

The Dynamics of Physiologically Structured
Populations: A Mathematical Framework and
Modelling Explorations

O. Diekmann

M. Gyllenberg
A.M. de Roos

J.A.J. Metz

October 13, 2012

Chapter 1

Age Structure

1.1 Population models

When we write

$$(1.1.1) \quad \frac{dN}{dt} = \beta N - \mu N = rN$$

and declare N to be the size of a population (perhaps in the form of the uniform spatial density), β the per capita birth rate, μ the per capita death rate and $r = \beta - \mu$ the Malthusian parameter, also known as the intrinsic rate of natural increase (or decline, if less than zero), we ignore many things. In particular

1. The difference between males and females. If there are always enough males to inseminate all females, one may interpret (1.1.1) as an equation for the female part of the population, with β pertaining to the daughters only.
2. Demographic stochasticity. Individuals are discrete units that either do or do not die and either do or do not reproduce, but if they do, they produce an integer number of offspring.
3. Maturation delay. Newborn individuals are, as a rule, not able to reproduce, they need to develop first. To distinguish individuals from one another, one may introduce the notion of i -state (i for individual), allow the i -state to take a continuum of values, and model how i -state changes in the course of time.
4. Aging. In general, life time is not exponentially distributed. Maturation has its negative sides too!

5. Dependence. The linear equation (1.1.1) ignores that β may depend on, for example, food density and μ on predator density and that, in turn, food density is influenced by consumption and predator density by being consumed. This feedback to the environmental condition creates dependence and, in the deterministic description, nonlinearity.
6. Environmental variability. The time-translation invariant equation (1.1.1) ignores seasonality as well as spatial heterogeneity. Yet often spatio-temporal fluctuations have an impact on population dynamics.

In this book we focus on 3, 4 and 5, while referring to [16] for 2 and [30] for 6.

In much of this chapter we consider a constant environmental condition, that is, we not only ignore 6 but also 5. The key point is that under constant conditions we can relate the i -state to the combination of age and state-at-birth in a once and for all manner. Initially we assume that individuals are born equal (perhaps in a stochastic sense, see Ex. 1.2.2 below), i.e., they can be treated as if there is but one i -state at birth, but in Section 1.5 we allow for finitely many different states-at-birth.

1.2 The ingredients

In a data-driven approach, it is natural to describe an age-structured population model in terms of

- the survival probability to age a , denoted by $\mathcal{F}(a)$
- the average number of offspring produced by age a , denoted by $L(a)$.

Provided \mathcal{F} is sufficiently smooth, one can define the age-specific per capita death rate (i.e., the probability per unit of time of dying) by

$$(1.2.1) \quad \mu(a) = -\frac{d}{da} \ln \mathcal{F}(a) \Leftrightarrow \mathcal{F}(a) = e^{-\int_0^a \mu(\alpha) d\alpha}.$$

Likewise one can define the age-specific average per capita birth rate (i.e., the average number of births per unit of time) by

$$(1.2.2) \quad \beta(a) = \frac{1}{\mathcal{F}(a)} \frac{dL}{da}(a) \Leftrightarrow L(a) = \int_0^a \beta(\alpha) \mathcal{F}(\alpha) d\alpha.$$

If L and \mathcal{F} are determined from data, there is no need to introduce β and μ . But often we use a model to deduce the consequences at the p -level (p for population) of (quasi-) mechanistic assumptions concerning i -behaviour and then it is often more natural to start from β and μ .

Example 1.2.1 *“Daphnia” under constant conditions*

Suppose all Daphnia are born with size ξ_b and that their growth rate is given by $g(\xi, S)$, where ξ denotes the size and S the food/algae concentration, here assumed to be constant. Let $\xi(a)$ denote the solution of

$$(1.2.3) \quad \frac{d\xi}{da} = g(\xi, S), \quad \xi(0) = \xi_b.$$

Let $\tilde{\beta}(\xi, S)$ be the per capita rate of producing offspring, given size ξ and food concentration S and let, likewise, $\tilde{\mu}(\xi, S)$ be the per capita death rate. Then we may put

$$(1.2.4) \quad \beta(a) = \tilde{\beta}(\xi(a), S), \quad \mu(a) = \tilde{\mu}(\xi(a), S).$$

The point is that one can use energy budget considerations, see Section 2.8 below and scaling laws of individual behaviour characteristics to motivate expressions for g and $\tilde{\beta}$ and, to a lesser extent, $\tilde{\mu}$.

Example 1.2.2. *Daphnia under constant conditions, but with variable birth size*

If ξ_b is variable, one should write $\xi(a, \xi_b)$ to denote the solution of (1.2.3). If ξ_b is a stochastic variable with density f , one simply introduces

$$(1.2.5) \quad \begin{aligned} \mathcal{F}(a) &= \int_{\Omega_b} \tilde{\mathcal{F}}(a, \xi_b) f(\xi_b) d\xi_b \\ L(a) &= \int_{\Omega_b} \tilde{L}(a, \xi_b) f(\xi_b) d\xi_b \end{aligned}$$

where Ω_b denotes the set of all possible sizes-at-birth, and next uses the first identity in formulas (1.2.1) and (1.2.2) to define μ and β . Practical considerations, in particular the need to do numerical calculations, may motivate us to replace the density f by a measure concentrated in a finite number of points.

1.3 Bookkeeping

The equation

$$(1.3.1) \quad n(t, a) = b(t - a)\mathcal{F}(a)$$

relates the age density n at time t to the p -birth rate b in the past and the survival probability \mathcal{F} . It simply expresses that a fraction $\mathcal{F}(a)$ of the large cohort born at time $t - a$ survived till time t and age a . (But one should always keep in mind that both n and b have dimension 1/time and that only integration over age (in the case of n) or time (in the case of b) leads to numbers, so it is dangerous to speak about a "cohort" born at a certain time.)

The equation

$$(1.3.2) \quad b(t) = \int_0^{\infty} \beta(a)n(t, a)da$$

expresses that the p -birth rate is obtained by adding contributions of individuals. Combining these two equations we arrive at the *renewal* equation

$$(1.3.3) \quad b(t) = \int_0^{\infty} \beta(a)\mathcal{F}(a)b(t - a)da$$

which alternatively can be written in the form

$$(1.3.4) \quad b(t) = \int_0^{\infty} b(t - a)L(da)$$

where the so-called Stieltjes integral is defined by

BOX to be written

(note the very natural biological interpretation!)

If we start an experiment at time $t = 0$ with an (assumed to be known) initial age density $n(0, a)$, the identity (1.3.1) only holds for $0 \leq a < t$. For $a \geq t$ we have instead (conditional survival probability)

$$n(t, a) = \frac{\mathcal{F}(a)}{\mathcal{F}(a - t)}n(0, a - t).$$

So (1.3.2) now leads to

$$(1.3.5) \quad b(t) = \int_0^t \beta(a) \mathcal{F}(a) b(t-a) da + f(t)$$

with

$$(1.3.6) \quad f(t) = \int_t^\infty \beta(a) \frac{\mathcal{F}(a)}{\mathcal{F}(a-t)} n(0, a-t) da = \int_0^\infty \beta(\alpha+t) \frac{\mathcal{F}(\alpha+t)}{\mathcal{F}(\alpha)} n(0, \alpha) d\alpha.$$

An alternative way to arrive at (1.3.5), is to assume that (1.3.3) holds for $t \geq 0$ and that the p -birth rate in the past (relative to time $t = 0$), so $b(\theta)$ for $\theta < 0$, is somehow known/given. In fact the two ways of prescribing an “initial condition”, respectively $n(0, a)$ and $b(\theta)$, are completely equivalent. Indeed, if we take $t = 0$ in (1.3.1) we find

$$(1.3.7) \quad n(0, a) = b(-a) \mathcal{F}(a), \quad a \geq 0$$

showing how to compute $b(\theta)$ given $n(0, a)$ or $n(0, a)$ given $b(\theta)$.

Both (1.3.5) and (1.3.3) are called a *renewal equation*. For questions of existence and uniqueness of solutions one considers (1.3.5). As we will see soon, the translation invariant form (1.3.3) is more informative when dealing with questions concerning the asymptotic behaviour for large time.

As an alternative for (1.3.1), one may formulate the first order partial differential equation

$$(1.3.8) \quad \frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} = -\mu n.$$

The equation (1.3.2), rewritten as

$$(1.3.9) \quad n(t, 0) = \int_0^\infty \beta(a) n(t, a) da$$

then provides a boundary condition at $a = 0$. This condition is called “non-local” to emphasize that the right hand side involves values of n at points far away from $a = 0$ (which is biologically obvious, in fact necessary: mothers should have an age that exceeds some minimum age).

Note that $\frac{\partial n}{\partial a}$ equals the divergence of the flux, the flux being the velocity times the density and the velocity being 1. Also note that the left hand side of (1.3.9) equals the flux at the boundary. These observations are important if one generalizes (1.3.8)-(1.3.9) to, for instance, size structure; see [22].

1.4 Growth or decline?

The basic reproduction number R_0 is defined as the expected life time production of offspring and hence is given by

$$(1.4.1) \quad R_0 := L(\infty) = \int_0^{\infty} \beta(a) \mathcal{F}(a) da.$$

Directly from the interpretation it follows that in our deterministic way of looking at things generations grow (if $R_0 > 1$) or decline (if $R_0 < 1$) in a geometric progression with ratio R_0 , that is, the k th generation is proportional to R_0^k . There is an asymmetry in the correction that results from the incorporation of demographic stochasticity: extinction is guaranteed if $R_0 < 1$, but if $R_0 > 1$ the population may also go extinct, instead of growing exponentially, see [18, 16]. So, from a stochastic perspective, R_0 measures the *potential* for population growth.

One can prove (see below) that in real time the population grows like

$$e^{rt}$$

where r is the real root of the Euler-Lotka equation

$$(1.4.2) \quad 1 = \int_0^{\infty} \beta(a) \mathcal{F}(a) e^{-ra} da$$

Figure 1

Figure 1 shows the graph of the function $z \mapsto \int_0^{\infty} \beta(a) \mathcal{F}(a) e^{-za} da$ with real z , and illustrates that

$$(1.4.3) \quad \begin{aligned} R_0 > 1 &\Leftrightarrow r > 0 \\ R_0 = 1 &\Leftrightarrow r = 0 \\ R_0 < 1 &\Leftrightarrow r < 0 \end{aligned}$$

(but the last equivalence should be interpreted with care, as r need not exist, since the integral may cease to converge before the value 1 is reached). Under suitable conditions on β and \mathcal{F} one can formulate this more precisely and use the monotonicity of the function to provide a proof.

Fisher [11] interpreted the right hand side of (1.4.2) as a discounted reproduction number, where the discounting is based on the growth of the population (if we weigh a newborn individual with (population size at the time of birth)⁻¹ then the population growth rate r is such that the expected number of offspring, with this weight factor taken into account, equals one).

For the biological interpretation only the real root of the equation

$$(1.4.4) \quad 1 = \int_0^{\infty} \beta(a) \mathcal{F}(a) e^{-za} da$$

is relevant, but in the mathematical analysis complex roots play a role as well. From the inequality

$$(1.4.5) \quad \left| \int_0^{\infty} \beta(a) \mathcal{F}(a) e^{-za} da \right| \leq \int_0^{\infty} \beta(a) \mathcal{F}(a) e^{-\operatorname{Re} z a} da$$

which, under weak assumptions on β and \mathcal{F} , is strict for $\operatorname{Im} z \neq 0$, one sees that the real root is *dominant* (in the sense that $\operatorname{Re} z < r$ if z is a root with $z \neq r$). Here we use once more the monotone dependence on $\operatorname{Re} z$, which derives from the non-negativity of β and \mathcal{F} . (One should compare this result to the Perron-Frobenius theory of positive-off-diagonal matrices.)

Cautionary example. For cell division at exactly age 1, L jumps from zero to two at age 1 (if we ignore the possibility of cell death) and the difference equation

$$b(t) = 2b(t-1)$$

leads to the characteristic equation

$$1 = 2e^{-z}$$

which has roots

$$z = \ln 2 + k2\pi i, \quad k \in \mathbb{Z}.$$

Main results. There exists a constant $C > 0$ such that

$$(1.4.6) \quad b(t) = Ce^{rt} + o(e^{rt}), \quad t \rightarrow \infty$$

and hence, according to (1.3.1), we have

$$(1.4.7) \quad n(t, a) = C e^{rt} e^{-ra} \mathcal{F}(a) + o(e^{rt}), \quad t \rightarrow \infty$$

showing that the age distribution stabilizes to a distribution with density

$$(1.4.8) \quad \frac{e^{-ra} \mathcal{F}(a)}{\int_0^\infty e^{-r\alpha} \mathcal{F}(\alpha) d\alpha}$$

while the size of the population grows like e^{rt} .

Note that the age density is steeply declining in fast growing populations. The expression (1.4.8) also illustrates the aging of a population when r decreases. In this spirit, Aline de Koeijer [20] has observed that (assuming that BSE infection occurs, if it occurs at all, early in a cow's life) there are relatively far more young individuals infected in an outbreak situation than in the control induced decline situation afterwards. The moral is that the relationship between the p -growth rate r and the stable distribution can be used to deduce conclusions from data.

Sketch of the proof. Applying the Laplace transform to (1.3.5) we obtain

$$(1.4.9) \quad \bar{b} = \bar{K} \bar{b} + \bar{f}$$

where we have written K as a short-hand notation for the product of β and \mathcal{F} and denoted the Laplace transform of a function by a bar. If we solve for \bar{b} , the inversion formula yields

$$(1.4.10) \quad b(t) = \frac{1}{2\pi i} \int_{\gamma} e^{zt} \frac{\bar{f}(z)}{1 - \bar{K}(z)} dz$$

where γ is a vertical line to the right of r .

Figure 2

As W. Feller [10] showed (see also [6, 13, 17]) one may shift γ to the left, picking up a residue when passing r . This (together with exponential estimates for the integral along the shifted contour) justifies (1.4.6) and provides the expression

$$(1.4.11) \quad C = \frac{\bar{f}(r)}{\int_0^{\infty} a\beta(a)\mathcal{F}(a)e^{-ra}da}$$

for the constant C . □

From (1.3.6) we deduce

$$(1.4.12) \quad \begin{aligned} \bar{f}(r) &= \int_0^{\infty} \int_0^{\infty} n(0, a) \frac{\mathcal{F}(a+t)}{\mathcal{F}(a)} \beta(a+t) da e^{-rt} dt \\ &= \int_0^{\infty} n(0, a) \nu(a) da \end{aligned}$$

where

$$(1.4.13) \quad \nu(a) := \frac{e^{ra}}{\mathcal{F}(a)} \int_a^{\infty} \mathcal{F}(\tau) \beta(\tau) e^{-r\tau} d\tau$$

is called the *reproductive value* of an individual at age a since such an individual is expected to contribute $\nu(a)$ as much to future population sizes as a newborn (note that $\nu(0) = 1$). This concept was introduced by Fisher [11]. Mathematically we say that the *projection* onto the stable age distribution is given by

$$(1.4.14) \quad (P\phi)(a) = \frac{\int_0^{\infty} \nu(\alpha) \phi(\alpha) d\alpha}{\int_0^{\infty} \alpha \beta(\alpha) \mathcal{F}(\alpha) e^{-r\alpha} d\alpha} e^{-ra} \mathcal{F}(a).$$

The normalized distribution $\frac{L(a)}{L(\infty)}$ describes the “age at child bearing” of a cohort. It is *not* equal to the distribution of the age of mothers of newborn babies (given that the population is in the stable age distribution). For instance, the mean of “age at child bearing” is

$$\bar{a} = \frac{\int_0^{\infty} a\beta(a)\mathcal{F}(a)da}{\int_0^{\infty} \beta(a)\mathcal{F}(a)da}$$

while the mean age of mothers of newborn babies is

$$\int_0^{\infty} a\beta(a)\mathcal{F}(a)e^{-ra}da$$

and the two quantities differ if the population is growing or declining. This observation is very relevant in the context of SARS, where one observes r but needs to estimate R_0 in order to decide what control measures are needed. If one writes

$$(1.4.15) \quad R_0 = e^{rT}$$

with T interpreted as a "generalization length", one only shifts the problem to "how to estimate T from data?", see [32, 26].

Remark 1.4.1. (cf.[28]) Example 1.2.1 continued. Along with (1.2.3) one may numerically solve

$$(1.4.16) \quad \frac{d\mathcal{F}}{da} = -\tilde{\mu}(\xi, S)\mathcal{F}, \quad \mathcal{F}(0) = 1$$

and

$$(1.4.17) \quad \frac{dL}{da} = \tilde{\beta}(\xi, S)\mathcal{F}, \quad L(0) = 0$$

to compute $R_0 = L(\infty)$ as a function of the parameter S , with a stopping criterion based on \mathcal{F} decreasing beyond a chosen small level. If we replace (1.4.17) by

$$(1.4.18) \quad \frac{d\tilde{L}_z}{da}(a) = e^{-za}\tilde{\beta}(\xi(a), S)\mathcal{F}(a), \quad \tilde{L}_z(0) = 0$$

we may find the Malthusian parameter by solving

$$(1.4.19) \quad \tilde{L}_z(\infty) = 1$$

where again ∞ should not be taken literally and where the monotonicity and convexity with respect to real z guarantees rapid convergence of simple root finding routines. If both $\tilde{\beta}$ and $\tilde{\mu}$ are (more or less) constant for large a , say $\tilde{\beta}(\xi(a), S) = \beta_{\infty}(S)$ and $\tilde{\mu}(\xi(a), S) = \mu_{\infty}(S)$ for $a \geq \bar{a}$, one may use, for instance, (1.4.17) to compute $L(\bar{a})$ and then add

$$\frac{\beta_{\infty}(S)}{\mu_{\infty}(S)}\mathcal{F}(\bar{a})$$

to obtain $L(\infty)$. This provides an alternative to a stopping criterion based on \mathcal{F} decreasing beyond a chosen level.

