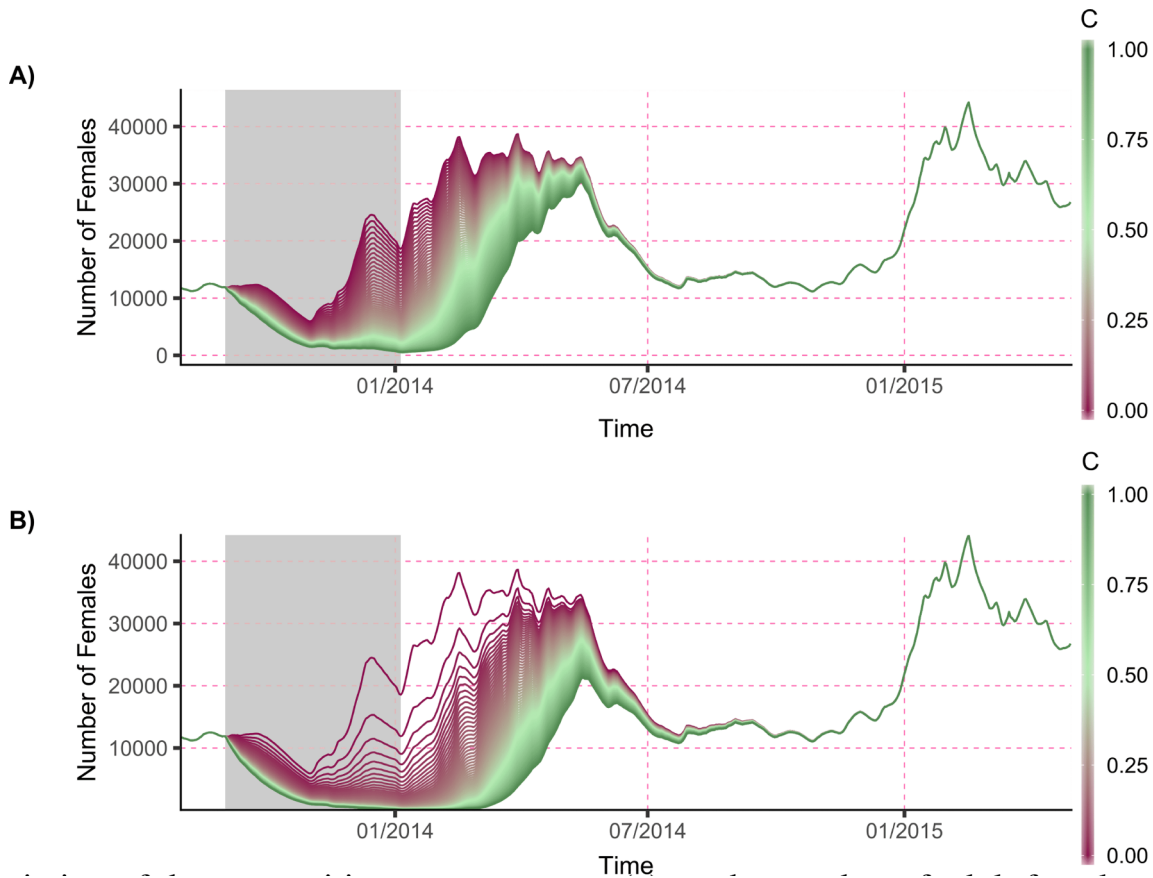


Fig. F2. Impact of the variation of the competitiveness parameter (c) on the number of adult females (nulliparous (F_n) + parous (F_p)). Competitiveness (c) increases from purple (c = 0: low competitiveness) to yellow (c = 1: high competitiveness). The grey background indicates the control period. Weather inputs were those of the Duparc Sector, Reunion Island. Parameter values and functions of the models are in Tables 1 and 2. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Appendix G. Variation of the proportion of pupae surviving to pyriproxyfen (ϕ) in the mALBORUN-BSIT model

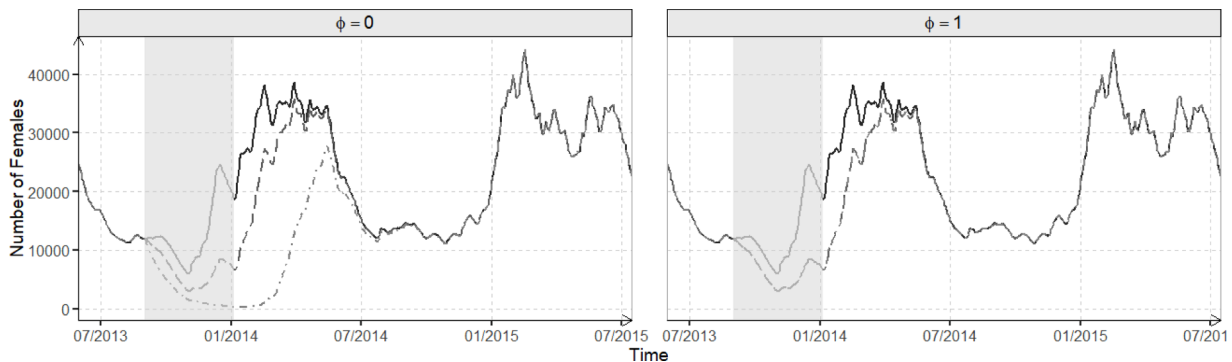


Fig. G1. Impact of the proportion of pupae surviving exposure to pyriproxyfen ϕ on the number of adult females (nulliparous (F_n) + parous (F_p)). Population dynamics without control (mALBORUN) is represented in solid line and the population dynamics controlled with SIT (mALBORUN-SIT) and boosted SIT (mALBORUN-BSIT) are represented in long dashed line and in dotted line respectively. When $\phi = 0$ (left), no emergence is possible so that the boosted SIT effect is maximum, for both population reduction and resilience; when $\phi = 1$ (right) all the pupae can emerge (e.g. resistance of *Ae. albopictus* to pyriproxyfen) so that the boosting effect is null. The grey background indicates the control period. Weather inputs were those of the Duparc sector, Reunion Island. Parameter values and functions of the models are in Tables 1 and 2.

