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Bifurcations and Exchance of Stability with Density Dependence in a Coinfection Model and an Age-structured Population Model

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ABSTRACT

In nature many pathogens and in particular strains of pathogens with negative effects on species coexists. This is for simplicity often ignored in many epidemiological models. It is however still of interest to get a deeper understanding how this coexistence affects the dynamics of the disease. There are several ways at which coexistence can influence the dynamics. Coinfection which is the simultaneous infection of two or more pathogens can cause increased detrimental health effects on the host [3]. Pathogens can also limit each others growth by the effect of cross immunity [1] as well as promoting isolation. On the contrary one pathogen can also aid another by making the host more vulnerable to as well as more inclined to spread disease [7].

Population dynamics is often analysed using mathematical models. These models may need to take into account various factors which each results in increased complexity. This increase in complexity limits what can be done analytically. In papers I-III we study the effects of density dependence in a system of two coexisting diseases. The density dependence is modelled the form of a carrying capacity on the host population.

Spread of disease is dependent on the density of the population. If a pathogen is able to spread or not, is strongly correlated with how many times individuals interact with each other. This in turn depends on how many individuals live in a given area. The aim of papers I-III is to provide an understanding how different factors including the carrying capacity of the host population affect the dynamics of two coexisting diseases.

In papers I-III we investigate how the parameters effects the long term solution in the form of a stable equilibrium point. In particular we want to provide an understanding of how changes in the carrying capacity affects the long term existence of each disease as well as the occurrence of coinfection.

The model that is studied in papers I-III is a generalisation of the standard susceptible, infected, recovered (SIR) compartmental model. The SIR model is generalised by the introduction of the second infected compartment as well as the coinfection compartment. We also use a logistic growth term à la Verhulst with associated carrying capacity K. In paper I and II we make the simplifying assumption that a coinfected individual has to, if anything, transmit both of the disease and simply not just one of them. This restriction is relaxed in paper III. In all papers I-III however we do restrict ourself by letting all transmission rates, that involves scenarios where the newly infected person does not move to same compartment as the infector, to be small. By small we here mean that the results at least hold when the relevant parameters are small enough.

In all paper I-III it turns out that for each set of parameters excluding K there exist a unique branch of mostly stable equilibrum points depending continuously on K. We differentiate the equilibrium points of the branch by which compartments are non-zero which we refer to as the type of the equilibrium. The way that the equilibrium point changes its type with K is made clear with the use of transition diagrams together with graphs for the stable susceptible population over K.

In paper I simple algebraic expression for each possible type of equilibrium point is derived with the notable exception of the inner equilibrium also referred to as the coexistence equilibrium point. The algebraic expression of the coexistence equilibrium point is to complicated to get any meaningful insight from. Two out of four different transition scenarios

of the equilibrium branch is derived involving two sets of parameter. These branches are stable for all K.

The complex expression of the coexistence equilibrium makes the stability analysis considerably harder for the remaining two choices of parameters which leads to equilibrium branches that involves an inner equilibrium. Therefore the original paper meant to study the model in paper I and II where separated into two part i.e. paper I and II.

In paper II we tackle the problem of deriving stability of the coexistence equilibrium with a certain bifurcation technique. This is in contrast to paper I where we only do the standard analysis of the Jacobian and its eigenvalues. The remaining two possibilities of transition is derived. The stability of the entire branch is derived for one of the scenarios while the possibility of loss of stability for large K resulting in a Hopf bifurcation is shown for the other scenario.

In paper III the introduction of certain parameters that was set to zero in paper I and II leads to changes in the transition scenarios. The number of possible transition scenarios are reduced to three. The equilibrium point is always stable in all scenarios. An important observation is that, in contrast to paper I and II, the existence of coinfection now implies the existence of both diseases as single infections. The solution in paper III is a small perturbation of the solution in paper I and II, consequently the results in paper I and II helps create an intuition of the dynamics in paper III.
In paper IV we consider a model for a single age-structured population á la Mckendric-von-Foerster with the addition of differing density dependence on the birth and death rates. Each vital rate is a function of age as well as a weighing of the population also referred to as a size. The birth rate influencing size and the death rate influencing size can be weighted differently allowing us to consider different age-groups to influence the birth and death rate in different proportions compared to other age groups.

It is commonly assumed that an increase of population density is detrimental to the survival of each individual. However, for various reasons, it is know that for some species survival is positively correlated with population density when the population is small. This is called the Allee effect and our model includes this scenario.

It is shown that the trivial equilibrium, which signifies extinction, is locally stable if the basic reproductive rate R_0 is less then 1. This implies global stability with certain extinction if no Allee effect is present. However if the Allee effect is present we show that the population can persist even if $R_0 < 1$.

Demographics is an important factor to take into consideration, since the total population does not by itself predict the size of the next generation and should at least be divided into juveniles and adults. Age-structure is also important when predicting the spread and consequences of disease. Diseases can effect the health of age-groups differently and some age-groups can be more inclined to spread the disease. Therefore there is a future desire to combine the models in paper I-III with paper IV.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Många sjukdomsframkallande ämnen eller organismer förekommer tillsammans i naturen. För enkelhets skull så ignoreras detta ofta i epidemiska modeller. Det är ändå av intresse att få en djupare förståelse för hur denna samexistens kan påverka smittspridningen. Det finns flera sätt på vilka samexisterande patogener kan påverka varandras smittspridning. Saminfektion, vilket inträffar då en individ drabbas av två eller flera patogener samtidigt, kan orsaka ökade negativa effekter hos de som drabbats. Patogener kan också motverka varandras spridning genom att motivera isolering. Anskaffad immunitet för en patogen kan också leda till immunitet mot en annan patogen. Däremot kan patogener även hjälpa varandras smittspridning genom att göra värddjuret mer mottaglig såväl som mer benägen att sprida sjukdomen.

Populationsdynamik analyseras ofta med matematiska modeller. Dessa modeller kan ta i beaktning en mängd olika faktorer vilka var och en leder till ökad komplexitet. Denna ökning I komplexitet begränsar vad som kan göras analytiskt. I papper I-III studeras hur populationstätheten hos värdpopulationen påverkar smittspridningen. Populationsstorleken och dess täthet antas bero på miljöns bärförmåga.

Spridning av smittoämnen är beroende av populationstätheten. En patogens förmåga att sprida sig till en annan individ beror på frekvensen av interaktioner mellan individer, vilket i sin tur beror på hur många individer som lever på en given levnadsyta. Målet med papper I-III är att ge en inblick i hur olika faktorer, där ibland populationstätheten hos värddjuret, påverkar dynamiken för två samexisterande patogener.

I papperna I-III undersöker vi hur de olika parametrar för modellen påverkar den långsiktiga smittdynamiken i form av stabila jämnviktspunkter. Speciellt så vill vi förse en förståelse för hur ändringar hos bärförmågan påverkar den långsiktiga existensen av vardera sjukdom såväl som förekomsten av saminfektion.

