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ANALYSE, OBSERVATION ET CONTRÔLE DE CERTAINS BIO-SYSTÈMES

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UNIVERSITÉ DE NICE SOPHIA ANTIPOLIS

Mémoire
présenté pour obtenir

l'HABILITATION À DIRIGER DES RECHERCHES

en Sciences
Spécialité : Automatique

par
Abderrahman Iggidr

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**ANALYSE, OBSERVATION ET CONTRÔLE DE CERTAINS
BIO-SYSTÈMES**

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Avant-propos

Dans le but donner une certaine unité à ce mémoire, nous n'avons exposé que nos travaux relatifs aux bio-systèmes avec un bref rappel de certains travaux antérieurs en théorie du contrôle (chapitre 1) dont nous avons utilisé certains résultats par la suite pour l'étude de certains bio-systèmes.

Nous commençons par une brève notice présentant les différentes activités et travaux ainsi que les thématiques de recherche.

L'essentiel de nos travaux concernant les systèmes halieutiques et épidémiologiques sont présentés dans les chapitres 2 et 3. Nous avons choisi de détailler certaines parties qui ne figurent pas dans les articles fournis ou qui ne sont pas publiées. Nous finirons par présenter quelques perspectives et projets de recherche que nous comptons développer.

En annexe, nous reproduisons sept articles qui contiennent les preuves et les détails techniques des résultats exposés dans les chapitres 1, 2 et 3.

Chapitre 1

Quelques (anciens) résultats de stabilisation

1.1 Stabilisation de systèmes non linéaires en temps continu.

La stabilisation par retour d'état de systèmes non linéaires en temps continu fait l'objet d'une intense activité de recherche en automatique non linéaire.

Un système

$$\begin{cases} \dot{x} = f(x, u) \\ x \in \mathbb{R}^n, u \in \mathbb{R}^p \end{cases} \quad (1.1)$$

est dit stabilisable s'il existe une fonction $u : \mathbb{R}^n \rightarrow \mathbb{R}^p$ suffisamment régulière (pour assurer l'existence et l'unicité des solutions) telle que l'origine soit un point d'équilibre asymptotiquement stable (localement ou globalement) pour le système bouclé

$$\dot{x} = f(x, u(x))$$

Si de plus la commande u est de classe C^1 , le système est dit C^1 -stabilisable.

Dans [29], nous considérons, en collaboration avec A. Ferfera, le problème de la stabilisation globale des systèmes non linéaires de la forme

$$\begin{cases} \dot{x} = f(x, y) & x \in \mathbb{R}^n, y \in \mathbb{R}^p \\ \dot{y} = Ay + Bu & u \in \mathbb{R}^k \end{cases} \quad (1.2)$$

Ces systèmes ont été beaucoup considérés (cf. [87] et sa bibliographie). Sous certaines conditions dont la stabilité asymptotique globale à l'origine de

$$\dot{x} = f(x, 0) \quad (1.3)$$

Saberi, Kokotovic et Sussmann ([87]) obtiennent une commande stabilisante à partir d'une fonction de Lyapunov $V(x)$ stricte pour (1.3) :

$$\langle \nabla V(x), f(x, 0) \rangle < 0, \forall x \neq 0$$

Il n'existe cependant pas de méthode systématique pour construire de telles fonctions de Lyapunov. Nous montrons dans [29] que la connaissance d'une fonction de Lyapunov large pour (1.3) :

$$\langle \nabla V(x), f(x, 0) \rangle \leq 0 \quad \forall x \in \mathbb{R}^n$$

vérifiant le principe d'invariance de Lasalle suffit pour obtenir une commande stabilisante pour (1.2). L'intérêt de notre démarche est que pour de très larges classes de systèmes, dont les systèmes mécaniques, il est plus facile de construire une fonction de Lyapunov large plutôt qu'une stricte.

Dans [7], nous donnons, en collaboration avec M. Bensoubaya et A. Ferfera, une condition suffisante de stabilisation globale par une commande régulière pour des systèmes non affines en contrôle de la forme (1.1) généralisant la condition de Jurdjevic-Quinn connue pour les systèmes affines en contrôle (cf. [59])

$$\dot{x} = X(x) + \sum_{i=1}^m u_i Y_i(x) \quad (1.4)$$

Historiquement, le résultat de [59] est l'un des premiers résultats significatifs sur la stabilisation. On peut le résumer ainsi : s'il existe une fonction de classe \mathcal{C}^∞ $V : \mathbb{R}^n \rightarrow \mathbb{R}$ définie positive et propre telle que

(i) la dérivée de Lie de V suivant le champ de vecteur X satisfait

$$X \cdot V(x) \leq 0, \quad \forall x \in \mathbb{R}^n$$

(ii) l'ensemble

$$W = \{x \in \mathbb{R}^n \mid X^{k+1} \cdot V(x) = X^k \cdot Y_i \cdot V(x) = 0, \quad k \in \mathbb{N}, \quad i = 1, \dots, m\}$$

est réduit à $\{0\}$;

alors, la dérivée de V le long des trajectoires du système (1.4) étant donnée par

$$\dot{V}(x) = X \cdot V(x) + \sum_{i=1}^m u_i Y_i \cdot V(x)$$

le feedback

$$u(x) = -(Y_1 \cdot V(x), \dots, Y_m \cdot V(x))^T$$

conduit à $\dot{V}(x) \leq 0$ et, par application du principe d'invariance de LaSalle, stabilise globalement (1.4).

Pour les systèmes non affines en contrôle de la forme générale (1.1), $\dot{V}(x)$ n'étant plus linéaire en u , la difficulté majeure est de prouver l'existence d'un feedback $u(x)$ conduisant à $\dot{V}(x) \leq 0$. Dans [7] on montre que si les champs de vecteurs :

$$X(x) = f(x, 0), \quad Y_i(x) = \frac{\partial f}{\partial u_i}(x, 0), \quad i = 1, \dots, m \quad (1.5)$$

satisfont (i) et (ii) alors un tel feedback existe et stabilise globalement (1.1). Dans [7] on donne une preuve constructive de ce résultat permettant de calculer explicitement le feedback stabilisant.

1.2 Stabilisation de systèmes non linéaires discrets.

Un système en temps discret :

$$x(k+1) = f(x(k), u(k)), \quad f(0, 0) = 0, \quad k = 0, 1, 2, \dots$$

où $x(k) \in \mathbb{R}^n$, $u(k) \in \mathbb{R}^m$ et f est continue au voisinage de $(0, 0)$, est stabilisable s'il existe une loi de commande $x \mapsto u(x)$ continue au voisinage de l'origine telle que pour le système bouclé :

$$x(k+1) = f(x(k), u(x(k)))$$

l'origine soit un point d'équilibre asymptotiquement stable.

Pour les systèmes non linéaires en temps discret, dont l'intérêt est croissant, il n'existe que fort peu de résultats de stabilisation.

Dans [8, 7, 9], en collaboration avec M. Bensoubaya et A. Ferfera, nous avons établi, en temps discret, une condition nécessaire de stabilisation, analogue à celle de Brockett [18] en temps continu, et nous avons donné des conditions suffisantes de stabilisation (conditions de type Jurdjevic-Quinn, utilisation de commandes $u(x, t)$ dépendant du temps pour des systèmes ne vérifiant pas la condition nécessaire) ainsi que des méthodes permettant de calculer la commande stabilisante pour certaines classes de systèmes non linéaires.

1.3 Stabilisation par retour d'état estimé par observateur.

Dans la quasi totalité des systèmes concrets, on a rarement accès à l'état x du système, mais plutôt à une approximation \hat{x} estimée par un observateur.

Etant donné un feedback stabilisant $x \mapsto u(x)$ dépendant de l'état, que se passe-t-il si, au lieu d'appliquer le retour d'état $u(x)$, on applique le retour d'état estimé $u(\hat{x})$? Le système obtenu est-il stable? Pour les systèmes non linéaires, il existe peu de résultats sur ce problème (cf. [33]).

Dans ECC93, nous avons étudié, en collaboration avec G. Sallet, le problème de la stabilisation par retour d'état estimé par observateur pour des systèmes qui peuvent s'écrire, après éventuellement un changement de coordonnées dans l'espace d'état et/ou l'espace des contrôles, sous la forme

$$\begin{cases} \dot{x} = Ax + Bu + g(x, u) \\ x \in \mathbb{R}^n, u \in \mathbb{R}^r, A \in M_{n,n}(\mathbb{R}), B \in M_{n,r}(\mathbb{R}), \end{cases} \quad (1.6)$$

où g est globalement Lipschitz et satisfait $g_i(x, u) = g_i(x_1, \dots, x_i, 0, \dots, 0, u)$ pour $i = 1 \dots n$.

1.4 Stabilisation de systèmes non linéaires stochastiques.

On aborde ici la stabilisation de systèmes stochastiques dans l'optique de l'étude de la robustesse au bruit. Les résultats obtenus concernent les calculs de feedback stabilisant pour des équations différentielles stochastiques contrôlées de la forme

$$\begin{cases} x_t = x_0 + \int_0^t f_0(x_s, u) ds + \sum_{j=1}^p \int_0^t f_j(x_s, u) d\omega_s^j \\ x \in \mathbb{R}^n, u \in \mathbb{R}^m, f_j(0, 0) = 0 \end{cases} \quad (1.7)$$

où $\omega = (\omega^1, \dots, \omega^p)$ est un processus de Wiener à valeurs dans \mathbb{R}^p défini sur un espace de probabilité usuel (Ω, \mathcal{F}, P) , avec $\omega^1, \dots, \omega^p$ indépendants, et où les intégrales stochastiques sont prises au sens de Itô. Les versions stochastiques des théorèmes de Lyapunov et du principe d'invariance de LaSalle sont à la base des résultats obtenus. Les systèmes stochastiques contrôlés de la forme (1.7) considérés dans la littérature ont la particularité d'avoir l'entrée u non affectée par le bruit, *i.e.* $(\partial f_j / \partial u) = 0$, pour $1 \leq j \leq p$. Ainsi l'intensité du bruit ne dépend pas de la commande du système, ce qui, dans la pratique, n'est pas très réaliste. En fait, cette hypothèse simplifie considérablement les choses et permet de transposer les résultats déterministes aux systèmes stochastiques de ce type de façon automatique. Ceci est loin d'être le cas pour les systèmes où le bruit affecte les variables aussi bien d'état que de contrôlé. Dans [12], à partir des champs $f_j(x, u)$, $0 \leq j \leq p$, sont associés au système $m + 1$ opérateurs différentiels du second ordre L_0, \dots, L_m . Ces opérateurs, qui constituent pour (1.7) l'analogie des opérateurs linéaires induits par les champs

X, Y_1, \dots, Y_m associés à (1.1) par (1.5), permettent alors d'établir la version stochastique du théorème de Jurdjevic-Quinn pour (1.7) : s'il existe $V : \mathbb{R}^n \rightarrow \mathbb{R}$ de classe \mathcal{C}^∞ définie positive et propre telle que $L_0 V(x) \leq 0, \forall x \in \mathbb{R}^n$, et l'ensemble $\{x \in \mathbb{R}^n \mid L_0^{k+1} V(x) = L_0^k L_i V(x) = 0, k \in \mathbb{N}, i = 1, \dots, m\}$ est réduit à $\{0\}$, alors le système stochastique (1.7) est globalement stabilisable par un feedback que l'on peut expliciter. Ce résultat a préalablement été annoncé en [10].

Notons que la forme (1.7) peut être considérée comme la plus générale dans le sens où, d'une part, le bruit affecte aussi bien la variable d'état que celle de commande, et d'autre part, les champs intervenant dans le système ne sont pas restreints à un type particulier de non linéarité comme pour les systèmes affines en contrôle par exemple. Notons aussi que l'approche stochastique pour l'étude des systèmes contrôlés permet de prendre en considération les perturbations aléatoires auxquelles est soumis un système déterministe (erreurs de modélisation, bruits sur les variables du système). De ce fait, les lois de commande stabilisantes calculées dans ce travail à partir de systèmes stochastiques sont robustes aux bruits, tout en stabilisant le système déterministe idéal associé obtenu en l'absence de bruits.

Enfin, [11] donne l'analogue discret du résultat de [12] pour les systèmes stochastiques discrets de la forme

$$x_{k+1}(\omega) = f(x_k(\omega), \omega, u)$$

où $f : \mathbb{R}^n \times \Omega \times \mathbb{R} \rightarrow \mathbb{R}$ vérifie $f(0, \omega, 0) = 0$.

Chapitre 2

Synthèse d'observateurs et contrôle de certains modèles de pêche

2.1 Introduction

Nous donnons ici quelques applications de la théorie du contrôle à des systèmes modélisant l'évolution au cours du temps de populations soumises à l'exploitation humaine. Ces modèles sont utilisés en "gestion des ressources renouvelables" et plus particulièrement en halieutiques. On retrouve aussi des modèles analogues en gestion de forêts. Autant les techniques de contrôle optimale ont été abondamment appliquées et utilisées dans le domaine de la gestion des ressources renouvelables, autant la théorie des observateurs a été peu utilisée dans ce domaine. En particulier, nous ne connaissons pas d'application des observateurs dans le domaine de l'halieutique. Nous nous sommes donc intéressés à l'utilisation des observateurs comme possible solution (alternative) au problème de l'estimation du stock.

Pour des modèles continus (l'évolution au cours du temps est décrite par des équations différentielles ordinaires), nous avons juste appliqué les méthodes de Gauthier et al. (voir par exemple [31, 32]) pour construire des observateurs (grand-gain et type Kalman) pour un modèle global ainsi que pour un modèle structuré. Le modèle global [25] décrit une population qui peut se déplacer entre deux zones : une zone où la pêche est autorisée et une autre où la pêche est interdite. Le modèle structuré [94, 95] décrit l'évolution d'une population structurée en plusieurs stades (qui peuvent être caractérisés par l'âge, la taille ou le poids par exemple) intégrant, en particulier, un stade de pré-recrutés. Pour ces deux systèmes, il est prouvé qu'il existe un domaine D compact qui est positivement invariant. Le champ de vecteur est donc globalement Lipschitz sur D . La construction d'observateurs pour ces deux

modèles nous a permis de montrer que le prolongement Lipschitzien du champ de vecteur à tout \mathbb{R}^n est nécessaire pour que l’observateur converge effectivement et ceci pas seulement pour des raisons de rigueur mathématique mais aussi pour l’application. Nous montrons dans [35, 37], en choisissant un jeu de paramètres de la littérature, que l’observateur explose en temps fini si le champ n’est pas prolongé en dehors de D . Par contre, si on construit un prolongement Lipschitz du champ (avec les mêmes paramètres) alors les états estimés calculés par l’observateur convergent bien (et vite) vers les états réels du système.

Nous avons aussi étudié le problème d’estimation de stock pour des modèles discrets : la dynamique et la sortie mesurable sont discrètes. Il s’agit de modèles classiques en halieutique. Nous considérerons un modèle structuré en âge et un autre structuré en “stades” qui est une sorte de généralisation du premier. Pour ces systèmes, nous n’avons pas appliqué des résultats existants mais nous avons construit un nouvel observateur pour cette classe de systèmes. Il faut dire que les résultats généraux concernant la synthèse d’observateurs globaux pour des systèmes discrets se limitent aux cas très restreint des systèmes linéaires ou linéarisables ainsi qu’aux systèmes dont les nonlinéarités ne dépendent que de la sortie. Autrement, la plupart des méthodes classiques de synthèse d’observateur pour les systèmes non linéaires utilisent des techniques de linéarisation autour d’un point d’équilibre et donc génèrent des observateurs locaux. Un observateur local n’a pas tellement d’intérêt pratique pour les systèmes qui nous intéressent, nous avons donc cherché à construire un observateur global dont nous développerons la construction dans la suite de ce chapitre.

Nous nous sommes aussi intéressé à la stabilisation par feedback de ces systèmes : calculer un effort de pêche (ou sa vitesse de variation) comme fonction de l’état du stock qui permet de ramener et de maintenir la population au voisinage d’une certaine configuration d’équilibre. Pour les modèles discrets considérés, nous avons réussi à calculer une commande stabilisante en utilisant la méthode décrite dans la section 1.2 mais seulement pour la fonction de recrutement de Beverton et Holt. Nous détaillerons ici la construction pour le modèle continu au dernier paragraphe de ce chapitre.

2.2 Estimation de stock pour une pêcherie

2.2.1 Modèle discret structuré en âge

Le modèle que nous considérons est le modèle classique à structure d’âge décrit dans le livre de Getz et Haight [34]. C’est un modèle discret non linéaire structuré en classes d’âge. L’importance des modèles structurés en halieutique a été résumé dans [76] par B. Mesnil qui a écrit :

“L’introduction des structures d’âge dans les modèles halieutiques résulte du constat que les différents groupes d’âge qui constituent une population fournissent, au fil du temps, des contributions distinctes à la production de biomasse, à la reproduction ou aux captures, ou sont inégalement affectés par les mesures de gestion. Ceci les distingue des modèles dits ”globaux” (e.g. Schaefer, 1954) plus simples qui décrivent la dynamique des stocks uniquement en termes de biomasse total.”

Nous expliquons brièvement comment le modèle que nous utilisons a été obtenu :

La dynamique de passage d’une classe à la suivante :

La population considérée est divisée en n classes d’âge. Le nombre d’individus de la $i^{\text{ème}}$ classe à l’instant k sera noté $x_i(k)$. la population est caractérisée par certains paramètres qui sont supposés ne dépendre que de l’âge des individus. Ces paramètres sont :

- b_i est le taux de fécondité des individus de la classe d’âge i ,
- M_i est le taux de mortalité des individus de la classe d’âge i ,
- q_i est la capturabilité des individus de la classe d’âge i
- $E(k)$ est l’effort de pêche à l’instant k qui représente l’ensemble des moyens de capture mis en œuvre pendant une période donnée et dans une zone déterminée.
- τ est la durée de la saison de pêche avec $0 < \tau < 1$.

On suppose que la pêche a lieu au début de l’intervalle de temps $[k, k + 1[$ avec un effort de pêche $E(k)$ qui reste constant pendant la saison de pêche $[k, k + \tau[$. Pendant cette période, il y a donc une mortalité supplémentaire due à la pêche et dont le taux pour la classe i est donné par $F_i(k) = q_i E(k)$. L’évolution de l’abondance de la classe i sur l’intervalle de temps $[k, k + 1[$ est gouvernée par l’équation différentielle [34] :

$$\frac{dx_i(t)}{dt} = \begin{cases} -(M_i + q_i E(k))x_i(t) & k \leq t < k + \tau \\ -M_i x_i(t) & k + \tau \leq t \leq k + 1 \end{cases} \quad (2.1)$$

En intégrant et en tenant compte du passage d’une classe à l’autre on obtient :

$$x_{i+1}(k + 1) = x_i(k)e^{-M_i - q_i \tau E(k)} \quad i = 1, 2, \dots, n - 2. \quad (2.2)$$

Etant donné que la dernière classe regroupe les individus d’âge n mais aussi les individus d’âge supérieur à n (quand il y en a), il faut ajouter les individus qui avaient déjà l’âge n à l’instant k et qui sont encore vivants à l’instant $k + 1$, ce qui donne :

$$x_n(k + 1) = x_{n-1}(k)e^{-M_{n-1} - q_{n-1} \tau E(k)} + x_n(k)e^{-M_n - q_n \tau E(k)} \quad (2.3)$$

Recrutement dans la première classe d'âge :

On suppose que l'âge 1 est l'âge d'entrée dans la phase exploitable : les individus peuvent être pêchés à partir de l'âge 1. Le nombre des nouveaux nés au temps k est donné par

$$x_0(k) = \sum_{i=1}^n b_i x_i(k) \quad (2.4)$$

Le nombre des nouveaux nés qui survivent jusqu'à l'âge 1 correspond à ce qui est appelé *recrutement*. A cause de plusieurs facteurs (prédation, compétition pour la nourriture, cannibalisme, etc.), le taux de survie des juvéniles est "densité-dependant". En particulier, il a été observé que ce taux décroît quand la nombre des juvéniles augmente. Ceci a amené à introduire une non linéarité dans la relation qui relie $x_1(k+1)$ et $x_0(k)$ de la forme :

$$x_1(k+1) = f\left(\sum_{i=1}^n b_i x_i(k)\right) = \left(\sum_{i=1}^n b_i x_i(k)\right) h\left(\sum_{i=1}^n b_i x_i(k)\right). \quad (2.5)$$

La fonction h est, en général, une fonction qui décroît vers zéro quand son argument tend vers $+\infty$. En halieutique, la fonction f est appelée une fonction de recrutement. Plusieurs fonctions de recrutement existent dans la littérature, les plus connues sont (α , β , γ et c étant des constantes positives)[34, 91, 82] :

$$\text{Beverton et Holt} \quad f(x_0) = \alpha x_0 / (1 + \beta x_0) ;$$

$$\text{Ricker} \quad f(x_0) = \alpha x_0 e^{-\beta x_0} ;$$

$$\text{Power function} \quad f(x_0) = \alpha x_0^{1-\beta} ;$$

$$\text{Shepherd} \quad f(x_0) = \alpha x_0 / (1 + \beta x_0^c) , \quad (c > 0).$$

$$\text{Deriso - Schnute} \quad f(x_0) = \alpha x_0 (1 - \beta x_0)^{1/\gamma};$$

$$\text{Saila - Lorda} \quad f(x_0) = \alpha x_0^\gamma e^{-\beta x_0}.$$

On a donc le système suivant qui décrit l'évolution de la population soumise à l'action de la pêche :

$$\left\{ \begin{array}{l} x_1(k+1) = f\left(\sum_{i=1}^n b_i x_i(k)\right) \\ x_2(k+1) = x_1(k)e^{-M_1 - q_1\tau E(k)} \\ \vdots \\ x_{n-1}(k+1) = x_{n-2}(k)e^{-M_{n-2} - q_{n-2}\tau E(k)} \\ x_n(k+1) = x_{n-1}(k)e^{-M_{n-1} - q_{n-1}\tau E(k)} + x_n(k)e^{-M_n - q_n\tau E(k)} \end{array} \right. \quad (2.6)$$

Dans la suite, on va utiliser la notation $v_i(k) = e^{-M_i - q_i\tau E(k)}$.

Calcul des captures :

Les captures en nombre sur un intervalle de temps $[k, k+1[$ sont données par :

$$y(k) = \sum_{i=1}^n \int_k^{k+1} q_i E(t) x_i(t) dt = \sum_{i=1}^n \int_k^{k+\tau} q_i E(t) x_i(t) dt.$$

Sur l'intervalle $[k, k+\tau[$, en utilisant (2.1), $x_i(t)$ est donnée par

$$x_i(t) = e^{-(M_i + q_i E(k))(t-k)} x_i(k)$$

Ce qui donne

$$y(k) = \sum_{i=1}^n \frac{q_i E(k)}{q_i E(k) + M_i} \left(1 - e^{-(M_i + q_i E(k))\tau}\right) x_i(k). \quad (2.7)$$

qui est de la forme :

$$y(k) = \sum_{i=1}^n c_i(k) x_i(k). \quad (2.8)$$

Remarquons que les $c_i(k)$ ne sont jamais nuls car d'une part tous les coefficients q_i sont non nuls (toutes les classes $i = 1 \dots n$ appartiennent à la partie exploitable de la population considérée) et d'autre part $E(k) \neq 0$ sinon cela voudrait dire qu'il n'y a pas eu de pêche pendant toute une saison.

Pour pouvoir utiliser les données des organisations qui s'occupent des pêcheries, on peut aussi exprimer les captures saisonnières en masse au lieu du nombre total

d'individus capturés. On peut aussi utiliser les taux de mortalité par pêche. Si nous notons par w_i le poids moyen individuel des poissons de la classe d'âge i , alors on peut exprimer la biomasse totale capturée $Y(k)$ par :

$$Y(k) = \sum_{i=1}^n \frac{q_i E(k)}{q_i E(k) + M_i} \left(1 - e^{-(M_i + q_i E(k))\tau}\right) w_i x_i(k).$$

Soit $F_i(k) = q_i E(k)$ le taux de mortalité par pêche de la classe d'âge i , alors on a :

$$Y(k) = \sum_{i=1}^n \frac{F_i(k)}{M_i + F_i(k)} (1 - e^{-(M_i + F_i(k))\tau}) w_i x_i(k). \quad (2.9)$$

Un observateur :

Nous cherchons à donner un outil qui permet d'estimer l'état du stock ainsi que sa répartition en classes en utilisant le modèle (2.6) avec la seule information dont on dispose à savoir la quantité d'individus capturés qui est donnée par (2.7) ou la relation (2.9). Pour cela nous construisons un *observateur* qui n'est autre qu'un système dynamique auxiliaire qui utilisera la sortie mesurable $y(k)$ ou $Y(k)$ du système (2.6) et qui devra fournir une estimation dynamique de l'état du système (2.6). Plus précisément cet observateur sera de la forme :

$$\hat{x}(k+1) = g(\hat{x}(k), y, E). \quad (2.10)$$

Il devra satisfaire la condition suivante : il existe $\rho < 1$ tel que l'on ait pour toute condition initiale $x(0)$ du système (2.6) et pour toute condition initiale $\hat{x}(0)$ du système (2.10), les solutions correspondantes satisfont

$$|\hat{x}(k) - x(k)| \leq \rho^k |\hat{x}(0) - x(0)|, \text{ pour tout } k \geq 0.$$

Etant donné que la fonction de recrutement est mal connue, nous cherchons à construire un observateur qui ne dépend pas de cette fonction. En fait on va la considérer comme une *entrée inconnue*. L'utilisation de $y(k+1)$ nous permettra d'éliminer cette entrée inconnue. Considérons les captures en nombre au temps $k+1$,

alors d'après la relation (2.7), avec $r_i(k) = e^{-(M_i + q_i E(k))\tau}$, on a :

$$\begin{aligned}
y(k+1) &= \sum_{i=1}^n \frac{q_i E(k+1)}{M_i + q_i E(k+1)} \left(1 - r_i(k+1)\right) x_i(k+1) \\
&= \frac{q_1 E(k+1)}{M_1 + q_1 E(k+1)} \left(1 - r_1(k+1)\right) x_1(k+1) \\
&\quad + \sum_{i=2}^n \frac{q_i E(k+1)}{M_i + q_i E(k+1)} \left(1 - r_i(k+1)\right) x_i(k+1) \\
&= \frac{q_1 E(k+1)}{M_1 + q_1 E(k+1)} \left(1 - r_1(k+1)\right) x_1(k+1) \\
&\quad + \sum_{i=1}^{n-1} \frac{q_{i+1} E(k+1)}{M_{i+1} + q_{i+1} E(k+1)} \left(1 - r_{i+1}(k+1)\right) x_{i+1}(k+1).
\end{aligned}$$

Pour $i = 2, \dots, n-1$ on a :

$$\begin{cases} x_{i+1}(k+1) = v_i(k)x_i(k), \text{ for } i = 1, \dots, n-2, \\ \text{and } x_n(k+1) = v_{n-1}(k)x_{n-1}(k) + v_n(k)x_n(k). \end{cases}$$

D'où on obtient :

$$\begin{aligned}
y(k+1) &= \frac{q_1 E(k+1)}{M_1 + q_1 E(k+1)} \left(1 - r_1(k+1)\right) x_1(k+1) \\
&\quad + \sum_{i=1}^{n-1} \frac{q_{i+1} E(k+1)}{M_{i+1} + q_{i+1} E(k+1)} \left(1 - r_{i+1}(k+1)\right) v_i(k)x_i(k) \\
&\quad + \frac{q_n E(k+1)}{M_n + q_n E(k+1)} \left(1 - r_n(k+1)\right) v_n(k)x_n(k).
\end{aligned}$$

L'observateur que nous proposons est donné par :

$$\left\{ \begin{array}{l} \hat{x}_1(k+1) = \frac{M_1 + q_1 E(k+1)}{q_1 E(k+1)(1 - r_1(k+1))} y(k+1) \\ \quad - \sum_{i=1}^{n-1} \frac{q_{i+1} (M_1 + q_1 E(k+1)) (1 - r_{i+1}(k+1))}{q_1 (M_{i+1} + q_{i+1} E(k+1)) (1 - r_1(k+1))} v_i(k) \hat{x}_i(k) \\ \quad - \frac{q_n (M_1 + q_1 E(k+1)) (1 - r_n(k+1))}{q_1 (M_n + q_n E(k+1)) (1 - r_1(k+1))} v_n(k) \hat{x}_n(k), \\ \hat{x}_2(k+1) = v_1(k) \hat{x}_1(k), \\ \vdots \\ \hat{x}_{n-1}(k+1) = v_{n-2}(k) \hat{x}_{n-2}(k), \\ \hat{x}_n(k+1) = v_{n-1}(k) \hat{x}_{n-1}(k) + v_n(k) \hat{x}_n(k), \end{array} \right. \quad (2.11)$$

Notons

$$\alpha_i(k) = - \frac{q_{i+1} (M_1 + q_1 E(k+1)) (1 - r_{i+1}(k+1))}{q_1 (M_{i+1} + q_{i+1} E(k+1)) (1 - r_1(k+1))} v_i(k), \quad \text{for } i = 1 \dots n-1$$

et

$$\alpha_n(k) = - \frac{q_n (M_1 + q_1 E(k+1)) (1 - r_n(k+1))}{q_1 (M_n + q_n E(k+1)) (1 - r_1(k+1))} v_n(k).$$

Alors le système (2.11) peut s'écrire sous la forme :

$$\hat{x}(k+1) = A(k) \hat{x}(k) + y(k+1) F(k), \quad (2.12)$$

avec

$$F(k) = \begin{pmatrix} \frac{M_1 + q_1 E(k+1)}{q_1 E(k+1)(1 - r_1(k+1))} \\ 0 \\ \vdots \\ 0 \end{pmatrix}$$

et

$$A(k) = \begin{pmatrix} \alpha_1(k) & \alpha_2(k) & \alpha_3(k) & \dots & \alpha_n(k) \\ v_1(k) & 0 & 0 & \dots & 0 \\ 0 & v_2(k) & 0 & \dots & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots \\ 0 & \dots & 0 & v_{n-1}(k) & v_n(k) \end{pmatrix}.$$

Remarquons que le système considéré (2.12) ou (2.11) ne fait intervenir que ses variables d'état $\hat{x}_i(k)$ ainsi que l'entrée et la sortie du système (2.6). Il n'utilise pas la fonction de recrutement.

Notons E_m la valeurs minimale de l'effort de pêche. Nous avons alors le résultat suivant :

Proposition 2.2.1 *Il existe η tel que si $E_m > \eta$ alors le système (2.11) est un observateur exponentiel global du système (2.6).*

La démonstration est détaillée dans [78] ainsi que dans la thèse de D. Ngom [79]. Nous donnons aussi l'expression de l'observateur quand la sortie correspond aux captures en poids et non en nombre :

$$\left\{ \begin{array}{l} \hat{x}_1(k+1) = \frac{Y(k+1)(M_1 + F_1(k+1))}{F_1(k+1)(1 - r_1(k+1))w_1} \\ - \sum_{i=1}^{n-1} \frac{F_{i+1}(k+1)(M_1 + F_1(k+1))(1 - r_{i+1}(k+1))}{F_1(k+1)(M_{i+1} + F_{i+1}(k+1))(1 - r_1(k+1))} \frac{w_i}{w_1} v_i(k) \hat{x}_i(k) \\ - \frac{F_n(k+1)(M_1 + F_1(k+1))(1 - r_n(k+1))}{F_1(k+1)(M_n + F_n(k+1))(1 - r_1(k+1))} \frac{w_n}{w_1} v_n(k) \hat{x}_n(k), \\ \hat{x}_2(k+1) = v_1(k) \hat{x}_1(k), \\ \vdots \\ \hat{x}_{n-1}(k+1) = v_{n-2}(k) \hat{x}_{n-2}(k), \\ \hat{x}_n(k+1) = v_{n-1}(k) \hat{x}_{n-1}(k) + v_n(k) \hat{x}_n(k). \end{array} \right. \quad (2.13)$$

Nous avons appliqué l'observateur construit à des données (mesures) disponibles concernant une pêcherie mono-espèce. La population est structurée en 7 classes d'âge, l'unité étant l'année. Ces données proviennent d'un rapport de la FAO disponible en ligne à l'adresse :

<http://www.fao.org/DOCREP/003/S4882F/S4882F09.htm>.

Les données sont synthétisées dans les tableaux 2.1 et 2.2. Ces tableaux donnent respectivement les quantités de poissons pêchés et les taux de mortalité par pêche. Il est à remarquer que le tableau 2.1 donne, pour chaque année, les captures totales ainsi que les captures par classe d'âge. Ceci dit si les captures totales constituent de vraies mesures réelles, il n'en est pas de même pour les valeurs des captures par classes qui, généralement, sont le résultat d'un échantillonnage. Notre méthode d'estimation du stock utilise seulement les valeurs des captures totales et n'a pas besoin des captures par classe contrairement à certaines méthodes classiques en halieutique telle l'analyse de cohortes (AC), désignée aussi par VPA (Virtual Population Analysis), qui utilise les captures par classe ce qui nécessite l'estimation de la composition en âge des captures. La figure 2.1 donne les estimations pour la classe d'âge 2 calculées par l'observateur avec deux conditions initiales prises au hasard. Elle compare aussi ces estimations avec celles de la FAO.

An- nées	Classes d'âge							Capture totale (1000t)	Capture totale en nombre
	1	2	3	4	5	6	7+		
72	1492,0	798,1	403,9	188,0	106,4	52,0	18,5	390,123	3058.9
73	2457,0	680,9	250,9	114,5	60,3	43,2	48,5	383,052	3625.3
74	3273,2	947,3	240,4	44,9	26,2	12,3	11,8	414,63	4562.8
75	2078,1	493,6	152,3	48,9	7,7	4,8	2,6	302,317	2803.9
76	3202,3	685,6	97,4	35,6	16,3	4,6	1,1	394,145	4060.3
77	2927,2	1391,2	380,3	52,1	12,0	6,3	1,4	392,572	4787.6
78	1650,4	1162,8	338,7	78,2	16,5	3,0	0,5	294,151	3268.1
79	1323,3	534,7	231,0	99,0	29,6	10,0	0,8	223,165	2246.1
80	150,2	676,6	582,1	799,6	306,6	86,0	11,4	503,081	2619.6
81	230,4	415,2	462,2	357,9	207,2	72,6	14,1	357,935	1764.0
82	310,5	840,4	542,4	254,1	71,5	8,1	1,1	310,464	2045.5
83	591,1	727,3	262,9	135,9	88,4	62,5	31,8	280,000	1886.6
84	424,6	621,4	274,9	167,1	105,7	68,4	41,9	300,000	1680.6
85	145,6	800,1	360,3	109,8	126,4	48,7	2,5	320,000	1609.4

TABLE 2.1 – *Trachurus* spp. : Captures en millions d'individus par classe d'âge (divisions 34.1.3. et 34.3.1) et captures totales en milliers de tonnes. (Les prises de 1972-1981 sont extraites de COPACE/PACE SERIES 83/27, et les prises totales pour 1982 de CECAF Statistical Bulletin 1984 N°4. Les prises de 1983, 1984 et 1985 sont estimées à un niveau respectif de 280, 300 et 320 milliers de tonnes.)

An- nées	Classes d'âge						
	1	2	3	4	5	6	7+
72	0,511725	0,788882	0,841723	0,767820	0,616278	0,322343	0,705246
73	0,710480	0,691405	0,962460	0,953076	0,933614	0,833445	0,850099
74	0,911205	1,462620	0,858620	0,660721	0,921245	0,740458	0,879356
75	0,351619	0,472105	0,686220	0,617037	0,312602	0,620453	0,488036
76	0,387599	0,261425	0,221046	0,483193	0,632487	0,445506	0,397193
77	0,258610	0,413621	0,318220	0,245832	0,424763	0,816728	0,332598
78	0,184893	0,215220	0,232136	0,136975	0,167873	0,248101	0,185781
79	0,233446	0,115179	0,082385	0,135158	0,096253	0,187148	0,132838
80	0,030647	0,250393	0,245816	0,651817	1,229370	0,641243	0,481579
81	0,045911	0,152152	0,383773	0,330540	0,502452	2,385422	0,283060
82	0,098016	0,327470	0,430687	0,546851	0,139337	0,043822	0,308936
83	0,168887	0,496638	0,224000	0,253589	0,540531	0,241525	0,337494
84	0,134262	0,380006	0,511330	0,341390	0,457392	0,010983	0,357427
85	0,063021	0,577001	0,577000	0,577000	0,577000	0,577000	0,530840
M	0,50	0,50	0,50	0,50	0,50	0,50	0,50
P	65,00	99,00	175,00	274,00	401,00	483,00	563,00

TABLE 2.2 – *Trachurus* spp. : Mortalités par pêche (divisions 34.1.3 et 34.3.1).
(P = poids moyen, M= mortalité naturelle)

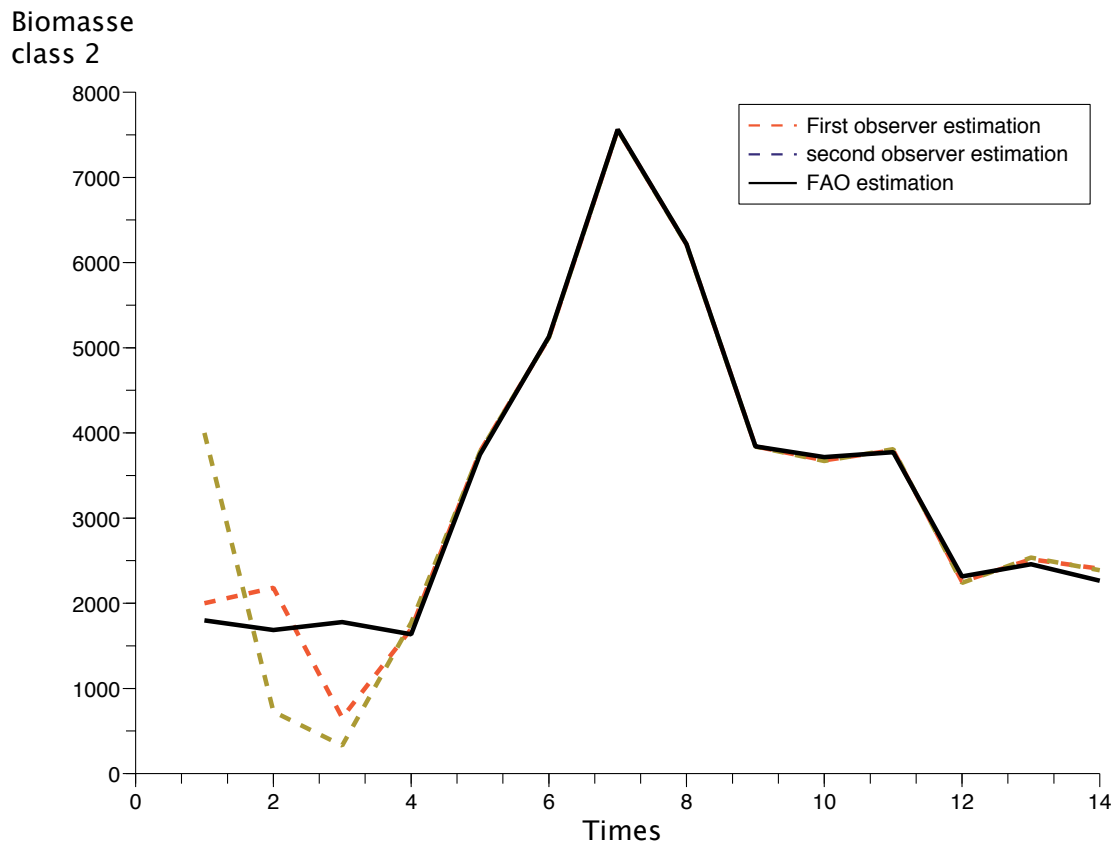


FIGURE 2.1 – Comparaison de l'estimation de la FAO et celle donnée par l'observateur (2.11).

2.2.2 Modèles structurés en "stades"

Dans la pratique et pour certaines populations, il est assez souvent plus facile de structurer une population en utilisant d'autres critères que l'âge. Pour les poissons on utilise souvent le poids ou la taille (qui sont plus faciles à mesurer que l'âge). On parlera alors de structuration en "stades" (en anglais stages). Notons p_i la proportion d'individus ($i = 1, \dots, n$) de la classe i qui arrive dans la classe $i+1$ après écoulement de l'intervalle de temps $[k, k+1[$. Alors $1 - p_i$ est la proportion d'individu de la classe i qui n'atteint pas le stade de classe $i + 1$. Par définition des p_i on a $p_n = 0$ car les individus qui atteignent le stade n y demeurent jusqu'à leur mort naturelle ou jusqu'à ce qu'ils soient capturés. On notera s_i le taux de survie des individus de la classe i qui représente la proportion des individus qui survivent de l'instant k à l'instant $k + 1$. Pour une population soumise à l'action de la pêche, nous avons vu que $s_i(k) = e^{-M_i - q_i \tau} E(k)$. Avec les mêmes hypothèses que celles faites pour le modèle structuré en âge (2.6), l'évolution au cours du temps d'une population structurée en "stades" sera décrite par le système suivant :

$$\left\{ \begin{array}{l} x_1(k+1) = (1 - p_1)s_1(k)x_1(k) + s_0 f\left(\sum_{i=1}^n b_i x_i(k)\right) \\ x_2(k+1) = p_1 s_1(k)x_1(k) + (1 - p_2)s_2(k)x_2(k) \\ \quad \quad \quad \vdots \quad \quad \quad \vdots \\ x_i(k+1) = p_{i-1} s_{i-1}(k)x_{i-1}(k) + (1 - p_i)s_i(k)x_i(k) \\ \quad \quad \quad \vdots \quad \quad \quad \vdots \\ x_{n-1}(k+1) = p_{n-2} s_{n-2}(k)x_{n-2}(k) + (1 - p_{n-1})s_{n-1}(k)x_{n-1}(k) \\ x_n(k+1) = p_{n-1} s_{n-1}(k)x_{n-1}(k) + s_n(k)x_n(k) \end{array} \right. \quad (2.14)$$

De la même façon que pour les modèles structurés en classes d'âge, nous avons construit un observateur pour le système (2.14) qui s'écrit :

$$\left\{ \begin{array}{l}
 z_1(k+1) = -\frac{c_2(k+1)p_1s_1(k)}{c_1(k+1)}z_1(k) \\
 \quad - \sum_{i=2}^{n-1} \left(p_i s_i(k) \frac{c_{i+1}(k+1)}{c_1(k+1)} + (1-p_i)s_i(k) \frac{c_i(k+1)}{c_1(k+1)} \right) z_i(k) \\
 \\
 z_2(k+1) = p_1s_1(k)z_1(k) + (1-p_2)s_2z_2(k) + \frac{p_1s_1}{c_1(k)}y(k), \\
 \vdots \\
 z_{n-1}(k+1) = p_{n-2}s_{n-2}(k)z_{n-2}(k) + (1-p_{n-1})s_{n-1}(k)z_{n-1}(k), \\
 z_n(k+1) = p_{n-1}s_{n-1}(k)z_{n-1}(k) + s_n(k)z_n(k), \\
 \\
 \hat{x}_1(k) = z_1(k) + \frac{1}{c_1(k)}y(k), \\
 \hat{x}_i(k) = z_i(k) \text{ for } i = 2, \dots, n.
 \end{array} \right. \tag{2.15}$$

Rappelons que $c_i(k) = \frac{q_i E(k)}{q_i E(k) + M_i} \left(1 - e^{-(M_i + q_i E(k))\tau} \right)$ qui peut aussi s'écrire en utilisant les taux de mortalité par pêche

$$c_i(k) = \frac{F_i(k)}{F_i(k) + M_i} \left(1 - e^{-(M_i + F_i(k))\tau} \right).$$

Nous avons appliqué cet observateur à des données concernant une population structurée en deux classes : immatures et matures. Ces données proviennent d'un rapport de l'IECS [2] et ont été reproduites et utilisées dans [100]. Les mesures concernent les captures entre 1946 et 2000, le rapport de l'ICES donne aussi les mortalités par pêche ainsi que les estimations de la biomasse pour chaque classe, nous en reproduisons une partie (voir Table 2.3) en ajoutant une colonne pour les captures totales (le tableau complet peut être consulté dans [100]). Nous avons pris comme taux de mortalité naturelle (autre que par pêche) les valeurs de [100] à savoir $M_1 = M_2 = 0.2$ et pour le taux de passage de la classe des immatures à celle des matures $p = 0.1$. Bien que les données fournissent les captures pour chacune des deux classes, nous n'utilisons pour l'observateur que les captures totales sans distinction entre individus

immatures ou matures. Les figures 2.2 et 2.3 permettent de comparer les estimations de l'ICES avec celles données par l'observateur (2.15). On obtient la même allure mais avec une légère surestimation de l'observateur (surtout pour les immatures) qui pourrait être due aux valeurs de M_i et de p choisies.

Biomasse (million de tonnes)			Captures (million de tonnes)			Taux de mortalité par pêche	
Année k	Immature x_1	Mature x_2	Immature $Y_1(k)$	Mature $Y_2(k)$	Total $Y(k)$	Immature (F_1)	Mature (F_2)
1946	3.3866	1.1206	0.4222	0.2633	0.6855	0.1247	0.2350
1947	2.7283	1.1740	0.4959	0.4688	0.9647	0.1818	0.3993
1948	2.8562	1.0264	0.5176	0.3510	0.8686	0.1812	0.3420
1949	2.5528	0.7360	0.5503	0.2563	0.8066	0.2156	0.3482
1950	2.5292	0.6206	0.4284	0.2444	0.6728	0.1694	0.3938
1951	3.0474	0.5741	0.5263	0.1940	0.7203	0.1727	0.3379
1952	3.4114	0.5271	0.6951	0.2428	0.9379	0.2038	0.4606
1953	3.8533	0.4010	0.5209	0.1425	0.6634	0.1352	0.3554
1954	3.9139	0.4350	0.7196	0.1691	0.8887	0.1839	0.3887
1955	3.2905	0.3512	0.9268	0.1526	1.0794	0.2817	0.4345
1956	3.1074	0.3034	1.1425	0.1421	1.2846	0.3677	0.4684
1957	2.6487	0.2103	0.7023	0.0900	0.7923	0.2651	0.4280
1958	2.1979	0.1978	0.6019	0.0830	0.6849	0.2739	0.4196
1959	2.2912	0.4382	0.6197	0.1806	0.8003	0.2705	0.4121
1960	2.0169	0.3890	0.4343	0.1629	0.5972	0.2153	0.4188

TABLE 2.3 – Biomasse et captures en million de tonnes du Arctic cod dans le Nord Est entre 1946 et 2000. Les données sont extraites de "ICES Advisory Committee on Fisheries Management" (Anon, 2001).

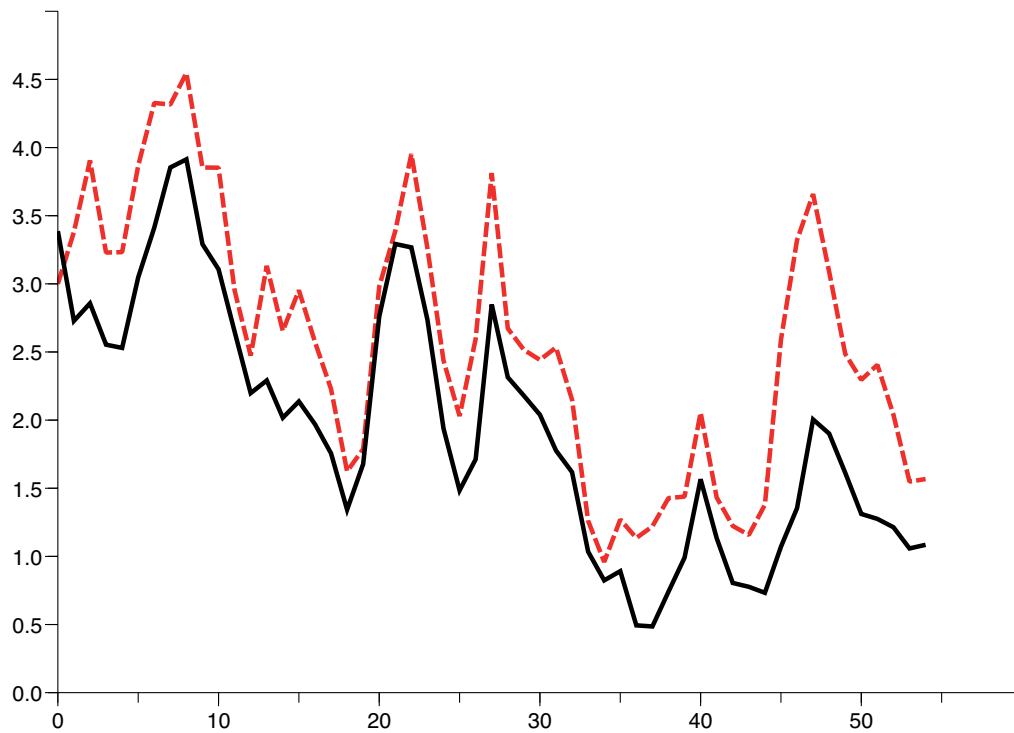


FIGURE 2.2 – Comparaison de l'estimation de la biomasse des immatures donnée par l'IECS (trait plein) et celle donnée par l'observateur (2.15) (en pointillé)

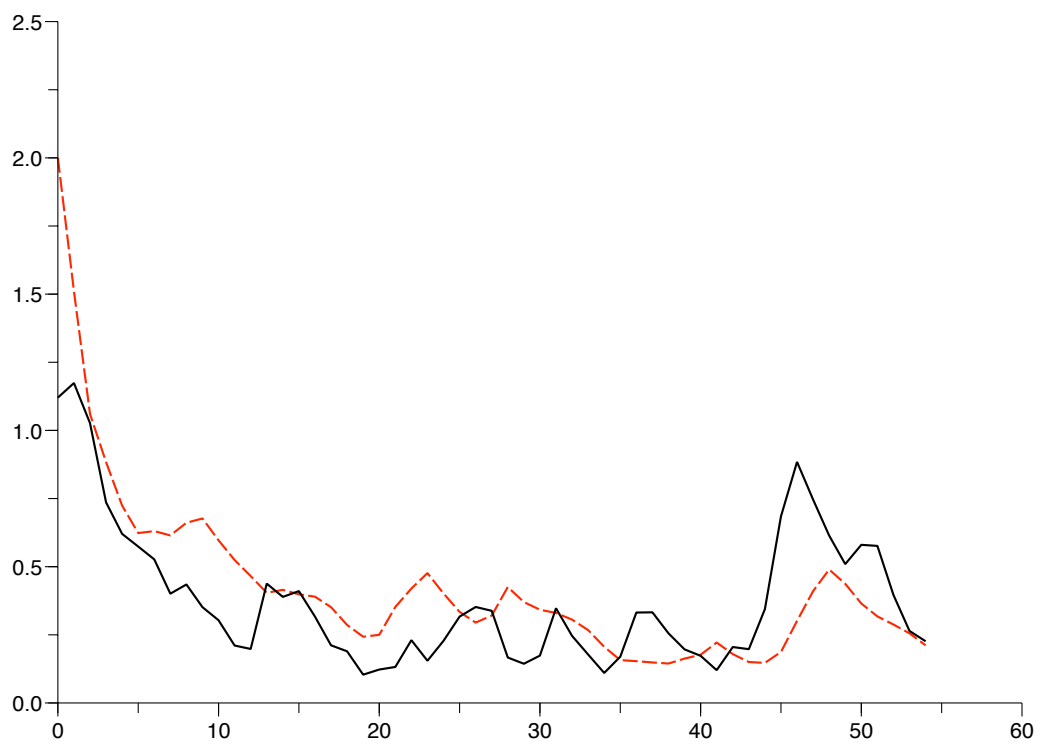


FIGURE 2.3 – Comparaison de l'estimation de la biomasse des matures donnée par l'IECS (trait plein) et celle donnée par l'observateur (2.15) (en pointillé)

2.3 Stabilisation d'un modèle continu de pêche

Nous considérons ici un modèle structuré en stades introduit dans [94, 95]. Ce modèle distingue $(n + 1)$ stades représentés par leurs effectifs $X_i(t)$. Le premier stade X_0 représente le stade des pré-recrutés (oeufs, larves, alevins, juvéniles). Chaque stade est caractérisé par ses coefficients de fécondité, mortalité et prédation. Il est aussi possible d'intégrer la pêche en introduisant au niveau des termes de mortalité l'effort de pêche $E(t)$.

$$\begin{cases} \dot{X}_0 = -\alpha_0 X_0 + \sum_{i=1}^n f_i l_i X_i - \sum_{i=0}^n p_i X_i X_0 \\ \dot{X}_1 = \alpha X_0 - (\alpha + M_1 + q_1 E) X_1 \\ \vdots \\ \dot{X}_{n-1} = \alpha X_n - (\alpha + M_n + q_n E) X_n \end{cases} \quad (2.16)$$

où

- p_0 : paramètre de compétition des juvéniles .
- p_i : coefficient de prédation de la classe i sur la classe 0.
- f_i : coefficient de fécondité de la classe i .
- l_i : efficacité de la reproduction de la classe i .
- q_i : capturabilité de la classe i .
- M_i : mortalité naturelle (autre que par pêche).
- α : coefficient de passage.
- E : effort de pêche (qui joue ici le rôle d'un contrôle).

Le but est de maintenir l'état du système (2.16) autour d'un point de fonctionnement (point d'équilibre) donné, en agissant sur l'effort de pêche ou sur sa vitesse de variation. Plus précisément, nous allons construire un feedback qui stabilise le système autour d'un point d'équilibre non trivial.

Dans la suite on notera $\alpha_i = \alpha + M_i$.

Pour un effort constant $E = \bar{E}$, il a été prouvé dans [94] que l'orthant positif $\Omega = \{X \in \mathbb{R}^{n+1} \mid X_i > 0, i = 0 \dots n + 1\}$ est positivement invariant et que le système admet un état d'équilibre non trivial X^* (en plus de l'équilibre trivial $X_{i=0}$) si les hypothèses de non linéarité et de survie suivantes sont satisfaites :

$$(H1) \quad \sum_{i=0}^n p_i \neq 0$$

$$(H2) \quad \sum_{i=1}^n f_i l_i \pi_i > \alpha_0$$

où

$$\pi_i = \frac{\alpha^i}{\prod_{j=1}^i (\alpha_j + q_j \bar{E})}.$$

Les coordonnées de X^* sont alors données par

$$\begin{cases} X_0^* = \frac{\sum_{i=1}^n f_i l_i \pi_i - \alpha_0}{p_0 + \sum_{i=1}^n p_i \pi_i} \\ X_i^* = \pi_i X_0^*. \end{cases} \quad (2.17)$$

Il a aussi été montré que si les hypothèses **(H1)**-**(H2)** sont satisfaites et si en plus on a :

$$\textbf{(H3)} \quad f_n l_n \neq 0$$

$$\textbf{(H4)} \quad X_0^* < \mu = \min_{i=1, \dots, n} \left(\frac{f_i l_i}{p_i} \right) \quad \text{pour } f_i l_i p_i \neq 0$$

alors l'origine est instable et il existe un domaine positivement invariant $\mathcal{D} = \prod_{i=1}^n [a_i, b_i]$, avec $0 < a_i < b_i$, tel que $X^* \in \mathcal{D}$, X^* est asymptotiquement stable et son domaine d'attraction contient \mathcal{D} .

Ceci a été prouvé en utilisant les propriétés des systèmes coopératifs.

Dans [81, 80] Nous montrons que le domaine d'attraction est l'orthant positif Ω . Notre démonstration est basée sur l'utilisation d'une fonction de Lyapunov. Cette méthode présente l'intérêt de donner un résultat global, en plus la fonction de Lyapunov considérée permet de stabiliser le système par un effort de pêche variable que l'on peut calculer explicitement. Nous montrons aussi comment agir sur la variation de l'effort de pêche [80] pour stabiliser le système au point d'équilibre non trivial.

Pour cela nous avons construit la fonction de Lyapunov suivante :

$$V(X) = \frac{1}{2} \left((X_0 - X_0^*)^2 + \sum_{i=1}^n \gamma_i \left(\frac{X_i - X_i^*}{\pi_i} \right)^2 \right) \quad (2.18)$$

avec

$$\gamma_i = \frac{\sum_{j=i}^n k_j \pi_j}{\alpha_i + q_i \bar{E}} \quad \text{et } k_i = l_i f_i - p_i X_0^* \quad \text{pour } i = 1, \dots, n \quad (2.19)$$

Cette fonction est définie positive si $p_i X_0^* < l_i f_i$ pour tout i , c'est à dire si **H4** est vérifiée.

Grâce à cette fonction et au principe d'invariance de LaSalle, nous avons établi les résultats suivants.

Proposition 2.3.1 *Soit \bar{E} un effort de pêche positif constant. Si les hypothèses **H1**, **H2**, **H3** et **H4** sont satisfaites alors X^* est un point d'équilibre globalement asymptotiquement stable pour le système (2.16).*

Proposition 2.3.2 *Soit \bar{E} un effort de pêche positif constant. Si les hypothèses **H1**, **H2**, **H3** et **H4** sont satisfaites alors on peut construire un effort de pêche qui dépend de l'état du système $X(t)$ (feedback) de la forme $E(X) = \bar{E} + u(X)$ de telle sorte que X^* soit un point d'équilibre globalement asymptotiquement stable pour le système (2.16) bouclé avec $E(X)$.*

Le feedback $u(X)$ est calculé en utilisant la formule de Jurdjevic-Quinn [59] légèrement modifiée pour que $E(X)$ soit toujours positif. En effet le système (2.16) avec $E = \bar{E} + u$ peut s'écrire

$$\dot{X} = F(X) + uG(X), \quad (2.20)$$

avec

$$F(X) = \begin{pmatrix} -\alpha_0 X_0 + \sum_{i=1}^n f_{il_i} X_i - \sum_{i=0}^n p_i X_i X_0 \\ \alpha X_0 - (\alpha_1 + q_1 \bar{E}) X_1 \\ \vdots \\ \alpha X_n - (\alpha_n + q_n \bar{E}) X_n \end{pmatrix}, \quad G(X) = \begin{pmatrix} 0 \\ -q_1 X_1 \\ \vdots \\ -q_n X_n \end{pmatrix}.$$

On peut prendre alors $u = \Phi(X) = -\langle G(X), \nabla V(X) \rangle$. ($\langle \cdot, \cdot \rangle$ est le produit scalaire dans \mathbb{R}^{n+1}) avec

$$\nabla V(X) = \begin{pmatrix} \frac{\partial V}{\partial X_0} \\ \frac{\partial V}{\partial X_1} \\ \vdots \\ \frac{\partial V}{\partial X_n} \end{pmatrix}.$$

Avec la fonction de Lyapunov définie ci-dessus, cela donne :

$$\Phi(X) = \sum_{i=1}^n \frac{q_i \gamma_i}{\pi_i^2} X_i (X_i - X_i^*). \quad (2.21)$$

Mais avec ce feedback, rien ne garantit que $E = \bar{E} + u(X)$ reste positif pour tout $X \in \Omega$. On prendra donc

$$u(X) = \frac{2\Phi(X)}{1 + \Phi^2(X)} \bar{E}. \quad (2.22)$$

Ce choix satisfait $|u(X)| \leq \bar{E}$ ce qui assure que : $0 \leq E(X) \leq 2\bar{E}$ pour tout $X \in \Omega$. Un autre choix [48] est donné par :

$$u(X) = \frac{4\bar{E}}{\sum_{i=1}^n \frac{q_i \gamma_i}{\pi_i^2} X_i^{*2}} \Phi(X)$$

qui assure la positivité de l'effort de pêche $E(X)$ car $\Phi(X) \geq -\sum_{i=1}^n \frac{q_i \gamma_i}{\pi_i^2} \frac{X_i^{*2}}{4}$.

On peut aussi stabiliser le système (2.16) en agissant sur la vitesse de la variation de l'effort de pêche ce qui revient à avoir une stratégie qui consiste à dire : pêcher plus ou pêcher moins en fonction de l'état du système. Cela revient à considérer le système suivant :

$$\begin{cases} \dot{X}_0 = -\alpha_0 X_0 + \sum_{i=1}^n f_i l_i X_i - \sum_{i=0}^n p_i X_i X_0 \\ \dot{X}_1 = \alpha X_0 - (\alpha_1 + q_1 E) X_1 \\ \vdots \\ \dot{X}_n = \alpha X_n - (\alpha_n + q_n E) X_n \\ \dot{E} = v \end{cases} \quad (2.23)$$

L'effort E devient ainsi une autre variable d'état et on contrôle le système en agissant sur \dot{E} la dérivée de E et non plus sur E directement. Sous les hypothèses **H1** et **H2** le système (2.23) admet (X^*, \bar{E}) comme point d'équilibre non trivial. On peut alors établir le résultat suivant :

Proposition 2.3.3 *Sous les hypothèses **H1**, **H2**, **H3** et **H4** le système (2.23) bouclé par le feedback*

$$v(X, E) = \bar{E} - E + \frac{4\bar{E}}{n} \sum_{i=1}^n \frac{q_i \gamma_i}{\pi_i^2} X_i (X_i - X_i^*), \quad (2.24)$$

est globalement asymptotiquement stable.

Là encore il faut s'assurer que l'effort de pêche reste positif. Pour cela il suffit que l'on ait $v(X, 0) \geq 0$. Comme $\sum_{i=1}^n \frac{q_i \gamma_i}{\pi_i^2} X_i (X_i - X_i^*) \geq -\sum_{i=1}^n \frac{q_i \gamma_i}{\pi_i^2} \frac{X_i^{*2}}{4}$, il s'en suit que $v(X, 0) \geq 0$.

Chapitre 3

Epidémiologie mathématique

3.1 Introduction

Cette partie s'intéresse essentiellement aux modèles déterministes appelés modèles compartimentaux.

Il est traditionnel en introduction de ce que l'on appelle l'épidémiologie mathématique de faire remonter cette discipline à Bernoulli [15, 24] en 1766. Klaus Dietz évoque la contribution de P.D. En'ko en 1889. En réalité on peut dire que les fondations de l'épidémiologie remonte à Sir Ronald Ross. Dans son livre [83] il introduit en 1911 le premier modèle différentiel compartimental de la transmission du paludisme. Celui-ci peut s'écrire en notant x_1 la proportion des humains infectieux et x_2 la proportion des moustiques infectieux :

$$\begin{cases} \dot{x}_1 = m a b_1 x_2 (1 - x_1) - \gamma x_1 \\ \dot{x}_2 = b_2 a (1 - x_2) x_1 - \mu x_2 \end{cases} \quad (3.1)$$

Ross a également écrit trois mémoires où il développe l'application des mathématiques à l'épidémiologie. Plus précisément Ross et Hudson [84, 86, 85] développent une théorie des épidémies entre 1916 et 1917. Ross l'appelle a-priori pathometry ou théorie des «happenings». On peut également noter que Lotka [73] a consacré plus de 120 pages au modèle (3.1) de Ross.

Le modèle épidémiologique auquel beaucoup se réfèrent est celui de Kermack et McKendrick en 1927[62]. En fait dans cet article, Kermack et McKendrick présentent une modélisation complexe dont le modèle dit de «Kermack et McKendrick» est un cas particulier de modèle compartimental simple :

$$\begin{cases} \dot{S} = -\beta S I \\ \dot{I} = \beta S I - \gamma I \\ \dot{R} = \gamma I \end{cases} \quad (3.2)$$

Les modèles compartimentaux de Ross ou de Kermack et McKendrick sont assez simples. Ces modèles considèrent différentes classes d'individus les susceptibles S , les infectés I et les «removed» R . Il est supposé que ces classes sont homogènes.