1.5 Multiple birth states

Suppose in a certain region there are a finite number of patches of suitable habitat for a plant species. Assume there are quality differences between the patches, for instance due to differences in soil type or micro-climatic conditions. The patch in which a seed lands may then have a large impact on the germination success, on subsequent growth of the plant, and ultimately on the production of seeds. Therefore we attach a label to a seed that identifies the patch in which it lands.

To deal with such situations, we only need to superimpose a certain amount of linear algebra on the formalism of earlier sections (and if we allow for infinitely many types, either still countable or a continuum, we should use functional analysis rather than linear algebra; but for the time being we refrain from considering such technically more complicated situations).

If we indicate the type by an index, we can replace (1.3.3) by

$$(1.5.1) \quad b_i(t) = \sum_j \int_0^\infty \beta_{ij}(a) \mathcal{F}_j(a) b_j(t-a) da$$

if we adopt the convention that the last of the two indices of β refers to the state-at-birth of the mother and the first to the state-at-birth of the offspring (Nota bene: probabilists usually do it the other way round). Instead of (1.4.1) we now define

R_0 := the dominant eigenvalue of the positive matrix $L(\infty)$,
where

$$(1.5.2) \quad L_{ij}(a) := \int_0^a \beta_{ij}(\alpha) \mathcal{F}_j(\alpha) d\alpha$$

and where we assume that $L(\infty)$ is *primitive*, i.e., for some power k all entries of $L(\infty)^k$ are strictly positive.

The corresponding eigenvector of $L(\infty)$ describes the stable distribution of state-at-birth in the generation process (which is, for growing or declining populations, in general different from the stable real time distribution of state-at-birth; the latter we denote below by ϕ).

If we define

$$(1.5.3) \quad K_{ij}(a) := \beta_{ij}(a) \mathcal{F}_j(a)$$

and define the Laplace transform of vectors and matrices by taking component-wise the transform, we can define the Malthusian parameter r as the real root of the equation

$$(1.5.4) \quad \det (I - \bar{K}(z)) = 0$$

obtained by substituting $b(t) = e^{zt}b(0)$, where $b(0)$ is now a vector, into the renewal equation (1.5.1). Note that for real z

- i) $\bar{K}(z)$ is primitive too, since it has strictly positive entries at exactly the same positions as $\bar{K}(0) = L(\infty)$
- ii) the dominant eigenvalue of $\bar{K}(z)$ is a strictly decreasing function of z , since so are all non-zero elements of $\bar{K}(z)$ and, in general for a matrix M depending on a parameter p , the derivative of a *simple* eigenvalue with respect to p is given by the formula

$$(1.5.5) \quad \lambda' = \frac{\langle \psi^*, M' \psi \rangle}{\langle \psi^*, \psi \rangle}$$

where ψ and ψ^* are the corresponding eigenvector and adjoint eigenvector, which are positive.

- iii) the dominant eigenvalue of $K(z)$ decreases to zero for $z \rightarrow \infty$

Main results There exists a constant $C > 0$ such that

$$(1.5.6) \quad b(t) = Ce^{rt}\phi + o(e^{rt}), \quad t \rightarrow \infty,$$

where ϕ is the eigenvector of $\bar{K}(r)$ corresponding to eigenvalue 1 (and normalized, for instance, such that $\sum_j \phi_j = 1$). As a consequence we have

$$(1.5.7) \quad n_i(t, a) = \mathcal{F}_i(a)b_i(t - a) = Ce^{rt}e^{-ra}\mathcal{F}_i(a)\phi_i + o(e^{rt})$$

showing that the distribution with respect to age and state-at-birth stabilizes. As we show below, the expression (1.4.11) for C generalizes to

$$(1.5.8) \quad C = \frac{\langle \phi^*, \bar{f}(r) \rangle}{-\langle \phi^*, \bar{K}'(r)\phi \rangle}$$

if we normalize ϕ^* such that $\langle \phi^*, \phi \rangle = 1$. (Note that $\overline{K}'(r)$ has entries $-\int_0^\infty a\beta_{ij}(a)\mathcal{F}_j(a)e^{-ra}da$.) We can rewrite

$$\langle \phi^*, \overline{f}(r) \rangle = \sum_j \int_0^\infty \sum_i \phi_i^* \nu_{ij}(a) n_j(0, a) da$$

and interpret

$$\sum_i \phi_i^* \nu_{ij}(a)$$

as the reproductive value of an individual of age a and state-at-birth j . Explicitly we have

$$(1.5.9) \quad \nu_{ij}(a) = \frac{e^{ra}}{\mathcal{F}_j(a)} \int_a^\infty \beta_{ij}(\tau) \mathcal{F}_j(\tau) e^{-r\tau} d\tau$$

and consequently $\sum_j \nu_{ij}(0) \phi_j = \phi_i$, which amounts to the normalization that a "stochastic" newborn individual with distribution ϕ has reproductive value 1.

Technical aside 1.5.1. Computation of C . To avoid ambiguities, we now need to take the dependence of ϕ, ϕ^* and λ on z into account in the notation. If we define $y(z) = \overline{b}(z)$, i.e.,

$$y(z) = (I - \overline{K}(z))^{-1} \overline{f}(z)$$

then

$$y(z) - \overline{K}(z)y(z) = \overline{f}(z)$$

and hence

$$\langle \phi^*(z), y(z) \rangle - \lambda(z) \langle \phi^*(z), y(z) \rangle = \langle \phi^*(z), \overline{f}(z) \rangle$$

which we rewrite as

$$\langle \phi^*(z), y(z) \rangle = (1 - \lambda(z))^{-1} \langle \phi^*(z), \overline{f}(z) \rangle.$$

Since

$$y(z) = \langle \phi^*(z), y(z) \rangle \phi(z) + R(z)$$

for a function R of z which is regular in $z = r$, the residue of $y(z)$ in $z = r$ equals the residue of $\langle \phi^*(z), y(z) \rangle \phi(z)$ in $z = r$, which equals

$$\frac{\langle \phi^*(r), \overline{f}(r) \rangle}{-\lambda'(r)} \phi(r).$$

Using (1.5.5) and once more the normalization $\langle \phi^*(z), \phi(z) \rangle = 1$, we arrive at (1.5.8).

Remark 1.5.2. Simplification for the case of a one-dimensional range of K . If the distribution of the state-at-birth of the offspring is independent of the state-at-birth of the mother, we are in a situation already known from Example 1.2.2: one can do the averaging once and for all. Mathematically this manifests itself in the matrix function K having one-dimensional range. In view of (1.5.3) this amounts to

$$(1.5.10) \quad \beta_{ij}(a) = p_i \tilde{\beta}_j(a), \text{ with } \sum_k p_k = 1.$$

A possible interpretation of (1.5.10) is that p_i measures the size of patch i and seed dispersal is random in the sense that *all* seeds, no matter where they are produced, have probability p_i to land in patch i , given that they land in a patch and not on unsuitable surface (so we incorporate the probability that they land in a patch and not on unsuitable surface as a factor in each of the $\tilde{\beta}_j$.)

If we nevertheless start from the system (1.5.1) we can make the Ansatz

$$b_i(t) = p_i \tilde{b}(t)$$

and derive the scalar renewal equation

$$\tilde{b}(t) = \int_0^\infty \tilde{\beta}(a) \tilde{b}(t-a) da$$

where

$$\tilde{\beta}(a) := \sum_j \tilde{\beta}_j(a) \mathcal{F}_j(a) p_j.$$

Occasionally one meets a case in which the range of the matrix K has a dimension in between 1 and the total number of types. Then one can reduce the dimension of (1.5.1) to that of the range of K .

1.6 Cannibalism, taking only negative effects into account

The deterministic view provides a simple dichotomy for population dynamics under prescribed constant environmental conditions: either $R_0 < 1$ and the

population is doomed to go extinct or $R_0 > 1$ and the population will grow exponentially with rate $r > 0$. We dismiss the critical case $R_0 = 1$ as too exceptional to be considered seriously.

A first effect of density dependence in the form of feedback to the environmental condition is that $R_0 = 1$ becomes, in a sense, the rule rather than the exception. The aim of the present section is to illustrate this phenomenon in the context of a model that incorporates a caricatural description of cannibalistic interaction. (It is always good to use caricatures to derive qualitative insights and to use numerical simulation studies of complex models to derive quantitative estimates, as the confrontation of the two approaches yields more understanding than each separately. The focus of the present book is on methods for studying what one could call relatively complex caricatures. But we start simple.)

To set the stage, consider a population consisting of juveniles and adults, with juveniles turning adults at exacty age $\bar{\tau}$. The chief distinction is that only adults reproduce. We assume that both the per capita birth rate and the per capita death rate of adults is a constant, i.e., independent of age, once age exceeds $\bar{\tau}$. We call these β and μ , respectively. It follows at once that

$$(1.6.1) \quad R_0 = \beta \frac{1}{\mu} \mathcal{F}(\bar{\tau})$$

since the last factor is the probability of reaching adulthood, the middle factor the expected life time as adult, given that the individual matures to become adult, and the first factor the rate of producing offspring during this period. If also the death rate of juveniles is a constant, i.e., independent of the actual age $a \in [0, \bar{\tau}]$, we speak of a *stage* structured model (but note that the age of juveniles *is* important, as it determines when they will mature; also note that ambiguity about the death rate *at* age $\bar{\tau}$ doesn't hurt, as the threshold $\bar{\tau}$ is crossed with non-zero speed and hence the survival probability is not affected by our choice for μ in that single point). In fact, to avoid a proliferation of parameters, we assume that the death rate of juveniles is equal to that of adults, that is, we assume

$$(1.6.2) \quad \mathcal{F}(\bar{\tau}) = e^{-\mu\bar{\tau}}.$$

The results from our earlier sections can now be summarized in the diagram depicted in Figure 3.

Figure 3

In this diagram, \bar{A} denotes the size of the subpopulation of adults, s means that the zero population state (usually called the trivial steady state) is stable and u that it is unstable (that in the latter case A grows to infinity is implicitly incorporated in the picture by the absence of "anything", meaning some attractor, other than the trivial steady state, except for the vertical line of neutrally stable steady states for $R_0 = 1$. How will this picture change if we incorporate the effect of cannibalism?

Cannibalism has two sides, that of the aggressor and that of the victim. In general, therefore, the attack rate is a function of two i -states. Here we assume (for no other reason than that we want to increase the tractability) that those two i -states have an independent influence or, in other words, that the function of two variables is in fact the product of a function of one variable and a function of the other variable. More precisely, we assume that the death rate of a juvenile of age a is, due to cannibalism, increased from μ to

$$\mu + h(a)A$$

meaning that adults (and only adults) practise cannibalism. The vulnerability h is assumed to have a graph somewhat like the one depicted in Figure 4.

Figure 4

Before proceeding with the formulation of the equations for population level quantities, we introduce a very important piece of notation: ϕ_t denotes the

history, relative to time t , of the function ϕ , in the sense that

$$(1.6.3) \quad \phi_t(\theta) := \phi(t + \theta) \text{ for } \theta \leq 0.$$

An individual born at time $t - a$ survives, to have age a at time t , with probability

$$(1.6.4) \quad \mathcal{F}(a, A_t) = e^{-\mu a - \int_0^a h(\alpha) A(t-a+\alpha) d\alpha}.$$

We now assume that, although cannibalism is a not infrequent cause of death of juveniles, the own species forms but a very minor part of the diet of adults. Or, in simpler words, we assume that the per capita birth rate of adults is a constant, again denoted by β . The renewal equation now reads

$$(1.6.5) \quad b(t) = \beta \int_{\bar{\tau}}^{\infty} \mathcal{F}(a, A_t) b(t-a) da.$$

By definition

$$(1.6.6) \quad A(t) = \int_{\bar{\tau}}^{\infty} \mathcal{F}(a, A_t) b(t-a) da.$$

We view (1.6.6) as an updating rule for A just as (1.6.5) is an updating rule for b . If the support of h is bounded away from $\bar{\tau}$, the values of the argument of A that matter at the right hand side are bounded away from t and one can proceed by steps (this is indeed called "the method of steps" in the theory of delay equations). In fact we can restrict to just one of the two equations, because our assumption concerning reproduction can also be stated as

$$(1.6.7) \quad b(t) = \beta A(t).$$

Either directly from the interpretation or by formal formula manipulation (using that in (1.6.6) we have $a \geq \bar{\tau}$ and that the support of h is restricted to $[0, \bar{\tau}]$), it follows that

$$(1.6.8) \quad \frac{dA}{dt}(t) = b(t - \bar{\tau}) \mathcal{F}(\bar{\tau}, A_t) - \mu A(t).$$

If we substitute (1.6.7) into (1.6.8) we obtain the single delay differential equation

$$(1.6.9) \quad \frac{dA}{dt}(t) = \beta A(t - \bar{\tau}) \mathcal{F}(\bar{\tau}, A_t) - \mu A(t).$$

Let us next pay attention to initial conditions. If we start an experiment at time $t = a$ with an (assumed to be known) initial age density $n(0, a)$, we should replace the right hand sides of (1.6.5), (1.6.6), (1.6.9) by more complicated expressions and, also, restrict to $t \geq 0$. For instance, for $0 \leq t \leq \bar{\tau}$ one should replace (1.6.9) by

$$\frac{dA}{dt}(t) = n(0, \bar{\tau} - t) e^{-\mu t - \int_0^t h(\bar{\tau} - t + \sigma) A(\sigma) d\sigma} - \mu A(t)$$

and put as initial condition

$$A(0) = \int_{\bar{\tau}}^{\infty} n(0, \alpha) d\alpha.$$

For $t > \bar{\tau}$ we can use (1.6.9) as it stands. The traditional mathematical way of formulating an initial condition for (1.6.9) is to prescribe A itself on an interval of length $\bar{\tau}$, i.e., to require that

$$(1.6.10) \quad A(\theta) = \psi(\theta), \quad -\bar{\tau} \leq \theta \leq 0$$

where ψ is a given continuous function. When we said “For $t > \bar{\tau}$ we can use (1.6.9) as it stands”, the statement implicitly included that $A_t(\theta)$ is a well-defined continuous function of θ on $[-\bar{\tau}, 0]$ for $t > \bar{\tau}$. Or, in other words, for $t > \bar{\tau}$ we can represent the population state by the history of the adult population size A , without losing any information that has an impact on dynamics.

Similarly we can equip the renewal equation

$$(1.6.11) \quad b(t) = \beta \int_{\bar{\tau}}^{\infty} \mathcal{F} \left(a, \frac{1}{\beta} b_t \right) b(t - a) da, \quad t > 0,$$

with an initial condition

$$(1.6.12) \quad b(\theta) = \phi(\theta), \quad -\infty < \theta \leq 0$$

where ϕ is a given integrable function. But a representation of the population state by the history of the population birth rate b need not be completely accurate (as far as dynamics is concerned) after finite time. It only applies asymptotically for $t \rightarrow \infty$.

Formula (1.3.7) shows that, in the case of a constant environment, there is a simple relationship between the age-density at time zero and the birth

rate in the past. Here the influence of A in the survival probability (1.6.4) makes that juvenile individuals experience a fluctuating environment. If we prescribe *both* the population birth rate b and the adult population size A in the past, we can compute the age-density at time zero as

$$(1.6.13) \quad n(0, a) = b(-a)\mathcal{F}(a, A_0)$$

(where, of course, $A_0(\theta) = A(\theta)$, $\theta \leq 0$). It clearly is impossible, however, to go in the other direction: one cannot recover $b(\theta)$ and $A(\theta)$ from $n(0, a)$ by using (1.6.13). So initial conditions of the form (1.6.10) or of the form (1.6.12) constitute a restriction on the initial age distribution $n(0, a)$. Hopefully the discussion above made clear that we do *not* miss anything related to large time dynamical behaviour if we accept such a restriction.

We conclude this section by computing steady states. For constant A we have

$$(1.6.14) \quad R_0(A) = \beta \frac{1}{\mu} e^{-\mu\bar{\tau} - HA}$$

where

$$(1.6.15) \quad H := \int_0^{\bar{\tau}} h(\sigma) d\sigma.$$

The equation

$$(1.6.16) \quad R_0(A) = 1$$

has the solution

$$(1.6.17) \quad A = \bar{A} = \frac{1}{H} \ln \left(\frac{\beta}{\mu} e^{-\mu\bar{\tau}} \right).$$

The biological interpretation requires A to be non-negative, so requires

$$\beta \geq \mu e^{\mu\bar{\tau}}.$$

Note that

$$\bar{b} = \beta \bar{A}$$

is a steady state for the Renewal Equation (1.6.11).

The analogue of Figure 3 is Figure 5, which shows a prototypical *transcritical bifurcation*. The Principle of the Exchange of Stability implies that the nontrivial steady state is stable for β a bit larger than $\mu e^{\mu\bar{\tau}}$ (see [1] and

the references given there; note once again that A needs to be positive to have biological relevance and that, if we concentrate on the branch of positive values of \bar{A} , we may call the bifurcation *supercritical*). The question mark in Figure 5 indicates that we do not know whether stability is, or is not, retained if β is increased. In Section 1.8 below we shall investigate this in detail. For now we just observe that negative feedback prevents exponential growth and that a steady state exists.