Modellen som studeras i papper I-III är en generalisation av den vanligt förekommande susceptible-infected-recovered (SIR) modellen där värdbefolkningen delas upp i mottagliga, infekterade och återhämtade. Vår SIR modell generaliseras genom att vi introducerar två extra uppdelningar, en för individer smittade med den introducerade extra smittan och en del bestående av saminfekterade individer. Vi introducerar också ett speciellt täthetsberoende i tillväxttermen med associerad bärförmåga K för den mottagliga delen av populationen. I papper I och II gör vi det förenklande antagandet att saminfekterade individer endast kan sprida båda sjukdomarna samtidigt och inte endast en av dem. Denna restriktion relaxeras i papper III. I alla papperna I-III begränsar vi oss dock genom att anta att det sällan sker smittoscenarior där den nyligen smittade inte överförs till samma indelning som personen som orsakade smittan.

I papperna I-III visar det sig att för varje mängd parametrar undantaget bärförmågan K så existerar det en förgrening av jämnviktspunkter som beror kontinuerligt på K. Vi väljer att differentiera jämnviktspunkterna i olika typer med avseende på vilka möjliga smittoämnen såväl som saminfektion som existerar. Hur ändringar i bärförmågan påverkar jämviktpunktens typ presenteras via övergångsdiagram tillsammans med grafer för den stabila mottagliga populationen som funktion av K.

I papper I tas enkla uttryck fram för varje typ av jämnviktspunkt förutom samexistensjämviktspunkten alltså den typ av jämnviktspunkt som inkluderar alla sjukdomsscenarior. Uttrycket för denna punkt är för komplext för att få någon meningsfull information från. Två av fyra olika övergångsscenarior av jämnviktsförgreningen härleds vilka inträffar för två

olika mängder av parametervärden. Dessa förgreningar är stabila för alla K. Det komplexa uttrycket för samexistensjämnviktspunkten gör stabilitets analysen betydligt svårare för de övriga förgreningsscenariorna vilka involverar denna punkt. Därför delades den ursprungliga artikeln som behandlade modellen i papper I och II upp i två delar, alltså papper I och II.

I papper II tar vi an problemet med att härleda stabilitet för samexistensjämnviktspunkten. De två kvarvarande förgreningsscenariorna tas fram. Den ena grenen är stabil för alla K medans den andra grenen förlorar sin stabilitet för stora K vilket leder till oscillerande lösningar kring jämnviktspunkten som då är en samexistenspunkt.

Introduktionen av vissa parametrar i papper III som tidigare var satta till noll leder till en förändring i hur grenen övergår mellan de olika typerna. Antalet möjliga scenarior reduceras till tre. Jämnviktspukterna på grenen är alltid stabila. En intressant observation är att till skillnad från de tidigare papperna så medför nu existens av saminfektion att det även måste förekommer isolerade infektioner av vardera smittoämne. Lösningen i papper III är mycket nära motsvarande lösning i papper I och II så resultatet i de tidigare papperna hjälper till att skapa en intuition över hur jämnviktspunkten ändras med bärförmågan.

I papper IV behandlar vi en modell för en enskild smittfri population med åldersstruktur. I modellen låter vi födelseantalet och dödstalet bero på var sin viktning av populationen. Viktningen görs efter ålder. Detta tillåter oss till exempel att anta att vuxna individer upptar mer av miljöns resurser än barn och därmed har större negativ verkan för andra individers överlevnad.

Vanligtvis antas en ökning av populationen ha en negativ effekt på individers möjlighet att överleva och reproduceras. Av diverse anledningar så uppvisar en del arter ett motsatt samband när populationen är tillräckligt liten. Detta fenomen kallas Allee effekten och våran modell inkluderar detta scenario. Vi härleder villkor som anger om population kommer att dö ut eller inte.

Demografi är en viktig faktor att ta i beaktning eftersom det totala antalet individer i en population i sig inte säger något om hur stor populationen kommer vara nästa generation. Vi måste också bland annat veta hur många som är i reproduktiv ålder. Åldersstruktur är också viktigt för att uppskatta spridning av sjukdom. Sjukdomars påverkan av hälsan kan variera mellan olika åldersgrupper. Vissa åldersgrupper kan även vara mer benägna att sprida smittan. Därför är det av framtida intresse att kombinera modellerna i papper I-III med papper IV.

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List of Papers

I. J. Andersson,S. Ghersheen,V. Kozlov, V. Tkachev, and U. Wennergren. *Effect of density dependence on coinfection dynamics.* Analysis and Mathematical Physics, 11(4), 2021.
Author contribution: Contribution to the model development and its analysis, writing of the draft

II. J. Andersson, S. Ghersheen, V. Kozlov, V. Tkachev, and U. Wennergren. *Effect of density dependence on coinfection dynamics : part 2.* Analysis and Mathematical Physics, 11(4), 2021.
Author contribution: Contribution to the model development and its analysis, writing of the draft

III. J. Andersson, V. Kozlov, V. Tkachev, and U. Wennergren. *Bifurcations and the exchange of stability with coinfection*, manuscript
Author contribution: Contribution to the model development and its analysis, writing of the draft

IV. J. Andersson, V. Kozlov, V. Tkachev, S. Radosavljevic. *Density–Dependent Feedback in Age–Structured Populations.* Journal of Mathematical Science 242, 2–24, 2019.

Contents

1 Modelling population dynamics

Populations, and consequently disease dynamics, can be modelled with the use of differential equations. The population is wrongfully modelled as being infinitely divisible and not consisting of a finite number of individuals. This relaxation, which is well motivated for large populations, is done in order to take advantage of established mathematical methods that can be applied to these differential systems. Many different models exists describing dynamical processes in nature like predator/prey relations, interspecies competition, spread of disease, evolution and more. The aim with these models are to explain and predict dynamical processes in populations.

A populations growth is determined by its vital rates, which are the birth rate and death rate. Migration between populations can also be considered but this is not done in this dissertation. The vital rates can in turn be dependent on a wide range of factors such as age, seasons, other populations, resources, population density and position. For a single homogeneous population, the population dynamics is determined by the differential equation

$$\frac{dN(t)}{dt} = (\beta - \mu)N(t) \tag{1.1}$$

where N is the population size and β, μ are the birth and death rates respectively. The vital rates β and μ are in general dependent on other parameters describing factors such as those mention above. If a collection of populations $N_1, N_2, ...N_k$ influence each others vital rates, perhaps through a predator prey relation, this will result in a system of differential equations,

$$\frac{\partial N_i}{\partial t} = (\beta_i(N_1, N_2, ..., N_k) - \mu_i(N_1, N_2, ..., N_k))N_i \quad i = 1, 2, ..., k.$$

The increase in the number of equations provide a significant increase in complexity.
A population does not need to be homogeneous and individuals can have different attributes resulting in different vital rates. There are two ways by which this can be modelled. Either one could divide the population into several subpopulations or one could model the population with a distribution. Integrating this distribution over a range of attributes then gives the size of the population having attributes in that range. Subpopulations in the model can introduce the possibility of individuals changing populations which gives rise to more complexity in the model. Some reasons for changing subpopulation are aging, migration, and becoming sick or healthy.
When constructing a model one has to decide which factors, influencing the vital rates, needs to be taken into consideration and in what way they should be modelled. It is important that the parameters can be measured to some accuracy but in many cases this could be hard or impossible. This often limits what can be taken into consideration in the model. Too many parameters can also results in models that are to complex to get any meaningful insights from. The way that the vital rates depend on different factors can be modelled in different ways often ranging from simpler less precise to more complex and precise formulas and methods. In many cases, where data is scarce, what is the more precise way is up to debate see [12].

