NET REPRODUCTION FUNCTIONS FOR NONLINEAR STRUCTURED POPULATION MODELS

JÓZSEF Z. FARKAS

Abstract. Our goal in this note is to present a general approach to define the net reproduction function/functional for a large class of nonlinear physiologically structured population models. In particular, we are going to show that this can be achieved in a natural way by reformulating a general nonlinear problem as a family of linear problems; each of the linear problems describing the evolution of the population in a different, but constant environment. The reformulation of a nonlinear population model as a family of linear ones is a new approach and provides an elegant way to study qualitative questions, in general. To define the net reproduction number for any fixed (constant) environment we use a fairly recent spectral theoretic result. For nonlinear models, varying the environment naturally leads to a net reproduction function or functional, depending on the dimension of the nonlinearity.

1. Prologue

Physiologically structured population models have been developed extensively in the past decades, see for example the well-known monographs [17, 34, 36, 43] for an in-depth introduction and review of the topic. Our general research agenda, to relate the stability of steady states of physiologically structured population models to biologically meaningful quantities, allowed us to obtain a number of interesting results, see e.g. [26, 28, 29, 30, 31]. In particular, as we have seen for example in [11, 26, 28, 29, 30, 31], the existence and stability of steady states of structured population models can often be characterised using an appropriately defined net reproduction function. In fact we note that stability questions of nonlinear matrix population models were already investigated in the same spirit, see for example the early paper [44]. However, we emphasize that previously, net reproduction functions/functionals were defined for concrete nonlinear models on an 'ad hoc' basis, but typically via analysing the corresponding steady state equations, see e.g. [11, 26, 27, 28, 29, 30, 31] for more details. It is our goal in this paper to present a general framework, which is applicable to a very large class of nonlinear models.

Date: June 1, 2017.

1991 Mathematics Subject Classification. 92D25, 35B35.

Key words and phrases. Physiologically structured populations, net reproduction number, positive operators.
Indeed, the existence of positive steady states is one of the most important questions, when studying nonlinear population models; and to establish the existence of non-trivial steady states is often challenging. This is especially the case for models formulated as infinite-dimensional dynamical systems, for example delay equations, partial differential equations or even integro-differential equations, see e.g. [32, 33]. To overcome some of the difficulties, we have developed a very general framework to treat steady state problems of some classes of nonlinear partial differential or partial integro-differential equations, see e.g. [9, 10, 11]. The power of our method becomes apparent for models with so-called infinite-dimensional nonlinearities, when in fact the existence of positive steady states cannot be completely characterised by appropriately defined net reproduction functions. More precisely, for models with infinite-dimensional nonlinearities it turns out (as we will also show later) that one can still define a net reproduction functional, which will necessarily take the value 1 at any positive steady state; but the condition $R(E_*) = 1$ ($E_*$ stands for the steady environment) is not necessarily sufficient for the existence of a positive steady state. This phenomenon was already noted for example in [31] for a hierarchic size-structured population model. It also turns out, as we are going to show later, that the approach we developed in [10] to study the existence of steady states of physiologically structured population models, can be utilised to define net reproduction functions/functionals for a variety of nonlinear population models. We also note that our approach to consider a nonlinear population model, and then recast it in the form of a parametrised family of linear problems is in some sense the opposite to the modelling framework elaborated in detail for example in [20, 21], wherein the starting point is a linear model and then nonlinearities are incorporated via interaction variables.

For linear models the basic (or net) reproduction number $R$, could be defined (heuristically, or from the biological point of view) as the average number of offspring 'produced' by a newborn individual in her expected lifetime. Note that, crucially, this definition assumes that the environment any given individual is experiencing remains constant throughout her lifetime. This is the case in a linear model, and hence we can talk about a universal constant, the net reproduction number, which then often determines the asymptotic behaviour of solutions, too.

As a motivating example consider the classic linear age-structured population model, see e.g. [34, 43].

\begin{align}
  u_t(a, t) + u_a(a, t) &= -\mu(a)u(a, t), \quad a \in (0, m), \quad (1.1) \\
  u(0, t) &= \int_0^m \beta(a)u(a, t) \, da. \quad (1.2)
\end{align}

For the basic age-structured model above one can introduce the so-called survival probability, as

$$
\pi(a) = \exp\left\{-\int_0^a \mu(r) \, dr\right\}, \quad a \in [0, m]. \quad (1.3)
$$
Then many people would agree that intuitively it is clear that the average number of offspring 'produced' by a newborn individual in her expected lifetime is
\[ R = \int_0^m \beta(a)\pi(a)\,da. \] (1.4)

The natural question arises, whether we can do this in a mathematically rigorous fashion; that is, to arrive at \( R \) as defined above in (1.4), using a rigorous mathematical framework. The answer is yes, but surprisingly enough it turns out that the mathematical machinery what one has to deploy to this end is rather involved; it requires us to lift the age-structured problem (1.1)-(1.2) into a bigger (than the natural) state space, in which the boundary condition becomes a positive perturbation of the main part of the generator. In the forthcoming paper [12] we present the details of this calculation (amongst other things). Interestingly, it turns out that the mathematical machinery becomes much less involved/cumbersome for models incorporating infinite states at birth, as we will also see later. This phenomenon is also interesting to note because in the alternative delay formulation of physiologically structured population models, see e.g. [19], this is usually the other way around; i.e. models with infinite states at birth are notoriously difficult to handle/analyse as the book-keeping (tracing back individual history) becomes intractable. It may be also worthwhile to note that possibly the first account of the notion of a net reproduction number is found in [24], in which Dublin and Lotka were trying to provide a systematic way of estimating the growth rate of the age-structured human population.