3.2 La prise en compte des hétérogénéités

Un des défis que rencontre la modélisation en épidémiologie est la prise en compte des hétérogénéités. L'hypothèse que les individus se rencontrent au hasard n'est pas réaliste. Beaucoup de populations sont divisées en sous-populations à l'intérieur desquelles on peut admettre l'hypothèse de rencontre aléatoire. En revanche les rencontres entre groupes différents sont soumis à une certaine structuration. Pour tenir compte des différentes source d'hétérogénéité de nouveaux modèles ont été introduits.

On a d'abord introduit d'autres compartiments : les individus latents (infectés mais non infectieux), les individus «removed» (qui ne transmettent plus l'infection), les vaccinés, les individus en quarantaine, ceux protégés par les anticorps de la mère. On a ainsi des modèles encore assez simples notés MSEIRVQ.

3.2.1 Les modèles multi-groupes

Les sources d'hétérogénéité sont nombreuses et de nature diverse. L'intérêt pour des modèles comportant des groupes est venue des différences de comportement. Ce sont les maladies sexuellement transmissibles qui ont donné naissance à ces modèles multi-groupes. En particulier l'article fondateur de Lajmanovich et Yorke [64] en 1976 introduit le premier modèle multi-groupes. La MST concernée est la gonorrhée encore appelée blennorragie gonococcique. Le modèle s'écrit

$$\dot{x}_i = (1 - x_i) \sum \tilde{\beta}_{i,j} x_j - \alpha_i x_i. \quad (3.3)$$

Pour $i = 1, \dots, n$. Le terme x_i représente la prévalence dans le groupe i . Chaque groupe a une population constante.

On peut remarquer que ce modèle pour $n = 2$ est exactement le modèle (3.1) de Ross. Ronald Ross en était particulièrement conscient car dans [83] il fait aussi la remarque que les maladies vénériennes peuvent être modélisées de la même façon :

«the venereal diseases may be looked upon as metaxenous diseases in which the two sexes take the part of the two hosts.»

Metaxenous le mot utilisé par Ross réfère aux parasites qui passent une partie de leur vie chez un hôte et le reste dans un autre.

Une monographie *la gonorrhée : dynamique de transmission et contrôle* par Hethcote et Yorke [44] en 1984 est une tentative sérieuse pour traduire les résultats mathématiques en recommandations de santé publique.

C'est la pandémie du VIH/SIDA qui va stimuler de façon importante l'attention sur les modèles multi-groupes [41, 90, 58, 19, 43] vers les années 1987. La distinction des groupes se fait par le comportement. En effet le comportement sexuel est un des facteurs principaux de la transmission du VIH. La transmission effective va dépendre des types de contacts sexuels entre les groupes.

Un autre facteur important est la longue période d'infectiosité avant que se déclare effectivement un SIDA. Cette période peut-être modélisée à l'aide d'une chaîne de compartiment afin de simuler un retard [53, 56, 54]. Enfin les études cliniques de la transmission du HIV montrent une variabilité de l'infectivité au cours de la longue période "asymptomatique" où l'individu séropositif n' a pas encore déclaré un SIDA. Cela constitue le troisième facteur. C'est la raison qui a motivé J.A. Jacquez [58] a introduire le concept d'individu passant par différent stades, chaque stade ayant une infectivité différente.

Sur un seul groupe le diagramme de flot est donné dans la figure suivante (3.1)

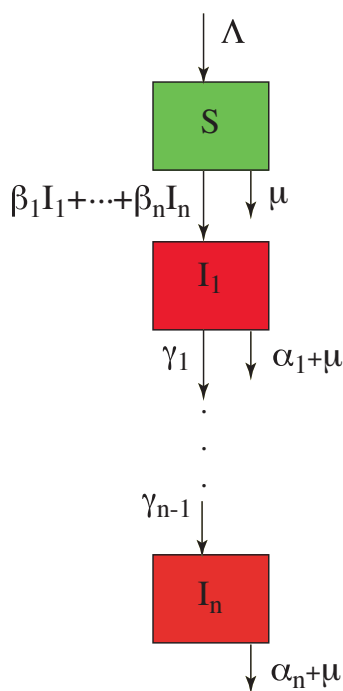


FIGURE 3.1 – Progression dans les stades d'infectiosité

La dynamique est représentée par le système d'équation différentielles :

$$\left\{ \begin{array}{l} \dot{S} = \Lambda - \mu S - S \sum_{j=1}^n \beta_j I_j \\ \dot{I}_1 = S \sum_{j=1}^n \beta_j I_j - (\gamma_1 + \mu + \alpha_1) I_1 \\ \dot{I}_2 = \gamma_1 I_1 - (\gamma_2 + \mu + \alpha_2) I_2 \\ \vdots \\ \dot{I}_j = \gamma_{j-1} I_{j-1} - (\gamma_j + \mu + \alpha_j) I_j \\ \vdots \\ \dot{I}_n = \gamma_{n-1} I_{n-1} - (\mu + \alpha_n) I_n \end{array} \right. \quad (3.4)$$

Le paramètre γ_j représente la fraction de vitesse de transfert du compartiment j au stage $j + 1$. Les termes I_j représentent les différentes classe d'infectieux. On peut remarquer qu'un infecté (latent) est un infectieux avec une infectiosité nulle. Ce modèle permet de prendre en compte les rémissions, les rechutes. Les nombreux compartiments servent d'une part à la prise en compte dans la modélisation de l'infectiosité et d'autre part à représenter phénoménologiquement des retards.

Par la suite ce modèle introduit par Jacquez a été baptisé par Hyman et al. [47] modèle à progression de stade (Stage progression SP).

L'introduction de groupes permet de considérer des groupes noyaux (core group) dans la transmission. Ces groupes jouent un rôle fondamental [57] dans la transmission.

Enfin on rencontre des porteurs asymptomatiques infectieux qui jouent un rôle dans la transmission de la maladie. Le modèle précédent permet de prendre en compte ces porteurs asymptomatiques. En général ces porteurs ont une infectivité moindre. Mais leur influence n'est pas négligeable. Un exemple célèbre est celui de Mary Mallon, connue sous le nom de «typhoid Mary». C'était une porteuse asymptomatique de la typhoïde. Cuisinière, au début du XXème siècle, dans plusieurs familles New-Yorkaises elle a transmis la typhoïde sans être elle-même malade. On utilisait anciennement le terme de porteur sains. On les qualifie de porteurs asymptomatiques plutôt que de porteurs sains (car ils sont réellement porteurs de la maladie). Un autre exemple est celui de certains oiseaux infectés par des souches grippales TP (très pathogènes) ou HP (hautement pathogènes) et qui peuvent excréter des virus sans aucun signe clinique ni aucune lésion observables à l'autopsie.

Parmi les maladies infectieuses pour lesquelles on peut introduire des porteurs asymptomatiques on a par exemple

- La tuberculose

- La typhoïde
- L’infection au HBV (Hépatite B)
- La méningite

Il existe une nombreuse littérature sur les modèles multi-groupes [92, 93, 42, 68, 57]. Les modèles multi-groupes peuvent représenter les maladies à transmission vectorielle. Le modèle fondateur de Ross en est l’exemple type.

Dans l’article [26] (joint), nous avons donné un résultat de stabilité qui nous a permis d’étudier un système constitué de n groupes de systèmes SIS , en particulier nous avons donné une démonstration plus simple du résultat de Lajmanovich et Yorke [64].

Nous avons étudié dans [51] (article joint) le modèle (3.4) avec une fonction de démographie $\varphi(S)$ plus générale qu’un simple recrutement constant Λ et on a introduit des classes de malades latents (ne transmettent pas la maladie). Le système que nous avons considéré est le suivant

$$\left\{ \begin{array}{l} \dot{S} = \varphi(S) - \mu_S S - S \sum_{i=k+1}^n \beta_i I_i \\ \dot{E}_1 = S \sum_{i=k+1}^n \beta_i I_i - \alpha_1 E_1 \\ \dot{E}_2 = \gamma_1 E_1 - \alpha_2 E_2 \\ \vdots \\ \dot{E}_k = \gamma_{k-1} E_{k-1} - \alpha_k E_k \\ \dot{I}_{k+1} = \gamma_k E_k - \alpha_{k+1} I_{k+1} \\ \dot{I}_2 = \gamma_{k+1} I_1 - \alpha_{k+2} I_2 \\ \vdots \\ \dot{I}_n = \gamma_{n-1} I_{n-1} - \alpha_n I_n \\ \dot{R} = \gamma_n I_n - \alpha_{n+1} R \end{array} \right. \quad (3.5)$$

avec $\alpha_i = \gamma_i + \mu_i$. Le paramètre γ_j représente la vitesse de transfert du compartiment j au stage $j + 1$ et le paramètre μ_j la mortalité spécifique du compartiment j . α_{n+1} est la mortalité du dernier compartiment, celui des guéris ou ”removed”.

Nous avons aussi considéré les modèles à infectivité différentielle **DI** (differential infectivity models) représentés par la figure 3.2.

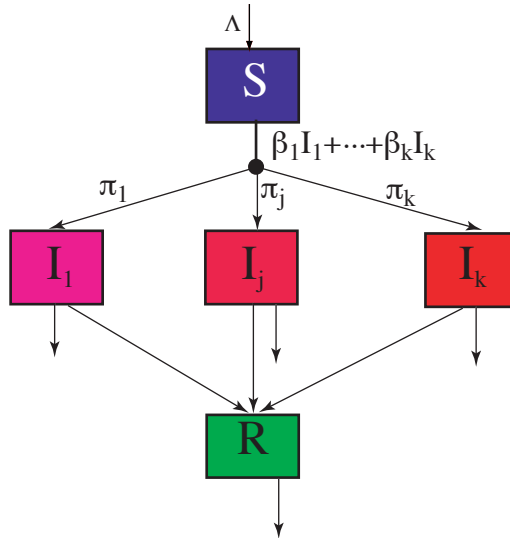


FIGURE 3.2 – Modèle à infectivité différentielle

La dynamique s'écrit :

$$\left\{ \begin{array}{l} \dot{S} = \varphi(S) - \mu_S S - S \sum_{i=1}^n \beta_i I_i \\ \dot{I}_1 = \pi_1 S \sum_{i=1}^n \beta_i I_i - (\mu_1 + \gamma_1) I_1 \\ \dot{I}_2 = \pi_2 S \sum_{i=1}^n \beta_i I_i - (\mu_2 + \gamma_2) I_2 \\ \vdots \\ \dot{I}_n = \pi_n S \sum_{i=1}^n \beta_i I_i - (\mu_n + \gamma_n) I_n \\ \dot{R} = \sum_{i=1}^n \gamma_i I_i - \mu_n R \end{array} \right. \quad (3.6)$$

avec $\sum_{i=1}^n \pi_i = 1$.

Nous avons réécrit ces modèles sous la forme générale suivante :

$$\left\{ \begin{array}{l} \dot{x} = \varphi(x) - x \beta^T \cdot y \\ \dot{y} = (x \beta^T \cdot y) \mathbf{b} + A y = (A + \mathbf{b} \beta^T) y \end{array} \right. \quad (3.7)$$

où $x \in \mathbb{R}_+$ représente la classe des susceptibles et $y \in \mathbb{R}_+^n$ est un vecteur qui regroupe toutes les autres classes (infectés, latents, guéris). Les vecteurs β et b ainsi

que la matrice A sont définis pour chaque modèle dans l'article joint. Nous avons alors établi la dissipativité de ces systèmes (existence d'un compact positivement invariant et absorbant), calculé \mathcal{R}_0 le taux de reproduction de base, étudié l'existence des points d'équilibre, prouvé la stabilité asymptotique globale du DFE (équilibre sans maladie) et surtout nous avons démontré la stabilité asymptotique globale de l'équilibre endémique quand il existe pour le modèle **SP** (3.5).

3.2.2 Les modèles à pathogènes comprenant des souches multiples

Jusqu'à présent la distinction s'est faite sur l'hôte. On sait bien que les pathogènes (virus, bactéries, ...) ont un polymorphisme génétique. Les souches sont plus ou moins virulentes. Cela se traduit par une infectiosité et une transmission différente. Voici par exemple le graphe de flux d'un modèle à progression de stades à 3 souches.

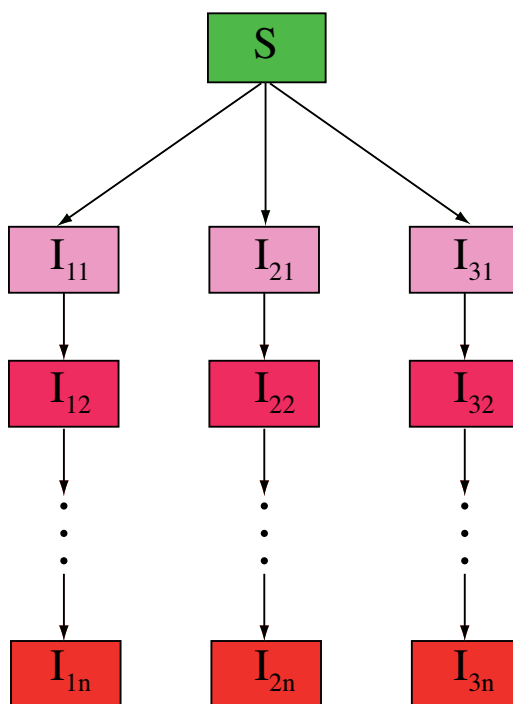


FIGURE 3.3 – Progression dans les stades d' infectiosité

Cette question a été jusqu'à présent relativement peu traitée[65, 17, 46, 1, 67, 20, 28, 66].

Les diverses souches entrent en compétition et souvent un principe de pessimisme s'applique [17, 23].

Notre contribution a constitué en l'étude des modèles intra-hôtes de paludisme décrivent la dynamique des stades sanguins des parasites, ainsi que leur interaction avec les cellules hôtes, en particulier les globules rouges et les effecteurs d'immunité. Durant cette dernière décennie, il y a eu un travail considérable en ce qui concerne la modélisation mathématique de l'infection à *Plasmodium falciparum*. Ce travail a fait l'objet de la publication [49] (jointe) où nous avons présenté un nouveau modèle qui tient compte de la structure d'âge des parasites de *Plasmodium* et qui inclut différentes souches pour le parasite. Nous avons donné une étude qualitative complète de ce modèle, en particulier nous avons affaibli une condition de stabilité donnée par De Leenheer et Smith [22] qui avaient étudié un système analogue (mais seulement avec trois variables d'état) qui modélise l'infection au VIH. Nous avons aussi établi un principe de compétition exclusive : génériquement, la souche la plus virulente l'emporte sur toutes les autres.

Le modèle original¹ est donné par le système suivant :

$$\begin{cases} \dot{x} = \Lambda - \mu_x x - \beta x m \\ \dot{y} = \beta x m - \mu_y y \\ \dot{m} = r \mu_y y - \mu_m m - \beta x m \end{cases} \quad (3.8)$$

La variable x désigne la concentration des globules rouges non parasités par microlitre, y la concentration des globules rouges parasités et m la concentration des mérozoïtes libres dans le sang. Les paramètres μ_x , μ_y et μ_m sont respectivement les taux de disparition naturelle des globules rouges sains, des globules rouges parasités et des mérozoïtes libres. Le paramètre β est la probabilité d'infection des globules rouges sains au contact des mérozoïtes. Les globules rouges non parasités sont recrutés au taux constant Λ de la moelle épinière et ont une espérance de vie de $1/\mu_x \times$ jours. De la disparition d'un globule rouge parasité, résulte la libération d'un nombre moyen de r mérozoïtes. Ces mérozoïtes libres disparaissent ou envahissent de nouveaux globules rouges. Certains auteurs ont négligé le terme $-\beta x m$ dans la dernière équation ce qui revient à supposer qu'un mérozoïte peut infecter plus qu'un globule rouge. Cette approximation rend l'étude mathématique du système (3.8) moins difficile.

Le modèle que nous avons proposé et étudié est décrit par le système ci-dessous avec

1. R.M. Anderson, R.M. May, and S. Gupta. Non-linear phenomena in host-parasite interactions. *Parasitology*, 99 :59–79, 1989.

k classes et n génotypes de parasites :

$$\left\{ \begin{array}{l} \dot{x} = f(x) - \mu_x x - x \sum_{i=1}^n \beta_i m_i \\ \text{pour } i = 1, \dots, n \\ \dot{y}_{1,i} = \beta_i x m_i - \alpha_{1,i} y_{1,i} \\ \dot{y}_{2,i} = \gamma_{1,i} y_{1,i} - \alpha_{2,i} y_{2,i} \\ \vdots \\ \dot{y}_{k,i} = \gamma_{k-1,i} y_{k-1,i} - \alpha_{k,i} y_{k,i} \\ \dot{m}_i = r_i \gamma_{k,i} y_{k,i} - \mu_{m_i} m_i - u \beta_i x m_i \end{array} \right. \quad (3.9)$$

Le recrutement des globules rouges sains x n'est plus constant mais dépend de leur densité. Le paramètre u est un nombre positif qui peut en particulier prendre la valeur zéro ou un et donc notre modèle permet de considérer aussi bien le cas où l'on tient compte du terme $-\beta x m$ dans l'équation \dot{m} que le cas où ce terme est négligé.

3.2.3 Les modèles à susceptibilité et à infectivité différentielles

Si la variation d'infectivité est une source d'hétérogénéité elle n'est pas la seule. On sait, par exemple, que les individus ne sont pas égaux devant la maladie. On est ainsi amené à introduire des classes différentes chez les susceptibles. On peut songer par exemple aux individus vaccinés. Tout vaccin n'est pas parfait par conséquent un individu vacciné est encore susceptible, mais peut, avec un risque diminué, contracter une infection. On peut également distinguer des groupes génétiques qui correspondent à des susceptibilités différentielles.

Enfin un autre exemple est l'âge. Ainsi on sait, dans le cas de l'hépatite B, que l'âge auquel est contractée l'infection joue un rôle dans la probabilité de développer une infection chronique (porteurs asymptomatiques). C'est ainsi qu'en dessous de un an, 90% des enfants développent une infection chronique si la mère est elle-même porteuse chronique. Au-delà de 5 ans ce pourcentage tombe à 5%.

Une étude des modèles à susceptibilité différentielle a fait l'objet d'une partie de l'article [26] (joint). Un travail concernant un système plus général où on tient compte des flux aussi bien entre les différents compartiments S_i qu'entre les compartiments I_j a fait l'objet de l'article [16] (article joint) où nous avons proposé et étudié le modèle suivant qui peut être représenté par le schéma 3.4 :

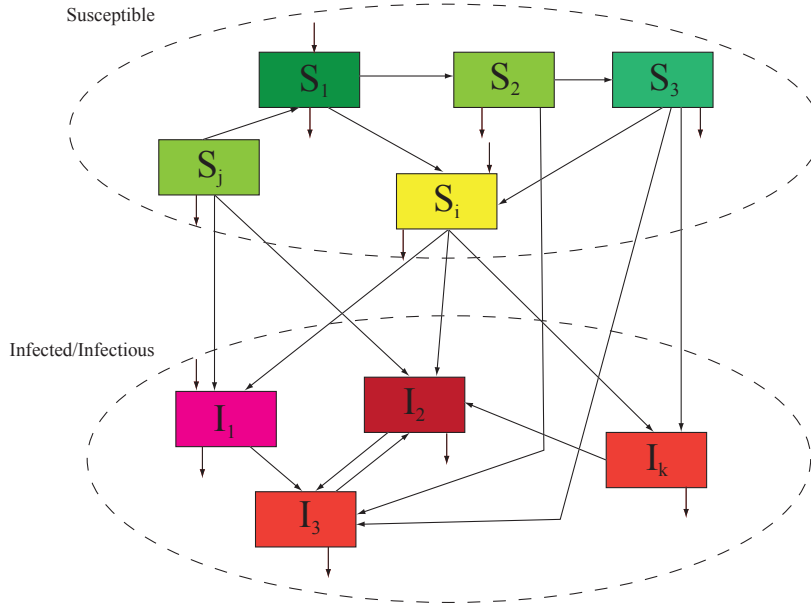


FIGURE 3.4 – Modèle à susceptibilité et infectivité différentielles **DSDI**

$$\begin{cases} \dot{S} = \Lambda - \text{diag}(\mu_S) S + A_S S - \text{diag}(B I) S, \\ \dot{I} = P \text{diag}(B I) S - \text{diag}(\mu_I + \gamma_I) I + A_I I, \\ \dot{R} = L I - \text{diag}(\mu_R) R + A_R R, \end{cases} \quad (3.10)$$

où $S \in \mathbb{R}_+^n$ représente les différents compartiments de susceptibles, $I \in \mathbb{R}_+^m$ les compartiments d'infectés (qu'ils participent à la transmission de la maladie ou non), $R \in \mathbb{R}_+^p$ les individus guéris ou immunisés. La matrice B , appelée matrice «WAIFW» (Who Acquire Infection From Whom) est définie par $B = (\beta_{ij})_{i,j}$ où β_{ij} est la probabilité de rencontre donnant lieu à la transmission de l'infection (contact adéquat) entre un susceptible du compartiment S_i avec un infecté du compartiment I_j . Il est à remarquer que $B > 0$ mais que $B \not\gg 0$ car $\beta_{ij} = 0$ pour les compartiments I_j d'individus infectés mains "non infectant". La matrice P (respectivement L) est une matrice stochastique-colonne de dimension $m \times n$ (respectivement $p \times m$) qui représente la distributions des susceptibles (respectivement des infectés) dans les différents compartiments I_j (respectivement R_k) après leur infection (respectivement

guérison) :

$$P = \begin{pmatrix} p_{11} & p_{12} & \dots & p_{1n} \\ p_{21} & p_{22} & \dots & p_{2n} \\ \vdots & \dots & \ddots & \dots \\ p_{m1} & p_{m2} & \dots & p_{mn} \end{pmatrix} \text{ avec } \sum_{j=1}^m p_{ji} = 1.$$

Ce modèle généralise les modèles existants dans la littérature et permet d'étudier entre autres l'infection au HBV pour laquelle nous disposons de données concernant le Sénégal. En tenant compte de ces données ainsi que certaines études expérimentales et statistiques (OMS, CDC, National Institute Health ...) qui montrent bien l'influence de l'âge au moment de l'infection sur l'évolution de la maladie, nous avons proposé un modèle dynamique avec cinq classes de susceptibles (0-1 mois, 1-6 mois, 7-12 mois, 1-5 ans et > 5 ans), deux compartiments d'infectés latents (ne transmettant pas l'infection) et de deux compartiments d'infectieux (infectieux symptomatiques et infectieux chroniques). Ce modèle du HBV peut se schématiser par la figure 3.5.

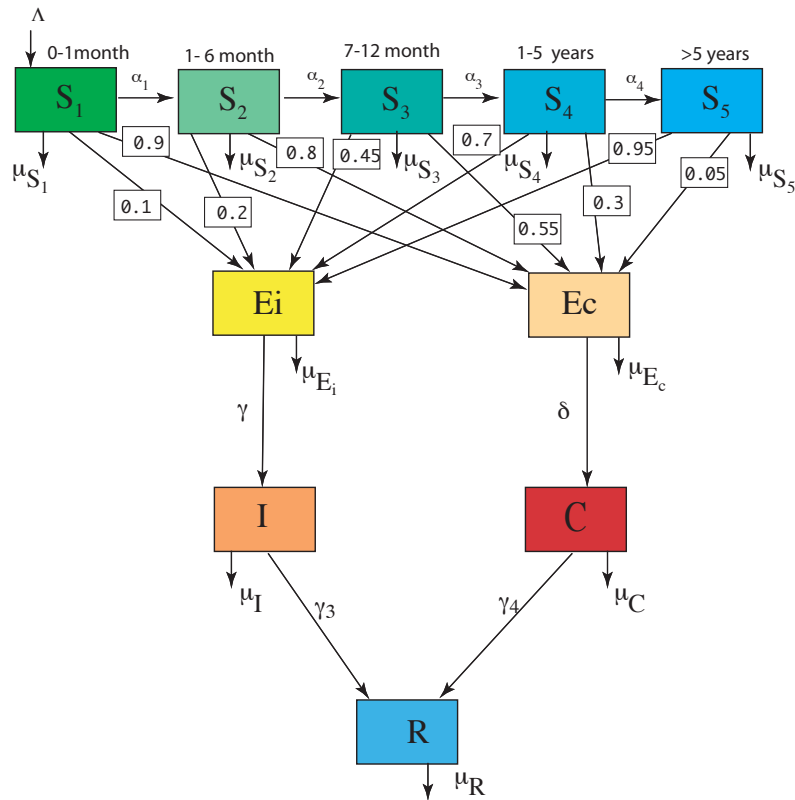


FIGURE 3.5 – Un modèle HBV

Le modèle représenté par le schéma 3.5 rentre bien dans la classe des systèmes (3.10) avec

$$B = \begin{pmatrix} 0 & 0 & \beta_{1,3} & \beta_{1,4} \\ 0 & 0 & \beta_{2,3} & \beta_{2,4} \\ 0 & 0 & \beta_{3,3} & \beta_{3,4} \\ 0 & 0 & \beta_{4,3} & \beta_{4,4} \\ 0 & 0 & \beta_{5,3} & \beta_{5,4} \end{pmatrix} \text{ et } P = \begin{pmatrix} p_1 & p_2 & p_3 & p_4 & p_5 \\ 1-p_1 & 1-p_2 & 1-p_3 & 1-p_4 & 1-p_5 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$A_S = \begin{pmatrix} -\alpha_1 & 0 & 0 & 0 & 0 \\ \alpha_1 & -\alpha_2 & 0 & 0 & 0 \\ 0 & \alpha_2 & -\alpha_3 & 0 & 0 \\ 0 & 0 & 0 & -\alpha_4 & 0 \\ 0 & 0 & 0 & \alpha_4 & 0 \end{pmatrix} \in \mathcal{M}_5(\mathbb{R})$$

Les valeurs des différents coefficients p_i proviennent des données du CDC.

3.2.4 L'hétérogénéité et les temps de séjours

Le temps de séjour dans un statut épidémiologique, autrement dit dans un compartiment n'est en général pas fixe. On peut parler de retards où de temps de séjour représenté par une fonction de densité de probabilité. Une technique pour représenter ce retard, quand la fonction est une combinaison linéaire convexe de fonctions d'Erlang, est d'introduire des compartiments supplémentaires [53, 54, 56]. Cette technique est appelée par McDonald le «linear chain trick» [74, 75]. Elle est aussi appelée par d'autres «method of stages» [69, 70]. L'article de Jacquez [56] contient une bibliographie complète sur cette technique.

On peut donc introduire des compartiments pour des raisons phénoménologiques, simuler un retard, en plus des raisons biologiques. Par exemple introduire un compartiment de latent correspond à une raison épidémiologique, mais on peut rajouter des compartiments afin d'avoir un temps de résidence correspondant à une fonction d'Erlang.

En effet il est bien connu que les équations différentielles avec des retards dont la fonction de densité de probabilité est la fonction d'Erlang

$$g_{n,\sigma} = \frac{t^{n-1}}{(n-1)!} \frac{1}{\sigma^n} e^{-\frac{t}{\sigma}}$$

peuvent se réduire à des équations différentielles ordinaires. L'utilisation d'un système caténaire de compartiments pour engendrer un retard est bien connu des ingénieurs automatismes. Györi dans [38] donne deux références dans la littérature russe et MacDonald [74] l'utilise sous le nom de l'astuce de la chaîne linéaire («linear chain trick»). Une littérature abondante considère l'apparition de retards dans des modèles

où il y a des variables cachées. C'est ainsi que Vogel consacre un livre [98] aux systèmes héréditaires et aux variables cachées. Une condition nécessaire et suffisante pour la réductibilité d'un système d'équations fonctionnelles à un système d'équations différentielles ordinaires est donné par Fargue [27]. Cette méthode est celle utilisée par MacDonald.

Nous allons revisiter cette méthode du point de vue de la théorie du contrôle. Cette approche avait déjà été proposée par Cooke et Grossman [21] en utilisant la transformée de Laplace. Nous utilisons une autre méthode qu'on va illustrer ici avec le modèle (3.1)

$$\begin{cases} \dot{x}_1 = m a b_1 (1 - x_1) x_2 - \gamma x_1, \\ \dot{x}_2 = a b_2 (1 - x_2) x_1 - \mu x_2. \end{cases} \quad (3.11)$$

Dans la deuxième équation, le terme $a b_2 (1 - x_2) x_1$ représente la proportion de «nouveaux» moustiques infectieux. On peut considérer ce terme comme un certain feedback $v(x)$ avec $x = (x_1, x_2)$. On réécrit le système (3.11) sous la forme

$$\dot{x} = f(x, v(x)) \quad (3.12)$$

qui correspond au schéma (3.6)

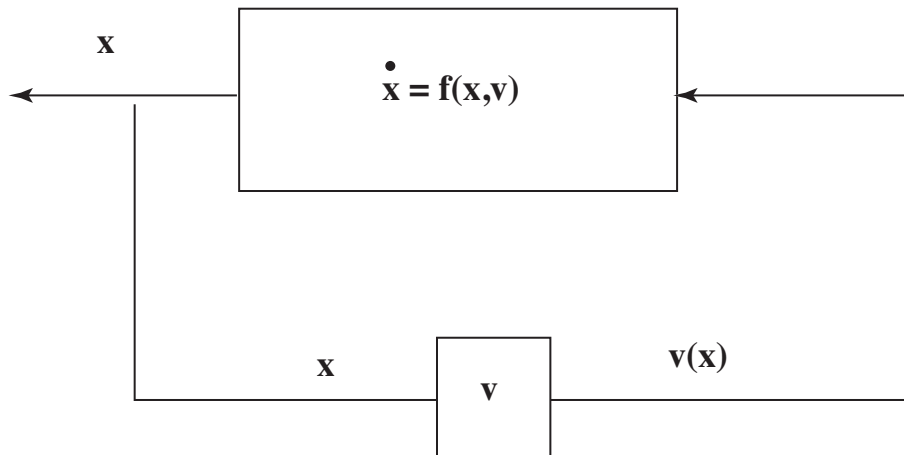


FIGURE 3.6 – Feedback

La vie moyenne d'un anophèle est de 5 jours, et le temps d'incubation, c'est à dire le temps qui s'écoule entre le moment où la femelle anophèle ingère des parasites du paludisme et celui où elle est infectante est de 6 jours en moyenne quand la température est de 30 degrés. On voit que l'hypothèse de considérer la période de latence comme négligeable est une approximation grossière. Si $h(\tau)$ est la probabilité de devenir infectieux, après τ unités de temps on obtient les nouveau x infectés par

la formule

$$b_2 a \int_{-\infty}^t h(\tau) (1 - x_2(t - \tau)) x_1(t - \tau) d\tau$$

Si on veut prendre en compte ce retard dans (3.11), cela revient à introduire un retard sur $v(x)$ dont la fonction de densité de probabilité est h , le système devient un système intégral-différentiel :

$$\dot{x} = f(x, \int_0^\infty v(x(t - \tau)) h(\tau) d\tau)$$

ou encore

(3.13)

$$\dot{x} = f(x, \int_{-\infty}^t v(x(\tau)) h(t - \tau) d\tau)$$

Supposons, pour simplifier l'exposé, que la fonction de densité de probabilité h est celle de la distribution d'Erlang (la même procédure est valable pour toute combinaison linéaire convexe de distributions d'Erlang) :

$$h(t) = h_{n,\sigma}(t) = \frac{t^{n-1}}{(n-1)!} \frac{1}{\sigma^n} e^{-\frac{t}{\sigma}}$$

Cette distribution est réalisée par le système linéaire caténaire représenté par le schéma 3.7.

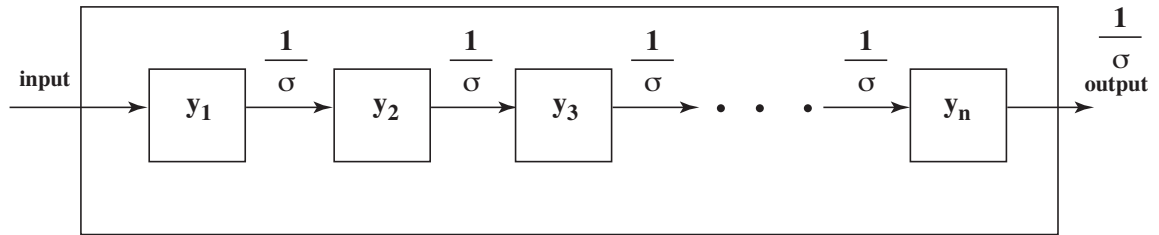


FIGURE 3.7 – réalisation de la distribution d'Erlang

En d'autres termes, on peut écrire

$$h(t) = C e^{tA} B Y(t)$$

avec $A = \frac{1}{\sigma} \begin{pmatrix} -1 & 0 & 0 & \cdots & 0 \\ 1 & -1 & 0 & \cdots & 0 \\ 0 & 1 & -1 & \cdots & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots \\ 0 & \cdots & 0 & 1 & -1 \end{pmatrix}$, $B = \begin{pmatrix} 1 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix}$, $C = \frac{1}{\sigma} (0, \dots, 0, 1)$ et $Y(t)$

est la fonction d'Heaviside.

On peut donc écrire

$$\begin{aligned}
 \int_{-\infty}^t v(x(\tau)) h(t - \tau) d\tau &= \int_{-\infty}^t C e^{(t-\tau)A} B v(x(\tau)) d\tau \\
 &= \int_{-\infty}^0 C e^{(t-\tau)A} B v(x(\tau)) d\tau + \int_0^t C e^{(t-\tau)A} B v(x(\tau)) d\tau \\
 &= C e^{tA} \int_{-\infty}^0 e^{-\tau A} B v(x(\tau)) d\tau + \int_0^t C e^{(t-\tau)A} B v(x(\tau)) d\tau.
 \end{aligned} \tag{3.14}$$

Considérons maintenant le système contrôlé linéaire suivant

$$\begin{cases} \dot{y} = A y + u B \\ z = C x. \end{cases} \tag{3.15}$$

D'après (3.14), on voit que $\int_{-\infty}^t v(x(\tau)) h(t - \tau) d\tau$ n'est autre que la sortie du système (3.15) correspondant à une entrée (contrôle) $u = v(x)$ et à une condition initiale

$$y_0 = y(0) = \int_{-\infty}^0 e^{-\tau A} B v(x(\tau)) d\tau$$

L'équation intégro-différentielle (3.13) peut donc être représentée par le dessin 3.8 ci-dessous

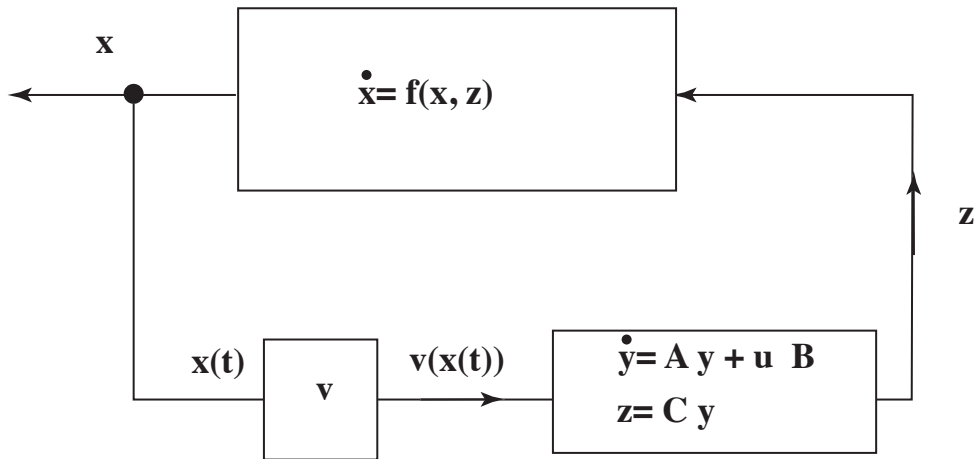


FIGURE 3.8 – mise en boucle des systèmes

Donc pour toute condition initiale $x(t) = \theta(t)$ sur \mathbb{R}_- , la solution de l'équation intégro-différentielle (3.13) associée à cette condition initiale est une solution du système

$$\begin{cases} \dot{x} = f(x, C y) \\ \dot{y} = A y + v(x) B \end{cases} \tag{3.16}$$

avec comme condition initiales $x(0) = \theta(0)$ et $y(0) = y_0 = \int_{-\infty}^0 e^{-\tau A} B v(\theta(\tau)) d\tau$.

Plus précisément, toute solution de (3.13) est une solution de (3.16) (cf [13] par exemple).

Revenons au modèle de Ross avec retard :

$$\begin{cases} \dot{x}_1 = m a b_1 (1 - x_1) x_2 - \gamma x_1, \\ \dot{x}_2 = a b_2 \int_{-\infty}^t h(\tau) (1 - x_2(t - \tau)) x_1(t - \tau) d\tau - \mu x_2. \end{cases} \quad (3.17)$$

Pour ce système, on a $v(x_1, x_2) = a b_2 (1 - x_2) x_1$.

L'étude des propriétés de (3.17) peut être donc déduite de celle du système suivant :

$$\begin{cases} \dot{x}_1 = m a b_1 (1 - x_1) x_2 - \gamma x_1, \\ \dot{x}_2 = \frac{1}{\sigma} y_n - \mu x_2, \\ \dot{y}_1 = \frac{-1}{\sigma} y_1 + a b_2 (1 - x_2) x_1, \\ \dot{y}_2 = \frac{1}{\sigma} (y_1 - y_2), \\ \vdots \\ \dot{y}_n = \frac{1}{\sigma} (y_{n-1} - y_n). \end{cases} \quad (3.18)$$

De la même façon, si l'infection des humains se fait aussi avec un retard distribué selon une loi d'Erlang $g(t) = g_{p,\alpha}(t) = \frac{t^{p-1}}{(p-1)!} \frac{1}{\alpha^p} e^{-\frac{t}{\alpha}}$, on obtient le système :

$$\begin{cases} \dot{x}_1 = m a b_1 \int_{-\infty}^t g(\tau) (1 - x_1(t - \tau)) x_2(t - \tau) d\tau - \gamma x_1, \\ \dot{x}_2 = a b_2 \int_{-\infty}^t h(\tau) (1 - x_2(t - \tau)) x_1(t - \tau) d\tau - \mu x_2. \end{cases} \quad (3.19)$$

Les propriétés de (3.19) peuvent se déduire de celles du système d'équations différentielles

ordinaires suivant :

$$\left\{ \begin{array}{l} \dot{x}_1 = \frac{1}{\alpha} w_n - \gamma x_1, \\ \dot{w}_1 = \frac{-1}{\alpha} w_1 + m a b_1 (1 - x_1) x_2, \\ \dot{w}_2 = \frac{1}{\alpha} (w_1 - w_2), \\ \quad \vdots \\ \dot{w}_p = \frac{1}{\alpha} (w_{p-1} - w_p) \\ \dot{x}_2 = \frac{1}{\sigma} y_n - \mu x_2, \\ \dot{y}_1 = \frac{-1}{\sigma} y_1 + a b_2 (1 - x_2) x_1, \\ \dot{y}_2 = \frac{1}{\sigma} (y_1 - y_2), \\ \quad \vdots \\ \dot{y}_n = \frac{1}{\sigma} (y_{n-1} - y_n). \end{array} \right. \quad (3.20)$$

Rappelons enfin que toute distribution peut-être "approximée" par une combinaison linéaire convexe de fonctions d'Erlang. Cela conduit à considérer des sous-systèmes, modèles multi-compartimentaux du type 3.9 :

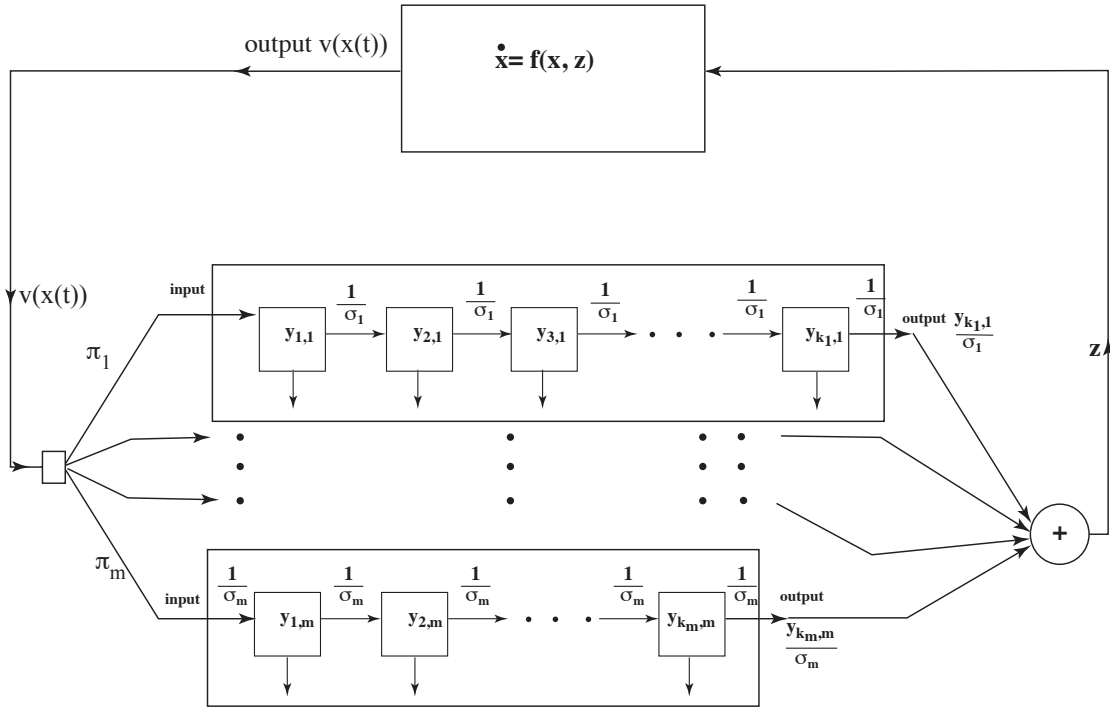


FIGURE 3.9 – combinaison linéaire convexe de fonctions d’Erlang

Par exemple Jacquez et al. utilisent des fonctions de densité d’Erlang en parallèle pour analyser le passage dans les tissus pulmonaires de différents médicaments [63]. L’utilisation de l’approche expliquée ci-dessus nous a permis d’étudier dans [50] le système à retard suivant qui modélise l’attaque de cellules saines par un parasite

$$\begin{cases} \dot{x} = \varphi(x) - \beta x v, \\ \dot{y} = \beta \int_0^\infty x(t - \tau) v(t - \tau) g(\tau) e^{-m\tau} d\tau - \mu_y y, \\ \dot{v} = r \mu_y y - \mu_v v - u \beta x v, \end{cases} \quad (3.21)$$

où x , y , et v représentent respectivement la densité des cellules cibles saines et susceptibles, la densité des cellules parasitées et celle des parasites libres. La fonction φ décrit la démographie des cellules saines en l’absence du parasite. Nous avons établi des résultats de stabilité globale dans le cas où la fonction de densité de probabilité g est une combinaison convexe de fonctions d’Erlang. L’application de ces résultats à des modèles intra-hôtes du VIH étudiés par Nelson et Perelson dans [77] nous a permis d’améliorer certains de leurs résultats.

3.2.5 L'hétérogénéité spatiale

Une dernière source d'hétérogénéité est la prise en compte des répartitions spatiales. Dans le cas du paludisme les zones urbaines, les banlieues et les villages en brousse jouent des rôles différents. A cela s'ajoute les mouvements entre ces différentes zones. La transmission d'une maladie infectieuse dans des régions géographiques discrètes se modélise par de modèles de métapopulations. Les zones appelées «patch» sont distinctes et isolées. Des mouvements de migration se font entre les patch. Les modèles de métapopulations sont classiques en écologie théorique[40, 39]. Leur apparition en épidémiologie est relativement récente[89, 72, 61, 60, 30, 71, 99, 5, 88, 3, 6].

Dans [52], nous avons étudié un modèle SIS pour une population répartie entre n régions distinctes (patches). La population est constituée de résidents (individus qui sont nés et qui vivent normalement dans la région considérée) et de voyageurs qui sont les individus qui ne se trouvent pas à l'instant considéré dans leurs régions de résidence. La population de chaque "patch" est divisée en individus susceptibles et individus infectés, la dynamique de la transmission de la maladie est donnée par un modèle SIS classique. Ce modèle avait été proposé par Sattenspiel et Dietz dans [89] et a été étudié par J. Arino et van den Driessche dans [4] en y ajoutant une dynamique de démographie (natalité et mortalité naturelles). Les auteurs de [4] ont calculé le taux de reproduction de base \mathcal{R}_0 et ont prouvé que l'équilibre sans maladie DFE (disease-free equilibrium) est localement asymptotiquement stable si $\mathcal{R}_0 < 1$ et qu'il est instable si $\mathcal{R}_0 > 1$. Ils ont aussi conjecturé, en se basant sur des simulations numériques, que si $\mathcal{R}_0 > 1$ alors le système admet un unique équilibre endémique qui est globalement attractif. Dans [52], nous avons prouvé la conjecture de [4]. Plus précisément nous avons établi, en utilisant les propriétés des systèmes fortement monotones [45], le résultat suivant :

Théorème 3.2.1

- *Il existe un compact $K \subset \mathbb{R}^{n^2}$ qui est positivement invariant et absorbant sous l'action du champ de vecteurs définissant le système étudié. Le compact K est en fait le domaine "biologique" du système.*
- *Si $\mathcal{R}_0 \leq 1$ alors le DFE $(\bar{N}, 0)$ est un état d'équilibre globalement asymptotiquement stable pour le système (3.28).*
- *Si $\mathcal{R}_0 > 1$ alors il existe un unique équilibre endémique (\bar{N}, \bar{I}) avec $\bar{I} \gg 0$ qui est globalement asymptotiquement stable sur $K \setminus \mathcal{U}$ où \mathcal{U} est la variété stable du DFE.*

Pour prouver ce théorème, nous allons commencer par rappeler le modèle de [4] puis nous l'écrirons sous une forme matricielle qui est plus adaptée pour prouver le résultat ci-dessus :

On note $N_{ij}(t)$ le nombre des résidents de la région i qui se trouvent à l'instant t dans la région j . Le nombre total des résidents de la région i est donné par $N_i^r = \sum_{j=1}^n N_{ij}$.

On notera N_i^p le nombre total des individus (résidents et voyageurs) qui se trouvent l'instant t dans la région i . Ce nombre est donné par

$$N_i^p = \sum_{j=1}^n N_{ji}.$$

En supposant que les tailles des populations sont suffisamment grandes, l'évolution des nombres d'individus peut être décrite par [4] :

$$\dot{N}_{ii} = d(N_i^r - N_{ii}) + \sum_{j=1}^n r_{ij} N_{ij} - g_i N_{ii} \quad (3.22)$$

et pour $j \neq i$

$$\dot{N}_{ij} = g_i m_{ji} N_{ii} - r_{ij} N_{ij} - d N_{ij} \quad (3.23)$$

Le nombre d est le taux de natalité supposé être le même pour toutes les régions et être égal au taux de mortalité. Les résidents de i quittent leur région avec le taux g_i . Une partie m_{ji} parmi eux vont dans le patch j : le terme $g_i m_{ji}$ représente le taux de voyage de i vers j . Le nombre r_{ij} représente le taux de retours de la région j des résidents de la région i vers leur région i . Ces différents taux vérifient : $m_{ii} = 0$, $\sum_{j=1}^n m_{ji} = 1$, $r_{ii} = 0$,

Il est facile d'établir que le nombre total des résidents d'une région est constant au cours du temps : $\dot{N}_i^r = 0$. Par contre le nombre N_i^p des individus présents dans une région i varie au cours du temps.

En notant $N = (N_{11}, N_{12}, \dots, N_{1n}, N_{21}, N_{22}, \dots, N_{2n}, \dots, N_{nn})^T \in [0, +\infty)^{n^2}$, le modèle de migration (3.22-3.23) peut s'écrire :

$$\dot{N} = \mathcal{M} N, \quad (3.24)$$

où \mathcal{M} est une matrice diagonale par blocs avec les coefficients appropriés.

Il a été prouvé dans [4] que le système (3.22-3.23) admet un équilibre \bar{N} qui est globalement asymptotiquement stable et qui est donné par :

$$\bar{N}_{ii} = \frac{1}{1 + g_i C_i} N_i^r, \quad \bar{N}_{ij} = g_i \frac{m_{ji}}{d + r_{ij}} \frac{1}{1 + g_i C_i} N_i^r \text{ avec } C_i = \sum_{k=1}^n \frac{m_{ki}}{d + r_{ik}}$$

Maintenant on écrit les équations régissant la transmission de la maladie dans chaque région. Comme $N_{ij} = S_{ij} + I_{ij}$, il suffit de considérer les équations pour les infectés I_{ij} qui s'écrivent :

$$\dot{I}_{ii} = \sum_{k=1}^n r_{ik} I_{ik} - g_i I_{ii} + \sum_{k=1}^n \kappa_i \beta_{iki} (N_{ii} - I_{ii}) \frac{I_{ki}}{N_i^p} - (\gamma + d) I_{ii}, \quad (3.25)$$

et pour $j \neq i$,

$$\dot{I}_{ij} = g_i m_{ji} I_{ii} - r_{ij} I_{ij} + \sum_{k=1}^n \kappa_j \beta_{ikj} (N_{ij} - I_{ij}) \frac{I_{kj}}{N_j^p} - (\gamma + d) I_{ij}. \quad (3.26)$$

Avec :

- β_{ijk} est la proportion des contacts dans la région j entre un susceptible de région i avec un infecté de la région k qui donnent lieu à la transmission de la maladie.
- $\kappa_j > 0$ est le nombre moyen par unité de temps des contacts dans la région j .
- γ est le taux de guérison supposé être le même pour toutes les régions.

On définit le vecteur \mathbf{N}^p par

$$\mathbf{N}^p = (N_1^p, N_2^p, \dots, N_n^p, N_1^p, N_2^p, \dots, N_n^p, \dots, N_n^p)^T \in]0, +\infty)^{n^2}.$$

De la même façon que pour le vecteur N , on définit le vecteur I par

$$I = (I_{11}, I_{12}, \dots, I_{1n}, I_{21}, I_{22}, \dots, I_{2n}, \dots, I_{nn})^T \in [0, +\infty)^{n^2}.$$

Le système (3.25-3.26) peut alors s'écrire

$$\dot{I} = \mathcal{D} I - (\gamma + d) I + \text{diag}(\kappa) \text{diag}(\mathbf{N}^p)^{-1} \text{diag}(N - I) B I \quad (3.27)$$

La matrice \mathcal{D} représente le terme de migration, c'est une matrice diagonale par blocs $\mathcal{D} = \text{diag}(D_{ii})$. Les matrices D_{ii} sont définies par :

$$D_{ii}(i, k) = r_{ik} \quad D_{ii}(k, i) = g_i m_{ki} \quad D_{ii}(i, i) = -g_i \quad D_{ii}(k, k) = -r_{ik}$$

Par exemple

$$D_{11} = \begin{bmatrix} -g_1 & r_{12} & r_{13} & \cdots & r_{1n} \\ g_1 m_{21} & -r_{12} & 0 & \cdots & 0 \\ g_1 m_{31} & 0 & -r_{13} & \cdots & 0 \\ \vdots & \vdots & \ddots & \ddots & \vdots \\ g_1 m_{n1} & 0 & \cdots & 0 & -r_{1n} \end{bmatrix}$$

La matrice B est définie par :

$$B^T e_{ij} = \sum_{k=1}^n \beta_{ikj} e_{kj}$$

où e_{ij} désigne la base canonique \mathbb{R}^{n^2} .

Finalement le système SIS que nous considérons s'écrit :

$$\begin{cases} \dot{N} = \mathcal{M} N \\ \dot{I} = \mathcal{D} I - (\gamma + d) I + \text{diag}(\kappa) \text{diag}(\mathbf{N}^p)^{-1} \text{diag}(N - I) B I \end{cases} \quad (3.28)$$

En considérant le vecteur constant (rappelons que $\dot{N}_i^r = 0$) :

$$\mathbf{N}^r = (N_1^r, N_1^r, \dots, N_1^r, N_2^r, N_2^r, \dots, N_2^r, \dots, N_n^r)^T,$$

on peut montrer en utilisant les expressions (3.22), (3.23), (3.25) et (3.26) :

Proposition 3.2.1 *L'ensemble K défini par*

$$K = \{(N, I) | 0 \leq N \leq \mathbf{N}^r; 0 \leq I \leq \mathbf{N}^r\}.$$

est un compact positivement invariant pour le système (3.28)

On va donc étudier le système dans cet ensemble K qui correspond au domaine "biologique" d'étude. Dans cet ensemble, Le système (3.28) est triangulaire, les solutions sont bornées et \bar{N} est un équilibre globalement asymptotiquement stable pour $\dot{N} = \mathcal{M}N$. Il suffit donc d'étudier le système réduit suivant

$$\dot{I} = \mathcal{D}I - (\gamma + d)I + \text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(\bar{N} - I)BI. \quad (3.29)$$

Calcul de \mathcal{R}_0 : Nous utilisons la méthode développée dans [96]. la vitesse d'apparition de nouveaux infectés, dans le compartiment des infectés est donnée par

$$\mathcal{F} = \text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(\bar{N} - I)BI.$$

Les autres transferts (autres que par transmission) sont donnés par la fonction

$$\mathcal{V} = \mathcal{D}I - (\gamma + d)I.$$

Les matrices Jacobiennes de ces fonctions au DFE ($I = 0$) sont :

$$F = \text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(\bar{N})B \text{ et } V = \mathcal{D} - (\gamma + d)I_{n^2}.$$

La matrice \mathcal{D} est une matrice de Metzler [55](tous les termes hors diagonaux sont positifs). La somme des éléments de chaque colonne de \mathcal{D} est nulle. Ceci implique que 0 est une valeur propre simple de \mathcal{D} et les autres valeurs propres sont à partie réelle strictement négative. Donc V est une matrice de Metzler stable et admet pour module de stabilité $-(\gamma + d)$ ce qui entraîne que V est inversible. On peut donc appliquer la formule de [96], ce qui donne en désignant par $\rho(A)$ le rayon spectral de la matrice A :

$$\mathcal{R}_0 = \rho(-FV^{-1}) = \rho\left(-\text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(\bar{N})B (\mathcal{D} - (\gamma + d)I_{n^2})^{-1}\right).$$

On peut maintenant démontrer le théorème 3.2.1. pour cela il suffit de considérer le système (3.29). Le champ associé au système (3.29) est :

$$X(I) = (F + V)I - \text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(I)BI.$$

C'est un champ de vecteurs \mathcal{C}^1 dont le flot laisse invariant l'ensemble $K_1 = \{0 \leq I \leq \mathbf{N}^r\}$ pour $t \geq 0$. La dérivée DX est :

$$DX(I) = \mathcal{D} - (\gamma + d) I_{n^2} + \text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(\bar{\mathbf{N}} - I) B \\ - \text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(B I).$$

Pour tout $I \in K_1$, $DX(I)$ est une matrice de Metzler irréductible. Il s'en suit que le flot de X est fortement monotone dans K_1 . D'autre part, comme chaque ligne de la matrice B est constituée d'éléments positifs avec au moins un terme non nul, l'application $I \mapsto DX(I)$ est strictement antimonotone : $I_1 < I_2 \Rightarrow DX(I_1) > DX(I_2)$. On est donc dans les conditions d'application du résultat de M. Hirsch ([45], page 55, théorème 6.1) :

- (a) soit toutes les trajectoires dans K_1 tendent vers l'origine ;
- (b) ou bien il existe un unique point d'équilibre \bar{I} à l'intérieur de K_1 et toutes les trajectoires dans K_1 convergent vers cet équilibre intérieur.

Le linéarisé du système (3.29) à l'origine est défini par la matrice $J(0) = F + V$. Comme $F \geq 0$ et V une matrice de Metzler inversible, $F + V$ est une décomposition régulière (regular splitting) de $J(0)$. On en déduit, d'après [97], que $\rho(-FV^{-1}) < 1$ est équivalent $\alpha(F + V) < 0$ où $\alpha(F + V) = \max_{\lambda \in \text{Spec}(F+V)} \text{Re}(\lambda)$ est le module de stabilité de la matrice $F + V$. Ceci montre que si $\mathcal{R}_0 = \rho(-FV^{-1}) < 1$ alors l'origine est asymptotiquement stable et donc il est globalement asymptotiquement stable dans K_1 d'après le résultat de Hirsch mentionné plus haut.

Si $\mathcal{R}_0 > 1$ alors $\alpha(J(0)) > 0$ et donc l'origine est instable ce qui implique, d'après toujours ([45], page 55, théorème 6.1) qu'il existe un unique point d'équilibre \bar{I} à l'intérieur de K_1 ($I \gg 0$) qui correspond à l'équilibre endémique et qui est globalement attractif. Il reste à montrer sa stabilité. Cet équilibre endémique \bar{I} satisfait

$$[\mathcal{D} - (\gamma + d)] \bar{I} + \text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(\bar{\mathbf{N}} - \bar{I}) B \bar{I} = 0.$$

En utilisant cette relation avec les propriétés de B et le fait que $\bar{I} \gg 0$, on obtient

$$DX(\bar{I}) \bar{I} = -\text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(B \bar{I}) \bar{I} \ll 0.$$

Comme $DX(\bar{I})$ est une matrice de Metzler, cette dernière relation implique que la matrice $DX(\bar{I})$ est stable grâce à [14](critère I_{28} du théorème 6.2.3). On a donc montré la stabilité de \bar{I} .

Il reste à étudier le cas $\mathcal{R}_0 = 1$ qui est équivalent à $\alpha(F + V) = 0$. Comme $F + V$ est une matrice de Metzler irréductible, $\alpha(F + V) = 0$ entraîne l'existence d'un vecteur strictement positif $\mathbf{v} \gg 0$ qui satisfait $(F + V)^T \mathbf{v} = 0$. On considère alors dans K_1 la fonction définie par

$$V(I) = \langle I | \mathbf{v} \rangle.$$

Sa dérivée le long des trajectoires est

$$\dot{V} = -\langle \text{diag}(\kappa) \text{diag}(\bar{\mathbf{N}}^p)^{-1} \text{diag}(I) B I | \mathbf{v} \rangle \leq 0.$$

Ceci prouve la stabilité de l'origine et donc on est nécessairement dans le cas **(a)** du théorème de Hirsch et par suite l'origine est globalement asymptotiquement stable quand $\mathcal{R}_0 = 1$. Ceci termine la preuve du théorème [3.2.1](#). ■

Chapitre 4

Quelques perspectives scientifiques

L'objectif est de développer et d'appliquer les méthodes de l'**automatique** et de la théorie des **systèmes dynamiques** à la modélisation mathématique des problèmes rencontrés en **épidémiologie, immunologie** et en gestion de certaines ressources renouvelables. Le paradigme de l'automatique qui consiste à décomposer des systèmes entrée-sortie en composantes plus simples (briques de base) qui sont interconnectés est bien adapté aux systèmes complexes rencontrés en épidémiologie. L'objectif de recherche est double. D'une part, il s'agit d'obtenir une meilleure compréhension des systèmes épidémiologiques, immunologiques ou halieutiques, d'autre part, l'objectif est aussi d'étudier les nouveaux problèmes mathématiques qui vont apparaître.

La première étape est celle de la modélisation. En théorie du contrôle, la modélisation a toujours été une forte composante de l'activité de recherche. Cependant la modélisation en épidémiologie a des spécificités que l'on ne rencontre pas en ingénierie. Les systèmes sont complexes et présentent des non linéarités. Une autre caractéristique est la rareté des données. Ces données, quand elles existent, sont souvent imprécises ou bruitées. Enfin des lois précises existent rarement, c'est une différence fondamentale avec l'ingénierie. Dans cette situation de modélisation, il doit y avoir des aller-retour entre le biologiste et le mathématicien. (par biologiste on entend chercheur en sciences du vivant, médecin, entomologiste, ...). On doit décider de ce qui est important et ce que l'on peut négliger. Ce n'est pas une tâche facile. En terme de structure un terme qui peut, de l'avis du biologiste, être négligé car « petit », donnera un comportement inattendu du système. D'un autre côté, le biologiste voudra avoir un système qui sera le plus complet possible au détriment d'une possibilité d'analyse mathématique complète. Ce projet demande donc une collaboration étroite avec les biologistes d'où l'intérêt de nos relations de coopération avec l'UR Géodes de l'I.R.D. et le laboratoire URBEP de l'IMTSSA (Institut de médecine tropicale du Service de santé des armées) <http://www.actu-pharo.com/>

html/urbep.html.

Une fois un modèle construit, il s'agit de le valider, le simuler et analyser mathématiquement ses propriétés. Cela fait aussi partie de la modélisation. Un modèle pourra être rejeté s'il ne s'adapte pas aux données ou parce qu'il a un comportement incompatible avec les connaissances biologiques et expérimentales.

Notre objectif final est de proposer et d'étudier des modèles épidémiologiques pour

- Analyser la propagation des maladies infectieuses transmissibles,
- obtenir une meilleure compréhension de la dynamique des épidémies,
- clarifier des hypothèses, préciser des paramètres,
- proposer des résultats conceptuels (seuils , \mathcal{R}_0 , robustesse),
- utiliser la simulation comme outils d'expérimentation,
- évaluer les résultats de terrain,
- planifier et évaluer les moyens d'intervention.

Nous nous concentrerons dans un premier temps sur les maladies tropicales à vecteur. Cela n'empêchera de nous intéresser à d'autres maladies, importantes en Afrique (Tuberculose, HBV, Ebola . . .) pour lesquelles nous avons des collaborations extérieures.

Il s'agira donc de construire des modèles en épidémiologie et immunologie. Ces modèles seront validés par des données de terrain. Un accent particulier sera porté sur la construction d'observateurs (voir plus loin) pour obtenir certaines variables ou estimer certains paramètres. L'analyse de ces modèles sera faite avec l'objectif d'évaluer certaines stratégies de contrôle en santé publique. Les systèmes considérés sont suffisamment génériques pour pouvoir s'adapter à d'autres maladies infectieuses.

Modélisation et observateurs :

Nous proposons une structure générale pour modéliser une maladie infectieuse. Pour donner un exemple, nous donnons la brique de base de la structure proposée :

$$\begin{cases} \dot{x} = \varphi(x) - x \langle \beta | C y \rangle \\ \dot{y} = x P \text{diag}(\beta) C y + A y - u x \text{diag}(\beta) C y \end{cases} \quad (4.1)$$

Dans ce modèle x représente la densité des individus susceptibles dans une zone (patch) donnée. S'il s'agit d'un modèle intra-hôte, ce sera de la concentration en cellule cibles (erythrocytes, CD^+4 , . . .). Les différentes composantes y_i de y représentent l'incidence de divers états : exposés à différents stades, infectés à différents stades, immunisés. Ce système peut représenter les modèles connus sous le nom de DI (differential infectivity) , SP (staged progression) ou DISP.

Ce que nous avons exposé ci-dessus nous amène à nous intéresser aux problèmes théoriques suivants :

1. Observabilité et Construction d'observateurs pour les systèmes continus-discrets : Il s'agit des systèmes qui peuvent s'écrire sous la forme :

$$\dot{x}(t) = f(x(t), u(t)), y_k = h(x_k) \quad (4.2)$$

L'étude de ces systèmes est motivée par le fait qu'en général les modèles épidémiologiques ont une dynamique continue mais les mesures (sorties) sont discrètes. Il existe quelques résultats dans la littérature mais ils concernent des classes de systèmes qui ne contiennent pas les systèmes épidémiologiques qui nous intéressent.