1.1 Interpreting the solution

In general an analytic expression for the solution of a system of differential equations can not be found or is to complex to get any meaningful insight from. It is up to the mathematician to instead derive properties of the solution that gives a meaningful insight into the ecological system. Often long term behaviour of the solution is of interest since the ecologic system is assumed to be unchanged for a long time. The populations of the model could either converge towards a stable equilibrium point or they could converge towards a periodic solution. Determining equilibria and deriving their stability is in general easier then expressing the analytical solution and still gives a satisfactory insight of the solution. When the populations can not be found to converge toward a expressible long term solution one can instead derive lower and upper bounds of the solution perhaps even bounds that are dependent on time.

2 Modelling coinfection

In this section we consider the related models for coinfection used in papers I,II,III. The model is based on the standard SIR model and describes the progression of two pathogens, perhaps two different strains of a disease. The strains influence each other by changing the vital rates and transmission rates of the host. The model considered in III is the most general and is given as follows

$$\Big(r(1-\frac{S}{K}) - \alpha_1 I_1 - \alpha_2 I_2 - (\beta_1+\beta_2+\alpha_3)I_{12}\Big)S = S', \tag{2.1}$$

$$(\alpha_1 S - \eta_1 I_{12} - \gamma_1 I_2 - \mu_1)I_1 + \beta_1 S I_{12} = I_1' \tag{2.2}$$

$$(\alpha_2 S - \eta_2 I_{12} - \gamma_2 I_1 - \mu_2)I_2 + \beta_2 S I_{12} = I_2', \tag{2.3}$$

$$(\alpha_3 S + \eta_1 I_1 + \eta_2 I_2 - \mu_3)I_{12} + (\gamma_1+\gamma_2)I_1 I_2 = I_{12}' \tag{2.4}$$

$$\rho_1 I_1 + \rho_2 I_2 + \rho_3 I_{12} - \mu_4' R = R', \tag{2.5}$$

where we use the following notation for the different compartments:

- S represents the susceptible class,
- I_1 and I_2 are infected classes from strain 1 and strain 2 respectively,
- I_{12} represents co-infected class,
- R represents the recovered class.

Since the recovered class does not influence the other compartments it is not important and can be ignored when studying the dynamics of the system. It can then be derived from I_1, I_2, I_{12}.

Following [8, 4, 5], we assume limited population growth by making the per capita growth rate depend on the density of the population. The density dependence is modelled à la Verhulst. We also consider the recovery of each infected class. The fundamental parameters of the system are:

- b is the birthrate,
- K is the carrying capacity,
- ρ_i is the recovery rate for each infected class ($i = 1, 2, 3$),
- μ_i' is the death rate of each class, ($i = 1, 2, 3, 4$) and $\mu_i = \rho_i + \mu_i', i = 1, 2, 3$,
- γ_i is the rate at which individuals infected with one strain get infected with the other strain from single infected individuals and move to the coinfected class ($i = 1, 2$).
- α_1, α_2, α_3 are the rates of transmission of strain 1, strain 2 and both strains (in the case of coinfection),
- β_i is the rate at which susceptibles contracts disease i but not the other disease from a coinfected individuals $i = 1, 2$
- and η_i is the rate at which individuals infected by one strain gets coinfected by the coinfected class ($i = 1, 2$).

It is convenient to introduce the parameters $\sigma_i = \frac{\mu_i}{\alpha_i} \quad i = 1, 2, 3$. The introduced parameter σ_i is the minimal population size of susceptibles at which disease i can start to propagate. Also $\frac{S}{\sigma_i}$ is the basic reproductive rate of the disease. In order to differentiate the two diseases we introduce the inequality

$$\sigma_1 < \sigma_2 \quad \sigma_i = \frac{\mu_i}{\alpha_i}. \tag{2.6}$$

The inequality (2.6) indicates that disease 1 is more inclined to spread through a naive population. In order to reduce the number of possible scenarios that needs to be handled, we throughout papers I-III make the following restriction

$$\sigma_1 < \sigma_2 < \sigma_3.$$

That is we assume that coinfection is less incline to spread than each of the diseases separately. One can motivate this assumption by for instance pointing out that coinfected individuals might be showing more symptoms and thus are more inclined to quarantine themselves.

2.1 Some notes on density dependence

Our logistic growth term provides no information on the specifics of why the population declines. We could imagine that the declined is caused by a decrease in birth rate and/or increase in death rate. In [13] it is assumed that the population density only impacts the birth rate and not the death rate. With no disease present the differential system of equations in [13] becomes the equation $S' = (b(1 - \frac{S}{K^*}) - \mu_0)S$, here the parameter K^* is no longer the carrying capacity since $S'(K^*) \neq 0$. By making the change of variable $K = \frac{K^*}{b}(b - \mu_0)$ we get the same logistic term as in paper I,II,III and thus we can easily translate any result from our model to the case where only the birth rate is impacted by population density.
Expanding to the case where disease is present i.e. (2.1)-(2.4) we note that the compartments of infection does not experience any logistic growth

2.2 Expanding on complementary theory

In [14] the equilibria and there stability are studied for model (2.1)-(2.5) for the special case $\beta_i, \gamma_i = 0$. In this case the model can be written in the form

$$\frac{\partial Y_i}{\partial t} = F_i(Y)Y_i \quad i = 0, \ldots, 3 \tag{2.7}$$

where we denote

$$F(Y) = -q + AY \tag{2.8}$$

with

$$Y^t = (Y_0, Y_1, Y_2, Y_3) = (S, I_1, I_2, I_{12}) > 0 \tag{2.9}$$

$$F(Y) = \begin{pmatrix} F_0(Y) \\ F_1(Y) \\ F_2(Y) \\ F_3(Y) \end{pmatrix}, \quad q = \begin{pmatrix} -r \\ \mu_1 \\ \mu_2 \\ \mu_3 \end{pmatrix}, \quad A = \begin{pmatrix} -\frac{r}{K} & -\alpha_1 & -\alpha_2 & \alpha_3 \\ \alpha_1 & 0 & 0 & -\eta_1 \\ \alpha_2 & 0 & 0 & -\eta_2 \\ \alpha_3 & \eta_1 & \eta_2 & 0 \end{pmatrix} \tag{2.10}$$

This structure of the problem is common for population models and corresponds with the well studied linear complementary problem (LCP). In [14] the well established LCP machinery is used to derive results for stability. In paper I-III however, since becoming infected does not necessarily mean that one moves to that same compartment as the infecter we get extra terms in (2.7) that are not dependent on Y_i. This thus adds to the complexity and we can no longer use the methods for the LCP.

