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A Singular Perturbation Theorem for Evolution Equations and Time-scale Arguments for Structured Population Models

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In this paper we present a generalization of a particular case of Tikhonov's singular perturbation theorem to Banach spaces. From this we obtain sufficient conditions under which a faithful simplification by a time-scale argument is justified for age-structured population models. An explicit formulation for the approximating, ordinary differential equation, model is obtained. Finally, we describe the precise class of structured population models for which we conjecture that a similar result holds.

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1. Introduction and motivation

General structured population models have the unfortunate tendency to be very complicated. It is therefore important to investigate systematic simplification methods for this class of models. One would like to elucidate under which conditions the general problem can be simplified in such a way that the essential information one would like to obtain from the model, is not lost. In [10] a number of general principles of model simplification are mentioned that operate on the level of the population (we are not concerned here with principles that pertain to the level of the individuals). One example in case is the so-called linear chain trickery: for some physiologies of the individuals the original infinite dimensional evolution system allows a representation as a finite set of ordinary differential equations, which is faithful to the full structured model as far as input-output relations on the population level are concerned. In [9], necessary and sufficient conditions are given for a structured population model to be linear

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chain trickable. In principle, this is the only exact ordinary differential equation representation possible.

However, an idea that seems to hover in the back of most people's minds when using ordinary differential equation population models is not linear chain trickery, but the exploitation of differences in time-scale. One implicitly argues that the use of an ordinary differential equation model is justified if the time-scale of changes in the population size is much slower than the time-scale at which the stable i-state distribution is reached. The motivation behind the present paper is that one would like to have a set of sufficient conditions for the implicit argument to be valid in the case of general structured population models.

That however, is still wishful thinking. In this paper we give such a set of sufficient conditions for general *age-structured* populations. In the process we obtain a function Q, which tells us exactly how the overall population parameters are linked to the parameters at the individual level. From a modelling point of view one should, instead of writing down an ordinary differential equation model right away, start with the age-structured model which is entirely based on mechanistic reasoning at the individual level (individual parameters are things we can measure). Subsequently, the time-scale argument in this paper gives the precise form of the ordinary differential equation model that approximates the full model. It would in general be very difficult, if not impossible, to write down the correct ordinary differential equation from scratch.

Time-scale arguments are most frequently used in finite systems of ordinary differential equations arising in applications wherever different time-scales can be distinguished, or introduced in some natural way (see e.g. [12]). The idea is that when one time-scale is very fast, as compared to the other time-scales inherent in the system, one assumes that the processes on the fast time-scale are actually in equilibrium at all times (however, this equilibrium changes slowly as the slower processes change in time). This then leads to a system of ordinary differential equations of lower dimension, capturing the essentials of the original bigger system. The equilibrium assumption is usually called the quasi-(or pseudo)-steady-state hypothesis. The mathematical counterpart of this intuitive notion starts by scaling the original system of differential equations in such a way that it can be rewritten as a singular perturbation problem. A precise set of sufficient conditions for the quasi-steady-state hypothesis to be valid, for finite dimensional systems of ordinary differential equations, is then given by the singular perturbation theorem of Tikhonov [13]. Models for structured populations come in the form of first order hyperbolic partial differential equations with an integral-type boundary condition, so the original Tikhonov theorem and the usual generalizations of it in the literature (see e.g. [7]) do not apply.

In section 2 a particular case of Tikhonov's theorem is generalized to infinite dimensional spaces, in such a way as to make it applicable to structured population models. Apart from this we think that the theorem is interesting in its own right. Based on the Tikhonov result we give, in section 3, a set of sufficient conditions for the quasi-steady-state hypothesis to hold for age-structured population models. Finally, we give a precise description of a more general class of structured population models for which we explicitly calculate the above mentioned function Q. We conjecture that, for this more general class, our approximation result still holds.

2. The singular perturbation theorem

The proof of Theorem 2.1 below makes frequent use of Gronwall's Lemma. We state it explicitly for easy reference, for a proof see e.g. [5].

Gronwall's Lemma: *Assume that* a, b, $u : [\tau, T] \to \mathbb{R}_+$ *are continuous functions,* $a \in C^1$, *such that*

$$u(t) \leq a(t) + \int_\tau^t b(s)u(s)ds \quad \text{for all} \quad t \in [\tau, T] .$$

Then for $t \in [\tau, T]$ one can estimate u as follows

$$u(t) \leq a(\tau)\exp\left(\int_\tau^t b(s)ds\right) + \int_\tau^t \dot{a}(s)\exp\left(\int_s^t b(\sigma)d\sigma\right)ds .$$