In more realistic models than (1.1)-(1.2), the environment that individuals are experiencing changes, due for example to the availability of resources, which may be affected by competition (e.g. by scramble or contest competition). Hence for nonlinear models, one ought to define a net reproduction function or functional, analogously. Then, one can evaluate such functions or functionals by fixing the environment, to obtain scalar quantities, i.e. net reproduction numbers. Hence we would like to emphasize that for nonlinear models, one has to really talk about a net reproduction function/functional, analogous to (1.4), but depending on the environment. Then \( R_0 \) for example is simply obtained by evaluating such functions/functionals at a fixed environment (for example at the extinction environment, i.e. we may define \( R_0 := R\big|_{E(0)} \)). In fact, as demonstrated in the papers [28, 29, 30, 31] for concrete examples, the stability of non-trivial steady states can be related to the derivative of the net reproduction function/functional, while the stability of the extinction steady state is related to \( R_0 \). Moreover, as shown for example by Cushing and later also by Walker, the value \( R_0 \) (if it is defined as \( R_0 := R\big|_{E(0)} \)) can be used as a bifurcation parameter to establish the existence of positive steady states, see e.g. [14] [15] [40] [41] [42].

The very natural idea of defining a scalar quantity, namely the net reproduction number \( R \), when fixing the environment, can be made mathematically rigorous, and at the same time allows us to derive some desirable qualitative properties of the model. Note that the notation \( R_0 \) itself (although it may well originate from [24], but it has
been adapted widely since then in the mathematical epidemiology community), possibly reflects the fact that mathematical epidemiologists for example may think about this number as (an approximation of) the number of secondary cases produced by a single infected individual in a completely susceptible population. This can be understood exactly in the sense as fixing the environment an infected individual experiences; for example (in a simple SIS model) assuming that everybody else is, and will remain, susceptible. Importantly note that, by fixing a different environment a newly infected individual experiences, assuming for example that approximately half of the population is (and will remain) susceptible, will arguably lead to a different value of $R_0$; and indeed we should really define $R_0(S)$, see Section 4 for an example to illustrate this. So we emphasize again, that also for nonlinear models of mathematical epidemiology one really ought to define a function or functional depending on the dimension of the nonlinearity incorporated in the model. In the context of population dynamical models, we argue that it seems reasonable to set $R_0 := R|_{E(0)}$, but of course there may also different choices of parametrisations leading to different operators $E$, see the subsequent sections.

We also mention that in recent years there has been a reinvigorated interest within the mathematical epidemiology community and beyond to define net reproduction numbers also for linear non-autonomous models, e.g. for models with explicitly time-dependent parameters (e.g. periodic vital rates). The interested reader will find many results in this direction for example in the fairly recent papers [3, 4, 5, 35]. Actually it turns out that the general idea we present here is clearly applicable to some linear non-autonomous models, see Section 4 for an illustrative example.

2. (Re)formulation of a nonlinear problem

Our starting point is a nonlinear evolution equation, which we assume to describe the dynamics of a physiologically structured population, formulated as a Cauchy problem on the Banach space $\mathcal{X}$ as follows.

$$\frac{d}{dt}u = Au, \quad D(A) \subseteq \mathcal{X}, \quad u(0) = u_0; \tag{2.5}$$

where $A$ (possibly multivalued) is assumed to generate a (nonlinear) strongly continuous semigroup of type $\omega$, on $\mathcal{X}$ (or possibly on a closed subset of $\mathcal{X}$); that is, we tacitly assume in the rest of the paper that the assumptions of the Crandall-Liggett Theorem hold true, see [13]. In other words, we assume that (at least) mild solutions to (2.5) exist in $\mathcal{X}$ for all times. For some of the other notions not introduced here explicitly we refer the interested reader to [2, 25, 37].

The new idea to recast the nonlinear problem (2.5) as a family of linear problems proved to be fruitful to establish results concerning the existence of steady states of model (2.5), see [3, 10, 11]. Here, we apply the same formulation but in a slightly more specific fashion, to show how this idea can also be used to define a net reproduction function/functional associated to the nonlinear model (2.5) (of course when it describes the
evolution of a biological population). In particular we assume that $\mathcal{X}, \mathcal{Y}$ are Banach lattices, $\mathcal{X}$ being the state space; while we call $\mathcal{Y}$ the parameter space. $\mathcal{Y}$ can be understood as the set of all of the possible environments an individual may experience throughout her/his lifetime. From the mathematical point of view, typically there is a natural choice of the space $\mathcal{Y}$, depending on the type of nonlinearity incorporated in model (2.5).