The equilibrium points and their stability

An equilibrium point of (2.1)- (2.5) is a point $(S^*, I_1^*, I_2^*, I_{12}^*)$ for which all compartments has zero derivative i.e. satisfies

$$\Big(r(1-\frac{S}{K}) - \alpha_1 I_1 - \alpha_2 I_2 - (\beta_1+\beta_2+\alpha_3)I_{12}\Big)S = 0, \tag{2.11}$$

$$(\alpha_1 S - \eta_1 I_{12} - \gamma_1 I_2 - \mu_1)I_1 + \beta_1 S I_{12} = 0 \tag{2.12}$$

$$(\alpha_2 S - \eta_2 I_{12} - \gamma_2 I_1 - \mu_2)I_2 + \beta_2 S I_{12} = 0, \tag{2.13}$$

$$(\alpha_3 S + \eta_1 I_1 + \eta_2 I_2 - \mu_3)I_{12} + (\gamma_1+\gamma_2)I_1 I_2 = 0 \tag{2.14}$$

By assuming at most one of the disease compartments to be non-zero we get explicit expressions for different non-trivial equilibria.

$$G_{000} = (S^*, 0, 0, 0), \qquad S^* = K, \tag{2.15}$$

$$G_{100} = \Big(S^*, \frac{r}{K\alpha_1}(K-S^*), 0, 0\Big), \qquad S^* = \sigma_1 \tag{2.16}$$

$$G_{010} = \Big(S^*, 0, \frac{r}{K\alpha_2}(K-S^*), 0\Big), \qquad S^* = \sigma_2 \tag{2.17}$$

$$G_{001} = \Big(S^*, 0, 0, \frac{r}{K\alpha_3}(K-S^*)\Big), \qquad S^* = \sigma_3 \tag{2.18}$$

$$\tag{2.19}$$

The subscripts in the notation G_{jkl} indicates if the respective compartment is present (= 1) or not (= 0). In the case $\beta = 0$ we also get simple expressions for equilibria for which both diseases are present in the population but where one of the diseases only exists together with the other as coinfection.

$$G_{101} = \Big(S^*, \frac{\alpha_3}{\eta_1}(\sigma_3 - S^*), 0, \frac{\alpha_1}{\eta_1}(S^* - \sigma_1)\Big), \qquad S^* = K(1-\frac{1}{\eta_1^*}), \tag{2.20}$$

$$G_{011} = (S^*, 0, \frac{\alpha_3}{\eta_2}(\sigma_3 - S^*), \frac{\alpha_2}{\eta_2}(S^* - \sigma_2)), \qquad S^* = K(1-\frac{1}{\eta_2^*}), \tag{2.21}$$

where

$$\eta_1^* = \frac{\eta_1}{A_1}, \qquad A_1 = \frac{\alpha_1\alpha_3}{r}(\sigma_3 - \sigma_1)$$
$$\eta_2^* = \frac{\eta_2}{A_2}, \qquad A_2 = \frac{\alpha_2\alpha_3}{r}(\sigma_3 - \sigma_2).$$

As we will see later η_1^* and η_2^* has a connection with the basic reproductive rate R_0 of the coinfection compartment. Comparing η_1^*, η_2^* and 1 gives us information about if coinfection can spread, in certain situations, in much the same way as when R_0 is compared with 1.
A common theme of these equilibria mentioned above is that they are independent on the parameters γ_i and β_i. These parameters distinguish themselves

by describing interactions where two compartments mix and increases a different third compartment.
In the special case where γ_i and β_i are zero we can get a relatively simple expression for the inner equilibria where all compartments coexist.

$$G_{111} = \Big(\frac{\Delta_\mu}{\Delta_\alpha}, \frac{rA_2}{\Delta_\alpha}\Big(1 - \eta_2^*\Big(1 - \frac{\Delta_\mu}{K\Delta_\alpha}\Big)\Big), \frac{rA_1}{\Delta_\alpha}\Big(\eta_1^*\Big(1 - \frac{\Delta_\mu}{K\Delta_\alpha}\Big) - 1\Big), \frac{rA_3}{\Delta_\alpha}\Big), \quad (2.22)$$

where

$$A_3 = \frac{\alpha_1\alpha_2}{r}(\sigma_2 - \sigma_1), \quad (2.23)$$

$$\Delta_\mu = \eta_1\mu_2 - \eta_2\mu_1, \quad (2.24)$$

$$\Delta_\alpha = \eta_1\alpha_2 - \eta_2\alpha_1. \quad (2.25)$$

For each equilibria, if we imagine that all basic parameter except K are fixed we see that that there exist K such that at least some compartment is negative and thus the equilibria does not correspond to any real large time behaviour, we say that it does not exist for such K. If K is such that the equilibria exists we still need to now if it is stable to deduce any long term behaviour of the system. This is done by examining if all the eigenvalues of the Jacobian matrix are negative.

2.3 The study of branches

Usually each type of equilibrium point is analysed separately. In this thesis we extend this approach and look at branches of equilibrium points parametrized by K. By an equilibrium branch we mean any continuous in $K \geq 0$ family of equilibrium points which are locally stable for all but finitely many threshold values of K. Branches typically bifurcates meaning that a sudden change in behaviour happens with a small change of the parameter. This usually occurs when a stable continuous family of equilibrium points coincides with an unstable one, resulting in an exchange of stability. In our case this translates into different compartments turning zero or non-zero for the stable branch, which indicates extinction and persistence respectively of the disease compartment. The study of branches gives us a more clear insight on how the behaviour of the system depends on the carrying capacity and also provides tools to analyse the more complex inner equilibrium point for which the analytic expression is too complicated to be written out. When studying branches we are interested in conditions for stability as well as deriving transition diagrams describing how the equilibrium points of the branch changes its type indicated by which compartments are present i.e are non-zero. This corresponds to different scenarios of development of disease. It is also convenient to look through the lens of branches in order to derive cyclic solutions resulting from a so called Hopf bifurcation. There are also other bifurcation scenarios that could potentially occur.

2.4 Transition dynamics for the simplest case

We now assume that coinfection spreads only through transmission between coinfected and healthy individuals. This corresponds to the special case $\gamma_i, \beta_i = 0$. By keeping all parameters except K fixed it turns out that for each K there exists only one stable equilibria. Furthermore this equilibria changes continuously with K, forming a branch of stable equilibrium points. The equilibrium point of the branch occasionally, with increasing K, transitions from one type to another. Depending on the fixed parameters we get one of the different transition scenarios described below. The expressions for the bifurcation points K_1, K_2, K_4, K_5, K_6 can be found in paper I.

(a) The branch $\mathcal{S}_1(K)$ is defined for $\eta_1^* < 1$ and consists of $G_{000}(K)$, $0 < K < \sigma_1$, and then of $G_{100}(K)$, $K > \sigma_1$. The bifurcation point is $K = \sigma_1$. We will use the diagram

$$G_{000} \to G_{100}$$

for this branch;

(b) The branch $\mathcal{S}_2(K)$ is defined for $\eta_2^* > \eta_1^* > 1$ and consists of the branch $G_{000}(K)$ for $0 < K < \sigma_1$, $G_{100}(K)$ for $\sigma_1 < K < K_1$, $G_{101}(K)$ for $K_1 < K < K_2$ and $G_{001}(K)$ for $K_2 < K$. There are three bifurcation points σ_1, K_1 and K_2. The diagram

$$G_{000} \to G_{100} \to G_{101} \to G_{001}$$

will be used for this branch;

(c) The third branch $\mathcal{S}_3(K)$ is met when $\eta_1^* > \eta_2^* > 1$ and consists of $G_{000}(K)$ for $0 < K < \sigma_1$, $G_{100}(K)$ for $\sigma_1 < K < K_1$, $G_{101}(K)$ for $K_1 < K < K_5$, $G_{111}(K)$ for $K_5 < K < K_6$, of $G_{011}(K)$ for $K_6 < K < K_4$ and of G_{001} for $K_4 < K$. There are five bifurcation points here: σ_1, K_1, K_5, K_6 and K_4. The following diagram

$$G_{000} \to G_{100} \to G_{101} \to G_{111} \to G_{011} \to G_{001}$$

corresponds to this branch.