In case b is constant, then the estimate reduces to

$$u(t) \leq a(\tau)e^{b(t-\tau)} + \int_\tau^t \dot{a}(s)e^{b(t-s)}ds .$$

We consider a system of evolution equations which depend on a small parameter $\varepsilon \in [0, \varepsilon_0]$ of the following form

$$\dot{\gamma}_\varepsilon(t) = f(\gamma_\varepsilon(t), w_\varepsilon(t), \varepsilon) \tag{2.1a}$$

$$\varepsilon \dot{w}_\varepsilon(t) = A_0 w_\varepsilon(t) + \varepsilon F(\gamma_\varepsilon(t), w_\varepsilon(t), \varepsilon) \tag{2.1b}$$

with an initial condition

$$\gamma_\varepsilon(0) = \bar{\gamma} \ , \ w_\varepsilon(0) = \bar{w} . \tag{2.1c}$$

The unknown function γ_ε has values in $\mathbb{R}^m$, while w_ε has values in an (infinite dimensional) Banach space X. We assume that A_0, f and F satisfy the following hypotheses:

1). A_0 generates a strongly continuous semigroup $\{T_0(t)\}$ on X which is assumed to be exponentially stable, i.e. there are constants $M_1 \geq 1$, $\sigma > 0$ such that $\|T_0(t)\| \leq M_1 e^{-\sigma t}$ for all $t > 0$.

2). Both $f : \mathbb{R}^m \times X \times [0, \varepsilon_0] \to \mathbb{R}^m$ and $F : \mathbb{R}^m \times X \times [0, \varepsilon_0] \to X$ are continuous and locally Lipschitz with respect to the first two variables, uniformly in ε.

These assumptions ensure that (2.1) has unique mild solutions for every ε and we always assume that these are maximal solutions, i.e. cannot be extended to a larger time interval. The notion of *mild solution* is the usual one, based on the variation-of-constants formula or (equivalently) satisfies the integrated version of (2.1), i.e.

$$\gamma_\varepsilon(t) = \bar{\gamma} + \int_0^t f(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon)ds \tag{2.2a}$$

$$w_\varepsilon(t) = T_0\left(\frac{t}{\varepsilon}\right)\bar{w} + \int_0^t T_0\left(\frac{t-s}{\varepsilon}\right)F(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon)ds \tag{2.2b}$$

(see [11] for further details and for conditions which ensure that a mild solution is a clasical one). We want to describe the behaviour of the solutions letting $\varepsilon \to 0$. This is a problem of *singular perturbation* of a similar kind as considered by Tikhonov [13]. Formally one expects that γ_ε converges to the solution of the following ordinary differential equation

$$\dot{\gamma}(t) = f(\gamma(t), 0, 0) \quad , \quad \gamma(0) = \bar{\gamma} \tag{2.2c}$$

while w_ε tends to 0 as $\varepsilon \to 0$. This actually is true, more precisely, the main result reads as follows.

Theorem 2.1 *Let $\gamma_0 : [0,T] \to \mathbb{R}^m$ be a solution of (2.2c). Then for every $\delta > 0$ there exists $\varepsilon_1 > 0$ such that for $\varepsilon \in (0, \varepsilon_1]$ the solution γ_ε, w_ε of (2.1) exists on $[0,T]$ and satisfies the following estimates*

$$|\gamma_\varepsilon(t) - \gamma_0(t)| \leq \delta \quad \text{for all} \quad t \in [0,T] \tag{2.3a}$$

$$\|w_\varepsilon(t)\| \leq \delta \quad \text{for all} \quad t \in [\delta, T] \tag{2.3b}$$

Note that the convergence of γ_ε is uniformly on the whole interval, while w_ε converges uniformly merely on intervals bounded away from 0. More cannot be proved since, in general, $w_\varepsilon(0) = \bar{w} \neq 0$.

We will prove this result in several steps, which we formulate as lemmas. The structure of the proof is as follows. We give an estimate for $|\gamma_\varepsilon(t) - \gamma_0(t)|$ in terms of $\|w_\varepsilon(t)\|$ in Lemma 2.5. Subsequently we estimate $\|w_\varepsilon(t)\|$ in terms of $|\gamma_\varepsilon(t) - \gamma_0(t)|$ in Lemma 2.6. These estimates are then combined in the main part of the proof.

As a consequence of the first lemma below we can assume that the solutions of (2.1) are defined on all $\mathbb{R}_+$.

Lemma 2.2 *If Theorem 2.1 is true for f and F globally Lipschitz (w.r.t the first two variables), then it is also true for f and F locally Lipschitz (w.r.t the first two variables).*

Proof: We start by recalling two standard facts:

1) Given a compact set K and an open set V in a Banach space Y satisfying $K \subset V$, then there exists a globally Lipschitz function $\varphi : Y \to \mathbb{R}_+$ such that $\{y \in Y : \varphi(y) = 1\}$ is a neighbourhood of K and $\operatorname{supp} \varphi \subset V$.