Appendix H. Autonomous and non-autonomous models

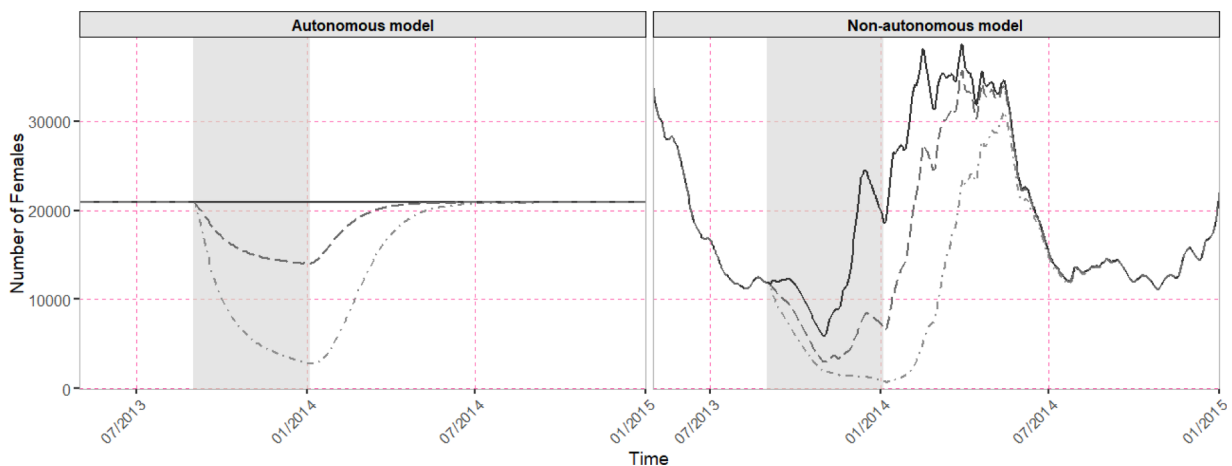


Fig. H1. Number of adult females (nulliparous (F_n) + parous (F_p)) in autonomous and non-autonomous models. Temperature and precipitation of the autonomous model were set at the average value of temperatures and precipitation recorded in the Duparc sector from 2011 to 2016. Population dynamics without control (mALBORUN) is represented in solid line and the population dynamics controlled with SIT (mALBORUN-SIT) and boosted SIT (mALBORUN-BSIT) are represented in long dashed line and in dotted line respectively. The grey background indicates the control period. Weather inputs were those of the Duparc sector, Reunion Island. Parameter values and functions of the models are in Tables 1 and 2.

4 Annexes de l'article 2

A Optimization of the sterile males releases date

To identify the best period for the sterile males releases, we optimized the starting date of releases similarly to Haramboure *et al.*⁷¹. The effectiveness of the SIT and BSIT was quantified by gathering 5 model outputs into a single value (3): the mean reduction rate over the releases (no units), the resilience (years), the sterility rate (no units), the emergence reduction rate (no units) and the increase rate of female population (no units). These outputs were computed relatively to the control model (without any vector control actions). Since the increase in female population during releases is an undesirable effect, the female increase rate was subtracted to lower down effectiveness estimator. The release starting day (T_{start}) was optimized to find the overall maximal effectiveness value. Both global and local optimizations were performed using the algorithm from `nloptr` R package (<https://cran.r-project.org/web/packages/nloptr/index.html>).

$$\begin{aligned}
 Effectiveness &= f(T_{start}) \\
 &= \sum_y \sum_p Reduction\ rate_{yp} + Sterility\ rate_{yp} + Resilience_{yp} \\
 &\quad + Emergence\ reduction_{yp} - Increase\ rate_{yp},
 \end{aligned} \tag{3}$$

$$\text{with } \begin{cases} p & \in \text{Parcels,} \\ y & \in [2015 - 2017]. \end{cases}$$

Optimization of SIT and boosted SIT consisted of maximizing their respective effectiveness. Because of inter-annual weather variations and field heterogeneity, these effectiveness were computed in three different years (2015, 2016 and 2017) and on the four Reunion Island-like parcels linked to the Montpellier meteorological stations (see Methods). It thus takes into account weather variability and field heterogeneity in both SIT and boosted SIT efficiency.

We defined the best release period as the time-frame of vector control actions that allows to reach at least 95% of the maximal potential effectiveness.

The best starting period was found to be late March in the temperate climate. A 3.5-months interval extending from February to mid-May allows reaching at least 95% of the maximum SIT and BSIT potential (Figure 5(A)). The 99% interval, mainly driven by resilience augmentation, is much shorter and lasts 40 days for both SIT and BSIT. It takes place within the firsts months of the favorable period, when the adult population is very low (Figure 5 (B)).

During control, and similarly in SIT and BSIT, the female population is heavily lowered during summer, approaching extinction (Figure 5 (B)). A few individuals nevertheless survive and breed, leading to the population recovery the year after.