2. Observateurs adaptatifs : Il s'agit de construire des observateurs pour les systèmes de la forme

$$\dot{x}(t) = f(x, u) = F(x, u) + G(x, u, t)\theta, y(k) = h(x(k)) \quad (4.3)$$

Le but étant d'estimer, en utilisant les sorties discrètes $y(k)$, l'état $x(t)$ du système ainsi que le paramètre (scalaire ou vectoriel) inconnu θ . La motivation de ce travail provient de l'étude des modèles épidémiologiques, en particulier les modèle intra-hôte (3.9) de la malaria (pour lequel nous disposons de données réelles grâce à C. Rogier de l'Institut de médecine tropicale du Service de santé des armées) ainsi que les modèles de propagation de l'infection au HBV. Ces modèles sont décrits par des systèmes continus mais les mesures (sorties) sont discrètes. Par exemple, considérons le modèle (3.9) avec $i = 1$ (une seule souche de parasite) qu'on rappelle ici :

$$\begin{cases} \dot{x} = f(x) - \mu_x x - \beta x m \\ \dot{y}_1 = \beta x m - \alpha_1 y_1 \\ \dot{y}_2 = \gamma_1 y_1 - \alpha_2 y_2 \\ \dots \\ \dot{y}_k = \gamma_{k-1} y_{k-1} - \alpha_k y_k \\ \dot{m} = r \gamma_k y_k - \mu_m m - \beta x m \end{cases} \quad (4.4)$$

Dans ce modèle, x représente la concentration en érythrocytes sain. La fonction $f(x)$ modélise le recrutement des globules rouges. Les y_i sont les différents stades des érythrocytes parasités, de la forme en anneau au vieux schizonte. La variable m représente la concentration en mérozoïtes. Certains paramètres peuvent être estimés à partir des connaissances biologiques : par exemple on connaît assez bien la durée de vie d'un globule rouge saint, d'un globule infecté ou d'un mérozoïte. D'autres paramètres sont inconnus. C'est le cas du paramètre essentiel β qui s'interprète

comme le taux d'infection des globules sains (des individus sains et susceptibles pour les autres modèles) par les parasites (les infectés transmettant l'infection).

On mesure par la technique de la goutte épaisse le nombre de globules infectés dans le sang périphérique ce qui correspond à mesurer y_1 car les autres y_i correspondent aux globules infectés qui sont dans l'organisme mais ne sont plus accessibles à la mesure par cette technique. L'efficacité du traitement dépend de son dosage en fonction de la charge parasitaire totale qui est $\sum y_i$ et non pas seulement y_1 qui est mesuré. Le but est donc d'essayer d'estimer $\sum y_i$ en utilisant le modèle et la mesure $y_1(k)$. L'autre objectif est d'estimer le paramètre β pour lequel il n'y a pas de méthodes "expérimentales" qui permettent de le mesurer.

Nous cherchons donc à construire un observateur qui permettra, à partir des mesures (par exemple de y_1), de reconstituer $x(t)$, tous les $y_i(t)$, $m(t)$ et estimer β . On comprend l'intérêt d'un tel observateur qui permettrait de connaître en temps réel la charge parasitaire totale, ainsi que l'identification de certains paramètres.

Il existe des méthodes de constructions d'observateurs adaptatifs pour certaines classes de systèmes non linéaires mais elles concernent toutes, à notre connaissance, des systèmes continus à sortie continue ou bien quelques systèmes discrets à sortie discrète. Ce travail est en cours et pour le moment nous avons un résultat préliminaire [36] qui concerne les systèmes linéaires.

3. Etude de modèles généraux à susceptibilité et infectivité différentielles.

Il s'agit d'étudier les propriétés dynamiques de modèles avec plusieurs classes de susceptibles et plusieurs classes d'infectés où on tient compte des flux entre les différents compartiments S_i ainsi que des flux entre les différents compartiments I_i . Ces systèmes peuvent s'écrire sous la forme

$$\begin{cases} \dot{S} &= \Lambda - \text{diag}(\mu_S) S + A_S S - \text{diag}(B I) S \\ \dot{I} &= P \text{diag}(B I) S - \text{diag}(\mu_I + \gamma_I) I + A_I I, \\ \dot{R} &= L I - \text{diag}(\mu_R) R + A_R R \end{cases} \quad (4.5)$$

Le système (4.5) est suffisamment général pour représenter la dynamique d'une grande classe d'épidémies. Nous avons déjà étudié ce système dans [16] : calcul de \mathcal{R}_0 , stabilité globale du DFE quand $\mathcal{R}_0 \leq 1$, existence d'un unique équilibre endémique quand $\mathcal{R}_0 > 1$. Cependant, nous n'avons prouvé la stabilité asymptotique globale de l'équilibre intérieur (endémique) quand il existe ($\mathcal{R}_0 > 1$) que pour $A_S = 0$ et une infection qui admet une seul compartiment (qu'on notera avec l'indice 1) d'infectés comme point d'entrée avant de progresser vers les autres compartiment, c-à-d, quand un susceptible est infecté, il rentre d'abord dans le compartiment I_1 avant d'aller

dans les autres compartiments. Cela revient à dire que la matrice P de distribution est $P = e_i \mathbf{1}^T$ (e_i étant une base de \mathbb{R}^m et $\mathbf{1} = (1, 1, \dots, 1)^T \in \mathbb{R}^n$).

Nous comptons donc explorer les propriétés de l'équilibre endémique quand $A_S \neq 0$ et (ou) quand la matrice P de distribution permet d'aller simultanément dans différents compartiments d'infectés (quand P ne peut pas s'écrire $P = e_i \mathbf{1}^T$).

Nous comptons aussi prendre en compte la transmission verticale (transmission de l'infection par la mère pendant la grossesse ou au moment de la naissance). Ceci revient à introduire dans le modèle (4.5) un recrutement dans la classe des infectés.

4. Contrôlabilité de certains modèles épidémiologiques : Il s'agit d'intégrer l'utilisation de certaines stratégies de santé publique (vaccination, traitement, mise en quarantaine, utilisation de moustiquaires imprégnées, ...) comme des termes de contrôle dans un modèle dynamique puis d'étudier les propriétés du système contrôlé obtenu : contrôlabilité, stabilisation. Par exemple, comment calculer le taux de vaccination, comme fonction de l'état de la population considérée (feedback) et non seulement comme un taux fixe, en vue d'éradiquer l'épidémie ou (quand cela n'est pas possible) maintenir la prévalence en dessous d'un certain seuil : cela nous amène à un problème de stabilisation avec contraintes aussi bien sur l'état que sur le contrôle.

5. Etude de modèles de métapopulations : Le but est de tenir compte des mouvements des individus et de l'influence de ces mouvements dans la propagation de l'épidémie. L'approche suivie est de subdiviser l'espace en plusieurs régions discrètes. Dans chaque région l'épidémie est régie par un système dynamique et il y a des flux entre les différentes régions. Pour le moment nous cherchons à établir les propriétés du système dynamique global en fonction des propriétés des systèmes définies dans chaque région et des flux entre les régions. Un des objectifs est d'étudier (voire quantifier) l'influence de l'isolement de certaines régions sur la propagation de l'épidémie.

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Annexes : Reproduction d'articles

A Jurdjevic-Quinn-type theorem for stochastic nonlinear control systems

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A Jurdjevic-Quinn Type Theorem for Stochastic Nonlinear Control Systems

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Abstract— We consider stochastic nonaffine nonlinear control systems $x_t = x_0 + \int_0^t f(x_s, u)ds + \int_0^t g(x_s, u)d\omega_s$, (written in the sense of Itô), ω being a standard Wiener process, for which we give a sufficient condition for global stabilization by a bounded smooth state feedback which is explicitly given. This condition generalizes the well known Jurdjevic-Quinn result for deterministic affine control systems.

Keywords— Stochastic nonlinear control systems, stochastic stability, state feedback law, Lyapunov functions.

I. INTRODUCTION

This paper deals with the question of stabilizability for stochastic nonlinear control differential equations written in the sense of Itô:

$$x_t = x_0 + \int_0^t f_0(x_s, u)ds + \sum_{j=1}^p \int_0^t f_j(x_s, u)d\omega_s^j, \quad (1)$$

where $x_0 \in \mathbb{R}^n$, $u = (u_1, \dots, u_m)^T$ is a \mathbb{R}^m -valued control law, $\{\omega_t, t \geq 0\}$ is a standard \mathbb{R}^p -valued Wiener process defined on an usual probability space (Ω, \mathcal{F}, P) , and $f_j : \mathbb{R}^n \times \mathbb{R}^m \rightarrow \mathbb{R}^n$, $0 \leq j \leq p$, are smooth (C^∞) Lipschitz functions satisfying $f_j(0, 0) = 0$ and there exists a positive constant K such that, for any $x \in \mathbb{R}^n$ and any $u \in \mathbb{R}^p$, $\sum_{j=0}^p \|f_j(x, u)\| \leq K(1 + \|x\| + \|u\|)$.

Stochastic control systems (1) are of interest for various reasons. As well known, a multitude of physical, engineering, biological, social, and managerial phenomena are either well approximated or reasonably modelled by control differential equations $dx_t/dt = f_t(x_t, u)$, for which many of the most basic questions concern stabilization around the equilibrium.

Again one often has situations where the coefficients, say $f_t(x_t, u)$, are not deterministic but of the random form $f_t(x_t, u) = b(x_t, u) + \sigma(x_t, u) \cdot$ “noise”, where b and σ are some given functions and where one does not know the exact behaviour of the noise term, but only its probability distribution. Of course in such a situation stochastic control differential equations (1) are more natural models than deterministic ones $dx/dt = f_0(x, u)$. For instance during these past decades there has been increasing effort to describe various facets of dynamic economic interactions with the help of stochastic differential processes. Traditional mathematical economics modelling focusses on transient and equilibrium interrelationships among production and consumption factors. Stochastic differential processes provide a mechanism to incorporate the influences associated with randomness, uncertainties, and risk factors operating with respect to various economic units (stock prices, labour force, technology variables, etc.). Among other applications where stochastic differential equations occur to

describe phenomena one can cite theoretical ecology and population genetics, and electrical dynamical systems. For the literature dealing with applications see e.g. [1], [3], [5], [6], [9], [11], [14], [15], [18].

For deterministic nonlinear control systems many techniques to study the stabilizability problem and to design stabilizing feedback laws are known. Historically, one of the first significant results is due to Jurdjevic and Quinn [7] who used the LaSalle’s invariance principle to give a sufficient condition for the global stabilization of an affine nonlinear control system:

$$\dot{x} \triangleq \frac{dx}{dt} = X_0(x) + \sum_{i=1}^m u_i Y_0^i(x). \quad (2)$$

with a linear (i.e. $X(x) = Ax$) and dissipative drift. Since then, various Jurdjevic-Quinn type sufficient conditions have been developed by several authors [8], [13], [16], [17]. In [16], it is proved that if there exists a positive definite and proper smooth function $V : \mathbb{R}^n \rightarrow \mathbb{R}$ such that: (i) the Lie derivative $X_0V(x) = \langle X_0(x), \nabla V(x) \rangle$ of V with respect to vector field X_0 satisfies $X_0V(x) \leq 0$, $\forall x \in \mathbb{R}^n$; (ii) the set $\{x \in \mathbb{R}^n | X_0^{k+1}V(x) = X_0^k Y_0^i V(x) = 0, k \in \mathbb{N}, 1 \leq i \leq m\}$ is reduced to $\{0\}$; then the derivative of V along the trajectories of system (2) being given by $\dot{V}(x) = X_0V(x) + \sum_{i=1}^m u_i Y_0^i V(x)$, the smooth state feedback control law $u_i(x) = -Y_0^i V(x)$, $1 \leq i \leq m$, yields $\dot{V}(x) \leq 0$, that is to say a Lyapunov stable closed-loop system, and by application of LaSalle’s invariance principle it stabilizes globally system (2).

In [4], Florchinger extends Jurdjevic-Quinn theorem to the particular class of stochastic affine control systems:

$$x_t = x_0 + \int_0^t \left(X_0(x_s) + \sum_{i=1}^m u_i Y_0^i(x_s) \right) ds + \sum_{j=1}^p \int_0^t X_j(x_s) d\omega_s^j, \quad (3)$$

where only the drift term is corrupted by a noise. For these systems, the associated infinitesimal generator \mathcal{L} satisfies $\mathcal{L}V(x) = L_0V(x) + \sum_{i=1}^m u_i Y_0^i V(x)$, $\forall x \in \mathbb{R}^n$, where L_0 is the second order differential operator defined by $L_0V(x) = X_0V(x) + (1/2) \sum_{j=1}^p \langle X_j(x), (\partial^2 V / \partial x^2)(x) X_j(x) \rangle$ and V is a given smooth positive definite and proper function. So, it follows that if: (i') $L_0V(x) \leq 0$ for all $x \in \mathbb{R}^n$; (ii') the set $\{x \in \mathbb{R}^n | L_0^{k+1}V(x) = L_0^k Y_0^i V(x) = 0, k \in \mathbb{N}, 1 \leq i \leq m\}$ is reduced to $\{0\}$; then the smooth state feedback control law $u_i(x) = -Y_0^i V(x)$ yields $\mathcal{L}V(x) \leq 0$, which allows, as in [16] for the deterministic case, to state in [4], by application of the stochastic versions of Lyapunov theorem (see [10]) and LaSalle’s invariance principle (see [12]), that the stochastic affine system (3) is globally asymptotically stabilizable in probability by the feedback law $u_i(x) = -Y_0^i V(x)$.

In order to illustrate the peculiar difficulty of the stochastic case in comparison with the deterministic one, which disappears for system (3), consider now affine control sys-

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tems of the form:

$$\begin{aligned} x_t &= x_0 + \int_0^t \left(X_0(x_s) + \sum_{i=1}^m u_i Y_0^i(x_s) \right) ds \\ &+ \sum_{j=1}^{p_0} \int_0^t X_j(x_s) d\omega_{0s}^j \\ &+ \sum_{i=1}^m \sum_{j=1}^{p_i} \int_0^t u_i Y_j^i(x_s) d\omega_{is}^j, \end{aligned} \quad (4)$$

where ω_i , $0 \leq i \leq m$, is a standard \mathbb{R}^{p_i} -valued Wiener process such that ω_i and $\omega_{i'}$ are independent for $i \neq i'$. Contrary to system (3), for system (4) where every thing is corrupted by a noise, the associated infinitesimal generator \mathcal{L} , applied to a Lyapunov function V , leads to:

$$\begin{aligned} \mathcal{L}V(x) &= L_0V(x) + \sum_{i=1}^m u_i Y_0^i V(x) \\ &+ \frac{1}{2} \sum_{i=1}^m u_i^2 \sum_{j=1}^{p_i} \langle Y_j^i(x), \frac{\partial^2 V}{\partial x^2}(x) Y_j^i(x) \rangle. \end{aligned}$$

So, it appears that the Jurdjevic-Quinn feedback $u_i(x) = -Y_0^i V(x)$, under conditions (i') and (ii'), is no more a stabilizing feedback for (4).

More generally for stochastic nonlinear systems of the form (1), for which the random parametric excitation depends on the control, $\mathcal{L}V(x)$ is a nonlinear expression on u which depends explicitly on the corrupted terms $f_j(x, u)$, $1 \leq j \leq p$. So, if one assumes that there exists a feedback $u(x)$ such that $\langle f_0(x, u(x)), \nabla V(x) \rangle \leq 0$, the most difficult problem is now to prove the existence of a feedback law $\tilde{u}(x)$ yielding $\mathcal{L}V(x) \leq 0$ and satisfying $\tilde{u}(x) = u(x)$ for $f_j = 0$, $1 \leq j \leq p$.

In [2], it is proved that Jurdjevic-Quinn type conditions (i') and (ii') remain sufficient for the stochastic affine control system (4) to be globally asymptotically feedback stabilizable in probability.

In this work, we give an extended version of these conditions under which the stochastic nonaffine control system (1) is globally asymptotically stabilizable in probability with a bounded smooth stabilizing feedback law $u = u(x)$ with $u(0) = 0$ and with an arbitrary choice of the bound. We make a constructive proof of this fact which provides an explicit design of bounded smooth stabilizing feedback laws.

it is worth while to point out that the above mentioned difficulty, that is peculiar to the stochastic case in comparison with the deterministic one, does not appear with the hypothesis that the coefficients associated with the noise in system (1) do not depend on the control, that is to say $\partial f_j / \partial u = 0$, $1 \leq j \leq p$. In this case the stochastic stabilization procedure is close to the deterministic one.

II. NOTATIONS AND PRELIMINARIES

The first aim of this section is to recall some classical definitions and results on stability in probability of the zero solution of a stochastic differential equation (see e.g. [10]).

Let $(\Omega, \mathcal{F}, \mathcal{P})$ be an usual probability space and $\{\omega_t, t \geq 0\}$ be a standard \mathbb{R}^p -valued Wiener process defined on this space. Denote by $(\mathcal{F}_t)_{t \geq 0}$ the complete right-continuous filtration generated by ω .

Let x_t be the \mathbb{R}^n -valued process solution of the stochastic differential equation written in the sense of Itô,

$$x_t = x_0 + \int_0^t X_0(x_s) ds + \sum_{k=1}^p \int_0^t X_k(x_s) d\omega_s^k, \quad (5)$$

where $X_k(0) = 0$, $0 \leq k \leq p$. We assume that X_k are Lipschitz vector fields on \mathbb{R}^n such that there exists a positive constant K such that, for any x in \mathbb{R}^n , $\sum_{k=0}^p \|X_k(x)\| \leq K(1 + \|x\|)$. For any x_0 in \mathbb{R}^n , denote by $x_t(x_0)$, $t \geq 0$, the solution at time t of the stochastic differential equation (5) starting from the state x_0 . Then, the different notions of stochastic stability that are used in this paper are the following.

Definition 1: The solution $x_t \equiv 0$ of the stochastic differential equation (5) is said to be stable in probability if for any $\epsilon > 0$, $\lim_{x_0 \rightarrow 0} P(\sup_{t > 0} |x_t(x_0)| > \epsilon) = 0$. If, in addition, there exists a neighbourhood D of the origin such that $P(\lim_{t \rightarrow +\infty} |x_t(x_0)| = 0) = 1$, $\forall x_0 \in D$, the solution $x_t \equiv 0$ of the stochastic differential equation (5) is said to be asymptotically stable in probability. It is globally asymptotically stable in probability (GASP) if $D = \mathbb{R}^n$.

For $1 \leq i, j \leq n$, let \mathcal{L} be the infinitesimal generator associated with the stochastic differential equation (5) defined for any function Ψ in $C^2(\mathbb{R}^n)$ by:

$$\begin{aligned} \mathcal{L}\Psi(x) &= \langle X_0(x), \nabla \Psi(x) \rangle \\ &+ \frac{1}{2} \sum_{k=1}^p \langle X_k(x), \frac{\partial^2 \Psi}{\partial x^2}(x) X_k(x) \rangle, \end{aligned}$$

where $\langle \cdot, \cdot \rangle$ is the inner product in \mathbb{R}^n .

Then, following criteria in terms of Lyapunov function for the stochastic stability hold (see [1],[10]).

Theorem 1: If there exist a neighbourhood D of the point $x = 0$ in \mathbb{R}^n , and a Lyapunov function V defined in D (i.e. a positive definite and proper function V mapping D into \mathbb{R}) such that $\mathcal{L}V(x) \leq 0$ (resp. $\mathcal{L}V(x) < 0$), $\forall x \in D$, $x \neq 0$, then, the solution $x_t \equiv 0$ of the stochastic differential equation (5) is stable (resp. asymptotically stable) in probability. It is GASP if $\mathcal{L}V(x) < 0$, $\forall x \in \mathbb{R}^n$, $x \neq 0$.

By a *proper function* we mean a function $V : D \rightarrow \mathbb{R}$ such that $\{x \in \mathbb{R}^n \mid V(x) \leq \xi\}$ is compact for each $\xi > 0$.

Recall also that if the solution $x_t \equiv 0$ of the stochastic differential equation (5) is stable in probability and there exists a Lyapunov function V defined in D such that $\mathcal{L}V(x) \leq 0$, $\forall x \in D$, $x \neq 0$, then, the stochastic version of LaSalle's invariance principle (see [12]) allows to state that the stochastic process x_t converges in probability to the largest invariant set whose support is contained in the locus $\{x_t \mid \mathcal{L}V(x_t) = 0, \forall t \geq 0\}$.

Now, in order to state our results on the stabilization of stochastic control system (1), let us introduce the following notations and definitions.

Definition 2: The stochastic differential control system (1) will be said globally asymptotically feedback stabilizable in probability at the origin if there exists a feedback control law $u : \mathbb{R}^n \rightarrow \mathbb{R}^m$ with $u(0) = 0$ such that the zero solution $x_t \equiv 0$ of the closed-loop system $x_t = x_0 + \int_0^t f_0(x_s, u(x_s))ds + \sum_{j=1}^p \int_0^t f_j(x_s, u(x_s))d\omega_s^j$ is globally asymptotically stable in probability.

For $0 \leq j \leq p$ and $1 \leq i \leq m$, we associate with system (1) the vector fields X_j and Y_j^i defined by:

$$X_j(x) = f_j(x, 0), \quad Y_j^i(x) = \frac{\partial f_j}{\partial u_i}(x, 0), \quad (6)$$

and the second order differential operators L_0 and L_i defined for any function Ψ in $\mathcal{C}^2(\mathbb{R}^n)$ by:

$$\begin{aligned} L_0\Psi(x) &= \langle X_0(x), \nabla\Psi(x) \rangle \\ &+ \frac{1}{2} \sum_{j=1}^p \langle X_j(x), \frac{\partial^2\Psi}{\partial x^2}(x)X_j(x) \rangle, \quad (7) \end{aligned}$$

$$\begin{aligned} L_i\Psi(x) &= \langle Y_0^i(x), \nabla\Psi(x) \rangle \\ &+ \sum_{j=1}^p \langle X_j(x), \frac{\partial^2\Psi}{\partial x^2}(x)Y_j^i(x) \rangle. \quad (8) \end{aligned}$$

Definition 3: Stochastic nonlinear control system (1) is said to be a *Jurdjevic-Quinn type* stochastic system if there exists a positive definite and proper smooth function $V : \mathbb{R}^n \rightarrow \mathbb{R}$ such that: (h1) $LV(x) \leq 0, \forall x \in \mathbb{R}^n$; (h2) the set $\{x \in \mathbb{R}^n | L_0^{k+1}V(x) = L_0^k L_i V(x) = 0, k \in \mathbb{N}, i = 1, \dots, m\}$ is reduced to $\{0\}$.

Notice that for $f_j = 0$ (resp. $\partial f_j / \partial u = 0$), $1 \leq j \leq p$, conditions (h1) and (h2) reduce to (i) and (ii) (resp. (i') and (ii')).

Notice also that for the stochastic affine control system (4) that have been considered in [2], (h1) and (h2) reduce to (i') and (ii'). Indeed, set $p = \sum_{i=0}^m p_i$; $\tilde{\omega} = (\omega_0^1, \dots, \omega_0^{p_0}, \dots, \omega_m^1, \dots, \omega_m^{p_m})$; for $1 \leq i \leq m$ and $1 \leq j \leq p$, $\tilde{X}_j = X_j$ if $1 \leq j \leq p_0$ and $\tilde{X}_j = 0$ otherwise; $\tilde{Y}_j^i = Y_j^i$ if $\sum_{k=0}^{i-1} p_k + 1 \leq j \leq \sum_{k=0}^i p_k$ and $\tilde{Y}_j^i = 0$ otherwise. Then system (4) may be written on the form:

$$\begin{aligned} x_t &= x_0 + \int_0^t \left(X_0(x_s) + \sum_{i=1}^m u_i Y_0^i(x_s) \right) ds \\ &+ \sum_{j=1}^p \int_0^t \left(\tilde{X}_j(x_s) + \sum_{i=1}^m u_i \tilde{Y}_j^i(x_s) \right) d\tilde{\omega}_s^j \end{aligned}$$

and one gets, for $1 \leq i \leq m$, $L_i V(x) = \langle Y_0^i(x), \nabla V(x) \rangle$, because of $\tilde{X}_j(x) \tilde{Y}_j^i(x) = 0, 1 \leq j \leq p$.

Finally, for a Lyapunov function V , associate with system (1) the smooth function $\psi_V : \mathbb{R}^n \times \mathbb{R}^m \rightarrow \mathbb{R}^m$ defined by:

$$\begin{aligned} \psi_V(x, u) &= -g_0^T(x, u) \nabla V(x) \\ &- \sum_{j=1}^p g_j^T(x, u) \frac{\partial^2 V}{\partial x^2}(x) X_j(x) \\ &- \frac{1}{2} \sum_{j=1}^p g_j^T(x, u) \frac{\partial^2 V}{\partial x^2}(x) g_j(x, u) u, \quad (9) \end{aligned}$$

where

$$g_j(x, u) = \int_0^1 \frac{\partial f_j}{\partial u}(x, tu) dt, \quad 0 \leq j \leq p. \quad (10)$$

III. FIXED POINT STABILIZABILITY SUFFICIENT CONDITION

The following proposition can now be stated as a preliminary result of stabilizability of Jurdjevic-Quinn type stochastic systems.

Proposition 1: Assume that system (1) is of Jurdjevic-Quinn type and let V be a Lyapunov function satisfying conditions (h1) and (h2). Assume also that, for any $x \in \mathbb{R}^n$, the function $\psi_V(x, \cdot)$ has a fixed point $u(x) = \psi_V(x, u(x))$ which is smooth and such that $u(0) = 0$. Then $u(x)$ is a globally stabilizing feedback for the stochastic system (1).

Proof: the functions $f_j, 0 \leq j \leq p$, being smooth, one has from (6) and (10), $f_j(x, u) = X_j(x) + g_j(x, u)u$. Then denoting by \mathcal{L} the infinitesimal generator associated with the closed-loop system

$$\begin{aligned} x_t &= x_0 + \int_0^t f_0(x_s, u(x_s)) ds \\ &+ \sum_{j=1}^p \int_0^t f_j(x_s, u(x_s)) d\omega_s^j, \quad (11) \end{aligned}$$

one has for all $x \in \mathbb{R}^n$:

$$\begin{aligned} \mathcal{L}V(x) &= \langle X_0(x) + g_0(x, u(x))u(x), \nabla V(x) \rangle \\ &+ \frac{1}{2} \sum_{j=1}^p \left\langle X_j(x) + g_j(x, u(x))u(x), \right. \\ &\left. \frac{\partial^2 V}{\partial x^2}(x) [X_j(x) + g_j(x, u(x))u(x)] \right\rangle, \end{aligned}$$

and by a simple computation one gets from (7), (8) and (9), $\mathcal{L}V(x) = L_0 V(x) - \langle u(x), \psi_V(x, u(x)) \rangle$. Hence, from $u(x) = \psi_V(x, u(x))$ and assumption (h1) one has $\mathcal{L}V(x) = L_0 V(x) - \|u(x)\|^2 \leq 0, \forall x \in \mathbb{R}^n$, and according with theorem 1, the zero solution $x_t \equiv 0$ of the closed-loop system (11) is stable in probability.

Besides, according to the stochastic version of LaSalle's invariance principle (see [12]), the stochastic process x_t converges in probability to the largest invariant set whose support is contained in the locus $\mathcal{L}V(x_t) = 0$ for all $t \geq 0$. Therefore, in order to prove that the zero solution of the closed-loop system is GASP it must be shown that for any complete solution x_t of (11) along which $\mathcal{L}V(x_t) = 0$ for all $t \geq 0$, one has necessarily $x_t = 0 \forall t \geq 0$.

Notice that, from (6) and (10), one has $g_j(x, 0) = (Y_j^1(x) \dots Y_j^m(x))$, and from (9) and (8) it follows that:

$$\begin{aligned} \psi_V(x, 0) &= -(\langle Y_0^1(x), \nabla V(x) \rangle, \dots, \langle Y_0^m(x), \nabla V(x) \rangle)^T \\ &- \sum_{j=1}^p \left(\langle Y_j^1(x), \frac{\partial^2 V}{\partial x^2}(x) X_j(x) \rangle, \dots \right) \end{aligned}$$

$$\begin{aligned} & \dots, \langle Y_j^m(x), \frac{\partial^2 V}{\partial x^2}(x) X_j(x) \rangle)^T \\ & = (L_1 V(x), \dots, L_m V(x))^T. \end{aligned}$$

Now $\mathcal{L}V(x) = 0$ if and only if $L_0 V(x) = 0$ and $u(x) = 0$, and since $u(x) = \psi_V(x, u(x))$, it turns out that $\mathcal{L}V(x) = 0 \Rightarrow L_0 V(x) = \dots = L_m V(x) = 0$. So, for any complete solution x_t of the stochastic differential equation (11) for which $\mathcal{L}V(x_t) = 0$ for all $t \geq 0$, successive differentiations by means of Itô's formula yield $L_0^{k+1} V(x_t) = L_0^k L_i V(x_t) = 0$, for $t \geq 0$, $k \in \mathbb{N}$, and $i = 1, \dots, m$. Hence, by assumption (h2), it follows that $x_t = 0$ for all $t \geq 0$, which completes the proof. \blacksquare

Remark 1: As an application of proposition 1, one can deduce the result of [2] on the stabilization of stochastic affine control system (4) provided that it is of Jurdjevic-Quinn type thanks to a Lyapunov function V satisfying conditions (i') and (ii'). Notice that for system (4) the function ψ_V defined in (9) satisfies $\psi_{V,i}(x, u) = -Y_0^i V(x) - a_{V,i}(x)u_i$ where $a_{V,i}(x) = (1/2) \sum_{j=1}^{p_i} \langle Y_j^i(x), (\partial^2 V / \partial x^2)(x) Y_j^i(x) \rangle$, $1 \leq i \leq m$, and generally it has no smooth fixed point. Nevertheless, by using the static precompensator

$$u_i = (1 + a_{V,i}^2(x) - a_{V,i}(x))^{-1/2} \tilde{u}_i, \quad 1 \leq i \leq m, \quad (12)$$

one transforms system (4) into

$$\begin{aligned} x_t &= x_0 + \int_0^t \left(X_0(x_s) + \sum_{i=1}^m \tilde{u}_i \tilde{Y}_0^i(x_s) \right) ds \\ &+ \sum_{j=1}^{p_0} \int_0^t X_j(x_s) d\omega_{0s}^j \\ &+ \sum_{i=1}^m \sum_{j=1}^{p_i} \int_0^t \tilde{u}_i \tilde{Y}_j^i(x_s) d\omega_{is}^j, \end{aligned} \quad (13)$$

where $\tilde{Y}_j^i = (1 + a_{V,i}^2(x) - a_{V,i}(x))^{-1/2} Y_j^i$, $1 \leq i \leq m$, $0 \leq j \leq p_i$. Clearly (13) is of Jurdjevic-Quinn type in accordance with (4), and thanks to the same Lyapunov function V . Now, to system (13) one associates by (9) the function $\tilde{\psi}_V$ given by:

$$\begin{aligned} \tilde{\psi}_{V,i}(x, \tilde{u}) &= -\tilde{Y}_0^i V(x) - \frac{u_i}{2} \sum_{j=1}^{p_i} \left\langle \tilde{Y}_j^i(x), \frac{\partial^2 V}{\partial x^2}(x) \tilde{Y}_j^i(x) \right\rangle \\ &+ \frac{a_{V,i}(x) \tilde{u}_i}{\sqrt{1 + a_{V,i}^2(x) - a_{V,i}(x)}} \\ &= - \frac{Y_0^i V(x) + \frac{a_{V,i}(x) \tilde{u}_i}{\sqrt{1 + a_{V,i}^2(x) - a_{V,i}(x)}}}{\sqrt{1 + a_{V,i}^2(x) - a_{V,i}(x)}} \end{aligned}$$

which has a smooth fixed point $\tilde{u}(x)$ defined by $\tilde{u}_i(x) = -(1 + a_{V,i}^2(x) - a_{V,i}(x))^{1/2} (1 + a_{V,i}^2(x))^{-1} Y_0^i V(x)$. Therefore, following proposition 1, $\tilde{u}(x)$ stabilizes (13), and by (12) it yields the stabilizing feedback law $u_i(x) = -(1 + a_{V,i}^2(x))^{-1} Y_0^i V(x)$, for system (4). \blacksquare

IV. STABILIZABILITY OF JURDJEVIC-QUINN TYPE STOCHASTIC SYSTEMS

Following Remark 1, the question now is what about the stabilizability of general Jurdjevic-Quinn type stochastic systems of the form (1). The next theorem will establish that any such a system is globally asymptotically stabilizable in probability by an arbitrarily bounded smooth feedback law.

Theorem 2: Assume that system (1) is of Jurdjevic-Quinn type and let V be a Lyapunov function satisfying conditions (h1) and (h2). Then, for any positive constant η , system (1) is globally asymptotically stabilizable in probability by means of a feedback law $u(x)$ satisfying $u(0) = 0$ and $\|u(x)\| \leq \eta$, $\forall x \in \mathbb{R}^n$.

Proof: Let us begin by the following remark on the function ψ_V associated with system (1) by (9), and that will be useful for the proof. If there exists a smooth function $k(x) > 0$ such that, for any $x \in \mathbb{R}^n$, the function $k(x)\psi_V(x, \cdot)$ has a fixed point $u(x) = k(x)\psi_V(x, u(x))$ which is smooth and such that $u(0) = 0$, then $u(x)$ is a globally stabilizing feedback for the stochastic system (1). As a matter of fact, the preliminary feedback $u = \sqrt{k(x)} \tilde{u}$ changes the original system (1) into the system

$$x_t = x_0 + \int_0^t \tilde{f}_0(x_s, \tilde{u}) ds + \sum_{j=1}^p \int_0^t \tilde{f}_j(x_s, \tilde{u}) d\omega_s^j, \quad (14)$$

where $\tilde{f}_j(x, \tilde{u}) = f_j(x, \sqrt{k(x)} \tilde{u})$, $0 \leq j \leq p$. One may also verify that the vector fields and the second order differential operators defined respectively by (6), (7) and (8) are changed into $\tilde{X}_j = X_j$, $\tilde{Y}_j^i = \sqrt{k} Y_j^i$, $\tilde{L}_0 = L_0$, and $\tilde{L}_i = \sqrt{k} L_i$. Therefore, (14) is a Jurdjevic-Quinn type stochastic system in accordance with (1). Besides, if one denotes by ψ_V and $\tilde{\psi}_V$ the functions associated respectively with systems (1) and (14), a straightforward calculation shows that $\tilde{\psi}_V(x, \tilde{u}) = \sqrt{k(x)} \psi_V(x, \sqrt{k(x)} \tilde{u})$. So, if $u(x) = k(x)\psi_V(x, u(x))$, $u(0) = 0$, is a smooth fixed point of the function $k(x)\psi_V(x, \cdot)$, then one has: $\tilde{\psi}_V(x, u(x)/\sqrt{k(x)}) = \sqrt{k(x)} \psi_V(x, u(x)) = u(x)/\sqrt{k(x)}$. Hence, one can deduce from proposition 1 that $\tilde{u}(x) = u(x)/\sqrt{k(x)}$ stabilizes system (14), and accordingly $u(x)$ stabilizes system (1).

Now, for $\eta > 0$, let $K_1(x)$ and $K_2(x)$ be any smooth non-negative real valued functions satisfying, for any $x \in \mathbb{R}^n$, $K_1(x) + K_2(x) \neq 0$, $K_1(x) \geq \sup_{\|u\| \leq \eta} \|\psi_V(x, u)\|$ and $K_2(x) \geq \sup_{\|u\| \leq \eta} \|(\partial \psi_V / \partial u)(x, u)\|$. Let $\alpha : \mathbb{R}^n \times \mathbb{R}^m \rightarrow \mathbb{R}^m$ be the smooth function defined by $\alpha(x, u) = \eta(K_1(x) + 2\eta K_2(x))^{-1} \psi_V(x, u)$. Then, for any $x \in \mathbb{R}^n$ and any $u \in \mathbb{R}^m$ such that $\|u\| \leq \eta$, one has $\|\alpha(x, u)\| \leq \eta$ and $\|(\partial \alpha / \partial u)(x, u)\| \leq 1/2$. So, on the one hand, applying the fixed point theorem one can deduce that there exists a unique continuous function $\theta : \mathbb{R}^n \rightarrow \mathbb{R}^m$, with $\theta(0) = 0$, satisfying for all $x \in \mathbb{R}^n$, $\|\theta(x)\| \leq \eta$ and $\alpha(x, \theta(x)) = \theta(x)$. On the other hand, the implicit function theorem applies to the function $\gamma(x, u) = \alpha(x, u) - u$ in each $x_0 \in \mathbb{R}^n$ since $\gamma(x_0, \theta(x_0)) = 0$ and the jacobian matrix $(\partial \gamma / \partial u)(x_0, \theta(x_0)) = (\partial \alpha / \partial u)(x_0, \theta(x_0)) - I_m$ is invertible. So, there exist a neighbourhood $\mathcal{V} \times \mathcal{U}$ of $(x_0, \theta(x_0))$

and $v : \mathcal{V} \rightarrow \mathcal{U}$ such that $v(x_0) = \theta(x_0)$ and $\gamma(x, v(x)) = 0$, $\forall x \in \mathcal{V}$. Now $v \in \mathcal{C}^\infty(\mathcal{V}, \mathcal{U})$ because of γ is \mathcal{C}^∞ , but the equation $\gamma(x, u) = 0$ has a unique solution $\theta(x)$ defined on \mathbb{R}^n , and so, $\theta|_{\mathcal{V}} = v$ and then θ is \mathcal{C}^∞ .

By setting $k(x) = \eta(K_1(x) + 2\eta K_2(x))^{-1}$, it turns out from the remark in the beginning of the proof that $u(x) = \theta(x)$ is a globally asymptotically stabilizing feedback for system (1), and the proof is completed. ■

In order to illustrate the feasibility of theorem 2, let us apply it to a stochastic affine control system of the form:

$$\begin{aligned} x_t = & x_0 + \int_0^t \left(X_0(x_s) + \sum_{i=1}^m u_i Y_0^i(x_s) \right) ds \\ & + \sum_{j=1}^p \int_0^t \left(X_j(x_s) + \sum_{i=1}^m u_i Y_j^i(x_s) \right) d\omega_s^j \end{aligned} \quad (15)$$

which is assumed to be of Jurdjevic-Quinn type thanks to a Lyapunov function V . Since $f_j(x, u) = X_j(x) + \sum_{i=1}^m u_i Y_j^i(x)$, one gets by a simple computation from (9) and (10) $\psi_v(x, u) = -h_v(x) - H_v(x)u$ where $h_v(x) = (L_1 V(x), \dots, L_m V(x))^T$ and $H_v(x)$ is the $m \times m$ matrix whose (i, k) th entry is $(1/2) \sum_{j=1}^p \langle Y_j^i(x), (\partial^2 V / \partial x^2)(x) Y_j^k(x) \rangle$. Hence, for a fixed $\eta > 0$, by taking $k(x) = \eta(K_1(x) + 2\eta K_2(x))^{-1}$ where $K_1(x)$ and $K_2(x)$ are smooth functions such that $K_1(x) + K_2(x)$ does not vanish on \mathbb{R}^n , $K_1(x) \geq \sup_{\|u\| \leq \eta} \|h_v(x) + H_v(x)u\|$ and $K_2(x) \geq \|H_v(x)\|$, one gets $k(x)\psi_v(x, u) = -k(x)h_v(x) - k(x)H_v(x)u$. Now, for all $x \in \mathbb{R}^n$, the $m \times m$ matrix $k(x)H_v(x)$ satisfies $\|k(x)H_v(x)\| \leq 1/2$, and so, the matrix $I_m + k(x)H_v(x)$ is invertible. Therefore, the fixed point $u(x)$ of the function $k(x)\psi_v(x, \cdot)$, which satisfies $u(0) = 0$ and $\|u(x)\| \leq \eta$, can actually be explicitly computed: $u(x) = -(I_m + k(x)H_v(x))^{-1} k(x)h_v(x)$, and it is a globally asymptotically stabilizing feedback law for system (15).

In particular, for Jurdjevic-Quinn type stochastic affine control systems of the form (4), one has $h_v(x) = (Y_0^1 V(x), \dots, Y_0^m V(x))^T$ and $H_v(x) = \text{diag}(a_{v,1}(x), \dots, a_{v,m}(x))$. Thus, the above procedure yields bounded feedback laws of the form $u_i(x) = -\eta(K_1(x) + 2\eta K_2(x))^{-1} Y_0^i V(x)$, where a possible choice of K_1 and K_2 is given by $K_1(x) = 1 + \sum_{i=1}^m (Y_0^i V(x))^2 + \eta \sum_{i=1}^m (1 + a_{v,i}^2(x))$ and $K_2(x) = \sum_{i=1}^m (1 + a_{v,i}^2(x))$.

V. EXPLICIT DESIGN OF STABILIZING FEEDBACK

Notice that, as established above, theorem 2 gives an existential stabilizability result in the sense that, even if for particular cases as Jurdjevic-Quinn type stochastic affine control systems of the form (15) the fixed point can be exactly computed, it does not yield, in general, explicitly the stabilizing feedback control law. By providing an explicit design of such a feedback, the next theorem is more close to practical preoccupations in automatic control.

the functions f_j , $1 \leq j \leq p$, being smooth, recall that,

from the Taylor expansion formula, one has:

$$f_j(x, u) = f_j(x, 0) + \frac{\partial f_j}{\partial u}(x, 0)u + \tilde{f}_j(x, u, u), \quad (16)$$

where $\tilde{f}_j : \mathbb{R}^n \times \mathbb{R}^m \times \mathbb{R}^m \rightarrow \mathbb{R}^n$, is defined by

$$\tilde{f}_j(x, v, w) = \int_0^1 (1-t) \frac{\partial^2 f_j}{\partial u^2}(x, tv)(w, w) dt.$$

The notation $(\partial^2 f_j / \partial u^2)(x, tv)$ is used for the second order derivative of f_j with respect to u at (x, tv) , that is to say the bilinear application from $\mathbb{R}^m \times \mathbb{R}^m$ to \mathbb{R}^n defined by $(\partial^2 f_j / \partial u^2)(x, tv)(w, \tilde{w}) = (w^T (\partial^2 f_j^1 / \partial u^2)(x, tv) \tilde{w}, \dots, w^T (\partial^2 f_j^p / \partial u^2)(x, tv) \tilde{w})^T$ with f_j^1, \dots, f_j^p the component functions of f_j .

Besides, for a Lyapunov function V , let $\varphi_v : \mathbb{R}^n \times \mathbb{R}^m \times \mathbb{R}^m \rightarrow \mathbb{R}$ be the smooth function defined by:

$$\begin{aligned} \varphi_v(x, v, w) = & \langle \tilde{f}_0(x, v, w), \nabla V(x) \rangle \\ & + \frac{1}{2} \sum_{j=1}^p \text{Tr} \left(A_j(x, v, w) \frac{\partial^2 V}{\partial x^2}(x) \right) \end{aligned} \quad (17)$$

where the $n \times n$ matrix $A_j(x, v, w)$ is defined by:

$$\begin{aligned} A_j(x, v, w) = & X_j(x) \tilde{f}_j^T(x, v, w) + \tilde{f}_j(x, v, w) X_j^T(x) \\ & + \sum_{i=1}^m v_i \left[Y_j^i(x) \tilde{f}_j^T(x, v, w) + \tilde{f}_j(x, v, w) Y_j^{iT}(x) \right] \\ & + \sum_{i_1, i_2=1}^m w_{i_1} w_{i_2} Y_j^{i_1}(x) Y_j^{i_2 T}(x) + \tilde{f}_j(x, v, v) \tilde{f}_j^T(x, v, w). \end{aligned}$$

Notice that the real valued function φ_v is homogeneous of degree 2 with respect to w . Then one can state:

Theorem 3: Assume that system (1) is of Jurdjevic-Quinn type and let V be a Lyapunov function satisfying conditions (h1) and (h2). Then for any $\eta > 0$ and any smooth functions $K_1(x)$ and $K_2(x)$ satisfying, $\forall x \in \mathbb{R}^n$, $K_1(x) + K_2(x) \neq 0$ and

$$K_1(x) \geq \sup_{\|v\| \leq \eta, \|w\|=1} |\varphi_v(x, v, w)|, \quad (18)$$

$$K_2(x) \geq \|(L_1 V(x), \dots, L_m V(x))\|, \quad (19)$$

the stochastic control system (1) is globally stabilizable by means of the feedback:

$$u(x) = \frac{-\eta}{\eta K_1(x) + K_2(x)} (L_1 V(x), \dots, L_m V(x))^T, \quad (20)$$

which satisfies $\|u(x)\| \leq \eta$, $\forall x \in \mathbb{R}^n$.

Proof: The inequality $\|u(x)\| \leq \eta$ is an immediate consequence of (19), and (20). Moreover, from (6), and (16) the closed-loop system (1-20) is given by the stochastic differential equation:

$$\begin{aligned} x_t = & x_0 + \int_0^t \left(X_0(x_s) + \sum_{i=1}^m u^i(x_s) Y_0^i(x_s) \right. \\ & \left. + \tilde{f}_0(x_s, u(x_s), u(x_s)) \right) ds \end{aligned}$$

$$\begin{aligned}
& + \sum_{j=1}^p \int_0^t \left(X_j(x_s) + \sum_{i=1}^m u^i(x_s) Y_j^i(x_s) \right. \\
& \quad \left. + \tilde{f}_j(x_s, u(x_s), u(x_s)) \right) d\omega_s^j \quad (21)
\end{aligned}$$

Then, denoting by \mathcal{L} the infinitesimal generator associated with the stochastic differential equation (21), one has:

$$\begin{aligned}
\mathcal{L}V(x) &= \left\langle X_0(x_s) + \sum_{i=1}^m u^i(x_s) Y_0^i(x_s) \right. \\
& \quad \left. + \tilde{f}(x_s, u(x_s), u(x_s)), \nabla V(x) \right\rangle \\
& + \frac{1}{2} \sum_{j=1}^p \left\langle \left[X_j(x_s) + \sum_{i=1}^m u^i(x_s) Y_j^i(x_s) \right. \right. \\
& \quad \left. \left. + \tilde{f}_j(x_s, u(x_s), u(x_s)) \right] \right. \\
& \quad \left. \frac{\partial^2 V}{\partial x^2}(x) \left[X_j(x_s) + \sum_{i=1}^m u^i(x_s) Y_j^i(x_s) \right. \right. \\
& \quad \left. \left. + \tilde{f}_j(x_s, u(x_s), u(x_s)) \right] \right\rangle
\end{aligned}$$

and by a simple computation one gets from (7), (8) and (17), $\mathcal{L}V(x) = L_0V(x) + \sum_{i=1}^m u^i(x)L_iV(x) + \varphi_v(x, u(x), u(x))$. It follows that, for $x \in \mathbb{R}^n$ such that $u(x) = 0$ one has $\mathcal{L}V(x) = L_0V(x)$, and otherwise, from (20) and the homogeneity property of $\varphi_v(x, v, w)$ with respect to w one gets:

$$\mathcal{L}V(x) = L_0V(x) - \frac{\|u(x)\|^2 \left[1 - K(x) \varphi_v \left(x, u(x), \frac{u(x)}{\|u(x)\|} \right) \right]}{K(x)}$$

where $K(x) = \eta(\eta K_1(x) + K_2(x))^{-1}$. Besides, one has $1 - K(x) \varphi_v(x, u(x), u(x)/\|u(x)\|) \geq 0$ because of (18) and $\|u(x)\| \leq \eta$, and so one gets from assumption (h1), $\mathcal{L}V(x) \leq 0$, $\forall x \in \mathbb{R}^n$. Hence, according with theorem 1, the zero solution $x_t \equiv 0$ of the stochastic differential equation (21) is stable in probability. Moreover, it follows from (19), (19) and (20) that if $u(x) \neq 0$ then $K_2(x) \neq 0$ and so $1 - K(x) \varphi_v(x, u(x), u(x)/\|u(x)\|) \neq 0$, and, from (20), it turns out that $\mathcal{L}V(x) = 0$ if and only if $L_iV(x) = 0$, $i = 1, \dots, m$. Therefore, the proof can be continued, thanks to the stochastic version of LaSalle's invariance principle, exactly as in the proof of Proposition 1. ■

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An observer for a nonlinear age-structured model of a harvested fish population

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AN OBSERVER FOR A NONLINEAR AGE-STRUCTURED MODEL OF A HARVESTED FISH POPULATION

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ABSTRACT. We consider an age-structured model of a harvested population. This model is a discrete-time system that includes a nonlinear stock-recruitment relationship. Our purpose is to estimate the stock state. To achieve this goal, we built an observer, which is an auxiliary system that uses the total number of fish caught over each season and gives a dynamical estimation of the number of fish by age class. We analyse the convergence of the observer and we show that the error estimation tends to zero with exponential speed if a condition on the fishing effort is satisfied. Moreover the constructed observer (dynamical estimator) does not depend on the poorly understood stock-recruitment relationship. This study shows how some tools from nonlinear control theory can help to deal with the state estimation problem in the field of renewable resource management.

1. Introduction. The problem of natural stock management has received great attention during the last decades. Developers of management policies in the exploitation of renewable resource stocks need to have a good estimate of the available resource. Current mathematical models together with computer simulations are useful in describing the evolution of complex systems. One of the important problems in control theory is to reconcile the available data with the used mathematical model. This problem is known as the observability problem, and it is

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related to the construction of “observers” (called some times software sensors) for dynamical systems. In this paper, we show how to apply this theory to address the stock estimation problem for an exploited fish population. The biological model we use is the standard fisheries age-structured model (see for instance [8, 7, 16]):

$$\left\{ \begin{array}{l} x_1(k+1) = f\left(\sum_{i=1}^n b_i x_i(k)\right) \\ x_2(k+1) = x_1(k)e^{-M_1-q_1\tau E(k)} \\ \vdots \\ \vdots \\ x_{n-1}(k+1) = x_{n-2}(k)e^{-M_{n-2}-q_{n-2}\tau E(k)} \\ x_n(k+1) = x_{n-1}(k)e^{-M_{n-1}-q_{n-1}\tau E(k)} + x_n(k)e^{-M_n-q_n\tau E(k)} \end{array} \right. \quad (1)$$

where

- n is the number of age-classes,
- $x_i(k)$ is the number of individuals in the i th class at time k ,
- b_i is the fecundity rate of class i ,
- M_i is the natural mortality rate of class i ,
- q_i is the catchability coefficient of individuals of the i th class,
- $E(k)$ is the fishing effort at time k ,
- τ is the length of harvesting season,
- f is the stock-recruitment function.

We suppose that the number of fish harvested over each period $[k, k+1)$ is available for measurement. This number can be expressed as follows (see [7] pp. 146-148, for instance):

$$y(k) = \sum_{i=1}^n \frac{q_i \tau E(k)}{q_i \tau E(k) + M_i} \left(1 - e^{-M_i - q_i \tau E(k)}\right) x_i(k). \quad (2)$$

The goal of this paper is to give a simple tool that would allow us to give a dynamical estimation of the state $(x_1(k), \dots, x_n(k))$ of the stock using the available information which is the value of the captures. To achieve this goal we shall build an observer for system (1).

To fix the ideas let us take a peculiar three-dimensional numerical example of model (1) with the depensatory stock-recruitment function $f(x_0) = \frac{x_0^2}{1 + \beta x_0^2}$:

$$\left\{ \begin{array}{l} x_1(k+1) = f\left(\sum_{i=1}^3 b_i x_i(k)\right) = \frac{(\sum_{i=1}^3 b_i x_i(k))^2}{1 + \beta (\sum_{i=1}^3 b_i x_i(k))^2}, \\ x_2(k+1) = x_1(k)e^{-M_1-q_1\tau E(k)}, \\ x_3(k+1) = x_2(k)e^{-M_2-q_2\tau E(k)} + x_3(k)e^{-M_3-q_3\tau E(k)} \end{array} \right. \quad (3)$$

with the following parameters:

Depensation recruitment function parameter	$\beta = 0.6$
Fecundity parameters	$b = [2 \ 3 \ 3]$,
Catchability coefficients	$q = [0.12 \ 0.24 \ 1]$,
Natural mortality rates	$M = [0.8 \ 0.8 \ 0.8]$,
Length of harvesting season	$\tau = 1$,
Fishing effort	$E(k) = 10$.

The variables $x_i(k)$ give the number in millions of individuals of the class i at time k . If we can measure the state of (3) at some time k_0 , then the equation (3) allow us to compute the values of $x_1(k)$, $x_2(k)$ and $x_3(k)$ for all time $k \geq k_0$. Suppose, for instance, that the real state of the stock at time $k = 0$ is known and it is given by $x_1(0) = 0.181$, $x_2(0) = 0.021$ and $x_3(0) = 0.015$ (in millions of individuals); then by (3), the state of the stock will be (for instance) at time $k = 19$:

$$x_1(19) = 27.1 \times 10^{-3}, \quad x_2(19) = 8.37 \times 10^{-3}, \quad \text{and} \quad x_3(19) = 0.55 \times 10^{-3}.$$

It can moreover be shown that the above initial condition leads to the extinction of the considered population; that is, $x_i(k)$ tends toward zero as time k tends toward infinity. In practice, the stock will vanish as soon as k becomes larger than 20. However, in practice we do not have access to the values of $x_1(0)$, $x_2(0)$ and $x_3(0)$. All we can measure is the output of the system. Here it is the value of the captures defined by equation (2). For (3) associated to the above parameters values, its expression is given by:

$$y(k) = 0.518799 x_1(k) + 0.719428 x_2(k) + 0.925907 x_3(k).$$

Therefore, at time $k = 0$ we know only that $y(0) = 0.122899$. This value of the output corresponds to the real unknown initial condition, but it also corresponds to the following possible values: $\bar{x}_1(0) = 0.16$, $\bar{x}_2(0) = 0.05$, $\bar{x}_3(0) = 0.0042336$, since $0.518799 \times 0.16 + 0.719428 \times 0.05 + 0.925907 \times 0.0042336 = 0.122899$. Hence, one can take $(\bar{x}_1(0), \bar{x}_2(0), \bar{x}_3(0))$ as an initial condition for system (3), and in this case the state of the stock will be at time $k = 19$:

$$\bar{x}_1(19) = 1474 \times 10^{-3}, \quad \bar{x}_2(19) = 199 \times 10^{-3}, \quad \text{and} \quad \bar{x}_3(19) = 8.13 \times 10^{-3}.$$

These values are different from the values obtained for the real initial condition. Moreover, the simulations show that the solution of (3) corresponding to the initial condition $(\bar{x}_1(0), \bar{x}_2(0), \bar{x}_3(0))$ will converge to a positive steady state whose coordinates are $(1.474, 0.199, 0.008)$, while the real state will tend toward $(0, 0, 0)$. To summarize, the dynamical model (3) does not suffice to compute the value of the state at a given time k nor to predict the behavior of the system, because one needs to know the value of the real initial condition, which is unavailable for measurement. To overcome this difficulty we shall use a tool from control theory called an observer. That is, we shall construct another dynamical system whose state $\hat{\mathbf{x}}$ will provide an estimate of the real unmeasured state of the considered model, and this will be true regardless of the observer's initial condition: we need not care about the choice of the initial condition of the observer. For (3), the state of the observer will converge rapidly to the real state of the system (issued from the supposed real initial condition $\mathbf{x}(\mathbf{0}) = (0.181, 0.021, 0.015)$), even if we take as an initial condition for the observer the false one $\bar{\mathbf{x}}(\mathbf{0}) = (0.16, 0.05, 0.0042336)$. This is shown in Table 1, which compares the values obtained at different times by system (3) initialized respectively at the true initial condition $\mathbf{x}(\mathbf{0})$ and at the false one $\bar{\mathbf{x}}(\mathbf{0})$, as well as the values obtained by the observer also initialized at the false initial condition $\bar{\mathbf{x}}(\mathbf{0})$. For lack of space we only give the values of the first component, but the same observations are valid for the second and the third component of the state. It can be seen that the values provided by the observer are practically equal to the values of the real state as soon as time k becomes larger than 3. The simulations summarized in the table below have been done with SCILAB.

TABLE 1. Simulation values for system (3).

k	$x_1(k) \times 10^3$	$\bar{x}_1(k) \times 10^3$	$\hat{x}_1(k) \times 10^3$
0	181.0000	160.0000	160.0000
1	195.0483	204.4220	196.8801
2	192.2349	202.3581	192.0978
3	192.6023	210.1368	192.6010
4	192.4746	221.8007	192.4745
10	189.0404	990.8104	189.0404
15	152.3006	1471.1720	152.3006
17	99.0640	1473.7021	99.0640
19	27.1224	1473.9699	27.1224
20	6.5337	1473.9912	6.5337
21	0.6299	1473.9981	0.6299
24	0.0000	1474.0014	0.0000

Now we briefly recall the definition of an *observer* in control theory. Suppose that the dynamical evolution of some phenomena is modelled by the following system:

$$\begin{cases} \mathbf{x}(\mathbf{k} + 1) = \mathbf{G}(\mathbf{x}(\mathbf{k}), \mathbf{u}(\mathbf{k})) \\ \mathbf{y}(\mathbf{k}) = \mathcal{O}(\mathbf{x}(\mathbf{k}), \mathbf{u}(\mathbf{k})) \end{cases} \quad (4)$$

where $\mathbf{x}(\mathbf{k}) \in \mathbb{R}^n$ is the state of the system at time k , and $\mathbf{u}(\mathbf{k}) \in U \subset \mathbb{R}^m$ is the input or the control. We usually do not have access to the whole state: we can observe or measure only a part (or some function) of the actual state of the system. Therefore we introduce another variable, $\mathbf{y}(\mathbf{k}) \in \mathbb{R}^q$, which is called the measurable output of the system. For instance, the state of the fishery model (1) is given by the number of fish in each class, the control is the fishing effort E or the fishing mortality $q_i E$, and the measurable output corresponds to the captures. The expression of the function \mathcal{O} is given by (2).

An observer for the the system (4) is a dynamical system whose inputs are the inputs and outputs of the system (4), which produces an estimate $\hat{\mathbf{x}}(\mathbf{k})$ of the state $\mathbf{x}(\mathbf{k})$ such that the estimation error $\mathbf{x}(\mathbf{k}) - \hat{\mathbf{x}}(\mathbf{k})$ tends to zero as time k goes to infinity and must remain small if it starts small (see [23],[9]). The observer will be said to be an exponential observer if there exists $\rho < 1$ such that, for all $k \geq 0$ and if for all initial conditions $(\mathbf{x}(\mathbf{0}), \hat{\mathbf{x}}(\mathbf{0}))$, one has

$$| \hat{\mathbf{x}}(\mathbf{k}) - \mathbf{x}(\mathbf{k}) | \leq \rho^k | \hat{\mathbf{x}}(\mathbf{0}) - \mathbf{x}(\mathbf{0}) | .$$

For linear systems

$$\begin{cases} \mathbf{x}(k + 1) = \mathbf{A}\mathbf{x}(k) + \mathbf{B}\mathbf{u}(k), \\ \mathbf{y}(k) = \mathbf{C}\mathbf{x}(k), \\ \mathbf{x}(k) \in \mathbb{R}^n, \mathbf{u}(k) \in \mathbb{R}^m, \mathbf{y}(k) \in \mathbb{R}^p, \\ \mathbf{A} \text{ is a } n \times n \text{ square matrix, } \mathbf{B} \text{ is a } m \times n \text{ matrix and } \mathbf{C} \text{ is a } p \times n \text{ matrix,} \end{cases} \quad (5)$$

the observer design has been completely solved by the Luenberger observer [15] which is simply given by

$$\hat{\mathbf{x}}(\mathbf{k} + 1) = \mathbf{A}\hat{\mathbf{x}}(\mathbf{k}) + \mathbf{B}\mathbf{u}(\mathbf{k}) + \mathbf{K}(\mathbf{y}(\mathbf{k}) - \mathbf{C}\hat{\mathbf{x}}(\mathbf{k})).$$

The Luenberger observer converges; that is, $| \hat{\mathbf{x}}(\mathbf{k}) - \mathbf{x}(\mathbf{k}) |$ tends to zero exponentially if it is possible to find a matrix \mathbf{K} in such a way that the eigenvalues

of the matrix $\mathbf{A}-\mathbf{K}\mathbf{C}$ are all with modulus less than one. It has been proved that such a matrix \mathbf{K} exists if the pair (\mathbf{C}, \mathbf{A}) is observable or at least detectable. The system (5) (or the pair (\mathbf{C}, \mathbf{A})) is observable if any two distinct initial conditions produce two distinct outputs; that is, $\mathbf{x}(\mathbf{0}) \neq \bar{\mathbf{x}}(\mathbf{0}) \implies \mathbf{C}\mathbf{x}(\mathbf{k}) \neq \mathbf{C}\bar{\mathbf{x}}(\mathbf{k})$, where $\mathbf{x}(\mathbf{k})$ (respectively $\bar{\mathbf{x}}(\mathbf{k})$) is the solution of system (5) emanating from the initial condition $\mathbf{x}(\mathbf{0})$ (respectively from $\bar{\mathbf{x}}(\mathbf{0})$). This is equivalent to the following: $\mathbf{C}\mathbf{x}(\mathbf{k}) \equiv 0 \implies \mathbf{x}(\mathbf{k}) \equiv \mathbf{0}$. The pair (\mathbf{C}, \mathbf{A}) is detectable if the following holds: $\mathbf{C}\mathbf{x}(\mathbf{k}) \equiv 0 \implies \lim_{k \rightarrow +\infty} \mathbf{x}(\mathbf{k}) = \mathbf{0}$. A simple algebraic criterion allows one to check whether a pair of matrices (\mathbf{C}, \mathbf{A}) is observable. The pair (\mathbf{C}, \mathbf{A}) is observable if and only if the matrix

$$\mathbf{O}_{(\mathbf{C}, \mathbf{A})} = \begin{pmatrix} \mathbf{C} \\ \mathbf{C}\mathbf{A} \\ \mathbf{C}\mathbf{A}^2 \\ \vdots \\ \mathbf{C}\mathbf{A}^{n-1} \end{pmatrix}$$

is of rank n . In this case, we say that the system (5) or the pair (\mathbf{C}, \mathbf{A}) satisfies the Kalman rank condition for observability [23]. When the pair (\mathbf{C}, \mathbf{A}) (or the linear system (5)) is not observable (i.e., $\text{rank } \mathbf{O}_{(\mathbf{C}, \mathbf{A})} = r < n$), then there exists an invertible matrix \mathbf{P} such that $\mathbf{P}\mathbf{A}\mathbf{P}^{-1} = \begin{pmatrix} \mathbf{A}_{11} & \mathbf{0} \\ \mathbf{A}_{21} & \mathbf{A}_{22} \end{pmatrix}$, and $\mathbf{C}\mathbf{P}^{-1} = (\mathbf{C}_1 \quad \mathbf{0})$, where \mathbf{A}_{11} is a $r \times r$ matrix, \mathbf{C}_1 is a $p \times r$ matrix, and the pair $(\mathbf{C}_1, \mathbf{A}_{11})$ is observable. The pair (\mathbf{C}, \mathbf{A}) is detectable if all the eigenvalues λ_i of the matrix \mathbf{A}_{22} satisfy $|\lambda_i| < 1$.