2) If g is locally Lipschitz on a Banach space Y, then to every compact set $K \subset Y$ there exist a bounded open set $V \supset K$ such that the restriction $g_{|V}$ is globally Lipschitz on V. Moreover, if g_ε is locally Lipschitz uniformly with respect to $\varepsilon \subset [0, \varepsilon_0]$, then V can be chosen independent of ε and the restrictions $g_{\varepsilon|V}$ have a common Lipschitz constant.

Thus for the compact set $\{(\gamma_0(s), 0) : s \in [0,T]\} \subset Y := \mathbb{R}^m \times X$ there exists a bounded open set $V \supset K$ such that all the restrictions $f_{\varepsilon|V}$ and $F_{\varepsilon|V}$ are Lipschitz with a common Lipschitz constant. Choosing to K and V a globally Lipschitz function $\varphi : \mathbb{R}^m \times X \to \mathbb{R}_+$ as described in 1) above, and defining $\tilde{f}$, $\tilde{f}(\beta, x, \varepsilon) := \varphi(\beta, x) f(\beta, x, \varepsilon)$ and $\tilde{F}$, $\tilde{F}(\beta, x, \varepsilon) := \varphi(\beta, x) F(\beta, x, \varepsilon)$ then $\tilde{f}$ and $\tilde{F}$ are globally Lipschitz with respect to the first two variables, uniformly in ε. Moreover, f and $\tilde{f}$ coincide on a neighbourhood of K and the same holds for F and $\tilde{F}$. Thus a mild solution $(\tilde{\gamma}_\varepsilon(.), \tilde{\omega}_\varepsilon(.))$ of problem (2.1) for $\tilde{f}$ and $\tilde{F}$ which is close to $(\gamma_0(.), 0)$ is also the mild solution of the original problem. ◇

From here on in this section we will always assume that f and F are globally Lipschitz with respect to the first two variables with constant L. Hence we do not have to care on the domains of the solutions and have estimates uniform with respect to ε. This is stated in the next lemma.

Lemma 2.3 *Assume f and F are globally Lipschitz with constant L. Then (2.1) has solutions defined on $\mathbb{R}_+$ and the following estimate holds:*

$$|\gamma_\varepsilon(t)| + \|w_\varepsilon(t)\| \leq \left(|\bar{\gamma}| + M_1 \|\bar{w}\| + N_1 (t + \frac{1}{L})\right) \exp(L(1 + M_1)t) \tag{2.4}$$

where M_1 is as in hypothesis 1 and $N_1 := \sup_{0 \leq \varepsilon \leq \varepsilon_0} \{|f(0,0,\varepsilon)| + M_1 \|F(0,0,\varepsilon)\|\}$.

Proof: From the variation-of-constants formulas (2.2a-b) we obtain

$$\begin{aligned}|\gamma_\varepsilon(t)| + \|w_\varepsilon(t)\| &\le |\bar\gamma| + \int_0^t |f(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon)|ds + \|T_0(\frac{t}{\varepsilon})\bar w\| \\ &\quad + M_1 \int_0^t \|F(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon)\|ds \\ &\le (|\bar\gamma| + M_1\|\bar w\|) + \int_0^t |f(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon) - f(0,0,\varepsilon)|ds \\ &\quad + M_1 \int_0^t \|F(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon) - F(0,0,\varepsilon)\|ds + tN_1.\end{aligned}$$

Now use the Lipschitz continuity of F and f and apply Gronwall's Lemma to the function $t \mapsto |\gamma_\varepsilon(t)| + \|w_\varepsilon(t)\|$. ♢

Lemma 2.4 *For every $\delta > 0$ there exist $\tau_1 > 0$ and $\varepsilon_1 > 0$ such that for $\varepsilon \le \varepsilon_1$ we have*

$$\|w_\varepsilon(\varepsilon\tau_1)\| < \delta \quad \text{and} \tag{2.5a}$$

$$t \le \varepsilon\tau_1 \Rightarrow |\gamma_\varepsilon(t) - \bar\gamma| < \delta. \tag{2.5b}$$

Proof: We choose τ_1 such that $\|T_0(\tau_1)\bar w\| < \frac{\delta}{2}$. This is possible due to assumption 1. By Lemma 2.3 $\{(\gamma_\varepsilon(s), w_\varepsilon(s)) : 0 \le s \le \tau_1, 0 < \varepsilon \le \varepsilon_0\}$ is bounded in $\mathbb{R}^m \times X$. Thus $|f(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon)|$ and $\|F(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon)\|$ are uniformly bounded by a constant N say. The variation-of-constants formulas imply

$$|\gamma_\varepsilon(t) - \bar\gamma| \le Nt$$

$$\|w_\varepsilon(t) - T_0(\frac{t}{\varepsilon})\bar w\| \le N \int_0^t \|T_0(\frac{t-s}{\varepsilon})\|ds \le M_1 N t.$$