(d) The last branch $\mathcal{S}_4(K)$ is defined when $\eta_1^* > 1 > \eta_2^*$ and consists of $G_{000}(K)$ for $0 < K < \sigma_1$, $G_{100}(K)$ for $\sigma_1 < K < K_1$, $G_{101}(K)$ for $K_1 < K < K_5$ and $G_{111}(K)$ for $K_5 < K$. There are three bifurcation points in this case: σ_1, K_1 and K_5. The diagram

$$G_{000} \to G_{100} \to G_{101} \to G_{111}$$

will be used for this branch.

Even if the equilibrium branches are continuous with respect to K the unique stable equilibrium can change discontinuously with respect to other parameters. If K is large and we change η_1^* and or η_2^* in such a way that we get a new transition scenario with a different type of equilibrium for large K, then the stable equilibrium point and thus the dynamics of the system changes discontinuously.

2.5 The relationship between η_1^*, η_2^* and the basic reproductive rate of coinfection

From the previous section we see that comparing η_1^* and η_2^* with 1 tells us how the stable equilibrium branch progresses with K. This is very similar to how the basic reproductive rate predicts the size of a population.
As we will see there is a relationship between η_1^* and the basic reproductive rate of coinfection. In particularly the reproductive rate at the most ideal scenario ($K = \infty$) provided that only the first disease is present. The basic reproductive rate of coinfection denoted $R_{I_{12}}$, i.e the expected number of secondary infection that causes coinfection that a coinfected indivual causes before getting removed from the coinfection compartment, can be calculated by dividing the total rate at which a coinfected person spreads the disease by the rate at which the person gets removed from the coinfected state. The basic reproductive rate of coinfection depends on the size of the other compartments. We will use the notation $R_{I_{12}}^{xyz}(K)$, where $x, y, z = 0, 1$, to indicate the reproductive rate of coinfection at a point of type xyz and carrying capacity K. When only the first disease is present the reproductive rate of coinfection is

$$R_{I_{12}}^{100}(K) = \frac{\alpha_3 S + \eta_1 I_1}{\mu_3}. \tag{2.26}$$

In the ideal scenario where $R_{I_{12}}^{100} = R_{I_{12}}^{100}(\infty)$ we get the following equality between η_1^* and $R_{I_{12}}^{100}$

$$\eta_1^* = \frac{R_{I_{12}}^{100}\sigma_3 - \sigma_1}{\sigma_3 - \sigma_1}. \tag{2.27}$$

From this we can also deduce the following relation

$$\frac{\eta_1^* - 1}{R_{I_{12}}^{100} - 1} > 1, \tag{2.28}$$

that is $R_0^{100}(\infty)$ is always between η_1^* and 1. Next we do a similar comparison between $R_{I_{12}}^{010}(\infty)$ and η_2^* we get the reproductive rate $R_{I_{12}}^{010}$ of coinfection at point $G_{010}(K)$

$$R_{I_{12}}^{010}(K) = \frac{\alpha_3 S + \eta_2 I_2}{\mu_3} \tag{2.29}$$

In the ideal scenario where $R^{010}_{I_{12}} = R^{010}_{I_{12}}(\infty)$ we get the following equality between η^*_2 and $R^{010}_{I_{12}}$

$$\eta^*_2 = \frac{R^{010}_{I_{12}}\sigma_3 - \sigma_2}{\sigma_3 - \sigma_2} \tag{2.30}$$

From this we can also deduce the following relation

$$\frac{\eta^*_2 - 1}{R^{010}_{I_{12}} - 1} > 1 \tag{2.31}$$

i.e $R^{010}_{I_{12}}$ is somewhere in between η^*_2 and 1.

2.6 Making sense of the transition dynamics

In order to understand how and when new strains are introduced in a population it is beneficiary to first study the simple case with only one strain.

$$S' = (r(1 - \frac{S}{K}) - \alpha I)S \tag{2.32}$$

$$I' = (\alpha S - \mu)I \tag{2.33}$$

This system has a globally stable equilibrium point

$$(S^*, I^*) = (\sigma, \frac{r}{\alpha_1}(1 - \frac{\sigma}{K})) \quad \text{for } K \geq \sigma = \frac{\mu}{\alpha}$$

If $K < \sigma$ then $(S^*, I^*) = (K, 0)$ for the globally stable equilibrium point. Especially we note that any increase in K above σ has no effect on the size of the stable susceptible population and the infected compartment increases toward $\frac{r}{\alpha}$. With this in mind the first transition from $G_{000} \to G_{100}$ in each transition diagram becomes evident.

The dynamics of the coinfection model can be easier understood by viewing the two different diseases as species competing for the resource in the form of susceptibles and under the predation of coinfection that also feed on susceptibles. From (2.3) we see that the propagation of the less transmissible disease, is decided by the size of the susceptible population. Since the susceptible population does not change for G_{100} with increasing K we do not expect it to be able to spread at such equilibrium. The spread of coinfection however does also depend on the size of I_1 and so we could expect that if the stable I_1 population becomes large enough the coinfection will start to spread. To get the most optimistic condition for coinfection to spread at a point close to G_{100} we assume $K = \infty$. In order to see if this results in the spread of coinfection we plug in $G_{100}(\infty) = (\sigma_1, \frac{r}{\alpha_1}, 0, 0)$ into (2.4) and get

$$I'_{12} = (\sigma_3 - \sigma_1)(\eta^*_1 - 1)I_{12} \tag{2.34}$$

From this we see that $\eta^*_1 > 1$ is a requirement for I_{12} to be able to spread in this ideal scenario, which explains the transition $G_{100} \to G_{101}$ for all cases

with $\eta_1^* > 1$. Curiously the susceptible population increases with K for G_{101}. This can be explained if we think of the coinfection as being analogous to a predator that prey on the diseases. In order for the primary disease to be able to sustain itself when under predation there needs to be more resources in form susceptibles to compensate.
Next the lesser disease is able to spread alone if the susceptible population is above σ_2 but since it is under the "predation" of coinfection we require the susceptibles to be well above σ_2. By the competitive exclusion principle, the lesser disease also needs to be better to spread, when its population is small, then the primary disease. This can only happen if it is less effected by predation. Similarly as before we look at the most ideal situation for the secondary disease to spread, this is when the coinfected compartment is large enough so that the secondary disease gets a competitive advantage over primary disease. We accomplish this by letting K be the highest possible K for which G_{101} exists i.e. $K = \frac{\sigma_3\eta_1^*}{\eta_1^*-1}$ and plug in $G_{101}(\frac{\sigma_3\eta_1^*}{\eta_1^*-1}) = (\sigma_3, 0, 0, \frac{\alpha_1}{\eta_1}(\sigma_3-\sigma_1))$ into (2.3), we get

$$I_2' = \frac{r\eta_2}{\alpha_3\eta_1^*\eta_2^*}(\eta_1^* - \eta_2^*)I_2 \tag{2.35}$$