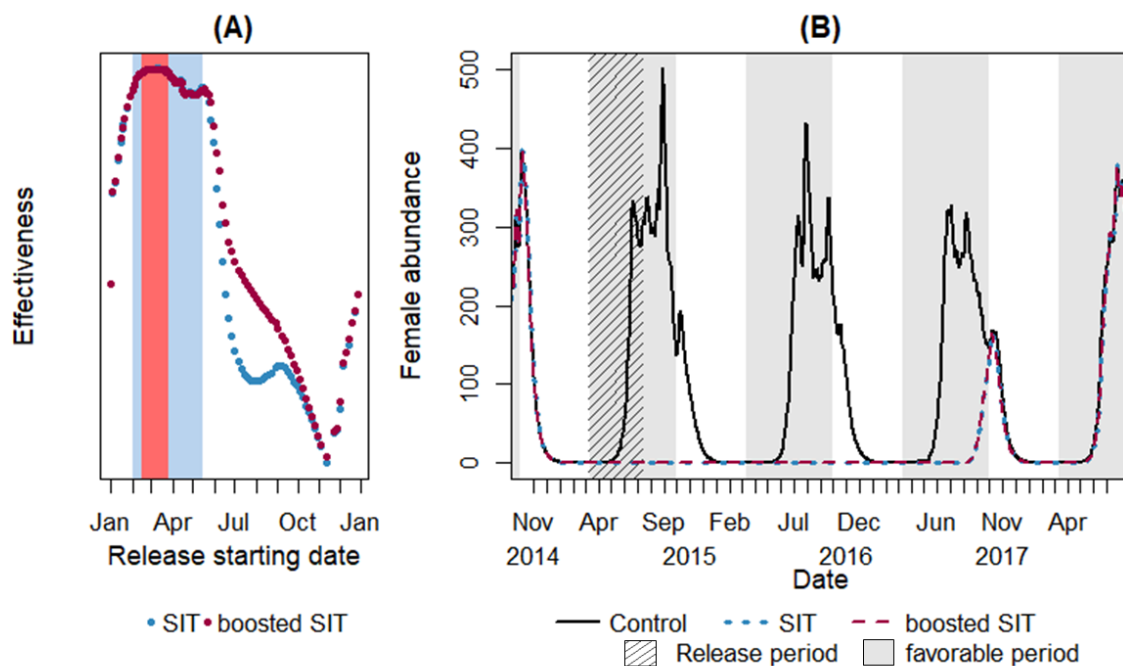


Figure 5. Best release starting date in the temperate climate for a maximum SIT and BSIT effect. (A) Effectiveness at different starting dates for SIT (blue) and BSIT (red). Periods reaching at least 95% and 99% of the maximum effect are respectively filled in blue and red. (B) SIT and BSIT effect on female dynamics over time. The release starts at its optimal day (March, the 24th) in year 2015. The scenario consists of 18 releases of 1000 males during a period of 4 months. Grey background represents the mosquitoes favorable period, *i.e.*, when no diapause occurs.

B Undesirable increase in female abundance

When started late in the mosquito season, SIT with late releases of less than 1100 males per hectare, has been found to cause a temporary increase in female abundance (see Results), which is not a desirable effect of control. This undesirable increase of female abundance has been reported in several studies^{60,80,81}. We further investigated the causes by running two sets of three simulations for SIT, BSIT and a control, one with larval competition and the other without (*i.e.*, removing the competition term $1 + \frac{P}{k_P(1-a)r_{prev}}$, eq. (4)). To allow comparison while avoiding the burst in population induced by the removal of larval competition, the total numbers of adult males and females were capped at 200 individuals.

An increase in female abundance was observed for SIT, which disappeared with the removal of larval competition from the model (Figure 6), suggesting that the sterile males releases induce a reduced larval competition, leading temporarily to more emergence. This increase is not observed with BSIT, either with or without larval competition, probably because the pp-contamination of breeding sites heavily lower down the larval population and overcome the effect of any competition process.

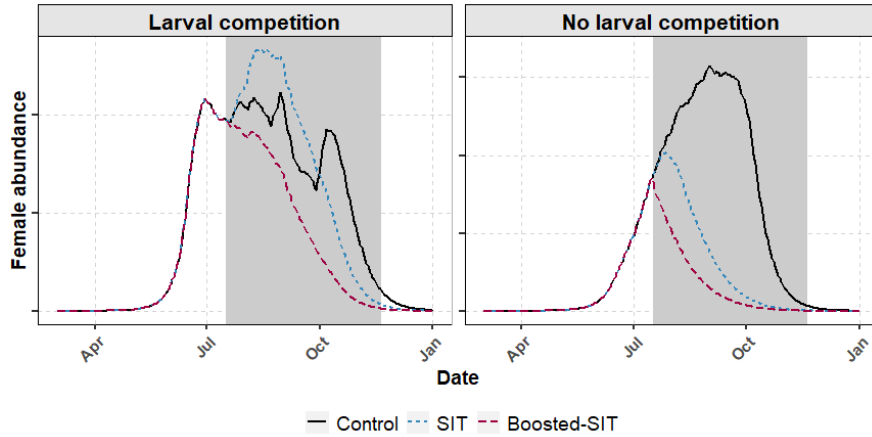


Figure 6. Population dynamics during late implementation of SIT or BSIT, with or without pupal competition. The release period is filled in grey. We bounded the adult females abundance to avoid exponential growth of population when the density-dependent (*i.e.*, the competition) process are removed.

C Model validation in the temperate climate

The simulated population dynamic without any sterile male releases (eq. (4) : $\lambda_{M_s} = \lambda_{M_{sc}} = 0$ and $a = 0$) has been validated on entomological data recorded by the "Entente Interdépartementale de Démoustication (EID) Méditerranée", the public agency in charge of the mosquito control in the southeast France.

Ovitrap were placed in 5 residential areas (Table 3) located in Montpellier (Vert-bois, Pompigane Sud and Aiguelongue) or in the adjacent city of Castelnau-Le-Lez (Volhe and Chevalerie) (Figure 7). Studied areas were described as discontinuous medium to dense urban fabrics by the reference CORINE, an European reference describing the land-cover structure based on satellite imagery¹⁰⁹. Ovitrap were mostly placed in sites shaded by vegetation. They consisted of 3L plastic black buckets filled with 2L of tap water, in which a floating polystyrene square (5 x 5cm) acted as an ovipositing support. Biolarvicide *Bacillus thuringiensis israelensis* was added into the bucket to prevent the production of mosquitoes from the trap.

The number of trapped eggs were monitored weekly between April and November, in 2015, 2016 and 2017 (Table 3). The trapping network in each parcel was composed of 8 to 25 ovitrap. We considered that a reasonable-enough trapping effort was performed to get an accurate description of the local *Ae. albopictus* population dynamics. Hatched and unhatched eggs were removed from the trap each week for identification and count at the laboratory.

Table 3. Entomological record of *Ae. albopictus* in the Montpellier area

Location	Year	Beginning	End	Number of traps	Surface of trapping area (ha)	Maximum mean number of eggs per trap per capture session
Vert-Bois	2015	30 Avr	18 Nov	25	9.739	434.36
Vert-Bois	2016	12 Mai	24 Nov	11	9.739	395.7
Vert-Bois	2017	26 Avr	19 Oct	19	9.739	294.2
Chevalerie	2016	12 Mai	24 Nov	10	5.876	377.2
Chevalerie	2017	26 Avr	19 Oct	8	5.876	259.25
South Pompignane	2016	12 Mai	24 Nov	10	12.313	334.9
Volhe	2016	12 Mai	24 Nov	10	9.954	483
Volhe	2017	26 Avr	19 Oct	11	9.954	228.36
Aiguelongue	2017	26 Avr	5 Oct	20	5.026	200.4

These observed data were then compared to the predictions of the model using a Spearman correlation test. The predicted numbers of new eggs produced per week were independently computed as $(\gamma_{gc}(\beta_n F_n + \beta_p F_p))$. Model simulations were highly consistent with the dynamics recorded in the field, with a significant correlation of 61% ($p_{value} \simeq 10^{-27}$).