We can choose $\varepsilon_1 > 0$ such that $\varepsilon_1 N \tau_1 < \delta$ and $\varepsilon_1 M_1 N \tau_1 < \frac{\delta}{2}$. Then obviously (2.5b) is satisfied and for $\varepsilon \le \varepsilon_1$: $\|w_\varepsilon(\varepsilon\tau_1)\| \le \|w_\varepsilon(\varepsilon\tau_1) - T_0(\tau_1)\bar w\| + \|T_0(\tau_1)\bar w\| < \frac{\delta}{2} + \frac{\delta}{2} = \delta$. ♢

Lemma 2.5 *For $0 \le \tau < t$ the following estimate holds*

$$\begin{aligned}|\gamma_\varepsilon(t) - \gamma_0(t)| &\le \Big(|\gamma_\varepsilon(\tau) - \gamma_0(\tau)| + M_2(t,\varepsilon)\Big)\exp(L(t-\tau)) \\ &\quad + \int_\tau^t L\exp(L(t-s))\|w_\varepsilon(s)\|ds\end{aligned} \tag{2.6}$$

where $M_2(t,\varepsilon) \to 0$ for $\varepsilon \to 0$ uniformly on bounded $t-$intervals.

Proof: We have

$$\gamma_\varepsilon(t) - \gamma_0(t) = \gamma_\varepsilon(\tau) - \gamma_0(\tau) + \int_\tau^t (f(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon) - f(\gamma_0(s), 0, 0))ds\ .$$

Hence

$$\begin{aligned}|\gamma_\varepsilon(t) - \gamma_0(t)| &\le |\gamma_\varepsilon(\tau) - \gamma_0(\tau)| + \int_\tau^t |f(\gamma_0(s), 0, \varepsilon) - f(\gamma_0(s), 0, 0)|ds + \\ &\quad + \int_\tau^t |f(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon) - f(\gamma_0(s), 0, \varepsilon)|ds\end{aligned}$$

$$\leq |\gamma_\varepsilon(\tau) - \gamma_0(\tau)| + (t-\tau)\tilde{M}_2(t,\varepsilon) + \int_\tau^t L\|w_\varepsilon(s)\|ds + \int_\tau^t L|\gamma_\varepsilon(s) - \gamma_0(s)|ds$$

where $\tilde{M}_2(t,\varepsilon) := \sup_{0\leq s\leq t} |f(\gamma_0(s),0,\varepsilon) - f(\gamma_0(s),0,0)|$. Applying Gronwall's Lemma to the function $s \mapsto |\gamma_\varepsilon(s) - \gamma_0(s)|$ and the interval $[\tau, t]$, (hereby estimating $\tilde{M}_2(s,\varepsilon)$ by the 'constant' $\tilde{M}_2(t,\varepsilon)$!) yields

$$|\gamma_\varepsilon(t) - \gamma_0(t)| \leq |\gamma_\varepsilon(\tau) - \gamma_0(\tau)| \exp(L(t-\tau)) + \int_\tau^t (\tilde{M}_2(t,\varepsilon) + L\|w_\varepsilon(s)\|) \exp(L(t-s))ds \ .$$

From this the estimate (2.6) follows, with $M_2(t,\varepsilon) := \tilde{M}_2(t,\varepsilon)/L$. Note also that continuity of f implies that $\tilde{M}_2(t,\varepsilon)$ converges to 0 uniformly on bounded t-intervals. ◊

Lemma 2.6 *For ε sufficiently small ($\varepsilon < \frac{\sigma}{LM_1}$) and $0 \leq \tau < t$ the following estimate holds:*

$$\|w_\varepsilon(t)\| \leq M_1\|w_\varepsilon(\tau)\| + \varepsilon M_3(t) + \int_\tau^t LM_1 \exp\left((LM_1 - \frac{\sigma}{\varepsilon})(t-s)\right)|\gamma_\varepsilon(s) - \gamma_0(s)|ds \quad (2.7)$$

Here M_1, and σ are as in assumption 1 and $M_3(t)$ is a suitable constant not depending on ε.