For nonlinear systems, there is unfortunately no “universal” solution. The observer design problem for nonlinear systems is still a very active research area in control theory. Several methods have been developed for some classes of systems, especially for continuous-time systems [13, 14, 18, 12, 25, 6]. This is not an exhaustive list, because the literature on the subject is extensive (339 references in MathScinet). Some applications of nonlinear observers to continuous biological models have been done (see, for instance, [1, 6, 5]). However there are fewer results concerning nonlinear discrete-time systems. Among them, one can mention [3, 22, 17, 11, 24, 4]. Most of the available results are local (the observer converges only for small initial error) or involve the solvability of some nonlinear functional equations. Moreover these results assume that the function \mathbf{G} modeling the dynamics of the system is completely and precisely known. Here we are interested in the design of a global observer for the fishery system (1), which exhibits an additional difficulty because the recruitment function f is poorly known. Many mathematical expressions have been proposed for the stock-recruitment relationship in the literature. The widely-used recruitment functions [7, 2, 16, 20, 21] are $(\alpha, \beta$ and γ are

positive parameters) as follows:

$$\begin{aligned}
 \text{Beverton and Holt} & \quad f(x_0) = \alpha x_0 / (1 + \beta x_0) ; \\
 \text{Ricker} & \quad f(x_0) = \alpha x_0 e^{-\beta x_0} ; \\
 \text{Power function} & \quad f(x_0) = \alpha x_0^{1-\beta} ; \\
 \text{Shepherd} & \quad f(x_0) = \alpha x_0 / (1 + \beta x_0^c) , \quad (c > 0). \\
 \text{Deriso - Schnute} & \quad f(x_0) = \alpha x_0 (1 - \beta x_0)^{1/\gamma} ; \\
 \text{Saila - Lorda} & \quad f(x_0) = \alpha x_0^\gamma e^{-\beta x_0}.
 \end{aligned}$$

Here $x_0 = \sum_{i=1}^n b_i x_i$ represents the number of newborns.

Therefore, to use model (1) to estimate the stock for a given population or to use it for fisheries management, one must choose the appropriate recruitment function. This is not an easy task because criteria for making the “good” choice are not generally available. Here we shall build an estimator (observer) which is independent of the recruitment function f . The observer we built will actually work even in the case where the stock-recruitment relationship is stochastic. More precisely, the observer will give a dynamical estimate $\hat{\mathbf{x}}(\mathbf{k})$ of the state $\mathbf{x}(\mathbf{k})$ of the model (1) without using the recruitment function f . The convergence of the observer will be guaranteed if the minimal value of the fishing effort is larger than some positive constant. Previous tentatives to solve this problem have been done in [10] for $n = 3$ (three age classes) and for n age classes in [19]. However the constructions made in [10] and [19] were done with the following output $y(k) = \sum_{i=1}^n x_i(k) e^{-M_i} (1 - e^{-q_i \tau E(k)})$, which was assumed to be the number of harvested fish. Unfortunately, this is not correct. Moreover, our sufficient condition for the convergence of the observer is weaker than that of [19].

2. Stock estimation with an observer. Our aim is to propose an observer for system (1) considered with the output given by equation (2). To this end we introduce the following notations:

$$E_{min} \leq E(k) \leq E_{max} \quad \forall k \geq 0,$$

$$q_{min} \leq q_i \leq q_{max} \quad \text{for } i = 1 \dots n,$$

$$m \leq M_i \leq M \quad \text{for } i = 1 \dots n,$$

and we assume that $q_1 \neq 0$.

Now let us consider the following candidate observer:

$$\left\{ \begin{array}{l} \hat{x}_1(k+1) = \frac{M_1 + q_1\tau E(k+1)}{q_1\tau E(k+1)(1-v_1(k+1))} y(k+1) \\ \quad - \sum_{i=1}^{n-1} \frac{q_{i+1}(M_1 + q_1\tau E(k+1))(1-v_{i+1}(k+1))}{q_1(M_{i+1} + q_{i+1}\tau E(k+1))(1-v_1(k+1))} v_i(k)\hat{x}_i(k) \\ \quad - \frac{q_n(M_1 + q_1\tau E(k+1))(1-v_n(k+1))}{q_1(M_n + q_n\tau E(k+1))(1-v_1(k+1))} v_n(k)\hat{x}_n(k), \\ \hat{x}_2(k+1) = v_1(k)\hat{x}_1(k), \\ \vdots \\ \hat{x}_{n-1}(k+1) = v_{n-2}(k)\hat{x}_{n-2}(k), \\ \hat{x}_n(k+1) = v_{n-1}(k)\hat{x}_{n-1}(k) + v_n(k)\hat{x}_n(k), \end{array} \right. \quad (6)$$

where $v_i(k) = e^{-M_i - q_i\tau E(k)}$. This system can be written in a condensed form as

$$\hat{\mathbf{x}}(\mathbf{k}+1) = \mathbf{A}(\mathbf{k})\hat{\mathbf{x}}(\mathbf{k}) + y(k+1)\mathbf{F}(\mathbf{k}), \quad (7)$$

where the matrix $A(k)$ is given in the proof of Proposition 1 and

$$\mathbf{F}(\mathbf{k}) = \begin{pmatrix} \frac{M_1 + q_1\tau E(k+1)}{q_1\tau E(k+1)(1-v_1(k+1))} \\ 0 \\ \vdots \\ 0 \end{pmatrix}.$$

The main result can then be stated as follows

Proposition 1. *There exists $\eta > 0$ such that if $E_{min} > \eta$, then the system (6) is a global exponential observer for system (1).*

Proof. We have

$$\begin{aligned} y(k+1) &= \sum_{i=1}^n \frac{q_i\tau E(k+1)}{M_i + q_i\tau E(k+1)} (1-v_i(k+1))x_i(k+1) \\ &= \frac{q_1\tau E(k+1)}{M_1 + q_1\tau E(k+1)} (1-v_1(k+1))x_1(k+1) \\ &\quad + \sum_{i=2}^n \frac{q_i\tau E(k+1)}{M_i + q_i\tau E(k+1)} (1-v_i(k+1))x_i(k+1) \\ &= \frac{q_1\tau E(k+1)}{M_1 + q_1\tau E(k+1)} (1-v_1(k+1))x_1(k+1) \\ &\quad + \sum_{i=1}^{n-1} \frac{q_{i+1}\tau E(k+1)}{M_{i+1} + q_{i+1}\tau E(k+1)} (1-v_{i+1}(k+1))x_{i+1}(k+1). \end{aligned}$$

Thanks to (1), we have

$$\begin{cases} x_{i+1}(k+1) = v_i(k)x_i(k), \text{ for } i = 1, \dots, n-2, \\ \text{and } x_n(k+1) = v_{n-1}(k)x_{n-1}(k) + v_n(k)x_n(k). \end{cases}$$

Therefore,

$$\begin{aligned} y(k+1) &= \frac{q_1\tau E(k+1)}{M_1 + q_1\tau E(k+1)} (1 - v_1(k+1))x_1(k+1) \\ &\quad + \sum_{i=1}^{n-1} \frac{q_{i+1}\tau E(k+1)}{M_{i+1} + q_{i+1}\tau E(k+1)} (1 - v_{i+1}(k+1))v_i(k)x_i(k) \\ &\quad + \frac{q_n\tau E(k+1)}{M_n + q_n\tau E(k+1)} (1 - v_n(k+1))v_n(k)x_n(k). \end{aligned}$$

Let $\mathbf{e}(\mathbf{k}) = \mathbf{x}(\mathbf{k}) - \hat{\mathbf{x}}(\mathbf{k})$ be the error. Then, taking into account the dynamical equations of the system (1) and of the observer (6), we can write

$$\begin{aligned} e_1(k+1) &= x_1(k+1) - \hat{x}_1(k+1) \\ &= - \sum_{i=1}^{n-1} \frac{q_{i+1}(M_1 + q_1\tau E(k+1))(1 - v_{i+1}(k+1))}{q_1(M_{i+1} + q_{i+1}\tau E(k+1))(1 - v_1(k+1))} v_i(k)e_i(k) \\ &\quad - \frac{q_n(M_1 + q_1\tau E(k+1))(1 - v_n(k+1))}{q_1(M_n + q_n\tau E(k+1))(1 - v_1(k+1))} v_n(k)e_n(k), \end{aligned}$$

and

$$e_i(k+1) = v_{i-1}(k)x_{i-1}(k) - v_{i-1}(k)\hat{x}_{i-1}(k) = v_{i-1}(k)e_{i-1}(k) \text{ for } i = 2 \dots n-1,$$

and

$$e_n(k+1) = v_{n-1}(k)e_{n-1}(k) + v_n(k)e_n(k).$$

We denote by α_i the following functions:

$$\alpha_i(k) = - \frac{q_{i+1}(M_1 + q_1\tau E(k+1))(1 - v_{i+1}(k+1))}{q_1(M_{i+1} + q_{i+1}\tau E(k+1))(1 - v_1(k+1))} v_i(k), \text{ for } i = 1 \dots n-1$$

and

$$\alpha_n(k) = - \frac{q_n(M_1 + q_1\tau E(k+1))(1 - v_n(k+1))}{q_1(M_n + q_n\tau E(k+1))(1 - v_1(k+1))} v_n(k).$$

With these notations we can write

$$\mathbf{e}(\mathbf{k}+1) = \mathbf{A}(\mathbf{k})\mathbf{e}(\mathbf{k}), \quad (8)$$

where the time-varying matrix $\mathbf{A}(\mathbf{k})$ is defined as follows:

$$\mathbf{A}(\mathbf{k}) = \begin{pmatrix} \alpha_1(k) & \alpha_2(k) & \alpha_3(k) & \dots & \alpha_n(k) \\ v_1(k) & 0 & 0 & \dots & 0 \\ 0 & v_2(k) & 0 & \dots & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots \\ 0 & \dots & 0 & v_{n-1}(k) & v_n(k) \end{pmatrix}.$$

We shall use the following matrix norm: $\|\mathbf{A}(\mathbf{k})\|_1 = \max_j \sum_{i=1}^n |a_{ij}(k)|$. To prove that system (6) is a global exponential observer for system (1), it is sufficient to prove that $\|\mathbf{A}(\mathbf{k})\|_1 \leq \delta < 1$.

For $i = 1 \dots n$, let: $s_i(k) = \left| \frac{\alpha_i(k)}{v_i(k)} \right|$. We have

$$\text{for } i = 1 \dots n - 1, s_i(k) = \frac{M_1 q_{i+1} (1 - v_{i+1}(k+1))}{q_1 (M_{i+1} + q_{i+1} \tau E(k+1)) (1 - v_1(k+1))} + \frac{q_{i+1} q_1 \tau E(k+1) (1 - v_{i+1}(k+1))}{q_1 (M_{i+1} + q_{i+1} \tau E(k+1)) (1 - v_1(k+1))}.$$

Since $\frac{q_{i+1} q_1 \tau E(k+1)}{q_1 (M_{i+1} + q_{i+1} \tau E(k+1))} < 1$, we can write

$$s_i(k) \leq \frac{M_1 q_{i+1} (1 - v_{i+1}(k+1))}{q_1 (M_{i+1} + q_{i+1} \tau E(k+1)) (1 - v_1(k+1))} + \frac{1 - v_{i+1}(k+1)}{1 - v_1(k+1)}.$$

The map $x \mapsto \frac{1 - e^{-x}}{x}$ is decreasing; hence

$$\frac{1 - v_{i+1}(k+1)}{M_{i+1} + q_{i+1} \tau E(k+1)} = \frac{1 - e^{-M_{i+1} - q_{i+1} \tau E(k+1)}}{M_{i+1} + q_{i+1} \tau E(k+1)} \leq \frac{1 - e^{-m - q_{min} \tau E_{min}}}{m + q_{min} \tau E_{min}}.$$

So we obtain

$$s_i(k) \leq \frac{M q_{max}}{q_1} \frac{(1 - e^{-m - q_{min} \tau E_{min}})}{m + q_{min} \tau E_{min}} \frac{1}{1 - v_1(k+1)} + \frac{1 - v_{i+1}(k+1)}{1 - v_1(k+1)}.$$

Since $0 < v_{i+1}(k+1) = e^{-M_{i+1} - q_{i+1} \tau E(k+1)} \leq 1$, we have $1 - v_{i+1}(k+1) \leq 1$. Therefore, we have for $i = 1 \dots n - 1$,

$$s_i(k) \leq \frac{M q_{max}}{q_1} \frac{(1 - e^{-m - q_{min} \tau E_{min}})}{m + q_{min} \tau E_{min}} \frac{1}{1 - v_1(k+1)} + \frac{1}{1 - v_1(k+1)}.$$

The same thing can be done for $s_n(k)$, which gives

$$s_n(k) \leq \frac{M q_{max}}{q_1} \frac{(1 - e^{-m - q_{min} \tau E_{min}})}{m + q_{min} \tau E_{min}} \frac{1}{1 - v_1(k+1)} + \frac{1}{1 - v_1(k+1)}.$$

The map $x \mapsto \frac{1}{1 - e^{-x}}$ is decreasing, it follows that

$$\frac{1}{1 - v_1(k+1)} = \frac{1}{1 - e^{-M_1 - q_1 \tau E(k+1)}} \leq \frac{1}{1 - e^{-m - q_{min} \tau E_{min}}}.$$

Therefore,

$$s_i(k) \leq \frac{M q_{max}}{q_1} \frac{1}{m + q_{min} \tau E_{min}} + \frac{1}{1 - e^{-m - q_{min} \tau E_{min}}}, \forall i = 1, \dots, n.$$

And hence we have for all $i = 1 \dots n$,

$$\begin{aligned} |\alpha_i(k)| + |v_i(k)| &= s_i(k)v_i(k) + v_i(k) = (s_i(k) + 1)v_i(k) \\ &\leq \left(\frac{M q_{max}}{q_1} \frac{1}{m + q_{min} \tau E_{min}} + \frac{1}{1 - e^{-m - q_{min} \tau E_{min}}} + 1 \right) e^{-m - q_{min} \tau E_{min}}. \end{aligned}$$

Therefore $\|\mathbf{A}(\mathbf{k})\|_1 \leq \delta(E_{min})$, where

$$\delta(E_{min}) = \left(\frac{Mq_{max}}{q_1} \frac{1}{m + q_{min}\tau E_{min}} + \frac{1}{1 - e^{-m - q_{min}\tau E_{min}}} + 1 \right) e^{-m - q_{min}\tau E_{min}}.$$

We will show now that there exists $\eta > 0$ in such a way that $E_{min} > \eta$ implies $\delta(E_{min}) < 1$.

Let $X = e^{-m - q_{min}\tau E_{min}}$ and consider $P(X) = -\frac{Mq_{max}X}{q_1 \text{Log}(X)} + \frac{X}{1 - X} + X - 1$. One can remark that $P(X) = \delta(E_{min}) - 1$.

We have $\lim_{X \rightarrow 0} P(X) = -1$ and $\lim_{X \rightarrow 1} P(X) = +\infty$. So, there exists $x_1 \in]0, 1[$ such that $P(x_1) = 0$. Let $x^* = \inf\{x \in]0, 1[/ P(x) = 0\}$; then, we have $P(X) < 0$ for all X satisfying $0 < X < x^*$. Now, $0 < X < x^*$ is equivalent to $E_{min} > \frac{-\text{Log}(x^*) - m}{q_{min}\tau}$ since $X = e^{-m - q_{min}\tau E_{min}}$. It is then sufficient to choose $\eta = \frac{-\text{Log}(x^*) - m}{q_{min}\tau}$, and this completes the proof of Proposition 1. \square

Remark 1. When the natural mortality rates are all equal, it is possible to give a weaker condition on the minimal value of the fishing effort that ensures the convergence of the observer.

Proposition 2. Assume that $q_1 \leq q_i \forall i = 2, \dots, n$, and moreover that the natural mortality coefficient is the same for all stages, that is, $M_1 = M_2 = \dots = M_n = m$. Then, the system (6) is a global exponential observer for the system (1) if

$$E_{min} > \frac{1}{q_1\tau} \left(\text{Log} \left[\frac{q_{max}}{q_1} + 1 \right] - m \right).$$

Proof. We have

$$\begin{aligned} |\alpha_i(k)| + |v_i(k)| &= \left(\frac{q_{i+1} \left(M_1 + q_1\tau E(k+1) \right) \left(1 - e^{-M_{i+1} - q_{i+1}\tau E(k+1)} \right)}{q_1 \left(M_{i+1} + q_{i+1}\tau E(k+1) \right) \left(1 - e^{-M_1 - q_1\tau E(k+1)} \right)} + 1 \right) e^{-M_i - q_i\tau E(k)} \\ &= \left(\frac{q_{i+1} \left(m + q_1\tau E(k+1) \right) \left(1 - e^{-m - q_{i+1}\tau E(k+1)} \right)}{q_1 \left(m + q_{i+1}\tau E(k+1) \right) \left(1 - e^{-m - q_1\tau E(k+1)} \right)} + 1 \right) e^{-m - q_i\tau E(k)} \\ &= \left(\frac{q_{i+1} \frac{1 - e^{-m - q_{i+1}\tau E(k+1)}}{m + q_{i+1}\tau E(k+1)}}{q_1 \frac{1 - e^{-m - q_1\tau E(k+1)}}{m + q_1\tau E(k+1)}} + 1 \right) e^{-m - q_i\tau E(k)}. \end{aligned}$$

Since $q_1 \leq q_i$, we have

$$m + q_1\tau E(k+1) \leq m + q_{i+1}\tau E(k+1),$$

and using the fact that the map $x \mapsto \frac{1}{1 - e^{-x}}$ is decreasing, we get

$$\frac{1 - e^{-m - q_{i+1}\tau E(k+1)}}{m + q_{i+1}\tau E(k+1)} \leq \frac{1 - e^{-m - q_1\tau E(k+1)}}{m + q_1\tau E(k+1)}.$$

Thus, $|\alpha_i(k)| + |v_i(k)| \leq \left(\frac{q_{i+1}}{q_1} + 1\right) e^{-m - q_i \tau E(k)} \leq \left(\frac{q_{i+1}}{q_1} + 1\right) e^{-m - q_1 \tau E(k)}$. It follows that

$$\|\mathbf{A}(\mathbf{k})\|_1 \leq \left(\frac{q_{i+1}}{q_1} + 1\right) e^{-m - q_1 \tau E(k)}.$$

And hence, $\|\mathbf{A}(\mathbf{k})\|_1 < 1$ if $E_{min} > \frac{1}{q_1 \tau} \left(\text{Log} \left[\frac{q_{max}}{q_1} + 1\right] - m\right)$. □

Remark 2. When it is possible to have the number of harvested individuals from the first class ($i = 1$) (i.e., when the output

$$y_1(k) = \frac{q_1 \tau E(k)}{q_1 \tau E(k) + M_1} \left(1 - e^{-M_1 - q_1 \tau E(k)}\right) x_1(k)$$

is available for measurement), then the construction of the observer is simpler and does not involve any condition on the fishing effort except that it does not vanish during the harvesting season. The dynamical equation of the observer in this case is given by the following:

$$\left\{ \begin{array}{l} \hat{x}_1(k+1) = \frac{q_1 \tau E(k+1) + M_1}{q_1 \tau E(k+1)(1 - v_1(k+1))} y_1(k+1) \\ \hat{x}_2(k+1) = v_1(k) \hat{x}_1(k) \\ \vdots \\ \hat{x}_n(k+1) = v_{n-1}(k) \hat{x}_{n-1}(k) + v_n(k) \hat{x}_n(k) \end{array} \right. \quad (9)$$

Remark 3. In general, the fishery’s literature provides the fishing mortality rates instead of the catchability parameters. On the other hand the available catch data usually gives the total weight of the fish caught during a season. Therefore, we will consider that the measurable output is the seasonal biomass yield (i.e., the total weight of harvested fishes over each period $[k, k + 1)$) instead of their number. If we denote by w_i the mean weight of individuals of class i , then the seasonal biomass yield is

$$Y(k) = \sum_{i=1}^n \frac{q_i \tau E(k)}{M_i + q_i \tau E(k)} (1 - e^{-M_i - q_i \tau E(k)}) w_i x_i(k). \quad (10)$$

Let $\varphi_i(k) = q_i \tau E(k)$ be the fishing mortality rate of class i , then we can write:

$$Y(k) = \sum_{i=1}^n \frac{\varphi_i(k)}{M_i + \varphi_i(k)} (1 - e^{-M_i - \varphi_i(k)}) w_i x_i(k).$$

With these notations and defining $v_i(k) = e^{-M_i - \varphi_i(k)}$, an observer for system (1) whose output is the seasonal biomass yield $Y(k)$ can be written as

$$\left\{ \begin{array}{l} \hat{x}_1(k+1) = \frac{Y(k+1)(M_1 + \varphi_1(k+1))}{\varphi_1(k+1)(1 - v_1(k+1))w_1} \\ - \sum_{i=1}^{n-1} \frac{\varphi_{i+1}(k+1)(M_1 + \varphi_1(k+1))(1 - v_{i+1}(k+1))v_i(k)w_i \hat{x}_i(k)}{\varphi_1(k+1)(M_{i+1} + \varphi_{i+1}(k+1))(1 - v_1(k+1))w_1} \\ \frac{\varphi_n(k+1)(M_1 + \varphi_1(k+1))(1 - v_n(k+1))v_n(k)w_n \hat{x}_n(k)}{\varphi_1(k+1)(M_n + \varphi_n(k+1))(1 - v_1(k+1))w_1}, \\ \hat{x}_2(k+1) = v_1(k)\hat{x}_1(k), \\ \vdots \\ \hat{x}_{n-1}(k+1) = v_{n-2}(k)\hat{x}_{n-2}(k), \\ \hat{x}_n(k+1) = v_{n-1}(k)\hat{x}_{n-1}(k) + v_n(k)\hat{x}_n(k). \end{array} \right. \quad (11)$$

3. Numerical examples.

3.1. An oscillating system. To illustrate the efficiency of the observer, we give a simulation that shows the observer works well even if the system (1) does not have a stable steady state. To this end we consider a three-age-class system with a Ricker stock-recruitment function $f(x_0) = x_0 e^{-\beta x_0}$, with $x_0 = \sum_{i=1}^3 b_i x_i$. We use the following parameters:

Ricker function parameters	$\alpha = 1, \beta = 0.003,$
Fecundity parameters	$b = [15 \ 20 \ 20],$
Catchability coefficients	$q = [0.24 \ 0.36 \ 0.42],$
Natural mortality rates	$M = [0.2 \ 0.2 \ 0.2],$
Length of harvesting season	$\tau = 2/3,$
Fishing effort	$E(k) = 8.33 + e^{-t}.$

With these parameters the model exhibits oscillations. The simulations have been done with Scilab. The time evolutions of the state variables x_1, x_2 and x_3 , as well as their estimates \hat{x}_1, \hat{x}_2 and \hat{x}_3 , are drawn in Figures 1, 2, and 3. It can be seen that the convergence of the estimate variable \hat{x}_i to the real state x_i is quite fast.

3.2. An example with a stable equilibrium. We now consider the system (1) with the Beverton-Holt stock-recruitment function $\alpha x_0 / (1 + \beta x_0)$ associated to the following parameters:

Beverton-Holt function parameters	$\alpha = 1, \beta = 0.0002,$
Fecundity parameters	$b = [8 \ 10 \ 10],$
Catchability coefficients	$q = [0.24 \ 0.36 \ 0.42],$
Natural mortality rates	$M = [0.2 \ 0.2 \ 0.2],$
Length of harvesting season	$\tau = 2/3,$
Fishing effort	$E = 8.$

The corresponding three-dimensional dynamical system has a globally asymptotically stable steady state whose coordinates are (4527, 1030, 135). Once again the estimates \hat{x}_1 , \hat{x}_2 and \hat{x}_3 delivered by the observer converge rapidly to the real states x_1 , x_2 and x_3 , as seen in Figures 4, 5, and 6.

4. Conclusion. An observer for a standard age-structured model has been presented and explicitly constructed. This observer is simple to use and to implement. It allows one to obtain a dynamical estimate of the state of the stock by using as the only available data the values of the captures. This means that if one can measure the output $y(k)$ (here, it is the total catch), then the observer will give an estimation of the number of individuals by age classes $x_1(k), \dots, x_n(k)$ that are not measurable in practice or are at least difficult or expensive (acoustic methods for example) to measure. A good estimate of the stock is important, at least for establishing management policies. The observer's convergence is quite fast. It has the advantage of not using the stock-recruitment function.

The estimator developed in this paper can not be used directly for prediction when we do not know the analytical expression of the recruitment function f , because it uses the output at time $k + 1$; that is, to calculate the estimate $\hat{x}(k + 1)$, the observer needs the value of the output at the same time $k + 1$. However, the estimator can indirectly help in prediction when the expression of the recruitment function and the map $k \mapsto E(k)$ are available in the following way. When the observer allows recovery of a good estimate $\hat{\mathbf{x}}(\mathbf{k}_0)$ (with the desired precision) of the real unknown state $\mathbf{x}(\mathbf{k}_0)$ and then model (1) can be used for prediction for $k \geq k_0$ by taking $\hat{\mathbf{x}}(\mathbf{k}_0)$ as an initial condition (for instance in example (3.2)), one can take $k_0 = 4$, since for this value of time the values of $\mathbf{x}(\mathbf{k}_0)$ and $\hat{\mathbf{x}}(\mathbf{k}_0)$ are practically equal. In practice we do not have the values of $\mathbf{x}(\mathbf{k})$, and so we can not compare with the values delivered by the observer in order to determine the value k_0 of time for which we have $|\mathbf{x}(\mathbf{k}_0) - \hat{\mathbf{x}}(\mathbf{k}_0)| < \epsilon$, where ϵ is the desired precision. To determine k_0 , it is sufficient to simulate the observer with different initial conditions, and then k_0 is the first time for which the different curves coincide. We have done this for example (3.2). Figure 7 gives the time evolution of the third coordinate \hat{x}_3 corresponding to three different initial conditions for the observer dynamical system (6). This shows that one can take $k_0 = 4$, and the same conclusion can be derived from the curves corresponding to the two other components \hat{x}_1 and \hat{x}_2 .

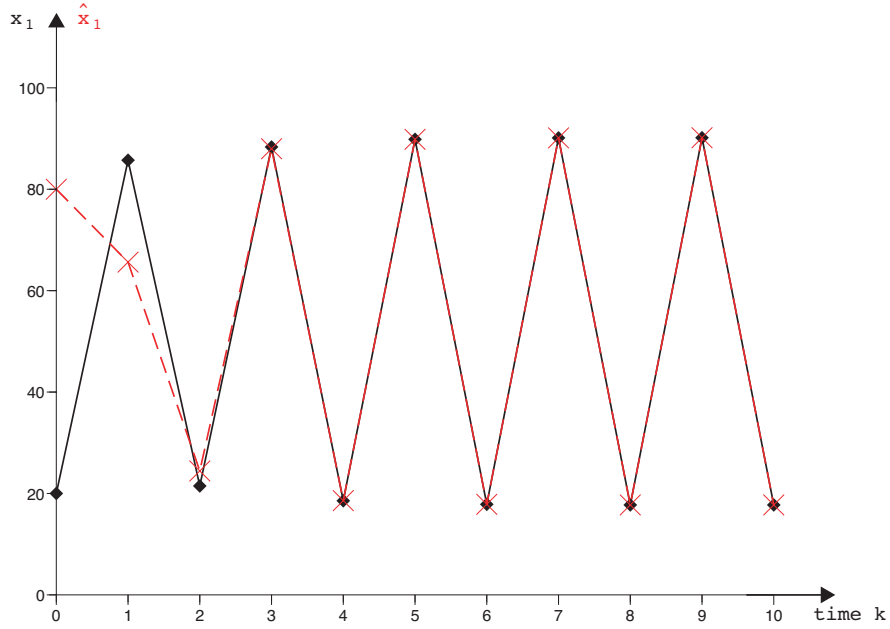
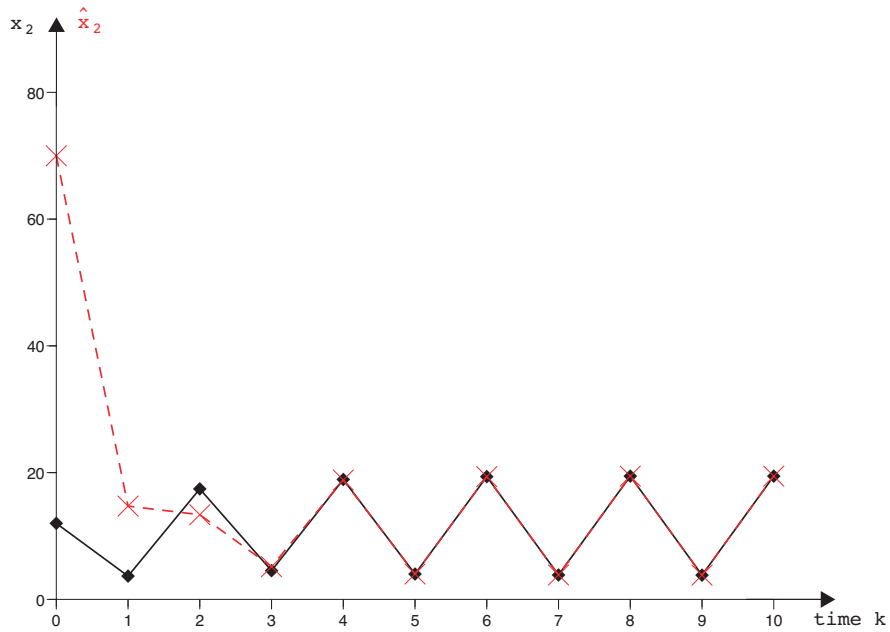
The condition on the fishing effort that allows the convergence of the observer can be weakened and the convergence can be made faster if we add a corrective term to the observer dynamics (6) as follows: the output (2) can be written in a matrix form $y(k) = \mathbf{C}(\mathbf{k})\mathbf{x}(\mathbf{k})$ where the time varying matrix $\mathbf{C}(\mathbf{k})$ depends on $E(k)$; the new candidate observer is then

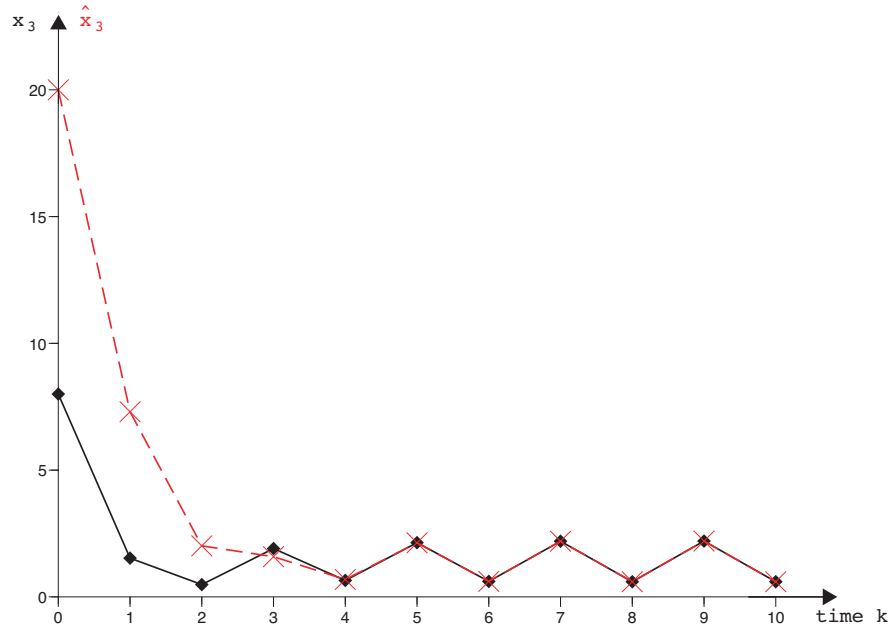
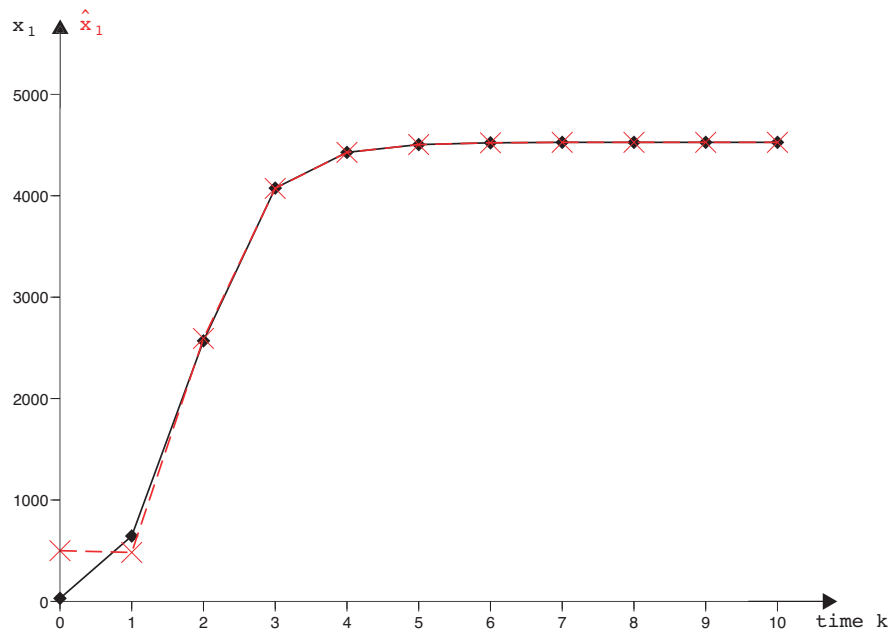
$$\hat{\mathbf{x}}(\mathbf{k} + 1) = \mathbf{A}(\mathbf{k})\hat{\mathbf{x}}(\mathbf{k}) + y(k + 1)\mathbf{F}(\mathbf{k}) + \mathbf{L}(\mathbf{k})(y(k) - \mathbf{C}(\mathbf{k})\hat{\mathbf{x}}(\mathbf{k})),$$

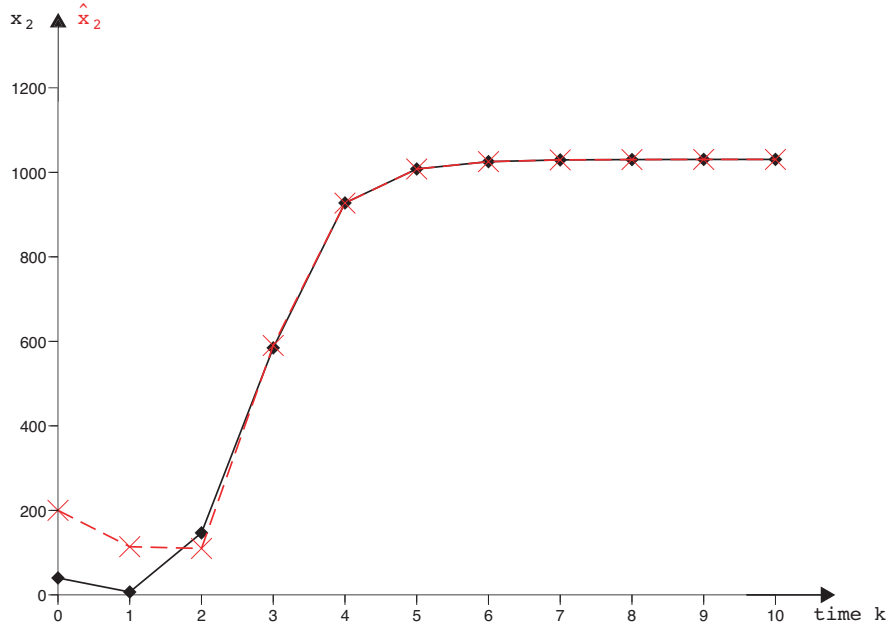
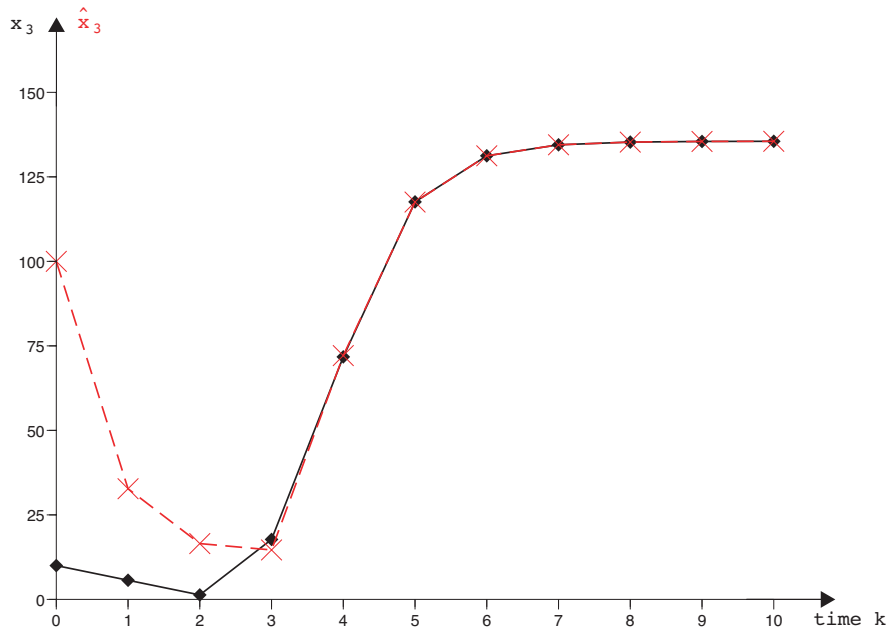
where the matrix $\mathbf{L}(\mathbf{k})$ has to be computed. A work in this direction is in progress.

Optimal control theory has been widely used in renewable resource management. The present work indicates that the estimation problem can be investigated from the point of view of control engineering.

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FIGURE 1. x_1 (solid line) and its estimate \hat{x}_1 (dashed line)FIGURE 2. x_2 (solid line) and its estimate \hat{x}_2 (dashed line)

FIGURE 3. x_3 (solid line) and its estimate \hat{x}_3 (dashed line)FIGURE 4. x_1 (solid line) and its estimate \hat{x}_1 (dashed line)

FIGURE 5. x_2 (solid line) and its estimate \hat{x}_2 (dashed line)FIGURE 6. x_3 (solid line) and its estimate \hat{x}_3 (dashed line)

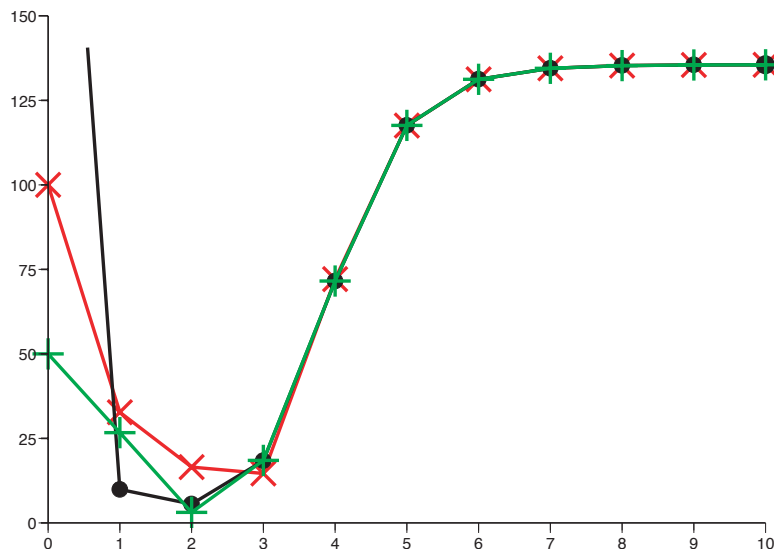


FIGURE 7. Time evolution of \hat{x}_3 corresponding to different initial conditions for the observer.

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On the stock estimation for some fishery systems

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Abstract

In this work we address the stock estimation problem for two fishery models. We show that a tool from nonlinear control theory called "observer" can be helpful to deal with the resource stock estimation in the field of renewable resource management. It is often difficult or expensive to measure all the state variables characterising the evolution of a given population system, therefore the question arises whether from the observation of certain indicators of the considered system, the whole state of the population system can be recovered or at least estimated. The goal of this paper is to show how some techniques of control theory can be applied for the approximate estimation of the unmeasurable state variables using only the observed data together with the dynamical model describing the evolution of the system. More precisely we shall consider two fishery models and we shall show how to build for each model an auxiliary dynamical system (the observer) that uses the available data (the total of caught fish) and which produces a dynamical estimation $\hat{x}(t)$ of the unmeasurable stock state $x(t)$. Moreover the convergence speed of $\hat{x}(t)$ towards $x(t)$ can be chosen.

Keywords: Fishery models, Stage-structured population models, Estimation, Harvested Fish Population, Observers.

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1 Introduction and a short survey of *observers design*

The stock estimation is one of the most important problem in fishery science. One can quote J.A. Gulland [17]: *A major emphasis in fishery science has been on the problems of estimating current and past level using catch levels and fishing effort data.*

To make a policy decision about the exploitation of renewable resources, it is necessary to take into account the state of the resource stocks. This implies the need of a good estimate of the available resource. Mathematical models are more and more used to describe the evolution of biological systems. Here, we consider two mathematical models for fishery resources. The first one is a "stage structured" model [43, 44] that describes the dynamics of a population divided in stage-classes (according to age, length or weight) and submitted to the fishing action. The second model is a "global" model that describes the evolution of a fish population that can move between an area where it can be harvested and a reserve area where no fishing is allowed [9]. Both models are given by systems of differential equations of the form

$$\dot{x} = f(x, E), \tag{1}$$

where E is the fishing effort (it can be seen as a control or an input) and $x(t)$ is the state of the system at time t . The state variable $x(t)$ represents the density of the population or the number of individuals by stage. For both models, the state $x(t)$ is not available for measurement. In practice, the only available information at time t is the value of the captures: this means that one can measure the total catch at each time t . The value of the captures can be seen as the measurable output of system (1). The output is in general a function of the state variable and the input, that is, $y(t) = h(x(t), E)$.

Now assuming that (1) is a "good" model of the system under consideration, if it is possible to have the value of the state at some time t_0 then it is possible to compute $x(t)$ for all $t \geq t_0$ by integrating the differential equation with the initial condition $x(t_0)$. Unfortunately, it is often not possible to measure the whole state at a given time and therefore it is not possible to integrate the differential equation because one does not know an initial condition. One can only have a partial information of the state and this partial information is precisely given by $y(t)$ the output of the system. Therefore we shall show how to use this partial information $y(t)$ together with the given model in order to have a dynamical estimate $\hat{x}(t)$ of the real unknown state variable $x(t)$. This estimate will be produced by an auxiliary dynamical system which uses the information $y(t)$ provided by the system (1). This dynamical system is generally of the form

$$\dot{\hat{x}} = g(\hat{x}, E, y). \tag{2}$$

It can be represented by Schema 1 The estimate error is given by $e(t) = \hat{x}(t) - x(t)$ and it satisfies the following "error equation"

$$\dot{e} = g(\hat{x}, E, y) - f(x, E) \tag{3}$$

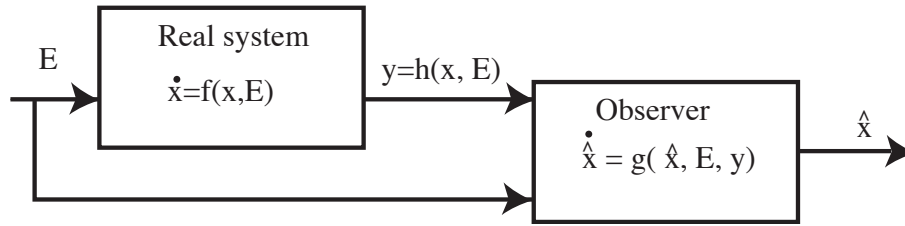


Figure 1: A schematic representation of an observer

39 The function g has to be determined in such a way that the solutions of (1) and (2)
 40 satisfy $x(t) - \hat{x}(t) \rightarrow 0$ as $t \rightarrow +\infty$ regardless of the respective initial conditions of
 41 system (1) and system (2).

42 A dynamical system (2) satisfying this conditions is called an "observer" for sys-
 43 tem (1). When the convergence of $\hat{x}(t)$ towards $x(t)$ is exponential, the system (2) is
 44 an "exponential observer". More precisely, system (2) is an exponential observer for
 45 system (1) if there exists $\lambda > 0$ such that, for all $t \geq 0$ and for all initial conditions
 46 $(x(0), \hat{x}(0))$, the corresponding solutions of (1) and (2) satisfy

$$\|\hat{x}(t) - x(t)\| \leq \exp(-\lambda t) \|\hat{x}(0) - x(0)\|.$$

47 In this situation a good estimate of the real unmeasured state is rapidly obtained.
 48 One must notice that we need not care about the choice of the initial condition of the
 49 observer since the convergence of $\hat{x}(t)$ towards the real state $x(t)$ does not depend
 50 on this choice.

51 When the system under consideration is a linear system, i.e., it can be written as
 52 follows

$$\begin{cases} \dot{x}(t) = Ax(t) + Bu(t), \\ y(t) = Cx(t), \\ x(t) \in \mathbb{R}^n, u(t) \in U \subset \mathbb{R}^m, y(t) \in \mathbb{R}^q, \\ A, B, \text{ and } C \text{ are respectively } n \times n, n \times m \text{ and } q \times n \text{ matrices,} \end{cases} \quad (4)$$

53 then an exponential observer (called *Luenberger Observer*)[30] for this system is
 54 given by

$$\dot{\hat{x}}(t) = A\hat{x}(t) + Bu(t) + K(y(t) - C\hat{x}(t)) \quad (5)$$

55 where the $n \times q$ matrix K has to be computed. The Luenberger observer converges,
 56 i.e., $|\hat{x}(k) - x(k)|$ tends to zero exponentially fast if it is possible to find a matrix K
 57 in such a way that the eigenvalues of the matrix $A - KC$ are all with negative real
 58 part. It has been proved that such a matrix K exists if the pair (C, A) is observable.

59 The pair (C, A) is observable if and only if the matrix:

$$O_{(C,A)} = \begin{pmatrix} C \\ CA \\ CA^2 \\ \vdots \\ CA^{n-1} \end{pmatrix}$$

60 is of rank n . In this case we say that the system (4), or the pair (C, A) , satisfies the
61 Kalman rank condition for observability (one can see for more details and examples
62 [39] or [20]).

63 The construction of observers for highly nonlinear systems is still a very active
64 research area in Control Theory. Several methods have been developed for some
65 classes of systems (one can see for instance the references [30, 27, 28, 26, 47, 13] that
66 represent different approaches). This is not an exhaustive list, because the literature
67 on the subject is very extensive. This active research has resulted in the emergence
68 of many nonlinear observer design techniques. The most classical one is based on
69 the "feedback linearization" and the observer normal form (see for instance [6], [22],
70 [27], [46]) Roughly speaking, this method consists in finding change of coordinates
71 $x = \kappa(z)$, $u = \zeta(E)$, $y = \eta(w)$ in the state space as well as in the input space and in
72 the output space in such a way that equation (1) is transformed into

$$\begin{cases} \dot{x} = Ax + \chi(w, u), \\ w = Cx. \end{cases} \quad (6)$$

73 In this case a Luenberger type observer can be easily constructed. However the
74 conditions under which the appropriate changes of coordinates exist are restrictive.
75 These changes of coordinates often exist only locally and hence the derived observer
76 design works only locally.

77 The second famous method is the high gain construction ([41],[7],[13],[14], [15], [21],
78 [4]). A short survey is given in [4]. This method is developed hereafter and will be
79 used in this paper.

80 Another design method uses an on-line optimization approach ([24] , [2], [33], [34],
81 [47]) such as moving horizon observers that use the integral output prediction error
82 in the estimation process, and the observer using Newtons method. In this case,
83 the state is estimated by minimizing a certain norm of the difference between the
84 ob- server output and the measured output. The advantage of the online optimiza-
85 tion method is the capability of dealing with a variety of nonlinear systems includ-
86 ing time-varying systems, chaotic systems, and systems with unknown parameters.
87 Moreover this method does not require the use of any canonical form. However, the
88 corresponding observer computations are generally quite heavy and may prevent the
89 use of these observers for systems with very fast dynamics.

90 Historically observability theory and observers design have been developed for arti-
91 ficial engineering systems but nowadays they are more and more applied to "natural

92 systems". We outline here some applications of nonlinear observers to biological
93 models. Once again the list is not exhaustive.

94 In [5] the well-known Droop model which describes the growth of a population
95 of phytoplanktonic cells is considered. Observers for this model are built and are
96 used to discuss the validity of this model by comparing the prediction of the state
97 computed by the observer with direct measurements of this state.

98 In [10], observers are used to estimate the kinetic rates in bioreactors. The efficiency
99 of the observer design is illustrated with examples dealing with the microbial growth
100 and biosynthesis reactions.

101 A robust nonlinear asymptotic observer with adjustable convergence rate has been
102 proposed in [1]. This observer has been applied to a model of an anaerobic digestion
103 process used for wastewater treatment.

104 The authors of [29] consider a system of populations described by the classical Lotka-
105 Volterra model with one predator and two preys. The only available information is
106 the total quantity of population preys without distinction between them. An ob-
107 server is constructed that allows to estimate all the state variables. It is also shown
108 how the observer can be used for the estimation of the level of an abiotic effect on
109 the population system. It must be, however, noticed that the proposed observer in
110 [29] is a local observer, i.e., its convergence is guaranteed only if the initial estimate
111 error is small.

112 A high gain observer is used in [42] to study a system describing a one-gene regulation
113 circuit. The observer is used to rebuild the non-measured concentrations of the
114 mRNA and the protein.

115 The use of observer theory in fishery is scarce, we have done some works in this
116 sense (see [35], [16]). In [35], an observer has been constructed for a stage structured
117 discrete-time fishery model that exhibits an unknown recruitment function. In [16],
118 a stage structured continuous model is considered and it is assumed that only the
119 last class (mature individuals) is harvested. The present work is a continuation and
120 a generalization of [16].

121 The goal of this paper is twofold. First we shall show that some tools from control
122 theory are helpful to address the stock estimation problem for an exploited fish
123 population. More precisely we shall built exponential observers for the two models
124 under consideration. These observers will allow to give an estimate of the respective
125 stocks. The second is to show that the application of mathematical tools to biological
126 systems has to be done carefully. One of the most efficient way to build an observer
127 for a nonlinear system has been given in [13]. We briefly recall the method developed
128 in [13]. To simplify matters we consider systems without control. Roughly speaking,
129 the result of [13] concerns systems that can be written (possibly after a coordinates

130 change):

$$\left\{ \begin{array}{l} \dot{z}(t) = \underbrace{\begin{pmatrix} 0 & 1 & 0 & \dots & 0 \\ 0 & 0 & 1 & \dots & 0 \\ \cdot & \cdot & \cdot & \cdot & \cdot \\ 0 & 0 & \dots & 0 & 1 \\ 0 & 0 & \dots & 0 & 0 \end{pmatrix}}_A z(t) + \begin{pmatrix} 0 \\ 0 \\ \vdots \\ 0 \\ \psi(z(t)) \end{pmatrix} = X(z(t)) \\ y(t) = z_1(t) = \underbrace{(1, 0, \dots, 0)}_C z(t). \end{array} \right. \quad (7)$$

131 The state of the system at time t is $z(t) = (z_1(t), z_2(t), \dots, z_n(t)) \in \mathbb{R}^n$, and its
 132 measurable output is $y(t)$. The fact that $y(t) = z_1(t)$ means that one can measure
 133 only the first component of the state and hence the other components are not avail-
 134 able for measurement. Assume that the function ψ is globally Lipschitz on \mathbb{R}^n , that
 135 is, there exists $K > 0$ such that $|\psi(z) - \psi(x)| \leq K|z - x|$ for all $(z, x) \in \mathbb{R}^n \times \mathbb{R}^n$.
 136 It has then been proved in [13] that for $\theta \geq 1$ large enough, an exponential observer
 137 (a *Luenberger type observer*) for the system (7) is given by the following dynamical
 138 system:

$$\dot{\hat{z}} = X(\hat{z}) - S_\theta^{-1} C^T (C \hat{z} - y), \quad (8)$$

139 with S_θ being the solution of

$$\theta S_\theta + A^T S_\theta + S_\theta A = C^T C.$$

140 System (8) is an exponential observer for system (7) means that the solutions of
 141 (8) converge to the solutions of system (7) with an exponential speed regardless the
 142 values of the respective initial conditions $z(0)$ and $\hat{z}(0)$. To prove this result the
 143 authors of [13] use the fact that the function ψ is globally Lipschitz on the **whole**
 144 state space \mathbb{R}^n . The global Lipschitz assumption is very restrictive. Biological
 145 systems always evolve in a bounded domain \mathcal{D} of \mathbb{R}^n and hence the global Lipschitz
 146 assumption is satisfied on \mathcal{D} . However, it must be noticed that the fact that the
 147 domain \mathcal{D} is positively invariant for system (7) and that the map ψ is globally
 148 Lipschitz on \mathcal{D} does not guarantee the convergence of the observer (8) even if one
 149 take the initial values inside \mathcal{D} . Indeed, the domain \mathcal{D} is positively invariant for the
 150 system (7) but it is **not** a positively invariant set for the system (8) defining the
 151 equations of the observer. More precisely, for a given initial condition $(z(0), \hat{z}(0)) \in$
 152 $\mathcal{D} \times \mathcal{D}$, the corresponding solution $(z(t), \hat{z}(t))$ of (7-8) can leave the set $\mathcal{D} \times \mathcal{D}$ in
 153 finite time: the component $z(t)$ will actually belong to \mathcal{D} for all positive time but
 154 there is no reason that the same property will be true for $\hat{z}(t)$. In order to built
 155 an exponential observer for the considered system in this situation, one has first to
 156 extend the function ψ from \mathcal{D} to the whole \mathbb{R}^n by a function $\tilde{\psi}$ which is globally
 157 Lipschitz on \mathbb{R}^n and then to consider the systems (7-8) defined on $\mathbb{R}^n \times \mathbb{R}^n$ after
 158 replacing the function ψ by its prolongation $\tilde{\psi}$. The stage-structured fishery model
 159 we consider here will illustrate this fact. For this model, there is a domain $\mathcal{D} \subset \mathbb{R}^3$
 160 which is positively invariant, and the system dynamics are defined by a vector field
 161 X which is globally Lipschitz on \mathcal{D} . We shall show that the observer works well

162 when we extend the vector field X to the whole space \mathbb{R}^3 and it fails to work
 163 when the prolongation is not done. The same things are valid for the global model.
 164 This shows that the Lipschitz extension of the vector field mentioned in [13] is not
 165 only for mathematical sophistication purpose but it is also necessary for application
 166 purpose. Here we construct simply a continuous Lipschitz extension of the function
 167 ψ . For more details concerning the design of Lipschitz extensions one can see for
 168 instance [38].

169 The paper is organized as follows. In Section 2, we present the stage-structured
 170 model and we built an observer for this system. The construction is made for a three
 171 stages model. It can be done for an arbitrary number of stages but the calculus are
 172 longer and more complicated. Section 3 is devoted to the stock estimation problem
 173 for a "global" model. Once again, for clarity reasons, we have preferred to deal
 174 with a model with two fishing areas but the observer construction can be done for a
 175 system describing the dynamics of a fish population that can move between different
 176 fishing zones (an example of such a system has been considered in [32]).

177 2 A Stage-structured model

178 In this section, we consider a class of a structured model in fishery with three classes.
 179 The first class x_0 is constitute of the pre-recruits i.e the eggs, larvae and the juveniles.
 180 The second and the third classes are the post-recruits or the exploited phase of the
 181 population.

182 The dynamics of the system are modeled by the following three dimensional system
 183 (see [43, 44], [36]) :

$$\begin{cases} \dot{x}_0(t) = -\alpha_0 x_0(t) + \sum_{i=1}^2 f_i l_i x_i(t) - \sum_{i=1}^2 p_i x_i(t) x_0(t) - p_0 x_0^2(t) \\ \dot{x}_1(t) = \alpha x_0(t) - (\alpha_1 + q_1 E) x_1(t) \\ \dot{x}_2(t) = \alpha x_1(t) - (\alpha_2 + q_2 E) x_2(t) \end{cases} \quad (9)$$

184 where :

- 185 x_i : the number of fish in the stage i .
- 186 α : linear aging coefficient (in time⁻¹)
- 187 m_i : natural mortality rate of class i (in time⁻¹)
- 188 $\alpha_i = m_i + \alpha$ (in time⁻¹)
- 189 p_0 : juvenile competition parameter (in time⁻¹.number⁻¹)
- 190 f_i : fecundity rate of class i (no dimension)
- 191 l_i : reproduction efficiency of class i (in time⁻¹)
- 192 p_i : predation rate of class i on class 0 (time⁻¹.num⁻¹)
- 193 q_i : capturability coefficient of class i (in unit effort⁻¹)
- 194 E : instantaneous fishing effort. (in unit effort \times time⁻¹).

195 We assume that the total catch is available for measurement. This total catch can

196 be considered as a measurable output of the system(9) and it is given by

$$y(t) = q_1 E x_1(t) + q_2 E x_2(t) \quad (10)$$

197 We then obtain the following coupled system:

$$\begin{cases} \dot{x}_0(t) = -\alpha_0 x_0(t) + \sum_{i=1}^2 f_i l_i x_i(t) - \sum_{i=1}^2 p_i x_i(t) x_0(t) - p_0 x_0^2(t) \\ \dot{x}_1(t) = \alpha x_0(t) - (\alpha_1 + q_1 E) x_1(t) \\ \dot{x}_2(t) = \alpha x_1(t) - (\alpha_2 + q_2 E) x_2(t) \\ y(t) = q_1 E x_1(t) + q_2 E x_2(t) \end{cases} \quad (11)$$

198 We consider system (11) which is a nonlinear system. Our aim is to construct an
199 observer (estimator) i.e an auxiliary system which will give a dynamical estimate
200 $(\hat{x}_0(t), \hat{x}_1(t), \hat{x}_2(t))$ of the state $(x_0(t), x_1(t), x_2(t))$ of system (9). For the construction
201 of such auxiliary system, we shall use a method called High Gain construction (see
202 for instance [13]). This construction provide an exponential observer; the estimation
203 error will converges to zero with exponential speed, i.e.,

$$\|\hat{x}(t) - x(t)\| \leq \exp(-\lambda t) \|\hat{x}(0) - x(0)\|.$$

204 2.1 High Gain observer design for (11)

205 The system (11) is the system (9) coupled with the output (10). For the observer
206 design, we will use the High Gain observer techniques (Gauthier et al.([13])) to
207 construct a High Gain observer for system (9).

208 It has been proved in [43] that there is a positively invariant compact set for sys-
209 tem (9). This set is of the form $D = [a_0, b_0] \times [a_1, b_1] \times [a_2, b_2]$, where the numbers a_i
210 can be chosen as small as we need and the numbers b_i are function of the parameters
211 f_i, l_i and p_i . More precisely:

$$\begin{aligned} b_i &= \pi_i \mu \\ \text{with } \pi_i &= \frac{\alpha^i}{\prod_{j=1}^i (\alpha_j + q_j E)}, \\ \text{and } \mu &= \min_{i:p_i \neq 0} \left\{ \frac{f_i l_i}{p_i} \right\} \end{aligned}$$

212 Let us denote by F the vector field defining the dynamics of the system (9), and h
213 the output function, that is $y(t) = h(x(t)) = q_1 E x_1(t) + q_2 E x_2(t)$ and

$$214 \quad F(x(t)) = \begin{pmatrix} -\alpha_0 x_0(t) + \sum_{i=1}^2 f_i l_i x_i(t) - \sum_{i=1}^2 p_i x_i(t) x_0(t) - p_0 x_0^2(t) \\ \alpha x_0(t) - (\alpha_1 + q_1 E) x_1(t) \\ \alpha x_1(t) - (\alpha_2 + q_2 E) x_2(t) \end{pmatrix}$$

215 Let Φ be the function $\Phi : \overset{\circ}{D} \rightarrow \mathbb{R}^3$ ($\overset{\circ}{D}$ is the interior of D), defined as follows:

216 $\Phi(x) = \begin{pmatrix} h(x) \\ L_F h(x) \\ L_F^2 h(x) \end{pmatrix}$, where L denotes the Lie derivative operator with respect to
 217 the vector field F . Thus,

$$\Phi(x) = E \begin{pmatrix} q_1 x_1 + q_2 x_2 \\ \alpha q_1 x_0 + \left(\alpha q_2 - q_1(\alpha_1 + q_1 E) \right) x_1 - q_2(\alpha_2 + q_2 E) x_2 \\ \left(-\alpha_0 \alpha q_1 + \alpha^2 q_2 - \alpha q_1(\alpha_1 + q_1 E) \right) x_0 \\ + \left(\alpha q_1 f_1 l_1 - \alpha q_2(\alpha_1 + q_1 E) + q_1(\alpha_1 + q_1 E)^2 - \alpha q_2(\alpha_2 + q_2 E) \right) x_1 \\ + \left(\alpha q_1 f_2 l_2 + q_2(\alpha_2 + q_2 E)^2 \right) x_2 \\ - \alpha q_1 p_0 x_0^2 - \alpha q_1 p_1 x_1 x_0 - \alpha q_1 p_2 x_2 x_0 \end{pmatrix}$$

218 The Jacobian of Φ can be written:

$$\frac{d\Phi}{dx} = \begin{pmatrix} 0 & q_1 E & q_2 E \\ \alpha q_1 E & \gamma_1 & \gamma_2 \\ \gamma_3 & \gamma_4 & \gamma_5 \end{pmatrix},$$

and

$$\left[\frac{d\Phi}{dx} \right]^{-1} = \frac{1}{\Gamma} \begin{pmatrix} \beta_1 & \beta_2 & \beta_3 \\ \beta_4 & \beta_5 & \beta_6 \\ \beta_7 & \beta_8 & \beta_9 \end{pmatrix},$$

219 where:

$$220 \Gamma = \text{Det} \left(\frac{d\Phi}{dx} \right) = q_1 E \gamma_2 \gamma_3 + \alpha q_1 q_2 E^2 \gamma_4 - q_2 E \gamma_1 \gamma_3 - \alpha q_1^2 E^2 \gamma_5$$

$$221 \gamma_1 = \alpha q_2 E - q_1 E(\alpha_1 + q_1 E)$$

$$222 \gamma_2 = -q_2 E(\alpha_2 + q_2 E)$$

$$223 \gamma_3 = \alpha^2 q_2 E - \alpha_0 \alpha q_1 E - \alpha q_1 E(\alpha_1 + q_1 E) - 2\alpha q_1 E p_0 x_0 - \alpha q_1 E p_1 x_1 - \alpha q_1 E p_2 x_2$$

$$224 \gamma_4 = q_1 E(\alpha_1 + q_1 E)^2 - \alpha q_2 E(\alpha_1 + q_1 E) - \alpha q_2 E(\alpha_2 + q_2 E) + \alpha q_1 f_1 l_1 E - \alpha q_1 E p_1 x_0$$

$$225 \gamma_5 = q_2 E(\alpha_2 + q_2 E)^2 + \alpha q_1 f_2 l_2 E - \alpha q_1 E p_2 x_0$$

$$226 \beta_1 = \gamma_1 \gamma_5 - \gamma_2 \gamma_4$$

$$227 \beta_2 = -q_1 E \gamma_5 + q_2 E \gamma_4$$

$$228 \beta_3 = q_1 E \gamma_2 - q_2 E \gamma_1$$

$$229 \beta_4 = -\alpha q_1 E \gamma_5 + \gamma_2 \gamma_3$$

$$230 \beta_5 = -q_2 E \gamma_3$$

$$231 \beta_6 = \alpha q_1 q_2 E^2$$

$$232 \beta_7 = \alpha q_1 E \gamma_4 - \gamma_1 \gamma_3$$

$$233 \beta_8 = q_1 E \gamma_3$$

234 $\beta_9 = -\alpha q_1^2 E^2.$

235 The determinant of $\frac{d\Phi}{dx}$ can be written

$$\Gamma(x_0, x_1, x_2) = \text{Det}\left(\frac{d\Phi}{dx}\right) = (c + a_0x_0 + a_1x_1 + a_2x_2) E^3,$$

236 where c and a_i are functions of the parameters. The map $(x_0, x_1, x_2) \mapsto \Gamma(x_0, x_1, x_2)$
 237 is affine on the polyhedron D , hence it reaches its extrema on the vertexes of D . For
 238 a given set of parameters, it is then sufficient to compute the values of $\Gamma(x_0, x_1, x_2)$
 239 on the vertexes of D in order to see if $\Gamma(x_0, x_1, x_2)$ vanishes in D or not.