We then recast the nonlinear model (2.5) as follows.

$$\frac{du}{dt} = (B_p + C_p) u, \quad D(B_p + C_p) \subseteq \mathcal{X}, \quad u(0) = u_0, \quad p \in \mathcal{Y}. \quad (2.6)$$

Note that, as we have fixed the environment, for every $p \in \mathcal{Y}$, $B_p$ and $C_p$ are linear operators; with $B_p$ describing mortality and individual development, such as growth; and $C_p$ describing recruitment/reproduction of individuals. Note that, mortality and fertility being some of the basic ingredients of most population models, it seems to be natural from the biological point of view to distinguish the operators $B_p$ and $C_p$ in this way.

At this point we would like acknowledge, that of course there are models, even natural ones, for which there can be an ambiguity as for example what can be considered recruitment/reproduction, as discussed for example in the most recent papers [6, 18]; but we shall not be focusing on such models here. Rather we note that of course different splittings of $A$ may also result in serious technical advantages, especially in the context of mathematical epidemiology. For example in the context of an epidemiological model different splittings will result in different formulas for $R_0$, some of which may be easier to compute due for example to the availability of different types of patient data, see e.g. the recent paper [17] in this direction.

From the mathematical point of view it is clear that if $B_p$ describes mortality and individual development, then it will naturally have a negative spectral bound, while the recruitment operator $C_p$ is a positive operator, by definition (of course, when fixing the ‘natural’ positive cone of the state space). Moreover, in the absence of mortality, it seems reasonable to assume that the spectral bound of $B_p$ is zero. That is, for example jumps between individual states (transitions), such as in the interesting example presented in Section 2 of [18], should be incorporated naturally into $B_p$. Any modification of this splitting would also destroy the natural mathematical properties of $B_p$ and $C_p$.

There is a natural (and important) relationship between elements of the parameter space $p \in \mathcal{Y}$, and elements $u \in \mathcal{X}$ of the state space. The relationship is determined by the so-called environmental operator:

$$E : \mathcal{X} \to \mathcal{Y}, \quad E(u) = p. \quad (2.7)$$

From the biological point of view, $E$ typically determines how the standing population (and in turn the environment) affects individual mortality, development and fertility, hence the terminology. From the mathematical point of view, $E$ is in general a nonlinear operator (although in many of the concrete applications problem (2.7) can be set up in such a way that $E$ is in fact positive linear, which can be convenient), associated to the
type of nonlinearity incorporated in (2.5). In particular, if it is possible to recast the nonlinear problem (2.5) in the form of (2.6) with a particular choice of \( E \), such that its range is contained in \( \mathbb{R}^n \) for some \( n \in \mathbb{N} \) then we say that problem (2.6) incorporates (finite) \( n \)-dimensional nonlinearity. On the other hand, if naturally \( Y \) itself is an infinite dimensional vector space (e.g. a Banach space), then we say that problem (2.6) incorporates an infinite dimensional nonlinearity.

We recall e.g. from [1, 8, 27] a structured distributed states at birth model as an example to illustrate the parametrisation and splitting in (2.6).

\[
\begin{align*}
\frac{du(s,t)}{dt} + (\gamma(s,\mathbf{P}(t))u(s,t))_s &= -\mu(s,\mathbf{P}(t))u(s,t) + \int_{s_{\min}}^{s_{\max}} \beta(s,\sigma,\mathbf{P}(t))u(\sigma,t) \, d\sigma, \\
\gamma(s_{\min},\mathbf{P}(t))u(s_{\min},t) &= 0, \quad \mathbf{P}(t) = \int_{s_{\min}}^{s_{\max}} u(s,t) \, ds, \quad 0 \leq s_{\min} < s_{\max} < \infty.
\end{align*}
\]

(2.8)

As in [1, 8, 27] we set the state space \( X = L^1(s_{\min}, s_{\max}) \), the Banach space of equivalence classes of Lebesgue integrable functions. Model (2.8) could be considered as a nonlinear size-structured counterpart of the classic age-structured model (1.1)-(1.2). Note that in this example scramble competition effects are introduced via density dependence through individual mortality (\( \mu \)), fertility (\( \beta \)) and growth/development (\( \gamma \)) rates. (We do not specify here the necessary regularity assumptions on the ingredients, but instead refer the interested reader to [1, 8, 27].) In model (2.8), the environment individuals are experiencing is simply determined by the total population size (scramble competition), and therefore we have

\[
E(u) = \int_{s_{\min}}^{s_{\max}} u(s) \, ds = \mathbf{p} \in \mathbb{R} = Y,
\]

(2.9)

and so in this example \( E \) is a positive linear operator. With this setting, the linear operators \( B_p, C_p \) can be naturally defined as follows (assuming that \( \gamma \) and \( \beta \) are sufficiently smooth, for example it suffices to assume that they are continuously differentiable).

\[
\begin{align*}
B_p u &= - (\gamma(\cdot, \mathbf{p})u)' - \mu(\cdot, \mathbf{p})u, & D(B_p) &= \{ u \in W^{1,1}(s_{\min}, s_{\max}) \mid u(s_{\min}) = 0 \}, \\
C_p u &= \int_{s_{\min}}^{s_{\max}} \beta(\cdot, y, \mathbf{p})u(y) \, dy, & D(C_p) &= X.
\end{align*}
\]

(2.10)

Note that in the natural splitting above, \( B_p \) describes individual development (growth) and mortality (death), while \( C_p \) determines the recruitment of individuals into the population (birth).