Proof: The variation-of-constants formula yields

$$w_\varepsilon(t) = T_0(\frac{t-\tau}{\varepsilon})w_\varepsilon(\tau) + \int_\tau^t T_0(\frac{t-s}{\varepsilon})F(\gamma_\varepsilon(s), w_\varepsilon(s), \varepsilon)ds$$

hence

$$\|w_\varepsilon(t)\| \leq \|T_0(\frac{t-\tau}{\varepsilon})\|\|w_\varepsilon(\tau)\| + \int_\tau^t \|T_0(\frac{t-s}{\varepsilon})\|\|F(\gamma_0(s),0,\varepsilon)\|ds +$$
$$+ \int_\tau^t \|T_0(\frac{t-s}{\varepsilon})\|\|F(\gamma_\varepsilon(s), w_\varepsilon(s),\varepsilon) - F(\gamma_0(s),0,\varepsilon)\|ds \ .$$

We have $\|T_0(t)\| \leq M_1 \exp(-\sigma t)$ by assumption 1, F is Lipschitz with constant L and define $N(t) := \sup_{s\leq t} \|F(\gamma_0(s),0,\varepsilon)\|$. Then

$$\|w_\varepsilon(t)\| \leq M_1 \exp(-\frac{\sigma}{\varepsilon}(t-\tau))\|w_\varepsilon(\tau)\| + \int_\tau^t M_1 N(t) \exp(-\frac{\sigma}{\varepsilon}(t-s))ds +$$

$$+ \int_\tau^t LM_1 \exp(-\frac{\sigma}{\varepsilon}(t-s))|\gamma_\varepsilon(s) - \gamma_0(s)|ds + \int_\tau^t LM_1 \cdot \exp(-\frac{\sigma}{\varepsilon}(t-s))\|w_\varepsilon(s)\|ds \ .$$

Now we apply Gronwall's Lemma to the function $s \mapsto \exp(\frac{\sigma}{\varepsilon}s)\|w_\varepsilon(s)\|$ (hereby considering $N(t)$ as a constant) and obtain

$$\exp(\frac{\sigma}{\varepsilon}t)\|w_\varepsilon(t)\| \leq M_1 \exp(\frac{\sigma}{\varepsilon}\tau)\|w_\varepsilon(\tau)\| \exp(LM_1(t-\tau)) +$$

$$\int_\tau^t M_1 N(t) \exp(\frac{\sigma}{\varepsilon}s) \exp(LM_1(t-s))ds + \int_\tau^t M_1 L \exp(\frac{\sigma}{\varepsilon}s)|\gamma_\varepsilon(s) - \gamma_0(s)| \exp(LM_1(t-s))ds$$

From this one easily deduces (2.7), where we write $M_3(t) := M_1 N(t)/(\frac{\sigma}{\varepsilon} - LM_1)$. ◊

With the estimates proved in Lemma 2.5 and Lemma 2.6 and we can now give the proof of Theorem 2.1.

Proof of Theorem 2.1: To get an estimate on $|\gamma_\varepsilon(t)-\gamma_0(t)|$ we insert (2.7) in (2.6) thus obtaining

$$\begin{aligned}|\gamma_\varepsilon(t)-\gamma_0(t)| \le \Big(|\gamma_\varepsilon(\tau)-\gamma_0(\tau)| + M_2(t,\varepsilon)\Big)\exp(L(t-\tau))\\ +(M_1\|w_\varepsilon(\tau)\| + \varepsilon M_3(t))\frac{1}{L}(\exp(L(t-\tau))-1)+ \\ +\int_\tau^t L\exp(L(t-s))\int_\tau^s LM_1\exp\left((LM_1-\frac{\sigma}{\varepsilon})(s-r)\right)|\gamma_\varepsilon(r)-\gamma_0(r)|\,dr\,ds\end{aligned} \tag{2.8}$$

Introduce $\rho_\varepsilon := LM_1 - \frac{\sigma}{\varepsilon}$ (then $\rho_\varepsilon < 0$, provided that $\varepsilon < \frac{\sigma}{LM_1}$), and $M_4(\varepsilon) := LM_1/(L-\rho_\varepsilon)$ (then $M_4(\varepsilon) \to 0$ as $\varepsilon \downarrow 0$). The last term of (2.8) equals

$$\int_\tau^t LM_4(\varepsilon)\Big(\exp(L(t-s)) - \exp(-\rho_\varepsilon(t-s))\Big)|\gamma_\varepsilon(s)-\gamma_0(s)|\,ds$$

and can be estimated by

$$\int_\tau^t LM_4(\varepsilon)\exp(L(t-s))|\gamma_\varepsilon(s)-\gamma_0(s)|\,ds\ .$$

The remaining terms in (2.8) can be estimated by an expression of the form

$$\Big(M_1(|\gamma_\varepsilon(\tau)-\gamma_0(\tau)| + \|w_\varepsilon(\tau)\|) + M_5(\varepsilon)\Big)\exp(L(t-\tau))$$

where $M_5(\varepsilon)$ tends to zero for $\varepsilon \to 0$. Thus applying once more Gronwall's Lemma (to the function $t \mapsto \exp(-Lt)|\gamma_\varepsilon(t)-\gamma_0(t)|$) we obtain

$$|\gamma_\varepsilon(t)-\gamma_0(t)| \le \Big(M_1\left(|\gamma_\varepsilon(\tau)-\gamma_0(\tau)| + \|w_\varepsilon(\tau)\|\right) + M_5(\varepsilon)\Big)\exp(L(M_4(\varepsilon)+1)(t-\tau)) \tag{2.9}$$