which suggest that η_1^* needs to be larger than η_2^* for the secondary disease to be able to spread. This explains the transition $G_{101} \to G_{111}$ in scenarios (c) and (d). If the secondary disease is not able to spread then we would expect coinfection to eventually with increasing K be able to outcompete the primary disease since it is able to feed on two resources.
If the secondary disease is able to spread we will have a coexistence branch with all compartments present. Interestingly the stable susceptible population is constant for coexistence equilibrium points. This suggest that the combined rate of infection onto susceptibles from all disease compartments is constant and only the structure of the disease compartments changes. Interesting still is that the coinfection compartment is also constant. This can be motivated with the competitive exclusion principle. The competitive exclusion principle states that two different species occupying the same niche can not stably coexist. If the coinfection compartment was any higher the primary disease would be outcompeted and the coinfection compartment would decrease since the secondary disease compartment is harder to coinfect. On the other hand if the coinfection compartment was any lower the primary disease would win and coinfection would be easier to spread. But why does the ratio between the primary and secondary disease not remain constant with K? The answer is that despite the susceptible and coinfection compartments staying the same we get a difference in living condition of the two disease compartments since the renewal rate of the susceptibles increases. This implies that there must be an increased pressure from the disease compartments in order to keep the susceptibles size constant. This allows for an increase of the disease compartments, but since the coinfection compartment needs to stay the same for

coexistence, the primary disease has to decrease with K.
Since the secondary disease compartment is bounded it could be that the primary disease still keeps on coexisting at infinite carrying capacity. Otherwise the primary disease will go extinct. A necessary condition for this is that the coinfected population should be able to sustain itself when no primary disease is present i.e. $\eta_2^* > 1$.

2.7 Transition dynamics paper I and II

Papers I,II and III investigates the model (2.1)-(2.5) by deriving the transition scenarios for the special case when the coinfection rates γ_i and β_i are small. In particular $\beta_i = 0$ in papers I and II whilst $\beta_i > 0$ in paper III. Since γ_i and β_i are supposed to be small the systems together with their stable equilibrium branches in papers (I-II) and III only differs by a small perturbation. However, even though the solutions are almost the same the transition scenarios differs quite substantially between the papers. Since β_i and γ_i only have an impact on the system for coexistence equilibra we exclusively get a difference in the transition scenarios when the inner equilibrium becomes part of the transition i.e. η_1 is greater than 1 and η_2. The transition diagrams when $\beta_i = 0$ stays the same

(iii) $G_{000} \to G_{100} \to G_{101} \to G_{111} \to G_{011} \to G_{001} \quad \eta_2^* > 1$;

(iv) $G_{000} \to G_{100} \to G_{101} \to G_{111} \quad \eta_2^* < 1$.

However, the transition to the inner equilibria now happens at

$$K = \hat{K}_1 = \frac{\Delta_\mu + \mu_3\gamma_2}{\Delta_\alpha + \alpha_3\gamma_2} \cdot \frac{\eta_1^*}{\eta_1^* - 1}$$

and the transition from the inner equilibria happens at

$$K = \hat{K}_2 = \frac{\Delta_\mu - \gamma_1\mu_3}{\Delta_\alpha - \gamma_1\alpha_3} \frac{\eta_2^*}{\eta_2^* - 1}$$

.

All non-coexistence equilibria are stable and the inner equilibria G_{111} start off as being stable when G_{101} bifurcates into G_{111} but might lose its stability in scenario iv) for large $(\gamma_1 + \gamma_2) \cdot K$. In this case a so called Hopf bifurcation will occur and the solution will start to oscillate and approach a limit cycle.

2.8 Stability of the inner equilibrium point and Hopf bifurcation

The stability of the inner equilibrium is determined by the eigenvalues of the Jacobian matrix

$$J_8 = \mathrm{d}iag(S, I_1, I_2, I_{12})B, \quad B = \begin{pmatrix} -\frac{r}{K} & -\alpha_1 & -\alpha_2 & -\alpha_3 \\ \alpha_1 & 0 & -\gamma_1 & -\eta_1 \\ \alpha_2 & -\gamma_2 & 0 & -\eta_2 \\ \alpha_3 & \eta_1 + \overline{\gamma} r_2 & \eta_2 + \overline{\gamma} r_1 & -\overline{\gamma} r_1 r_2 \end{pmatrix},$$

where

$$r_1 = \frac{I_1}{I_{12}}, \quad r_2 = \frac{I_2}{I_{12}}. \tag{2.36}$$

For $K > K_1$ close to K_1 the Jacobian is stable with all four eigenvalues having negative real part. In order to change stability at least one of the eigenvalues must pass the imaginary axis as K increases. If the determinant of the Jacobian stays positive, which it does for small γ_i, β_i, then the only possible scenario for J_8 to lose its stability is for a complex conjugate pair of eigenvalues to reach the imaginary axis this can only happen if $K(\gamma_1 + \gamma_2)$ is large enough, which implies that this can only happen in scenario iv). It is shown in paper II that the inner equilibrium indeed can become unstable . In this case there is an Hopf bifurcation and oscillations will appear.

2.9 Transition dynamics paper III

In paper III we get a much more simplified transition diagram. This is because the introduction of the β variables guarantees that $I_1 > 0$ and $I_2 > 0$ whenever $I_{12} > 0$. We get the following alternative transition scenario when $\eta_1^* > 1$

$$G_{000} \to G_{100} \to G_{111}$$

with the transition to the inner equilibria at $K = \frac{\eta_1^* \sigma_1}{\eta_1^* - 1} + O(\beta_2 \bar{\gamma})$. Even tough this transition scenario is different from the scenarios when $\beta_i = 0$ our previous results regarding the transition dynamics still has value since the equilibrium branch when $\beta_i > 0$ will still be close to the equilibrium branch with $\beta_i = 0$, as long as β_i is small.

3 Introducing density dependence in the age-structured Mckendrick-von-Foerster equation

3.1 Age-structure

Paper IV deals with a mathematical model for a population with age structure. Age structure can be a crucial factor to take into consideration when predicting the future development of a population. For example in many developed countries the population is growing despite the fertility rate being less then one daughter per woman. How can this be? Well, currently, due to improved living conditions during the last century, with women on average having more then one daughter, the ratio between woman in there fertile years and the women that are not is relatively high and the population of today experience growth simply because currently a large proportion of women are in their child bearing years. This however will change and many developed countries will experience negative population growth within this century see [2]. A model that does not take into consideration age-structure would predict a steadily increase of the population if vital rates stayed the same. Current models that does take age-structure into consideration however predict that many countries currently experiencing population growth will see their populations decline this century. This shows the importance of incorporating age-structure into the model.

Age-structure can also be very important when studying the spread of diseases that disproportionally affect a certain age group. A much relevant example during the currently ongoing pandemic is the spread of COVID-19,

which affects older people to a much larger extent then young ones. When predicting how much the number of patients will increase due to COVID-19, as well as what needs to be done in order to prevent spread of disease and deaths, it is of course crucial to know the age distribution of the population. If there are many old people in the population the health care should expect a higher pressure on staff and resources then otherwise. The ratio of old to young is not the only thing of importance when it comes to age-structure. Spread of disease in the younger population can be increasingly detrimental for the older population if, to a greater extent, older people tends to live together with young people. For example according to a study on SARS-CoV-2 from the Imperial College London's Department of Mathematics [11] only the age group between 20 and 49 years old had a reproductive number above 1 during the measured period. This effectively means that the older generation would eventually be free of disease if they totally abstain from contacts with this age group.