240 We assume that the parameters are such that the map Φ is a diffeomorphism from
 241 $\overset{\circ}{D}$ to $\Phi(\overset{\circ}{D})$. This implies that system (11) is observable.

242 In the new coordinates defined by $(z_1, z_2, z_3)^T = z = \Phi(x) = (h(x), L_F h(x), L_F^2(x))^T$,
 243 our system can be written in the canonical form as follow:

$$\begin{cases} \dot{z}(t) = \underbrace{\begin{pmatrix} 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 0 \end{pmatrix}}_A z(t) + \begin{pmatrix} 0 \\ 0 \\ \psi(z(t)) \end{pmatrix} \\ y(t) = z_1(t) = \underbrace{(1, 0, 0)}_C z(t). \end{cases} \quad (12)$$

244 where : $\psi(z) = L_F^3 h(\Phi^{-1}(z)) = L_F^3 h(x) = \varphi(x)$

245 The function φ is smooth (it is a polynomial function of $x = (x_0, x_1, x_2)$) on the
 246 compact set D . Hence, it is globally Lipschitz on D . Therefore it can be extended
 247 by $\tilde{\varphi}$, a Lipschitz function on \mathbb{R}^3 which satisfies $\tilde{\varphi}(x) = \varphi(x)$, for all $x \in D$. In the
 248 same way we define $\tilde{\psi}$ the Lipschitz prolongation of the function ψ .

249 So we have the following system (13) defined on the whole space \mathbb{R}^3 . The restriction
 250 of (13) to the domain D is the system (12):

$$\begin{cases} \dot{z} = Az + \begin{pmatrix} 0 \\ 0 \\ \tilde{\psi}(z) \end{pmatrix}, \\ y = Cz. \end{cases} \quad (13)$$

251 Hence, we have shown that system (11) satisfies the conditions of the following result
 252 which provides the observer construction.

253 **Proposition 2.1** ([13]) *Under the assumptions that*

254 **H1:** Φ is a diffeomorphism from $\overset{\circ}{D}$ to $\Phi(\overset{\circ}{D})$. ($\overset{\circ}{D}$ is the interior of D).

255 **H2:** φ can be extended from D to \mathbb{R}^3 by a C^∞ function, globally Lipschitz on \mathbb{R}^3 .

256 Then an exponential observer for system (13) is given by the following system :

$$\dot{\hat{z}} = A\hat{z} + \psi(\hat{z}) + S^{-1}(\theta)C^T(y - C\hat{z}). \quad (14)$$

257 where $S(\theta)$ is the solution of

$$0 = -\theta S(\theta) - A^T S(\theta) - S(\theta)A^T + C^T C,$$

258 and θ is large enough.

259 Here, $S(\theta) = \begin{pmatrix} \theta^{-1} & -\theta^{-2} & \theta^{-3} \\ -\theta^{-2} & 2\theta^{-3} & -3\theta^{-4} \\ \theta^{-3} & -3\theta^{-4} & 6\theta^{-5} \end{pmatrix}.$

260 Precisely $\theta \geq 2ncK\sqrt{S}$, where K is the lipschitz coefficient of the function ψ , n is
261 the dimension of the space, and $S = \sup_{i,j} |S(1)_{i,j}|$.

262 For the proof one can see [13].

263 Going back to the our original system (9) via the transformation Φ^{-1} , we have :

$$\dot{\hat{x}} = \tilde{F}(\hat{x}) + \left[\frac{d\Phi}{dx} \right]_{x=\hat{x}}^{-1} \times S(\theta)^{-1}C^T(y - h(\hat{x})) \quad (15)$$

264 The restriction of this system to D is the following system :

$$\left\{ \begin{array}{l} \dot{\hat{x}}_0 = -\alpha_0 \hat{x}_0 + \sum_{i=1}^2 f_{il} \hat{x}_i - \sum_{i=1}^2 p_i \hat{x}_i \hat{x}_0 - p_0 \hat{x}_0^2 \\ \quad + (3\theta\beta_1 + 3\theta^2\beta_2 + \theta^3\beta_3)(y - q_1 E \hat{x}_1 - q_2 E \hat{x}_2) \\ \dot{\hat{x}}_1 = \alpha \hat{x}_0 - (\alpha_1 + q_1 E) \hat{x}_1 \\ \quad + (3\theta\beta_4 + 3\theta^2\beta_5 + \theta^3\beta_6)(y - q_1 E \hat{x}_1 - q_2 E \hat{x}_2) \\ \dot{\hat{x}}_2 = \alpha \hat{x}_1 - (\alpha_2 + q_2 E) \hat{x}_2 \\ \quad + (3\theta\beta_7 + 3\theta^2\beta_8 + \theta^3\beta_9)(y - q_1 E \hat{x}_1 - q_2 E \hat{x}_2) \end{array} \right. \quad (16)$$

265 which is the observer for the fishery model (9). This observer is particularly simple
266 since it is only a copy of (9), together with a corrective term depending on θ .

267 2.2 Simulations and comments

268 We present here some simulation results that show the efficiency of the observer of
269 system (9). The simulations have been done with the free software SCILAB.

270 **Remarque 2.1** For the simulations we extend the function φ by continuity in order
271 to make it globally lipschitz on \mathbb{R}^3 in the following way: We denote $\tilde{\varphi}$ the prolonga-
272 tion of φ to \mathbb{R}^3 and the function π the projection on the domain D and we construct
273 $\tilde{\varphi} = \varphi \circ \pi$. The extended function $\tilde{\varphi}$ has the same Lipschitz coefficient as φ . The
274 projection π is defined as follows: for $x \in \mathbb{R}^3$, $\pi(x) = \bar{x}$, where $\bar{x} \in D$ is such that
275 $\text{dist}(x, D) = \|x - \bar{x}\|$, i.e., \bar{x} satisfies $\|x - \bar{x}\| = \min_{u \in D} \|u - x\|$. The extension algorithm
276 is described in *Appendix B.*

277 We use the following fishery parameters [36], [43].

278 $\alpha_0 = 1.3; \alpha_1 = 0.9;$

279 $\alpha_2 = 0.85; p_0 = 0.2;$

280 $p_1 = 0.1; p_2 = 0.1;$

281 $q_1 = 0.07; q_2 = 0.15;$

282 $f_1 = 0.5; f_2 = 0.5;$

283 $l_1 = 10; l_2 = 10;$

284 $E = 0.5; \alpha = 0.8.$

285 For these parameter the Jacobian of the function Φ is expressed as:

286

$$\frac{d\Phi}{dx} = \begin{pmatrix} 0 & 0.035 & 0.075 \\ 0.028 & 0.027275 & -0.069375 \\ -0.01458 - 0.0112x_0 & 0.0589979 - 0.0028x_0 & 0.191338 - 0.0028x_0 \\ -0.0028x_1 - 0.0028x_2 & & \end{pmatrix}$$

The determinant of this matrix is:

$$\text{Det}\left(\frac{d\Phi}{dx}\right) = 1.612 \times 10^{-6} + 0.00004697x_0 + 0.0000125265x_1 + 0.0000125265x_2.$$

287 The states x_0, x_1 and x_2 are time varying but remain in the positive orthant; so the
 288 $\text{Det}\left(\frac{d\Phi}{dx}\right)$ does not vanish. Therefore $\frac{d\Phi}{dx}$ is invertible and then $\Phi(x)$ is a diffeomor-
 289 phism.

290 With the parameters defined in the top of this section, we compute the coor-
 291 dinates of the higher corner B of the parallelepiped D ([43]) and we get $B =$
 292 $(25; 20.639; 17.868).$

293 The nontrivial equilibrium point is $x^* = (18.572; 15.89; 13.743).$

294 The construction of the high gain observer (15) is done with $\theta = 17$. For the
 295 simulations we have taken $x(0) = [21; 20; 15]$ and $\hat{x}(0) = [35; 40; 10]$.

296 **Comments:** Using the same parameters values, when we do not use the Lipschitz
 297 prolongation of the function φ to the whole \mathbb{R}^3 , the state estimation $\hat{x}(t)$ computed
 298 by the observer tends to infinity in finite time. This actually happens in the begin-
 299 ning of the integration process as it can be seen in Figures 2, 4 and 6. When the
 300 Lipschitz prolongation of the function φ to the whole \mathbb{R}^3 is done, the convergence
 301 of the estimates delivered by the observer is quite fast (Figures 3, 5 and 7).

302 3 A global model

303 3.1 The model and the observer

304 Here we consider the dynamics of a fish population moving between two zones (see
 305 [9]). The first zone is a free fishing area, and the second zone is a reserve area

306 where no fishing is allowed. Let $x_1(t)$ be the biomass density at time t of the fish
 307 population in the free fishing area and $x_2(t)$ be the biomass density at a time t of
 308 the fish population in the reserved areas. For $(i, j) \in \{1, 2\}^2$, we denote by m_{ij}
 309 the migration rate from the zone i to the zone j . In the free fishing area, the total
 310 fishing effort is denoted by E . The growth of the two sub-population in each zone
 311 follows logistic model. The dynamics of the fish subpopulations in unreserved and
 312 reserved ares are then assumed to be governed by the following autonomous system
 313 of differential equations [9].

$$\begin{cases} \dot{x}_1 = r_1 x_1 \left(1 - \frac{x_1}{K_1}\right) - m_{12} x_1 + m_{21} x_2 - q E x_1 \\ \dot{x}_2 = r_2 x_2 \left(1 - \frac{x_2}{K_2}\right) + m_{12} x_1 - m_{21} x_2. \end{cases} \quad (17)$$

314 r_1 and r_2 represent the intrinsic growth of each fish sub-population, respectively,
 315 K_1 and K_2 are the carrying capacities of fish species in the unreserved and reserved
 316 areas, respectively; q is the catchability coefficient of fish species in the unreserved
 317 area. The parameters $r_1, r_2, q, m_{12}, m_{21}, K_1$ and K_2 are positives constants.

318 To the system (17) we associate the capture (i.e. the output) $y = q E x_1$ (the total
 319 of caught fish in the unreserved area), with this output, we show the observability
 320 condition of system (17) and construct an auxiliary system that will give a dynamical
 321 estimation of the state of system (17).

322 It is possible to find a positive real number w_0 in such a way that for any $w \geq w_0$
 323 the following compact set D_w is positively invariant for system (17). This compact
 324 set is given

$$D_w = \{(x_1, x_2) \in \mathbb{R}_+^2 : x_1 + x_2 \leq w\},$$

325 The proof of this fact as well as the computation of w_0 as a function of the parameters
 326 are given in [Appendix A.](#)

327 Let us denote by f the vector field that defines the system (17):

$$f(x) = \begin{pmatrix} r_1 x_1 \left(1 - \frac{x_1}{K_1}\right) - (m_{12} + qE)x_1 + m_{21} x_2 \\ r_2 x_2 \left(1 - \frac{x_2}{K_2}\right) + m_{12} x_1 - m_{21} x_2 \end{pmatrix}.$$

328 Let $z = \begin{pmatrix} z_1 \\ z_2 \end{pmatrix}$, $y(t) = h(x) = q E x_1(t)$ and

$$329 \quad \Phi(x) = \begin{pmatrix} y \\ \dot{y} \end{pmatrix} = \begin{pmatrix} q E x_1 \\ r_1 q E x_1 \left(1 - \frac{x_1}{K_1}\right) - (m_{12} + qE)q E x_1 + m_{21} q E x_2 \end{pmatrix}.$$

$$330 \quad \text{Therefore } \frac{d\Phi}{dx} = \begin{pmatrix} qE & 0 \\ r_1 qE - \frac{2r_1 qE x_1}{K_1} - (m_{12} + qE)qE & m_{21} qE \end{pmatrix}$$

331 and $\text{Det}\left(\frac{d\Phi}{dx}\right) = q^2 E^2 m_{21}$.

332 As the parameters q , E and m_{21} are positive ($\neq 0$), we can conclude that $\text{Det}\left(\frac{d\Phi}{dx}\right) \neq$
 333 0 , and then, Φ is a diffeomorphism from \mathbb{R}^2 to $\Phi(\mathbb{R}^2)$, thus system (17) is observable.
 334 Thanks to ([13]) the observer can be expressed as follows:

$$\dot{\hat{x}} = \tilde{f}(\hat{x}) + \left(\frac{d\Phi}{dx}\right)^{-1} \times S(\theta)^{-1} C^T (y - h(\hat{x})), \quad (18)$$

335 where \tilde{f} is a Lipschitz extension of the function f from the invariant domain D_w to
 336 the whole \mathbb{R}^2 space, $C = (1, 0)$ and

$$337 S(\theta)^{-1} = \begin{pmatrix} 2\theta & \theta^2 \\ \theta^2 & \theta^3 \end{pmatrix}, \text{ with } \theta \geq 1.$$

338 The restriction of the estimator (18) to the invariant domain D_w is given by the
 339 equations:

$$\begin{cases} \dot{\hat{x}}_1 = r_1 \hat{x}_1 \left(1 - \frac{\hat{x}_1}{K_1}\right) - m_{12} \hat{x}_1 + m_{21} \hat{x}_2 - qE \hat{x}_1 + 2\theta(x_1 - \hat{x}_1) \\ \dot{\hat{x}}_2 = r_2 \hat{x}_2 \left(1 - \frac{\hat{x}_2}{K_2}\right) + m_{12} \hat{x}_1 - m_{21} \hat{x}_2 \\ \quad + 2\theta \left(\frac{qE}{m_{21}} - \frac{1}{m_{21}} + \frac{m_{12}}{qEm_{21}} + \frac{2r_1 x_1}{m_{21}} + \frac{\theta}{m_{21}}\right) (x_1 - \hat{x}_1), \end{cases} \quad (19)$$

340 3.2 Simulation

341 Simulations for the model (17) together with its observer (18) have been done with
 342 the following parameters :

$$343 r_1 = \frac{7}{10}; r_2 = \frac{5}{10},$$

$$344 q = \frac{25}{100}, E = \frac{9}{10},$$

$$345 K_1 = 10, K_2 = \frac{22}{10},$$

$$346 m_{12} = \frac{2}{10}, m_{21} = \frac{1}{10},$$

347 Thanks to formula (20) we compute $w_0 = 8.987$ and we take $w = 20$.

348 With these parameters, the invariant domain is the triangle defined by $O(0, 0)$,
 349 $A(w, 0) = A(20, 0)$ and $B(0, w) = B(0, 20)$, and we take $\theta = 4$.

350 Using the SCILAB free software, the time evolution of the states as well as the
 351 respective estimates when the Lipschitz extension is done are drawn in Figures 8
 352 and 10. When the Lipschitz extension has not been done, the simulations are given
 353 in Figures 9 and 11.

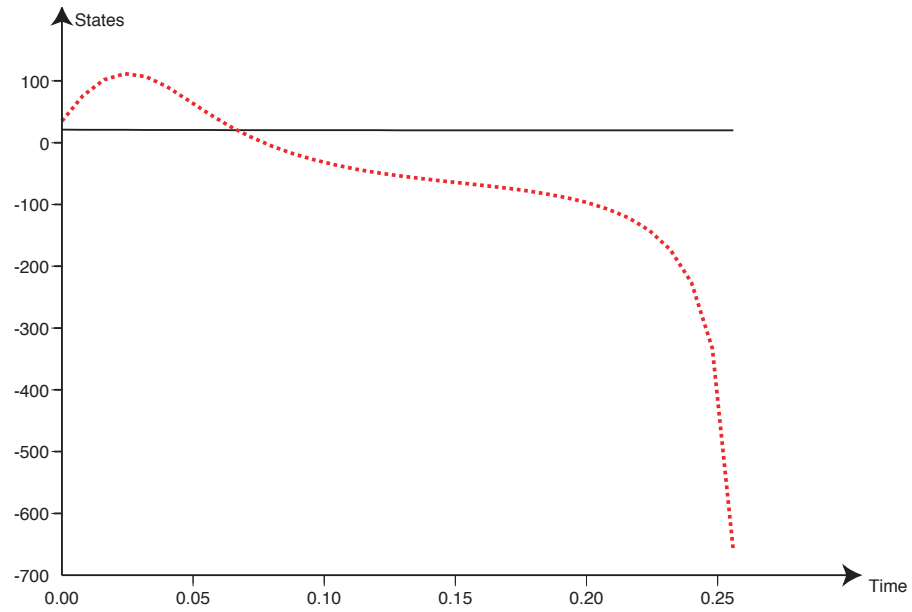


Figure 2: Simulation of system (9) with its observer (15): x_0 (solid line) and its estimate \hat{x}_0 (dashed line) when φ is not extended

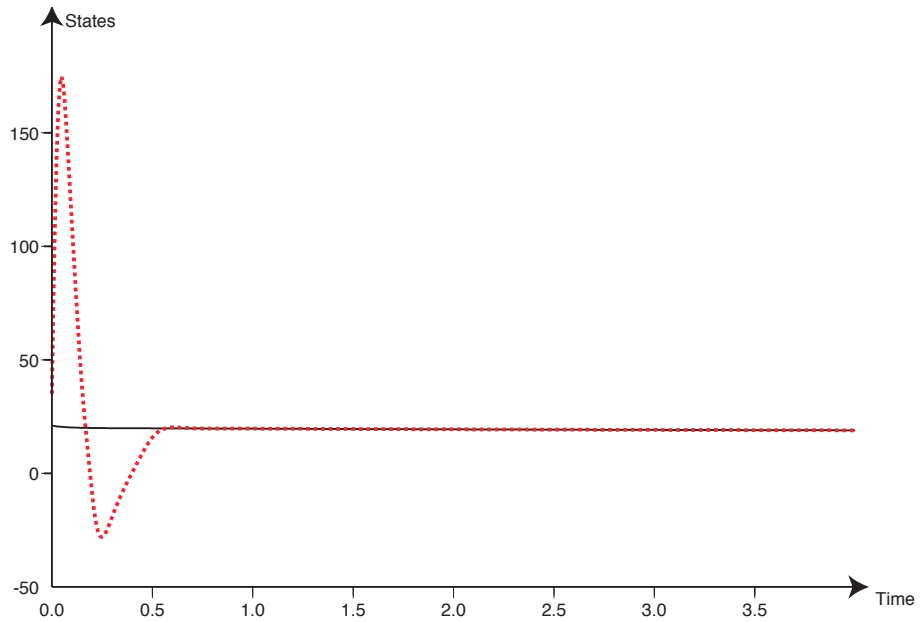


Figure 3: Simulation of system (9) with its observer (15): x_0 (solid line) and its estimate \hat{x}_0 (dashed line) when φ is extended

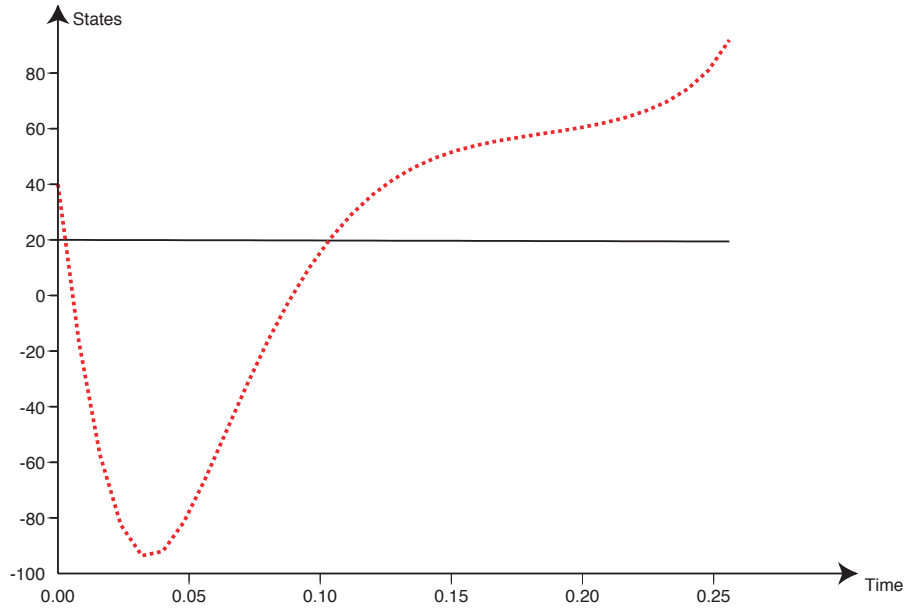


Figure 4: Simulation of system (9) with its observer (15): x_1 (solid line) and its estimate \hat{x}_1 (dashed line) when φ is not extended

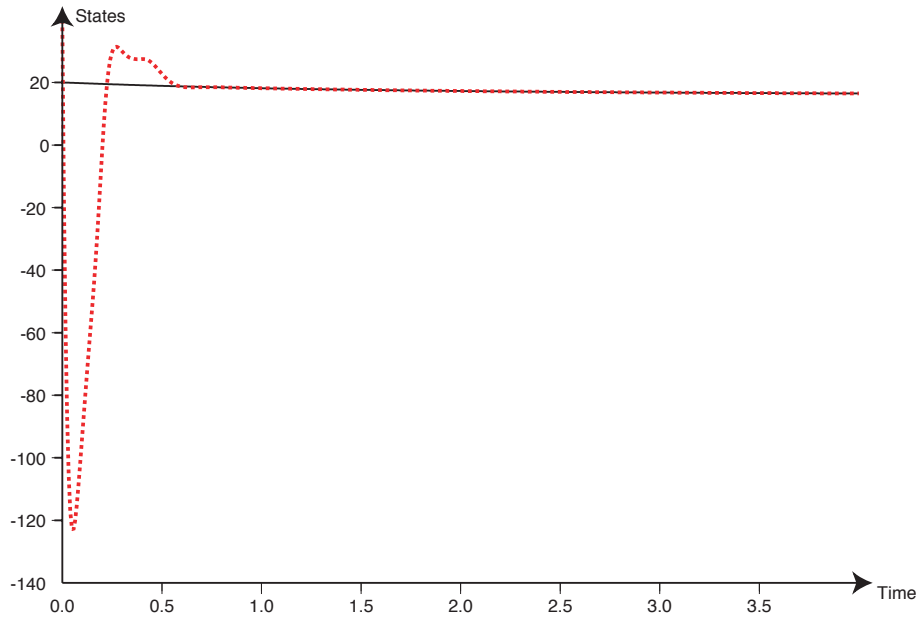


Figure 5: Simulation of system (9) with its observer (15): x_1 (solid line) and its estimate \hat{x}_1 (dashed line) when φ is extended

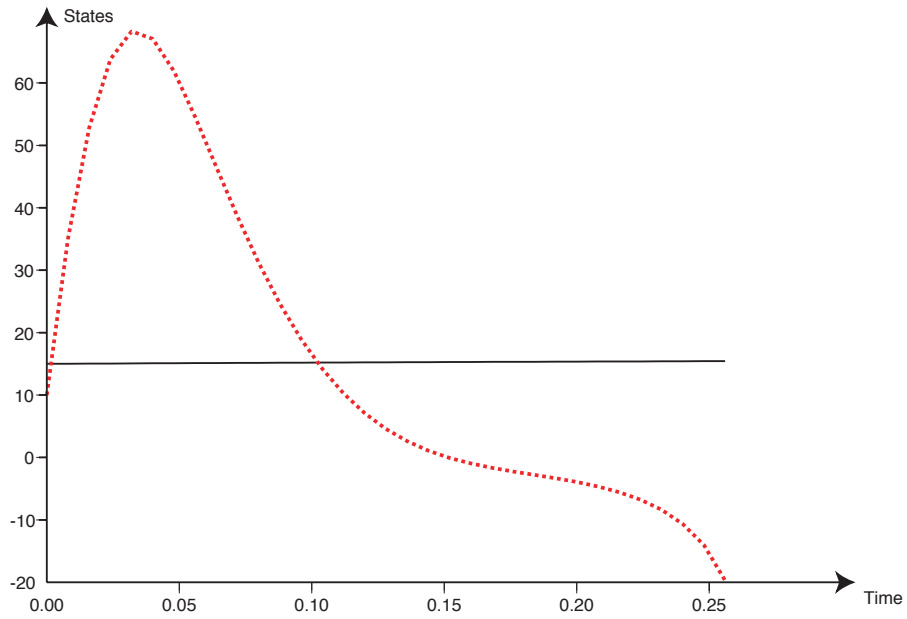


Figure 6: Simulation of system (9) with its observer (15): x_2 (solid line) and its estimate \hat{x}_2 (dashed line) when φ is not extended

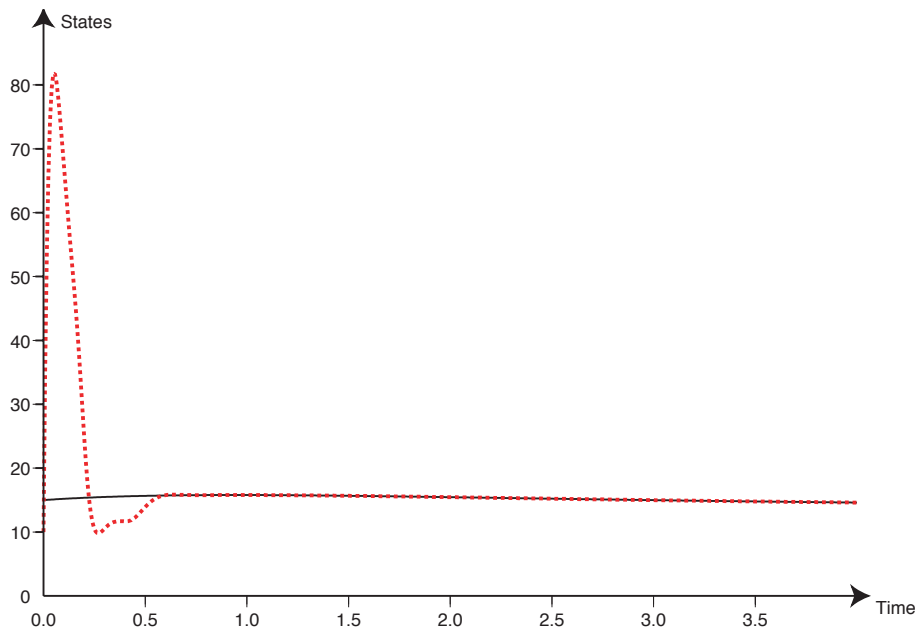


Figure 7: Simulation of system (9) with its observer (15): x_2 (solid line) and its estimate \hat{x}_2 (dashed line) when φ is extended

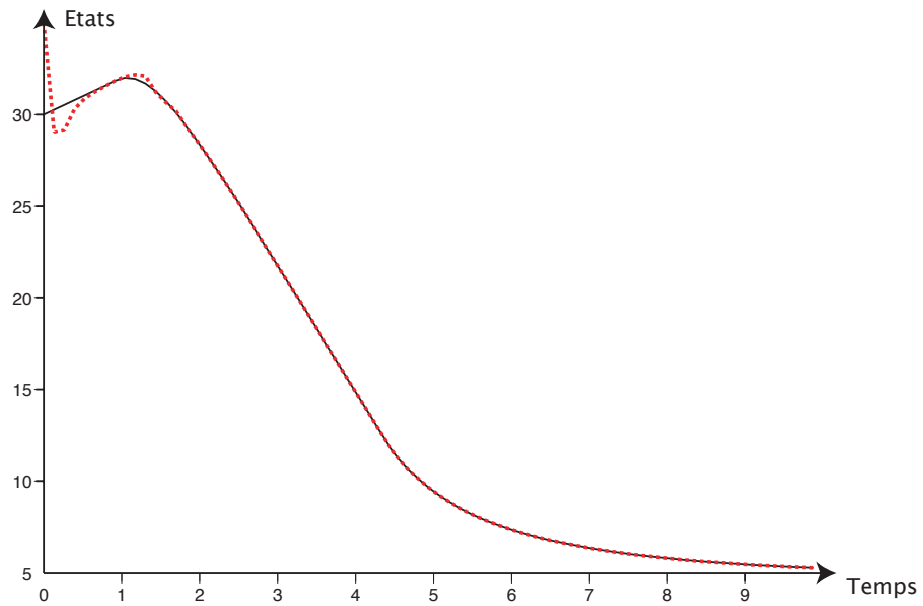


Figure 8: Simulation of system (17) with its observer (18): x_1 (solid line) and its estimate \hat{x}_1 (dashed line) when f is extended

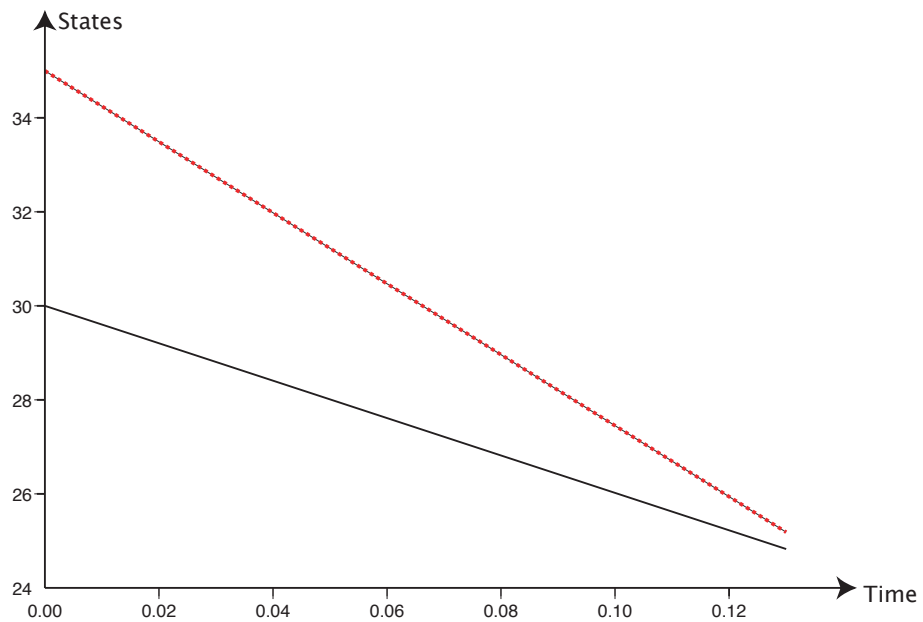


Figure 9: Simulation of system (17) with its observer (18): x_1 (solid line) and its estimate \hat{x}_1 (dashed line) when f is not extended

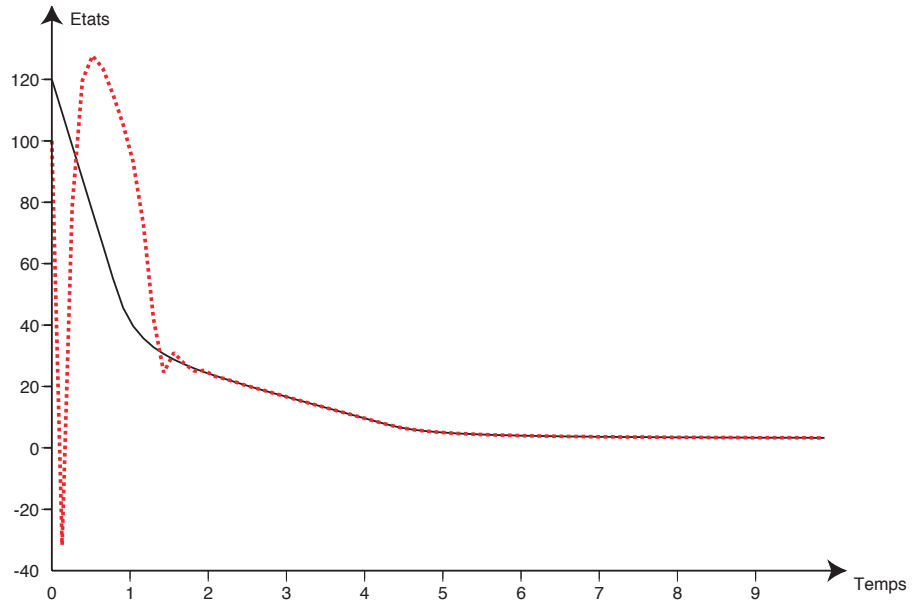


Figure 10: Simulation of system (17) with its observer (18): x_2 (solid line) and its estimate \hat{x}_2 (dashed line) when f is extended

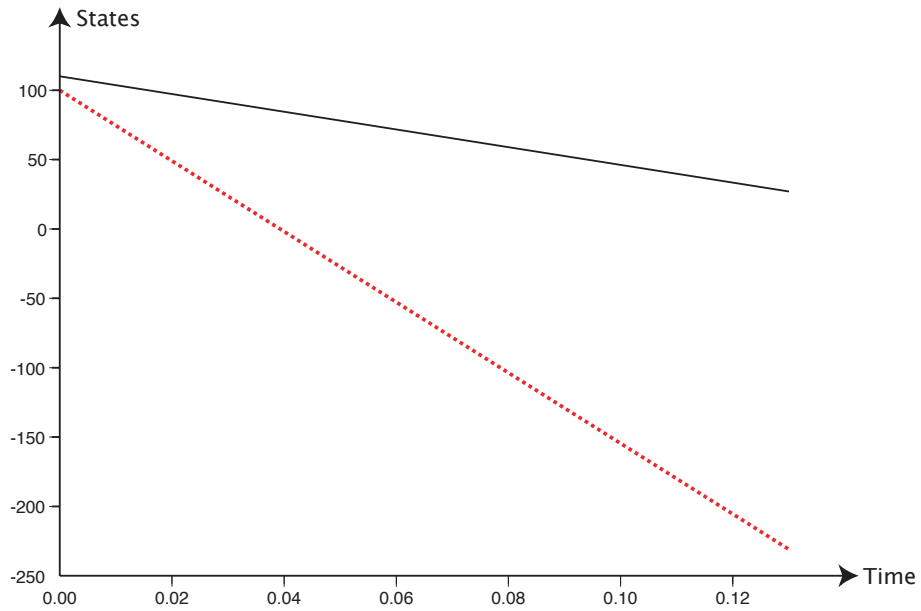


Figure 11: Simulation of system (17) with its observer (18): x_2 (solid line) and its estimate \hat{x}_2 (dashed line) when f is not extended

354 4 Conclusion

355 We have tried to combine modern Control Theory, Computer Science and Mathe-
356 matics to address the state estimation problem for systems that model the dynamics
357 of fish populations submitted to a fishing action. Indeed one of the important prob-
358 lems in fishery sciences is to estimate the state of the resource using the available
359 data, in order to produce scientific opinions that can be helpful for developing man-
360 agement policies that need to have a good estimate of the available resource.

361 In this work, we have constructed High Gain observers for some fishery models.
362 With the use of judicious value of the gain parameter θ we obtain satisfactory es-
363 timation of the real state. The observer's convergence is quite fast and does not
364 depend on the initial conditions choice. Therefore one can get a "good" estimate of
365 the unmeasurable real state very quickly. It is interesting to notice that the state
366 estimator built in this paper for the stage-structured model use only the total catch
367 to give not only an estimate of the total stock but also an estimate of the number
368 of individuals in each stage class. The classical techniques like the Cohort Analysis
369 (CA) or the Virtual Population Analysis (VPA) use the total catch for each stage-
370 class in order to give estimates of the number of individuals in each stage class.
371 In practice it is easier to measure the total catch (without doing any distinction
372 between individuals) than to measure the catch for each stage class. However the
373 observers given in this paper assume that the model is good enough and that the
374 parameters values are available.

375 Nonlinear control techniques are useful for studying and controlling complex systems.
376 Although they have been initially developed for mechanical and electrical systems
377 their applications to biological and environmental problems are growing. Tools of
378 optimal control theory have been extensively used in renewable resource management
379 ([8], [3] [23] [18] [25],[31],[45],[12],[32]). The present paper shows that the estimation
380 problem in fisheries management can also be investigated from the point of view of
381 control engineering.

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497 Appendix A. Positive invariance of D_w

498 Let $N = x_1 + x_2$.

$$499 \dot{N} = -qEx_1 + r_1 \left(1 - \frac{x_1}{K_1}\right) x_1 + (N - x_1) \left(1 - \frac{N - x_1}{K_2}\right) r_2$$

500 Let w be a positive real number, for $N = w$, we have

$$501 \dot{N} = -qEx_1 + r_1 \left(1 - \frac{x_1}{K_1}\right) x_1 + (w - x_1) \left(1 - \frac{w - x_1}{K_2}\right) r_2 = g(x_1)$$

502 The function g is defined for $0 \leq x_1 \leq w$.

$$503 g(0) = w \left(1 - \frac{w}{K_2}\right) r_2$$

$$504 g(w) = -quw + w \left(1 - \frac{w}{K_1}\right) r_1$$

$$505 g'(x_1) = r_1 - r_2 - qu + \frac{2wr_2}{K_2} - 2 \left(\frac{r_1}{K_1} + \frac{r_2}{K_2}\right) x_1$$

$$506 g'(x_1) = 0 \Leftrightarrow x_1 = \bar{x}_1 = \frac{K_1(K_2r_1 - K_2r_2 - quK_2 + 2wr_2)}{2(K_2r_1 + K_1r_2)}$$

507 The maximum value of the function g is then given by the expression

$$508 \frac{K_1K_2(qu - r_1 + r_2)^2 + (4K_2r_1r_2 + K_1(-4qur_2 + 4r_1r_2))w - 4(r_1r_2)w^2}{4(K_2r_1 + K_1r_2)}$$

509 It is therefore clear that this maximum is non positive if $w \geq w_0$ with

$$w_0 = \frac{r_1r_2(K_1 + K_2) - quK_1r_2 + \sqrt{r_2(K_2r_1 + K_1r_2)(K_1(-qu + r_1)^2 + K_2r_1r_2)}}{2r_1r_2} \quad (20)$$

510 This shows that for any real number $w \geq w_0$, the compact set

$$D_w = \{(x_1, x_2) \in \mathbb{R}_+^2 : x_1 + x_2 \leq w\}$$

511 is positively invariant for system (17).

512 Appendix B. Construction of the Lipschitz extension of φ

514 The function φ is Lipschitz on the compact set $D = [a_0, b_0] \times [a_1, b_1] \times [a_2, b_2]$. Our aim
515 is to extend it to a function $\tilde{\varphi}$ which is Lipschitz with the same Lipschitz coefficient
516 in the whole \mathbb{R}^3 .

517 Let $a(a_0, a_1, a_2)$, (respectively $b(b_0, b_1, b_2)$), the lower corner, (respectively the upper
518 corner) of the domain D and $x(x_0, x_1, x_2)$ an unspecified point of \mathbb{R}^3 .

519 The problem of the extension is set for point $x \notin D$; in this situation we have 26
520 possibilities according to the situation of x . The different situations correspond to
521 $x_i \leq a_i$, $a_i \leq x_i \leq b_i$, or $x_i \geq b_i$.

522 The principle of this prolongation is to compose the function φ with the function π
523 (the projection function of the point x on the domain D).

524 The extension of function φ is described by the following algorithm:

525 if $x_0 \leq a_0$ then

526 if $x_1 \leq a_1$ then

```

527     if  $x_2 \leq a_2$  then
528          $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(a_0, a_1, a_2)$ 
529     else
530         if  $x_2 \leq b_2$  then
531              $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(a_0, a_1, x_2)$ 
532         else
533              $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(a_0, a_1, b_2)$ 
534         end.
535     end.
536 else
537     if  $x_1 \leq b_1$  then
538         if  $x_2 \leq a_2$  then
539              $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(a_0, x_1, a_2)$ 
540         else
541             if  $x_2 \leq b_2$  then
542                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(a_0, x_1, x_2)$ 
543             else
544                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(a_0, x_1, b_2)$ 
545             end.
546         end.
547     else
548         if  $x_2 \leq a_2$  then
549              $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(a_0, b_1, a_2)$ 
550         else
551             if  $x_2 \leq b_2$  then
552                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(a_0, b_1, x_2)$ 
553             else
554                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(a_0, b_1, b_2)$ 
555             end.
556         end.
557     end.
558 end.
559 else
560     if  $x_0 \leq b_0$  then
561         if  $x_1 \leq a_1$  then
562             if  $x_2 \leq a_2$  then
563                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(x_0, a_1, a_2)$ 
564             else
565                 if  $x_2 \leq b_2$  then
566                      $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(x_0, a_1, x_2)$ 
567                 else
568                      $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(x_0, a_1, b_2)$ 
569                 end.
570             end.
571         else
572             if  $x_1 \leq b_1$  then

```



```

573         if  $x_2 \leq a_2$  then
574              $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(x_0, x_1, a_2)$ 
575         else
576             if  $x_2 \leq b_2$  then
577                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(x_0, x_1, x_2)$ 
578             else
579                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(x_0, x_1, b_2)$ 
580             end.
581         end.
582     else
583         si  $x_2 \leq b_2$  then
584              $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(x_0, b_1, x_2)$ 
585         else
586              $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(x_0, b_1, b_2)$ 
587         end.
588     end.
589 end.
590 else
591     if  $x_1 \leq a_1$  then
592         if  $x_2 \leq a_2$  then
593              $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(b_0, a_1, a_2)$ 
594         else
595             if  $x_2 \leq b_2$  then
596                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(b_0, a_1, x_2)$ 
597             else
598                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(b_0, a_1, b_2)$ 
599             end.
600         end.
601     else
602         if  $x_1 \leq b_1$  then
603             if  $x_2 \leq a_2$  then
604                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(b_0, x_1, a_2)$ 
605             else
606                 if  $x_2 \leq b_2$  then
607                      $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(b_0, x_1, x_2)$ 
608                 else
609                      $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(b_0, x_1, b_2)$ 
610                 end.
611             end.
612         else
613             if  $x_2 \leq a_2$  then
614                  $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(b_0, b_1, a_2)$ 
615             else
616                 if  $x_2 \leq b_2$  then
617                      $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(b_0, b_1, x_2)$ 
618                 else

```

```
619              $\tilde{\varphi}(x_0, x_1, x_2) = \varphi(b_0, b_1, b_2)$ 
620         end.
621     end.
622 end.
623 end.
624 end.
625 end.
```

Global analysis of new malaria intrahost models with a competitive exclusion principle.

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GLOBAL ANALYSIS OF NEW MALARIA INTRAHOST MODELS WITH A COMPETITIVE EXCLUSION PRINCIPLE*

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Abstract. In this paper we propose a malaria within-host model with k classes of age for the parasitized red blood cells and n strains for the parasite. We provide a global analysis for this model. A competitive exclusion principle holds. If \mathcal{R}_0 , the basic reproduction number, satisfies $\mathcal{R}_0 \leq 1$, then the disease-free equilibrium is globally asymptotically stable. On the contrary if $\mathcal{R}_0 > 1$, then generically there is a unique endemic equilibrium which corresponds to the endemic stabilization of the most virulent parasite strain and to the extinction of all the other parasites strains. We prove that this equilibrium is globally asymptotically stable on the positive orthant if a mild sufficient condition is satisfied.

Key words. nonlinear dynamical systems, intrahost models, global stability, *Plasmodium falciparum*, competitive exclusion principle

AMS subject classifications. 34A34, 34D23, 34D40, 92D30

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1. Introduction. In this paper we consider intrahost models for malaria. These models describe the interaction of a parasite, namely a protozoa *Plasmodium falciparum*, with its target cells, the red blood cells (RBC). During the past decade there has been considerable work on the mathematical modeling of *Plasmodium falciparum* infection [2, 14, 21, 22, 24, 23, 25, 28, 30, 52, 55, 56, 58, 64]. A review has been done by Molineaux and Dietz in [59].

We give a brief review of the features of malaria. Malaria in a human begins with an inoculum of *Plasmodium* parasites (sporozoites) from a female *Anopheles* mosquito. The sporozoites enter the liver within minutes. After a period of asexual reproduction in the liver the parasites (merozoites) are released in the bloodstream where the asexual erythrocyte cycle begins. The merozoites enter RBC, grow, and reproduce over a period of approximately 48 hours after which the erythrocyte ruptures releasing 8–32 “merozoites” daughter parasites that quickly invade a fresh erythrocyte to renew the cycle. This blood cycle can be repeated many times, in the course of which some of the merozoites instead develop in the sexual form of the parasites: gametocytes. Gametocytes are benign for the host and are waiting for the mosquitoes.

The first mathematical model of the erythrocyte cycle was proposed by Anderson, May, and Gupta [3]. This original model has been extended in different directions [2, 3, 21, 25, 28, 30, 64].

The original model [3] is given by the following system:

$$(1.1) \quad \begin{cases} \dot{x} = \Lambda - \mu_x x - \beta x m, \\ \dot{y} = \beta x m - \mu_y y, \\ \dot{m} = r \mu_y y - \mu_m m - \beta x m. \end{cases}$$

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The state variables are denoted by x , y , and m . The variable x denotes the concentration of uninfected RBC, y the concentration of parasitized red blood cells (PRBC), and m the concentration of the free merozoites in the blood.

We briefly sketch the interpretation of the parameters. Parameters μ_x , μ_y , and μ_m are the death rates of the RBC, PRBC, and free merozoites, respectively. The parameter β is the contact rate between RBC and merozoites. Uninfected blood cells are recruited at a constant rate Λ from the bone marrow and have a natural life-expectancy of $\frac{1}{\mu_x}$ days. Death of a PRBC results in the release of an average number of r merozoites. Free merozoites die or successfully invade a RBC.

This system is isomorphic to numerous systems considered in the mathematical modeling of virus dynamics; see [60, 61, 62] and the references therein. Some authors ignore the loss term $-\beta x m$ that should appear in the m equation. Indeed without this loss term, merozoites can infect RBC without themselves being absorbed, and this allows one merozoite to infect more than one RBC.

The original and the derived malaria models were intended to explain observations, namely parasitaemia, i.e., the concentration y of PRBC and also the decrease of the healthy RBC leading to anaemia. An important characteristic of *Plasmodium falciparum*, the most virulent malaria parasite, is sequestration. At the halfway point of parasite development, the infected erythrocyte leaves the circulating peripheral blood and binds to the endothelium in the microvasculature of various organs where the cycle is completed. A measurement of *Plasmodium falciparum* parasitaemia taken from a blood smear therefore samples young parasites only. Physician treating malaria use the number of parasites in peripheral blood smears as a measure of infection, and this does not give the total parasite burden of the patient. In some respects this is a weak point of the model (1.1). Moreover antimalarial drugs are known to act preferentially on different stages of parasite development. These facts lead some authors to give a general approach to modeling the age structure of *Plasmodium* parasites [22, 23, 24, 57]. Their model is a linear catenary compartmental model. This model is based on a finite number of compartments, each representing a stage of development of the parasite inside the PRBC. The models describe only the dynamics of the morphological stage evolution of the parasites and make no allowance for the dynamics of the healthy RBC.

In this paper we propose a model which combines the advantages of the two approaches. We also consider this model with different strains for the parasites. To encompass the different models of the literature we allow, in this model, to ignore or not the loss term in the m equation. To begin we consider the model with one strain:

$$(1.2) \quad \begin{cases} \dot{x} = f(x) - \mu_x x - \beta x m, \\ \dot{y}_1 = \beta x m - \alpha_1 y_1, \\ \dot{y}_2 = \gamma_1 y_1 - \alpha_2 y_2, \\ \dots \\ \dot{y}_k = \gamma_{k-1} y_{k-1} - \alpha_k y_k, \\ \dot{m} = r \gamma_k y_k - \mu_m m - u \beta x m. \end{cases}$$

In this system $f(x) - \mu_x x$ is the density-dependent growth rate of RBC. The other parameters are positive. In the model of Gravenor et al. [21] $\alpha_i = \gamma_i + \mu_i$, and hence $\alpha_i > \gamma_i$. We do not need this requirement, which implies that our model is not necessarily a catenary compartmental model. In the literature the parameter u takes the values $u = 0$ when the loss of the merozoite when it enters a RBC is ignored or takes $u = 1$ when this loss is not ignored. In our analysis u is simply a nonnegative

parameter. Except for these generalizations this system has already been suggested by Gravenor and Lloyd [21] in their reply to the criticism of Saul [64]. We provide a global analysis of this system related to the basic reproduction ratio \mathcal{R}_0 of the considered model.

One problem is how to decide upon the number of parasite compartments in the model. A starting point can be the morphological appearance of the parasite. But if the objective is to reflect the distribution of cycle lengths, the number of compartment can be increased to obtain a gamma distribution. Finally the two approaches can be combined: some compartments are for morphological reasons and others are for behavioral reasons. Then this model can also be interpreted as the application of the method of stages (or the linear chain trick) to the life cycle of PRBC [3, 31, 47, 49, 48, 51]. In other words a chain of compartments is included to generate a distribution of lags. It is also possible to add a class y_{k+1} in order to allow for the production of gametocytes. Different numbers of stages, ranging from 5 to 48, are used in [20, 22, 23, 24].

It is well grounded that a *falciparum* infection consists of distinct parasite genotypes. The model of Anderson, May, and Gupta has been extended in this direction [25, 66]. With regard to such features we propose a model with k stages for the infected RBC, production of gametocytes, and n genotypes, in the population of parasites.

One of the important principles of theoretical ecology is the competitive exclusion principle which states that no two species can indefinitely occupy the same ecological niche [7, 8, 11, 17, 25, 39, 53, 54]. We provide a global analysis of this model and obtain a generic competitive exclusion result within one host individual. This confirms the simulation results obtained in [25]. We compute the basic reproduction ratio \mathcal{R}_0 of the model. For this model there is always a disease-free equilibrium (DFE). To put it more precisely this equilibrium corresponds to the extinction of all the parasites, including the free parasites and the intraerythrocyte parasites. We prove that if $\mathcal{R}_0 \leq 1$, then the DFE is globally asymptotically stable (GAS); in other words the parasites are cleared. If $\mathcal{R}_0 > 1$, then, generically, a unique endemic equilibrium exists corresponding to the extinction of all the strains of parasites but one. We prove that this equilibrium is GAS on the positive orthant under a mild condition. For example this condition is automatically satisfied when $u = 0$ and $f(x) = \Lambda - \mu_x x$. When $u \neq 0$ the criteria, obtained for deciding the winning strain, differs from other results in the literature. To each i -strain can be associated a basic reproduction number \mathcal{R}_0^i and a threshold \mathcal{T}_0^i . It turns out, when $u \neq 0$, that this is precisely this threshold \mathcal{T}_0^i which distinguishes the fate of the strain and not \mathcal{R}_0^i at the difference of [7, 11].

The paper is organized as follows. In section 2 we introduce the model with k stages for the infected RBC and one parasite strain, with and without gametocyte production. We compute the basic reproduction number and provide a stability analysis.

In section 3 we consider the model of Anderson, May, and Gupta with n distinct genotypes and production of gametocytes. This model with a constant recruitment function for the erythrocytes, two strains, and one class of age has been proposed in [25]. We have studied this model in [1]. Here using the computation of section 2, we prove for the general n strain k class of age model that if $\mathcal{R}_0 \leq 1$, then the parasites are cleared and if $\mathcal{R}_0 > 1$, then generically the different genotypes cannot coexist. Namely a unique equilibrium exists, for which only one genotype is positive, and which is GAS on a dense subset of the nonnegative orthant. This result confirms the simulations given in [25].

Global results of stability for the DFE as well for the endemic equilibrium for epidemic models are not so common [26, 27, 33, 43, 65, 67, 68]. Global stability

results for the endemic equilibrium have often been obtained by using monotone system techniques [29, 36]. Usually the Poincaré–Bendixson property of monotone systems in dimension 3 is used [40, 41, 42, 43, 44, 45]. Our results generalize the results of [13].

2. Stability analysis of a one strain model with k stages. We consider a general class of systems. The haemopoiesis is a complex system. In the cited references the recruitment of RBC is given by $\Lambda - \mu_x x$. In this paper we will use a more general function $\varphi(x)$. In a more complex system the haemopoiesis could be an input coming from another system:

$$(2.1) \quad \begin{cases} \dot{x} = f(x) - \mu_x x - \beta x m = \varphi(x) - \beta x m, \\ \dot{y}_1 = \beta x m - \alpha_1 y_1, \\ \dot{y}_2 = \gamma_1 y_1 - \alpha_2 y_2, \\ \dots \\ \dot{y}_k = \gamma_{k-1} y_{k-1} - \alpha_k y_k, \\ \dot{m} = r \gamma_k y_k - \mu_m m - u \beta x m. \end{cases}$$

We denote by y the column vector $(y_1, \dots, y_k)^T$. The parameter u is nonnegative. The reason for this parameter is to encompass some malaria models in which the term $-\beta x m$ can appear or not. In [2] Anderson has considered a system without the $-\beta x m$ in the \dot{m} equation. In [60] all the basic models of virus dynamics are also without this term. One feature of *Plasmodium falciparum*, responsible for the deadly case of malaria, is that more than one parasite can invade RBC. In this case u is the mean number of parasites invading RBC and thus disappearing from the circulating blood.

Some authors [25, 56] have included in the model production of gametocytes. In the course of the production of merozoites from bursting erythrocytes, some invading merozoites develop into the sexual, nonreplicating transmission stages known as gametocytes. The gametocytes are benign and transmissible to mosquitoes. We can also, following these authors, include a production of gametocytes in our model. If we denote by y_{k+1} the “concentration of gametocytes,” the model becomes

$$(2.2) \quad \begin{cases} \dot{x} = f(x) - \mu_x x - \beta x m = \varphi(x) - \beta x m, \\ \dot{y}_1 = \beta x m - \alpha_1 y_1, \\ \dot{y}_2 = \gamma_1 y_1 - \alpha_2 y_2, \\ \dots \\ \dot{y}_k = \gamma_{k-1} y_{k-1} - \alpha_k y_k, \\ \dot{y}_{k+1} = \rho \gamma_k y_k - \alpha_{k+1} y_{k+1}, \\ \dot{m} = r \gamma_k y_k - \mu_m m - u \beta x m. \end{cases}$$

We start to analyze the system with minimal hypothesis on f but nevertheless plausible from the biological point of view. The function f gives the production of erythrocytes from the bone marrow. The function $\varphi(x) = f(x) - \mu_x x$ models the population dynamic of RBC in the absence of parasites. The RBC have a finite lifetime, and then μ_x represents the average per capita death rate of RBC. The function f models in some way homeostasis. In this paper we suppose that f depends only on x . It could be assumed that the recruitment function depends on x and the total population of erythrocytes $x + \sum_i y_i$. In this paper we will analyze the simplified case which is the model considered in all the referenced literature. The rationale behind this simplification is that in a malaria primo-infection typically y is in the order of 10^{-1}

to 10^{-4} of the concentration of healthy erythrocytes x . This can be confirmed from the data of malaria therapy. In the last century neurosyphilitic patients were given malaria therapy, which was routine care at that time. Some of them were infected with *Plasmodium falciparum*. Data were collected at the National Institutes of Health laboratories in Columbia, SC and Milledgeville, GA during the period 1940 to 1963 [12].

We assume that f is a C^1 . Since homeostasis is maintained we assume that the dynamic without parasites is asymptotically stable. In other words, for the system

$$\dot{x} = f(x) - \mu_x x = \varphi(x)$$

there exists a unique $x^* > 0$ such that

$$(2.3) \quad \varphi(x^*) = 0, \quad \text{and } \varphi(x) > 0 \quad \text{for } 0 \leq x < x^*, \quad \text{and } \varphi(x) < 0 \quad \text{for } x > x^*.$$

2.1. Notation. We will rewrite systems (2.1) and (2.2) in a condensed simpler form.

Before we introduce some classical notation.

We identify vectors of \mathbb{R}^n with $n \times 1$ column vectors. $\langle | \rangle$ denotes the euclidean inner product. $\|z\|_2^2 = \langle z | z \rangle$ is the usual euclidean norm.

The family $\{e_1, \dots, e_n\}$ denotes the canonical basis of the vector space \mathbb{R}^n . For example $e_1 = (1, 0, \dots, 0)^T$. We denote by e_ω the last vector of the canonical basis, $e_\omega = (0, \dots, 0, 1)^T$.

If $z \in \mathbb{R}^n$, we denote by z_i the i th component of z . Equivalently $z_i = \langle z | e_i \rangle$.

For a matrix A we denote by $A(i, j)$ the entry at the row i , column j . For matrices A, B we write $A \leq B$ if $A(i, j) \leq B(i, j)$ for all i and j , $A < B$ if $A \leq B$ and $A \neq B$, and $A \ll B$ if $A(i, j) < B(i, j)$ for all i and j .

A^T denotes the transpose of A . Then $\langle z_1 | z_2 \rangle = z_1^T z_2$. The notation A^{-T} will denote the transpose of the inverse of A .

For this section we rewrite the systems (2.1) and (2.2) under a unique form:

$$(2.4) \quad \begin{cases} \dot{x} = \varphi(x) - \beta x \langle e_\omega | z \rangle, \\ \dot{z} = \beta x \langle e_\omega | z \rangle e_1 + A_0 z - u \beta x \langle e_\omega | z \rangle e_\omega. \end{cases}$$

In the case of the system (2.1) we have for A_0

$$(2.5) \quad A_0 = \begin{bmatrix} -\alpha_1 & 0 & 0 & \cdots & 0 & 0 \\ \gamma_1 & -\alpha_2 & 0 & \cdots & 0 & 0 \\ 0 & \gamma_2 & -\alpha_3 & \cdots & 0 & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots & \vdots \\ 0 & \cdots & 0 & \gamma_{k-1} & -\alpha_k & 0 \\ 0 & \cdots & 0 & 0 & r\gamma_k & -\mu_m \end{bmatrix}$$

and an analogous formula for (2.2).

We define the matrix $A(x) = A_0 - \beta x e_\omega e_\omega^T$. This a Metzler stable matrix. (A Metzler matrix is a matrix with nonnegative off-diagonal entries [5, 32, 50].)

It is not difficult to check that the nonnegative orthant is positively invariant by (2.4) and that there exists a compact absorbing set K for this system. An absorbing set D is a neighborhood such that a trajectory of the system starting from any initial condition enters and remains in D for a sufficiently large time T .

2.2. Global stability results. We can now give the main result of this section.

THEOREM 2.1. *We consider the system (2.4) with the hypothesis (2.3) on φ satisfied. We define the basic reproduction ratio of the system (2.1) and (2.2) by*

$$(2.6) \quad \mathcal{R}_0 = \frac{r\beta x^*}{\mu_m + u\beta x^*} \frac{\gamma_1 \cdots \gamma_k}{\alpha_1 \cdots \alpha_k}.$$

1. *The system (2.1) is GAS on \mathbb{R}_+^{k+2} (respectively, (2.2) on \mathbb{R}_+^{k+3}) at the DFE $(x^*, 0, \dots, 0)$ if and only if $\mathcal{R}_0 \leq 1$.*

2. *If $\mathcal{R}_0 > 1$, then the DFE is unstable and there exists a unique endemic equilibrium (EE) in the positive orthant, $(\bar{x}, \bar{z}) \gg 0$, given by*

$$(2.7) \quad \begin{cases} \bar{x} = \frac{\mu_m}{\beta \left[r \frac{\gamma_1 \cdots \gamma_k}{\alpha_1 \cdots \alpha_k} - u \right]}, \\ \bar{z} = \varphi(\bar{x}) (-A_0)^{-1} (e_1 - u e_\omega). \end{cases}$$

Denoting $\alpha^* = -\max_{x \in [0, x^*]} (\varphi'(x))$, if

$$(2.8) \quad u\beta\varphi(\bar{x}) \leq \alpha^* \mu_m,$$

then the EE is GAS on the nonnegative orthant, except for initial conditions on the x -axis.

Proof of Theorem 2.1. To begin we will consider the system (2.1) without gametocytes, i.e., the system (2.4) with A_0 as defined in (2.5). The stability analysis for (2.2) follows easily from the stability analysis of (2.1).

In a first step we will compute \mathcal{R}_0 . We use our preceding notation and define $A^* = A(x^*)$, i.e., the matrix computed at the equilibrium x^* of φ , which is a stable Metzler matrix. We will use, repeatedly in what follows, the property that if M is a stable Metzler matrix, then $-M^{-1} \geq 0$ [5]. The expression of \mathcal{R}_0 is obtained easily by using the next generation matrix of the system (2.1) [9, 15, 16]. We have for the basic reproduction number

$$\mathcal{R}_0 = \beta x^* \left\langle -(A^*)^{-1} e_1 \mid e_\omega \right\rangle.$$

If we remark that the matrix A^* is the matrix A_0 modified by a rank-one matrix, namely $A^* = A_0 - u\beta x^* e_\omega e_\omega^T$, we can use the Sherman–Morrison–Woodbury formula

$$-(A^*)^{-1} = -A_0^{-1} - \frac{u\beta x^*}{1 + u\beta x^* e_\omega^T (-A_0)^{-1} e_\omega} (-A_0)^{-1} e_\omega e_\omega^T (-A_0)^{-1}$$

or equivalently

$$-(A^*)^{-1} = -A_0^{-1} - \frac{u\beta x^*}{\mu_m + \beta x^*} e_\omega e_\omega^T (-A_0)^{-1}.$$

This shows that $-(A^*)^{-1}$ is obtained from $-A_0^{-1}$ by multiplying the last line of $-A_0^{-1}$ by $\frac{\mu_m}{\mu_m + u\beta x^*}$. Then we get

$$\mathcal{R}_0 = \beta x^* \frac{\mu_m}{\mu_m + u\beta x^*} \left\langle -(A_0)^{-1} e_1 \mid e_\omega \right\rangle,$$

and then in computing the last entry of the first column of A_0 we obtain (2.6).

We remark that $\mathcal{R}_0 > 1$ is equivalent to the following threshold condition:

$$(2.9) \quad \mathcal{T}_0 = \frac{\beta x^*}{\mu_m} \left[\mu_m \langle -(A_0)^{-1} e_1 \mid e_\omega \rangle - u \right] = \beta x^* \langle -(A_0)^{-1} (e_1 - u e_\omega) \mid e_\omega \rangle > 1.$$

We are now ready to analyze the stability of the DFE.

It is well known that if $\mathcal{R}_0 > 1$, then the DFE is unstable [15], which implies that the condition $\mathcal{R}_0 \leq 1$ is necessary for stability.

To prove the sufficiency, in a second step, we consider the following function defined on the nonnegative orthant:

$$(2.10) \quad V_{DFE}(z) = \beta x^* \langle e_\omega \mid (-A_0^{-1})z \rangle.$$

Its time derivative along the trajectories of system (2.4) is

$$\dot{V}_{DFE} = \beta x \langle e_\omega \mid z \rangle \beta x^* \langle e_\omega \mid (-A_0)^{-1} (e_1 - u e_\omega) \rangle - \beta x^* \langle e_\omega \mid z \rangle$$

or equivalently, using the expression of \mathcal{T}_0 given in (2.9),

$$(2.11) \quad \dot{V}_{DFE} = \beta \langle e_\omega \mid z \rangle (\mathcal{T}_0 x - x^*).$$

Now we take as a candidate Liapunov function, defined on the nonnegative orthant minus the hyperplane face $x = 0$,

$$V = (x - x^* \ln x) - x^*(1 - \ln x^*) + V_{DFE}(z).$$

This function is positive definite (relatively to the DFE) on $\mathbb{R}_{+,x>0}^{k+2} = \{(x, y, m) \in \mathbb{R}_+^{k+2} : x > 0\}$. Its time derivative is given by

$$\dot{V} = \frac{x - x^*}{x} \varphi(x) - (x - x^*) \beta \langle e_\omega \mid z \rangle + \beta \langle e_\omega \mid z \rangle (\mathcal{T}_0 x - x^*)$$

or assuming $\mathcal{R}_0 \leq 1$

$$\dot{V} = \frac{x - x^*}{x} \varphi(x) + \beta x \langle e_\omega \mid z \rangle (\mathcal{T}_0 - 1) \leq 0.$$

By assumption (2.3) we have $(x - x^*)\varphi(x) \leq 0$ for all $x \geq 0$. Therefore $\dot{V} \leq 0$ for all $(x, z) \in \mathbb{R}_{+,x>0}^{k+2}$, which proves the stability of the DFE. Its attractivity follows from LaSalle’s invariance principle [6, 37, 38], since the largest invariant set contained in $\{(x, z) \in \mathbb{R}_{+,x>0}^{k+2} : \dot{V} = 0\}$ is reduced to the DFE. On the other hand the vector field is strictly entrant on the face $x = 0$. Hence the whole orthant \mathbb{R}_+^{k+2} belongs to the region of attraction of the DFE.