3. The definition and basic properties of the net reproduction function

Since for every fixed environment \( \mathbf{p} \) (2.8) is a linear problem, we can define a net reproduction number \( \mathcal{R} \) corresponding to each of such fixed environments. Since in principle we can do this for every \( \mathbf{p} \in Y \), we can write \( \mathcal{R}(\mathbf{p}) \), with \( \mathcal{R} : Y \to \mathbb{R}_+ \), and
therefore introduce the notion of a net reproduction function/functional, depending on the dimension of the parameter space $\mathcal{Y}$. We recall from [39] Thieme’s theorem, which naturally gives rise to define $R(p)$.

**Theorem 3.1.** [39, Theorem 3.5] Let $B$ be a resolvent-positive operator on $\mathcal{X}$, $s(B) < 0$, and $A = B + C$ a positive perturbation of $B$. If $A$ is resolvent-positive then

$$s(A) \geq 0 \iff r\left(-C B^{-1}\right) - 1 \geq 0.$$  

(3.11)

Note that (at least in our opinion) the beauty of Theorem 3.1 is that its hypotheses exactly correspond to the biologically natural splitting of the generator $B_p + C_p$. If (2.6) describes a family of linear population models, then (for each fixed $p$) it is naturally governed by a positive semigroup, with its generator $A_p = B_p + C_p$ being resolvent positive according to Definition 3.1 in [39]. Similarly, $B_p$ is resolvent positive, and since it incorporates mortality and individual development (but not recruitment) its spectral bound is necessarily negative. Finally $C_p$ describing recruitment (only) is necessarily a positive perturbation of $B_p$ as long as it is defined (at least) on the domain of $B_p$. We note that, typically $C_p$ can be defined on a larger set than the domain of $B_p$ (depending of course on the regularity assumptions we impose on the model ingredients), for example in the case of the distributed states at birth model (2.8), see also [1, 27] for more details.

We note at this point, that for example if mortality is large enough, then of course it would be possible to incorporate part of the recruitment operator $C_p$ into $B_p$, while preserving all of the mathematical properties of the operators required to apply Theorem 3.1 but would this be rather unnatural? Of course there could be a greater ambiguity as to how to split individual development/transitioning (if any) as discussed for example in [18].

We now apply Theorem 3.1 at every fixed environment $p$ to arrive at the definition of the net reproduction function/functional. We tacitly assume that the operators in (2.6) satisfy the assumptions of Theorem 3.1.

**Definition 3.2.** The net reproduction function/functional for model (2.6) is defined as

$$R(p) := r\left(-C_p B_p^{-1}\right).$$  

(3.12)

Note that although this definition is mathematically inspired, the idea of defining the net reproduction number by fixing the environment (the standing population, essentially) seems to be rather natural. We also note that of course for concrete applications it may be very difficult (if not impossible) to compute the operator $-C_p B_p^{-1}$ (this was done for model (2.8) in [1]), and also in particular its spectral radius (again this was computed for the distributed states at birth model (2.8) in some special cases in [1]). For the age-structured (single state at birth) model (1.1)-(1.2) this is done in [12].

Next we note that an immediate and desirable consequence of the definition above is that in general it implies a strong connection between the existence of positive steady states $u_*$ of the nonlinear evolution equation (2.5) and parameter values $p_*$, such that $R(p_*) = 1$ holds. This is a very desirable property from the biological point of view,
as one would naturally expect that non-trivial steady states of a population model may arise, when the net reproduction number equals 1. For a large class of population models this connection is rigorously established as follows.

**Proposition 3.3.** Assume that $B_p + C_p$ generates a positive irreducible and eventually compact semigroup for all $p \in \mathcal{Y}$ on $X$. Then, if equation (2.5) admits a strictly positive steady state $u_\ast$, then $R(p_\ast) = 1$, with $p_\ast = E(u_\ast)$ holds.