Now given δ as in Theorem 2.1 we can choose, according to Lemma 2.4, ε_1 and τ_1 such that

$$|\gamma_\varepsilon(\varepsilon\tau_1)-\gamma_0(\varepsilon\tau_1)| + \|w_\varepsilon(\varepsilon\tau_1)\| < (M_1\exp(L(M_1+1)T))^{-1}\frac{\delta}{2}, \quad \forall\varepsilon \le \varepsilon_1.$$

Since $\lim_{\varepsilon\to 0} M_5(\varepsilon) = 0$ one can achieve (by making ε_1 smaller) that

$$M_1\left(|\gamma_\varepsilon(\varepsilon\tau_1)-\gamma_0(\varepsilon\tau_1)| + \|w_\varepsilon(\varepsilon\tau_1)\|\right) + M_5(\varepsilon) < (\exp(L(M_1+1)T))^{-1}\frac{\delta}{2}, \quad \forall\varepsilon \le \varepsilon_1. \tag{2.10}$$

From (2.2a) and the boundedness of $V := \{(\gamma_\varepsilon(s), w_\varepsilon(s)) : 0 \le s \le \tau_1,\ 0 \le \varepsilon \le \varepsilon_0\}$ it follows that

$$|\gamma_0(t) - \bar\gamma| \le Kt \tag{2.11}$$

for $K := \sup_V f(\gamma_\varepsilon(\sigma), w_\varepsilon(\sigma), \varepsilon)$. Now choose

$$\varepsilon < \min(\varepsilon_0, \varepsilon_1, \frac{\delta}{2\tau_1 K}, \frac{\sigma}{LM_1}).$$

Then the estimates (2.9) and (2.10) with $\tau := \varepsilon\tau_1$ give (2.3a) for $t \in [\varepsilon\tau_1, T]$. Furthermore estimate (2.11) together with Lemma 2.4 gives $|\gamma_\varepsilon(t)-\gamma_0(t)| \le |\gamma_\varepsilon(t)-\bar\gamma| + |\bar\gamma-\gamma_0(t)| < \delta$ for

$t \in [0, \varepsilon\tau_1]$. To prove (2.3$b$) one starts with inserting (2.6) in (2.7) and proceeds in a similar fashion. ◊

3. Time-scale arguments for structured populations

We start by briefly describing the nature of general models for (age)-structured populations. We refer to [8] for an extensive treatment of many aspects of model-building for structured populations.

Suppose the individuals that make up a certain population, are distinguished from one another on the basis of a certain set of characteristics, called the i-state. Let Ω denote the set of all possible i-states. In this paper we will take $\Omega \subset \mathbb{R}$. At the level of the individuals, a model would consist of a specification of birth- and death rates for individuals and a description of how the i-state of an individual changes with time. In general these rates of change will depend on the condition of the environment. One can think of, e.g. food availability, temperature, population density of predators (of course, what actually constitutes the environment depends on the nature of the i-states and the mechanisms that are taken into account). If the population, in turn, influences the condition of the environment, then our model becomes non-linear. We assume however that the future behaviour of an individual can be determined from its present state if the time evolution of the environment is known, so if the environment can be expressed as a *known* function of time, the model is linear.

We assume from now on that only the birth- and death rates are influenced by the environment, but that the rate of change of the i-state is not (so the key i-state variable we have in mind is age).

If the population, or rather the environment, is well mixed, the population state (p-state) corresponds to an element of some Banach space X of functions (or measures) over Ω. In our case we only consider $X = L_1(\Omega)$, the space of integrable functions on Ω, or $X = M(\Omega)$ the space of regular Borel measures of bounded variation on Ω (with the standard variation norm). In the latter case, the measures give, for each measurable subset of Ω, the total spatial density of individuals whose i-states are elements of that subset. From the model on the individual level one can, by doing the bookkeeping correctly, derive balance laws that describe the time evolution of the p-state. Basically this corresponds to the Kolmogorov forward equation from probability theory (for details see [3],[8],[9]). Let us denote the condition of the environment by a variable E taking values in some $\mathbb{R}^n$. The state u of our structured population then satisfies an abstract equation of the form

$$\frac{du}{dt}(t) = A(E(t))u(t), \quad u(0) = u^0, \tag{3.1}$$

where $A(\hat{E})$ is a linear, usually unbounded, operator on X for each possible fixed condition of the environment $\hat{E}$.

Our model should now be completed by specifying some output quantities. In our case these are necessarily of the form $\langle \psi, u \rangle$, where $\psi \in C_0(\Omega)$, the space of continuous functions on Ω that vanish at infinity (and $\langle \cdot, \cdot \rangle$ denotes the duality pairing between $M(\Omega)$ and its predual $C_0(\Omega)$). If Ω is bounded then one possibility is to take the total population size as a function of time $N(t) = \langle \Xi_\Omega, u \rangle$, where Ξ_Ω is the characteristic function on Ω. Finally, if the population and the environment influence each other then we have to specify the dynamics of the environment.