However, the model tends to underestimate the number of new eggs produced at the beginning of the favorable period (April). An early egg peak is observed in 2017 in all studied areas (Figure 8). This burst is not captured by our simulations and could not be explained by temperature or rainfall fluctuations. It is probably responsible for the lower correlation (52%, $p_{value} \simeq 0.01$) observed in the Aiguelongue area where the few records (24) provided were all performed in 2017. Eggs measured in Chevalerie, Volhe and Vert-bois areas, were followed for more than one year and show higher correlation coefficients: 0.75 ($p_{value} \simeq 10^{-11}$),

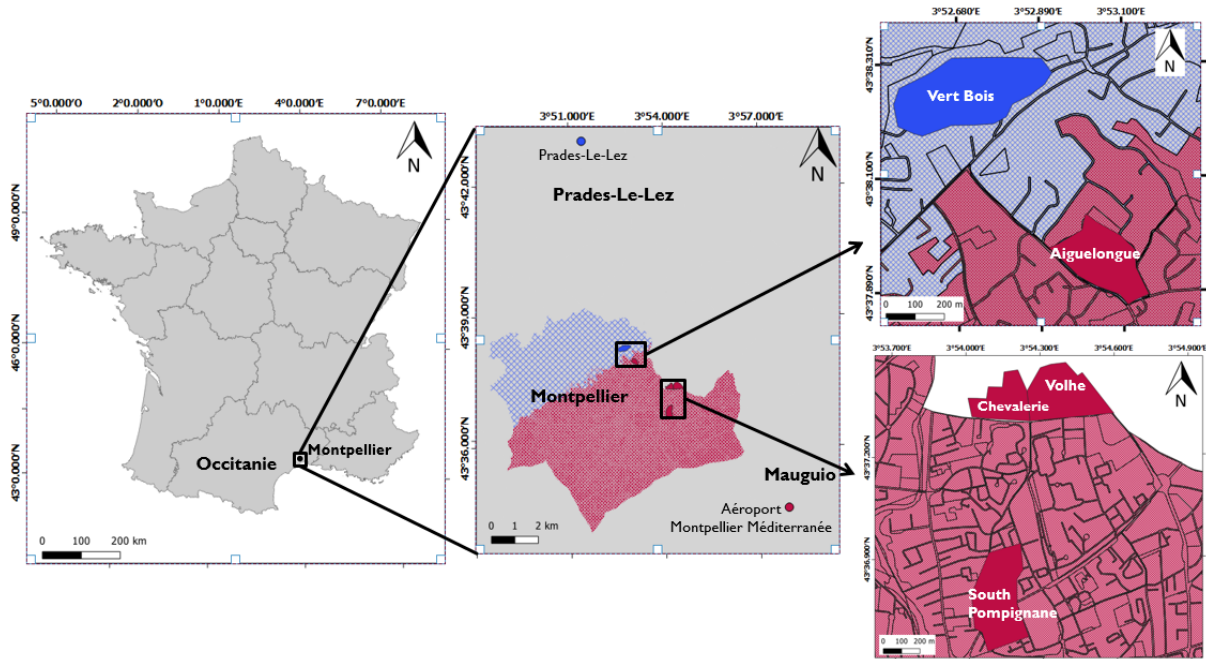


Figure 7. Study area. Colored points represent the two meteorological stations (blue for Prades-Le-Lez and red for Montpellier's airport) of the area. The same color code was used to link each parcel with its closest meteorological station. Entomological data were provided for 5 parcels : Vert-Bois, Aiguelongue, South Pompignade, Chevalerie and Volhe (filled parcels).

0.69 ($p_{value} \simeq 10^{-9}$) and 0.65 ($p_{value} \simeq 10^{-11}$), respectively. The best fit to the entomological data was observed in the South Pompignane neighborhood with a significant correlation of 86% ($p_{value} \simeq 10^{-9}$); this area is the only one where no records were performed in year 2017.

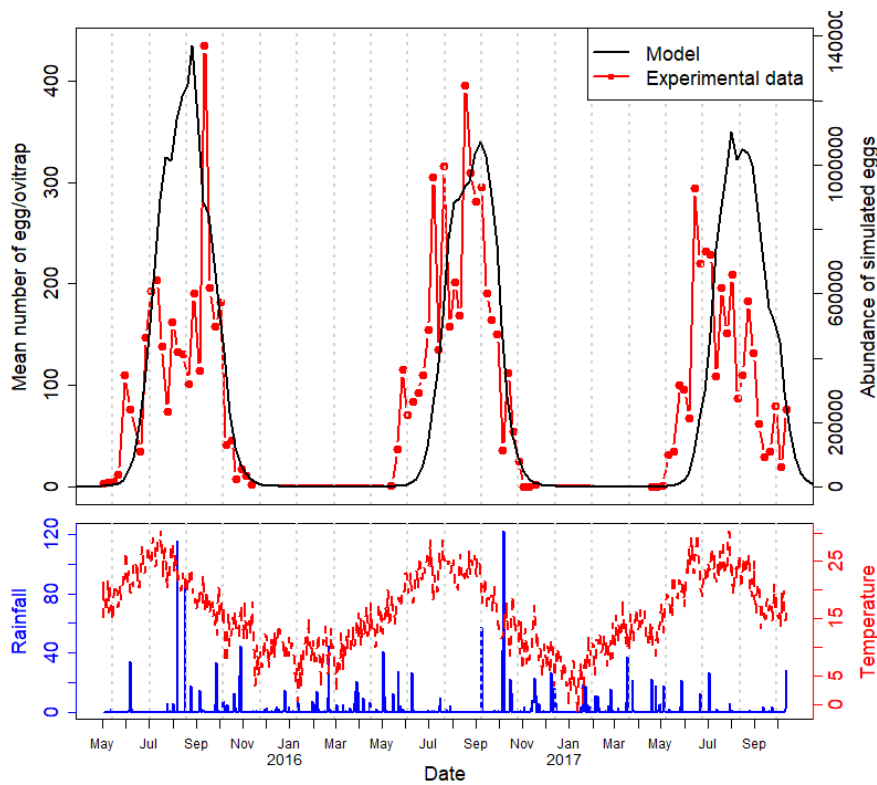


Figure 8. Model vs. observed data in the Vert-bois area. (Top panel) Comparison of the numbers of new eggs sampled each week in the entomological collection (red) and predicted by the model (black). (Bottom panel) Temperature and rainfall records from Prades-Le-Lez meteorological station.