Figure 5

Side remark 1.6.1. The observation that the total population size \bar{N} equals the rate of "inflow" \bar{b} times the sojourn time, usually called the life expectancy, is often helpful. The latter equals

$$\int_0^{\infty} \mathcal{F}(a, \bar{A}) da.$$

Indeed, omitting the parameter \bar{A} from the notation, we have as distribution function $1 - \mathcal{F}(a)$ and partial integration leads to

$$-\int_0^{\infty} a \mathcal{F}(da) = \int_0^{\infty} \mathcal{F}(\alpha) d\alpha.$$

1.7 Cannibalism, with positive effects incorporated

Next, let's incorporate that cannibalistic food increases reproduction and change (1.6.5) into

$$(1.7.1) \quad b(t) = (\beta + B(t)) \int_{\bar{\tau}}^{\infty} \mathcal{F}(a, A_t) b(t-a) da$$

with

$$(1.7.2) \quad B(t) := \int_0^{\bar{\tau}} E(\alpha)h(\alpha)\mathcal{F}(\alpha, A_t)b(t-\alpha)d\alpha.$$

So $E(\alpha)$ converts the food value of a juvenile of age a into the ability to produce offspring. The dynamical system is now defined in terms of solutions of (1.7.1) and (1.6.8), here repeated as

$$(1.7.3) \quad \frac{dA}{dt}(t) = b(t-\bar{\tau})\mathcal{F}(\bar{\tau}, A_t) - \mu A(t)$$

with B given by (1.7.2) and \mathcal{F} by (1.6.4). A peculiarity is that if we rewrite (1.7.1) in the form

$$(1.7.4) \quad b(t) = (\beta + B(t))A(t)$$

we can work with initial conditions of the form

$$(1.7.5) \quad \begin{aligned} b(\theta) &= \varphi(\theta), \\ A(\theta) &= \psi(\theta), \end{aligned} \quad -\bar{\tau} \leq \theta \leq 0$$

(this means that if we are prepared to assume that A on the interval $-\bar{\tau} \leq \theta \leq 0$ is related to b in the distant past as one would expect on the basis of the model, then the information about the distant past of b is redundant as far as future dynamics is concerned). To find steady states, we first of all require that the steady environmental condition is such that $R_0 = 1$, i.e.,

$$(1.7.6) \quad 1 = R_0(A, B) = (\beta + B) \frac{1}{\mu} e^{-\mu\bar{\tau} - HA}.$$

We supplement this equation by the feedback conditions

$$(1.7.7) \quad \begin{aligned} A &= b \frac{1}{\mu} e^{-\mu\bar{\tau} - HA} \\ B &= b \int_0^{\bar{\tau}} E(\alpha)h(\alpha) e^{-\mu\alpha - A \int_0^{\alpha} h(\sigma)d\sigma} d\alpha \end{aligned}$$

Together these are three equations in the three unknowns A, B and b . But by writing the first equation of (1.7.7) as

$$(1.7.8) \quad b = \mu A e^{\mu\bar{\tau} + HA}$$

and next substituting this into the second equation of (1.7.7) and finally the resulting expression for B into (1.7.6), one reduces the system to the single equation

$$(1.7.9) \quad \beta = \mu e^{\mu\bar{\tau}+HA} - \mu A e^{\mu\bar{\tau}+HA} \int_0^{\bar{\tau}} E(\alpha) h(\alpha) e^{-\mu\alpha - A \int_0^{\alpha} h(\sigma) d\sigma} d\alpha$$

for A . For given β , this is an equation for A and we call the solution \bar{A} . But inversely it is an *explicit* expression for β as a function of $A = \bar{A}$, making it rather easy to make a picture like Figure 5. Note that $A = 0$ corresponds to $\beta = \mu e^{\mu\bar{\tau}}$, as is to be expected. A natural question now is: will the bifurcation at this critical value of β be supercritical or subcritical? In other words, will positive values of A correspond to $\beta > \mu e^{\mu\bar{\tau}}$ or to $\beta < \mu e^{\mu\bar{\tau}}$?

To answer this question, we simply differentiate the expression on the right in (1.7.9) with respect to A and then put $A = 0$ (so we can be lazy and not even compute certain terms in the derivative of the second term, since these will have a factor A and so become zero upon putting $A = 0$). The result is

$$\left. \frac{d\beta}{dA} \right|_{A=0} = H \mu e^{\mu\bar{\tau}} \left(1 - \frac{1}{H} \int_0^{\bar{\tau}} E(\alpha) h(\alpha) e^{-\mu\alpha} d\alpha \right)$$

and we conclude that the bifurcation is *supercritical* if

$$(1.7.10) \quad \frac{1}{H} \int_0^{\bar{\tau}} E(\alpha) h(\alpha) e^{-\mu\alpha} d\alpha < 1$$

and *subcritical* if

$$(1.7.11) \quad \frac{1}{H} \int_0^{\bar{\tau}} E(\alpha) h(\alpha) e^{-\mu\alpha} d\alpha > 1$$

Interlude 1.7.1 Biological interpretation of the condition for the direction of bifurcation.

For A negligibly small, the age distribution of victims has density $\sim h(a)e^{-\mu a}$. In terms of *newborns*, a victim of age a means a loss $e^{\mu a}$ and a gain $E(a)$. Therefore the gain exceeds the loss if and only if

$$\int_0^{\bar{\tau}} (E(a) - e^{\mu a}) h(a) e^{-\mu a} da > 0,$$

that is, if and only if the condition (1.7.11) for subcritical bifurcation holds.

But if the branch of non-trivial steady states starts as a subcritical bifurcation, how does it continue? To get some insight, we take the caricature to its extreme by letting h depend on a parameter in such a way that, in the sense of distributions, $h_\varepsilon(a) \rightarrow \delta(a - \hat{\tau})H$ for $\varepsilon \downarrow 0$, where δ is the Dirac “function”. In fact this amounts to assuming that, as $\varepsilon \downarrow 0$,

$$\mathcal{F}(a, A_t) \rightarrow \begin{cases} e^{-\mu a}, & a < \hat{\tau} \\ e^{-\mu a - HA(t-a+\hat{\tau})}, & a > \hat{\tau} \end{cases}$$

and

$$\begin{aligned} A \int_0^{\bar{\tau}} E(\alpha) h(\alpha) e^{\mu\alpha - A \int_0^\alpha h(\sigma) d\sigma} d\alpha &= - \int_0^{\bar{\tau}} E(\alpha) e^{-\mu\alpha} d_\alpha e^{-A \int_0^\alpha h(\sigma) d\sigma} \\ &\rightarrow E(\hat{\tau}) e^{-\mu\hat{\tau}} (1 - e^{-HA}) \end{aligned}$$

so that (1.7.9) can, in the limit $\varepsilon \downarrow 0$, be written as

$$(1.7.12) \quad \beta = \mu e^{\mu\bar{\tau} + HA} (1 - E(\hat{\tau}) e^{-\mu\hat{\tau}} (1 - e^{-HA})).$$

It follows that

$$(1.7.13) \quad \frac{d\beta}{dA}(A) = H\mu e^{\mu\bar{\tau} + HA} (1 - E(\hat{\tau}) e^{-\mu\hat{\tau}})$$

and we see that the local condition $E(\hat{\tau}) e^{-\mu\hat{\tau}} > 1$ is also the global condition for the branch to “go to the left”. A striking consequence is that we have

$$(1.7.14) \quad A = -\frac{1}{H} \ln (1 - e^{\mu\bar{\tau}} (E(\hat{\tau}))^{-1}) > 0$$

for $\beta = 0$: the population can persist if adults have nothing but juveniles of their own kind to eat! (And indeed, there are lakes in Northern Europe which have perch as the only fish [2, 25] . So all energy comes from the juveniles eating zooplankton.)

We conclude that the bifurcation diagram may look like Figure 6,

Figure 6

and that, accordingly, there may be the dichotomy that either the population goes extinct or it grows exponentially. This is a form of the Allee effect and one may as well call it *positive* density dependence.

If the support of h is larger than just a point, it may be that the larger/older individuals bring more than they cost while the smaller/younger individuals cost more than they yield. An increase in A shifts the distribution of the age of victims towards younger ages. As a result, the branch of nontrivial steady states may wiggle, as shown in Figure 7 (see [2]).

Figure 7

The argument just given suggests that a branch, which starts by going to the right, continues to the right. But actually this need not be the case [2]. The key point is once more that victims of cannibalism, which would anyhow not have made it into adulthood, come for free: if the distribution of the age of victims shifts towards younger ages, the energetic drawback may be more than compensated by the increase of victims among those that were anyhow bound to die before reaching age $\bar{\tau}$.

1.8 Stability boundaries in parameter space

In the preceding two sections we have found that, for our particular kind of dynamical systems, finding steady states is not too difficult. But how do we find out whether or not they are stable? Near a transcritical bifurcation the Principle of the Exchange of Stability may help, but, as indicated by the question mark in the diagram at the end of Section 1.6, this doesn't bring us very far.

The standard technique is to linearize and to use the Principle of Linearized Stability, which asserts that if we have exponential stability for the linearized system, we have it for the original nonlinear system as well, while if we find that the linearized system admits exponentially growing solutions, the steady state is unstable for the nonlinear system too (the second part is harder to prove than the first). Often one can, in particular for delay equa-

tions, decide about stability for the linearized system in terms of the position of the roots in the complex plane of a *characteristic equation*. The aim of the present section is to introduce these ideas in the context of a very simple example that can be analyzed in great detail (and therefore is, perhaps, misleadingly simple).

Remark 1.8.1. In our discussion so far we suggested that the (in)stability of a steady state is completely determined by the position of the roots of the corresponding characteristic equation in the complex plane. This is indeed true, but needs proof. We come back to this in Chapter ?.

We return to the cannibalism model with only negative effects taken into account and consider the delay differential equation (1.6.9) with \mathcal{F} given by (1.6.4). To reduce the notational burden, we scale A to make H , the integral of h , equal to 1 and we scale time to make $\bar{\tau} = 1$ (the latter means that when we write μ and β below, these correspond to $\mu\bar{\tau}$ and $\beta\bar{\tau}$ in terms of the original parameters). So we consider

$$(1.8.1) \quad \frac{dA}{dt}(t) = \beta A(t-1) e^{-\mu - \int_0^1 h(\sigma) A(t-1+\sigma) d\sigma} - \mu A(t)$$

and note that the nontrivial steady state is given by

$$(1.8.2) \quad \bar{A} = \ln\left(\frac{\beta}{\mu} e^{-\mu}\right).$$

If we put

$$(1.8.3) \quad A(t) = \bar{A} + z(t)$$

and assume that z is small, we can rewrite (1.8.1) as

$$\begin{aligned} \frac{dz}{dt}(t) = & \beta(\bar{A} + z(t-1)) e^{-\mu - \bar{A}} \left(1 - \int_0^1 h(\sigma) z(t-1+\sigma) d\sigma\right) + \text{h.o.t.} \\ & - \mu \bar{A} - \mu z(t) \end{aligned}$$

and hence, omitting the higher order terms (h.o.t.) and using $\beta e^{-\mu - \bar{A}} = \mu$, as

$$(1.8.4) \quad \frac{dz}{dt}(t) = \mu z(t-1) - \mu \bar{A} \int_0^1 h(\sigma) z(t-1+\sigma) d\sigma - \mu z(t).$$

By substituting a trial solution $z(t) = e^{\lambda t}$ into (1.8.4) we obtain the *characteristic equation*

$$(1.8.5) \quad \lambda = -\mu + \mu e^{-\lambda}(1 - \overline{A}\widehat{h}(-\lambda))$$

where the Laplace transform is now indicated by $\widehat{}$. Note that $\lambda = 0$ is never a root for $\overline{A} > 0$. This reflects that no steady states bifurcate along the branch of nontrivial steady states, neither by saddle-node bifurcations corresponding to turning points of the branch as in the diagram at the end of Section 1.7, nor by transcritical bifurcations corresponding to the crossing of another branch, as for $\beta = \mu e^\mu$ and $A = 0$. So if destabilization occurs, it has to occur by way of a pair of complex conjugated roots crossing the imaginary axis from left to right, and the corresponding bifurcation is a Hopf bifurcation: the birth of a periodic solution (with period-at-birth $\frac{2\pi}{\omega}$ if the roots cross at $\pm i\omega$).

By putting $\lambda = i\omega$ in (1.8.5) and letting ω vary, while considering the equation as conditions on the parameters (note that one complex equation amounts to two real equations), we may trace out the set in parameter space such that (1.8.5) has a root exactly on the imaginary axis. This works best if we single out two parameters (i.e., keep other parameters fixed), for then the set is a curve in a plane and humans are well-suited for the up-take and digestion of information that comes in the form of a two-dimensional picture! To illustrate this methodology, we now focus on egg-cannibalism. That is, we assume that h_ε converges for $\varepsilon \downarrow 0$ to the Dirac delta in $\tilde{\tau} = 0$ (recall the last part of the last section). In that case we have $\widehat{h}(-\lambda) = \widehat{h}(0) = 1$ and (1.8.5) reduces to

$$(1.8.6) \quad \lambda = -\mu + \mu(1 - \overline{A})e^{-\lambda}$$

which has exactly two *dimensionless* (due to the scaling) parameters μ and β/μ (recall that $\overline{A} = \ln(\frac{\beta}{\mu}e^{-\mu})$). But still we are going to use a two-step procedure: we first analyse

$$(1.8.7) \quad \lambda = \alpha_1 + \alpha_2 e^{-\lambda}$$

corresponding to

$$(1.8.8) \quad \frac{dz}{dt}(t) = \alpha_1 z(t) + \alpha_2 z(t-1)$$

and next let the results apply to (1.8.6) and the version

$$(1.8.9) \quad \frac{dz}{dt}(t) = -\mu z(t) + \mu(1 - \overline{A})z(t-1)$$

of (1.8.4) by means of

$$(1.8.10) \quad \begin{aligned} \mu &= -\alpha_1 & \alpha_1 &= -\mu \\ \frac{\beta}{\mu} &= e^{1+\frac{\alpha_2}{\alpha_1}-\alpha_1} & \alpha_2 &= \mu(1 - \ln(\frac{\beta}{\mu}e^{-\mu})) \end{aligned}$$

(and finally we have to undo the scaling by replacing μ and β by $\mu\bar{\tau}$ and $\beta\bar{\tau}$ respectively; note that this has no effect on the quotient β/μ).

If we put $\lambda = i\omega$ into (1.8.7) and split into real and imaginary part, we obtain two *linear* equations in the unknowns α_1 and α_2 . The linearity allows us to find the explicit solution

$$(1.8.11) \quad \alpha_1 = \frac{\omega \cos \omega}{\sin \omega} \quad \alpha_2 = -\frac{\omega}{\sin \omega}$$

which has singularities for $\omega = k\pi$, $k \in \mathbb{Z}$. An interval from $k\pi$ to $(k+1)\pi$, with $k = 0, 1, 2, \dots$, yields a curve that connects ∞ in the (α_1, α_2) -plane to itself,

Figure 8

In [6, Section XI.2] one finds a description of the simple computations that establish at which side of a curve the roots are in the right half plane. A summary is: if you follow a curve in the direction of increasing ω , then the critical roots are in the right half-plane in the parameter region to the left of the curve when $\det M < 0$ and to the right when $\det M > 0$, where

$$M = \begin{pmatrix} \frac{\partial G_1}{\partial \alpha_1} & \frac{\partial G_1}{\partial \alpha_2} \\ \frac{\partial G_2}{\partial \alpha_1} & \frac{\partial G_2}{\partial \alpha_2} \end{pmatrix}$$

with the entries of M evaluated for (α_1, α_2) on the curve and with the corresponding value of ω and $\mu = 0$. Here

$$\begin{aligned} G_1(\alpha_1, \alpha_2, \mu, \omega) &= \operatorname{Re} F(\alpha_1, \alpha_2, \mu + i\omega) \\ G_2(\alpha_1, \alpha_2, \mu, \omega) &= \operatorname{Im} F(\alpha_1, \alpha_2, \mu + i\omega) \end{aligned}$$

and the characteristic equation corresponds to $F = 0$. In this manner we obtain the picture above, where the numbers indicate the total number of roots in the right half plane for a particular region in parameter space.

An important insight can be deduced from this picture. If we put $\alpha_2 = 0$, we see that negative feedback is stabilizing: the region of stability on the α_1 -axis is precisely $\alpha_1 < 0$. But if we put $\alpha_1 = 0$, we see that *delayed negative feedback may actually destabilize*: if we make α_2 sufficiently negative, the steady state becomes unstable! The reason is overshoot, see Figure 9:

Figure 9

after z has passed the value 0, the decrease or increase continues for one unit of time and so oscillations occur with peaks that may (if $|\alpha_2|$ is small enough) or may not die out. Using (1.8.10) and undoing the scaling we obtain the diagram depicted in Figure 10.

Figure 10

Note that for $\frac{\beta}{\mu}e^{-\mu} > 1$ we have $\alpha_1 + \alpha_2 < 0$, so the curves with odd k are irrelevant for (1.8.6). Moreover, $\mu > 0$ gives $\alpha_1 < 0$, so only part of each curve with even k is relevant (also note that $\alpha_1 = 0$ is a singularity in the expression for β/μ in (1.8.10)). G.A. Enciso & E.D. Sontag [9] observed that such restrictions on parameters are sometimes overlooked in published work, leading to wrong conclusions.

We emphasize that the two-parameter analysis yields, in the end, essential information about the way the stability depends on a single parameter. For instance, varying $\bar{\tau}$ amounts to taking a horizontal section and one sees at once that, depending on the level of β/μ , there may be a number of pairs (possibly zero) that enter the right half plane but they all return to the left half plane if $\bar{\tau}$ is further increased (there are many papers in which such conclusions are reached in a far more complicated manner!). Varying β , on the other hand, amounts to taking a vertical section and one sees that now stability is bound to get lost and will never be regained.