Now we assume that $\mathcal{R}_0 > 1$. The equilibria (\bar{x}, \bar{z}) of the system, different from the DFE, are determined by the relations

$$\bar{z} = \beta \bar{x} \langle \bar{z} \mid e_\omega \rangle (-A_0)^{-1} (e_1 - u e_\omega).$$

Replacing \bar{z} in $\langle \bar{z} \mid e_\omega \rangle$ we obtain

$$(2.12) \quad \langle \bar{z} \mid e_\omega \rangle = \beta \bar{x} \langle \bar{z} \mid e_\omega \rangle \langle (-A_0)^{-1} (e_1 - u e_\omega) \mid e_\omega \rangle.$$

If $\langle \bar{z} \mid e_\omega \rangle = 0$, then $\varphi(\bar{x}) = 0$, we obtain $\bar{x} = x^*$, and hence $\bar{z} = 0$; i.e., the corresponding equilibrium is the DFE. In the other case, i.e., $\langle \bar{z} \mid e_\omega \rangle \neq 0$, the relation (2.12) gives

$$(2.13) \quad \beta \bar{x} \left\langle (-A_0)^{-1} (e_1 - u e_\omega) \mid e_\omega \right\rangle = 1.$$

Using $\langle (-A_0)^{-1} e_\omega \mid e_\omega \rangle = \frac{1}{\mu_m}$ we finally have

$$\bar{x} = \frac{\mu_m}{\beta \left[\mu_m \langle (-A_0)^{-1} e_1 \mid e_\omega \rangle - u \right]} = \frac{x^*}{\mathcal{T}_0}.$$

We deduce that if $\mathcal{R}_0 > 1$, then $0 < \bar{x} < x^*$, and hence $\varphi(\bar{x}) > 0$. Therefore

$$\bar{z} = \varphi(\bar{x}) (-A_0)^{-1} (e_1 - u e_\omega).$$

The last component of \bar{z} , $\langle \bar{z} \mid e_\omega \rangle = \bar{m}$, is given by

$$\bar{m} = \frac{\varphi(\bar{x})}{\beta \bar{x}} > 0.$$

The k first components of \bar{z} are given by the k first components of $\varphi(\bar{x}) (-A_0)^{-1} e_1$. It is straightforward to check that the first column of $(-A_0)^{-1}$ namely $(-A_0)^{-1} e_1 \gg 0$, which proves that $\bar{z} \gg 0$. We have then proved that there is a unique EE in the positive orthant if and only if $\mathcal{R}_0 > 1$.

Finally we will prove a sufficient condition for the global asymptotic stability of the EE. To this end we define the following candidate Liapunov function on the positive orthant minus the face corresponding to $x = 0$:

$$(2.14) \quad V_{EE}(x, y, m) = a(x - \bar{x} \ln x) + \sum_{i=1}^k b_i (y_i - \bar{y}_i \ln y_i) + b_{k+1} (m - \bar{m} \ln m).$$

This function has a unique global minimum in $(\bar{x}, \bar{y}, \bar{m})$. We will choose the coefficients a, b_i, b_{k+1} such that in the computation of \dot{V} , the linear terms in y_i and m and the bilinear terms in $x m$ cancel. Let us show that it is possible with positive coefficients. To this end we rewrite the function V_{EE} using the notation $z = (y, m)^T$, $\ln z = (\ln z_1, \ln z_2, \dots, \ln z_{k+1})^T$, and $b = (b_1, \dots, b_k, b_{k+1})^T$:

$$V_{EE}(x, z) = a(x - \bar{x} \ln x) + \langle b \mid z - \text{diag}(\bar{z}) \ln z \rangle.$$

Consider the block matrix

$$M = \begin{bmatrix} -1 & (e_1 - u e_\omega)^T \\ \beta \bar{x} e_\omega & A_0^T \end{bmatrix}.$$

Using classical Schur complement techniques and the relation (2.13) on \bar{x} , we have

$$\begin{aligned} \det(M) &= \det(A_0) [-1 + \beta \bar{x} (e_1 - u e_\omega)^T (-A_0^{-T}) e_\omega] \\ &= \det(A_0) [-1 + \beta \bar{x} \langle -A_0^{-1} (e_1 - u e_\omega) \mid e_\omega \rangle] = 0. \end{aligned}$$

Since the matrix M is obviously of codimension 1 (A_0 is nonsingular) the kernel of M is of dimension 1. Then there exists $a \in \mathbb{R}$ and $b \in \mathbb{R}^{k+1}$ such that

$$(2.15a) \quad a = (e_1 - u e_\omega)^T b = \langle b \mid e_1 - u e_\omega \rangle$$

and

$$(2.15b) \quad b = a \beta \bar{x} (-A_0^{-T}) e_\omega.$$

Since the kernel is one dimensional, a can be chosen arbitrarily. Thanks to the structure of A_0 , if $a > 0$, then $b \gg 0$.

The derivative of V along the trajectories of (2.4) is given by

$$\begin{aligned} \dot{V}_{EE} &= a \frac{x - \bar{x}}{x} \varphi(x) - a \beta x \langle e_\omega | z \rangle + a \beta \bar{x} \langle e_\omega | z \rangle + \beta x \langle e_\omega | z \rangle \langle b | e_1 - u e_\omega \rangle \\ &\quad + \langle b | A_0 z \rangle + \langle b | \text{diag}(\bar{z}) \text{diag}(z)^{-1} \dot{z} \rangle \\ &= a \frac{x - \bar{x}}{x} \varphi(x) + \langle b | \text{diag}(\bar{z}) \text{diag}(z)^{-1} \dot{z} \rangle \\ &\quad + a \beta \bar{x} \langle e_\omega | z \rangle + \langle b | A_0 z \rangle + \beta x \langle e_\omega | z \rangle (\langle b | e_1 - u e_\omega \rangle - a). \end{aligned}$$

Using the relation (2.15b) we see that

$$\langle b | A_0 z \rangle = -a \beta \bar{x} \langle (A_0^{-T}) e_\omega | A_0 z \rangle = -a \beta \bar{x} \langle e_\omega | z \rangle.$$

Therefore the linear terms in z cancel. The same is true for the bilinear terms thanks to the relation (2.15a). Finally we get

$$\dot{V}_{EE} = a \frac{x - \bar{x}}{x} \varphi(x) + \langle b | \text{diag}(\bar{z}) \text{diag}(z)^{-1} \dot{z} \rangle.$$

We choose $b_{k+1} = 1 = \langle b | e_\omega \rangle = a \beta \bar{x} \langle -A^{-T} e_\omega | e_\omega \rangle = a \beta \bar{x} \frac{1}{\mu_m}$. In other words $a = \frac{\mu_m}{\beta \bar{x}}$. With the hypothesis $\mathcal{R}_0 > 1$ we have $a > 0$, and hence $b \gg 0$ as wanted.

With this choice developing \dot{V} gives

$$\begin{aligned} \dot{V}_{EE} &= a f(x) - a \mu_x x - a f(x) \frac{\bar{x}}{x} + a \mu_x \bar{x} - b_1 \beta \bar{y}_1 \frac{xm}{y_1} - \sum_{i=2}^k b_i \gamma_{i-1} y_{i-1} \frac{\bar{y}_i}{y_i} \\ &\quad + \sum_{i=1}^k b_i \alpha_i \bar{y}_i - r \gamma_k y_k \frac{\bar{m}}{m} + u \beta \bar{m} x + \mu_m \bar{m}. \end{aligned}$$

We collect some useful relations between our coefficients at the EE. We have from the definitions of a and b , since $b_{k+1} = 1$,

$$(2.16) \quad \begin{cases} a + u = b_1, \\ b_1 \alpha_1 = \gamma_1 b_2, \\ b_2 \alpha_2 = \gamma_2 b_3, \\ \dots \\ b_{k-1} \alpha_{k-1} = \gamma_{k-1} b_k, \\ b_k \alpha_k = r \gamma_k. \end{cases}$$

From these relations and the properties of the EE \bar{z} we have

$$(2.17) \quad b_1 \beta \bar{x} \bar{m} = b_i \alpha_i \bar{y}_i = b_i \gamma_{i-1} \bar{y}_{i-1} = r \gamma_k \bar{y}_k$$

and

$$(2.18) \quad a \alpha_1 \bar{y}_1 = \mu_m \bar{m}.$$

Replacing, in the expression of \dot{V} , $a\mu_x\bar{x}$ by $a f(\bar{x}) - a\beta\bar{x}\bar{m} = a f(\bar{x}) - a\alpha_1 \bar{y}_1$ we obtain

$$\begin{aligned} \dot{V}_{EE} &= kr\gamma_k\bar{y}_k + a f(\bar{x}) + a f(x) + (u\beta\bar{x}\bar{m} - a\mu_x\bar{x})\frac{x}{\bar{x}} - a f(x)\frac{\bar{x}}{x} \\ &\quad - b_1\beta\bar{x}\bar{m}\frac{x}{\bar{x}}\frac{m}{\bar{m}}\frac{\bar{y}_1}{y_1} - \sum_{i=2}^k b_i\gamma_{i-1}\bar{y}_{i-1}\frac{y_{i-1}}{\bar{y}_{i-1}}\frac{\bar{y}_i}{y_i} - r\gamma_k\bar{y}_k\frac{y_k}{\bar{y}_k}\frac{\bar{m}}{m}. \end{aligned}$$

Using again the relations between the coefficients we get

$$\begin{aligned} \dot{V}_{EE} &= kr\gamma_k\bar{y}_k + a f(\bar{x}) + a f(x) + (r\gamma_k\bar{y}_k - a f(\bar{x}))\frac{x}{\bar{x}} - a f(x)\frac{\bar{x}}{x} \\ &\quad - r\gamma_k y_k \frac{x}{\bar{x}}\frac{m}{\bar{m}}\frac{\bar{y}_1}{y_1} - \sum_{i=2}^k r\gamma_k\bar{y}_k\frac{y_{i-1}}{\bar{y}_{i-1}}\frac{\bar{y}_i}{y_i} - r\gamma_k\bar{y}_k\frac{y_k}{\bar{y}_k}\frac{\bar{m}}{m} \end{aligned}$$

and finally

$$\begin{aligned} \dot{V}_{EE} &= a \left[f(x) + f(\bar{x}) - f(\bar{x})\frac{x}{\bar{x}} - f(x)\frac{\bar{x}}{x} \right] \\ &\quad + r\gamma_k\bar{y}_k \left[k + \frac{x}{\bar{x}} - \frac{x}{\bar{x}}\frac{m}{\bar{m}}\frac{\bar{y}_1}{y_1} - \sum_{i=2}^k \frac{y_{i-1}}{\bar{y}_{i-1}}\frac{\bar{y}_i}{y_i} - \frac{y_k}{\bar{y}_k}\frac{\bar{m}}{m} \right]. \end{aligned}$$

Now we will use the fact that there exists ξ in the open interval $\xi \in]x, \bar{x}[$ such that $f(x) = f(\bar{x}) + (x - \bar{x}) f'(\xi)$. Replacing in the preceding expression gives

$$\begin{aligned} \dot{V}_{EE} &= a f(\bar{x}) \left[2 - \frac{x}{\bar{x}} - \frac{\bar{x}}{x} \right] + a f'(\xi) \frac{(x - \bar{x})^2}{x} \\ &\quad + r\gamma_k\bar{y}_k \left[k + \frac{x}{\bar{x}} - \frac{x}{\bar{x}}\frac{m}{\bar{m}}\frac{\bar{y}_1}{y_1} - \sum_{i=2}^k \frac{y_{i-1}}{\bar{y}_{i-1}}\frac{\bar{y}_i}{y_i} - \frac{y_k}{\bar{y}_k}\frac{\bar{m}}{m} \right]. \end{aligned}$$

Using the relations (2.16)–(2.17) we have

$$a f(\bar{x}) = (b_1 - u) f(\bar{x}) = b_1(\mu_x\bar{x} + \beta\bar{x}\bar{m}) - u f(\bar{x}) = b_1\mu_x\bar{x} + r\gamma_k\bar{y}_k - u f(\bar{x}).$$

Replacing in the preceding expression of \dot{V} gives

$$\begin{aligned} \dot{V}_{EE} &= (b_1\mu_x\bar{x} - u f(\bar{x})) \left[2 - \frac{x}{\bar{x}} - \frac{\bar{x}}{x} \right] + a f'(\xi) \frac{(x - \bar{x})^2}{x} \\ &\quad + r\gamma_k\bar{y}_k \left[k + 2 - \frac{\bar{x}}{x} - \frac{x}{\bar{x}}\frac{m}{\bar{m}}\frac{\bar{y}_1}{y_1} - \sum_{i=2}^k \frac{y_{i-1}}{\bar{y}_{i-1}}\frac{\bar{y}_i}{y_i} - \frac{y_k}{\bar{y}_k}\frac{\bar{m}}{m} \right]. \end{aligned}$$

This can also be written

$$\begin{aligned} \dot{V}_{EE} &= \Phi(x, y, m) = - [b_1\mu_x\bar{x} - u f(\bar{x}) - a\bar{x} f'(\xi)] \frac{(x - \bar{x})^2}{x\bar{x}} \\ (2.19) \quad &\quad + r\gamma_k\bar{y}_k \left[k + 2 - \frac{\bar{x}}{x} - \frac{x}{\bar{x}}\frac{m}{\bar{m}}\frac{\bar{y}_1}{y_1} - \sum_{i=2}^k \frac{y_{i-1}}{\bar{y}_{i-1}}\frac{\bar{y}_i}{y_i} - \frac{y_k}{\bar{y}_k}\frac{\bar{m}}{m} \right]. \end{aligned}$$

The term between brackets in the last expression of \dot{V} is nonpositive by the inequality between the arithmetical mean and the geometrical mean. Then a sufficient condition for $\dot{V} \leq 0$ is

$$b_1 \mu_x \bar{x} - u f(\bar{x}) - a \bar{x} f'(\xi) \geq 0.$$

Moreover with this condition \dot{V} is negative, except at the EE for the system (2.1). This proves the global asymptotic stability of the EE on the positive orthant for the system (2.1).

The vector field associated with the system is strictly entrant on the faces of the orthant, except the x -axis, where it is tangent. The basin of attraction of the EE is then the orthant, except the x -axis, which is the stable manifold of the DFE.

Using the function $\varphi(x) = f(x) - \mu_x x$ the preceding condition is equivalent to

$$u \varphi(\bar{x}) \leq -a \bar{x} \varphi'(\xi),$$

or equivalently, replacing a by its value $a = \frac{\mu_m}{\beta \bar{x}}$, the condition becomes

$$u \beta \varphi(\bar{x}) \leq -\mu_m \varphi'(\xi).$$

Setting $\alpha^* = -\max_{x \in [0, x^*]} \varphi'(x)$ a sufficient condition for global asymptotic stability of the EE is

$$\mathcal{R}_0 > 1 \quad \text{and} \quad u \beta \varphi(\bar{x}) \leq \mu_m \alpha^*.$$

We have proved the theorem for the system without gametocytes. We have seen that \mathcal{R}_0 does not depend on the production of gametocytes. If $\mathcal{R}_0 \leq 1$, it is easy, integrating the linear stable y_{k+1} equations of (2.2) from the solutions of (2.1), to see that the DFE is asymptotically stable and that all the trajectories converge to the equilibrium. The same argument is used when $\mathcal{R}_0 > 1$. This ends the proof of Theorem 2.1. \square

Remark 1. If this model is a model for a within-host model of malaria, each coefficient α_i is made of the mortality of the i -class and the rate of transmission in the $i + 1$ -class: $\alpha_i = \mu_i + \gamma_i$. This implies that $\gamma_i \leq \alpha_i$. We do not need this assumption, and our conclusions are valid for our more general model. The only hypothesis is that the parameters of the system are positive.

Remark 2. In the proof of Theorem 2.1 the quantity

$$\beta x^* \left\langle -(A_0)^{-1} (e_1 - u e_\omega) \mid e_\omega \right\rangle,$$

which we have called \mathcal{T}_0 when $\mathcal{R}_0 > 1$, plays a prominent role. When $\mathcal{R}_0 \leq 1$ and $u \neq 0$ three cases occur: $0 < \mathcal{T}_0 \leq 1$ or $\mathcal{T}_0 < 0$ or $\mathcal{T}_0 = 0$.

In the two first cases we can define $\bar{x} = \frac{x^*}{\mathcal{T}_0}$, and we obtain an equilibrium (\bar{x}, \bar{z}) of the system which is not in the nonnegative orthant (either $\bar{x} < 0$ or $\bar{z} < 0$).

In the third case, the computations, done in the proof of Theorem 2.1, for the research of an equilibrium show that $\langle z \mid e_\omega \rangle = 0$, and hence $z = 0$, and finally the equilibrium is the DFE $(x^*, 0)$.

We introduce a definition of \mathcal{T}_0 that will simplify future computations. The case $\mathcal{T}_0 = 0$ is special, since $\mathcal{T}_0 = \frac{x^*}{\bar{x}}$ is no longer true. However this case can be thought, by convention and misuse of language, as $\bar{x} = +\infty$.

DEFINITION 2.2. We define for the system (2.1) the threshold

$$(2.20) \quad \mathcal{T}_0 = \frac{x^*}{\mu_m} = \beta x^* \left\langle -(A_0)^{-1} (e_1 - u e_\omega) \mid e_\omega \right\rangle. \\ \beta \left[r \frac{\gamma_1 \cdots \gamma_k}{\alpha_1 \cdots \alpha_k} - u \right]$$

When $\mathcal{T}_0 \neq 0$ we have also $\mathcal{T}_0 = \frac{x^*}{\bar{x}}$.

Remark 3. It should be pointed out that the kind of Liapunov function defined by (2.14) has a long history of application to Lotka–Volterra models [18, 19] and was originally discovered by Volterra himself, although he did not use the vocabulary and the theory of Liapunov functions. Since epidemic models are “Lotka–Volterra” like models, the pertinence of this function is not surprising. Similar Liapunov functions have been used in epidemiology [4, 34, 35, 46, 63], although with different parameters. We have already used this kind of function in a simplified version of this paper in [1].

2.3. Comparison with known results. Our stability result improves the one of De Leenheer and Smith [13] in two directions:

1. We introduce n stages for latent classes.
2. Our sufficient condition for the global asymptotic stability of the endemic equilibrium is weaker than the one provided in [13]; for instance the sufficient condition given in Theorem 2.1 is satisfied for malaria parameters given in [3], while the condition of [13] is not satisfied.

2.4. Application to the original AMG model [3]. The original Anderson–May–Guptka model is a three dimensional system (1.1) which has the same form as system (2.1) with $f(x) = \Lambda$. The sufficient condition (2.8) applied to the AMG model (1.1) can be written

$$(2.21) \quad \beta \Lambda \leq \frac{r}{r-1} \mu_x \mu_m.$$

For the system (1.1), it is possible to give a weaker sufficient stability condition.

PROPOSITION 2.3. If $\mathcal{R}_0 > 1$ and $\beta \Lambda \leq (\sqrt{r} + \sqrt{r-1})^2 \mu_x \mu_m$, then the EE is a GAS steady state for system (1.1) with respect to initial states not on the x -axis.

Since in general the parameter r is larger than 2 (see, for instance, [28]), we have $(\sqrt{r} + \sqrt{r-1})^2 > \frac{r}{r-1}$.

Proof. Thanks to the computations done before, we have for system (1.1)

$$\dot{V}_{EE} = (r-1)\Lambda \left[2 - \frac{x}{\bar{x}} - \frac{\bar{x}}{x} \right] + r \mu_y \bar{y} \left[1 + \frac{x}{\bar{x}} - \frac{y \bar{m}}{\bar{y} m} - \frac{x m}{\bar{x} \bar{m} y} \right].$$

Define $X = \frac{x}{\bar{x}}$ and $S = \frac{y \bar{m}}{\bar{y} m}$. Then one can write

$$\dot{V}_{EE} = -(r-1)\Lambda \frac{(X-1)^2}{X} + r \mu_y \bar{y} \left(1 + X - S - \frac{X}{S} \right) \\ = -(r-1)\Lambda \frac{(X-1)^2}{X} + r \mu_y \bar{y} \Psi(X, S).$$

We have $\Psi(X, S) \geq 0 \Leftrightarrow X \leq S \leq 1$ or $X \geq S \geq 1$. On the other hand $\Psi(X, S) \leq \Psi(X, \sqrt{X}) = (\sqrt{X} - 1)^2$. Therefore

$$(2.22) \quad \dot{V}_{EE} \leq (r-1)\Lambda (\sqrt{X} - 1)^2 \left(\frac{r \mu_y \bar{y}}{(r-1)\Lambda} - \left(1 + \frac{1}{\sqrt{X}} \right)^2 \right), \\ \dot{V}_{EE} \leq (r-1)\Lambda (\sqrt{X} - 1)^2 \left(\sqrt{\frac{r \mu_y \bar{y}}{(r-1)\Lambda}} + 1 + \frac{1}{\sqrt{X}} \right) \left(\sqrt{\frac{r \mu_y \bar{y}}{(r-1)\Lambda}} - 1 - \frac{1}{\sqrt{X}} \right).$$

We have $\frac{\mu_y \bar{y}}{\Lambda} = \frac{\Lambda - \mu_x \bar{x}}{\Lambda} < 1$. Hence for $X \leq X^* = \frac{x^*}{\bar{x}} = \frac{(r-1)\beta}{\mu_m} x^*$ we have the following: $\sqrt{\frac{r \mu_y \bar{y}}{(r-1)\Lambda}} - 1 - \frac{1}{\sqrt{X}} < \sqrt{\frac{r}{(r-1)}} - \frac{\sqrt{\mu_m}}{\sqrt{(r-1)\beta x^*}} - 1 \leq 0$, since by assumption $\frac{\beta x^*}{\mu_m} = \frac{\beta \Lambda}{\mu_x \mu_m} \leq (\sqrt{r} + \sqrt{r-1})^2$. Therefore, the derivative of V_{EE} along the trajectories of system (1.1) is negative definite on the set $\mathcal{D}_0 = \{(x, y, m) \in \mathbb{R}_+^3 : 0 < x \leq x^*, y > 0, m > 0\}$. By continuity, there exists $\epsilon > 0$ such that \dot{V}_{EE} is negative definite on the set $\mathcal{D}_\epsilon = \{(x, y, m) \in \mathbb{R}_+^3 : 0 < x < x^* + \epsilon, y > 0, m > 0\}$. The global asymptotic stability of the EE follows from the fact that \mathcal{D}_ϵ is an absorbing set for system (1.1). \square

3. The general case: n strains with k classes of parasitized erythrocytes. We define the following system with k classes and n parasite strains:

$$(3.1) \quad \begin{cases} \dot{x} = f(x) - \mu_x x - x \sum_{i=1}^n \beta_i m_i = \varphi(x) - x \sum_{i=1}^n \beta_i m_i \\ \text{and for } i = 1, \dots, n, \\ \dot{y}_{1,i} = \beta_i x m_i - \alpha_{1i} y_{1,i}, \\ \dot{y}_{2,i} = \gamma_{1,i} y_{1,i} - \alpha_{2,i} y_{2,i}, \\ \dots \\ \dot{y}_{k,i} = \gamma_{k-1,i} y_{k-1,i} - \alpha_{k,i} y_{k,i}, \\ \dot{g}_i = \delta_i y_{k,i} - \mu_{g_i} g_i, \\ \dot{m}_i = r_i \gamma_{k,i} y_{k,i} - \mu_{m_i} m_i - u \beta_i x m_i. \end{cases}$$

As in preceding sections we rewrite the system as

$$(3.2) \quad \begin{cases} \dot{x} = \varphi(x) - x \sum_{i=1}^n \beta_i \langle z_i | e_{i,\omega} \rangle \\ \text{and for } i = 1, \dots, n, \\ \dot{z}_i = x \beta_i \langle z_i | e_{i,\omega} \rangle e_{i,1} + A_i z_i - u x \beta_i \langle z_i | e_{i,\omega} \rangle e_{i,\omega}, \end{cases}$$

where the matrix A_i is the analogous of the matrix A_0 defined in section 2.2, but corresponding to the genotype i , and the vectors $e_{i,1}$ and $e_{i,\omega}$ are defined accordingly. We drop the index 0 in A for readability.

THEOREM 3.1. *We consider the system (3.1) with the hypotheses (2.3) satisfied. We define the basic reproduction ratio \mathcal{R}_0 of the system (3.1) by*

$$\mathcal{R}_0^i = \frac{r_i \beta_i x^*}{\mu_{m_i} + u \beta_i x^*} \frac{\gamma_{1,i} \cdots \gamma_{k,i}}{\alpha_{1,i} \cdots \alpha_{k,i}}$$

and

$$\mathcal{R}_0 = \max_{i=1, \dots, n} \mathcal{R}_0^i.$$

1. *The system (3.1) is GAS on \mathbb{R}_+ at the DFE $(x^*, 0, \dots, 0)$ if and only if $\mathcal{R}_0 \leq 1$.*

2. *If $\mathcal{R}_0 > 1$, then the DFE is unstable. If $\mathcal{R}_0^i > 1$, there exists an EE in the nonnegative orthant corresponding to the genotype i , the value for the other indexes*

$j \neq i$ are $y_j = m_j = 0$, and

$$(3.3) \quad \begin{cases} \bar{x}_i = \frac{\mu_{m_i}}{\beta_i \left[r_i \frac{\gamma_{1,i} \cdots \gamma_{k,i}}{\alpha_{1,i} \cdots \alpha_{k,i}} - u \right]}, \\ \bar{z}_i = \varphi(\bar{x}_i) (-A_i)^{-1} (e_{i,1} - u e_{i,\omega}), \\ \bar{g}_i = \frac{\delta_i}{\mu_{g_i}} \bar{z}_{i,k}, \end{cases}$$

where we denote by $\bar{z}_{i,k}$ the k th component of \bar{z}_i .

3. We assume $\mathcal{R}_0 > 1$. We define \mathcal{T}_0^i as in Definition 2.2. We assume that the generic conditions $\mathcal{T}_0^i \neq \mathcal{T}_0^j$ are satisfied for $i \neq j$. We suppose that the genotypes have been indexed such that

$$\mathcal{T}_0^1 > \mathcal{T}_0^2 \geq \cdots \geq \mathcal{T}_0^n.$$

Then the EE corresponding to \bar{x}_1 is asymptotically stable and the EEs corresponding to \bar{x}_j for $j \neq 1$ (for those which are in the nonnegative orthant) are unstable.

4. We assume that the preceding hypothesis $\mathcal{T}_0^1 > \mathcal{T}_0^j$ is satisfied with $\mathcal{R}_0 > 1$. We denote it by $\alpha^* = -\max_{x \in [0, x^*]} (\varphi'(x))$. Then if

$$u \beta_1 \varphi(\bar{x}_1) \leq \mu_{m_1} \alpha^*,$$

the equilibrium $(\bar{x}_1, \bar{y}_1, \bar{m}_1, \bar{g}_1, 0, \dots, 0)$ is GAS on the orthant minus the x -axis and the faces of the orthant defined by $y_1 = m_1 = g_1 = 0$. In other words the most virulent strain is the winner and the other strains go extinct.

Proof. As in Theorem 2.1 there exists a forward invariant compact absorbing set in the nonnegative orthant for the system (3.1), and hence all the forward trajectories are bounded. The variables g_i do not affect the dynamical evolution of the variables $x, y_{i,j}, m_i$, and so we can consider the system without the production of gametocytes. We use the Liapunov function

$$V_{DFE}(z) = \sum_{i=1}^n V_{DFE}(z_i) = \sum_{i=1}^n \beta_i x^* \langle e_{i,\omega} \mid (-A_i^{-1}) z_i \rangle.$$

Using the system written as (3.2) and the computation (2.11) we easily obtain

$$\dot{V}_{DFE} = \sum_{i=1}^n \beta_i \langle e_{i,\omega} \mid z_i \rangle (\mathcal{T}_0^i x - x^*).$$

Now we define the Liapunov function on the nonnegative orthant minus the hyperplane face $x = 0$

$$V(x, z) = (x - x^* \ln x) - x^*(1 - \ln x^*) + \sum_{i=1}^n V_{DFE}(z_i)$$

which gives

$$\begin{aligned} \dot{V} &= \frac{x - x^*}{x} \varphi(x) + \sum_{i=1}^n x^* \beta_i \langle z_i \mid e_{i,\omega} \rangle - \sum_{i=1}^n x \beta_i \langle z_i \mid e_{i,\omega} \rangle \\ &\quad + \sum_{i=1}^n \beta_i \langle e_{i,\omega} \mid z_i \rangle (\mathcal{T}_0^i x - x^*) \\ &= \frac{x - x^*}{x} \varphi(x) + \sum_{i=1}^n \beta_i \langle e_{i,\omega} \mid z_i \rangle x (\mathcal{T}_0^i - 1). \end{aligned}$$

Since $\mathcal{R}_0^i \leq 1$ for all index i , we have $\mathcal{T}_0^i \leq 1$, and hence $\dot{V} \leq 0$. The conclusion follows by Lasalle’s invariance principle and consideration of the boundary of the positive orthant.

Now we assume $\mathcal{R}_0 > 1$. The instability of the DFE follows from the properties of \mathcal{R}_0 [15]. We assume that the genotypes are indexed such that their corresponding threshold are in decreasing order $\mathcal{T}_0^1 > \mathcal{T}_0^2 \geq \dots \geq \mathcal{T}_0^n$.

We will define a Liapunov function on the nonnegative orthant minus the manifold defined by the equations $x = y_1 = m_1 = 0$. For this we need to recall the definition of the function $V_{EE}(x, y_1, m_1)$ defined in (2.14):

$$V_{EE}(x, y, m) = a(x - \bar{x} \ln x) + \sum_{i=1}^k b_{1,i} (y_{1,i} - \bar{y}_{1,i} \ln y_{1,i}) + b_{1,k+1} (m_1 - \bar{m}_1 \ln m_1).$$

The coefficients $(a, b_{1,i})$ are positive and defined from A_1 as in the proof of Theorem 2.1 from section 2.2. We also use the function V_{EE} defined in (2.10) to consider

$$V(x, z) = \mathcal{T}_0^1 V_{EE}(x, z_1) + a \sum_{i=2}^n V_{DFE}(z_i)$$

or equivalently

$$V(x, z) = \mathcal{T}_0^1 V_{EE}(x, z_1) + a \sum_{i=2}^n \beta_i x^* \langle e_{i,\omega} | (-A_i^{-1}) z_i \rangle.$$

Using the relation (2.19) and (2.11), we can compute the derivative of V along the trajectories of (3.2):

$$\begin{aligned} \dot{V} &= \mathcal{T}_0^1 \Phi(x, z_1) + a \mathcal{T}_0^1 \sum_{i=2}^n \beta_i \bar{x}_1 \langle e_{i\omega} | z_i \rangle - a \mathcal{T}_0^1 \sum_{i=2}^n \beta_i x \langle e_{i\omega} | z_i \rangle \\ &\quad + a \sum_{i=2}^n \beta_i \langle z_i | e_{i,\omega} \rangle (\mathcal{T}_0^i x - x^*). \end{aligned}$$

Using $\mathcal{T}_0^1 \bar{x}_1 = x^*$ from the Definition 2.2 for the threshold we get

$$\dot{V} = \mathcal{T}_0^1 \Phi(x, z_1) + a \sum_{i=2}^n \beta_i \langle z_i | e_{i,\omega} \rangle x (\mathcal{T}_0^i - \mathcal{T}_0^1) \leq 0.$$

By Liapunov theorem this ends the proof for the stability. The global asymptotic stability is obtained by a straightforward use of LaSalle’s invariance principle, which ends the proof of Theorem 3.1. \square

Remark 4. In the nongeneric case it can be shown, with the help of the Liapunov functions used in the theorem, that there exists a continuum of stable EE. We omit the proof.

In the generic case, the dynamics of the system are completely determined. The nonnegative orthant is stratified in the union of stable manifolds corresponding to the different equilibria. Only the equilibrium corresponding to the winning strain has a basin of attraction with a nonempty interior.

Remark 5. We have proved that the most virulent strain, that is, the strain which maximizes its respective threshold \mathcal{T}_0^i , eliminates the other. We obtain the

same kind of result as in [7], where the authors consider a *SIR* model with n strains of parasite. They consider that infection by one parasite strain excludes superinfection by other strains (this is also our case) and induces permanent immunity against all strains in case of recovery. They also guarantee limited population by considering a recruitment depending on the density in a monotone decreasing way. They find that the strain which maximizes the basic reproduction ratio eliminates the others. In the case considered by the authors, actually, using our notation, $\mathcal{R}_0 = \frac{x^*}{\bar{x}}$. In fact in this model \mathcal{T}_0 and \mathcal{R}_0 coincide. This is also the case in our model when $u = 0$. Hence our result compares with the result of [7]. However in the case $u \neq 0$ this is \mathcal{T}_0^i , and not \mathcal{R}_0^i , which distinguishes the fate of the strain. Our result is then different from [7], where this role is devoted to \mathcal{R}_0 . The same kind of remarks apply to [10] and [11].

Remark 6. In our model the chains are of equal length for each strain. If the chains are of unequal length, the proof is unchanged. We use equal length for notational convenience. A reason to have unequal length could be to model different behavior for two different strains of the parasite.

4. Conclusion. In this article we have given a parasitic within-host model and have provided a stability analysis of this model.

This model incorporates a number k of compartments for the parasitized target cells and considers n strains for the parasite. The rationale for including multicompartments can be multiple. One reason is to take into account biological reasons, e.g., consideration of morphological or age classes. The second is for behavioral modeling reasons, e.g., to model delays described by gamma distribution functions.

This model has been conceived from malaria infection, since it is well grounded that malaria is a multistrain infection. However other parasitic infections can be considered by this model.

We prove that if the basic reproduction number satisfies $\mathcal{R}_0 \leq 1$, then the DFE is GAS; i.e., the parasite is cleared from the host. Our stability result when $\mathcal{R}_0 > 1$ can be summarized as a competitive exclusion principle. To each i -strain we associate an individual threshold condition \mathcal{T}_0^i as in Definition 2.2. If $\mathcal{R}_0 > 1$, if one strain has its individual threshold strictly larger than the thresholds of the other strains and if a mild sufficient condition is satisfied (for a constant recruitment, i.e., $f(x) = \Lambda$, this condition is simply $u\beta\Lambda \leq \frac{r}{r-u} \mu_x \mu_m$), then there exists a GAS equilibrium on the positive orthant. This equilibrium corresponds to the extinction of all strains, except the strain with the largest threshold. This winning strain maximizes the threshold and not its individual basic reproduction number, which is different from previous analogous results of the literature.

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Epidemiological Models and Lyapunov Functions

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Epidemiological Models and Lyapunov Functions

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Abstract

We give a survey of results on global stability for deterministic compartmental epidemiological models. Using Lyapunov techniques we revisit a classical result, and give a simple proof. By the same methods we also give a new result on differential susceptibility and infectivity models with mass action and an arbitrary number of compartments. These models encompass the so-called differential infectivity and staged progression models. In the two cases we prove that if the basic reproduction ratio $\mathcal{R}_0 \leq 1$, then the disease free equilibrium is globally asymptotically stable. If $\mathcal{R}_0 > 1$, there exists a unique endemic equilibrium which is asymptotically stable on the positive orthant.

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1. Introduction

The primary objective of this paper is to give two results on global stability for some epidemiological models using Lyapunov techniques. Using a new result for systems of the type $\dot{x} = A(x)x$, we revisit

a celebrated result of Lajmanovitch and Yorke [39] and give a simple proof. The second result is for differential susceptibility and infectivity models with mass action. We generalize a result of [26, 29]. But before we will give an overview of the literature concerning the problem of stability in epidemiological models

In [59] J.A. Jacquez says:

A major project in deterministic epidemiological modeling of heterogeneous populations is to find conditions for local and global stability of the equilibria and to work out the relations among these stability conditions, the threshold of epidemic take-off, and endemicity, and the basic reproduction.

We denote in this paper by \mathcal{R}_0 the basic reproduction number. The basic reproduction number, a key concept in epidemiology, is defined as the expected number of new cases of infection caused by a typical infected individual in a population of susceptibles only and is an ingredient in almost all papers using mathematical modeling for infectious diseases. An abundant literature have been devoted to \mathcal{R}_0 (see [9, 10, 17, 18, 34, 59, 66, 67] and the references therein) after the seminal paper [8].

The citation before was written in 1982, at this time no too many results was known. What is the situation 25 year later ? As early as 1976 the stability analysis for the classic SIR or SIRS models was well known [20, 21]. The reason was that the study of stability for these models was reduced to the study of 2-dimensional systems, hence phase methods could be used : Poincaré-Bendixson theorem. Periodic orbits are ruled out using Dulac criteria or condition of Busenberg and van den Driessche [7].

For many infectious diseases the transmission occurs in a heterogeneous population, so the epidemiological model must divide the population into subpopulations or groups, in which the members have similar characteristics. This division into groups can be based not only on mode of transmission, contact patterns, latent period, infectious period, genetic susceptibility or resistance, and amount of vaccination or chemotherapy, but also on social, cultural, economic, demographic, or geographic factors. This is the rationale for the introduction of multi-group models. In the epidemiological literature, the term “multi-group” usually refers to the division of a heterogeneous population into several homogeneous groups based on individual behaviour. The interest in multi-group endemic models originally stems from sexual transmitted diseases such as gonorrhea or HIV/AIDS. The pioneering paper of Lajmanovitch and Yorke in 1976 [39] provides a complete description of the dynamics of n groups of SIS systems for subpopulations of constant size. The authors use Lyapunov techniques to prove that either all trajectories in \mathbb{R}_+^n tends to 0, or else there is a unique endemic equilibrium \bar{x} in the positive orthant and trajectories in $\mathbb{R}_+^n \setminus \{0\}$ tends to \bar{x} .

Other types of high dimensional systems are the so-called differential infectivity (DI) and staged progression (SP) models. The staged progression model [23, 34, 59] has a single uninfected compartment, and infected individuals progress through several stages of the disease with changing infectivity. This model is applicable to disease with changing infectivity during the infectious period such that HIV or disease with asymptomatic carriers such that HBV or tuberculosis. The differential infectivity model has been also introduced to take into account some specificity of HIV/AIDS. In a DI model the infected population is subdivided into subgroups of different infectivity. Upon infection, an individual enters some subgroup with a certain probability and stays in this subgroup until becoming inactive in transmission.

For multigroup SEIRS models of constant size many results have demonstrated the global stability of the disease free equilibrium when $\mathcal{R}_0 < 1$ and the local asymptotic stability of an unique endemic equilibrium when $\mathcal{R}_0 > 1$ [19, 64, 65]. The most difficult task is the global stability of the endemic equilibrium when $\mathcal{R}_0 > 1$, when this is possible. Actually for general multigroup models the uniqueness of the endemic equilibrium non longer holds and the disease free equilibrium may be locally, but not globally, asymptotically stable [34, 59, 67].

The global stability when $\mathcal{R}_0 > 1$ of SEIR models with constant size has long been conjectured but only proven in 1995 [45]. The proof relies heavily on the competitive structure of the system, and the fact that 3 dimensional competitive systems satisfy the Poincaré-Bendixson theorem [22, 60, 61]. When the system is not competitive another approach consists to show that the system satisfies a Bendixson criterion which is robust under C^1 perturbation [46, 49, 50, 62].

Since these path-breaking papers numerous results of global stability for the endemic equilibrium have been obtained for low dimensional systems;

- For SEIRS systems, with fraction of classes (then the system reduces to a 3-dimensional systems) for small or large temporary immunity [44],
- For SEIR model with vertical transmission [47]. The study of stability is reduced to a 3-dimensional system. Since this system is not competitive the second approach is used,
- For SEIR model with varying population size [43] for the system of fraction of classes,
- For SIRV models (V for vaccinate class) with constant population size and mild parameters constraints [2],
- For SVEIR models [14] with small mortality,
- For Staged progression models in dimension 3 and 4 [56],
- For SEI models with immigration of latent and infectious [55],
- A model of dengue which is reduced to a 3 dimensional competitive system [67],
- A 5 dimensional staged progression model [13], for which the asymptotic stability of the endemic equilibrium reduces to a 3 dimensional system permitting to apply the Li-Muldowney technique [46].

For arbitrary dimensional system, the most promising method may be that of Lyapunov. The systematic use of Lyapunov function in studying stability problems is relatively recent. The exception is the result of Lajmanovitch and Yorke evoked before. However, Lasalle-Lyapunov theory has been used in [34, 42, 57, 59] to study the stability of classic SIRS models.

In 2004, Korobeinikov and Maini using a Lyapunov function [38] demonstrate simply the result of Li and Muldowney for the endemic equilibrium. The Lyapunov function used is $V = \sum_{i=1}^n a_i(x_i - \bar{x} \ln x_i)$.

This function has a long history of application to Lotka-Volterra models [5, 12, 16, 63] and was originally discovered by Volterra himself, although he did not use the vocabulary and the theory of Lyapunov functions. Since epidemic models are "Lotka-Volterra" like models, the pertinence of this function is not surprising. This Volterra-Lyapunov function has been used in epidemiological models at the end of the eighties.

Beretta and Capasso [4] use a skew-symmetry condition on the Jacobian of the matrix of the system to give a necessary condition for the global stability of the endemic equilibrium.

For a SIRS multigroup model with constant subgroup sizes, Lin and So [41] show that the endemic equilibrium is globally asymptotically stable if the contact rate between subgroups is small. These two results are actually perturbation results of the situation where the endemic equilibrium is known to be globally stable.

Since the publication of the result of Korobeinikov and Maini the "Volterra-like" Lyapunov functions has been used to address the stability of high-dimensional systems with mass action. The difficulty is

in choosing the coefficient and in proving that the derivative is nonnegative. The global stability of DI model with mass action is demonstrated in [52]. The global stability of SP model, eventually with latent classes, with mass action is proved in [15, 31]. Stability of intra-host models with different strains [30] (which contained as a particular case, $SE_1 \cdots E_k IR$ models with multiple strains) is treated in [1, 30]. The stability of differential and staged progression latent classes, with one infectious class is solved in [31]. Two models of tuberculosis are studied in [53]. The stability of a model with complex graph interaction between latent classes and one infectious class is addressed in [54].

We give a brief outline of the paper. In Section 2, we consider a system similar to the system in [39]. We compute \mathcal{R}_0 and prove that if $\mathcal{R}_0 \leq 1$, the DFE is globally asymptotically stable and if $\mathcal{R}_0 > 1$, then a unique equilibrium exists which is globally asymptotically stable on $\mathbb{R}_+^n \setminus \{0\}$. In Section 3, we present a system with different classes of susceptible individuals and staged progression through latency and infectious classes. Using a ‘‘Volterra-like’’ Lyapunov function we obtain results as before: if $\mathcal{R}_0 \leq 1$ the DFE is globally asymptotically stable and if $\mathcal{R}_0 > 1$ then a unique equilibrium exists which is globally asymptotically stable on the positive orthant.

2. A n Groups SIS Model

Throughout the paper we will use the following classical notations. We identify vectors of \mathbb{R}^n with $n \times 1$ column vectors. The euclidean inner product is denoted by $\langle \cdot | \cdot \rangle$, then $\|z\|_2^2 = \langle z | z \rangle$ is the usual euclidean norm. The family $\{e_1, \dots, e_n\}$ denotes the canonical basis of the vector space \mathbb{R}^n . We denote by $\mathbf{1}$ the vector with all components equal to 1, i.e. $\mathbf{1} = e_1 + \dots + e_n$.

If $x \in \mathbb{R}^n$ we denote by x_i the i -th component of x . Equivalently $x_i = \langle x | e_i \rangle$. For a matrix A we denote by $A(i, j)$ the entry in row i , column j . For matrices A, B we write $A \leq B$ if $A(i, j) \leq B(i, j)$ for all i and j , $A < B$ if $A \leq B$ and $A \neq B$, $A \ll B$ if $A(i, j) < B(i, j)$ for all i and j . The notation A^T denotes the transpose of A . Then $\langle v_1 | v_2 \rangle = v_1^T v_2$. The notation A^{-T} will denote the transpose of the inverse of A . If $x \in \mathbb{R}^n$, we denote by $\text{diag}(x)$ the diagonal matrix whose diagonal elements are given by x .

A Metzler matrix A is a matrix such that $A(i, j) \geq 0$ for any indices $i \neq j$ [6, 35, 51]. These matrices are also called quasipositive matrices [61]. Metzler matrices are the opposite of M -matrices [6, 67]. We prefer to use Metzler matrices since they appear naturally in compartmental systems.

In this section we will consider the following system

$$\dot{x} = \left[D + B - \text{diag}(x) B \right] x. \quad (2.1)$$

where D is a stable Metzler matrix and $B \geq 0$ is a nonnegative irreducible matrix.

To motivate the consideration of such a system we consider n groups with constant population size and a disease which confer no immunity after recovery. We model the contact by the mass action law. If we denote by S_i and I_i the respective number of susceptible and infectious individuals in group i , $N_i = S_i + I_i$, the system is, for $i = 1, \dots, n$

$$\begin{cases} \dot{S}_i = \mu_i N_i - \mu_i S_i - \sum_{j=1}^n \beta_{i,j} \frac{S_i}{N_i} I_j + \gamma_i I_i \\ \dot{I}_i = \sum_{j=1}^n \beta_{i,j} \frac{S_i}{N_i} I_j - (\gamma_i + \mu_i) I_i. \end{cases} \quad (2.2)$$

Since the population is constant, it is sufficient to know the I_i . If we set $x_i = \frac{I_i}{N_i}$, $\tilde{\beta}_{i,j} = \beta_{i,j} N_j$ and $\alpha_i = \gamma_i + \mu_i$ we obtain a system of ODE

$$\dot{x}_i = (1 - x_i) \sum \tilde{\beta}_{i,j} x_j - \alpha_i x_i. \quad (2.3)$$

that we can write in compact form

$$\dot{x} = [D + B - \text{diag}(x) B] x. \quad (2.4)$$

with $B = (\tilde{\beta}_{i,j})$ and $D = -\text{diag}(\alpha_i)$. This system is the system considered in [39], where the system addressed has the structure of (2.1). In this model, the matrix B describes the contact interaction between groups. We recall the following definition [6, 61, 66].

Definition 2.1. A matrix A of size $n \times n$, $n \geq 2$ is called irreducible if for any proper subset I of $\{1, \dots, n\}$ there are $i \in I$ and $j \notin I$ such that $A(i, j) \neq 0$.

Epidemiologically speaking the irreducibility of B (or Q) means that no group is contact isolated in and out from the remaining groups. It is now easy to interpret the meaning of the system (2.1). The matrix D describes the transfer of individuals out of compartments and $B - \text{diag}(x) B$ the disease transmission. The model can also be written $\dot{x} = [D + \text{diag}(1 - x) B] x$. It is clear that $[0, 1]^n$ is a compact positively invariant absorbing set for this system.

2.1. The Basic Reproduction Number

We denote by $\rho(A)$ the spectral radius of a matrix A , which is defined, if $\text{Sp}(A)$ denotes the spectrum of A , by

$$\rho(A) = \max\{|\lambda| \mid \lambda \in (\text{Sp}(A))\}$$

and the stability modulus $\alpha(A)$

$$\alpha(A) = \max\{\Re(\lambda) \mid \lambda \in (\text{Sp}(A))\}.$$

Using the framework of [67] the matrix $-D^{-1}B$ is the next generation matrix of (2.1) and the basic reproduction number is $\mathcal{R}_0 = \rho(-D^{-1}B)$. We now will use a result of Varga [68, 69] (rewritten in term of Metzler matrices).

Definition 2.2. [Regular splitting] For a real Metzler matrix \mathbf{M} , $\mathbf{M} = \Lambda + \mathbf{N}$ is a regular splitting if Λ is a Metzler stable matrix and $\mathbf{N} \geq \mathbf{0}$ is a nonnegative matrix.

Now we can give the following classical theorem.

Proposition 2.3. [Varga, 1962, Theorem 3.13, [69]] Let $\mathbf{M} = \Lambda + \mathbf{N}$ be a regular splitting of \mathbf{M} , a real Metzler matrix. Then \mathbf{M} is Metzler stable if and only if $\rho(-\mathbf{N}\Lambda^{-1}) < 1$.

The proof of Proposition 2.3 is in Varga (1960). It is also in Bermann and Plemmons [6]: the condition N_{45} expressed in terms of M -matrices. We see from this proposition, by a continuity argument, that for any regular splittings of a Metzler matrix \mathbf{M} we have

$$\begin{aligned} \alpha(\mathbf{M}) < 0 &\iff \rho(-\mathbf{N}\Lambda^{-1}) < 1, \\ \alpha(\mathbf{M}) = 0 &\iff \rho(-\mathbf{N}\Lambda^{-1}) = 1. \end{aligned} \quad (2.5)$$

Thus any regular splitting gives an equivalent threshold condition $\alpha(M)$ on the parameters. This has a consequence for our system : $D + B$ is a regular splitting and the stability of $D + B$ is completely related to \mathcal{R}_0 and its position relatively to 1. Since this equivalence is independent from the splitting, we can replace the system (2.1) by the same system where we assume that D is a diagonal matrix and incorporating the off-diagonal elements in B , this modification let the new matrix B still irreducible. This does not change the generality of the conclusion. However only the original $\rho(-D^{-1}B)$ has a biological meaning, the others are equivalent thresholds. From now on we will assume that D is a diagonal matrix.

2.2. Existence and Uniqueness of an Endemic Equilibrium

We will show that there exists a unique equilibrium $\bar{x} \gg 0$ if and only if $\mathcal{R}_0 > 1$. An equilibrium such that $\bar{x} \gg 0$ is called a strongly endemic equilibrium. The method of proof is inspired by the methods used by Thieme [19, 64, 66]. We show that if there exists an endemic equilibrium $\bar{x} > 0$ then $\mathcal{R}_0 > 1$. For the convenience of the reader we recall the following result on Metzler matrices [6].

Theorem 2.4. Let A be an irreducible Metzler matrix

1. If there exists $x > 0$ such that $Ax > \lambda x$ then $\alpha(A) > \lambda$.
2. If there exists $x > 0$ such that $\mu x > Ax$ then $\mu > \alpha(A)$.

If A is only Metzler, the preceding relations hold with $>$ replaced by \geq . If A is an irreducible nonnegative matrix, we have analogous inequalities, obtained in replacing the stability modulus $\alpha(A)$ by the spectral radius $\rho(A)$ in the preceding inequalities.

If there exists an endemic equilibrium $\bar{x} > 0$ it satisfies

$$\bar{x} = -D^{-1}B\bar{x} + \text{diag}(\bar{x})D^{-1}B\bar{x}.$$

Since D is a Metzler matrix, then $-D^{-1} > 0$ [61]. As B is irreducible and $-D$ diagonal, with positive diagonal terms, $-D^{-1}B$ is also irreducible. Therefore $-D^{-1}B\bar{x} \gg 0$ and from the preceding relation, we deduce $\bar{x} \gg 0$. A consequence is also $\text{diag}(\bar{x})D^{-1}B\bar{x} \ll 0$. Finally we obtain

$$\bar{x} < -D^{-1}B\bar{x}.$$

which in turn implies using Theorem 2.4.

$$\mathcal{R}_0 = \rho(-D^{-1}B) > 1.$$

Conversely, we have to show that if $\mathcal{R}_0 > 1$, then there exists a unique strongly endemic equilibrium. An equilibrium satisfies

$$(D + B)\bar{x} = \text{diag}(\bar{x})B\bar{x},$$

equivalently,

$$\bar{x} + \text{diag}(\bar{x})(-D^{-1}B\bar{x}) = \bar{x} + \text{diag}(-D^{-1}B\bar{x})\bar{x} = -D^{-1}B\bar{x},$$

which can be written

$$[I + \text{diag}(-D^{-1}B\bar{x})]\bar{x} = -D^{-1}B\bar{x}.$$

Hence

$$\bar{x} = [\text{diag}(\mathbf{1} - D^{-1}B\bar{x})]^{-1}(-D^{-1}B)\bar{x}.$$

We are reduced to find a fixed point for the application $H: [0, 1]^n$ in $[0, 1]^n$

$$H(x) = [\text{diag} (1 - D^{-1} B x)]^{-1} (-D^{-1} B) x.$$

Let be $A = D^{-1} B$ the next generation matrix. Since $\mathcal{R}_0 = \rho(-D^{-1} B)$ and $A = -D^{-1} B$ is a nonnegative irreducible matrix, from the Perron-Frobenius Theorem there exists $v \gg 0$ such that

$$A v = \mathcal{R}_0 v.$$

We choose ε sufficiently small such that for any index i

$$1 + \varepsilon \mathcal{R}_0 v_i \leq \mathcal{R}_0.$$

This is possible since $\mathcal{R}_0 > 1$. We deduce

$$1 \leq \frac{\mathcal{R}_0}{1 + \varepsilon \mathcal{R}_0 v_i},$$

and

$$\varepsilon v_i \leq \frac{\mathcal{R}_0 \varepsilon v_i}{1 + \varepsilon \mathcal{R}_0 v_i} = \frac{(A \varepsilon v)_i}{1 + (A \varepsilon v)_i}.$$

We have proved that there exists $\varepsilon > 0$ such that $\varepsilon v \leq H(\varepsilon v)$. We also have $\varepsilon > 1$ and $\varepsilon v \leq v$. A similar argument shows that we can choose λ with $0 < \lambda v_i \leq 1$ and λ large enough such that

$$\frac{\mathcal{R}_0}{1 + \mathcal{R}_0 \lambda v_i} \leq 1,$$

which is equivalent to $\frac{\mathcal{R}_0 - 1}{\mathcal{R}_0} \leq \lambda v_i$. This implies $H(\lambda v) \leq \lambda v$. Choosing $\varepsilon \leq \lambda$ we have $\varepsilon v \leq H(\varepsilon v)$ and $H(\lambda v) \leq \lambda v \leq 1$. Since H is a monotone function, H maps the parallelepiped

$$K = \{x \mid \varepsilon v \leq x \leq \lambda v\} \subset]0, 1[^n,$$

into itself. By Brouwer fixed point Theorem we know that H has a fixed point ω in K . This is an endemic equilibrium since $0 \ll \varepsilon v \leq \omega$.

It remains to show the uniqueness.

Lemma 2.5. If $\omega \gg 0$ is a strongly endemic equilibrium and if \bar{x} is another equilibrium then $\bar{x} \leq \omega$.

Proof. Let $\xi = \max_{i=1, \dots, n} \frac{\bar{x}_i}{\omega_i}$. We have $\bar{x} \leq \xi \omega$ and there exists an index i_0 such that $\bar{x}_{i_0} = \xi \omega_{i_0}$. Since A is nonnegative and \bar{x} a fixed point of H we have the following inequalities

$$\bar{x}_{i_0} = \frac{(A \bar{x})_{i_0}}{1 + (A \bar{x})_{i_0}} \leq \frac{(A \xi \omega)_{i_0}}{1 + (A \xi \omega)_{i_0}} = \frac{\xi (A \omega)_{i_0}}{1 + \xi (A \omega)_{i_0}}.$$

By contradiction assume that $\xi > 1$. From the last inequality we have

$$\bar{x}_{i_0} < \frac{\xi (A \omega)_{i_0}}{1 + (A \omega)_{i_0}}.$$

But since $\bar{\omega}$ is a fixed point

$$\bar{x}_{i_0} < \frac{\xi (A \omega)_{i_0}}{1 + (A \omega)_{i_0}} = \xi \omega_{i_0} = \bar{x}_{i_0}.$$

Therefore we obtain a contradiction. ■

We need a second lemma to end the proof.

Lemma 2.6. If $\omega > 0$ is an endemic equilibrium and if A is irreducible then $\omega \gg 0$.

Proof. Since $\omega > 0$ and A is irreducible, then we have $A \omega \gg 0$. Since components of ω are given by

$$\omega_j = \frac{(A \omega)_j}{1 + (A \omega)_j} > 0,$$

the assertion of the lemma is obtained. ■

The two lemmas prove that there exists an unique strongly endemic equilibrium.

2.3. A Theorem on Stability

To study the stability we need the following result which can be considered as a dual result to LaSalle's theorem [40].

Theorem 2.7. Let G be an open set, containing the origin, which is positively invariant for the system $\dot{x} = A(x).x$, where $A(x)$ is a Metzler matrix, depending continuously on x . We assume that there exists $c^T \gg 0$ such that $c^T A(x) \ll 0$ for any $x \in G, x \neq 0$. Then the origin is globally asymptotically stable on G .

Proof. Let us consider on G the Lyapunov function

$$V(x) = \sum_{i=1}^n c_i |x_i|.$$

We define $\varepsilon_z = \text{sign}(z)$, i.e. $|x_i| = \varepsilon_{x_i} x_i$. This function is locally Lipschitz. The Dini derivative can be defined [40]. We have

$$\begin{aligned} \dot{V} &= \sum_{i=1}^n c_i \varepsilon_{x_i} \dot{x}_i \\ &= \sum_{i=1}^n c_i \varepsilon_{x_i} \sum_{j=1}^n a_{ij} x_j \\ &= \sum_{i=1}^n \sum_{j=1}^n c_i \varepsilon_{x_i} a_{ij} x_j \\ &= \sum_{j=1}^n \varepsilon_{x_j} x_j \sum_{i=1}^n c_i \varepsilon_{x_j} \varepsilon_{x_i} a_{ij} \\ &= \sum_{j=1}^n \varepsilon_{x_j} x_j \left[c_j a_{jj} + \sum_{i \neq j} c_i \varepsilon_{x_j} \varepsilon_{x_i} a_{ij} \right] \\ &\leq \sum_{j=1}^n \varepsilon_{x_j} x_j \left[c_j a_{jj} + \sum_{i \neq j} c_i a_{ij} \right] = \sum_{j=1}^n |x_j| (c^T A)_j \leq 0. \end{aligned}$$

Since $c^T A(x) \ll 0$ on G , then the function \dot{V} is negative definite. This ends the proof by the Lyapunov theorem. ■

2.4. Global Stability of the DFE

We have the following result.

Theorem 2.8. The DFE of the system (2.1), which is the origin, is globally asymptotically stable if and only if $\mathcal{R}_0 \leq 1$.

Proof. Assume that $\mathcal{R}_0 = \rho(-D^{-1}B) \leq 1$. We have seen from Proposition 2.3 that this is equivalent to the stability of the matrix $D + N$. From the Perron-Frobenius theorem, since $D + B$ is irreducible, it follows that there exists an eigenvector $c \gg 0$ such that $(D + B)^T c = \alpha(D + B)c$. We choose the Lyapunov function

$$V(x) = \langle c | x \rangle,$$

positive definite on \mathbb{R}_+^n and we have

$$\dot{V}(x) = \langle (D + B)^T c | x \rangle - \langle \text{diag}(x)Bx | c \rangle \leq 0.$$

If $D + B$ is stable, i.e. $\alpha(D + B) < 0$, the proof is finished, since this quantity is negative definite. It remains to study the case where $\alpha(D + B) = 0$, or equivalently $\mathcal{R}_0 = 1$.

We apply Lasalle's invariance principle. We consider the largest invariant set contained in

$$E = \{x \mid \text{diag}(x)Bx = 0\}.$$

The irreducibility of B implies $\mathcal{L} = \{0\}$. Indeed if $x \in \mathcal{L} \subset E$ we have for all (i, j) , $x_i \sum_j \beta_{ij} x_j = 0$.

The quantities are positive, this implies that for any couple of indices $\beta_{ij} x_i x_j = 0$. By contradiction assume that i_0 is such that $x_{i_0} \neq 0$. There exists an index i_1 such that $\beta_{i_1, i_0} \neq 0$, from the irreducibility of B . It follows $x_{i_1} = 0$. The trajectory $x(t)$ from x , satisfies for a small positive time $x(t)_{i_0} \neq 0$. Hence $x(t)_{i_1} = 0$. By invariance of \mathcal{L} we must have

$$\dot{x}_{i_1} = - \sum_j \beta_{i_1, j} x_j = 0.$$

Which in turn implies $x_{i_2} = 0$ for any $\beta_{i_1, i_2} \neq 0$. In the other words, if the node i_2 is connected by an oriented path to the node i_1 , then $x_{i_2} = 0$. By a finite induction we deduce that we have $x_i = 0$ for any node connected to the node i_1 . Since by irreducibility [6] the graph associated to B is strongly connected, we have $x_{i_0} = 0$. This gives a contradiction. ■

2.5. Global Stability of the Endemic Equilibrium

Theorem 2.9. The endemic equilibrium of the system (2.1) is globally asymptotically stable on $\mathbb{R}^n \setminus \{0\}$ if and only if $\mathcal{R}_0 > 1$.

Proof. Since $\mathcal{R}_0 > 1$, then there exists an unique equilibrium $\omega \gg 0$. We write (2.4) under new coordinates $x + X + \omega$. Using the definition of ω : $(D + B)\omega - \text{diag}(x)Bx = 0$, we get

$$\dot{X} = [D + \text{diag}(1 - X - \omega)B - \text{diag}(B\omega)]X. \quad (2.6)$$

Since ω is in $]0, 1[$ which is an absorbing set, it is sufficient to consider (2.1) on this set, or equivalently, when $x \leq 1$. In this case $\text{diag}(1 - X - \omega) = \text{diag}(1 - x)$ and the matrix

$$A(X) = D + \text{diag}(1 - X - \omega)B - \text{diag}(B\omega)$$

is Metzler. X is in the compact set $-\omega + [0, 1]^n$.

We apply (2.7). We know that for any irreducible $B \geq 0$, for any Metzler stable D such that $\rho(-D^{-1}B) > 1$ there exists $\omega \gg 0$ such that

$$(D - \text{diag}(B\omega) + B)\omega = 0.$$

In other words $A(-\omega)$ satisfies $A(-\omega)\omega = 0$. From Proposition (2.4) we deduce $\alpha(A(-\omega)) = 0$. Since this matrix is irreducible, and transposing, we know that there exists $c \gg 0$ such that

$$c^T A(-\omega) = c^T (D - \text{diag}(B\omega) + B) = 0.$$

Then for $X + \omega \gg 0$ (i.e. $x \gg 0$, we have

$$c^T A(X) = -c^T (X + \omega) B \ll 0.$$

This proves the stability on $]0, 1[^n$. Since the vector field is strictly entrant, this ends the proof on $\mathbb{R}^n \setminus \{0\}$. ■

3. A Differential Susceptibility and Infectivity Model

We consider the following model

$$\begin{cases} \dot{S} = \Lambda - \mu S - \text{diag}(B I) S \\ \dot{I} = \langle B I | S \rangle e_1 + A I, \end{cases} \quad (3.1)$$

where $S \in \mathbb{R}_+^n$ is the state of susceptible individuals and $I \in \mathbb{R}_+^k$ is the state of infectious. The matrix $B \geq 0$ represents the coefficients of infectivity, actually $B(i, j)$ is the contact and infectivity of I_j in the group S_i . As usual, e_1 is the first vector of the canonical basis of \mathbb{R}^k . Finally, A is a stable Metzler matrix and represents the evolution through the infectious stages. This model encompasses known models of DI, SP, or differential susceptibility models. We generalize the results obtained in [26, 29].