D Full model, modified from Haramboure *et al.* ⁷¹

The original model was developed for Reunion Island (southwest Indian Ocean, tropical climate) by Haramboure *et al.* ⁷¹. The present model is an adaptation that allows for the temperate climate, using Montpellier (southern France, Mediterranean

temperate climate, *i.e.*, hot and dry summers vs. mild and humid winters) as a reference:

$$\left\{ \begin{array}{l}
\frac{dE}{dt} = \gamma_{gc}(\beta_n F_n + \beta_p F_p) - (\mu_E + z f_E)E, \\
\frac{dL}{dt} = z f_E E - \left(m_L \left(1 + \frac{L}{k_L(\mathbf{1} - \mathbf{a} \mathbf{r}_{\text{prev}})} \right) + f_L \right) L, \\
\frac{dP}{dt} = f_L L - (m_P + f_P)P, \\
\frac{dF_{em}}{dt} = \sigma f_P P \exp \left(-\mu_{F_{em}} \left(1 + \frac{P}{k_P(\mathbf{1} - \mathbf{a} \mathbf{r}_{\text{prev}})} \right) \right) \left(1 - \frac{B_c}{B_{tot}(\mathbf{1} - \mathbf{a} \mathbf{r}_{\text{prev}})} (1 - \phi) \right) \\
\qquad \qquad \qquad - (m_F + \gamma_{F_{em}})F_{em}, \\
\frac{dF_n}{dt} = \gamma_{F_{em}} F_{em} \left(1 - \frac{\omega(M_{sc} + M_s)}{\omega(M_{sc} + M_s) + M} \right) - (m_F + \mu_r + \gamma_{gc}(\mathbf{1} + \mathbf{a}(\mathbf{c}_{F_g, O_T} + \mathbf{c}_{F_{hs}, BGS}))) F_n, \\
\frac{dF_p}{dt} = \gamma_{gc} F_n - (m_F + \mu_r + \mathbf{a}(\mathbf{c}_{F_g, O_T} + \mathbf{c}_{F_{hs}, BGS}) \gamma_{gc}) F_p, \\
\frac{dF_s}{dt} = \gamma_{F_{em}} F_{em} \frac{\omega(M_{sc} + M_s)}{\omega(M_{sc} + M_s) + M} - (m_F + \mu_r + \gamma_{gc} \mathbf{a}(\mathbf{c}_{F_g, O_T} + \mathbf{c}_{F_{hs}, BGS})) F_s, \\
\frac{dM}{dt} = (1 - \sigma) f_P P \exp \left(-\mu_{F_{em}} \left(1 + \frac{P}{k_P(\mathbf{1} - \mathbf{a} \mathbf{r}_{\text{prev}})} \right) \right) \left(1 - \frac{B_c}{B_{tot}(\mathbf{1} - \mathbf{a} \mathbf{r}_{\text{prev}})} (1 - \phi) \right) \\
\qquad \qquad \qquad - (\mu_M + \mathbf{a} \boldsymbol{\varepsilon} \mathbf{c}_{M_{all}, BGS}) M, \\
\frac{dM_s}{dt} = \frac{F_{tot}}{\omega(M_{sc} + M_s) + M} \frac{\omega M_{sc}}{\kappa_F} - (\mu_{M_s} + \mathbf{a} \boldsymbol{\varepsilon} \mathbf{c}_{M_{all}, BGS}) M_s \\
\frac{dM_{sc}}{dt} = - \frac{F_{tot}}{\omega(M_{sc} + M_s) + M} \frac{\omega M_{sc}}{\kappa_F} - (\mu_{M_s} + \mathbf{a} \boldsymbol{\varepsilon} \mathbf{c}_{M_{all}, BGS}) M_{sc}, \\
\frac{dB_c}{dt} = \left(\frac{\omega M_{sc}}{\omega(M_{sc} + M_s) + M} + \mathbf{a} \mathbf{c}_{F_g, S_T} \right) (F_n + F_p + F_s) \kappa_{Bc} \gamma_{gc} \left(1 - \frac{B_c}{B_{tot}(\mathbf{1} - \mathbf{a} \mathbf{r}_{\text{prev}})} \right) - \nu B_c, \\
M_x(T_{start} + n\tau^+) = M_x(T_{start} + n\Delta_t) + \lambda_{M_x}, \quad n = 1, 2, 3, \dots; \quad n\Delta_t \leq \tau; \quad x \in \{sc, s\}, \\
F_{tot} = F_{em} + F_n + F_p + F_s.
\end{array} \right. \quad (4)$$

$$\text{with } z = \begin{cases} 0 & \text{if } d_{start} \leq t \leq d_{end} \text{ (diapause)} \\ 1 & \text{otherwise} \end{cases} \quad \text{and} \quad \mathbf{a} = \begin{cases} \mathbf{1} & \text{during vector control} \\ \mathbf{0} & \text{otherwise} \end{cases}$$

Constant parameters are in Greek letters. They include mortality rates (μ_X being the mortality rate of compartment X , 11 compartments in total, see text), and the transition rates from emerging to nulliparous females ($\gamma_{F_{em}}$), and from nulliparous to parous females (γ_{gc}). γ_{gc} is then multiplied by the number of eggs laid per ovipositing nulliparous (β_n) and parous (β_p) females to compute the egg-laying rate. An additional mortality rate is added for female compartments, due to their host-seeking behaviour (μ_r). σ is the sex ratio at emergence. Each male being able to fertilize several females, we assumed that the mating probability for females was 1, *i.e.*, independent of the male density.

Latin letters are weather-dependent functions that act on the mortality rates (m_x), the transition rates (f_x) and the environment-defined carrying capacities (k_x) for the aquatics stages. Carrying capacities drive the density-dependent mortality at larval stage ($m_L \left(1 + \frac{L}{k_L} \right)$) and the pupae density-dependent success for adult emergence ($\exp \left(-\mu_{F_{em}} \left(1 + \frac{P}{k_P} \right) \right)$). Temperature impacts m_x and f_x , whereas k_x is rainfall-dependent.

During diapause (d_{start}, d_{end}), observed only in the temperate climate, the transition between the eggs and larvae compartments is stopped by the z parameter that represents the egg dormancy process⁷⁴.