When incorporation age-structure into differential population model, there are two possible ways this can be done. Either one can, similarly to the SIR model, divide the population into several age compartments. Another more precise way is to use an age-distribution $n(a,t)$. The age-distribution measures the density of people with a certain age a at the time t. Here, the word "density" implies that in order to evaluate the number of people between ages a_1 and $a_2 > a_1$ we calculate the integral

$$\int_{a_1}^{a_2} n(a,t)da. \tag{3.1}$$

We thus get the whole population $N(t)$ from the following expression

$$N(t) = \int_0^\infty n(a,t)da. \tag{3.2}$$

A cohort $n(a,t)$ of individuals, with age a at time t, experiencing a death rate $\mu(a,t)$ will satisfy the equation

$$\frac{dn(a+h,t+h)}{dh} = \frac{\partial n(a,t)}{\partial t} + \frac{\partial n(a,t)}{\partial a} = -\mu(a)n(a,t). \tag{3.3}$$

This equation is called the McKendrik-von-Foerster equation. Together with the boundary condition

$$n(0,t) = \int_0^\infty \beta(a)n(a,t)\,da, \quad t > 0, \tag{3.4}$$

where $\beta(a)$ is the birth rate of individuals at age a, and the initial condition given by:

$$n(a,0) = g(a), \quad a > 0, \tag{3.5}$$

this is enough to fully describe the dynamics of the population. Equation (3.9) is called the renewal equation and simply states that the number of newborns is the sum of each cohorts contribution to the births.

3.2 Density dependence and weighted populations

Paper IV studies the effect of density dependence on a single age-structured population. With the introduction of age-structure it is now possible to differentiate the impact that individuals have on each others vital rates. We might perhaps consider grown ups to take up more resources, in terms of food, than individuals that are not fully grown. This would result in adults having a more negative impact of the vital rate than juveniles. We might also consider only individuals in their childbearing years to have a positive impact on others birth rate. A more denser fertile population can have a significant positive impact on the ability to find a mate [6].

In paper IV we make a rather general approach to density dependence by introducing the weighted populations $P(t)$ and $Q(t)$ defined by

$$P(t) = \int_0^\infty p(a)n(a,t)\,da \tag{3.6}$$

and

$$Q(t) = \int_0^\infty q(a)n(a,t)\,da, \tag{3.7}$$

where $p(a)$ and $q(a)$ are the weight functions. The weighted population $P(t)$ is regarded as impacting the death rate $\mu(a, P(t))$ while the weighted population $Q(t)$ is thought to impact the birth rate $\beta(a, Q(t))$. This way of modelling density dependence should however not be seen as a complete generalisation. We make the constricting assumption that each age group is effected by the other age groups in equal proportions. Examples where this would not be a good way to model density dependence is when juveniles and adults occupies vast different niches such as with alligators.

3.3 The model setup

In summary, incorporating density dependence, in terms of dependence of two weighted populations, into the McKendrik-von-Foerster model leads to the following partial differential equation which we refer to as the balance equation:

$$\frac{\partial n(a,t)}{\partial t} + \frac{\partial n(a,t)}{\partial a} = -\mu(a, P(t))n(a,t), \quad a, t > 0. \tag{3.8}$$

The boundary condition is given by

$$n(0,t) = \int_0^\infty \beta(a, Q(t))n(a,t)\,da, \quad t > 0. \tag{3.9}$$

The initial condition is given by:

$$n(a,0) = g(a), \quad a > 0. \tag{3.10}$$

As stated in Section 5.1 of [10], using the change of variables $a = x$ and $t = x+y$ and integrating along characteristic lines $y = C$, where C is a constant, the balance equation (3.8) becomes

$$n(a,t) = \begin{cases} \rho(t-a)e^{-\int_0^a \mu(v,P(v+t-a))dv}, & a < t, \\ f(a-t)e^{-\int_{a-t}^a \mu(v,P(v+t-a))dv}, & a \geq t. \end{cases} \tag{3.11}$$

where $\rho(t) = n(0,t)$. Despite being a distribution ρ is referred to as the number of newborns. From (3.9), and (3.11) we obtain:

$$\begin{aligned} \rho(t) = &\int_0^t \beta(a,Q(t))\rho(t-a)e^{-\int_0^a \mu(v,P(v+t-a))dv}\,da \\ &+ \int_t^\infty \beta(a,Q(t))f(a-t)e^{-\int_{a-t}^a \mu(v,P(v+t-a))dv}\,da, \end{aligned} \tag{3.12}$$

$$\begin{aligned} P(t) = &\int_0^t p(a)\rho(t-a)e^{-\int_0^a \mu(v,P(v+t-a))dv}\,da \\ &+ \int_t^\infty p(a)f(a-t)e^{-\int_{a-t}^a \mu(v,P(v+t-a))dv}\,da, \end{aligned} \tag{3.13}$$

and

$$\begin{aligned} Q(t) = &\int_0^t q(a)\rho(t-a)e^{-\int_0^a \mu(v,P(v+t-a))dv}\,da \\ &+ \int_t^\infty q(a)f(a-t)e^{-\int_{a-t}^a \mu(v,P(v+t-a))dv}\,da. \end{aligned} \tag{3.14}$$

In summary, we get a system of integral equations with the unknown variables ρ,P, and Q.
Equation (3.12) can be written on the form

$$\rho = K\rho(t) + F(t). \tag{3.15}$$

This formulation has the advantage that if $P(t)$ and $Q(t)$ are given then one can approximate ρ arbitrary close using the the iterative formula

$$\rho_{j+1}(t) = K\rho_j(t) + F(t), \quad \rho_0(t) = F(t) \tag{3.16}$$

Existence and uniqueness of the solution, is proved in [10].
It is in general impossible to find analytic expressions to (ρ, P, Q). However we can still deduce some properties of the solution. If $\rho_-(t)$ and $\rho_+(t)$ are functions satisfying

$$\rho_-(t) < K\rho_-(t) + F(t) \tag{3.17}$$

$$\rho_+(t) > K\rho_+(t) + F(t) \tag{3.18}$$

then $\rho_- < \rho < \rho_+$ i.e. ρ_- and ρ_+ are lower and upper solutions. Upper and lower solution are important since they can be used to show long term behaviour of the population like extinction, permanence and boundedness.

3.4 Assumptions on the vital parameters

The boundary-initial value problem (3.8)–(3.10), together with the weighted age-class-functions (3.6) and (3.7), constitutes a density-dependent population growth model. In order for the death rates dependence on population density to correspond to natural phenomena we assume that $\mu(a, P)$ goes to infinity when either a or P goes to infinity. In more detail we make the following assumption on the death and birth rates.

(H_1) The death rate $\mu(a, x)$ is assumed to be of the form

$$\mu(a, x) = \mu_0(a) + \mathscr{M}(a, x), \tag{3.19}$$

where for some $a_\dagger > 0$ which indicates the maximal lifespan we have

$$\mu_0(a) \geq 0 \quad \text{a.e. in } [0, a_\dagger], \ \int_0^{a_\dagger} \mu_0(\sigma) d\sigma = +\infty \tag{3.20}$$

(H_2) The birth rate β satisfies

$$0 \leq \beta(a, x) \leq \beta_+ \quad \text{a.e. in} \quad [0, a_\dagger] \times \mathbb{R}_+. \tag{3.21}$$

In addition we assume that $\beta(a, x)$ and $\mu(a, x)$ are Lipschitz continuous with respect to the second argument on bounded sets, uniformly on $a \in [0, a_\dagger]$. That is, for all $M > 0$ there exists a constant $H(M) > 0$ such that, if $x, \bar{x} \in [0, M]$, then

$$|\mu(a, x) - \mu(a, \bar{x})| \leq H(M)|x - \bar{x}|, \tag{3.22}$$

$$|\beta(a, x) - \beta(a, \bar{x})| \leq H(M)|x - \bar{x}|. \tag{3.23}$$

For a more complete list of assumptions made on the parameters see paper IV. These assumptions can also be found in [10].