If the environment is constant, then the problem (3.1) is linear. Assume that the operator A in (3.1) is the generator of a (positive) semigroup $\{S(t)\}$, $t \geq 0$, on X and has a strictly dominant eigenvalue λ_d. Let ϕ_d be the eigenvector associated with λ_d, and let ϕ_d^* be the corresponding eigenvector of the adjoint of A. We normalize such that $\|\phi_d\| = 1$ and $\langle \phi_d, \phi_d^* \rangle = 1$. Under some conditions on the semigroup generated by A (irreducibility and a condition on the growth bound, see e.g. [6],[8]) one proves that there exist constants $\delta, M > 0$ such that for all $u \in X$ the following estimate holds

$$\|e^{-\lambda_d t} S(t)u - \langle u, \phi_d^* \rangle \phi_d\| \leq M e^{-\delta t} \|u\|,$$

$t \geq 0$. The eigenvector ϕ_d is called the *stable distribution* of the population over the i-state space Ω. The dominant eigenvalue λ_d has the biological interpretation of the intrinsic growth rate of the total population (see [8]). So as $t \to \infty$, the distribution of individuals over the different i-states approaches ϕ_d and becomes fixed. The sizes of the various classes of individuals then only grow or diminish, depending on whether the total population size N grows or diminishes.

We now proceed with the time-scale argument for the type of structured population models described above for the case that $X = L_1(\Omega)$. We attach a subscript ε to A in (3.1) for our special purpose, and we make the following assumptions.

I. $A_\varepsilon(E)u = A_0 u + H_\varepsilon(E)u$, and

a.) A_0 is a linear operator and generates a C_0-semigroup $\{S_0(t)\}$ on X; the strictly dominant eigenvalue of A_0 is zero; there exist unique (up to scalars) eigenfunctions $\phi_0 \in X$ and $\phi_0^* \in X^*$, corresponding to the eigenvalue 0, for A_0 and its adjoint A_0^* respectively (we normalize such that $\langle \phi_0, \phi_0^* \rangle = 1$, and $\|\phi_0\| = 1$); the following estimate for the semigroup $\{S_0(t)\}$ holds

$$\|S_0(t)u - \langle u, \phi_0^* \rangle \phi_0\| \leq M e^{-\delta t}$$

for some $M \geq 1, \delta > 0$.

b.) $H : [0, \varepsilon_0] \times \mathbb{R}^n \times X \to X$ is locally Lipschitz continuous in the last two arguments.

c.) $H_\varepsilon(E)u \to 0$ in the strong sense for $\varepsilon \downarrow 0$; the limit

$$\lim_{\varepsilon \to 0} \frac{1}{\varepsilon} \langle H_\varepsilon(E)\phi_0, \phi_0^* \rangle$$

exists.

II. Either

a.) Environmental feedback is direct: $E = G(u)$ for some sufficiently nice operator G, or

b.) Environmental feedback is indirect: $\frac{dE}{dt} = K(u, E)$. Here K satisfies the condition: $\forall\, u \in X\ \exists\, !G(u) \in \mathbb{R}^n$ such that $K(u, G(u)) = 0$ and $E = G(u)$ is a globally stable steady state of $\frac{dE}{dt} = K(u, E)$.

Let $u_\varepsilon(t)$ denote the solution to (3.1) (subject to the conditions I, II) at time t. The fact that a mild solution u_ε exists follows from the theory of semi-linear evolution systems [11].

Theorem 3.1 *Under assumptions I, II the following holds*

$\forall\, T > 0$ we have $\|u_\varepsilon(t/\varepsilon) - N(t)\phi_0\| \to 0$ for $\varepsilon \downarrow 0$ on $(0, T]$, uniformly on intervals bounded away from zero. Here N denotes the total population size when the population-state has reached its stable distribution ϕ_0, and N is the solution of

$$\frac{dN}{dt}(t) = \lim_{\varepsilon \downarrow 0} \frac{1}{\varepsilon} \langle H_\varepsilon(G(N\phi_0))\phi_0, \phi_0{}^* \rangle N =: Q(N)N, \qquad N(0) = \langle u^0, \phi_0^* \rangle. \tag{3.2}$$

Any other population output, specified by some $\psi \in C_0(\Omega)$ *is obtained as* $N(t)\langle\psi, \phi_0\rangle$.

Proof: We first prove the result under assumptions I, IIa. We suppress the subscript ε below, but keep in mind that our functions depend on ε.