In conclusion of this section we note that along the *stability boundary* (i.e., the curve separating the region of stability from the region of instability) ω varies from $\pi/2$ to π and hence the period from 2 to 4. If we undo the scaling we find $2\bar{\tau} < \text{period} < 4\bar{\tau}$. Gurney, Nisbet and co-workers [23] found that such kind of inequalities can be seen as traces of how exactly density dependence acts. We shall return to this point in Section 2.7.

If only juveniles of exactly age $\tilde{\tau}$ are cannibalized (with $0 \leq \tilde{\tau} \leq 1$), (1.8.5) reads

$$(1.8.12) \quad \lambda = -\mu + \mu e^{-\lambda} - \mu \bar{A} e^{-\lambda(1-\tilde{\tau})}.$$

For $\tilde{\tau} = 1$ (“almost adult” cannibalism) this is again of the form (1.8.7),

but with $\alpha_2 = \mu > 0$ and $\alpha_1 + \alpha_2 = -\mu\bar{A} < 0$, showing that stability is guaranteed. This illustrates our earlier observation that negative feedback needs to come with a delay in order to be destabilizing. If we increase $\tilde{\tau}$, the stability boundary in the $(\mu\bar{\tau}, \beta/\mu)$ plane shifts upwards and eventually disappears at infinity when $\tilde{\tau} = 1$.

Chapter 2

Size structure

2.1 The case of *Daphnia*

Waterfleas mature when they reach a certain size (to be indicated by ξ_A in the following). So the length of their juvenile period equals the time they need to grow from size-at-birth (to be indicated by ξ_b in the following) to ξ_A . Accordingly the length of the juvenile period depends on food supply, which in turn is influenced by consumption. This raises the following question: what is the impact of density dependent maturation delay on the dynamics at the p -level?

Long ago the question of how to extrapolate the measured effects of toxic substances on *Daphnia* population dynamics under lab conditions to field conditions, motivated the development of energy budget models [21]; see [24] for the state-of-the-art. Such models specify rules for the i -level partitioning of the energy derived from ingested food to growth, reserves, maintenance and reproduction. Two aspects require special attention and remain somewhat controversial: 1) what does exactly happen at the juvenile-adult transition? 2) what happens under starvation conditions, i.e., when the food supply is insufficient to cover maintenance, in particular the energy costs of basic metabolism? Here we will not go into these modelling issues. Instead we focus on the influence of variable maturation delay on consumer resource interaction, in the spirit of de Roos et al. [27]. In particular we will not consider a reserve compartment but declare that the size ξ of an individual serves as the i -state. If we think of ‘size’ as length, then the surface is proportional to ξ^2 and the volume to ξ^3 . Since waterflies are filter feeders, the uptake of food (algae) is proportional to ξ^2 . Maintenance costs, on the other hand, are proportional to ξ^3 and as a result individuals will grow slower and slower towards a maximal size that depends on the prevailing algae

concentration (assumed here to be constant, just to explain this particular phenomenon of a maximal individual size).

Mechanistic considerations of this kind should provide us with the following ingredients for a model of the behaviour of individual *Daphnia*, given its size ξ and given that the algae concentration equals S :

- $g(\xi, S)$ the rate of growth
- $\beta(\xi, S)$ the probability per unit of time of giving birth
- $\mu(\xi, S)$ the probability per unit of time of dying
- $\gamma(\xi, S)$ the rate of food consumption.

Throughout this chapter we assume that the size-at-birth is fixed at ξ_b . To complete a consumer-resource model we need as a fifth ingredient

- $f(S)$ the rate of change of S in the absence of consumers.

It should be clear that, even though we shall keep speaking about *Daphnia* and algae, the model applies to any size-structured population that consumes an unstructured resource.

2.2 Programmed instruction: how to build a “*Daphnia*” population model?

Step 1 specify g, μ as functions of ξ and S

Step 2 for any $a \geq 0$ and any non-negative continuous function ψ defined on at least $[-a, 0]$ construct $\Xi(a, \psi)$ and $\mathcal{F}(a, \psi)$ as follows: compute $\xi(\tau) = \xi(\tau; a, \psi)$ and $\mathfrak{f}(\tau) = \mathfrak{f}(\tau; a, \psi)$ by solving the system of ode's

$$\begin{aligned}
 \frac{d\xi}{d\tau}(\tau) &= g(\xi(\tau), \psi(-a + \tau)) \\
 \xi(0) &= \xi_b \\
 \frac{d\mathfrak{f}}{d\tau}(\tau) &= -\mu(\xi(\tau), \psi(-a + \tau))\mathfrak{f}(\tau) \\
 \mathfrak{f}(0) &= 1
 \end{aligned}
 \tag{2.2.1}$$

and then put

$$\Xi(a, \psi) = \xi(a), \quad \mathcal{F}(a, \psi) = \mathfrak{f}(a)
 \tag{2.2.2}$$

2.2. PROGRAMMED INSTRUCTION: HOW TO BUILD A “DAPHNIA” POPULATION MODEL?

(Note that the equation for ξ is decoupled from the one for f .) The interpretation is that $\Xi(a, \psi)$ is the size of an individual of age a , given the food history as described by ψ and given that it survived till age a . The probability that an individual born a time units ago survived till now, given the food history ψ , is $\mathcal{F}(a, \psi)$.

Step 3 specify β, γ as functions of ξ and S as well as f as function of S .

Step 4 Let $b(t)$ denote the population level birth rate of Daphnia at time t , then the p -level equations are

$$(2.2.3) \quad \begin{aligned} b(t) &= \int_0^{\infty} \beta(\Xi(a, S_t), S(t)) \mathcal{F}(a, S_t) b(t-a) da \\ \frac{dS}{dt}(t) &= f(S(t)) - \int_0^{\infty} \gamma(\Xi(a, S_t), S(t)) \mathcal{F}(a, S_t) b(t-a) da. \end{aligned}$$

(These follow straight from the interpretation; note that we do the bookkeeping in terms of age and that we need the history of the environmental interaction variable S in order to know how age determines size, also note the linearity in b , which reflects that all dependence is mediated by S .)

Initial conditions are a subtle issue. One option is to prescribe

$$(2.2.4) \quad \begin{aligned} b(\theta) &= \varphi(\theta), \quad \theta \leq 0 \\ S(\theta) &= \psi(\theta), \end{aligned}$$

and to consider (2.2.3) as a system of delay equations, i.e., as rules to extend the functions b and S into the future, given their past. It is natural to think of φ as an L_1 -function (since one needs to integrate the birth rate to obtain a number) and of ψ as a continuous function. But if the model does not guarantee that $\mathcal{F}(a, \psi)$ becomes zero for $a \geq a_{\max}$ for all feasible food histories ψ , we are dealing with infinite delay and the behaviour at $-\infty$ needs special attention. For instance, in steady state b is constant, so we definitely want that constant functions belong to the space of functions from which we take φ . We shall achieve this by incorporating an exponential weight function in the L_1 -norm (and likewise in the supremum norm, when we consider ψ).

The second option is to prescribe

$$(2.2.5) \quad \begin{aligned} n(0, \xi) &\text{ the size-density at time zero} \\ S(0) & \end{aligned}$$

and to modify (2.2.3) on the basis of a modified version of (2.2.1) for individuals that have a given size at a given time. (We here restrict our attention to an initial size distribution described by a density, but see [4, 7, 29] for formulations in terms of measures.) We present details below.

The advantage of option 1 is technical: it leads to many results since \odot *-calculus can be used, see [6, 8, 5].

The advantage of option 2 is conceptual: it corresponds exactly to the description of a population as a distribution over the i -state space specifying the size and composition of that population.

Fortunately one can relate the two options to each other and have the best of both. First note that an initial condition of the form (2.2.4) yields a size-density at time zero and, of course, a value of S at time zero, so an initial condition of the form (2.2.5). However, conditions of the form (2.2.4) correspond to a restricted class of initial conditions of the form (2.2.5), as it is in general impossible to reconstruct the history of both b and S from $n(0, \xi)$ and $S(0)$. If we solve (2.2.3) with (2.2.4) then the up-dated histories (b_t, S_t) also belong to this class, which in more fancy terminology means that the class is *forward invariant*. If there happens to be a maximal age a_{\max} and we solve the variant of (2.2.3) corresponding to (2.2.5), we find $(n(t, \cdot), S(t))$ that belongs to the class for $t \geq a_{\max}$. In general, the distance of $(n(t, \cdot), S(t))$ to the class will go to zero exponentially for $t \rightarrow \infty$, with an exponent that relates to a lower bound for the per capita death rate μ for large ages, uniformly in S . In more fancy terminology: the class is globally attracting.

So when studying stability and bifurcation issues, we shall adopt (2.2.4), but keep in mind that the conclusions also pertain to (2.2.5).

For completeness we show how to modify (2.2.3) when using (2.2.5). Define $H(t) = H(t; \xi)$ and $G(t) = G(t; \xi)$ by solving the system of ode

$$\begin{aligned}
 \frac{dH}{dt}(t) &= g(H(t), S(t)) \\
 H(0) &= \xi \\
 \frac{dG}{dt}(t) &= -\mu(H(t), S(t))G(t) \\
 G(0) &= 1
 \end{aligned}
 \tag{2.2.6}$$

then $H(t; \xi)$ is the size of an individual at time t , given that it had size ξ at time zero and it is still alive, while $G(t; \xi)$ is the probability that that individual is indeed still alive. We now split the integrals over $[0, \infty)$ into an integral over $[0, t)$ and an integral over the sizes of the individuals that were

already present at time zero:

$$\begin{aligned}
 (2.2.7) \quad b(t) &= \int_0^t \beta(\Xi(a, S_t), S(t)) \mathcal{F}(a, S_t) b(t-a) da \\
 &\quad + \int_{\xi_b}^{\infty} \beta(H(t; \xi), S(t)) G(t; \xi) n(0, \xi) d\xi \\
 \frac{dS}{dt}(t) &= f(S(t)) - \int_0^t \gamma(\Xi(a, S_t), S(t)) \mathcal{F}(a, S_t) b(t-a) da \\
 &\quad - \int_{\xi_b}^{\infty} \gamma(H(t; \xi), S(t)) G(t; \xi) n(0, \xi) d\xi
 \end{aligned}$$

(see also [29, (3.7), (3.8)]; in that paper the author also shows that solutions of (2.2.7) can be used to obtain solutions, in the distributional sense, of the partial differential equation with boundary condition coupled with an ordinary differential equation.

$$\begin{aligned}
 \frac{\partial}{\partial t} n(t, \xi) + \frac{\partial}{\partial \xi} (g(\xi, S(t), n(t, \xi))) &= -\mu(\xi, S(t)) n(t, \xi), \\
 g(\xi_b) n(t, \xi_b) &= \int \beta(\xi, S(t)) n(t, \xi) d\xi, \\
 \frac{dS}{dt}(t) &= f(S(t)) - \int \gamma(\xi, S(t)) n(t, \xi) d\xi.
 \end{aligned}$$

2.3 Steady states

From the first equation of (2.2.3) we infer that steady state requires

$$(2.3.1) \quad 1 = R_0(S) := \int_0^{\infty} \beta(\Xi(a, S), S) \mathcal{F}(a, S) da$$

where S twice denotes a positive number and twice the constant function having that number as its only value. As in Sections 1.6 and 1.7 we find that the steady environmental condition should be such that $R_0 = 1$ or, equivalently, $r = 0$. Under very reasonable conditions one has that R_0 is an increasing function of S , assuming values less than one for small S and

bigger than one for large S , so that (2.3.1) has a unique root (which we shall sometimes denote by \bar{S} and sometimes simply by S ; when the substrate S is toxic for large concentrations, the monotonicity gets lost and there may exist multiple roots of (2.3.1)).

Once S is known, the second equation of (2.2.3) yields an explicit expression for the steady population birth rate

$$(2.3.2) \quad b = \frac{f(S)}{\int_0^{\infty} \gamma(\Xi(a, S), S) \mathcal{F}(a, S) da}$$

Of course we should have $f(S) > 0$ for this to be biologically meaningful. Very often (but not always) f is positive for S between 0 and S_{cc} (where the subscript cc stands for carrying capacity) and negative for $S > S_{cc}$. Then the condition $f(S) > 0$ can be translated into the interpretable condition $R_0(S_{cc}) > 1$: the consumer population should be able to grow exponentially if the food concentration is held fixed at its carrying capacity level in the absence of consumers.

Under constant conditions, there is a fixed age-size relation and, in order to limit the notational burden as much as possible, we denote it by $\xi(a)$. So

$$(2.3.3) \quad \xi(a) = \Xi(a, S)$$

with S the root of (2.3.1). Likewise we put

$$(2.3.4) \quad \mathbf{f}(a) = \mathcal{F}(a, S)$$

(note that this is not inconsistent with (2.2.1)). The stable age distribution has density \mathbf{f} divided by the integral of \mathbf{f} . The corresponding stable size distribution has density $\xi \mapsto \mathbf{f}(a(\xi))/g(\xi, S)$ divided by the integral of \mathbf{f} . This can most easily be seen by transformation of the integration variable:

$$\int_{a_1}^{a_2} \mathbf{f}(a) da = \int_{\xi_1}^{\xi_2} \mathbf{f}(a(\xi)) \frac{da}{d\xi}(\xi) d\xi = \int_{\xi_1}^{\xi_2} \frac{\mathbf{f}(a(\xi))}{g(\xi, S)} d\xi$$

where $\xi \mapsto a(\xi)$ is the inverse function of $a \mapsto \xi(a)$.

2.4 Stage structure à la Gurney & Nisbet

In order to reduce the number of parameters, one may assume that

- juveniles grow at a rate that depends only on S , not on their size; likewise their per capita death and consumption rate depends only on S
- the size of adults is irrelevant: their per capita reproduction, death, and consumption rate depends only on S (one may, for instance, assume that adults don't grow at all).

In the following we provide μ and γ with an index 1 when juveniles are concerned and with an index 2 when they pertain to adults. The symbol g denotes the growth rate of juveniles and the symbol β the reproduction rate of adults, see Figure 11.

Figure 11

As our bookkeeping will be based on age, it is obviously important to be able to tell from the age whether an individual is, or is not, an adult. The answer depends on the food history. The word "history" already indicates that we can only look back (if we don't know the food supply, we cannot predict the maturation delay).

Let $\tau = \tau(\psi)$ be the age of the individuals that mature at the present time, given food history ψ , then

$$(2.4.1) \quad \int_{-\tau}^0 g(\psi(\theta))d\theta = \xi_A - \xi_b.$$

(Note that the existence and uniqueness of a solution for τ , given ψ , is guaranteed if g is bounded away from zero.) If ψ is of the form S_t we may consider $\tau(S_t)$ as a function of time. For the purpose of numerical computation it may now help to formulate an up-dating rule for $\tau(S_t)$ in the form of a differential equation. With $\psi = S_t$ we can rewrite (2.4.1) as

$$(2.4.2) \quad \int_{t-\tau(S_t)}^t g(S(\sigma))d\sigma = \xi_A - \xi_b$$

which upon differentiation with respect to t and reorganization yields the delay differential equation

$$(2.4.3) \quad \frac{d}{dt}\tau(S_t) = 1 - \frac{g(S(t))}{g(S(t - \tau(S_t)))}.$$

Note that $\frac{d\tau}{dt} < 1$ so that, reassuringly, individuals can never lose the adult status!

In order to compute survival probabilities, we also need to know how long ago an adult acquired that status. Let, for $a \geq \tau(\psi)$, $\tilde{\tau} = \tilde{\tau}(\psi, a)$ be the time it took an adult of age a to mature, given the food history ψ . Then

$$(2.4.4) \quad \int_0^{\tilde{\tau}} g(\psi(-a + \theta))d\theta = \xi_a - \xi_b.$$

There are two things to be noted:

$$(2.4.5) \quad \tilde{\tau}(\psi, \tau(\psi)) = \tau(\psi)$$

$$(2.4.6) \quad \tilde{\tau}(S_t, a + t) \text{ does not depend on } t$$

(here a is the age the individual has at $t = 0$).