3.5 The net reproductive rate and the Allee effect

With the introduction of age structure the net reproductive rate for a population with weighted sizes P and Q becomes

$$R = \int_0^\infty \beta(a, Q) e^{-\int_0^a \mu(v, P) dv} da.$$

That is it measure how many, on average, daughters each female will produce during her lifetime given that the vital rates stays the same. If $P, Q = 0$ we get the basic reproductive number R_0. If $R_0 > 0$ it will according to the model be impossible for the population to go extinct. However, if $R_0 < 1$ we are only guaranteed that the population will go extinct if the population is small enough that the net reproductive rate is guaranteed to be less then one for the

rest of time. When only considering individuals to have a negative impact on each others vital rates, $R_0 < 1$ will guarantee that $R < 1$ and the population will go extinct. In nature however we often see vital rates having a positive density dependence for small population, the so called Allee effect. Such a population would be able to exist in large numbers but risk to experience a sudden extinction if the population size passes a certain threshold.

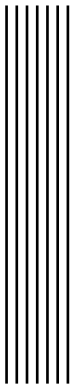
One of our main assumptions is that mortality rate tends to infinity with the population size. This assumption is having a biological explanation: intraspecific competition is increasing in any large population due to limited resources in the habitat. An important consequence of this assumption, is existence of an upper bound for a population. Moreover, this result is an improvement of a similar result in [9], which is made possible by allowing two different weight functions for the mortality and fertility rates and by relaxing condition of Lipschitz continuity for the weight functions.

A stability analysis is performed on the trivial equilibrium $(\rho, P, Q) = (0, 0, 0)$. The stability of the trivial equilibrium depends on the basic reproductive rate

$$R_0 = \int_0^\infty \beta(a,0) e^{-\int_0^a \mu(v,0)dv} da.$$

We study the global stability of the system in terms of newborns only. Initially we restrain the mortality rate to be increasing with P and thus we do not incorporate the Allee effect on the mortality. Under this assumption we derive conditions based on the net reproduction rate R_0 for extinction and permanence. In the case $R_0 \leq 1$ the population will go extinct and in the case $R_0 > 1$ the population will be persistent.

In the later part of paper IV we remove the restriction on the mortality function. This allows for the Allee effect. If $R_0 < 1$ we conclude that the population either becomes extinct or is persistent. We note that if the number of newborns ever is small enough then this implies extinction. This effectively means that the trivial equilibrium is locally stable.



Discussion

Papers I-III contributes to the understanding of the dynamics of a pair of coexisting pathogens with full or strong cross immunity. Logistic growth for the susceptible population is modelled with a carrying capacity K and we see that K is vital in determining which of the diseases that persists. For most K the solution converges to a unique equilibrium point that can either be on the boundary (which signifies that at least one of the disease compartments is not present) or inside the positive cone. For some choices of parameters the solution approaches an orbit when K is large.

Throughout the papers we successively introduce more ways of transmission into the model and derive transition scenarios with increasing K for the unique equilibrium branch. If we only allow for an infected individual to move into the infectors compartment, the different transition scenarios of the branch can be understood with the help of the competitive exclusion principle and understanding of the role of the derived parameters η_1^* and η_2^*. The introduced parameters η_1^* and η_2^*, which in a way measures the optimal basic reproductive rate of the coinfection given certain requirements, are important in determining permanence of the coinfection class.

Introducing the possibility of single infected individuals to become coinfected from non coinfected individuals we get the same expressions of equilibria and transition scenarios as before with exceptions for when the coexistence equilibria is involved. The transition to and from the coexistence equilibrium point now happens at slightly different K and the expression for the inner equilibria is different. Specifically the susceptible and coinfected class are no

longer constant with K but instead changes slightly. Perhaps a bit peculiar, the susceptible compartment decreases with K implying the paradox of enrichment.

Each equilibrium branch changes continuously with K but small changes in $\eta_1^\star$ and $\eta_2^\star$ can lead to sudden changes of the equilibrium. The competitive exclusion principle is observed for relative small K resulting in that the more transmissible disease competes out the less transmittable disease. The lesser disease however might, depending on the parameters, get an advantage and avoid extinction as a single infection when K is large enough for coinfection to spread.

In paper III we allow for susceptibles to move to one of the non coinfection compartments when infected by a coinfected person. This significantly simplifies the possible transition scenarios. We still have value of our understanding of the transition scenario in the previous papers since the branch is close to the branches in previous papers. Even though no analysis has been done yet, we highly suspect that, similarly to papper I-II, we could get a Hopf bifurcation for large K given certain parameters.

Currently it can be hard to fully motivate our models ability to describe existing coinfection scenarios. However there are several ways to improve the analysis of the model and to make it more realistic. We could for instance remove the restricting assumption regarding the coinfections ability to spread compared to each of the single infections throughout paper I-III. After all coinfection does not necessarily need to be the least transmittable class. It is also interesting to know what happens if we ease the condition for some of the transmission rates to be small.

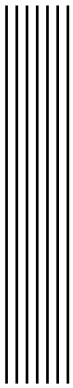
Further introductions of factors can also make the model more in-line with real life disease scenarios. Some appropriate factors to include are loss of immunity, age dependence and density dependence for the disease compartment.

The main reason our model has a stable non trivial equilibria, in contrast with the regular density independent SIR model, is that the susceptible population replenishes itself through birth. Any achieved herd immunity will thus only last a limited time. For rapidly transmitting diseases, our model might overestimate the time taken to replenish the susceptible population above the critical value σ_1. This is if immunity against the disease is lost in a time much shorter than the average susceptibles lifespan.

Unless the disease causes infertility, it is appropriate to assume that the disease compartments also contributes to fertility and is effected by the same density dependence as susceptibles. It is believed however that our model is somewhat self correcting in this matter. The negative displacement from the original carrying capacity size of the susceptible population causes an increased birth rate according to the model which does not make much sense if the infected population still consumes the resources of the habitat. We can instead interpret this increase of birth as birth cause by infected individuals.

Age dependence is a crucial factor to consider. In paper IV the age-structure is modelled using an age-distribution, however because of its complexity it is believed to be more appropriate to instead consider multiple age departments when expanding the coinfection model.
Paper IV deals with an age-structured population model for a single population using an age-distribution. Each vital rate depends on separate weightings of the population. Integrating along characteristic lines results into a complex system of integrals with the number of newborns and each weighted population as variables. We derive upper and lower solutions by assuming lower and upper bounds on the vital rates. We conclude that for the non Allee effect scenarios the population persists if the basic reproductive rate R_0 is greater than one and goes extinct for $R_0 < 1$. When the Allee effect is present the condition $R_0 < 1$ does no longer guarantee extinction but we also require the number of newborns to be small enough.

It is desirable in the future to make the weight function also dependent on the age of the impacted individual. This would allow us to consider cases where the young and old occupy vastly different niches.



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Papers

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