**Proof.** If $u_\ast$ is a strictly positive positive steady state of (2.6) then we have $u_\ast \in \text{Ker}(B_{E(u_\ast)} + C_{E(u_\ast)})$, that is 0 is an eigenvalue of $(B_{E(u_\ast)} + C_{E(u_\ast)})$. If however, the semigroup generated by $(B_{E(u_\ast)} + C_{E(u_\ast)})$ is irreducible and eventually compact, then the spectral bound is the only eigenvalue, which admits a corresponding strictly positive eigenvector (see e.g. [2, 25, 37]), and therefore we have $s(B_{E(u_\ast)} + C_{E(u_\ast)}) = 0$, which by Theorem 3.1 implies that $R(p_\ast) = 1$, where $p_\ast = E(u_\ast) \in \mathcal{Y}$. □

Note that if in addition we assume that $E$ is positive (which can be the case for concrete applications, as seen e.g. in the previous section for model (2.8)), then we can restrict ourselves to parameter values $p \in \mathcal{Y}_+$. Importantly, note that Proposition 3.3 says that $R(p_\ast) = 1$ is a necessary condition for the existence of a positive steady state. But it cannot always shown to be sufficient, as already noted for example in [10, 31]. However, for a large class of models with one dimensional nonlinearities this condition can in fact shown to be sufficient, too.

To this end, we impose some further restrictions on the environmental operator $E$. In particular, we hypothesize that $E$ is of the form $E = \hat{E} + r$, for some $r \in \mathbb{R}$; where $\hat{E} : X \to \mathbb{R}$ is such that $\forall \alpha \in \mathbb{R}, \forall x \in X$ we have $\hat{E}(\alpha x) = \alpha \hat{E}(x)$, and $\hat{E}(x) \neq 0$, unless $x \equiv 0$. We may say that the operator $E$ is affine, but strictly speaking it is not as $\hat{E}$ is not necessarily assumed to be linear.

**Proposition 3.4.** Assume that $\dim(\mathcal{Y}) = 1$, and that for every $p \in \mathcal{Y}$ the operators $B_p, C_p$ satisfy the assumptions of Theorem 3.1; moreover assume that $E$ satisfies the hypothesis above. Then, if there exists a $p_\ast \in \mathcal{Y}$ such that $R(p_\ast) = 1$, then the nonlinear equation (2.5) admits a steady state.

**Proof.** If there exists a $p_\ast \in \mathbb{R}$ such that $R(p_\ast) = 1$, then by Theorem 3.1 we have that $s(B_{p_\ast} + C_{p_\ast}) = 0$, with a corresponding eigenspace $V_{p_\ast} \subseteq X$, with $\dim(V_{p_\ast}) \geq 1$, in general. Note that we only need to show that there exists a $v_\ast \in V_{p_\ast}$ such that $\hat{E}(v_\ast) = p_\ast$ holds. However, it follows from our assumptions on $E$ that for every $0 \neq x \in X$ the equation

$$\alpha \hat{E}(x) + r = p_\ast$$

has a solution $\alpha \in \mathbb{R}$. □

Note that to allow a greater generality (than for example in [10]) we did not the assert the existence of a strictly positive steady state in Proposition 3.4. Imposing further
assumptions on the family of operators $B_p + C_p$ (such that they generate eventually compact and irreducible semigroups), and on $E$, would allow us to obtain more information about the eigenspace $V_{u^*}$, and in turn guarantee for example the existence of a strictly positive steady state.

We proceed by formulating two conjectures, which further underpin the significance of the definition of the net reproduction function/functional in (3.12), and more generally the idea of reformulating a nonlinear evolution problem as a parametrised family of linear problems (2.6). Below by linearisation of (2.5) we mean the linear approximation of the nonlinear operator $A$ using its Fréchet derivative (if it exists). We also note that in fact this assumption could be weakened by assuming only that $A$ is Gâteaux differentiable in the direction of the positive cone of $X$.

**Conjecture 3.5.** Assume that the linearisation of (2.5) at the trivial steady state $u^* \equiv 0$ exists, and that $E(0) = 0$. Then, the trivial steady state $u^* \equiv 0$ is locally asymptotically stable if $R(0) < 1$; and it is unstable if $R(0) > 1$.

This first conjecture can be translated as follows. The linearisation of (2.5) at the steady state $u^* \equiv 0$ (if it exists) coincides with the following linear Cauchy problem.

$$\frac{du}{dt} = (B_{E(u^*, \equiv 0)} + C_{E(u^*, \equiv 0)}) u, \quad u(0) = u_0. \quad (3.14)$$

This in fact can be verified directly for all of the structured population models (including both single, and infinite states at birth) we studied via linearisation techniques for example in [26, 27, 28, 29, 31].

The second conjecture we formulate could appear slightly far-fetched for the cautious reader, however we point out that there is a strong connection between the dissipativity condition of a generator of a linear (quasi-)contraction semigroup and the accretive condition of the generator of a nonlinear contraction semigroup, see e.g. [13, 25]. Also note that here no linearisation of $A$ is required, so potentially it is applicable to a wider class of models.

**Conjecture 3.6.** Assume that $E(0) = 0$, and that there exists an $\varepsilon > 0$ such that for every $p \in \mathcal{P}$, $R(p) < 1 - \varepsilon$ holds. Then the trivial steady state $u^* \equiv 0$ of (2.5) is globally asymptotically stable.

The second conjecture can be translated as follows. If the net reproduction number is strictly less than 1 for all possible environments (and in fact we have a uniform upper bound), then the population dies out, irrespective of the initial population density.