Under these assumptions and with this notation in place we can write (2.2.3) in the form

$$(2.4.7) \quad \begin{aligned} b(t) &= \beta(S(t)) \int_{\tau(S_t)}^{\infty} b(t - a) e^{-\mu_1 \tilde{\tau}(S_t, a) - \mu_2 (a - \tilde{\tau}(S_t, a))} da \\ \frac{dS}{dt}(t) &= f(S(t)) - \gamma_1(S(t)) \int_0^{\tau(S_t)} b(t - a) e^{-\mu_1 a} da \\ &\quad - \gamma_2(S(t)) \int_{\tau(S_t)}^{\infty} b(t - a) e^{-\mu_1 \tilde{\tau}(S_t, a) - \mu_2 (a - \tilde{\tau}(S_t, a))} da. \end{aligned}$$

If we want to use available and well tested software (eg., SOLVER [reference]) for the numerical solution of delay differential equations or for numerical bifurcation analysis of such equations (e.g., DDE-biftool Engelborghs, <http://www.cs.kuleuven.ac.be/cwis/research/twr/research/software/delay/ddebiftool.shtml>) (list of software at this website) we may reformulate (2.4.7) by first introducing the sizes A and J of the subpopulations of adults, respectively, juveniles:

$$(2.4.8) \quad \begin{aligned} A(t) &:= \int_{\tau(S_t)}^{\infty} b(t-a)e^{-\mu_1 \tilde{\tau}(S_t, a) - \mu_2 (a - \tilde{\tau}(S_t, a))} da \\ J(t) &:= \int_0^{\tau(S_t)} b(t-a)e^{-\mu_1 a} da. \end{aligned}$$

If we transform the integration variable a into $\sigma = t - a$ and next differentiate we obtain (using that $\tilde{\tau}(S_t, t - \sigma)$ does not depend on t)

$$(2.4.9) \quad \begin{aligned} \frac{dA}{dt}(t) &= b(t - \tau(S_t))e^{-\mu_1 \tau(S_t)} \frac{g(S(t))}{g(S(t - \tau(S_t)))} - \mu_2 A(t) \\ \frac{dJ}{dt}(t) &= b(t) - b(t - \tau(S_t))e^{-\mu_1 \tau(S_t)} \frac{g(S(t))}{g(S(t - \tau(S_t)))} - \mu_1 J(t). \end{aligned}$$

Finally, we may substitute in these differential equations the identity

$$(2.4.10) \quad b(t) = \beta(S(t))A(t)$$

and supplement them by

$$(2.4.11) \quad \frac{dS}{dt} = f(S) - \gamma_1(S)J - \gamma_2(S)A$$

and (2.4.3) to obtain a closed system of four delay differential equations. But a word of warning is needed: in order to avoid artefacts one has to make sure that the initial condition for τ , say τ_0 , and the initial condition for S , say ψ , satisfy the compatibility condition

$$(2.4.12) \quad \int_{-\tau_0}^0 g(\psi(\sigma))d\sigma = \xi_A - \xi_b$$

(a related phenomenon is that the linearization has a spurious eigenvalue zero, which is introduced by the differentiation of (2.4.2), and which gives problems when solving the system numerically.)

2.5 Quasi-steady-state-approximation (QSSA)

With reference to the second equation of (2.2.3), we note that sometimes both f and γ have a multiplicative parameter that is large relative to β , g

and μ , implying that food dynamics is fast relative to consumer maturation and demography. In an attempt to make the analysis simpler, one may then replace the differential equation for S by the constraint

$$(2.5.1) \quad f(S(t)) = \int_0^{\infty} \gamma(\Xi(a, S_t), S(t)) \mathcal{F}(a, S_t) b(t-a) da$$

provided this constraint can serve as an up-date rule, which isn't guaranteed since both sides depend in a nonlinear way on $S(t)$. Things become easier if

$$(2.5.2) \quad \gamma(\xi, S) = h(S) \tilde{\gamma}(\xi)$$

and, in addition, the equation

$$(2.5.3) \quad \frac{f(S)}{h(S)} = c$$

has a unique solution $S = \tilde{S}(c)$. Indeed, then we can replace (2.5.1) by

$$(2.5.4) \quad S(t) = \tilde{S} \left(\int_0^{\infty} \tilde{\gamma}(\Xi(a, S_t)) \mathcal{F}(a, S_t) b(t-a) da \right).$$

For example, if $f(S) = D - \varepsilon S$ and $h(S) = S$ we find

$$(2.5.5) \quad S(t) = \frac{S_0}{\varepsilon + \int_0^{\infty} \tilde{\gamma}(\Xi(a, S_t)) \mathcal{F}(a, S_t) b(t-a) da}$$

while if $f(S) = rS(1 - \frac{S}{K})$ and $h(S) = S$ we obtain

$$(2.5.6) \quad S(t) = K \left(1 - \frac{1}{r} \int_0^{\infty} \tilde{\gamma}(\Xi(a, S_t)) \mathcal{F}(a, S_t) b(t-a) da \right).$$

Note that in the case of stage structure we have

$$(2.5.7) \quad \int_0^{\infty} \tilde{\gamma}(\Xi(a, S_t)) \mathcal{F}(a, S_t) b(t-a) da = \tilde{\gamma}_1 J + \tilde{\gamma}_2 A$$

2.6 The linearized system

If we substitute into (2.2.3)

$$(2.6.1) \quad \begin{aligned} b(t) &= \bar{b} + y(t), \\ S(t) &= \bar{S} + z(t) \end{aligned}$$

with \bar{S} the solution of (2.3.1) and \bar{b} given by (2.3.2), perform Taylor expansion around $(y, z) = (0, 0)$ and neglect higher order terms, we obtain a system of the form

$$(2.6.2) \quad \begin{aligned} y(t) &= c_1 z(t) + \int_0^\infty (k_{11}(a)y(t-a) + k_{12}(a)z(t-a))da \\ \frac{dz}{dt}(t) &= c_2 z(t) + \int_0^\infty (k_{21}(a)y(t-a) + k_{22}(a)z(t-a))da. \end{aligned}$$

The coefficients c_i reflect the dependence of the right hand side of (2.2.3) on the value of S in the point t . They are given by

$$(2.6.3) \quad \begin{aligned} c_1 &= b \int_0^\infty \frac{\partial \beta}{\partial S}(\xi(a), S) \mathfrak{f}(a) da, \\ c_2 &= f'(S) - b \int_0^\infty \frac{\partial \gamma}{\partial S}(\xi(a), S) \mathfrak{f}(a) da. \end{aligned}$$

The components k_{11} and k_{21} of the kernel $k(a)$ reflect the dependence on the history of b . Since the right hand side of (2.2.3) is linear in b_t , we don't have to do any computations to conclude that

$$(2.6.4) \quad \begin{aligned} k_{11}(a) &= \beta(\xi(a), S) \mathfrak{f}(a) \\ k_{22}(a) &= -\gamma(\xi(a), S) \mathfrak{f}(a). \end{aligned}$$

The difficult part is to compute the components k_{12} and k_{22} , since these reflect the rather implicit dependence on the history of S via the solutions of (2.2.1). We shall first deal with the case where g, μ, β and γ are smooth functions of ξ and S and next with the case that these functions do have a jump discontinuity at $\xi = \xi_A$, but are otherwise smooth.

Let, as in Section 2.2, the functions $\xi(\tau; a, \psi)$ and $\mathfrak{f}(\tau; a, \psi)$ be defined by (2.2.1). Let

$$(2.6.5) \quad \eta(\tau) := D_3 \xi(\tau; a, S) \psi$$

be the derivative with respect to the third variable, evaluated at the constant function S and acting on some function ψ . Then we can compute η by solving the ode

$$(2.6.6) \quad \begin{aligned} \frac{d\eta}{d\tau}(\tau) &= \frac{\partial g}{\partial \xi}(\xi(\tau), S)\eta(\tau) + \frac{\partial g}{\partial S}(\xi(\tau), S)\psi(-a + \tau) \\ \eta(0) &= 0. \end{aligned}$$

We find that

$$(2.6.7) \quad \eta(\tau) = \int_0^\tau K(\tau, \alpha)\psi(-a + \alpha)d\alpha$$

with

$$(2.6.8) \quad K(\tau, \alpha) := e^{\alpha \int_0^\tau \frac{\partial g}{\partial \xi}(\xi(\theta), S)d\theta} \frac{\partial g}{\partial S}(\xi(\alpha), S).$$

Now recall (2.2.2) (but be aware of the fact that there $\xi(a) = \xi(a; a, \psi)$ while in (2.6.6) and (2.6.7) above ξ denotes this function for the special case that ψ is constant and equal to S , the solution of (2.3.1)) and take $\tau = a$ to obtain

$$(2.6.9) \quad D_2\Xi(a, S)\psi = \eta(a) = \int_0^a K(a, \alpha)\psi(-a + \alpha)d\alpha.$$

Similarly we find that

$$(2.6.10) \quad \zeta(\tau) := D_3\mathfrak{f}(\tau; a, S)\psi$$

satisfies

$$(2.6.11) \quad \begin{aligned} \frac{d\zeta}{d\tau}(\tau) &= -\mu(\xi(\tau), S)\zeta(\tau) - \rho(\tau), \\ \zeta(0) &= 0 \end{aligned}$$

with

$$(2.6.12) \quad \rho(\tau) := \frac{\partial \mu}{\partial \xi}(\xi(\tau), S)\eta(\tau)\mathfrak{f}(\tau) + \frac{\partial \mu}{\partial S}(\xi(\tau), S)\psi(-a + \tau)\mathfrak{f}(\tau).$$

Using the expression (2.6.7) for η and a bit of formula manipulation we deduce that

$$(2.6.13) \quad \zeta(\tau) = \int_0^\tau L(\tau, \theta)\psi(-a + \theta)d\theta$$

with

$$(2.6.14) \quad L(\tau, \theta) := -f(\tau) \left\{ \int_{\theta}^{\tau} \frac{\partial \mu}{\partial \xi}(\xi(\alpha), S) K(\alpha, \theta) d\alpha + \frac{\partial \mu}{\partial S}(\xi(\theta), S) \right\}.$$

In view of (2.2.2) we conclude that

$$(2.6.15) \quad D_2 \mathcal{F}(a, S) \psi = \zeta(a) = \int_0^a L(a, \theta) \psi(-a + \theta) d\theta.$$

The final results

$$(2.6.16) \quad k_{12}(a) = b \int_0^{\infty} \left\{ \beta(\xi(a+\theta), S) L(a+\theta, \theta) + \frac{\partial \beta}{\partial \xi}(\xi(a+\theta), S) K(a+\theta, \theta) f(a+\theta) \right\} d\theta$$

and

$$(2.6.17) \quad k_{22}(a) = -b \int_0^{\infty} \left\{ \gamma(\xi(a+\theta), S) L(a+\theta, \theta) + \frac{\partial \gamma}{\partial \xi}(\xi(a+\theta), S) K(a+\theta, \theta) f(a+\theta) \right\} d\theta$$

are obtained from (2.2.3) by differentiation while using the chain rule, (2.6.9), (2.6.15) and a change in the order of integration.

We next investigate how these expressions should be adapted if the ingredients are allowed to have, as a function of ξ , a jump discontinuity at ξ_A . If individuals are allowed to linger at this juvenile-adult transition, where their behaviour is ill-defined, one runs into technical difficulties that reflect modelling ambiguities, as explained in detail in [29]. To avoid such difficulties, we want that the size of an individual passes the critical size ξ_A with positive speed. If we assume that

$$(2.6.18) \quad g(\xi_A-, S) > 0 \quad \text{and} \quad g(\xi_A+, S) > 0$$

this is guaranteed in the steady state situation and hence, by continuity, for nearby values of the food concentration. To discuss linearization at the steady state, this suffices.

The analogue of (2.4.1) is the equation

$$(2.6.19) \quad \Xi(a, \psi) = \xi_A$$

and we shall denote the solution by $a = \tau(\psi)$, to conform to the notation that is already in use. We define $\bar{\tau} = \tau(S)$. If we assume that juveniles don't

reproduce, i.e., $\beta(\xi, S) = 0$ for $\xi < \xi_A$, then the first equation of (2.2.3) can be written in the form

$$(2.6.20) \quad b(t) = \int_{\tau(S_t)}^{\infty} b(t-a)\beta(\Xi(a, S_t), S(t))\mathcal{F}(a, S_t)da.$$

The lower integration boundary yields in the linearized equation an extra term (recall (2.6.1))

$$(2.6.21) \quad -b\beta(\xi_{A+}, S)f(\bar{\tau})D\tau(S)z_t.$$

Similarly we find for the second equation of (2.2.3) an extra term

$$(2.6.22) \quad b(\gamma(\xi_{A+}, S) - \gamma(\xi_{A-}, S))f(\bar{\tau})D\tau(S)z_t.$$

In order to compute $D\tau(S)\psi$ we differentiate the identity

$$\Xi(\tau(\psi), \psi) = \xi_A.$$

This yields

$$D_1\Xi(\bar{\tau}, S)D\tau(S)\psi + D_2\Xi(\bar{\tau}, S)\psi = 0$$

which amounts to (recall (2.6.9))

$$g(\xi_{A-}, S)D\tau(S)\psi + \eta(\bar{\tau}) = 0$$

and hence to

$$(2.6.23) \quad D\tau(S)\psi = -\frac{\eta(\bar{\tau})}{g(\xi_{A-}, S)}.$$

The terms (2.6.21) and (2.6.22) capture the effect of, respectively, the jump in β and the jump in γ . We still need to determine the effect of the jump in g and the effect of the jump in μ . We first deal with the jump in g .

We choose to let η be defined by (2.6.7), with $\frac{\partial g}{\partial \xi}$ and $\frac{\partial g}{\partial S}$ in (2.6.8) taken as piece-wise smooth functions. Then, as we will show below, (2.6.5) should be replaced by

$$(2.6.24) \quad D_3\xi(\tau; a, S)\psi = \eta(\tau) + \left(\frac{g(\xi_{a+}, S)}{g(\xi_{A-}, S)} - 1\right)\eta(\bar{\tau})H(\tau - \bar{\tau})$$

where H denotes the Heaviside function, i.e., $H(\sigma) = 0$ for $\sigma < 0$ and $H(\sigma) = 1$ for $\sigma \geq 0$. To justify (2.6.24), we first observe that (2.6.5) remains

valid for $\tau < \bar{\tau}$. For $\tau > \bar{\tau}$ let, for a given ψ, ε be so small that $\tau > \tilde{\tau}(a, S + \varepsilon\psi)$ as well, where, in analogy with (2.4.4), we denote the solution (whenever it exists, so for $a > \tau(\psi)$) of

$$(2.6.25) \quad \xi(\sigma; a, \psi) = \xi_A$$

by $\sigma = \tilde{\tau}(a, \psi)$. Then

$$\begin{aligned} & \xi(\tau; a, S + \varepsilon\psi) - \xi(\tau; a, S) \\ &= \int_{\tilde{\tau}(a, S + \varepsilon\psi)}^{\tau} g(\xi(\sigma; a, S + \varepsilon\psi), S + \varepsilon\psi(-a + \sigma)) d\sigma - \int_{\bar{\tau}}^{\tau} g(\xi(\sigma; a, S), S) d\sigma \\ &= \int_{\tilde{\tau}(a, S + \varepsilon\psi)}^{\bar{\tau}} g(\xi(\sigma; a, S), S) d\sigma \\ &+ \int_{\tilde{\tau}(a, S + \varepsilon\psi)}^{\tau} \{g(\xi(\sigma; a, S + \varepsilon\psi), S + \varepsilon\psi(-a + \sigma)) - g(\xi(\sigma; a, S), S)\} d\sigma \\ &= -\varepsilon g(\xi_{A+}, S) D_2 \tilde{\tau}(a, S) \psi + o(\varepsilon) + \varepsilon \{\eta(\tau) - \eta(\bar{\tau})\} + o(\varepsilon). \end{aligned}$$

Dividing by ε and taking the limit $\varepsilon \downarrow 0$ we obtain

$$D_3 \xi(\tau; a, S) \psi = \eta(\tau) - \eta(\bar{\tau}) - g(\xi_{A+}, S) D_2 \tilde{\tau}(a, S) \psi.$$

By differentiation of the identity

$$\xi(\tilde{\tau}(a, \psi); a, \psi) = \xi_A$$

with respect to ψ and evaluation of the result in S we find

$$D_1 \xi(\bar{\tau}; a, S) D_2 \tilde{\tau}(a, S) \psi + D_3 \xi(\bar{\tau}; a, S) \psi = 0$$

and therefore

$$(2.6.26) \quad D_2 \tilde{\tau}(a, S) \psi = -\frac{\eta(\bar{\tau})}{g(\xi_{A-}, S)}$$

Inserting this result into the formula for $D_3 \xi(\tau; a, S) \psi$ above we arrive at (2.6.24) for $\tau > \bar{\tau}$.