When SIT, or BSIT, starts (T_{start}), a quantity of sterile males (λ_X , with $X = M_s$ or M_{sc} , resp.), is periodically released into the population (Δ_t) during a given period of time τ . The sterile males have a probability to mate with an emerging females (F_{em}) depending of their relative availability compared to the overall number of males, *i.e.*, their proportion adjusted by the competition parameter ω : $p = \frac{\omega X}{\omega X + M}$. No eggs produced by sterile females will hatch. Emerging females that encounter a sterile male thus become sterile (F_s), while the other become nulliparous (F_n , probability $1 - p$).

Moreover, for BSIT the released sterile males (M_{sc}) are also coated with pyriproxyfen (PP). Males attempt to mate with any females of the population ($F_{tot} = F_{em} + F_n + F_p + F_s$), even if already fertilized. Each encounter of a contaminated male with a

female makes it lose a part of its PP coating until total decontamination after κ_F matings : $\left(\frac{\omega M_{sc}}{\omega(M_{sc}+M_s)+M} \frac{F_{tot}}{\kappa_F}\right)$. The eventually decontaminated males nevertheless keep their ability to sterilize females (M_s). While laying eggs at each gonotrophic cycle (γ_{gc}), PP-contaminated females transfer the contaminant to the breeding sites $\left(\frac{\omega M_{sc}}{\omega(M_{sc}+M_s)+M} (F_n + F_p + F_s) \gamma_{gc}\right)$, but only to the non-contaminated fraction $\left(1 - \frac{B_c}{B_{tot}}\right)$, with B_c the number of contaminated sites among all breeding sites (B_{tot}). Females lose part of the contaminant at each oviposition, until total decontamination after κ_{Bc} gonotrophic cycles. Pupae emergence rate is affected by the probability of the pupae to 1) grow in a contaminated breeding site and 2) to survive PP with a probability ϕ $\left(1 - \frac{B_c}{B_{tot}}(1 - \phi)\right)$. Finally, breeding site become decontaminated at a rate ν .

Bold sections of the equation (eq. (4)) model the vector control methods that are not based on sterile males releases : ADT (O_T, S_T), oviscans (O_T), BGS-traps (BGS) and prevention (r_{prev}) through breeding site destruction.

E Model parameters

Parameters and weather-dependent function have been adjusted according to expert knowledge and literature (Table 4 and 5).

The density of breeding sites B_{tot} was estimated from the urbanization level in each delimited subarea, as the mean number of breeding sites per household (10 – 20) multiplied by the number of households per hectare (25 – 30) and the surface of the parcel. All were estimated from field observations, as well as the distinction between permanent and rainfall-dependent breeding sites.

Table 4. Parameters values in the temperate climate

Parameter	Definition	Value	Reference
σ	Sexe ratio at emergence	0.5	110
β_n	Eggs laid by ovipositing nulliparous female (per female)	95	111
β_p	Eggs laid by ovipositing parous female (per female)	75	111
γ_{Fem}	Transition rate from emerging female to nulliparous female (/day)	0.4	74
γ_{gc}	Length of the gonotrophic cycle (/day)	0.2	74
μ_E	Egg mortality rate (/day)	0.05	(Lacour, unpublished)
μ_L	Minimum larva mortality rate (/day)	0.02	(Lacour, unpublished)
μ_P	Minimum pupa mortality rate (/day)	0.02	(Lacour, unpublished)
μ_{Fem}	Mortality rate during adult emergence (/day)	0.1	(Lacour, unpublished)
μ_r	Female mortality rate related to seeking behaviour (/day)	0.058	current work
μ_M	Male mortality rate (/day)	0.0735	110
μ_F	Female mortality rate (/day)	0.02	110
k_{Lfix}	Standard rainfall-independent environment carrying capacity for larvae		To our best knowledge
k_{Lvar}	Standard rainfall-dependent environment carrying capacity for larvae		To our best knowledge
k_{Pfix}	Standard rainfall-independent environment carrying capacity for pupae		To our best knowledge
k_{Pvar}	Standard rainfall-dependent environment carrying capacity for pupae		To our best knowledge
T_E	Minimal temperature needed for egg development (°C)	10	110
TDD_E	Total number of degree-day necessary for egg development (°C)	110	(Lacour, unpublished)
d_{start}	Beginning of the diapause period	30 Sept	112
d_{end}	End of the diapause period	10 Mar	112

Table 5. Functions adjusted for temperate conditions⁷⁴. R is the rainfall and T , the temperature at time t .

Function	Definition	Expression
f_E	Transition function from egg to larvae	$(T(t) - T_E) / TDD_E$
f_L	Transition function from larvae to pupae	$-0007T^2 + 0.0392T - 0.3911$
f_P	Transition function from pupae to emerging adult	$0.0008T^2 - 0.0051T + 0.0319$
m_L	Larva mortality	$\mu_L + 0.0007exp(0.1838(T - 10))$
m_P	Pupa mortality	$\mu_P + 0.0003exp(0.2228(T - 10))$
m_F	Female mortality	$\mu_F + 0.0003exp(0.1745(T - 10))$
R_{norm}	Normalized weekly rainfall amount	$(\sum_{i=t-14}^t R(i)) / 100$
k_L	Environmental carrying capacity for larvae	$k_{Lfix} + \min(k_{Lvar}R_{norm}(t), k_{Lvar})$
k_P	Environmental carrying capacity for pupae	$k_{Pfix} + \min(k_{Pvar}R_{norm}(t), k_{Pvar})$

F Sensitivity analysis

A sensitivity analysis (SA) was performed on the model outputs to identify the key parameters of SIT and BSIT. Four model outputs were studied : the reduction rate, the resilience, the reduction rate of BSIT compared SIT and the undesirable female augmentation.

SIT parameters (λ_{M_s} , ω , μ_{M_s}), BSIT parameters ($\lambda_{M_{sc}}$, v , κ_{Bc} , κ_F , $\mu_{M_{sc}}$) and parameters describing the release period (T_{start} , τ , Δ_t) were varied one by one through 100 trajectories to complete a Morris Sensitivity analysis¹¹³ with the sensitivity R package. The grid of parameters space was discretized by 10 levels and the walking step was defined as $\frac{10}{2}$, following Morris's recommendations.

Each parameter space (Table 1)) was determined from literature or expert knowledge, except for T_{start} , which was just estimated.