Finally we note that the ultimate (mathematical) advantage to recast (and study) the nonlinear model (2.5) in the form of a family of linear problems (2.6) is that, with the appropriate choice of the environmental operator $E$ and parameter space $Y$, we may preserve the natural positivity properties of the original nonlinear problem; which are typically lost for example when approaching the nonlinear problem (2.5) with classical linearisation techniques. But we emphasize again that for a given nonlinear problem (2.5)
typically there may be different ways to define the environmental operator $E$, which then lead to different parametrisations (2.6), some of them being potentially more advantageous for specific purposes.

4. Further examples

In this section we present two further (but completely different) examples to illustrate the general ideas presented in the previous sections. In fact it is worth mentioning that these two examples do not fit explicitly into the framework presented in the previous sections. In particular first we consider a simple SIS model, in which infected individuals are structured with respect to the bacterium/virus load they are carrying. We do not have a specific disease in mind, rather we consider a generic (‘toy’ model) to illustrate our approach (we note that a somewhat similar model, but with a super-linear term for the infectives, was considered and analysed in [11]).

\[
\begin{align*}
\frac{d}{dt} \left( \int_0^\infty i(x, t) \, dx + S(t) \right) &= 0, \\
\alpha(0) i(0, t) &= 0, \\
i(x, 0) &= i_0(x), \\
S(0) &= S_0.
\end{align*}
\] (4.15)

Above, $\varrho$ denotes the recovery rate, $\alpha$ determines the rate at which bacteria/virus replicate inside an infected host individual thereby increasing their bacterial/viral load, while $\Lambda$ determines the rate at which infected individuals pass on the disease to susceptibles upon contact. A newly infected individual may have any bacterial/viral load in principle, hence we do not impose any restrictions on $\Lambda$. The function $f$ accounts for the fact that the number of contacts per unit time does not always linearly increase with the susceptible population size $S$. Note that in the classic bilinear case we would simply have $f(S) \equiv S$, but in different applications $f$ may be sub or super-linear. It suffices to assume that the model ingredients $\alpha, \varrho, \Lambda$ are positive and continuously differentiable, and also integrable on $(0, \infty)$; and it is also natural to assume that $\alpha(\infty) = 0$. $f$ is also assumed to be positive and continuous. Note that there is no population dynamics incorporated in model (4.15), and indeed every solution $(i, S)$ satisfies

\[
\frac{d}{dt} \left( \int_0^\infty i(x, t) \, dx + S(t) \right) = 0.
\]

The natural state space for (4.15) is $\mathcal{X} = L^1(0, \infty) \times \mathbb{R}$ and it turns out that the most convenient parametrisation of (4.15) arises when defining the environmental operator as

\[
E : \mathcal{X} \to \mathcal{Y} = \mathbb{R}, \quad E \begin{pmatrix} i \\ S \end{pmatrix} = S \in \mathbb{R}.
\] (4.16)

Note that previously we used $p$ to denote the parameter, but here we emphasize that the parameter is actually the susceptible population size, and hence we denote it by $S$. 


In this case we can rewrite the nonlinear problem (4.15) as the family of linear ones as in (2.6).

\[ B_i = -\left(\alpha(\cdot)i\right)' - \varphi(\cdot)i, \quad D(B) = \{ i \in W^{1,1}(0, \infty) \mid i(0) = 0 \}, \]

\[ C_S i = f(S) \int_0^\infty \Lambda(\cdot, y)i(y) \, dy, \quad D(C_S) = L^1(0, \infty). \]  

(4.17)

Note that since the only nonlinearity in model (4.17) is due to the infection process, \( B \) naturally does not depend on \( S \). Also note that since the susceptible population size is chosen as the parameter \( S \), the second equation in (4.15) becomes 'void' after the parametrisation, in fact it is simply the integral of the first one (at the steady state). Hence the net reproduction number is given as the spectral radius of the integral operator \( L_S = -C_S B^{-1} \), which is computed as

\[ L_S \phi = f(S) \int_0^\infty \frac{\Lambda(\cdot, y)}{\alpha(y)} \int_0^y \exp \left\{ -\int_r^y \frac{\varphi(\sigma)}{\alpha(\sigma)} \, d\sigma \right\} \phi(r) \, dr \, dy, \quad D(L_S) = L^1(0, \infty); \]  

(4.18)

that is

\[ R(S) = r(L_S). \]  

(4.19)

In this example the spectral radius, and therefore \( R \), as a function of the susceptible population size \( S \), behaves as \( f \). For example in the classic bilinear case (i.e. when \( f(S) \equiv S \)) it is a monotone increasing function of the susceptible population size \( S \), as expected. It can be computed explicitly in special cases, for example when \( \Lambda \) is separable, in which case \( L_S \) is of rank one. Also note that endemic steady states may arise at different values of \( S \), depending on the behaviour of the function \( f \). At endemic steady states clearly we have \( R(S) = 1 \), but in general \( R(S) \) determines the expected number of secondary cases at any susceptible population density \( S \). In fact the interested reader may recall from the celebrated paper [23] the universal definition of the net reproduction number. Indeed it is already clear from [23] that \( R \) should be a function of the variable \( S \), despite the fact that the authors in [23] define a universal constant by referring to a 'typical individual' and 'linearized equation'.