It remains to determine the effect of the jump in μ . Again nothing changes for $\tau < \bar{\tau}$, so we focus on $\tau > \bar{\tau}$. For (a, ψ) with $a < \tau(\psi)$ we can write

$$\mathcal{F}(a, \psi) = e^{-\int_0^{\tilde{\tau}(a, \psi)} \mu(\xi(\sigma; a, \psi), \psi(-a + \sigma)) d\sigma} - \int_{\tilde{\tau}(a, \psi)}^a \mu(\xi(\sigma; a, \psi), \psi(-a + \sigma)) d\sigma$$

and conclude that, relative to the smooth situation, there is an extra term

$$(2.6.27) \quad (\mu(\xi_{A+}, S) - \mu(\xi_{A-}, S))f(a)D_2\tilde{\tau}(a, S)z_t.$$

Gathering the bits and pieces we arrive at

$$(2.6.28) \quad \begin{aligned} k_{12}(a) = & \bar{b} \int_{\max\{0, \bar{\tau}-a\}}^{\infty} \left\{ \beta(\bar{\xi}(a+\theta), \bar{S})L(a+\theta, \theta) + \frac{\partial\beta}{\partial\xi}(\bar{\xi}(a+\theta), \bar{S})K(a+\theta, \theta)\bar{\mathcal{F}}(a+\theta) \right\} d\theta \\ & + \chi_{[0, \bar{\tau}]}(a)\bar{b} \int_{\bar{\tau}}^{\infty} \frac{\partial\beta}{\partial\xi}(\bar{\xi}(\sigma), \bar{S})\bar{\mathcal{F}}(\sigma)d\sigma \left(\frac{g(\xi_{A+}, \bar{S})}{g(\xi_{A-}, \bar{S})} - 1 \right) K(\bar{\tau}, \bar{\tau}-a) \\ & + \bar{b} \frac{\mu(\xi_{A-}, \bar{S}) - \mu(\xi_{A+}, \bar{S})}{g(\xi_{A-}, \bar{S})} \int_{\max\{0, \bar{\tau}-a\}}^{\bar{\tau}} \beta(\bar{\xi}(a+\theta), \bar{S})\bar{\mathcal{F}}(a+\theta)K(\bar{\tau}, \theta)d\theta \\ & + \chi_{[0, \bar{\tau}]}(a)\bar{b} \frac{\beta(\bar{\xi}_{A+}, \bar{S})\bar{\mathcal{F}}(\bar{\tau})}{g(\xi_{A-}, \bar{S})} K(\bar{\tau}, \bar{\tau}-a). \end{aligned}$$

$$(2.6.29) \quad \begin{aligned} k_{22}(a) = & -\bar{b} \int_0^{\infty} \left\{ \gamma(\bar{\xi}(a+\theta), \bar{S})L(a+\theta, \theta) + \frac{\partial\gamma}{\partial\xi}(\bar{\xi}(a+\theta), \bar{S})K(a+\theta, \theta)\bar{\mathcal{F}}(a+\theta) \right\} d\theta \\ & - \chi_{[0, \bar{\tau}]}(a)\bar{b} \int_{\bar{\tau}}^{\infty} \frac{\partial\gamma}{\partial\xi}(\bar{\xi}(\sigma), \bar{S})\bar{\mathcal{F}}(\sigma)d\sigma \left(\frac{g(\xi_{A+}, \bar{S})}{g(\xi_{A-}, \bar{S})} - 1 \right) K(\bar{\tau}, \bar{\tau}-a) \\ & - \bar{b} \frac{\mu(\xi_{A-}, \bar{S}) - \mu(\xi_{A+}, \bar{S})}{g(\xi_{A-}, \bar{S})} \int_{\max\{0, \bar{\tau}-a\}}^{\bar{\tau}} \gamma(\bar{\xi}(a+\theta), \bar{S})\bar{\mathcal{F}}(a+\theta)K(\bar{\tau}, \theta)d\theta \\ & - \chi_{[0, \bar{\tau}]}(a)\bar{b} \frac{\gamma(\bar{\xi}_{A+}, \bar{S}) - \gamma(\bar{\xi}_{A-}, \bar{S})}{g(\xi_{A-}, \bar{S})} \bar{\mathcal{F}}(\bar{\tau})K(\bar{\tau}, \bar{\tau}-a). \end{aligned}$$

Now that we know how to compute the vector c and the matrix kernel $k(a)$, we return to the linearized system (2.6.2) and ask ourselves how we should analyse it. As before the key information is obtained by looking for $\lambda \in \mathbb{C}$ such that (2.6.2) admits a solution of the special separation-of-variables form

$$(2.6.30) \quad \begin{pmatrix} y(t) \\ z(t) \end{pmatrix} = e^{\lambda t} \begin{pmatrix} y_0 \\ z_0 \end{pmatrix}$$

Substitution of (2.6.30) into (2.6.2) yields the linear algebra problem

$$\begin{aligned} y_0 &= c_1 z_0 + \hat{k}_{11}(\lambda)y_0 + \hat{k}_{12}(\lambda)z_0 \\ \lambda z_0 &= c_2 z_0 + \hat{k}_{21}(\lambda)y_0 + \hat{k}_{22}(\lambda)z_0 \end{aligned}$$

which has a non-trivial solution iff the determinant of the matrix

$$\begin{pmatrix} 1 - \widehat{k}_{11}(\lambda) & -c_1 - \widehat{k}_{12}(\lambda) \\ -\widehat{k}_{21}(\lambda) & \lambda - c_2 - \widehat{k}_{22}(\lambda) \end{pmatrix}$$

equals zero. So λ should be a root of

$$(2.6.31) \quad (1 - \widehat{k}_{11}(\lambda))(\lambda - c_2 - \widehat{k}_{22}(\lambda)) - \widehat{k}_{21}(\lambda)(c_1 + \widehat{k}_{12}(\lambda)) = 0$$

which is called the *characteristic equation* of (2.6.2). In the next section we shall take a closer look at this characteristic equation in the setting of a stage structured population, as described in Section 2.4.

2.7 Stability criteria for stage structured models

In this section we shall assume that the per capita death rates μ_1 and μ_2 are independent of the resource concentration S . In case of stage structure, the steady maturation delay $\bar{\tau}$ and the steady state food concentration S relate to each other according to (cf. (2.4.1))

$$(2.7.1) \quad g(S)\bar{\tau} = \xi_A - \xi_b.$$

From (2.4.7) we infer that the $R_0 = 1$ condition can be written as

$$(2.7.2) \quad \frac{\beta(S)}{\mu_2} e^{-\mu_1 \bar{\tau}} = 1$$

and that the steady population birth rate b is given by

$$(2.7.3) \quad b = \frac{f(S)}{\gamma_1(S) \frac{1 - e^{-\mu_1 \bar{\tau}}}{\mu_1} + \gamma_2(S) \frac{e^{-\mu_1 \bar{\tau}}}{\mu_2}} = \frac{f(S)}{\frac{\gamma_1(S)}{\beta(S)} \frac{\beta(S) - \mu_2}{\mu_1} + \frac{\gamma_2(S)}{\beta(S)}}.$$

Using (2.7.1) we can rewrite (2.7.2) as

$$(2.7.4) \quad \frac{\beta(S)}{\mu_2} e^{-\mu_1 \frac{\xi_A - \xi_b}{g(S)}} = 1$$

and if both β and g are increasing functions of S , the left hand side is an increasing function of S as well. So if this function is smaller than one for small S and bigger than one for large S , there is a unique root which, with some abuse of notation, we simply denote by S . In order to make (2.7.3) meaningful we assume that $f(S) > 0$.

The steady state survival probability is given by

$$(2.7.5) \quad \mathbf{f}(a) = \begin{cases} e^{-\mu_1 a}, & a \leq \bar{\tau} \\ e^{-\mu_1 \bar{\tau} - \mu_2 (a - \bar{\tau})}, & a \geq \bar{\tau}. \end{cases}$$

Directly from (2.6.3) we deduce, using (2.7.2)

$$(2.7.6) \quad \begin{aligned} c_1 &= b \frac{\beta'(S)}{\beta(S)} \\ c_2 &= f'(S) - b \left\{ \frac{\gamma_1'(S)}{\beta(S)} \frac{\beta(S) - \mu_2}{\mu_1} + \frac{\gamma_2'(S)}{\beta(S)} \right\}. \end{aligned}$$

Likewise we obtain from (2.6.4), by computing the Laplace transform of \mathbf{f} defined by (2.7.5), that

$$(2.7.7) \quad \begin{aligned} \widehat{k}_{11}(\lambda) &= \frac{\mu_2}{\lambda + \mu_2} e^{-\lambda \bar{\tau}} \\ \widehat{k}_{21}(\lambda) &= -\frac{\gamma_1(S)}{\beta(S)} \frac{\beta(S) - \mu_2 e^{-\lambda \bar{\tau}}}{\lambda + \mu_1} - \frac{\gamma_2(S)}{\beta(S)} \frac{\mu_2}{\lambda + \mu_2} e^{-\lambda \bar{\tau}}. \end{aligned}$$

From (2.6.8) we deduce that

$$(2.7.8) \quad K(\tau, \alpha) = g'(S) \text{ if } 0 \leq \alpha < \bar{\tau} \text{ and zero otherwise}$$

and from (2.6.14) that

$$(2.7.9) \quad L(\tau, \theta) = 0.$$

With a bit of effort one can now compute that (2.6.28) and (2.6.29) lead to

$$(2.7.10) \quad \begin{aligned} \widehat{k}_{12}(\lambda) &= b \frac{g'(S)}{g(S)} (1 - e^{-\lambda \bar{\tau}}) \left(\frac{\mu_1}{\lambda} - \frac{\mu_2 - \mu_1}{\mu_2 + \lambda} \right) \\ \widehat{k}_{22}(\lambda) &= b \frac{g'(S)}{g(S)} (1 - e^{-\lambda \bar{\tau}}) \left(\frac{\mu_2 \gamma_1(S) - \mu_1 \gamma_2(S)}{\lambda \beta(S)} - \frac{(\mu_2 - \mu_1) \gamma_2(S)}{(\mu_2 + \lambda) \beta(S)} \right) \end{aligned}$$

We now first collect a number of assumptions that help to simplify some of these expressions:

i) if the γ_i are linear in S which we shall, with abuse of notation, write as

$$(2.7.11) \quad \gamma_i(S) = \gamma_i S, \quad i = 1, 2,$$

then

$$(2.7.12) \quad c_2 = f'(S) - \frac{f(S)}{S}$$

ii) if we adopt the QSSA as described in Section 2.5, the term λ in the second factor in (2.6.31) disappears and the characteristic equation becomes

$$(2.7.13) \quad (1 - \widehat{k}_{11}(\lambda))(-c_2 - \widehat{k}_{22}(\lambda)) - \widehat{k}_{21}(\lambda)(c_1 + \widehat{k}_{12}(\lambda)) = 0$$

iii) if g is constant, i.e., the i -growth does not depend on S , then both $\widehat{k}_{12}(\lambda)$ and $\widehat{k}_{22}(\lambda)$ reduce to zero. Note that in this case $\bar{\tau}$ is the fixed maturation delay for all food concentrations (and not just the steady state value for a particular food concentration)

iv) if β is constant, i.e., the per capita reproduction rate does not depend on S , then $c_1 = 0$

v) if $\mu_1 = \mu_2 = \mu$ and $\gamma_1(S) = \gamma_2(S) = \gamma(S)$ then

$$b = \mu \frac{f(S)}{\gamma(S)} \quad c_2 = f'(S) - \frac{\gamma'(S)}{\gamma(S)} f(S)$$

$$\widehat{k}_{21}(\lambda) = -\frac{\gamma(S)}{\lambda + \mu} \quad \widehat{k}_{12}(\lambda) = \frac{bg'(S)}{g(S)} \mu \frac{1 - e^{-\lambda\bar{\tau}}}{\lambda} \quad \widehat{k}_{22}(\lambda) = 0.$$

To illustrate how one can use the characteristic equation in order to contrast the effects of various forms of density dependence (once more inspired by work of Gurney & Nisbet [14]) we now consider a few special cases.

1. No destabilization with fixed maturation delay

We assume that the growth rate g is independent of S and, for consistency, that the juveniles have a different (and constant) food source and do not consume S . So we assume $g' = 0$ and $\gamma_1 = 0$. Then

$$b = \frac{\beta(S)f(S)}{\gamma_2(S)}, \quad c_1 = \frac{\beta'(S)f(S)}{\gamma_2(S)}, \quad c_2 = f'(S) - \frac{\gamma_2'(S)f(S)}{\gamma_2(S)}$$

and the characteristic equation is given by

$$\left(1 - \frac{\mu_2}{\lambda + \mu_2} e^{-\lambda\bar{\tau}}\right) \left(\lambda - f'(S) + \frac{\gamma_2'(S)}{\gamma_2(S)} f(S)\right) + \frac{\mu_2}{\lambda + \mu_2} \frac{\beta'(S)}{\beta(S)} f(S) e^{-\lambda\bar{\tau}} = 0.$$

If we multiply by $\lambda + \mu_2$ and re-organize, we can bring the characteristic equation in the form

$$\frac{\mu_2}{\lambda + \mu_2} e^{-\lambda\bar{\tau}} \frac{\lambda - f'(S) + \frac{\gamma_2'(S)}{\gamma_2(S)} f(S) - \frac{\beta'(S)}{\beta(S)} f(S)}{\lambda - f'(S) + \frac{\gamma_2'(S)}{\gamma_2(S)} f(S)} = 1.$$

We now consider each of the three factors at the left hand side for $\lambda = i\omega$. Clearly for $\omega \neq 0$

$$\left| \frac{\mu_2}{i\omega + \mu_2} \right| = \frac{\mu_2}{\sqrt{\mu_2^2 + \omega^2}} < 1 \quad \text{and} \quad |e^{-i\omega\bar{\tau}}| = 1.$$

So if also the absolute value of the third factor is less than one, then there will never be a root on the imaginary axis and destabilization by Hopf bifurcation does not occur. The condition is that

$$\left| -f'(S) + \frac{\gamma_2'(S)}{\gamma_2(S)}f(S) - \frac{\beta'(S)}{\beta(S)}f(S) \right| < \left| -f'(S) + \frac{\gamma_2'(S)}{\gamma_2(S)}f(S) \right|$$

and if we make the plausible assumptions that

$$f'(S) < 0, \quad \gamma_2'(S) > 0, \quad \beta'(S) > 0,$$

this condition is fulfilled.

2. Destabilization with variable maturation delay

Let us now assume that the birth rate β is independent of S and, for consistency, that the adults have a different (and constant) food source and do not consume S . So we assume that $\beta' = 0$ and $\gamma_2 = 0$. On top of that we make the QSSA .

Then

$$\bar{\tau} = \frac{\ln \beta - \ln \mu_2}{\mu_1} \quad \text{and} \quad S = g^{-1} \left(\frac{\xi_A - \xi_b}{\bar{\tau}} \right).$$

Moreover

$$b = \frac{\mu_1 \beta f(S)}{\gamma_1(S)(\beta - \mu_2)}, \quad c_1 = 0, \quad c_2 = f'(S) - \frac{\gamma_1'(S)}{\gamma_1(S)}f(S)$$

and the characteristic equation is given by

$$\begin{aligned} & \left(1 - \frac{\mu_2}{\lambda + \mu_2} e^{-\lambda\bar{\tau}} \right) \left(\lambda - f'(S) + \frac{\gamma_1'(S)}{\gamma_1(S)}f(S) - \frac{\mu_1 \mu_2 f(S)}{\beta - \mu_2} \frac{g'(S)}{g(S)} \frac{1 - e^{-\lambda\bar{\tau}}}{\lambda} \right) \\ & + \frac{\beta - \mu_2 e^{-\lambda\bar{\tau}}}{\lambda + \mu_1} \frac{\mu_1 f(S)}{\beta - \mu_2} \frac{g'(S)}{g(S)} (1 - e^{-\lambda\bar{\tau}}) \left(\frac{\mu_1}{\lambda} + \frac{\mu_2 - \mu_1}{\mu_2 + \lambda} \right) = 0. \end{aligned}$$

If we multiply by $\lambda + \mu_2$ and re-organize, we can bring the characteristic equation in the form

$$\lambda + \alpha_1(1 - e^{-\lambda\bar{\tau}}) + \alpha_2 \frac{1 - e^{-\lambda\bar{\tau}}}{\lambda} = 0$$

with

$$(2.7.14) \quad \alpha_1 = \mu_2 - \frac{\mu_1 \mu_2}{\beta - \mu_2} \frac{g'(S)}{g(S)} \frac{\gamma_1(S) f(S)}{\gamma_1'(S) f(S) - f'(S) \gamma_1(S)}$$

$$(2.7.15) \quad \alpha_2 = \mu_1 \mu_2 \frac{g'(S)}{g(S)} \frac{\gamma_1(S) f(S)}{\gamma_1'(S) f(S) - f'(S) \gamma_1(S)}.$$

For $\lambda = i\omega$ we can rewrite (2.7.14) as the two real equations

$$(2.7.16) \quad \begin{aligned} 0 &= \omega + \alpha_1 \sin \omega \bar{\tau} - \alpha_2 \frac{1 - \cos \omega \bar{\tau}}{\omega} \\ 0 &= \alpha_1 (1 - \cos \omega \bar{\tau}) + \alpha_2 \frac{\sin \omega \bar{\tau}}{\omega}. \end{aligned}$$

Solving for the parameters in terms of the frequency ω we find

$$\begin{pmatrix} \alpha_1 \\ \alpha_2 \end{pmatrix} = \begin{pmatrix} \frac{\omega \sin \omega \bar{\tau}}{2(\cos \omega \bar{\tau} - 1)} \\ \frac{\omega^2 / 2}{\omega^2 / 2} \end{pmatrix} = \frac{1}{2} \begin{pmatrix} \frac{-\omega \cos \frac{\omega \bar{\tau}}{2}}{\sin \omega \bar{\tau} / 2} \\ \omega^2 \end{pmatrix}$$

Note: If (2.7.14) implies that necessarily $\alpha_1 > 0$, then $\bar{\tau} < \text{period} < 2\bar{\tau}$ [19].

Chapter 3

Size structured cell populations

3.1 A continuum of possibilities for state-at-birth

The difference between the preceding chapter and this one is not so much the biological nature of the organisms that constitute the population (though the peculiarities of multiplication by division will play a role in this chapter) but rather the variation among the organisms of state-at-birth: in Chapter 2 we assumed that newborns had one and the same size, while here we shall consider the situation that there is a continuum of possibilities for state-at-birth. So we need to work with $b(t, x)$, where t is time, x is size-at-birth and b is the rate at which newborn individuals enter the population. And our task is, as before, to derive the renewal equation for b from model ingredients and to analyse it. One can still think of b as a function of time, but now this function of time takes on values which are functions of x and in that sense we deal with an infinite-dimensional renewal equation.

In Section 3.2 we introduce the model ingredients describing, respectively, the growth of cells, their propensity to divide, the force of mortality and the size of the two daughters, given the size of the mother. In Section 3.3 we derive the renewal equation for b . In Section 3.4 we establish the connection between the renewal equation and the more traditional formulation in terms of a partial differential equation (PDE). At the same time we also show how the interpretation may help to construct solutions of the PDE. Readers not interested in PDE may skip Section 3.4. In general, infinite dimensional renewal equations are rather prohibitive when it comes to their analysis, so it is important to find meaningful simplifications. In Section 3.5 we shall make extra assumptions that allow us to do the bookkeeping in terms of the traffic of cells at a so-called renewal point. The happy outcome is a scalar

renewal equation! In Section 3.6 we shall introduce a very special type of nonlinearity by assuming that cells may be either quiescent or proliferating, with the rate of going from one state to the other depending on the (weighted) total population.