It is straightforward to check that the nonnegative orthant is positively invariant by this system, that there exists a compact positively invariant absorbing set. The DFE is given by $(S^*, 0) \in \mathbb{R}_+^n \times \mathbb{R}_+^k$ where $S^* = \frac{1}{\mu} \Lambda$.

3.1. Basic Reproduction Ratio

We can give a simple elegant formula for the \mathcal{R}_0 (compare with [26, 29]). To obtain \mathcal{R}_0 we can use the techniques developed in [67]. We claim that

$$\mathcal{R}_0 = \langle B(-A^{-1}) e_1 | S^* \rangle. \quad (3.2)$$

We use the expression $(-A^{-1})$ to put the emphasis on the fact that $(-A^{-1}) > 0$ because A is Metzler stable. Using the framework of [67], we denote by $\mathcal{F}_i(S, I)$ the rate of appearance of new infections in compartment i , and by $\mathcal{V}_i(S, I)$ the rate of transfer of individuals in and out the compartment i by all other means. The matrix \mathcal{V} is the ‘‘mass’’ balance of the compartments. Note that our \mathcal{V} is the opposite of the same used in [67]. Then

$$\mathcal{F}(S, I) = \begin{bmatrix} 0 \\ \langle B I | S \rangle e_1 \end{bmatrix},$$

and

$$\mathcal{V}(S, I) = \begin{bmatrix} \Lambda - \mu S - \text{diag}(BI) S \\ AI \end{bmatrix}.$$

The Jacobian matrices are

$$D\mathcal{F}(x, y) = \begin{bmatrix} 0 & 0 \\ e_1 (BI)^T & e_1 S^T B \end{bmatrix}, \quad D\mathcal{V}(x, y) = \begin{bmatrix} -\mu I - \text{diag}(BI) & -\text{diag}(S) B \\ 0 & A \end{bmatrix}$$

Noting that we have sorted the variables in the reverse order in comparison with [67], we set $F = x^* \mathbf{b} \beta^T$ and $V = A$. It is proved in [67] that the basic reproduction number is the spectral radius of the next generation matrix for the model, namely $-FV^{-1}$ computed at the DFE (the minus sign comes from Metzler matrices used in place of M -matrices),

$$\mathcal{R}_0 = \rho(-FV^{-1}) = \rho(e_1 S^{*T} B (-A^{-1})).$$

It is clear that $e_1 S^{*T} B (-A^{-1})$ is a rank one matrix, the only nonzero eigenvalue is given by $S^{*T} B (-A^{-1}) e_1$, which is exactly our claim.

3.2. Global Stability of the DFE

We have the following theorem.

Theorem 3.1. If $\mathcal{R}_0 \leq 1$ then the DFE is globally asymptotically stable on the nonnegative orthant. If $\mathcal{R}_0 > 1$ the DFE is unstable.

Proof. We will introduce some notation to simplify the exposition of the proof. Actually these notations are used in MATLAB and SCILAB. For two matrices M and N of same size we denote by $D = M./N$ the matrix which is defined by $D(i, j) = M(i, j)/N(i, j)$. In the same spirit $L = \ln M$ will denote the matrix defined by $L(i, j) = \ln(M(i, j))$. We can now define the Lyapunov-LaSalle function on $\mathbb{R}_+^n \times \mathbb{R}_+^k \setminus \{S^*\} \times \mathbb{R}_+^k$:

$$V_{DFE}(S, I) = \mathcal{R}_0 \langle \mathbf{1} | S - S^* \rangle - \mathcal{R}_0 \langle S^* | \ln S - \ln S^* \rangle + \langle B(-A^{-1}) I | S^* \rangle.$$

We have, using the fact that $\Lambda = \mu S^*$:

$$\begin{aligned} \dot{V}_{DFE} &= \mu \mathcal{R}_0 \langle \mathbf{1} | S^* \rangle - \mathcal{R}_0 \langle \mathbf{1} | \text{diag}(BI) S \rangle - \mu \mathcal{R}_0 \langle \mathbf{1} | S \rangle \\ &\quad - \mu \mathcal{R}_0 \langle S^* ./ S | S^* \rangle + \mathcal{R}_0 \langle \text{diag}(BI) \mathbf{1} | S^* \rangle + \mu \mathcal{R}_0 \langle \mathbf{1} | S^* \rangle \\ &\quad + \langle BI | S \rangle \langle B(-A^{-1}) e_1 | S^* \rangle - \langle BI | S^* \rangle. \end{aligned} \quad (3.3)$$

Taking into account the formula (3.2) on \mathcal{R}_0 with the relations

$$\langle \mathbf{1} | \text{diag}(BI) S \rangle = \langle BI | S \rangle, \quad \langle \text{diag}(BI) \mathbf{1} | S^* \rangle = \langle BI | S^* \rangle$$

and $\langle \mathbf{1} | S \rangle = \langle S^* | S./S^* \rangle$ the preceding equation becomes

$$\dot{V}_{DFE} = \mu \mathcal{R}_0 \langle \mathbf{2} - S^* ./ S - S./S^* | S^* \rangle + (\mathcal{R}_0 - 1) \langle BI | S^* \rangle.$$

The inequality between the arithmetic and the geometric means and $\mathcal{R}_0 \leq 1$ imply $\dot{V}_{DFE} \leq 0$. The largest invariant set contained in the set $\{(S, I) | \dot{V}_{DFE}(S, I) = 0\}$ satisfies the relation $S = S^*$. Since A is a stable Metzler matrix, by Lasalle's invariance principle [40] the DFE is globally asymptotically stable. This ends the proof. \blacksquare

3.3. Endemic Equilibrium

Theorem 3.2. There exists a unique endemic equilibrium in the nonnegative orthant if and only if $\mathcal{R}_0 > 1$.

Proof. We look for an equilibrium (\bar{S}, \bar{I}) with $\bar{I} > 0$. From the relations

$$\begin{cases} 0 &= \Lambda - \mu \bar{S} - \text{diag}(\bar{B} \bar{I}) \bar{S}, \\ 0 &= \langle \bar{B} \bar{I} | \bar{S} \rangle e_1 + A \bar{I} \end{cases} \quad (3.4)$$

we deduce, since A is Metzler stable, that $\bar{I} = \langle \bar{B} \bar{I} | \bar{S} \rangle (-A^{-1}) e_1$. From the second relation of (3.4) and taking the inner product with e_1 we obtain $\langle \bar{B} \bar{I} | \bar{S} \rangle = -\langle A \bar{I} | e_1 \rangle$. Finally

$$\bar{I} = -\langle A \bar{I} | e_1 \rangle (-A^{-1}) e_1. \quad (3.5)$$

Then to compute \bar{I} it is sufficient to find $-\langle A \bar{I} | e_1 \rangle$.

Again with the expression $\bar{I} = \langle \bar{B} \bar{I} | \bar{S} \rangle (-A^{-1}) e_1$, we get

$$\langle \bar{B} \bar{I} | \bar{S} \rangle = \langle \bar{B} \bar{I} | \bar{S} \rangle \langle B(-A^{-1})e_1 | \bar{S} \rangle.$$

If $\langle \bar{B} \bar{I} | \bar{S} \rangle \neq 0$ then we have

$$\langle B(-A^{-1})e_1 | \bar{S} \rangle = 1. \quad (3.6)$$

From the first equation in (3.4) we have

$$\bar{S} = [\text{diag}(\mu \mathbf{1} + B\bar{I})]^{-1} \Lambda = \left[\text{diag} \left(\mathbf{1} + \frac{1}{\mu} B\bar{I} \right) \right]^{-1} S^*. \quad (3.7)$$

Using this value of \bar{S} and of $B\bar{I}$ in (3.6) gives

$$\left\langle B(-A^{-1})e_1 \mid \left[\text{diag} \left(\mathbf{1} - \frac{\langle A \bar{I} | e_1 \rangle}{\mu} B(-A^{-1})e_1 \right) \right]^{-1} S^* \right\rangle = 1.$$

In other words $-\langle A \bar{I} | e_1 \rangle$ is a solution of $H(x) = 1$ with

$$H(x) = \left\langle B(-A^{-1})e_1 \mid \left[\text{diag} \left(\mathbf{1} + \frac{x}{\mu} B(-A^{-1})e_1 \right) \right]^{-1} S^* \right\rangle.$$

It is clear that $H(x)$ is a strictly decreasing function satisfying $\lim_{x \rightarrow +\infty} H(x) = 0$. Then a unique positive solution exists if and only if $H(0) > 1$. Since $H(0) = \mathcal{R}_0$ we have a positive solution. Since, from (3.7) we have $\bar{S} \gg 0$ and from (3.5), with $-\langle A \bar{I} | e_1 \rangle > 0$, $\bar{I} > 0$, then the equilibrium is endemic. Moreover $\langle \bar{B} \bar{I} | \bar{S} \rangle \neq 0 > 0$. From the preceding analysis we see that if $\mathcal{R}_0 = 1$ then the unique equilibrium is the DFE. In the case $\mathcal{R}_0 < 1$ we have $\bar{I} < 0$, that is the equilibrium is not biologically feasible. ■

3.4. Global Stability of the Endemic Equilibrium

To prove the global stability of the endemic equilibrium we need to study in more detail the structure of A . We will treat in this section one example. For the sake of brevity we will consider a model of two susceptible classes and two infective classes with stage progression. It is not difficult, but certainly more involved, to treat exactly in the same way the case of n susceptible compartments and k infectious compartments. The compartmental model is represented in figure 1.

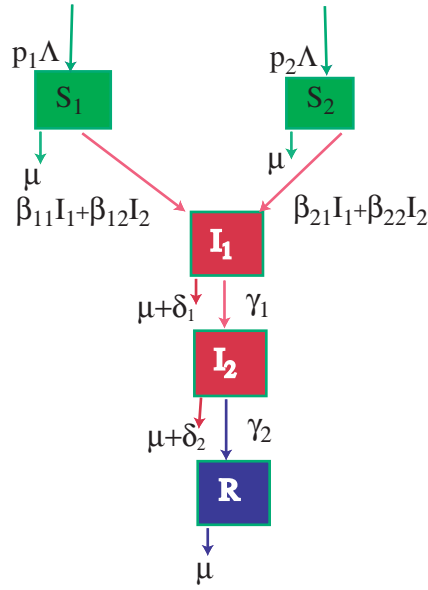


Figure 1: The two susceptible classes and two infectious classes model

The model is given by the following system of ordinary differential equations.

$$\begin{cases} \dot{S}_1 = p_1 \Lambda - \mu S_1 - \beta_{11} I_1 S_1 - \beta_{12} I_2 S_1 \\ \dot{S}_2 = p_2 \Lambda - \mu S_2 - \beta_{21} I_1 S_2 - \beta_{22} I_2 S_2 \\ \dot{I}_1 = \beta_{11} I_1 S_1 + \beta_{12} I_2 S_1 + \beta_{21} I_1 S_2 + \beta_{22} I_2 S_2 - (\mu + \gamma_1 + \delta_1) I_1 \\ \dot{I}_2 = \gamma_1 I_1 - (\mu + \gamma_1 + \delta_2) I_2 \\ \dot{R} = \gamma_2 I_2 - \mu R. \end{cases} \quad (3.8)$$

Theorem 3.3. If $\mathcal{R}_0 > 1$, then the unique endemic equilibrium is globally asymptotically stable. The basic reproduction number is given by

$$\mathcal{R}_0 = \frac{\gamma_1(\beta_{12}S_1^* + \beta_{22}S_2^*) + (\mu + \gamma_1 + \delta_2)(\beta_{11}S_1^* + \beta_{21}S_2^*)}{(\mu + \gamma_1 + \delta_1)(\mu + \gamma_1 + \delta_2)}.$$

Proof. The basic reproduction ratio is obtained by applying (3.2). From the general theory we know that there exists a unique endemic equilibrium which satisfies the following relations

$$\begin{cases} p_1 \Lambda = \mu \bar{S}_1 + \beta_{11} \bar{I}_1 \bar{S}_1 + \beta_{12} \bar{I}_2 \bar{S}_1 \\ p_2 \Lambda = \mu \bar{S}_2 + \beta_{21} \bar{I}_1 \bar{S}_2 + \beta_{22} \bar{I}_2 \bar{S}_2 \\ \beta_{11} \bar{I}_1 \bar{S}_1 + \beta_{12} \bar{I}_2 \bar{S}_1 + \beta_{21} \bar{I}_1 \bar{S}_2 + \beta_{22} \bar{I}_2 \bar{S}_2 = (\mu + \gamma_1 + \delta_1) \bar{I}_1 \\ \gamma_1 \bar{I}_1 = (\mu + \gamma_1 + \delta_2) \bar{I}_2 \\ \gamma_2 \bar{I}_2 = \mu \bar{R}. \end{cases} \quad (3.9)$$

Let us consider a possible Lyapunov function

$$V_{EE} = (S_1 - \bar{S}_1 \ln S_1) + (S_2 - \bar{S}_2 \ln S_2) + (I_1 - \bar{I}_1 \ln I_1) + \left(\frac{\beta_{12}\bar{S}_1 + \beta_{22}\bar{S}_2}{(\mu + \gamma_1 + \delta_2)} \right) (I_2 - \bar{I}_2 \ln I_2)$$

Setting $d = \frac{\beta_{12}\bar{S}_1 + \beta_{22}\bar{S}_2}{(\mu + \gamma_1 + \delta_2)}$, its derivative along the trajectories of (3.8) is

$$\begin{aligned} \dot{V}_{EE} = & \left[p_1 \Lambda - \mu S_1 - \beta_{11} I_1 S_1 - \beta_{12} I_2 S_1 - p_1 \Lambda \frac{\bar{S}_1}{S_1} + \mu \bar{S}_1 + \beta_{11} I_1 \bar{S}_1 + \beta_{12} I_2 \bar{S}_1 \right] \\ & + \left[p_2 \Lambda - \mu S_2 - \beta_{21} I_1 S_2 - \beta_{22} I_2 S_2 - p_2 \Lambda \frac{\bar{S}_2}{S_2} + \mu \bar{S}_2 + \beta_{21} I_1 \bar{S}_2 + \beta_{22} I_2 \bar{S}_2 \right] \\ & + \left[\beta_{11} I_1 S_1 + \beta_{12} I_2 S_1 + \beta_{21} I_1 S_2 + \beta_{22} I_2 S_2 - (\mu + \gamma_1 + \delta_1) I_1 \right. \\ & \left. - \beta_{11} \bar{I}_1 S_1 - \beta_{12} I_2 \frac{\bar{I}_1}{I_1} S_1 - \beta_{21} \bar{I}_1 S_2 - \beta_{22} I_2 \frac{\bar{I}_1}{I_1} S_2 + (\mu + \gamma_1 + \delta_1) \bar{I}_1 \right] \\ & + d \left[\gamma_1 I_1 - (\mu + \gamma_1 + \delta_2) I_2 - \gamma_1 I_1 \frac{\bar{I}_2}{I_2} + (\mu + \gamma_1 + \delta_2) \bar{I}_2 \right]. \end{aligned}$$

By using the endemic relations in the system (3.9) we obtain,

$$\begin{aligned} \dot{V}_{EE} = & \left[\mu \bar{S}_1 + \beta_{11} \bar{I}_1 \bar{S}_1 + \beta_{12} \bar{I}_2 \bar{S}_1 - \mu \bar{S}_1 \frac{S_1}{\bar{S}_1} \right. \\ & \left. - (\mu \bar{S}_1 + \beta_{11} \bar{I}_1 \bar{S}_1 + \beta_{12} \bar{I}_2 \bar{S}_1) \frac{\bar{S}_1}{S_1} + \mu \bar{S}_1 + \beta_{11} I_1 \bar{S}_1 + \beta_{12} I_2 \bar{S}_1 \right] \\ & + \left[\mu \bar{S}_2 + \beta_{21} \bar{I}_1 \bar{S}_2 + \beta_{22} \bar{I}_2 \bar{S}_2 - \mu \bar{S}_2 \frac{S_2}{\bar{S}_2} \right. \\ & \left. - (\mu \bar{S}_2 + \beta_{21} \bar{I}_1 \bar{S}_2 + \beta_{22} \bar{I}_2 \bar{S}_2) \frac{\bar{S}_2}{S_2} + \mu \bar{S}_2 + \beta_{21} I_1 \bar{S}_2 + \beta_{22} I_2 \bar{S}_2 \right] - (\mu + \gamma_1 + \delta_1) I_1 \\ & - \beta_{11} \bar{I}_1 \bar{S}_1 \frac{S_1}{\bar{S}_1} - \beta_{12} \bar{I}_2 \bar{S}_1 \frac{S_1}{\bar{S}_1} \frac{\bar{I}_1}{I_1} \frac{I_2}{\bar{I}_2} + \beta_{21} \bar{I}_1 \bar{S}_2 \frac{S_2}{\bar{S}_2} - \beta_{22} \bar{I}_2 \bar{S}_2 \frac{S_2}{\bar{S}_2} \frac{\bar{I}_1}{I_1} \frac{I_2}{\bar{I}_2} \\ & + \beta_{11} \bar{I}_1 \bar{S}_1 + \beta_{12} \bar{I}_2 \bar{S}_1 + \beta_{21} \bar{I}_1 \bar{S}_2 + \beta_{22} \bar{I}_2 \bar{S}_2 \\ & + d \left[\gamma_1 I_1 - (\mu + \gamma_1 + \delta_2) I_2 - \gamma_1 I_1 \frac{\bar{I}_2}{I_2} + \gamma_1 \bar{I}_1 \right] \\ = & \mu \bar{S}_1 \left[2 - \frac{\bar{S}_1}{S_1} - \frac{S_1}{\bar{S}_1} \right] + \mu \bar{S}_2 \left[2 - \frac{\bar{S}_2}{S_2} - \frac{S_2}{\bar{S}_2} \right] \\ & + \beta_{11} \bar{I}_1 \bar{S}_1 \left[2 - \frac{\bar{S}_1}{S_1} - \frac{S_1}{\bar{S}_1} \right] + \beta_{12} \bar{I}_2 \bar{S}_1 \left[2 - \frac{\bar{S}_1}{S_1} - \frac{S_1}{\bar{S}_1} \frac{\bar{I}_1}{I_1} \frac{I_2}{\bar{I}_2} \right] \\ & + \beta_{21} \bar{I}_1 \bar{S}_2 \left[2 - \frac{\bar{S}_2}{S_2} - \frac{S_2}{\bar{S}_2} \right] + \beta_{22} \bar{I}_2 \bar{S}_2 \left[2 - \frac{\bar{S}_2}{S_2} - \frac{S_2}{\bar{S}_2} \frac{\bar{I}_1}{I_1} \frac{I_2}{\bar{I}_2} \right] \\ & + (\beta_{11} \bar{S}_1 + \beta_{21} \bar{S}_2 + d \gamma_1 - (\mu + \gamma_1 + \delta_1)) I_1 \\ & + (\beta_{12} \bar{S}_1 + \beta_{22} \bar{S}_2 - d (\mu + \gamma_1 + \delta_2)) I_2 - d \gamma_1 \bar{I}_1 \frac{I_1}{\bar{I}_1} \frac{\bar{I}_2}{I_2} + d \gamma_1 \bar{I}_1. \end{aligned}$$

Using the expression for d , we observe that

$$\beta_{12}\bar{S}_1 + \beta_{22}\bar{S}_2 - d(\mu + \gamma_1 + \delta_2) = 0$$

and

$$\begin{aligned} & \beta_{11}\bar{S}_1 + \beta_{21}\bar{S}_2 + d\gamma_1 - (\mu + \gamma_1 + \delta_1) \\ &= \beta_{11}\bar{S}_1 + \beta_{21}\bar{S}_2 + \frac{\beta_{12}\bar{S}_1 + \beta_{22}\bar{S}_2}{(\mu + \gamma_1 + \delta_2)}\gamma_1 - (\mu + \gamma_1 + \delta_1) \\ &= \frac{(\mu + \gamma_1 + \delta_2)(\beta_{11}\bar{S}_1 + \beta_{21}\bar{S}_2) + \gamma_1(\beta_{12}\bar{S}_1 + \beta_{22}\bar{S}_2)}{(\mu + \gamma_1 + \delta_2)} - (\mu + \gamma_1 + \delta_1) \\ &= (\mu + \gamma_1 + \delta_1) \left[\frac{(\mu + \gamma_1 + \delta_2)(\beta_{11}\bar{S}_1 + \beta_{21}\bar{S}_2) + \gamma_1(\beta_{12}\bar{S}_1 + \beta_{22}\bar{S}_2)}{(\mu + \gamma_1 + \delta_1)(\mu + \gamma_1 + \delta_2)} - 1 \right] \\ &= 0. \end{aligned}$$

Substituting the endemic relations in the third equation of system (3.9), we obtain

$$\begin{aligned} & \beta_{11}\bar{I}_1\bar{S}_1 + \beta_{12}\bar{I}_2\bar{S}_1 + \beta_{21}\bar{I}_1\bar{S}_2 + \beta_{22}\bar{I}_2\bar{S}_2 = (\mu + \gamma_1 + \delta_1)\bar{I}_1, \\ & (\beta_{11}\bar{S}_1 + \beta_{21}\bar{S}_2 + \frac{\gamma_1}{(\mu + \gamma_1 + \delta_2)}(\beta_{12}\bar{S}_1 + \beta_{22}\bar{S}_2)) = (\mu + \gamma_1 + \delta_1), \\ & \frac{(\mu + \gamma_1 + \delta_2)(\beta_{11}\bar{S}_1 + \beta_{21}\bar{S}_2) + \gamma_1(\beta_{12}\bar{S}_1 + \beta_{22}\bar{S}_2)}{(\mu + \gamma_1 + \delta_1)(\mu + \gamma_1 + \delta_2)} = 1, \end{aligned}$$

$$\begin{aligned} d\gamma_1\bar{I}_1 &= \frac{\beta_{12}\bar{S}_1 + \beta_{22}\bar{S}_2}{(\mu + \gamma_1 + \delta_2)}\gamma_1\bar{I}_1 \\ &= \frac{\gamma_1}{(\mu + \gamma_1 + \delta_2)}(\beta_{12}\bar{I}_1\bar{S}_1 + \beta_{22}\bar{I}_1\bar{S}_2) \\ &= \beta_{12}\bar{I}_2\bar{S}_1 + \beta_{22}\bar{I}_2\bar{S}_2. \end{aligned}$$

and finally we have the following expression for \dot{V}_{EE}

$$\begin{aligned} \dot{V}_{EE} &= \mu\bar{S}_1 \left[2 - \frac{\bar{S}_1}{S_1} - \frac{S_1}{\bar{S}_1} \right] + \mu\bar{S}_2 \left[2 - \frac{\bar{S}_2}{S_2} - \frac{S_2}{\bar{S}_2} \right] \\ &+ \beta_{11}\bar{I}_1\bar{S}_1 \left[2 - \frac{\bar{S}_1}{S_1} - \frac{S_1}{\bar{S}_1} \right] + \beta_{12}\bar{I}_2\bar{S}_1 \left[3 - \frac{\bar{S}_1}{S_1} - \frac{S_1}{\bar{S}_1} \frac{\bar{I}_1}{I_1} \frac{I_2}{\bar{I}_2} - \frac{I_1}{\bar{I}_1} \frac{\bar{I}_2}{I_2} \right] \\ &+ \beta_{21}\bar{I}_1\bar{S}_2 \left[2 - \frac{\bar{S}_2}{S_2} - \frac{S_2}{\bar{S}_2} \right] + \beta_{22}\bar{I}_2\bar{S}_2 \left[3 - \frac{\bar{S}_2}{S_2} - \frac{S_2}{\bar{S}_2} \frac{\bar{I}_1}{I_1} \frac{I_2}{\bar{I}_2} - \frac{I_1}{\bar{I}_1} \frac{\bar{I}_2}{I_2} \right] \\ &\leq 0 \end{aligned}$$

Using the comparison between the arithmetical and the geometrical means we see that \dot{V}_{EE} is negative definite. This ends the proof of the theorem. \blacksquare

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MULTI-COMPARTMENT MODELS

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ABSTRACT. We consider models with a general structure which, for example, encompasses the so-called DI, SP or DISP models with mass action incidence. We give a very simple formula for the basic reproduction ratio \mathcal{R}_0 . If $\mathcal{R}_0 \leq 1$ we prove that the disease free equilibrium is globally asymptotically stable on the nonnegative orthant. If $\mathcal{R}_0 > 1$, we prove the existence of a unique endemic equilibrium in the positive orthant and give an explicit formula. We prove the global asymptotic stability of the endemic equilibrium, when $\mathcal{R}_0 > 1$ for SP model.

1. Introduction. The objective of this paper is to provide a stability analysis for models with a general structure and mass action incidence. The structure can deal with various complex interactions between different classes of infectiousness. We do not consider difference in susceptibilities as it is the case for example in [10]. We also consider mass action incidence. Mass action incidence is plausible in number of cases (see e.g [15]) or when variables considered are concentration (as number by unit area). Or as was pointed out in [21, 38], if the number of contacts per person, in general, is a function of the population size. For certain diseases, such as influenza and measles, or in certain ranges of population sizes, it is appropriate to assume that the number of contacts is proportional to the population size. Then the rate of infection has a bilinear form.

Our structure can handle models with different classes of latency and infectiousness. Models with variation in infectiousness have been considered since a long time in the literature [28, 1, 26, 42, 43]. Many reasons can be invoked to consider such models. If the infectiousness changes over the infectious period, one can model this fact by using different values of β for each stage. Most models of HIV infection are

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with four or more stages of infection. The case of infection with carriers is also such example. This is the case of HBV infection, tuberculosis ([40]), cholera or typhoid. A second reason is that a chain of compartments gives an Erlang distribution for the residence time [28, 23, 36, 35].

Actually introducing different stages in the simple *SEIR* model can be motivated by biological reasons or phenomenological reasons. For example in within-host models of malaria the introduction of different class of parasitised erythrocytes is sensible [14, 13]. On the other side if the density function of residence period in a stage is measured, then a linear chain or parallel linear chains can give a good phenomenological model [24]. The SI models with different infectiousness has now a long story in the literature. The first models has been introduced for the transmission of HIV [28, 2]. These models have been called Staged progression models (SP) in [22], where another structure is also introduced the differential infectivity models (DI).

Our models encompass the so-called staged-progression models and differential infectivity models with mass action incidence, but can also represent more complex relations between different infectious classes as for example CBPP models (Continuous Bovine Pleuro Pneumonia)[3] [45, 22]. These models represent also within-host models of parasites such that HIV or malaria plasmodium [7, 14, 13, 41]

We consider k latent classes E_1, \dots, E_k and $n - k$ infectious classes I_{k+1}, \dots, I_n . The SP models with latent classes are given by the following system.

$$\left\{ \begin{array}{l} \dot{S} = \varphi(S) - S \sum_{i=k+1}^n \beta_i I_i \\ \dot{E}_1 = S \sum_{i=k+1}^n \beta_i I_i - \alpha_1 E_1 \\ \dots \\ \dot{E}_k = \gamma_{k-1} E_{k-1} - \alpha_h E_k \\ \dot{I}_{k+1} = \gamma_k E_k - \alpha_{k+1} I_{k+1} \\ \dots \\ \dot{I}_n = \gamma_{n-1} I_{n-1} - \alpha_n I_n \\ \dot{R} = \gamma_{n+1} I_n - \alpha_{n+1} R \end{array} \right. \quad (1)$$

where S is the density of susceptible individuals (for example area density), the function φ is usually $\varphi(S) = \Lambda - \mu_S S$, I_i is the density of infectious individuals of class i . We denote by $\alpha_i = \gamma_i + \mu_i$ the sum of the progression rate in the next compartment and the specific death of the i -th compartment. For the last compartment α_{n+1} is simply the death-rate, however we keep this notation for homogeneity of the formulation.

We will consider this system with a class C^1 function φ such that the system $\dot{x} = \varphi(x)$ has a unique globally asymptotically stable equilibrium $x^* > 0$ on \mathbb{R}^+ . This means that the population, when there is no disease, stabilizes to a demographic equilibrium x^* .

With this hypothesis $\alpha_i \geq \gamma_i$. We remark that we do not need this assumption on the parameters. In some models, as for example in within-host models for HIV or Malaria ([14, 7]), some γ_i can be greater than α_i to take in account the multiplication of parasites when leaving an infected cell.

In these models different class of latent (infected but not infectious) individuals can also be introduced, simply in setting some β_i to 0, giving a *SEIR* staged-progression model.

On the contrary a DI model is a model in which individuals enter a specific group when they become infected and stay in that group until they are no longer involved in transmission.

$$\begin{cases} \dot{S} = \Lambda - \mu_S S - S \sum_{i=1}^n \beta_i I_i \\ \dot{I}_1 = \pi_1 S \sum_{i=1}^n \beta_i I_i - \alpha_1 I_1 \\ \dots \\ \dot{I}_i = \pi_i S \sum_{i=1}^n \beta_i I_i - \alpha_i I_i \\ \dots \\ \dot{I}_n = \pi_n S \sum_{i=1}^n \beta_i I_i - \alpha_n I_n \\ \dot{R} = \sum_{i=1}^n \gamma_i I_i - \alpha_n R \end{cases} \quad (2)$$

with $\sum_{i=1}^n \pi_i = 1$.

The meaning of the coefficients is the same as before.

Finally DISP models can be considered, i.e. parallel linear chains of different length. All these models can be written under one single form.

The models considered in this paper have the following structure.

$$\begin{cases} \dot{x} = \varphi(x) - x \beta^T . y \\ \dot{y} = (x \beta^T . y) \mathbf{b} + A y = (A + \mathbf{b} \beta^T) y \end{cases} \quad (3)$$

where $x \in \mathbb{R}_+$ represents the class of susceptible individuals, $y \in \mathbb{R}_+^n$, as a column vector, represents the different class of latent, infectious and removed individuals. The different infectiousness coefficient are in $\beta \in \mathbb{R}_+^k$ a nonnegative vector. We denote by β^T the transposition, hence $\beta^T . y$ is the inner product of β and y . The vector $\mathbf{b} \in \mathbb{R}_+^n$ is nonnegative and A is a stable Metzler matrix [25, 37] (A Metzler matrix is a matrix with off-diagonal entries nonnegative, some authors also call these matrices quasipositive)

The function φ represents the demography of the population. For example φ can be the widely used function $\varphi(x) = \Lambda - \mu_x x$. Hence we assume that φ is of class \mathcal{C}^1 function and that the system $\dot{x} = \varphi(x)$ has a unique positive, globally asymptotic equilibrium x^* on \mathbb{R}^+ . In other words when there is no disease the population stabilize to a demographic equilibrium x^* . This hypothesis is usual in the literature.

There are two schools for matrices like A . The first one, uses Metzler matrices and is represented by J.A. Jacquez, D. Luenberger or H. Thieme [24, 25, 37, 44]. The second one uses M -matrices, the opposite of Metzler matrices, represented by Bermans and Plemmons or van den Driessche ([5, 45]). We choose to stick to the Jacquez point of view, natural for compartment models, since our matrix A represents the exchanges between compartments (and also with the outside world).

Or expressed differently $\dot{y} = Ay$ describes the dynamic of the infected compartments when the recruitment of infected is blocked.

In this paper, we will give a simple formula for \mathcal{R}_0 , prove that if $\mathcal{R}_0 \leq 1$ then the disease free equilibrium is globally asymptotically stable, prove that if $\mathcal{R}_0 > 1$ there exists a unique endemic equilibrium. We will prove the global stability for SP and DI models. These results generalize the results obtained in [21, 22]

2. Notations and applications. We show in this section how our structure can take into account the DI,SP, and DISP models with mass action incidence. It is straightforward to represent more complex relation between infected (exposed and infectious) compartments.

The usual euclidean norm of a vector x is denoted by $\|x\|_2^2$. The canonical basis of \mathbb{R}^n is denoted by $\{e_1, \dots, e_n\}$. For example $e_1 = [1, 0, \dots, 0]^T$.

If $x \in \mathbb{R}^n$ we denote by x_i the i -th component of x . Equivalently $x_i = x^T \cdot e_i$.

For matrices A, B we write $A \leq B$ if $a_{ij} \leq b_{ij}$ for all i and j , $A < B$ if $A \leq B$ and $A \neq B$, $A \ll B$ if $a_{ij} < b_{ij}$ for all i and j . For a matrix A we denote by $A(i, j)$ the entry at the row i , column j .

I_n denotes the $n \times n$ identity matrix. $I_{m,n}$ the $m \times n$ matrix with 1 on the diagonal. $0_{p,q}$ is the $p \times q$ zero matrix.

We also denote by A^{-T} the transpose of the inverse of A .

For later references we precise in this section the different values of the parameters of the general system (3) for different particular system.

2.1. SP systems. The system (1) is a particular case of (3) with

$$A = \begin{bmatrix} -\alpha_1 & 0 & 0 & \dots & 0 \\ \gamma_1 & -\alpha_2 & 0 & \dots & 0 \\ 0 & \gamma_2 & -\alpha_3 & \dots & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots \\ 0 & \dots & 0 & \gamma_n & -\alpha_{n+1} \end{bmatrix}$$

$$\beta = [\beta_1, \dots, \beta_n, 0]^T ; \quad \mathbf{b} = e_1$$

It is sufficient to consider the k first components of β equal to 0 to obtain a $SE_1 \dots E_k I_{k+1} \dots E_n R$ model

2.2. DI systems. The system 2 is can be written as (3) with

$$A = \begin{bmatrix} -\alpha_1 & 0 & 0 & \dots & 0 \\ 0 & -\alpha_2 & 0 & \dots & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots \\ 0 & \dots & 0 & -\alpha_n & 0 \\ \gamma_1 & \dots & \gamma_{n-2} & \gamma_{n-1} & -\alpha_{n+1} \end{bmatrix}$$

$$\beta = [\beta_1, \dots, \beta_n, 0]^T ; \quad \mathbf{b} = \pi_1 e_1 + \dots + \pi_n e_n$$

2.3. DISP systems. Similarly we can define DISP models of k parallel linear chains of different lengths. Introducing dummy class we can suppose that the length of the parallel chains are equal. Then the system can be written under the general form (3) with A a diagonal bloc matrix $A = \text{diag}(A_1, \dots, A_k)$ where each A_i is a matrix similar to A defined in section 2.1, and if we identify the state space of the system with $\mathbb{R} \times (\mathbb{R}^n)^k$ the vector \mathbf{b} is

$$\mathbf{b} = \pi_1 e_1 + \dots + \pi_n e_n$$

where e_i is the first vector of the canonical basis of the i -th component of $(\mathbb{R}^n)^k$.

3. Dissipativity and global stability of the DFE. We consider the general structured model (3). We only assume that the coefficients are nonnegative. We denote by x^* the global asymptotic equilibrium of φ on \mathbb{R} . This is the demographic equilibria of the population without disease. The disease free equilibrium is then $(x^*, 0, \dots, 0)$.

3.1. Positive Invariance of the nonnegative orthant. With the hypothesis on the parameters of (3) it is straightforward to check the positive invariance of the nonnegative orthant \mathbb{R}_+^{n+1} by this system.

3.2. Boundedness and dissipativity. We will prove that there always exists a convex compact positively invariant absorbing set K_ρ for the system (3).

Since A is Metzler stable matrix (equivalently $-A$ is a M -matrix [5]) there exists a positive vector $c \gg 0$ such that $A^T c \ll 0$. We define

$$V_B(x, y) = c^T \cdot \mathbf{b} x + c^T y$$

Since $c \gg 0$ we have $c \cdot \mathbf{b}^T \gg 0$. The derivative \dot{V}_B of V_B along the trajectories of (3) is

$$\begin{aligned} \dot{V}_B &= c^T \cdot \mathbf{b} \varphi(x) - x c^T \cdot \mathbf{b} \beta^T \cdot y + x c^T \cdot \mathbf{b} \beta^T \cdot y + c^T \cdot A y \\ &= c^T \cdot \mathbf{b} \varphi(x) + c^T \cdot A y \end{aligned} \tag{4}$$

We set $\Phi = \max_{x \in \mathbb{R}_+} \varphi(x)$ and we define

$$\delta = \frac{\|c\|_2 c^T \cdot \mathbf{b} \Phi}{\min_i (-A^T c)_i} + c^T \cdot \mathbf{b} x^* \tag{5}$$

We now consider for $\rho \geq \delta$ the set K_ρ defined by

$$K_\rho = V_B^{-1} [0, \rho] \cap \mathbb{R}_+^{n+1}$$

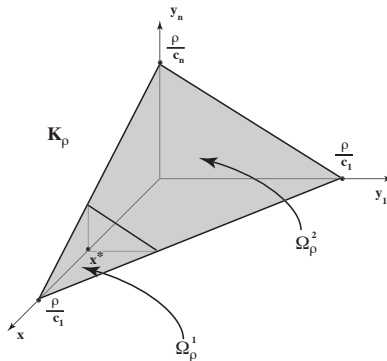


FIGURE 1. simplex

K_ρ is a compact set of the nonnegative orthant which contain $[x^*, 0, \dots, 0]^T$ in its interior. Actually K_ρ is the $n + 1$ -dimensional simplex. We will prove that K_ρ is a compact positively invariant set for (3) if $\rho \geq \delta$. Since the nonnegative orthant

is positively invariant it is sufficient to prove that no trajectory of (3) can leave K_ρ by its boundary Ω_ρ where

$$\Omega_\rho = V^{-1} \{ \rho \} \cap \mathbb{R}_+^{n+1}$$

This is equivalent to prove that $\dot{V} \leq 0$ on Ω_ρ . For this we divide Ω_ρ in two parts

$$\Omega_\rho^1 = \Omega_\rho \cap \{ (x, y) \in \mathbb{R}_+^{n+1} \mid x \geq x^* \}$$

and

$$\Omega_\rho^2 = \Omega_\rho \cap \{ (x, y) \in \mathbb{R}_+^{n+1} \mid x^* \geq x \}$$

Since x^* is globally asymptotically stable, on Ω_ρ^1 , $\varphi(x) \leq 0$ and by (4), we have $\dot{V} \leq 0$ on Ω_ρ^1 .

By definition of Ω_ρ on Ω_ρ^2 we have $V_B(x, y) = \rho = c^T \mathbf{b} x + c^T y$.

By Cauchy-Schwarz inequality, on Ω_ρ^2 we have

$$\|c\|_2 \|y\|_2 \geq \langle c^T \mid y \rangle = \rho - c^T \cdot \mathbf{b} x \geq \delta - c^T \cdot \mathbf{b} x^* = \frac{\|c\|_2 c^T \cdot \mathbf{b} \Phi}{\min_i (-A^T c)_i}$$

Which implies

$$\|y\|_2 \geq \frac{c^T \mathbf{b} \Phi}{\min_i (-A^T c)_i}$$

Therefore on Ω_ρ^2 the following inequalities are satisfied

$$-c^T \cdot A y \geq \min_i (-A^T c)_i (y_1 + \dots + y_n) \geq \min_i (-A^T c)_i \|y\|_2 \geq c^T \cdot \mathbf{b} \Phi$$

Hence

$$\dot{V}_B = c^T \cdot \mathbf{b} \varphi(x) + c^T \cdot A y \leq c^T \cdot \mathbf{b} \Phi + c^T \cdot A y \leq 0$$

on Ω_ρ^2 .

This ends the proof of the positive invariance of Ω_ρ for $\rho \geq \delta$.

Since $V(x, y) \rightarrow +\infty$ when $(x, y) \rightarrow +\infty$, any initial condition (x_0, y_0) in the nonnegative orthant is contained in a K_ρ . This proves that any trajectory is forward bounded.

We will now prove that K_ρ is a compact absorbing set for any $\rho > \delta$. An absorbing set D is a neighborhood such that a trajectory of the system starting from any initial condition enters and remains in D for a sufficiently large time T . Let consider an initial condition (x_0, y_0) and the forward trajectory from this initial condition. We assume $(x_0, y_0) \notin K_\rho$ otherwise since we have proved that K_ρ is positively invariant we are finished. We will prove by contradiction that this trajectory enters K_ρ . We suppose, by contradiction, that the trajectory stays always out of K_ρ . In other words for any points (x, y) of the trajectory $V(x, y) > \rho > \delta$. An analogous computation as the preceding one implies $\dot{V} \leq 0$. The function V is decreasing on the trajectory. Now since any trajectory is bounded the set Ω_{x_0, y_0} of ω -limit points of the trajectory is non empty and by hypothesis is contained in the closure of the complementary set of K_ρ , the set $\overline{\{(x, y) \notin K_\rho\}}$. By LaSalle's invariance principle $\Omega_{x_0, y_0} \subset \{\dot{V} = 0\} \cap \overline{\{(x, y) \notin K_\rho\}}$. Since $\dot{V}(x, y) = c^T \cdot \beta \varphi(x) + c^T \cdot A y$ we have $\{\dot{V} = 0\} = \{(x^*, 0, \dots, 0)\}$. The point $(x^*, 0, \dots, 0)$ is in the interior of K_ρ , this implies that $\Omega_{x_0, y_0} = \emptyset$, hence a contradiction.

3.3. Basic reproduction ratio. As usual the basic reproduction number is the expected number of secondary cases produced in a completely susceptible population, by a typical infected individual during its entire period of infectiousness [17, 45, 9, 8]. We can give a simple elegant formula for the \mathcal{R}_0 (compare with [22, 38]).

To obtain \mathcal{R}_0 we can use the techniques developed in [45]. We claim

$$\mathcal{R}_0 = x^* \beta^T (-A^{-1}) \mathbf{b} \quad (6)$$

We use the expression $(-A^{-1})$ to put the emphasis on the fact that $(-A^{-1}) > 0$ because A is Metzler stable.

Using the frame of [45], we define by $\mathcal{F}_i(x, y)$ the rate of appearance of new infections in compartment i , and by $\mathcal{V}_i(x, y)$ the rate of transfer of individuals in and out the compartment i by all other means. The matrix \mathcal{V} is the “mass” balance of the compartments. Note that our \mathcal{V} is the opposite of the same used in [45]. Then

$$\mathcal{F}(x, y) = \begin{bmatrix} 0 \\ x \beta^T .y \mathbf{b} \end{bmatrix}$$

and

$$\mathcal{V}(x, y) = \begin{bmatrix} \varphi(x) - x \beta^T .y \\ Ay \end{bmatrix}$$

The Jacobian matrices are

$$D\mathcal{F}(x, y) = \begin{bmatrix} 0 & 0 \\ \beta^T .y \mathbf{b} & x \mathbf{b} \beta^T \end{bmatrix} \quad D\mathcal{V}(x, y) = \begin{bmatrix} \varphi'(x) - \beta^T .y & -x \beta^T \\ 0 & A \end{bmatrix}$$

Noting that we have sorted the variables in the reverse order of [45], we set $F = x^* \mathbf{b} \beta^T$ and $V = A$

It is proved in [45] that the basic reproduction number is the spectral radius of the next generation matrix for the model, namely $-FV^{-1}$ (the minus sign comes from Metzler matrices used in place of M -matrices)

$$\mathcal{R}_0 = \rho(-FV^{-1}) = \rho(-x^* \mathbf{b} \beta^T A^{-1})$$

It is clear that $-x^* \mathbf{b} \beta^T A^{-1}$ is a rank one matrix, the only nonzero eigenvalue is given by $-x^* \beta^T A^{-1} \mathbf{b}$, which exactly our claim.

3.4. Equilibria. We will also obtain a simple formula for the equilibria.

There exists an evident equilibrium for (3) which is $(x^*, 0, \dots, 0)$. We call this equilibrium the disease free equilibrium. We also denote this equilibrium by DFE. Any equilibrium (\bar{x}, \bar{y}) satisfies

$$\begin{aligned} \varphi(\bar{x}) &= \bar{x} \beta^T \bar{y} \\ \bar{x} \beta^T \bar{y} \mathbf{b} &= A \bar{y} \end{aligned}$$

which gives $\bar{y} = \bar{x} \beta^T \bar{y} (-A^{-1}) \mathbf{b}$ and consequently

$$\beta^T \bar{y} = \bar{x} \beta^T \bar{y} \beta^T (-A^{-1}) \mathbf{b}$$

If $\beta^T \bar{y} = 0$, since A is stable, hence nonsingular, we get $\bar{y} = 0$ and $\bar{x} = x^*$ which is the DFE. The other case $\beta^T \bar{y} \neq 0$ gives

$$\bar{x} = \frac{1}{\beta^T (-A^{-1}) \mathbf{b}} = \frac{x^*}{\mathcal{R}_0} \quad (7)$$

and

$$\bar{y} = \varphi(\bar{x}) (-A^{-1}) \mathbf{b} \quad (8)$$

Since x^* is globally asymptotically stable $\varphi(\bar{x})$ is positive if and only if $\bar{x} < x^*$, hence if and only if $\mathcal{R}_0 > 1$. Using that A is a Metzler stable matrix we deduce $\bar{y} > 0$ if and only if $\mathcal{R}_0 > 1$.

We have proved that a unique endemic equilibrium exists (in the nonnegative orthant) if and only $\mathcal{R}_0 > 1$. This endemic equilibrium is in the compact absorbing set K_ρ

4. Global asymptotic stability of the DFE. We give a simple proof for the system (3) with a general stable Metzler matrix A

The system (3) is globally asymptotically stable at the disease free equilibrium (DFE) $(x^*, 0, \dots, 0)$ if and only if $\mathcal{R}_0 = \beta^T (-A^{-1}) \mathbf{b} x^* \leq 1$.

Proof: In a first step we will prove that if $\mathcal{R}_0 \leq 1$, the DFE is globally asymptotically stable on nonnegative orthant. It is well know that if $\mathcal{R}_0 > 1$ then the DFE is unstable. Thus the condition $\mathcal{R}_0 \leq 1$ is necessary.

To prove the sufficiency we consider the following Lyapunov function (in LaSalle's sense [30, 31]) defined on the positive orthant.

$$V_{DFE}(x, y) = \frac{1}{x^*}(x - x^* \ln x) - \beta^T A^{-1}y - \frac{1}{x^*}(x^* - x^* \ln x^*) \tag{9}$$

This function is nonnegative in general, since we only knows that $\beta^T A^{-1} > 0$.

It's time derivative along the trajectories of system (3) is

$$\dot{V}_{DFE} = \frac{1}{x^*} \left[\frac{x - x^*}{x} \varphi(x) - x \beta^T y + x^* \beta^T y \right] - x \beta^T y \beta^T A^{-1} \mathbf{b} - \beta^T y$$

simplifying and using the expression for \mathcal{R}_0 we obtain

$$\dot{V} = \frac{1}{x^*} \left[\frac{x - x^*}{x} \varphi(x) - x \beta^T y \right] + x \beta^T y \frac{\mathcal{R}_0}{x^*}$$

or equivalently

$$\dot{V} = \frac{x - x^*}{x^* x} \varphi(x) + \frac{x}{x^*} \beta^T y (\mathcal{R}_0 - 1) \tag{10}$$

With the hypothesis that x^* is globally asymptotically stable on \mathbb{R}_+ for the system $\dot{x} = \varphi(x)$, we have $(x - x^*)\varphi(x) \leq 0$ for all $x \geq 0$. Therefore $\dot{V} \leq 0$ for all (x, y) in the positive orthant. We restrict our attention, for the moment, to the positively invariant compact set K_ρ . The attractivity of the DFE follows from LaSalle invariance principle since the largest invariant set contained in $\{(x, y) \in K_\rho \mid \dot{V} = 0\}$ is reduced to the DFE. This proves the global asymptotic stability on K_ρ ([6], Theorem 3.7.11, page 346). Since K_ρ is absorbing this proves the global asymptotic stability on the nonnegative orthant.

5. Global stability of the endemic equilibrium. Global results of stability for the DFE as well for the endemic equilibrium for epidemic models are not so common [17, 44]. Global stability results for the endemic equilibrium using the Li-Muldowney techniques ([33]) bear upon properties of monotone systems. Usually the Poincaré-Bendixson property of monotone systems in dimension 3 is used. [15, 33, 40]. These techniques are far from being straightforward for high dimensional systems. In recent years Lyapunov methods have been used. A Volterra-like Lyapunov function has been used in [29] to prove global stability of the endemic equilibrium for SEIR models. This function has a long history of application to Lotka-Volterra models [12] and was originally discovered by Volterra himself, although he did not use

the vocabulary and the theory of Lyapunov functions. Since epidemic models are “Lotka-Volterra” like models, the pertinence of this function is not surprising. The global stability for DI models, with any number of compartments, with mass action incidence has been proved in [38]. For the SP model only local results are known. We will use a Volterra-like Lyapunov function. The difficulty is in the choice of the coefficients and in proving the negative definiteness of the derivative. We propose a general technique for finding the coefficients. The proof of the negativity is more involved and bear upon additional properties of A .

In this section we will describe a method to prove the global stability of the endemic equilibrium. We will apply this method to the SP model with mass action incidence, to establish the global stability, which improve results of [22, 21]

5.1. The general strategy. The proof is based on a Volterra-like Lyapunov function, defined on the positive orthant

$$V_{EE}(x, y) = a_0 (x - \bar{x} \ln x) + \sum_{i=1}^n a_i (y_i - \bar{y}_i \ln y_i) + K$$

Where K is the constant $K = a_0 (\bar{x} - \bar{x} \ln \bar{x}) + \sum_{i=1}^n a_i (\bar{y}_i - \bar{y}_i \ln \bar{y}_i)$. This function is positive on the positive orthant.

We first prove that we can choose the coefficients such that, in the expression of \dot{V}_{EE} , there are no linear terms in y and no bilinear terms.

It is sufficient to show that, if we set $a = (a_1, \dots, a_n)$, there is a nonnegative solution of

$$\begin{bmatrix} -1 & \mathbf{b}^T \\ \bar{x} \beta & A^T \end{bmatrix} \begin{bmatrix} a_0 \\ a \end{bmatrix} = 0 \quad (11)$$

Since

$$\det \begin{bmatrix} -1 & \mathbf{b}^T \\ \bar{x} \beta & A^T \end{bmatrix} = -1 + \mathbf{b}^T (-A^{-T}) \bar{x} \beta = -1 - \beta^T A^{-1} \mathbf{b} = -1 + 1 = 0$$

using the relation (7) for \bar{x}

The matrix is a codimension 1 matrix, the kernel is one dimensional, then we have one degree of freedom with $a = -a_0 \bar{x} A^{-T} \beta$. Any positive value for a_0 gives a nonnegative a . We choose.

With this choice, denoting $\text{diag}(a)$ the diagonal matrix with elements of a on the diagonal

$$\begin{aligned} \dot{V}_{EE} = & a_0 \frac{x - \bar{x}}{x} \varphi(x) - a_0 x \beta^T y + \underline{a_0 \bar{x} \beta^T y} + \\ & x \beta^T y a^T \mathbf{b} + a^T A y \\ & - x \beta^T y a^T \text{diag}(\bar{y}) (\text{diag}(y))^{-1} \mathbf{b} - a^T \text{diag}(\bar{y}) (\text{diag}(y))^{-1} A y \end{aligned}$$

Since $a_0 = \mathbf{b}^T a = a^T \mathbf{b}$ and $a = a_0 \bar{x} (-A^{-T}) \beta$ the terms $-a_0 x \beta^T y$ and $x \beta^T y a^T \mathbf{b}$ (respectively $a_0 \bar{x} \beta^T y$ and $a^T A y$) cancel.

Which gives

$$\dot{V}_{EE} = a_0 \frac{x - \bar{x}}{x} \varphi(x) - x \beta^T y a^T \text{diag}(\bar{y}) (\text{diag}(y))^{-1} \mathbf{b} - a^T \text{diag}(\bar{y}) (\text{diag}(y))^{-1} A y \quad (12)$$

The problem is now to rewrite the last expressions.

5.2. **The SP model.** We will apply the general strategy to a SP model with latent classes. Then we consider a $SE_1 \cdots E_k I_{k+1} \cdots I_n$ model, and we prove the global asymptotic stability of the endemic equilibrium when $\mathcal{R}_0 > 1$ for the usual demographic function $\Lambda - \mu_X x$ and give a sufficient condition for global asymptotic stability in the general case. If we remark that in this model, the latent classes can be considered as infected classes with 0 transmission, i.e. $\beta_i = 0$ for $i = 1, \dots, k$.

Theorem 1. For the system (1) when $\mathcal{R}_0 > 1$ there is a unique endemic equilibrium. This endemic is then globally asymptotically stable for the function $\varphi(S) = \Lambda - \mu_S S$. More generally for a class C^1 function φ , if $\max \varphi' \leq \frac{\beta_1}{\alpha_1} \varphi(\frac{x^*}{\mathcal{R}_0})$ the endemic equilibrium is globally asymptotically stable.

We consider the equations defining the endemic equilibrium.

$$\begin{aligned} \varphi(\bar{x}) &= (\sum_{i=1}^n \beta_i \bar{I}_i) \bar{x} \\ (\sum_{i=1}^n \beta_i \bar{I}_i) \bar{x} &= \alpha_1 \bar{I}_1 \\ \gamma_1 \bar{I}_1 &= \alpha_2 \bar{I}_2 \\ \gamma_2 \bar{I}_2 &= \alpha_3 \bar{I}_3 \\ &\dots\dots\dots \\ \gamma_{n-1} \bar{I}_{n-1} &= \alpha_n \bar{I}_n \end{aligned}$$

The relation (11) between the coefficients can be developed in

$$\begin{cases} b_1 - a = 0 \\ a\beta_1 \bar{x} - b_1 \alpha_1 + b_2 \gamma_1 = 0 \\ a\beta_2 \bar{x} - b_2 \alpha_2 + b_3 \gamma_2 = 0 \\ \dots\dots\dots \\ a\beta_n \bar{x} - b_n \alpha_n = 0 \end{cases}$$

We deduce for the endemic equilibrium

$$\begin{aligned} b_1 \alpha_1 \bar{I}_1 &= a\beta_1 \bar{x} \bar{I}_1 + b_2 \gamma_1 \bar{I}_1 \\ &= a\beta_1 \bar{x} \bar{I}_1 + b_2 \alpha_2 \bar{I}_2 \\ &= a\beta_1 \bar{x} \bar{I}_1 + a\beta_2 \bar{x} \bar{I}_2 + b_3 \alpha_3 \bar{I}_3 \\ &\dots\dots\dots \\ &= a\beta_1 \bar{x} \bar{I}_1 + a\beta_2 \bar{x} \bar{I}_2 + \dots + a\beta_n \bar{x} \bar{I}_n \end{aligned}$$

More generally we have

$$\begin{aligned} b_i \alpha_i \bar{I}_i &= a\beta_i \bar{x} \bar{I}_i + \dots + a\beta_n \bar{x} \bar{I}_n \\ &= \sum_{j=i}^n a\beta_j \bar{x} \bar{I}_j \end{aligned}$$

and

$$\begin{aligned} b_{i+1}\gamma_i\bar{I}_i &= a\beta_{i+1}\bar{x}\bar{I}_{i+1} + \cdots + a\beta_n\bar{x}\bar{I}_n \\ &= \sum_{j=i+1}^n a\beta_j\bar{x}\bar{I}_j \end{aligned}$$

The derivative of V_{EE} expressed in (12) is

$$\dot{V} = a\varphi(x)\left(1 - \frac{\bar{x}}{x}\right) + \sum_{i=1}^n b_i\alpha_i\bar{I}_i - a\beta_1\bar{x}\bar{I}_1\frac{x}{\bar{x}} - \sum_{i=2}^n a\beta_i\bar{x}\bar{I}_i\frac{\bar{I}_1}{I_1}\frac{x}{\bar{x}}\frac{I_i}{\bar{I}_i} - \sum_{i=1}^{n-1} \gamma_i b_{i+1}\bar{I}_i\frac{I_i}{\bar{I}_i}\frac{\bar{I}_{i+1}}{I_{i+1}}$$

But we can also write

$$\sum_{i=1}^n b_i\alpha_i\bar{I}_i = \sum_{j=1}^n a_j\beta_j\bar{x}\bar{I}_j$$

Then

$$\begin{aligned} \sum_{i=1}^{n-1} \gamma_i b_{i+1}\bar{I}_i\frac{I_i}{\bar{I}_i}\frac{\bar{I}_{i+1}}{I_{i+1}} &= \sum_{i=1}^{n-1} \left(\sum_{j=i+1}^n a\beta_j\bar{x}\bar{I}_j \right) \frac{I_i}{\bar{I}_i}\frac{\bar{I}_{i+1}}{I_{i+1}} \\ &= \sum_{j=2}^n a\beta_j\bar{x}\bar{I}_j \left(\sum_{i=1}^{j-1} \frac{I_i}{\bar{I}_i}\frac{\bar{I}_{i+1}}{I_{i+1}} \right) \end{aligned}$$

rearranging this equation gives

$$\begin{aligned} \dot{V} &= a\varphi(x)\left(1 - \frac{\bar{x}}{x}\right) + \sum_{j=1}^n a_j\beta_j\bar{x}\bar{I}_j - a\beta_1\bar{x}\bar{I}_1\frac{x}{\bar{x}} \\ &\quad - \sum_{j=2}^n a\beta_j\bar{x}\bar{I}_j\frac{\bar{I}_1}{I_1}\frac{x}{\bar{x}}\frac{I_j}{\bar{I}_j} - \sum_{j=2}^n a\beta_j\bar{x}\bar{I}_j \left(\sum_{i=1}^{j-1} \frac{I_i}{\bar{I}_i}\frac{\bar{I}_{i+1}}{I_{i+1}} \right) \end{aligned}$$

or equivalently

$$\begin{aligned} \dot{V} &= a\varphi(x)\left(1 - \frac{\bar{x}}{x}\right) + a\beta_1\bar{x}\bar{I}_1 - a\beta_1\bar{x}\bar{I}_1\frac{x}{\bar{x}} \\ &\quad + \sum_{j=2}^n a\beta_j\bar{x}\bar{I}_j \left[j - \frac{\bar{I}_1}{I_1}\frac{x}{\bar{x}}\frac{I_j}{\bar{I}_j} - \sum_{i=1}^{j-1} \frac{I_i}{\bar{I}_i}\frac{\bar{I}_{i+1}}{I_{i+1}} \right] \end{aligned}$$

If we group the terms in brackets in order to have the geometrical mean equal to 1, we will have

$$\begin{aligned} \dot{V} &= a\varphi(x)\left(1 - \frac{\bar{x}}{x}\right) + a\beta_1\bar{x}\bar{I}_1\left(1 - \frac{x}{\bar{x}}\right) + \sum_{j=2}^n a\beta_j\bar{x}\bar{I}_j\left(\frac{\bar{x}}{x} - 1\right) \\ &\quad + \sum_{j=2}^n a\beta_j\bar{x}\bar{I}_j \left[(j+1) - \frac{\bar{x}}{x} - \frac{\bar{I}_1}{I_1}\frac{x}{\bar{x}}\frac{I_j}{\bar{I}_j} - \sum_{i=1}^{j-1} \frac{I_i}{\bar{I}_i}\frac{\bar{I}_{i+1}}{I_{i+1}} \right] \end{aligned}$$

But we also know that

$$a\varphi(\bar{x}) = a\alpha_1\bar{I}_1 = \sum_{j=1}^n a\beta_j\bar{x}\bar{I}_j$$

So

$$\begin{aligned} \dot{V} = & a\varphi(x)\left(1 - \frac{\bar{x}}{x}\right) + a\varphi(\bar{x})\left(\frac{\bar{x}}{x} - 1\right) + a\beta_1\bar{x}\bar{I}_1\left(2 - \frac{x}{\bar{x}} - \frac{\bar{x}}{x}\right) \\ & + \sum_{j=2}^n a\beta_j\bar{x}\bar{I}_j \left[\left(j + 1\right) - \frac{\bar{x}}{x} - \frac{\bar{I}_1}{I_1} \frac{x}{\bar{x}} \frac{I_j}{\bar{I}_j} - \sum_{i=1}^{j-1} \frac{I_i}{\bar{I}_i} \frac{\bar{I}_{i+1}}{I_{i+1}} \right] \end{aligned}$$

we have

$$a\varphi(x)\left(1 - \frac{\bar{x}}{x}\right) + a\varphi(\bar{x})\left(\frac{\bar{x}}{x} - 1\right) + a\beta_1\bar{x}\bar{I}_1\left(2 - \frac{x}{\bar{x}} - \frac{\bar{x}}{x}\right) = a \frac{x - \bar{x}}{x} \left[\varphi(x) - \varphi(\bar{x}) - \beta_1\bar{x}\bar{I}_1 \frac{x - \bar{x}}{x} \right]$$

By observing that $\varphi(x) = \varphi(\bar{x}) + (x - \bar{x})\varphi'(c)$ where $c \in]\bar{x}, x[$, we have

$$\begin{aligned} \dot{V} = & a \frac{(x - \bar{x})^2}{x} [\varphi'(c) - \beta_1\bar{I}_1] \\ & + \sum_{j=2}^n a\beta_j\bar{x}\bar{I}_j \left[\left(j + 1\right) - \frac{\bar{x}}{x} - \frac{\bar{I}_1}{I_1} \frac{x}{\bar{x}} \frac{I_j}{\bar{I}_j} - \sum_{i=1}^{j-1} \frac{I_i}{\bar{I}_i} \frac{\bar{I}_{i+1}}{I_{i+1}} \right] \end{aligned}$$

Then we have $\dot{V} \leq 0$ if and only if $\varphi'(c) - \beta_1\bar{I}_1 \leq 0$; but we already have $\alpha_1\bar{I}_1 = \varphi(\bar{x})$ So the condition for the \dot{V} to be definite negative is

$$\dot{V} \leq 0 \quad \text{iff} \quad \varphi'(c) \leq \frac{\beta_1}{\alpha_1} \varphi(\bar{x})$$

which is obviously satisfied for $\varphi(x) = \Lambda - \mu_x x$.

Remark 1. This proof establishes a slightly more general result and gives a sufficient condition for more general demographic function $\varphi(x)$

6. Conclusion. In this paper we propose a class of epidemiological systems with mass action incidence with a general structure. We provide a very simple formula for the basic reproduction ratio \mathcal{R}_0 . When $\mathcal{R}_0 \leq 1$ we prove the global asymptotic stability for the disease free equilibrium. When $\mathcal{R}_0 > 1$ we prove the uniqueness of an endemic equilibrium and provide a simple explicit formula for the components of the endemic equilibrium. Since our class of systems encompass the DI,SP and DISP models we improves the results of [21, 22, 20] We propose a strategy for proving the global stability and apply it to SP model. The result is new.

The authors wants to thanks anonymous referee whose suggestions have improved the manuscript. The results in this paper have been exposed in june 2006 at the AIMS conference in Poitiers. We recently learned that similar results have been obtained in [16]. However our result is more general and simpler.

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Stability of differential susceptibility and infectivity epidemic models

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Stability of Differential Susceptibility and Infectivity Epidemic Models

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Abstract

We introduce classes of differential susceptibility and infectivity epidemic models. These models address the problem of flows between the different susceptible, infectious and infected compartments and differential death rates as well. We prove the global stability of the disease free equilibrium when the basic reproduction ratio $\mathcal{R}_0 \leq 1$ and the existence and uniqueness of an endemic equilibrium when $\mathcal{R}_0 > 1$. We also prove the global asymptotic stability of the endemic equilibrium for a differential susceptibility and staged progression infectivity model, when $\mathcal{R}_0 > 1$. Our results encompass and generalize those of [18, 22].