Finally we mention that the same general idea can be applied to models incorporating explicitly time-dependent vital rates. As an example consider the linear, but non-autonomous version of the distributed states at birth model (2.6).

\[ u_t(s, t) + (\gamma(s, t)u(s, t))_s = -\mu(s, t)u(s, t) + \int_{s_{\text{min}}}^{s_{\text{max}}} \beta(s, \sigma, t)u(\sigma, t) \, d\sigma, \]

\[ \gamma(s_{\text{min}}, t)u(s_{\text{min}}, t) = 0, \quad 0 \leq s_{\text{min}} < s_{\text{max}} < \infty. \]  

(4.20)
It is clear that by fixing the time in the vital rates $\gamma, \beta, \mu$ we arrive at a parametrised family of linear evolution problems by defining the linear operators $B_t, C_t$ as follows.

$$B_t u = - (\gamma(\cdot, t)u)' - \mu(\cdot, t)u, \quad D(B_t) = \{ u \in W^{1,1}(s_{\text{min}}, s_{\text{max}}) \mid u(s_{\text{min}}) = 0 \},$$

$$C_t u = \int_{s_{\text{min}}}^{s_{\text{max}}} \beta(\cdot, y, t)u(y) \, dy, \quad D(C_t) = \mathcal{X}. \quad (4.21)$$

From this parametrisation, similarly as before we arrive for every fixed $t$ at the linear integral operator

$$L_t \phi = \int_{s_{\text{min}}}^{s_{\text{max}}} \frac{\beta(\cdot, y, t)}{\gamma(\cdot, t)} \int_0^y \exp \left\{ - \int_r^y \frac{\mu(\sigma, t)}{\gamma(\sigma, t)} \, d\sigma \right\} \phi(r) \, dr \, dy, \quad D(L_t) = L^1(s_{\text{min}}, s_{\text{max}}); \quad (4.22)$$

and in turn at the explicitly time-dependent net reproduction function

$$R(t) = r(L_t). \quad (4.23)$$

Acknowledgements

I thank Ángel Calsina and Odo Diekmann for the careful reading of the manuscript, and also for the many insightful discussions (TBC).

References

[1] Ackleh AS, Farkas JZ. On the net reproduction rate of continuous structured populations with distributed states at birth. Computers and Mathematics with Applications 2013; 66:1685-1694.

[2] Arendt W, Graboso A, Greiner G, Groh U, Lotz HP, Moustakas U, Nagel R, Neubrand F, Schlotterbeck U. One-Parameter Semigroups of Positive Operators, Springer-Verlag: Berlin, 1986.

[3] Bacaër N. Approximation of the basic reproduction number $R_0$ for vector-borne diseases with a periodic vector population. Bulletin of Mathematical Biology 2007; 69:1067-1091.

[4] Bacaër N, Ait Dads E. On the biological interpretation of a definition for the parameter $R_0$ in periodic population models. Journal of Mathematical Biology 2012; 65:601-621.

[5] Bacaër N, Khaladi M. On the basic reproduction number in a random environment. Journal of Mathematical Biology 2013; 67:1729-1739.

[6] Barril C, Calsina À, Ripoll J. On the reproduction number of a gut microbiota model. preprint.

[7] Browne C, Webb GF. A nosocomial epidemic model with infection of patients due to contaminated rooms. Mathematical Biosciences and Engineering 2015; 12:761-787.

[8] Calsina À, Diekmann O, Farkas JZ. Structured populations with distributed recruitment: from PDE to delay formulation. Mathematical Methods in the Applied Sciences 2016; 39:5175-5191.

[9] Calsina À, Farkas JZ. Positive steady states of nonlinear evolution equations with finite dimensional nonlinearities. SIAM Journal on Mathematical Analysis 2014; 46:1406-1426.

[10] Calsina À, Farkas JZ. Positive steady states of nonlinear evolution equations with finite dimensional nonlinearities. SIAM Journal on Mathematical Analysis 2014; 46:1406-1426.

[11] Calsina À, Farkas JZ. Spectral bounds and steady states of structured populations. manuscript.

[12] Calsina À, Farkas JZ. Spectral bounds and steady states of structured populations. manuscript.

[13] Crandall MG, Liggett TM. Generation of semi-groups of nonlinear transformations on general Banach spaces. American Journal of Mathematics 1971; 93:265-298.
[14] Cushing JM. Equilibria in structured populations. *Journal of Mathematical Biology* 1985; **23**:15-39.

[15] Cushing JM. Global branches of equilibrium solutions of the McKendrick equations for age-structured population growth. *Computers and Mathematics with Applications* 1985; **11**:175-188.

[16] Cushing JM. The dynamics of hierarchical age-structured populations. *Journal of Mathematical Biology* 1994; **32**:705-729.

[17] Cushing JM. *An Introduction to Structured Population Dynamics*, SIAM: Philadelphia, 1998.