3.2 Model ingredients (for the case of a constant environment)

We consider a population of cells and assume that the state of a cell is fully characterized by its size (realising that this is a gross oversimplification). Here size may mean the radius of a spherically cell or the length of a rod-shaped cell or the total amount of some crucial chemical substance or Size is a real number. The set of all possible sizes we denote by Ω and the set of all possible sizes of daughters that just arose by division of the mother we denote by Ω_b .

We assume that the growth of a cell is deterministic and described by the ODE

$$(3.2.1) \quad \frac{dy}{da} = g(y).$$

The solution of this equation with initial condition $y(0) = \xi$ we denote by $X(a, \xi)$ so

$$(3.2.2) \quad X(t, \xi) \quad \text{is the size of a cell at time } t \text{ if at time zero} \\ \text{it had size } \xi \text{ (and it did neither die nor divide} \\ \text{in the time interval } [0, t))$$

We also define

$$(3.2.3) \quad A(x, \xi) := \int_{\xi}^x \frac{d\sigma}{g(\sigma)},$$

which is the time a cell needs in order to grow from size ξ to size x . Note that

$$(3.2.4) \quad X(A(x, \xi), \xi) = x \quad \text{and} \quad A(X(t, \xi), \xi) = t$$

or, in other words, for given ξ the functions $t \mapsto X(t, \xi)$ and $x \mapsto A(x, \xi)$ are inverse to each other.

3.2. MODEL INGREDIENTS (FOR THE CASE OF A CONSTANT ENVIRONMENT) 57

Next we look at the chances that a cell of a certain size divides. Here there are two options. We can introduce

(3.2.5) $\gamma(y)$ is the probability per unit of *time* that a cell of size y divides,

but instead we may also work with

(3.2.6) $\frac{\gamma(y)}{g(y)}$ is the probability per unit of *size* that a cell of size y divides.

Before explaining more precisely what we mean by two options, we clarify the notion of “probability per unit of size” by considering the survival function

$$(3.2.7) \quad \exp\left(-\int_0^t \gamma(X(\tau, \xi)) d\tau\right)$$

which gives the probability that a cell with size ξ at time zero does not divide in the time interval $[0, t]$, given that it does not die. If we change the integration variable τ to the integration variable y , where τ and y are related through

$$(3.2.8) \quad \tau = A(y, \xi)$$

then (3.2.7) transforms into

$$(3.2.9) \quad \exp\left(-\int_{\xi}^{X(t, \xi)} \frac{\gamma(y)}{g(y)} dy\right)$$

and we conclude that the probability that a cell with size ξ , given that it does not die, does not divide before reaching size x is

$$(3.2.10) \quad \exp\left(-\int_{\xi}^x \frac{\gamma(y)}{g(y)} dy\right)$$

and this is the precise meaning of the statement (3.2.6).

By “two options” we meant that one can either take survival functions of time-intervals or survival functions of size-intervals as fundamental ingredient. In the present case of constant conditions and deterministic growth one can, as we did above, relate one to the other by a simple transformation. But if conditions are not constant, one has to make a modelling decision [22]!

(A far-fetched analogy is the rule for determining the tariff of a taxicab: by distance, by time, or by a combination of these).

Similarly we can introduce

(3.2.11) $\mu(y)$ is the probability per unit of time that a cell of size y dies

and the overall survival function

$$(3.2.12) \quad \mathcal{F}(x, \xi) := \exp \left(- \int_{\xi}^x \frac{\mu(y) + \gamma(y)}{g(y)} dy \right),$$

which gives the probability that a cell grows from size ξ to size x without dying or dividing.

It remains to specify the sizes of the two daughters of a mother of size y . If “size” is a conserved quantity and the two daughters are exactly equal, both necessarily have size $\frac{1}{2}y$. But more generally one may imagine that the size of a daughter follows some probability distribution (with strong dependence between the two daughters). For instance, one may postulate that, for $y \in \Omega$ and ω a (measurable) subset of Ω_b

(3.2.13) $P(\omega, y)$ is the probability that a daughter of a
mother of size y has a size that belongs to ω

(note that consistency with size-conservation then requires that $P(f_y(\omega), y) = P(\omega, y)$ where $f_y(x) = y - x$).

The special case of division into two equal halves corresponds to

$$(3.2.14) \quad P(\omega, y) = \delta_{\frac{1}{2}y}(\omega) = \delta(\omega - \frac{1}{2}y),$$

where δ_z is the point mass (Dirac measure) concentrated at z . Apart from this special case, we shall consider only the situation in which for each y the probability measure $P(\cdot, y)$ has a density $\pi(\cdot, y)$, i.e.,

$$(3.2.15) \quad P(\omega, y) = \int_{\omega} \pi(x, y) dx$$

with $\pi(y - x, y) = \pi(x, y)$ and, as a consequence,

$$(3.2.16) \quad \int_{\Omega_b} x \pi(x, y) dx = \frac{1}{2}y,$$

meaning that the expected size of a daughter is half the size of the mother.

3.3 The renewal equation

We shall first formulate the renewal equation for the case in which the probability distribution P of the size of daughters has a density π and next for the special situation of two exactly equal daughters. To facilitate the description we shall use words like "survive" and "alive" to indicate that neither death nor division has occurred.

Consider a cell of age a which was born with size ξ . Its current size is $X(a, \xi)$ if it is still alive, which is the case with probability $\mathcal{F}(X(a, \xi), \xi)$. It divides with probability per unit of time $\gamma(X(a, \xi))$ to produce two daughters, each of which has size x with probability density $\pi(x, X(a, \xi))$.

To obtain the rate at which newly produced daughters enter the population, we classify their mothers in terms of age a and their size-at-birth ξ and then simply add all contributions. Hence

$$(3.3.1) \quad b(t, x) = 2 \int_0^\infty \int_{\Omega_b} b(t-a, \xi) \mathcal{F}(X(a, \xi), \xi) \gamma(X(a, \xi)) \pi(x, X(a, \xi)) d\xi da.$$

If, alternatively, we classify mothers in terms of their size-at-birth ξ and their current size η , and make the transformation

$$(3.3.2) \quad a = A(\eta, \xi) \Leftrightarrow X(a, \xi) = \eta$$

we obtain that (3.3.1) transforms into

$$(3.3.3) \quad b(t, x) = 2 \int_{\Omega_b} \int_{\{\eta: \eta \geq \xi\}} b(t - A(\eta, \xi), \xi) \mathcal{F}(\eta, \xi) \gamma(\eta) \pi(x, \eta) \frac{1}{g(\eta)} d\eta d\xi.$$

The renewal equation for the case of division into two equal halves reads

$$(3.3.4) \quad b(t, x) = 4 \frac{\gamma(2x)}{g(2x)} \int_{\Omega_b \cap \{\xi: \xi \leq 2x\}} b(t - A(2x, \xi), \xi) \mathcal{F}(2x, \xi) d\xi$$

and one can understand almost all of the logic behind it by looking at (3.3.3) and realising that in order for the daughter to have size x , the mother *must* have exactly size $2x$. The puzzling aspect is the factor 4 instead of 2. But once one observes that mothers with size in the interval $[x, x + dx]$ produce daughters in the interval $[\frac{1}{2}x, \frac{1}{2}x + \frac{1}{2}dx]$, which is only half as long, one can understand that this shrinking of the interval must be compensated by a

doubling of the density in order to keep numbers right, And indeed, if we integrate (3.3.4) with respect to x we find the identity

$$\begin{aligned}
 (3.3.5) \quad \int_{\Omega_b} b(t, x) dx &= 4 \int_{\Omega_b} \frac{\gamma(2x)}{g(2x)} \int_{\Omega_b \cap \{\xi: \xi \leq 2x\}} b(t - A(2x, \xi), \xi) \mathcal{F}(2x, \xi) d\xi dx \\
 &= 2 \int_{\Omega} \frac{\gamma(\eta)}{g(\eta)} \int_{\Omega_b \cap \{\xi: \xi \leq \eta\}} b(t - A(\eta, \xi), \xi) \mathcal{F}(\eta, \xi) d\xi d\eta \\
 &= 2 \int_0^\infty \int_{\Omega_b} b(t - a, \xi) \mathcal{F}(X(a, \xi), \xi) \gamma(X(a, \xi)) d\xi
 \end{aligned}$$

which has a factor 2, just as it should.

Note that alternatively we may write (3.3.4) as
(3.3.6)

$$b(t, x) = 4 \frac{\gamma(2x)}{g(2x)} \int_0^\infty b(t - a, X(-a, 2x)) \mathcal{F}(2x, X(-a, 2x)) g(X(-a, 2x)) da$$

since a cell which has size $2x$ at age a must have been born with size $X(-a, 2x)$.

3.4 The connection with the PDE formulation (a short interlude)

Since the more traditional formulation of size-structured cell population models is in terms of a partial differential equation for the size-density $n(t, x)$, we shall explain in this section the bookkeeping operations that relate n and b . Readers who have no affinity with the PDE formulation may skip this section. We restrict our attention to the special case of division into two daughters that each have exactly half the size of the mother.

The PDE

$$(3.4.1) \quad \frac{\partial n}{\partial t}(t, x) + \frac{\partial}{\partial x} (g(x)n(t, x)) = -\mu(x)n(t, x) - \gamma(x)n(t, x) + 4\gamma(2x)n(t, 2x)$$

takes into account that the growth of cells does not change the number of cells but that death and division do. The factor 4 should as before be read as 2 times 2 where one factor 2 accounts for the two daughters and the other for the shrinking of intervals which, since *numbers* are conserved, should be compensated by an increase in the density.

The quantity $g(x)n(t, x)$ is the *flux*, i.e., the “traffic” of cells through x . If we define

$$(3.4.2) \quad m(t, x) = g(x)n(t, x)$$

put the right hand side of (3.4.1) equal to zero and next multiply the equation by $g(x)$, we obtain

$$(3.4.3) \quad \frac{\partial m}{\partial t}(t, x) + g(x)\frac{\partial m}{\partial x}(t, x) = 0.$$

The solutions of (3.4.3) should satisfy (recall (3.2.3))

$$(3.4.4) \quad m(t, x) = m(t - A(x, y), y).$$

This identity just states that the cells that have size x at time t are, if we ignore death and division, exactly those that had size y at time $t - A(x, y)$. Using (3.4.2) we can rewrite (3.4.4) as

$$(3.4.5) \quad n(t, x) = \frac{g(y)}{g(x)}n(t - A(x, y), y).$$

The factor $g(y)/g(x)$ takes care of adjusting the density when velocities change, in order to conserve the number, see [22]. In other words, we have just verified the well-known fact that the left hand side of (3.4.1) is an infinitesimal formulation of the conservation of numbers of growing cells.

If we only remove the last term at the right hand side of (3.4.1), we need to replace (3.4.4) with (recall (3.2.12))

$$(3.4.6) \quad m(t, x) = m(t - A(x, y), y)\mathcal{F}(x, y)$$

to take into account that, for $x > y$, the cells that have size x at time t are those that had size y at time $t - A(x, y)$ and did neither die nor divide on their way to x .

Directly from the interpretation we conclude that

$$(3.4.7) \quad b(t, x) = 4\gamma(2x)n(t, 2x).$$

In general, the flux at x at time t consists of contributions of cells that were already present at the starting time and of cells that arose from divisions since the starting time. If we supplement the PDE (3.4.1) with the boundary condition that the flux at some conveniently chosen small size is zero, the first contribution will, if g is bounded away from zero, vanish after a finite time (which does not depend on x). This motivates us to ignore the first

contribution altogether (which amounts to putting the starting time at $-\infty$). Then

$$m(t, x) = \int^x b(t - A(x, \xi), \xi) \mathcal{F}(x, \xi) d\xi$$

and hence

$$(3.4.8) \quad n(t, x) = \frac{1}{g(x)} \int^x b(t - A(x, \xi), \xi) \mathcal{F}(x, \xi) d\xi,$$

where we leave the lower integration boundary unspecified since we have not yet introduced any notation for the lowest size at which cells are born.

Now note that (3.4.7) expresses b in terms of n , while (3.4.8) expresses n in terms of b , allowing us to go back and forth between the two formulations. Also note that if we use (3.4.8) to rewrite the right hand side of (3.4.7), we recover the renewal equation (3.3.4). So if we solve the renewal equation, we can use (3.4.8) to obtain a solution of the PDE. The only difference between (3.3.4) and (3.4.1) + boundary condition is in the way we impose an initial condition. In this respect the renewal equation is more restricted, but in a way that only matters for the transient behaviour of solutions. Concerning long time behaviour, (3.4.1) and (3.3.4) are equivalent!

3.5 Reducing the renewal equation by taking advantage of the existence of a renewal point

Suppose there exists a size, say $x = \alpha$, such that a newborn cell necessarily has size $x < \alpha$ while also a dividing cell necessarily has size $x > \alpha$, i.e., $\gamma(x) = 0$ for $x < \alpha$ (so in particular it is impossible that a newborn cell does immediately divide). The implication is that every cell attains size α in between being born and dividing. We call α a renewal point, to express that by concentrating on the traffic of cells at α we capture, quite literally, those aspects of the life cycle that drive the population dynamics. We may even go so far as to call the passing of α the “birth”, taking for granted that then there is life, and even death, before birth.

We shall illustrate this reduction method (and the way in which the various bookkeeping schemes relate to each other) in the context of division into two equal halves, so for the infinite-dimensional renewal equation (3.3.4). To begin with, we assume that cells have a maximal size, say $x = 1$ (this may

3.5. REDUCING THE RENEWAL EQUATION BY TAKING ADVANTAGE OF THE EXISTENCE

either be achieved by letting $g(x)$ go to zero for $x \uparrow 1$ or by letting $\gamma(x) \uparrow \infty$ in a non-integrable manner for $x \uparrow 1$, since the key point is that the survival probability $\mathcal{F}(x, \xi)$ defined in (3.2.12) goes to zero for $x \uparrow 1$). Then Ω_b extends to $x = \frac{1}{2}$. Next assume that $\gamma(x) = 0$ for $x < \alpha$ with $\alpha > \frac{1}{2}$, and that $\gamma(x) > 0$ for $x > \alpha$. Then $\Omega_b = (\frac{\alpha}{2}, \frac{1}{2}]$ or $\Omega_b = [\frac{\alpha}{2}, \frac{1}{2}]$, depending on whether $\gamma(\alpha) = 0$ or $\gamma(\alpha) > 0$, but the difference does not matter at all. We copy (3.3.4) here in the form

$$(3.5.1) \quad b(t, x) = 4 \frac{\gamma(2x)}{g(2x)} \int_{\alpha/2}^{1/2} b(t - A(2x, \xi), \xi) \mathcal{F}(2x, \xi) d\xi, \quad \frac{\alpha}{2} \leq x \leq \frac{1}{2}.$$

Now observe that for $\xi \leq \frac{1}{2}$ and $2x > \alpha$ we may write

$$(3.5.2) \quad \mathcal{F}(2x, \xi) = \mathcal{F}(2x, \alpha) \mathcal{F}(\alpha, \xi)$$

and put the factor $\mathcal{F}(2x, \alpha)$ outside the integral. The only remaining x -dependence inside the integral is then in the time argument of b . This suggests that we might be able to separate variables and reduce the problem to a scalar equation for the time dependence. And indeed, this is possible! But the easiest way to find out how to do it, is to first derive the scalar renewal equation from first principles. So that is what we do next.

Consider a cell of size α . It reaches size $x > \alpha$ with probability $\mathcal{F}(x, \alpha)$. It divides at this size with probability per unit of time $\gamma(x)$ and hence with probability per unit of size $\gamma(x)/g(x)$. After division the daughters have size $\frac{x}{2}$. They reach size α with probability $\mathcal{F}(\alpha, \frac{x}{2})$. The time needed for this cycle is

$$(3.5.3) \quad A(x, \alpha) + A\left(\alpha, \frac{x}{2}\right) = A\left(x, \frac{x}{2}\right)$$

and the encompassing survival probability is

$$(3.5.4) \quad \mathcal{F}(x, \alpha) \mathcal{F}\left(\alpha, \frac{x}{2}\right) = \mathcal{F}\left(x, \frac{x}{2}\right).$$

Now we lift these considerations to the p -level. Let $b_\alpha(t)$ denote the flux at size α . Then

$$(3.5.5) \quad b_\alpha(t) = 2 \int_{\alpha}^1 b_\alpha\left(t - A\left(x, \frac{x}{2}\right)\right) \mathcal{F}\left(x, \frac{x}{2}\right) \frac{\gamma(x)}{g(x)} dx.$$

The same considerations show, in addition, that

$$(3.5.6) \quad b(t, x) = 4b_\alpha(t - A(2x, \alpha)) \mathcal{F}(2x, \alpha) \frac{\gamma(2x)}{g(2x)}.$$

And indeed, if we substitute (3.5.6) as an Ansatz into (3.5.1) we find that the equation is indeed satisfied provided b_α satisfies (3.5.5). In other words, by way of (3.5.6) we obtain solutions of (3.5.1) in terms of the much simpler scalar renewal equation (3.5.5). The only difference is once again in the way we impose an initial condition. In this respect the scalar renewal equation is more restricted, but in a way that only matters for the transient behaviour of solutions. Concerning long time behaviour, (3.5.1) and (3.5.5) are equivalent when α is a renewal point.

Equation (3.5.5) has solutions of the form $b_\alpha(t) = e^{\lambda t}$ if and only if λ satisfies the characteristic equation

$$(3.5.7) \quad 1 = 2 \int_{\alpha}^1 e^{-\lambda A(x, \frac{x}{2})} \mathcal{F} \left(x, \frac{x}{2} \right) \frac{\gamma(x)}{g(x)} dx.$$

As usual, we denote the real root of this equation by r and call it the Malthusian parameter. Likewise we define

$$(3.5.8) \quad R_0 = 2 \int_{\alpha}^1 \mathcal{F} \left(x, \frac{x}{2} \right) \frac{\gamma(x)}{g(x)} dx$$

since the right hand side is indeed the expected number of daughters that reach size α of a cell that has size α . The identity

$$(3.5.9) \quad \text{sign } r = \text{sign } (R_0 - 1)$$

holds.