As previously found for the tropical climate⁷¹, the main parameters influencing the mosquito population dynamics are essentially the same between SIT and BSIT (Figure 9). The elementary effect variance increases for most of the parameters according to the absolute value of the elementary effect. Most parameters have few or no influence on the output values.

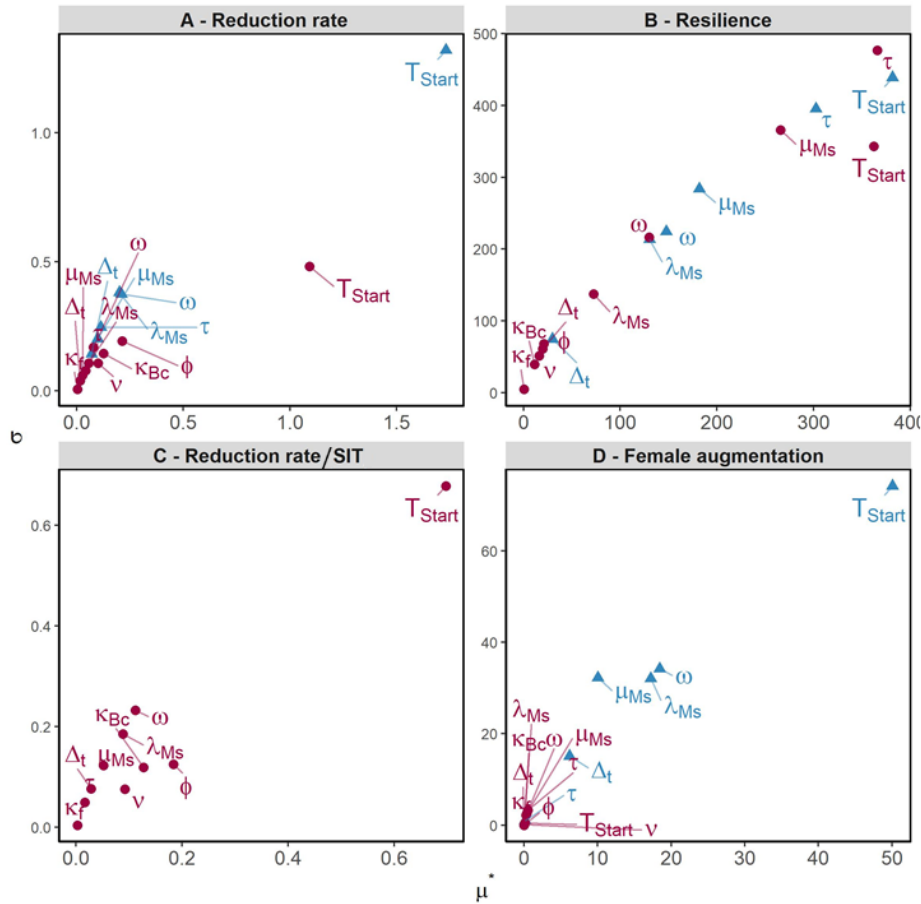


Figure 9. Keys parameters of SIT and BSIT. Sensitivity analysis performed on SIT (blue triangles) and BSIT (red points). Four outputs were studied, the reduction rate (A), the resilience (B), the reduction rate of BSIT compared to SIT (C), and the female population augmentation (D). The variance (σ) of each elementary effect is plotted against its absolute value (μ^*). Parameters without influence ($\sigma = 0$ and $\mu^* = 0$) were removed.

For 3 outputs out of 4, the date for the start of the releases (T_{start}) is by far the most influencing factor (Figure 9 (A, C, D)). Its elementary effect absolute value, describing its overall influence on the outputs, is 2 to 100 times higher than the effect of other parameters. Its participation to the output has either a non-linear relationship with the value, or a strong interaction with other inputs (high σ). The length of the release (τ) and the sterile male mortality (μ_s) are parameters that can significantly modify the population resilience after SIT or BSIT (Figure 9 (B)).

Even if the starting day of release remains by far the major influential parameter, BSIT is less sensitive than SIT to this

parameter for the reduction rate and resilience outputs (Figure 9 (A, B)). The reduction rate of BSIT compared to SIT is mostly influenced by the starting day of releases, and, to a much lesser extent, by sterile males competitiveness (ω) and the number of sterile males released (λ_{M_s}) (Figure 9 (C)). Male competitiveness, starting date of releases and the quantity of sterile males released drive an undesirable augmentation of the females number in SIT, while none has been observed for BSIT (Figure 9 (D)). These parameters may act in interaction (high σ). Boost related parameters (*e.g.* the decontamination rate, ν , the larval resistance to PP, ϕ and the PP transfers, κ_{Bc} and κ_F) have few or no influence in the outputs (Figure 9).

5 Annexes de l'article 3

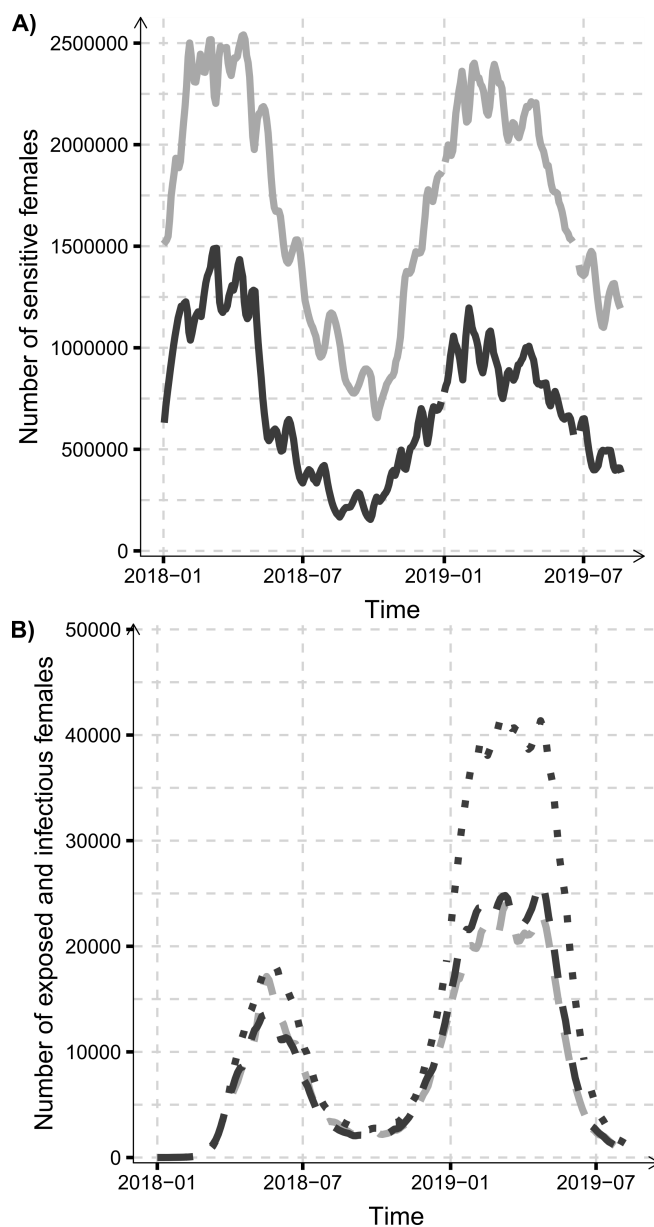
A Simulated abundance of *Ae. albopictus* females