Keywords : Nonlinear dynamical systems, global stability, Lyapunov methods, differential susceptibility models, reproductive number, HBV.

AMS subject classification : 34A34, 34D23, 34D40, 92D30

1 Introduction

The primary objective of this paper is to give results on global stability for epidemiological models with differentiation in susceptibility for infection and differentiation in infectivity. The first models with differential infectivity has been introduced for studying HIV infection [29, 28, 37] by Jacquez et al. circa 1990s. The term differential infectivity has been coined by Hyman et al. in [23, 18, 21, 19]. Models with differential susceptibility has been introduced in the references [18, 22].

The rationale to introduce differential infectivity and susceptibility is motivated by the heterogeneity, concerning the mode of infection, for the individuals.

For many reasons difference in susceptibility to infection can occur : genetic variations, different social behaviors, different states of immunization, different vaccines . . .

The infection by HBV, hepatitis B, is typically a disease where simultaneously differential susceptibility and infectivity appear :

Hepatitis B virus (HBV) is a bloodborne and sexually transmitted virus. The liver is the primary site of HBV replication. After a susceptible person is exposed, the virus enters the liver via the bloodstream. Hepatitis B is one of the major diseases of mankind and is a serious global public health problem. Of the 2 billion people who have been infected with the hepatitis B virus

(HBV), more than 350 million have chronic (lifelong) infections. Rates of new infection and acute disease are highest among adults, but chronic infection is more likely to occur in persons infected as infants or young children. These chronically infected persons are at high risk of death from cirrhosis of the liver and liver cancer, diseases that kill about one million persons each year. According to CDC and WHO, risk for chronic infection is inversely related to age at infection: approximately 90% of infected infants and 30% of infected children aged under 5 years become chronically infected, compared with 5% of adults. This difference in the evolution of infection introduces naturally differential susceptibility.

Indeed hepatitis B is a major public health problem in developing countries of Africa and Asia (where prevalence is greater than 8%). In much of the developing world, (sub-Saharan Africa, most of Asia, and the Pacific), most people become infected with HBV during childhood, and 8% to 10% of people in the general population become chronically infected. In these regions liver cancer caused by HBV figures among the first three causes death by cancer in men.

Asymptomatic carriers play an important role in the transmission of HBV. Usually asymptomatic carriers are considered as less infectious than acute carriers, which is a reason for incorporating differential susceptibility. Vaccination is recognized as the most efficient way of preventing hepatitis B. But the problem of imperfect vaccine introduce naturally differential susceptibility. Even if HBV vaccine is very efficient it does not offer 100% protection against infection. According WHO, Hepatitis B vaccine is 95% effective in preventing HBV infection and its chronic consequences, Then vaccinated individuals form a class of individual with different susceptibility.

In [2], May and Anderson consider a model of HBV infection. They distinguishes, in this model the susceptible individuals according to their response. They assume that a proportion of births to infected carriers are themselves infected carriers, while the remaining fraction of these births give susceptibles in the carrier carrier group. This model is clearly a differential susceptibility and infectivity model.

In [11], a SVEICR model is considered for modeling HBV infection.

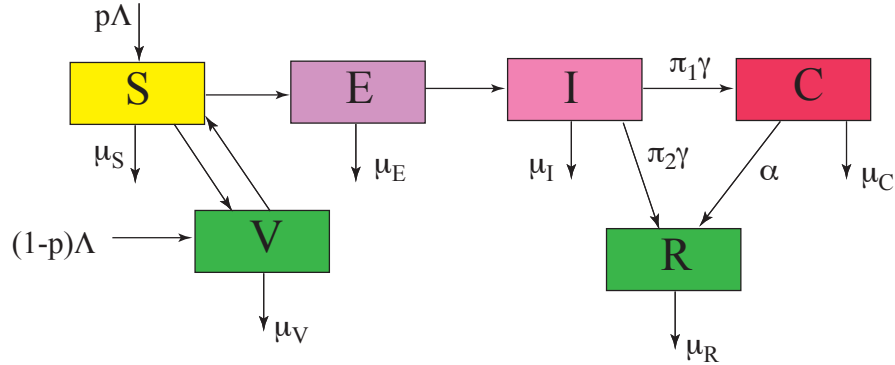


Figure 1: a Differential susceptibility and infectivity model

When different strains are taken into account differential susceptibility and infectivity models are given in [41, 42].

More generally the stage-progression HIV model with imperfect vaccine of [15] is also a differential susceptibility systems and infectivity model.

We consider a general class of differential susceptibility systems and infectivity models with bilinear mass action as in [18] and give stability results. We could have use a standard incidence mass action $c(N) \beta \frac{I}{N}$ [7, 36]. The stability results of the disease free equilibrium remain true by an easy adaptation. However the proof of existence and uniqueness of the endemic equilibrium, as well as the stability of this endemic equilibrium, work only with the bilinear mass action. This mass action becomes natural when N is constant or $c(N) = c_0 N$ or else when the model is dealing with proportions. For homogeneity of exposition, we will use bilinear mass action throughout the paper.

The models considered in this paper address the issue of flows between the different compartments of infected and infectious individuals as well as flows between the different compartment of susceptible individuals. Moreover the differences of death-rates between classes are also taken into account. These models encompass the models with bilinear mass action of [13, 14, 15, 22, 18].

We give a brief outline of the paper. In section 2 we introduce the class of system considered. Our models are differential susceptibility and infectivity epidemic models. These models take into account flows between the different classes of susceptible, infected and infectious compartments. The death rate

can be different for each compartment. Since our model is presented in a general setting we add hypotheses for biological soundness. These hypotheses are satisfied in the models in [15, 22, 18]. In this section we give, for natural subclasses of our general systems, a simple analytical expression for the basic reproduction ratio \mathcal{R}_0 . We prove the global stability of the disease free equilibrium (DFE) when $\mathcal{R}_0 \leq 1$ and the existence and uniqueness of a strongly endemic equilibrium when $\mathcal{R}_0 > 1$. The proof of the global stability of the endemic equilibrium is always a challenge. We give the global stability of the endemic equilibrium for a differential susceptibility and infectivity epidemic model which generalizes the results in [22, 18].

2 A general class of systems

Throughout this paper we will use the following notations. If x is a vector of \mathbb{R}^n then $\text{diag}(x)$ will be the $n \times n$ diagonal matrix, whose diagonal elements are the components of x . We will denote by $\langle | \rangle$ the usual inner product on \mathbb{R}^n . In \mathbb{R}^n Let $\{e_1, \dots, e_n\}$ be the canonical basis of \mathbb{R}^n . We will denote by $\mathbf{1}$ the vector given by $\mathbf{1} = (1, \dots, 1)^T = e_1 + \dots, e_n$, where the superscript T denotes transpose.

We use the ordering in \mathbb{R}^n generated by the cone \mathbb{R}_+^n . We write $x \leq y$, if $y - x \in \mathbb{R}_+^n$ and $x < y$ if $x \leq y$ and $x \neq y$. Finally $x \ll y$ will means $x_i < y_i$ for any index i .

We consider the following general model

$$\begin{cases} \dot{S} = \Lambda - \text{diag}(\mu_S) S + A_S S - \text{diag}(B I) S, \\ \dot{I} = P \text{diag}(B I) S - \text{diag}(\mu_I + \gamma_I) I + A_I I, \\ \dot{R} = L I - \text{diag}(\mu_R) R + A_R R, \end{cases} \quad (1)$$

where $S \in \mathbb{R}_+^n$ is the state of susceptible individuals, $I \in \mathbb{R}_+^m$ is the state of infectious and infected individuals and $R \in \mathbb{R}_+^p$ the state of recovered and immune individuals. The recruitment, in each susceptible compartment, is described by a nonnegative vector $\Lambda > 0$. The positive vector $\mu_S \gg 0$ represents the death rate of the different classes of susceptible individuals. The matrix A_S represents the flows between the susceptible compartments. In the words of Jacquez the coefficients of A_I are the *fractional transfer coefficients* [27]. Since A_S represents only the movement between the S

compartments, A_S is a compartmental Metzler matrix, whose column sums are zero, i.e., the sum of the elements of each column is zero.

The matrix $B > 0$ represents the coefficients of infectivity, actually $B(i, j) = \beta_{ij}$ is the contact and infectivity of I_j in the group S_i . The matrix B is also known as the WAIFW matrix (Who Acquire Infection From Whom [2]). The matrix P is a column-stochastic $m \times n$ matrix:

$$P = \begin{pmatrix} p_{11} & p_{12} & \cdots & p_{1n} \\ p_{21} & p_{22} & \cdots & p_{2n} \\ \vdots & \cdots & \ddots & \cdots \\ p_{m1} & p_{m2} & \cdots & p_{mn} \end{pmatrix}$$

This matrix represents the distribution of susceptible individual after infection. A susceptible individual in group S_i enters group I_j with probability

$$p_{ji}, \text{ hence } \sum_{j=1}^m p_{ji} = 1.$$

Analogously as before, the matrix A_I represents the movements between the I compartments. The vector $\mu_I \gg 0$ and $\gamma_I > 0$ represent respectively, the death rate and the recovery rate of the infectious-infected compartments I_i . The vector γ_I is supposed only nonnegative, since an infected individual does not necessarily recover and usually move in an infected compartment.

Finally, the matrix L represents the distribution of the I compartment toward the R compartments. The vector μ_R and the matrix A_R are defined as their corresponding analogue in the S and I compartments.

We remark that in this setting, since B is a non zero nonnegative matrix, the model (1) can contain compartments of infected individuals that are not infectious or latent individuals. They are simply the I_j compartments, with no transmission, i.e., for which $B_{i,j} = 0$, for any i . However the matrix B cannot contain a row whose elements are all zero. In other words, for all $i \in \{1, \dots, n\}$ there exist $k \in \{1, \dots, m\}$ such that $B_{i,k} \neq 0$, otherwise if there is an index i_0 such that $B_{i_0,k} = 0$ for all $k \in \{1, \dots, m\}$ this would mean that the individuals of compartment S_{i_0} can never be infected and hence the individuals of S_{i_0} would not be susceptible.

Using Gershgorin theorem it is clear that the matrices

$$-\text{diag}(\mu_S) + A_S, \quad -\text{diag}(\mu_I) + A_I, \quad \text{and} \quad -\text{diag}(\mu_R) + A_R$$

are stable Metzler matrices and are in particular non singular. This implies,

that when there is no transmission, the infected, infectious and the removed individuals disappear.

We will use the following properties repeatedly in the sequel : a Metzler matrix (off-diagonal entries are nonnegative) M is stable if and only if $-M^{-1} > 0$ [5, 38]. This also has for consequence that if $x \gg 0$ then $-M^{-1}x \gg 0$. There are two schools for matrices like these matrices. The first one, uses Metzler matrices (called also quasipositive matrices) and it is represented by J.A. Jacquez, D. Luenberger, H.L. Smith or H. Thieme [26, 27, 34, 39, 38]. The second one uses M -matrices : the negative of a stable Metzler matrix is a nonsingular M -matrix. This school is represented, for example, by Berman and Plemmons[5] or van den Driessche and Watmough ([40]). We choose to stick to the Jacquez formalism, natural for compartmental models, since our matrices A represent the exchanges between compartments.

For the stability analysis we can discard the last equation

$$\dot{R} = LI - \text{diag}(\mu_R) R + A_R R.$$

Since the variables R do not play a part in the preceding equations, the stability analysis can be reduced to the system (1) without the last equation. Therefore we will consider, from now on, the following system

$$\begin{cases} \dot{S} = \Lambda - \text{diag}(\mu_S) S + A_S S - \text{diag}(BI) S \\ \dot{I} = P \text{diag}(BI) S - \text{diag}(\mu_I + \gamma_I) I + A_I I, \end{cases} \quad (2)$$

Throughout the paper, we shall use the matrix \tilde{A}_I defined by

$$\tilde{A}_I = -\text{diag}(\mu_I + \gamma_I) + A_I$$

Supplementary assumptions: Our systems are general, we will add some hypotheses for to be biologically consistent. For formulating these hypothesis we will use some definitions from graph theory [5]. To our system we associate a directed graph as usual. We have $m+n$ vertices, n vertices corresponding to susceptible compartments, m vertices for infected or infectious compartments. Our system (2) can be rewritten under a canonical form for compartmental systems [27]:

$$\begin{bmatrix} \dot{S} \\ \dot{I} \end{bmatrix} = \begin{bmatrix} \Lambda \\ 0 \end{bmatrix} + \begin{bmatrix} -\text{diag}(\mu_S) + A_S - \text{diag}(BI) & 0 \\ 0 & \text{diag}(S)B - \text{diag}(\mu_I + \gamma_I) + A_I \end{bmatrix} \begin{bmatrix} S \\ I \end{bmatrix} \quad (3)$$

The matrix appearing in this equation is a compartmental Metzler matrix [27]. We denote by $M(S, I)$ this matrix.

$$M(S, I) = \begin{bmatrix} -\text{diag}(\mu_S) + A_S - \text{diag}(BI) & 0 \\ 0 & \text{diag}(S)B - \text{diag}(\mu_I + \gamma_I) + A_I \end{bmatrix}$$

In our associated graph an edge leads from a vertex j to a different vertex $i \neq j$ if $M(S, I)_{i,j} > 0$ for some (S, I) . We say that j has an access to i , if in the graph there is a path from j to i . This is equivalent to say that, for some $p > 0$, $M^p(S, I)_{i,j} > 0$ [5]. We thus shall assume that the following hypothesis is fulfilled:

H1 *We will assume in the sequel that any “susceptible” compartment is accessible from a “susceptible” compartment with recruitment.*

This property depends only of the matrix A_S and the location of recruitment. For any $x \geq 0$, the matrix $-\text{diag}(\mu_S) + A_S - \text{diag}(x)$ is a Hurwitz Metzler matrix. Hypothesis **H1** implies the following

Lemma 2.1 *For any $x \geq 0$, we have*

$$-[-\text{diag}(\mu_S) + A_S - \text{diag}(x)]^{-1} \Lambda \gg 0.$$

This implies, in particular, that the disease free equilibrium (DFE) of system (2) given by $(S^, 0) = (-[A_S - \text{diag}(\mu_S)]^{-1} \Lambda, 0)$ satisfies $S^* \gg 0$.*

Proof.

We have only to consider the connected components from the recruitment. If we denote by e_1 , the vector of the canonical basis, corresponding to a recruitment compartment, by $M(x)$ the matrix $[-\text{diag}(\mu_S) + A_S - \text{diag}(x)]$, we have to prove that for any e_i accessible from e_1 we have

$$\langle -M(x)^{-1} e_1 | e_i \rangle > 0.$$

Since the matrix $M(x)$ is Hurwitz, it satisfies $\int_0^\infty e^{tM(x)} dt = -M(x)^{-1}$. Thus we can write

$$\langle -M(x)^{-1} e_1 | e_i \rangle = \int_0^\infty \langle e^{tM(x)} e_1 | e_i \rangle dt.$$

The expression under the integral, in the right hand side, is nonnegative and analytic in t . Hence, it suffices to prove that $\left. \frac{d^k}{dt^k} \langle e^{tM(x)} e_1 | e_i \rangle \right|_{t=0} > 0$

for some $k > 0$. We choose for k the integer satisfying $\langle A_S^k e_1 | e_i \rangle > 0$ and $\langle A_S^p e_1 | e_i \rangle = 0$ for $0 \leq p < k$. This integer exists thanks to Assumption **H1**. We then have

$$\frac{d^k}{dt^k} \langle e^{tM(x)} e_1 | e_i \rangle \Big|_{t=0} = \langle M(x)^k e_1 | e_i \rangle$$

$\langle M(x)^k e_1 | e_i \rangle = \sum_{p=0}^k C_k^p (-1)^{k-p} (\mu_{S_1} + x_1)^{k-p} \langle A_S^p e_1 | e_i \rangle = \langle A_S^k e_1 | e_i \rangle > 0$. This completes the proof of the lemma. ■

An entry-point compartment for infection is an infected-infectious compartment with an edge coming from the susceptible compartments. Equivalently this is the compartment with index for which the components of $P \mathbf{1}$ are positive.

Since this model can deal with infected people that are not infectious, i.e., we allow the possibility of having some compartments I_j for which $B_{i,j} = 0$, we must add some hypotheses. The infectious individuals must appear from transmission. If we have, a typical set of different susceptible, $c \gg 0$, becoming infected, then distributed in the infected-infectious compartments as Pc we assume that all these individuals will evolve through all the infected-infectious compartments. This hypothesis is the analogous of the preceding hypothesis. This can also be formulated in the following manner:

H2 *Any infected-infectious compartment is accessible from at least one compartment which is an “entry-point” for infection.*

A consequence of hypothesis **H2** is $-\tilde{A}_I^{-1} P c \gg 0$ for any $c \gg 0$. The proof is similar to the proof of the preceding lemma.

Remark 2.1 *With these two hypotheses, when there are some infection, then the trajectories of our system are in the positive orthant. However our hypotheses are weaker than an irreducibility hypothesis on the flow graph of our system.*

This model encompasses known models of DI (differential infectivity), SP (staged progression), or differential susceptibility models, with bilinear mass action. We will generalize the results obtained in [22, 18, 4, 12]. In particular, we shall prove the global asymptotic stability of the endemic equilibrium when $\mathcal{R}_0 > 1$. This has been conjectured in [22] according to numerical simulations.

2.1 Basic reproduction ratio

It is not difficult using the results on \mathcal{R}_0 [10, 17, 9, 40, 16] to obtain a formula for the basic reproduction ratio. Since this formula expresses \mathcal{R}_0 as the spectral radius $\rho(\mathcal{G})$ of the next generation matrix \mathcal{G} , we cannot expect, in general, to obtain an analytical expression.

Using the techniques developed in [40], we claim that the basic reproduction ratio \mathcal{R}_0 for the general system (2) is

$$\mathcal{R}_0 = \rho\left(-P \operatorname{diag}(S^*) B \tilde{A}_I^{-1}\right) = \rho\left(-\tilde{A}_I^{-1} P \operatorname{diag}(S^*) B\right). \quad (4)$$

Where

$$\tilde{A}_I = -\operatorname{diag}(\mu_I + \gamma_I) + A_I.$$

We use the expression $(-\tilde{A}_I^{-1})$ to put the emphasis on the fact that the matrix $(-\tilde{A}_I^{-1}) > 0$ because the matrix A is Metzler stable. Using the framework of [40], we denote by $\mathcal{F}_i(S, I)$ the rate of appearance of new infections in compartment i , and by $\mathcal{V}_i(S, I)$ the rate of transfer of individuals in and out the compartment i by all other means. The matrix \mathcal{V} is the “mass” balance of the compartments. Note that our \mathcal{V} is the opposite of the one used in [40]. Then

$$\mathcal{F}(S, I) = \begin{bmatrix} 0 \\ P \operatorname{diag}(B I) S \end{bmatrix},$$

and

$$\mathcal{V}(S, I) = \begin{bmatrix} \Lambda - \operatorname{diag}(\mu_S) S + A_S S - \operatorname{diag}(B I) S \\ \tilde{A}_I I \end{bmatrix}.$$

The Jacobian matrices are

$$D\mathcal{F}(S, I) = \begin{bmatrix} 0 & 0 \\ P \operatorname{diag}(B I) & P \operatorname{diag}(S) B \end{bmatrix},$$

and

$$D\mathcal{V}(S, I) = \begin{bmatrix} -\operatorname{diag}(\mu_S) + A_S - \operatorname{diag}(B I) & -\operatorname{diag}(S) B \\ 0 & \tilde{A}_I \end{bmatrix}.$$

Noting that we have sorted the variables in the reverse order in comparison with [40], we set $F = P \operatorname{diag}(S^*) B$ and $V = \tilde{A}_I$. It is proved in [40] that the basic reproduction number is the spectral radius of the next generation

matrix for the model, namely $-FV^{-1}$, computed at the DFE (the minus sign comes from Metzler matrices used in place of M -matrices). This proves our claim.

However there are two cases where we can get explicit formulas. These cases are when the distribution stochastic matrix P or when the WAIFW matrix B are rank one matrices. We will now specialize to these two subcategories. In these two cases we can give a simple elegant formula for the basic reproduction ratio \mathcal{R}_0 (compare with [22, 18]).

2.1.1 Model with rank one stochastic distribution matrix P

We claim that in this case, the stochastic distribution matrix P we can always be written $P = p\mathbf{1}^T$, where $p \in \mathbb{R}^m$ is a nonnegative stochastic vector, i.e., $\sum_{i=1}^m p_i = 1$ and $\mathbf{1} \in \mathbb{R}^n$. This is quite evident since we can write, by Perron-Frobenius, $P = uv^T$ for two nonnegative vector $u \in \mathbb{R}^n$, $v \in \mathbb{R}^m$. Since upon infection a susceptible individual moves in the I compartments, we have $v \gg 0$. Using the stochasticity of P , the result follows. With this expression for P and the fact that

$$p\mathbf{1}^T \text{diag}(BI)S = \langle \mathbf{1} | \text{diag}(BI)S \rangle p = \langle BI | S \rangle p,$$

we obtain the following system

$$\begin{cases} \dot{S} = \Lambda - \text{diag}(\mu_S)S + A_S S - \text{diag}(BI)S \\ \dot{I} = \langle BI | S \rangle p - \text{diag}(\mu_I + \gamma_I)I + A_I I, \end{cases} \quad (5)$$

This model does not take into account the origin of the susceptible individuals upon infection. Once infected the individuals are distributed and enter the I compartment according to the stochastic vector p .

In this peculiar case, the hypothesis **H2** has for consequence $-\tilde{A}_I^{-1}p \gg 0$, which in turn implies $-B\tilde{A}_I^{-1}p \gg 0$.

We claim that for system (5), the basic reproduction number \mathcal{R}_0 is given by

$$\mathcal{R}_0 = \langle B(-\tilde{A}_I^{-1})p | S^* \rangle = S^{*T} B(-\tilde{A}_I^{-1})p. \quad (6)$$

Applying the preceding general formula (4) to system (5), we have

$$\mathcal{R}_0 = \rho\left(-p\mathbf{1}^T \text{diag}(S^*)B\tilde{A}_I^{-1}\right) = \rho\left(pS^{*T}B(-\tilde{A}_I^{-1})\right)$$

It is clear that $p S^{*T} B (-\tilde{A}_I^{-1})$ is a rank one matrix. The only nonzero eigenvalue is given by $S^{*T} B (-\tilde{A}_I^{-1}) p$, which is exactly our claim.

2.1.2 Model with rank one WAIFW matrix B

In this case we can write $B = \alpha \beta^T$, where $\alpha \gg 0$ is a positive vector of \mathbb{R}^n and $\beta > 0$ is a nonzero nonnegative vector of \mathbb{R}_+^m . From the modeling point of view, this means that for a given class of susceptible S_i , the infectivity factor of the different classes of infected is multiplied by a same coefficient α_i .

For this model $\mathcal{R}_0 = \rho \left((-\tilde{A}_I^{-1}) P \text{diag}(S^*) \alpha \beta^T \right)$

We again have a rank one matrix, then the spectral radius is given by

$$\mathcal{R}_0 = \left\langle \beta \mid -(\tilde{A}_I^{-1}) P \text{diag}(\alpha) S^* \right\rangle$$

2.2 A compact positively invariant absorbing set

We will show that there exists a compact positively invariant absorbing set K for (2). An absorbing set K for a dynamical system is a set K such that, for any initial condition, the forward trajectory starting from the initial condition enters for a positive time the set K .

We denote by $N(t)$ the total population at time t . We have $N = \langle S \mid \mathbf{1} \rangle + \langle I \mid \mathbf{1} \rangle$.

Using the fact that A_S, A_I are zero column sum matrices and P is a one column sum matrix we have the relations

$$\langle A_S S \mid \mathbf{1} \rangle = \langle S \mid A_S^T \mathbf{1} \rangle = 0, \quad \langle A_I I \mid \mathbf{1} \rangle = \langle I \mid A_I^T \mathbf{1} \rangle = 0,$$

and

$$\langle P \text{diag}(B I) S \mid \mathbf{1} \rangle = \langle \text{diag}(B I) S \mid P^T \mathbf{1} \rangle = \langle \text{diag}(B I) S \mid \mathbf{1} \rangle = \langle B I \mid S \rangle.$$

We get

$$\dot{N} = \langle \Lambda \mid \mathbf{1} \rangle - \langle \mu_S \mid S \rangle - \langle \mu_I + \gamma_I \mid I \rangle.$$

Let μ_0 be defined by $\mu_0 = \min(\mu_S, \mu_I + \gamma_I) > 0$, then we have

$$\dot{N} \leq \langle \Lambda \mid \mathbf{1} \rangle - \mu_0 N$$

Lemma 2.2 *Let $\mu_0 = \min(\mu_S, \mu_I + \gamma_I) > 0$. For any $\varepsilon > 0$, The subset K_ε of the nonnegative orthant $\mathbb{R}_+^n \times \mathbb{R}_+^m$, defined by*

$$K_\varepsilon = \left\{ (S, I) \mid S \geq 0 ; I \geq 0 ; N \leq (\langle \Lambda \mid \mathbf{1} \rangle + \varepsilon) / \mu_0 \right\},$$

is a positively invariant compact absorbing set for (2)

It is straightforward to check that the nonnegative orthant is positively invariant by the system (2). If we use the relation $\dot{N} \leq \langle \Lambda \mid \mathbf{1} \rangle - \mu_0 N$, then the lemma follows.

We also remark that $(S^*, 0) \in K_0$. Indeed we have $\langle \Lambda \mid \mathbf{1} \rangle = \langle \mu_S \mid S^* \rangle$, the conclusion follows from $\mu_0 \mathbf{1} \leq \mu_S$.

We have also a positively invariant set contained in K_ε .

Lemma 2.3 *The set Ω defined by*

$$\Omega = \left\{ (S, I) \in K_\varepsilon \mid S \leq S^* \right\},$$

is a positively invariant compact set for system (2).

On the boundary $S = S^*$ we have $\dot{S} = -\text{diag}(BI)S^* \leq 0$. This proves the positive invariance of Ω .

2.3 Global stability of the DFE

We will prove the global stability of the DFE for each category of models.

2.3.1 Model with rank one stochastic distribution matrix $P = p \mathbf{1}^T$

Theorem 2.1 *If $\mathcal{R}_0 \leq 1$ then the DFE of system (5) is globally asymptotically stable on the nonnegative orthant. If $\mathcal{R}_0 > 1$ the DFE is unstable.*

Proof.

If $\mathcal{R}_0 > 1$ the instability of the DFE is classical and is a consequence of the results of [10].

We suppose now that $\mathcal{R}_0 \leq 1$, and we consider the following candidate Lyapunov function

$$V_{DFE}(S, I) = \langle B(-\tilde{A}_I^{-1})I \mid S^* \rangle.$$

This function is nonnegative on the positive orthant and is zero at the DFE. The derivative of V along the trajectories is given by

$$\dot{V}_{DFE} = \langle BI | S \rangle \langle B(-\tilde{A}_I^{-1})p | S^* \rangle - \langle BI | S^* \rangle = \langle BI | \mathcal{R}_0 S - S^* \rangle.$$

Taking into account the formula (6) for \mathcal{R}_0 , it is clear that on the compact set Ω we have $\dot{V}_{DFE} \leq 0$.

We consider the largest invariant set \mathcal{L} , contained in the set

$$\{(S, I) \in \Omega \mid \dot{V}_{DFE}(S, I) = 0\}.$$

- For $\mathcal{R}_0 < 1$, using $S^* \gg 0$ (by hypothesis **H1**) we have if $S < S^*$ the relation $\mathcal{R}_0 S - S^* \ll 0$. This implies $BI = 0$, which gives $\dot{I} = \tilde{A}_I I$. Since \tilde{A}_I is Metzler stable, the largest invariant set contained in Ω satisfies $I = 0$, which in turn implies $S = S^*$. By Lasalle's invariance principle [32] (one can also see [6], Theorem 3.7.11, page 346) since we are in a positively invariant compact set, the DFE is globally asymptotically stable in Ω when $\mathcal{R}_0 < 1$.
- When $\mathcal{R}_0 = 1$, we have

$$\dot{V}_{DFE} = \langle BI | S - S^* \rangle \leq 0, \text{ for all } (S, I) \in \Omega.$$

Once again, it is sufficient to show that $\mathcal{L} = \{(S^*, 0)\}$. Let $(S, I) \in \mathcal{L}$, the trajectory of (5) corresponding to this initial point satisfy $\langle BI(t) | S(t) - S^* \rangle = 0$, for all $t \geq 0$. Suppose $I(0) > 0$, then by hypothesis **H2**, $BI(t) \gg 0$ for all $t > 0$ and hence, $S(t) - S^* = 0$ for all $t > 0$. This, together with the first equation of (5), would imply $BI(t) \equiv 0$ which contradict $I > 0$. Hence, if $(S, I) \in \mathcal{L}$ then necessarily $I = 0$ and so $S = S^*$ thanks to the first equation of (5). Therefore, the DFE is globally asymptotically stable in Ω when $\mathcal{R}_0 = 1$.

Since K_ε is absorbing, it remains to examine the trajectories starting in the set $K_\varepsilon \setminus \Omega$.

The set defined by $I = 0$ is invariant by the system. Therefore, any trajectory starting from a point in $K_\varepsilon \setminus \Omega$, with $I = 0$, will converge to $(S^*, 0)$.

Now if a starting point in $K_\varepsilon \setminus \Omega$ satisfies $I > 0$, then by hypothesis **H2**, $BI(t) \gg 0$, for all $t > 0$. Hence from the first equation the trajectory will enter Ω and then converge to the DFE. This proves the global asymptotic stability of the DFE $(S^*, 0)$ in the nonnegative orthant. ■

2.3.2 Model with rank one WAIFW matrix $B = \alpha \beta^T$

With rank one WAIFW matrix $B = \alpha \beta^T$ the system is

$$\begin{cases} \dot{S} = \Lambda - \text{diag}(\mu_S) S + A_S S - \langle \beta | I \rangle \text{diag}(\alpha) S, \\ \dot{I} = \langle \beta | I \rangle P \text{diag}(\alpha) S - \text{diag}(\mu_I + \gamma_I) I + A_I I. \end{cases} \quad (7)$$

Theorem 2.2 *Consider system (7). If $\mathcal{R}_0 \leq 1$, then the DFE is globally asymptotically stable on the nonnegative orthant. If $\mathcal{R}_0 > 1$, the DFE is unstable.*

We consider the following function

$$V(S, I) = \langle \beta | -\tilde{A}_I^{-1} I \rangle$$

We compute the derivative along the trajectories in Ω

$$\begin{aligned} \dot{V} &= \langle \beta | I \rangle \left\langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) S \right\rangle - \langle \beta | I \rangle \\ &= \langle \beta | I \rangle \left(\left\langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) S \right\rangle - 1 \right) \\ &\leq \langle \beta | I \rangle (\mathcal{R}_0 - 1) \leq 0 \end{aligned}$$

- For $\mathcal{R}_0 < 1$, the largest invariant set contained in the set $\dot{V} = 0$ contained in the compact set Ω , satisfies $\langle \beta | I \rangle = 0$. Since \tilde{A}_I is Metzler stable, this set is reduced to $I = 0$, which in turn, by invariance, implies $S = S^*$. By LaSalle invariance's principle, since we are in a positively invariant compact set [32, 6], the DFE is globally asymptotically stable in Ω . A similar argument, as in the proof of Theorem 2.1, permits to conclude to the global stability in the nonnegative orthant.

- For $\mathcal{R}_0 = 1$, we can write

$$\begin{aligned} \dot{V} &= \langle \beta | I \rangle \left\langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) S \right\rangle - \langle \beta | I \rangle \\ &= \langle \beta | I \rangle \left(\left\langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) S^* - \tilde{A}_I^{-1} P \text{diag}(\alpha) (S - S^*) \right\rangle - 1 \right) \\ &= \langle \beta | I \rangle \left(\left\langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) S^* \right\rangle + \left\langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) (S - S^*) \right\rangle - 1 \right) \\ &= \langle \beta | I \rangle \left(\mathcal{R}_0 - 1 + \left\langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) (S - S^*) \right\rangle \right) \\ &= \langle \beta | I \rangle \left\langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) (S - S^*) \right\rangle. \end{aligned}$$

Therefore $\dot{V}(S, I) = 0$ if and only if

$$\langle \beta | I \rangle = 0 \text{ or } \langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) (S - S^*) \rangle = 0.$$

Let $(S, I) \in \mathcal{L}$ the largest invariant set contained in $\{(S, I) \in \Omega : \dot{V}(S, I) = 0\}$. If $\langle \beta | I \rangle = 0$ then we conclude as in the case $\mathcal{R}_0 < 1$. Otherwise, we define $f(S) = \langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) S \rangle = \langle \text{diag}(\alpha) P^T (-\tilde{A}_I^{-1})^T \beta | S \rangle$

The map $f(S)$ is not identically null since $f(S^*) = \mathcal{R}_0$. Hence the vector $\text{diag}(\alpha) P^T (-\tilde{A}_I^{-1})^T \beta > 0$, i.e., it has at least one nonzero component, say, $(\text{diag}(\alpha) P^T (-\tilde{A}_I^{-1})^T \beta)_i \neq 0$ for some $i \in \{1, \dots, n\}$.

Thus $\langle \beta | -\tilde{A}_I^{-1} P \text{diag}(\alpha) (S - S^*) \rangle = 0$ implies at least that $S_i(t) \equiv S_i^*$. The equation governing the evolution of $S_i(t)$ is (e_i being the i th vector of the canonical basis of \mathbb{R}^n):

$$\dot{S}_i = -\mu_{S_i}(S_i(t) - S_i^*) + e_i^T A_S (S(t) - S^*) - \langle \beta | I(t) \rangle \alpha_i S_i(t)$$

Since $S_i(t) \equiv S_i^*$, the matrix A_S is a Metzler matrix and $S \leq S^*$ in Ω , we obtain $e_i^T A_S (S(t) - S^*) = \langle \beta | I(t) \rangle \alpha_i S_i^* = 0$. In particular we have $\langle \beta | I(t) \rangle = 0$ and so we can conclude as in the case $\mathcal{R}_0 < 1$.

2.4 Endemic equilibrium

The proofs for the two systems are similar and use the same principle. However the computations are different so we distinguishes the two proofs.

2.4.1 Model with rank one stochastic distribution matrix $P = p \mathbf{1}^T$

Theorem 2.3 *There exists a unique endemic equilibrium in the nonnegative orthant for system (5) if and only if $\mathcal{R}_0 > 1$.*

Proof. We look for an equilibrium (\bar{S}, \bar{I}) with $\bar{I} > 0$. From the relations

$$\begin{cases} 0 = \Lambda - \text{diag}(\mu_S) \bar{S} + A_S \bar{S} - \text{diag}(\bar{B} \bar{I}) \bar{S}, \\ 0 = \langle \bar{B} \bar{I} | \bar{S} \rangle p + \tilde{A}_I \bar{I} \end{cases} \quad (8)$$

we deduce, since \tilde{A}_I is Metzler stable, that $\bar{I} = \langle \bar{B} \bar{I} | \bar{S} \rangle (-\tilde{A}_I^{-1}) p$. From the second relation of (8) and taking the inner product with p we obtain, setting $\|p\|_2^2 = \langle p | p \rangle$

$$\|p\|_2^2 \langle \bar{B} \bar{I} | \bar{S} \rangle = -\langle \tilde{A}_I \bar{I} | p \rangle.$$

Finally

$$\bar{I} = -\frac{1}{\|p\|_2^2} \langle \tilde{A}_I \bar{I} | p \rangle (-\tilde{A}_I^{-1}) p. \quad (9)$$

Then to compute \bar{I} it is sufficient to find $-\langle \tilde{A}_I \bar{I} | p \rangle$.

Again with the expression $\bar{I} = \langle \bar{B} \bar{I} | \bar{S} \rangle (-\tilde{A}_I^{-1}) p$, we get

$$\langle \bar{B} \bar{I} | \bar{S} \rangle = \langle \bar{B} \bar{I} | \bar{S} \rangle \langle B(-\tilde{A}_I^{-1}) p | \bar{S} \rangle.$$

The condition $\langle \bar{B} \bar{I} | \bar{S} \rangle = 0$ implies, since \tilde{A}_I is Metzler stable, $\bar{I} = 0$, hence $\bar{S} = S^*$. We obtain the DFE and not an endemic equilibrium.

Then if $\langle \bar{B} \bar{I} | \bar{S} \rangle \neq 0$, by simplifying the preceding relation, we get

$$\langle B(-\tilde{A}_I^{-1}) p | \bar{S} \rangle = 1. \quad (10)$$

From the first equation in (8) we have

$$\bar{S} = -[-\text{diag}(\mu_S + B\bar{I}) + A_S]^{-1} \Lambda \quad (11)$$

Using the value of $B\bar{I}$ from relation (9) gives

$$\begin{aligned} \bar{S} &= -\left[-\text{diag}\left(\mu_S + \frac{(-\langle \tilde{A}_I \bar{I} | p \rangle)}{\|p\|_2^2} B(-\tilde{A}_I^{-1}) p\right) + A_S \right]^{-1} \Lambda \\ &= -M(-\langle \tilde{A}_I \bar{I} | p \rangle)^{-1} \Lambda. \end{aligned} \quad (12)$$

Where we have set, for $x \geq 0$

$$M(x) = -\text{diag}\left(\mu_S + \frac{x}{\|p\|_2^2} B(-\tilde{A}_I^{-1}) p\right) + A_S$$

The matrix $M(x)$ is a stable Metzler matrix depending linearly on the positive value x .

Replacing in relation (10), \bar{S} by the expression given by (12) gives

$$\left\langle B(-\tilde{A}_I^{-1})p \mid -M(-\langle \tilde{A}_I \bar{I} \mid p \rangle)^{-1} \Lambda \right\rangle = 1.$$

In other words the scalar $-\langle \tilde{A}_I \bar{I} \mid p \rangle$ is a solution of $H(x) = 1$ with

$$H(x) = \left\langle B(-\tilde{A}_I^{-1})p \mid -M(x)^{-1} \Lambda \right\rangle.$$

We claim that that $H(x)$ is a strictly decreasing function. The derivative of H is given by

$$H'(x) = \left\langle B(-\tilde{A}_I^{-1})p \mid -M(x)^{-1} \operatorname{diag} \left(\frac{B(-\tilde{A}_I^{-1})p}{\|p\|_2^2} \right) M(x)^{-1} \Lambda \right\rangle.$$

On the one hand, we have $B(-\tilde{A}_I^{-1})p \gg 0$ thanks to hypothesis **H2**. On the other hand hypothesis **H1** implies $-M(x)^{-1}\Lambda \gg 0$. Therefore $H'(x) < 0$. This proves that $H(x)$ is strictly decreasing.

The function $H(x)$ satisfies $\lim_{x \rightarrow +\infty} H(x) = 0$. Then a unique positive solution exists if and only if $H(0) > 1$. So we have a unique positive solution since $H(0) = \mathcal{R}_0 > 1$

From (11) we have $S^* > \bar{S} > 0$ and from (9), with $-\langle \tilde{A}_I \bar{I} \mid p \rangle > 0$ and hypothesis **H2** we deduce $\bar{I} \gg 0$, and then the equilibrium is endemic. An endemic equilibrium such that $\bar{I} \gg 0$ is also called a strongly endemic equilibrium [39].

From the preceding analysis we see that if $\mathcal{R}_0 = 1$ then the unique equilibrium is the DFE. In the case $\mathcal{R}_0 < 1$ we have $\bar{I} < 0$, which means that the equilibrium is not biologically feasible. \blacksquare

2.4.2 Model with rank one WAIFW matrix $B = \alpha \beta^T$

Theorem 2.4 *There exists a unique endemic equilibrium in the nonnegative orthant, for system (7) if and only if $\mathcal{R}_0 > 1$.*

Proof.

The proof is in the same spirit as the proof for the case of rank one stochastic distribution matrix. We have the relations for an equilibrium (\bar{S}, \bar{I})

$$\begin{cases} 0 &= \Lambda + \tilde{A}_S \bar{S} - \langle \beta | \bar{I} \rangle \text{diag}(\alpha) \bar{S}, \\ 0 &= \langle \beta | \bar{I} \rangle P \text{diag}(\alpha) \bar{S} + \tilde{A}_I \bar{I}. \end{cases} \quad (13)$$

Where as usual we set $\tilde{A}_S = -\text{diag}(\mu_S) + A_S$ and the analogous setting for \tilde{A}_I .

From the first equation we deduce, since the matrix $-\text{diag}(\mu_S) - \langle \beta | \bar{I} \rangle \text{diag}(\alpha) + A_S$ is Metzler stable for any \bar{I} ,

$$\begin{aligned} \bar{S} &= -[-\text{diag}(\mu_S) - \langle \beta | \bar{I} \rangle \text{diag}(\alpha) + A_S]^{-1} \Lambda \\ &= -M(\langle \beta | \bar{I} \rangle)^{-1} \Lambda. \end{aligned} \quad (14)$$

Where have set

$$M(x) = -\text{diag}(\mu_S + x \alpha) + A_S,$$

as a stable Metzler matrix, depending linearly on $x > 0$.

From the second equation, since \tilde{A}_I is Metzler stable, we get

$$\bar{I} = \langle \beta | \bar{I} \rangle (-\tilde{A}_I^{-1}) P \text{diag}(\alpha) \bar{S}. \quad (15)$$

Then it is sufficient to determine $\langle \beta | \bar{I} \rangle$ in order to compute (\bar{S}, \bar{I}) .

Using relation (15) we have

$$\langle \beta | \bar{I} \rangle = \langle \beta | \bar{I} \rangle \left\langle \beta \left| (-\tilde{A}_I^{-1}) P \text{diag}(\alpha) \bar{S} \right. \right\rangle.$$

If $\langle \beta | \bar{I} \rangle = 0$, then the relations (13) imply $\bar{I} = 0$ and $\bar{S} = S^*$, i.e., the DFE. Otherwise we can simplify and obtain

$$\left\langle \beta \left| (-\tilde{A}_I^{-1}) P \text{diag}(\alpha) \bar{S} \right. \right\rangle = 1.$$

Replacing \bar{S} by its value in (14)

$$\left\langle \beta \left| (-\tilde{A}_I^{-1}) P \text{diag}(\alpha) [-M(\langle \beta | \bar{I} \rangle)^{-1}] \Lambda \right. \right\rangle = 1.$$

In other words the scalar $\langle \beta | \bar{I} \rangle$ is a solution of $H(x) = 1$ with

$$H(x) = \left\langle \beta \left| (-\tilde{A}_I^{-1}) P \text{diag}(\alpha) [-M(x)^{-1}] \Lambda \right. \right\rangle.$$

We claim that $H(x)$ is a strictly decreasing function. The proof is identical to preceding proof of Theorem 2.3, we have just to check carefully that the derivative $H'(x)$ is negative.

$$H'(x) = \left\langle \beta \mid (-\tilde{A}_I^{-1}) P \operatorname{diag}(\alpha) M(x)^{-1} (-\operatorname{diag}(\alpha)) M(x)^{-1} \Lambda \right\rangle$$

By hypothesis **H1**, we have $-M(x)^{-1}\Lambda \gg 0$, and since $\alpha \gg 0$, we have $\operatorname{diag}(\alpha) M(x)^{-1} (-\operatorname{diag}(\alpha)) M(x)^{-1}\Lambda \gg 0$. Therefore, by hypothesis **H2**, we conclude $(-\tilde{A}_I^{-1}) P \operatorname{diag}(\alpha) M(x)^{-1} (-\operatorname{diag}(\alpha)) M(x)^{-1}\Lambda \ll 0$. This, with $\beta > 0$, implies $H'(x) < 0$.

Since $H(x)$ satisfies $\lim_{x \rightarrow +\infty} H(x) = 0$, a unique positive solution exists if and only if $H(0) > 1$. Since $H(0) = \mathcal{R}_0 > 1$, we then have a unique positive solution. Since, from (14) we have $S^* > \bar{S} \gg 0$ and from (15), with $\langle \beta \mid \bar{I} \rangle > 0$, we get $\bar{I} \gg 0$. Hence the equilibrium is strongly endemic.

From the preceding analysis we see that if $\mathcal{R}_0 = 1$ then the unique equilibrium is the DFE. In the case $\mathcal{R}_0 < 1$ we have $\bar{I} < 0$, which means that this equilibrium is not biologically feasible.

3 Global stability of the endemic equilibrium for differential susceptibility and staged progression infectivity models

To prove the global stability of the endemic equilibrium we need to use in more details the structure of A_I and A_S . We will treat in this section a differential susceptibility with staged progression infectivity model. This system has the same form as system (5) with $A_S = 0$.

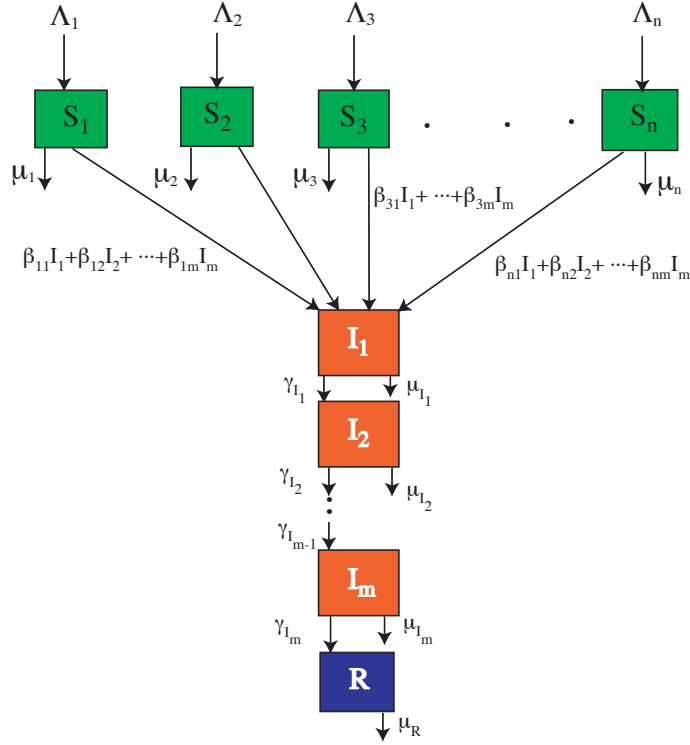


Figure 2: The n susceptible classes and m infected classes model

As before some I_i can be infected and non infectious compartments. For the stability analysis, we discard the removed compartments, by the argument given in the introduction.

The model is given by the following system of ordinary differential equations. We write for simplicity A in lieu of \dot{A}_I .

$$\begin{cases} \dot{S} = \Lambda - \text{diag}(\mu_S) S - \text{diag}(B I) S \\ \dot{I} = \langle B I | S \rangle e_1 + A I. \end{cases} \quad (16)$$

With e_1 the first vector of the canonical basis of \mathbb{R}^m and A the matrix given by

$$A = \begin{bmatrix} -\alpha_1 & 0 & 0 & \cdots & 0 \\ \gamma_1 & -\alpha_2 & 0 & \cdots & 0 \\ 0 & \gamma_2 & -\alpha_3 & \cdots & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots \\ 0 & \cdots & 0 & \gamma_{m-1} & -\alpha_m \end{bmatrix}.$$

Where we have set $\alpha_i = \gamma_{I_i} + \mu_{I_i}$ and $\gamma_i = \gamma_{I_i}$.

Using coordinates, system (16) can be written as follows

$$\begin{cases} \dot{S}_i = \Lambda_i - \mu_{S_i} S_i - \sum_{j=1}^{j=m} \beta_{ij} S_i I_j & \text{for } i = 1 \dots n \\ \dot{I}_1 = \sum_{i=1}^{i=n} \sum_{j=1}^{j=m} \beta_{ij} S_i I_j - \alpha_1 I_1 \\ \dot{I}_j = \gamma_{j-1} I_{j-1} - \alpha_j I_j & \text{for } j = 2 \dots m \end{cases}$$

For system (16), the stability of the DFE is addressed by Theorem 2.1.

Theorem 3.1 *If $\mathcal{R}_0 > 1$ then the unique endemic equilibrium of system (16) is globally asymptotically stable on $\mathbb{R}_+^{n+m} \setminus \{(S, I) : I = 0\}$ the nonnegative orthant minus the stable manifold of the disease free equilibrium.*

The stable manifold of the DFE is the set $\{(S, I) \in \mathbb{R}_+^{n+m} : I = 0\}$.

Proof

We use the following Lyapunov function on the positive orthant. This kind of Lyapunov function has been used, in a different way, in [33, 31, 30, 24, 1, 25, 4, 8]. The challenge is actually to prove that its derivative is nonpositive.

$$V_{EE}(S, I) = \left\langle S - \text{diag}(\bar{S}) \ln S \mid \mathbf{1} \right\rangle + \left\langle B(-A^{-1}) (I - \text{diag}(\bar{I}) \ln I) \mid \bar{S} \right\rangle - \Pi.$$

Where Π is given by $\Pi = \langle \bar{S} - \text{diag}(\bar{S}) \ln \bar{S} \mid \mathbf{1} \rangle + \langle B(-A^{-1}) (\bar{I} - \text{diag}(\bar{I}) \ln \bar{I}) \mid \bar{S} \rangle$.

With the matrix A in this section, we have $(-A^{-1}) e_1 \gg 0$, hence from subsection 2.4 we have $\bar{I} \gg 0$. An equilibrium such that $\bar{I} \gg 0$ is called a strongly endemic equilibrium.

We know that $\bar{S} \gg 0$. Then the assumption $B > 0$ implies $B^T \bar{S} > 0$. Since A is Metzler stable $-A^{-1} > 0$ we conclude that $-(A^{-1})^T B^T \bar{S} > 0$. Therefore $V(S, I)$ is nonnegative and that the endemic equilibrium satisfies $V(\bar{S}, \bar{I}) = 0$.

The derivative \dot{V}_{EE} along the trajectories of (16) is given by

$$\begin{aligned}\dot{V}_{EE} = & \langle \Lambda | \mathbf{1} \rangle - \langle \text{diag}(\mu_S) S | \mathbf{1} \rangle - \langle \text{diag}(BI) S | \mathbf{1} \rangle \\ & - \langle \bar{S} | \text{diag}(S)^{-1} \Lambda \rangle + \langle \bar{S} | \mu_S \rangle + \langle \bar{S} | \text{diag}(S)^{-1} \text{diag}(BI) S \rangle \\ & + \langle BI | S \rangle \langle B(-A^{-1}) e_1 | \bar{S} \rangle + \langle B(-A^{-1}) AI | \bar{S} \rangle \\ & - \langle BI | S \rangle \langle B(-A^{-1}) \frac{\bar{I}_1}{I_1} e_1 | \bar{S} \rangle - \langle B(-A^{-1}) \text{diag}(\bar{I}) \text{diag}(I)^{-1} AI | \bar{S} \rangle.\end{aligned}$$

This can be written

$$\begin{aligned}\dot{V}_{EE} = & \langle \Lambda | \mathbf{1} \rangle - \langle S | \mu_S \rangle - \langle BI | S \rangle - \langle \text{diag}(S)^{-1} \bar{S} | \Lambda \rangle + \langle \bar{S} | \mu_S \rangle + \langle \bar{S} | BI \rangle \\ & + \langle BI | S \rangle \langle B(-A^{-1}) e_1 | \bar{S} \rangle - \langle BI | \bar{S} \rangle \\ & - \langle BI | S \rangle \langle B(-A^{-1}) \frac{\bar{I}_1}{I_1} e_1 | \bar{S} \rangle - \langle B(-A^{-1}) \text{diag}(\bar{I}) \text{diag}(I)^{-1} AI | \bar{S} \rangle.\end{aligned}$$

Using the relation (10), $\langle B(-A^{-1}) e_1 | \bar{S} \rangle = 1$, we have

$$\begin{aligned}\dot{V}_{EE} = & \langle \Lambda | \mathbf{1} \rangle - \langle S | \mu_S \rangle - \langle \text{diag}(S)^{-1} \bar{S} | \Lambda \rangle + \langle \bar{S} | \mu_S \rangle \\ & - \frac{\bar{I}_1}{I_1} \langle BI | S \rangle - \langle B(-A^{-1}) \text{diag}(\bar{I}) \text{diag}(I)^{-1} AI | \bar{S} \rangle.\end{aligned}$$

Using the relation $\Lambda = \text{diag}(\mu_S) \bar{S} + \text{diag}(B\bar{I}) \bar{S}$ we obtain

$$\begin{aligned}\dot{V}_{EE} = & \langle \bar{S} | \mu_S \rangle + \langle B\bar{I} | \bar{S} \rangle - \langle S | \mu_S \rangle \\ & - \langle \text{diag}(S)^{-1} \bar{S} | \text{diag}(\mu_S) \bar{S} \rangle - \langle \text{diag}(S)^{-1} \bar{S} | \text{diag}(B\bar{I}) \bar{S} \rangle + \langle \bar{S} | \mu_S \rangle \\ & - \frac{\bar{I}_1}{I_1} \langle BI | S \rangle - \langle B(-A^{-1}) \text{diag}(\bar{I}) \text{diag}(I)^{-1} AI | \bar{S} \rangle.\end{aligned}$$

$$\begin{aligned}\dot{V}_{EE} = & \left\langle \text{diag}(\mu_S) \bar{S} | \mathbf{2} - \text{diag}(S)^{-1} \bar{S} - \text{diag}(\bar{S})^{-1} S \right\rangle \\ & + \langle B\bar{I} | \bar{S} \rangle - \langle \text{diag}(S)^{-1} \bar{S} | \text{diag}(B\bar{I}) \bar{S} \rangle \\ & - \frac{\bar{I}_1}{I_1} \langle BI | S \rangle - \langle B(-A^{-1}) \text{diag}(\bar{I}) \text{diag}(I)^{-1} AI | \bar{S} \rangle.\end{aligned}$$

The first line of the previous equation is non positive. We will prove that the sum of the 4 remaining expressions is also non positive. We will express the different expressions.

$$\Omega_1 = \langle B \bar{I} | \bar{S} \rangle = \sum_{i=1}^n \sum_{j=1}^m \beta_{ij} \bar{S}_i \bar{I}_j.$$

$$\Omega_2 = -\langle \text{diag}(S)^{-1} \bar{S} | \text{diag}(B \bar{I}) \bar{S} \rangle = -\sum_{i=1}^n \sum_{j=1}^m \beta_{ij} \bar{S}_i \bar{I}_j \frac{\bar{S}_i}{S_i}.$$

$$\Omega_3 = -\frac{\bar{I}_1}{I_1} \langle B I | S \rangle = -\sum_{i=1}^n \beta_{i1} \bar{S}_i \bar{I}_1 \frac{S_i}{\bar{S}_i} - \sum_{i=1}^n \sum_{j=2}^m \beta_{ij} \bar{S}_i \bar{I}_j \frac{S_i}{\bar{S}_i} \frac{\bar{I}_1}{I_1} \frac{I_j}{\bar{I}_j}$$

We will rewrite the last expression

$$\Omega_4 = -\left\langle B(-A^{-1}) \text{diag}(\bar{I}) \text{diag}(I)^{-1} A I | \bar{S} \right\rangle.$$

We have, for $k = 1, \dots, m-1$, the relations $A e_k = -\alpha_k e_k + \gamma_k e_{k+1}$ and for the last index $A e_m = -\alpha_m e_m$. Then

$$\begin{aligned} \Omega_4 &= -\sum_{k=1}^m I_k \left\langle B(-A^{-1}) \text{diag}(\bar{I}) \text{diag}(I)^{-1} A e_k | \bar{S} \right\rangle \\ &= \sum_{k=1}^m \alpha_k \bar{I}_k \left\langle B(-A^{-1}) e_k | \bar{S} \right\rangle - \sum_{k=1}^{m-1} I_k \gamma_k \frac{\bar{I}_{k+1}}{I_{k+1}} \left\langle B(-A^{-1}) e_{k+1} | \bar{S} \right\rangle. \end{aligned}$$

Let u_k be defined by $u_k = \langle B(-A^{-1}) e_k | \bar{S} \rangle$. We claim that the following relation holds for $k = 2, \dots, m$

$$\gamma_{k-1} u_k \bar{I}_{k-1} = \sum_{j=k}^m \bar{I}_j \langle B e_j | \bar{S} \rangle. \quad (17)$$

We will prove this expression later. For the moment we assume this relation. If we take into account $\alpha_k \bar{I}_k = \gamma_{k-1} \bar{I}_{k-1}$ for $k = 2, \dots, m$ and $\alpha_1 \bar{I}_1 = \langle B \bar{I} | \bar{S} \rangle$, we obtain

$$\begin{aligned} \Omega_4 &= \sum_{k=1}^m \left(\sum_{j=k}^m \bar{I}_j \langle B e_j | \bar{S} \rangle \right) - \sum_{k=1}^{m-1} \frac{I_k}{\bar{I}_k} \frac{\bar{I}_{k+1}}{I_{k+1}} \left(\sum_{j=k+1}^m \bar{I}_j \langle B e_j | \bar{S} \rangle \right), \\ &= \sum_{i=1}^n \sum_{j=1}^m j \beta_{ij} \bar{S}_i \bar{I}_j - \sum_{i=1}^n \sum_{j=2}^m \beta_{ij} \bar{S}_i \bar{I}_j \left(\sum_{k=1}^{j-1} \frac{I_k}{\bar{I}_k} \frac{\bar{I}_{k+1}}{I_{k+1}} \right). \end{aligned}$$

Then we get for the sum of these four expressions

$$\begin{aligned} \sum_{i=1}^4 \Omega_i &= \sum_{i=1}^n \beta_{i1} \bar{S}_i \bar{I}_1 \left[2 - \frac{\bar{S}_i}{S_i} - \frac{S_i}{\bar{S}_i} \right] \\ &\quad + \sum_{i=1}^n \sum_{j=2}^m \beta_{ij} \bar{S}_i \bar{I}_j \left[j + 1 - \frac{\bar{S}_i}{S_i} - \frac{S_i}{\bar{S}_i} \frac{\bar{I}_1}{I_1} \frac{I_j}{\bar{I}_j} - \sum_{k=1}^{j-1} \frac{I_k}{\bar{I}_k} \frac{\bar{I}_{k+1}}{I_{k+1}} \right]. \end{aligned}$$

Using the comparison between the arithmetical and the geometrical means we see that $\dot{V}_{EE} \leq 0$. It must be noticed however that \dot{V}_{EE} is not negative definite since some β_{ij} can be zero.

The endemic equilibrium satisfies

$$\langle \Lambda | \mathbf{1} \rangle - \langle \mu_S \bar{S} | \mathbf{1} \rangle + \langle A \bar{I} | \mathbf{1} \rangle = 0$$

Since $\langle A \bar{I} | \mathbf{1} \rangle = -\gamma_m \bar{I}_m - \langle \mu_I \bar{I} | \mathbf{1} \rangle$, and using the definition of μ_0 (Lemma 2.2), we get $\langle \bar{S} | \mathbf{1} \rangle + \langle \bar{I} | \mathbf{1} \rangle \leq \frac{\langle \Lambda | \mathbf{1} \rangle}{\mu_0}$ which proves that the endemic equilibrium (\bar{S}, \bar{I}) belongs to K_ε for all $\varepsilon \geq 0$.

Let \mathcal{L} be the largest invariant subset of K_ε , contained in $\dot{V}_{EE} = 0$. Each element (S, I) of \mathcal{L} must satisfy

$$\left\langle \text{diag}(\mu_S) | \mathbf{2} - \text{diag}(S)^{-1} \bar{S} - \text{diag}(\bar{S})^{-1} S \right\rangle = 0.$$

Since $\mu_S \gg 0$ this implies $S = \bar{S}$, and so in \mathcal{L} , we must have $\text{diag}(BI) \bar{S} = \Lambda - \text{diag}(\mu_S) \bar{S}$. On the other hand we have $\text{diag}(B \bar{I}) \bar{S} = \Lambda - \text{diag}(\mu_S) \bar{S}$. Thus in \mathcal{L} , the dynamics of I are governed by

$$\dot{I} = \langle B \bar{I} | \bar{S} \rangle - A I$$

Since A is stable the largest invariant set \mathcal{L} is then reduced to $\{(\bar{S}, \bar{I})\}$. This proves the global asymptotic stability of the endemic equilibrium (\bar{S}, \bar{I}) in the interior of K_ε by Lasalle's invariance principle [32, 6]. The global asymptotic stability of the endemic equilibrium on $\mathbb{R}_+^n \times \mathbb{R}_+^m \setminus \{(S, 0)\}$ follows from the fact that the set K_ε is an absorbing set and that the boundary of the positive orthant minus the stable manifold of the DFE is not invariant by (16).

To end the proof we have to prove our claim 17. The proof of the validity of our claim is made by induction on k .

We prove the claim for $k = 2$. We have, using $\langle B(-A^{-1})e_i | \bar{S} \rangle = 1$, the following equalities

$$\begin{aligned}
Ae_1 &= -\alpha_1 e_1 + \gamma_1 e_2 \\
-e_1 &= -\alpha_1 (-A^{-1})e_1 + \gamma_1 (-A^{-1})e_2 \\
\gamma_1 \bar{I}_1 \langle B(-A^{-1})e_2 | \bar{S} \rangle &= \alpha_1 \bar{I}_1 \langle B(-A^{-1})e_1 | \bar{S} \rangle - \bar{I}_1 \langle B(-A^{-1})e_1 | \bar{S} \rangle \\
\gamma_1 u_2 \bar{I}_1 &= \alpha_1 \bar{I}_1 - \bar{I}_1 \\
\gamma_1 u_2 \bar{I}_1 &= \langle B(-A^{-1})e_1 | \bar{S} \rangle \bar{I}_1 - \bar{I}_1 + \sum_{i=2}^m \langle B(-A^{-1})e_i | \bar{S} \rangle \\
\gamma_1 u_2 \bar{I}_1 &= \sum_{i=2}^m \langle B(-A^{-1})e_i | \bar{S} \rangle
\end{aligned}$$

We now suppose that

$$\gamma_{k-2} u_{k-1} \bar{I}_{k-2} = \sum_{j=k-1}^m \langle B(-A^{-1})e_j | \bar{S} \rangle$$

Then

$$\begin{aligned}
Ae_{k-1} &= -\alpha_{k-1} e_{k-1} + \gamma_{k-1} e_k \\
-e_{k-1} &= -\alpha_{k-1} (-A^{-1})e_{k-1} + \gamma_{k-1} (-A^{-1})e_k \\
\gamma_{k-1} \bar{I}_{k-1} \langle B(-A^{-1})e_k | \bar{S} \rangle &= \alpha_{k-1} \bar{I}_{k-1} \langle B(-A^{-1})e_{k-1} | \bar{S} \rangle \\
&\quad - \bar{I}_{k-1} \langle B(-A^{-1})e_{k-1} | \bar{S} \rangle \\
\gamma_{k-1} u_k \bar{I}_{k-1} &= \alpha_{k-1} \bar{I}_{k-1} u_{k-1} - \bar{I}_{k-1} \langle B(-A^{-1})e_{k-1} | \bar{S} \rangle \\
\gamma_{k-1} u_k \bar{I}_{k-1} &= \gamma_{k-2} \bar{I}_{k-2} u_{k-1} - \bar{I}_{k-1} \langle B(-A^{-1})e_{k-1} | \bar{S} \rangle \\
\gamma_{k-1} u_k \bar{I}_{k-1} &= \sum_{j=k-1}^m \langle B(-A^{-1})e_j | \bar{S} \rangle - \bar{I}_{k-1} \langle B(-A^{-1})e_{k-1} | \bar{S} \rangle \\
\gamma_{k-1} u_k \bar{I}_{k-1} &= \sum_{j=k}^m \langle B(-A^{-1})e_j | \bar{S} \rangle
\end{aligned}$$

This ends the proof of the theorem. ■