Just as we rewrote (3.3.4) in the form (3.3.5) by using age rather than size as label, we may attempt to perform the change of integration variable

$$(3.5.10) \quad a = A \left(x, \frac{x}{2} \right)$$

in (3.5.5). But we are in for a surprise:

$$(3.5.11) \quad \frac{d}{dx} A \left(x, \frac{x}{2} \right) = \frac{d}{dx} \int_{x/2}^x \frac{d\sigma}{g(\sigma)} = \frac{1}{g(x)} - \frac{1}{2g \left(\frac{x}{2} \right)}$$

and if $2g \left(\frac{x}{2} \right) = g(x)$, as it is whenever $g(x) = cx$ for some $c > 0$, this is identically zero. So in that situation (3.5.5) is actually the difference equation

$$(3.5.12) \quad b_\alpha(t) = R_0 b_\alpha(t - T)$$

(with T the constant value of $A\left(x, \frac{x}{2}\right)$), since the time a full cycle takes is independent of the exact size at which the cell divides! So in this case $r = \frac{\ln R_0}{T}$ and there are countably many roots of (3.5.7) on the line $\operatorname{Re} \lambda = r$, viz. $\lambda = r + k \frac{2\pi}{T} i$, $k \in \mathbb{Z}$. See [22, 12].

3.6 Limits to growth: incorporating the effects of hypoxia-induced arrest/quiescence

We continue to work with the setting of the preceding section: α is a renewal point and cells divide into two equal halves. Inspired by literature on the cell cycle, we call α a *restriction point* and interpret growth from the birth size to α as the G_1 phase and growth from α to the division size as the combined S and G_2 phase and, finally, the division itself as the M phase of negligible duration.

Let E denote the oxygen concentration. We assume that

- a fraction $p(E)$ of the cells that reach size α from below become quiescent
- quiescent cells don't grow
- quiescent cells return at rate $q(E)$ to the proliferating state, with size α but beyond the restriction point

Note that q is a rate, not a probability, and that in general $p + q \neq 1$.

Let

$$\begin{aligned} b_-(t) & \text{ denote the flux towards } \alpha, \\ b_+(t) & \text{ denote the flux away from } \alpha. \end{aligned}$$

Then

$$\begin{aligned} (3.6.1) \quad b_+(t) &= (1 - p(E(t)))b_-(t) + q(E(t))Q(t), \\ \frac{dQ}{dt}(t) &= p(E(t))b_-(t) - q(E(t))Q(t) - \mu Q(t), \\ b_-(t) &= 2 \int_{\alpha}^1 b_+ \left(t - A \left(x, \frac{x}{2} \right) \right) \mathcal{F} \left(x, \frac{x}{2} \right) \frac{\gamma(x)}{g(x)} dx, \end{aligned}$$

where $Q(t)$ is the concentration of quiescent cells which have, by assumption, death rate μ .

To derive an expression for E , we first introduce

$$\frac{dE}{dt} = 1 - E - EC,$$

where EC corresponds to oxygen consumption by the cells, but next make the quasi-steady-state assumption, which amounts to replacing the differential equation for E by the explicit expression

$$(3.6.2) \quad E = \frac{1}{1 + C}.$$

We complete the model formulation by putting

$$(3.6.3) \quad C = \int_{\alpha/2}^1 \varphi(y)n(t, y)dy + cQ(t),$$

where n is the cell size density and cells of size y are assumed to consume oxygen at the rate $\varphi(y)E$ if they are not quiescent, while quiescent cells consume oxygen at rate c . One may of course take $c = \varphi(\alpha)$, but it is also conceivable that quiescent cells consume substantially less oxygen than proliferating cells of the same size. One may take $\varphi(y)$ proportional to $g(y)$, to relate oxygen consumption to growth. Note, however, that we did not incorporate any effect of the oxygen availability on growth. The influence of the oxygen concentration is assumed to be restricted to the probability of going quiescent when reaching the restriction point and the rate of return to the proliferating state (we realise that this is a debatable restriction).

Directly from the interpretation we obtain the identities

$$(3.6.4) \quad n(t, x) = \begin{cases} \frac{1}{g(x)} b_+(t - A(x, \alpha)) \mathcal{F}(x, \alpha), & x > \alpha, \\ \frac{2}{g(x)} \int_{\alpha}^{\max(2x, 1)} b_+ \left(t - A(\xi, \alpha) - A \left(x, \frac{\xi}{2} \right) \right) \mathcal{F}(\xi, \alpha) \mathcal{F} \left(x, \frac{\xi}{2} \right) \frac{\gamma(\xi)}{g(\xi)} d\xi, & x < \alpha. \end{cases}$$

Consult the last two sections for more detailed explanation if you don't "see" this. Using (3.6.4) we can express C in terms of past values of b_+ and Q . So, since the last equation of (3.6.1) is an explicit expression for b_- in terms of past values of b_+ , we may consider (3.6.1) as a coupled system of delay equations for the variables b_+ and Q .

Our next step is to look for steady states. We shall do this in two steps: We first consider the case of a constant environment characterized by E as a

3.6. LIMITS TO GROWTH: INCORPORATING THE EFFECTS OF HYPOXIA-INDUCED ARREST

constant parameter and derive and analyse the equation $R_0(E) = 1$; secondly, we consider the feedback condition (3.6.2) with C given by (3.6.3).

To facilitate the formulation we abbreviate, for the time being, $p(E)$ to p and $q(E)$ to q and we introduce

$$(3.6.5) \quad K(x) := 2 \frac{\gamma(x)}{g(x)} \mathcal{F} \left(x, \frac{x}{2} \right).$$

With these notational conventions we can write (3.6.1) as

$$(3.6.6) \quad b_+(t) = (1-p) \int_{\alpha}^1 b_+ \left(t - A \left(x, \frac{x}{2} \right) \right) K(x) dx + qQ(t)$$

$$\frac{dQ}{dt}(t) = p \int_{\alpha}^1 b_+ \left(t - A \left(x, \frac{x}{2} \right) \right) K(x) dx - (q + \mu)Q(t).$$

Consider a cell growing away from α . It will produce an expected number $\int_{\alpha}^1 K(x) dx$ of daughters that reach α from below. Of these a fraction $1-p$ will grow immediately away from α and a fraction p will go quiescent. Of those that go quiescent a fraction $\frac{q}{q+\mu}$ will return to the proliferating state and then grow away from α . So

$$(3.6.7) \quad R_0 = (1-p + p \frac{q}{q+\mu}) \int_{\alpha}^1 K(x) dx.$$

Note that for $p=0$ we do indeed recover the expression (3.5.8) for R_0 .

The equation $R_0 = 1$ amounts to

$$(3.6.8) \quad \frac{\mu}{q(E) + \mu} p(E) = 1 - \frac{1}{\int_{\alpha}^1 K(x) dx}.$$

A first requirement for having a solution is that the right hand side should be positive, which translates into the condition

$$(3.6.9) \quad \int_{\alpha}^1 K(x) dx > 1,$$

meaning that in the total absence of quiescence we should have an exponentially growing population. So assume that (3.6.9) holds.

It is natural to assume that $p'(E) < 0$ and $q'(E) > 0$ and under these conditions the left hand side of (3.6.8) is a monotone decreasing function of E , implying that there is at most one solution. There will indeed be a unique solution if and only if

$$(3.6.10) \quad \frac{\mu}{q(\infty) + \mu} p(\infty) < 1 - \frac{1}{\int_{\alpha}^1 K(x) dx} < \frac{\mu}{q(0) + \mu} p(0).$$

Note that (3.6.10) cannot hold if (3.6.9) does not hold.

We arrived at the intermediate conclusion that, under natural monotonicity conditions for the dependence of p and q on E , there is a unique solution of the equation $R_0(E) = 1$ if (3.6.10) holds and no solution if this condition is strictly violated.

We have derived the expression (3.6.7) for R_0 by using the interpretation and likewise we have used the interpretation to argue that, in order to have a steady state, we should have $R_0(E) = 1$. Readers of the Doubting Thomas kind may now want to check that constant solutions (b_+, Q) of system (3.6.6) are found by solving

$$\begin{pmatrix} (1-p) \int_{\alpha}^1 K(x) dx - 1 & q \\ p \int_{\alpha}^1 K(x) dx & -(q + \mu) \end{pmatrix} \begin{pmatrix} b_+ \\ Q \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

and that the coefficient matrix in this equation is singular if and only if $R_0 = 1$. If indeed $R_0 = 1$, the null space of the coefficient matrix consists of (b_+, Q) with

$$(3.6.11) \quad Q = \frac{p \int_{\alpha}^1 K(x) dx}{q + \mu} b_+ = \frac{\int_{\alpha}^1 K(x) dx - 1}{\mu} b_+.$$

The idea is now to combine this relation with (3.6.4) and (3.6.3) to express C in terms of the constant b_+ . As a final step we then determine b_+ such that the feedback condition (3.6.2) holds when we take for E the solution of $R_0(E) = 1$. Thus the (unique) steady state is, if it exists, found by solving twice one equation in one unknown!

For constant b_+ the identities (3.6.4) reduce to

$$(3.6.12) \quad n(x) = \begin{cases} b_+ \frac{\mathcal{F}(x, \alpha)}{g(x)}, & x > \alpha, \\ b_+ \frac{2}{g(x)} \int_{\alpha}^{\max(2x, 1)} \mathcal{F}(\xi, \alpha) \mathcal{F}\left(x, \frac{\xi}{2}\right) \frac{\gamma(\xi)}{g(\xi)} d\xi, & x < \alpha. \end{cases}$$

3.6. LIMITS TO GROWTH: INCORPORATING THE EFFECTS OF HYPOXIA-INDUCED ARREST

If we substitute (3.6.11) and (3.6.12) into (3.6.3) and then the equation so obtained into (3.6.2) we arrive at the equation

(3.6.13)

$$\frac{1}{E} = 1 + b_+ \left(2 \int_{\alpha/2}^{\alpha} \frac{\varphi(y)}{g(y)} \int_{\alpha}^{\max(2y,1)} \mathcal{F}(\xi, \alpha) \mathcal{F}\left(y, \frac{\xi}{2}\right) \frac{\gamma(\xi)}{g(\xi)} d\xi dy + \int_{\alpha}^1 \frac{\varphi(y)}{g(y)} \mathcal{F}(y, \alpha) dy + c \frac{\int_{\alpha}^1 K(x) dx - 1}{\mu} \right)$$

for b_+ . Clearly this equation has a unique solution if $E < 1$ and no nontrivial solution if $E \geq 1$. So in retrospect we see that the condition (3.6.10) needs to be strengthened in order to let E belong to the range of the feedback map. To achieve $E < 1$ we replace (3.6.10) by

$$(3.6.14) \quad \frac{\mu}{q(1) + \mu} p(1) < 1 - \frac{1}{\int_{\alpha}^1 K(x) dx} < \frac{\mu}{q(0) + \mu} p(0).$$

Conclusion Assume that p is a strictly decreasing function of E and q a strictly increasing function. If (3.6.14) is not satisfied, there is no nontrivial steady state of (3.6.6). If (3.6.14) is satisfied, there is a unique nontrivial steady state. It is found by first solving (3.6.8) for E and next (3.6.13) for b_+ and by using (3.6.11) to express Q in terms of b_+ . The steady state size density is given by (3.6.12).

Remark If (3.6.14) is violated by way of

$$\frac{\mu p(1)}{q(1) + \mu} > 1 - \frac{1}{\int_{\alpha}^1 K(x) dx}$$

then the cell population will go extinct. If, on the other hand, (3.6.14) is violated by way of

$$\frac{\mu p(0)}{q(0) + \mu} < 1 - \frac{1}{\int_{\alpha}^1 K(x) dx},$$

then the quiescence mechanism is not able to prevent exponential growth of the cell population.

Bibliography

- [1] Boldin, B.: Introducing a population into a steady community: the critical case, the centre manifold and the direction of the bifurcation. *SIAM Journal on Applied Mathematics* **66** (2006) 1424-1453.
- [2] van den Bosch, F., de Roos, A.M., Gabriel, W., 1988. Cannibalism as a life boat mechanism, *Journal of Mathematical Biology* **26** 614-633.
- [3] *Matrix population models: construction, analysis, and interpretation*. Sinauer Associates, 2001.
- [4] Diekmann, O., Getto, P.: Boundedness, global existence and continuous dependence for nonlinear dynamical systems describing physiologically structured populations, *Journal of Differential Equations* **215** (2005) 268–319.
- [5] Diekmann, O. & Gyllenberg, M.: Equations with infinite delay: blending the abstract and the concrete, *Journal of Differential Equations* **252** (2012) 819-851.
- [6] Diekmann, O., van Gils, S.A., Verduyn Lunel, S.M. and Walther, H.-O.: *Delay Equations. Functional, Complex, and Nonlinear Analysis*, Springer-Verlag, New York, 1995.
- [7] Diekmann, O., Gyllenberg, M., Huang, H., Kirkilionis, M., Metz, J.A.J., Thieme, H.R.: On the formulation and analysis of general deterministic structured population models: II. Nonlinear theory. *Journal of Mathematical Biology* **43** (2001) 157–189.
- [8] Diekmann, O., Getto, Ph. and Gyllenberg, M.: Stability and bifurcation analysis of Volterra functional equations in the light of suns and stars, *SIAM Journal on Mathematical Analysis* **39** (2007) 1023-1069.
- [9] G.A. Enciso & E.D. Sontag: On the stability of a model of testosterone dynamics, *Journal of Mathematical Biology* **49** (2004) 627–634.

- [10] W. Feller, On the integral equation of renewal theory, *Annals of Mathematical Statistics* **12** (1941) 243–267;
- [11] Fisher, R.A.: *The Genetical Theory of Natural Selection*. Clarendon Press, Oxford, 1930
- [12] Greiner, G. & Nagel, R.: Growth of cell populations via one-parameter semigroups of positive operators. In: *Mathematics applied to science* (Jerome Goldstein, Steven Rosencrans and Gary Sod, Eds.) pp. 79105, Academic Press, Boston, MA, 1988.
- [13] Gripenberg, G., Londen, S.-O., Staffans, O.: *Volterra Integral and Functional Equations*, Cambridge University Press, Cambridge, UK, 1990.
- [14] Gurney, W. S. C. & Nisbet, R. M.: Fluctuation periodicity, generation separation, and the expression of larval competition, *Theoretical Population Biology* **28** (1985) 150–180.
- [15] Gurney, W. S. C. & Nisbet, R. M.: *Ecological Dynamics*. Oxford University Press, 1998.
- [16] Haccou, P., Jagers, P. and Vatutin, V.A.: *Branching Processes: Variation, Growth, and Extinction of Populations*, Cambridge University Press, 2005.
- [17] Iannelli, M.: *Mathematical theory of age-structured population dynamics*. Giardini, Pisa, 1995.
- [18] Jagers, P.: *Branching Processes with Biological Applications*. John Wiley and Sons, London, 1975.
- [19] A.E. Jones et al.: Period to delay ratio near stability boundaries for systems with delayed feedback, *JMAA* **135** (1988) 354-368.
- [20] de Koeijer, A., Heesterbeek, H., Schreuder, B., Oberthür, R., Wilesmith, J., van Roermund, H., de Jong, M.: Quantifying BSE control by calculating the basic reproduction ratio R_0 for the infection among cattle, *Journal of Mathematical Biology* **48** (2004) 1-22.
- [21] Koiyman, S.A.L.M & Metz, J.A.J.: On the dynamics of chemically stressed populations: the deduction of population consequences from effects on individuals. *Ecotox. Environ. Saf.* **8** (1984) 254-274.
- [22] Metz, J.A.J. & Diekmann, O. (Eds.): *The Dynamics of Physiologically Structured Populations*. Springer-Verlag, Berlin, 1986.

- [23] Nisbet, R.M. & Gurney, W.S.C.: *Modelling Fluctuating Populations*. John Wiley and Sons, Chechester, 1982
- [24] Kooijman, S.A.L.M: *Dynamic Energy Budget Theory for Metabolic Organisation*. Cambridge University Press, Third Edition, 2010.
- [25] O.A. Popova & L.A. Sytina: Food and feeding relations of eurasian perch (*Perca fluviatilis*) and pikeperch (*Stizostedion lucioperca*) in various waters of USSR. *Journal of the Fisheries Research Board of Canada* **10** (1977) 1559-1570
- [26] M.G. Roberts & J.A.P. Heesterbeek, Model-consistent estimation of the basic reproduction number from the incidence of an emerging inflection, *Journal of Mathematical Biology* **55** (2007) 803-816.
- [27] A.M. de Roos et al.
- [28] A.M. de Roos, Demographic analysis of continuous-time life-history models, *Ecology Letters* **11** (2008) 1-15
- [29] Thieme HR (1988) Well-posedness of physiologically structured population models for *Daphnia magna*, *Journal of Mathematical Biology* **26** 299-317.
- [30] Tuljapurkar, S.: *Population Dynamics in Variable Environments*, Springer-Verlag, 1990.
- [31] Tuljapurkar, S. & Caswell, H (Eds.): *Structured-Population Models in Marine, Terrestrial, and Freshwater Systems*. Springer-Verlag, 1997.
- [32] J. Wallinga & M. Lipsitch. How generation intervals shape the relationship between growth rates and reproductive numbers, *Proceedings of the Royal Society B* **274** (2007) 599–604.