Figure 6. Sum of simulated abundance of A) females susceptible and B) exposed and infectious females in all IRIS areas from La Reunion. The dark and light gray colors correspond to nulliparous and parous females respectively. The solid lines are for susceptible females, the long dotted lines are the exposed females, and the little dotted line are the infectious females.

B Impact of the vector control interventions

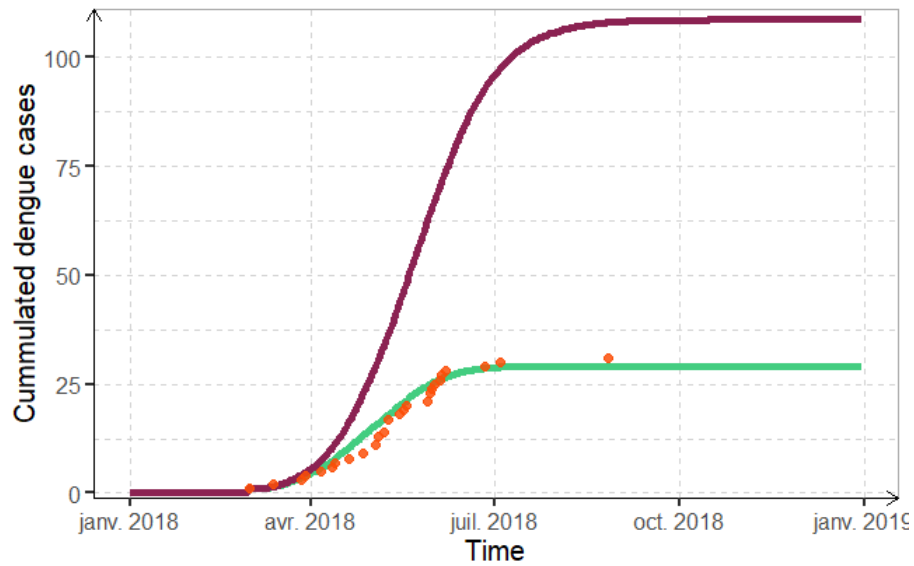


Figure 7. Taking into account the vector control interventions dramatically improves how predictions fit the observations. *The orange dots correspond to the cumulative number of observed cases. The purple line represents the cumulative sum of infected (H_I) and removed (H_R) cases predicted by the model without vector control interventions ($x = 0$). The green line represents the model predictions where control interventions increase adult mortality, with $x = 0.14$.*

Résumé

Le moustique tigre, *Aedes albopictus*, représente une menace sanitaire par la transmission de maladies virales humaines. Malgré l'existence de moyens de lutte, le contrôle des populations d'*Ae. albopictus* reste un enjeu contraint par une connaissance fine de leur dynamique dans l'espace et le temps. Dans ce contexte, les modèles mathématiques sont des outils de choix pour tester et optimiser ces stratégies de contrôle.

L'objectif de cette thèse était d'explorer les effets des méthodes de contrôle sur les populations d'*Ae. albopictus* en milieu tropical (La Réunion) et tempéré (Montpellier). L'étude s'est basée sur l'utilisation de modèle déterministe détaillant l'ensemble du cycle de vie du moustique, piloté par le climat et l'abondance de gîtes larvaires. Nous avons intégré au modèle les effets de différentes méthodes de lutte sur la dynamique des populations d'*Ae. albopictus*. Une attention particulière a été portée aux méthodes basées sur des lâchers de mâles stériles. L'analyse du modèle nous a permis de mieux comprendre et identifier les stratégies de lutte efficaces en terme de réduction et résilience des populations d'*Ae. albopictus*, afin de les optimiser en conséquence.

Les stratégies de lutte intégrée ont pour objectif final de prévenir l'émergence d'épidémie. C'est pourquoi le modèle de dynamique des populations à La Réunion a été couplé avec un modèle épidémiologique. Des études supplémentaires devront être réalisées pour ajuster les prédictions du modèle avant de pouvoir étudier l'impact de stratégies de lutte intégrée sur la transmission de la dengue.

Mots clés : *Aedes albopictus*, modélisation, climat, lutte intégrée, dengue

Abstract

The tiger mosquito, *Aedes albopictus*, poses a health threat through the transmission of human diseases. Despite fighting facilities, controlling the *Ae. albopictus* populations remains a stake constrained by a precise knowledge of their dynamics in space and time. In this context, mathematical models are a tool of choice to test and optimize these control strategies.

The objective of this thesis was to explore the effects of control methods on *Ae. albopictus* populations from tropical (La Réunion) and temperate (Montpellier) areas. The study was based on a deterministic model detailing the life cycle of the mosquito, driven by weather and the abundance of larval breeding sites. We incorporated into the model the effects of different control methods on the *Ae. albopictus* populations dynamics. We gave a particular attention to methods based on sterile male released. Analysis of the model allowed us to better understand and identify effective control strategies in terms of reduction and resilience of *Ae. albopictus* populations, in order to optimize them accordingly.

The main purpose of integrated control management is to prevent the emergence of epidemics. We had therefore coupled the population dynamics model from La Réunion with an epidemiological model. Further studies will need to be realized to adjust the model predictions before being able to study impact of integrated control strategies on dengue transmission.

Key words : *Aedes albopictus*, modelling, climate, integrated control management, dengue