[18] Cushing JM, Diekmann O. The many guises of $R_0$ (a didactic note). *Journal of Theoretical Biology* 2016; **404**:295-302.

[19] Diekmann O, Gyllenberg M. Abstract delay equations inspired by population dynamics, in "Functional Analysis and Evolution Equations" (Eds. H. Amann, W. Arendt, M. Hieber, F. Neubrander, S. Nicaise and J. von Below), Birkhäuser, 2007; 187–200.

[20] Diekmann O, Gyllenberg M, Huang H, Kirkilionis M, Metz JAJ, Thieme HR. On the formulation and analysis of general deterministic structured population models. II. Nonlinear theory. *Journal of Mathematical Biology* 2001; **43**:157-89.

[21] Diekmann O, Gyllenberg M, Metz JAJ. Steady-state analysis of structured population models. *Theoretical Population Biology* 2003; **63**:309-338.

[22] Diekmann O, Heesterbeek JAP. *Mathematical Epidemiology of Infectious Diseases*, John Wiley & Sons, 2000.

[23] Diekmann O, Heesterbeek JAP, Metz JAJ. On the definition and the computation of the basic reproduction ratio $R_0$ in models for infectious diseases in heterogeneous populations. *Journal of Mathematical Biology* 1990; **28**:365-382.

[24] Dublin LI, Lotka AJ. On the true rate of natural increase. *Journal of the American Statistical Association* 1925; **20**:305-339.

[25] Engel K-J, Nagel R. *One-Parameter Semigroups for Linear Evolution Equations*, Springer-Verlag: New York, 2000.

[26] Farkas JZ. On the linearized stability of age-structured multispecies populations. *Journal of Applied Mathematics* 2006; Art. ID 60643, 8 pp.

[27] Farkas JZ, Green DM, Hinow P. Semigroup analysis of structured parasite populations. *Mathematical Modelling of Natural Phenomena* 2010; **8**:94-114.

[28] Farkas JZ, Hagen T. Stability and regularity results for a size-structured population model. *Journal of Mathematical Analysis and Applications* 2007; **328**:119-136.

[29] Farkas JZ, Hagen T. Linear stability and positivity results for a generalized size-structured Daphnia model with inflow. *Applicable Analysis* 2007; **86**:1087-1103.

[30] Farkas JZ, Hagen T. Asymptotic behavior of size-structured populations via juvenile-adult interaction. *Discrete and Continuous Dynamical Systems. Series B* 2008; **9**:249-266.

[31] Farkas JZ, Hagen T. Hierarchical size-structured populations: the linearized semigroup approach. *Dynamics of Continuous, Discrete & Impulsive Systems. Series A. Mathematical Analysis* 2010; **17**:639-657.

[32] Farkas JZ, Morozov AY. Modelling effects of rapid evolution on persistence and stability in structured predator-prey systems. *Mathematical Modelling of Natural Phenomena* 2014; **9**:26-46.

[33] Farkas JZ, Morozov, AY, Arashkevich EG, Nikishina A. Revisiting the stability of spatially heterogeneous predator-prey systems under eutrophication. *Bulletin of Mathematical Biology* 2015; **77**:1886-1908.

[34] Iannelli M. *Mathematical Theory of Age-Structured Population Dynamics*, Giardini Editori: Pisa, 1994.

[35] Inaba H. On a new perspective of the basic reproduction number in heterogeneous environments. *Journal of Mathematical Biology* 2012; **65**:309-348.

[36] Metz JAJ, Diekmann O. *The Dynamics of Physiologically Structured Populations*, Springer-Verlag: Berlin, 1986.
[37] Schäfer HH. *Banach Lattices and Positive Operators*, Springer-Verlag: Berlin, 1974.

[38] Thieme HR. Remarks on resolvent positive operators and their perturbation. *Discrete and Continuous Dynamical Systems* 1998; 4:73-90.

[39] Thieme HR. Spectral bound and reproduction number for infinite-dimensional population structure and time heterogeneity. *SIAM Journal on Applied Mathematics* 2009; 70:188-211.

[40] Walker Ch. Positive equilibrium solutions for age- and spatially-structured population models. *SIAM Journal on Mathematical Analysis* 2009; 41:1366-1387.

[41] Walker Ch. Global bifurcation of positive equilibria in nonlinear population models. *Journal of Differential Equations* 2010; 248:1756-1776.

[42] Walker Ch. On nonlocal parabolic steady-state equations of cooperative or competing systems. *Nonlinear Analysis Real World Applications* 2011; 12:3552-3571.

[43] Webb GF. *Theory of Nonlinear Age-Dependent Population Dynamics*, Marcel Dekker: New York, 1985.

[44] Yicang Z, Cushing JM. Stability conditions for equilibria of nonlinear matrix population models. *Journal of Difference Equations and Applications* 1998; 4:95-126.

József Z. Farkas, Division of Computing Science and Mathematics, University of Stirling, Stirling, FK9 4LA, United Kingdom

E-mail address: jozsef.farkas@stir.ac.uk