Decompose X as

$$X = \mathbb{R} \oplus Y$$

where $P : X \to Y$ is the projection given by

$$Pu = u - \langle u, \phi_0^* \rangle \phi_0.$$

Write $Pu =: \tilde{w}$ and $\langle u, \phi_0^* \rangle =: \tilde{\gamma}$ then $u = \tilde{\gamma}\phi_0 + \tilde{w}$ with $\tilde{\gamma} : \mathbb{R}_+ \to \mathbb{R}$ and $\tilde{w} : \mathbb{R}_+ \to Y$. Then (3.1) is transformed into the system

$$\tilde{\gamma}' = \langle H_\varepsilon(E)(\tilde{\gamma}\phi_0 + \tilde{w}), \phi_0^* \rangle =: H_0(\varepsilon, \tilde{\gamma}, \tilde{w}) \tag{3.3}$$
$$\tilde{w}' = B_0\tilde{w} + P(H_\varepsilon(E)(\tilde{\gamma}\phi_0 + \tilde{w})) =: H_1(\varepsilon, \tilde{\gamma}, \tilde{w}). \tag{3.4}$$

In (3.4) the operator B_0 is the restriction of A_0 to Y. Furthermore we define a semigroup $\{T_0(t)\}$ as the restriction of $S_0(t)$ to Y. It is easy to see that S_0 and P, and A_0 and P, commute, so $\{T_0(t)\}$ is actually the C_0-semigroup generated by B_0. By assumption Ia this semigroup is exponentially stable.

If we now scale time with a factor $1/\varepsilon$ and put $\gamma(t) := \tilde{\gamma}(t/\varepsilon)$ and $w(t) := \tilde{w}(t/\varepsilon)$, then the system reads

$$\gamma' = f(\varepsilon, \gamma, w) \tag{3.5}$$
$$\varepsilon w' = B_0 w + \varepsilon F(\varepsilon, \gamma, w), \tag{3.6}$$

where $f(\varepsilon, \gamma, w) := \frac{1}{\varepsilon} H_0(\varepsilon, \gamma, w)$ and $F(\varepsilon, \gamma, w) := \frac{1}{\varepsilon} H_1(\varepsilon, \gamma, w)$. Due to the assumptions on H we have that f and F are continuous and locally Lipschitz in the last two arguments, and that both $f(0,0,0)$ and $F(0,0,0)$ are zero.

We have transformed our original problem into the frame of the singular perturbation result from section 2, system (2.1). Denote the solution to the unperturbed form of equation (3.5) by $N(t)$. The only solution to the unperturbed form of equation (3.6) is $w(\gamma) \equiv 0$. Application of Theorem 1 to the system (3.5, 3.6) now gives

$$\begin{aligned} \|u_\varepsilon(t/\varepsilon) - N(t)\phi_0\| &= \|\tilde{\gamma}(t/\varepsilon)\phi_0 + \tilde{w}(t/\varepsilon) - N(t)\phi_0\| \\ &= \|\gamma(t)\phi_0 + w(t) - N(t)\phi_0\| \\ &\leq \|w\| + \mid \gamma(t) - N(t) \mid \|\phi_0\| \to 0 \end{aligned}$$

uniformly on $(0, T]$, and the first part of the theorem follows.

The proof of the theorem for the case of assumptions I, IIb is completely analogous to the one given above. Instead of the single equation (3.1) we then treat the system

$$\frac{dz}{dt} = Vz, \qquad z(0) = z^0,$$

where $z \in Z := X \times \mathbb{R}^m$ is the vector $z = \binom{u}{E}$, and $V : Z \to Z$ is an operator that maps the vector z into $Vz = \binom{A_\varepsilon(E)u}{G(u,E)}$. As above we decompose our space as

$$Z = \mathbb{R} \oplus \mathcal{P}Z,$$

where $\mathcal{P}$ is the projection given by

$$\mathcal{P}\begin{pmatrix} u \\ E \end{pmatrix} := \begin{pmatrix} u \\ E \end{pmatrix} - \begin{pmatrix} \langle u, \phi_0^* \rangle \phi_0 \\ 0 \end{pmatrix}.$$

The rest of the proof is a straightforward analogy to the case of assumptions I, IIa. ◇

Let us explain, in somewhat more detail, what the gist of the result is. Let E_0 denote the 'virgin environment', i.e. the condition of the environment when the population that we study is not 'present'. Then the auxiliary parameter ε can, for example, be interpreted as the inverse of the doubling time for the population after introduction into E_0 (i.e. a measure for the time scale of population growth). So if population growth is slow, then ε is small. If $\varepsilon = 0$ then the operator that describes the (abstract) time-evolution is given by A_0. Our assumptions assure that the solution u will approach a stable distribution of individuals over the i-state space, and that this distribution is given by the eigenvector ϕ_0 of A_0 corresponding to the dominant eigenvalue $\lambda_d = 0$. For $\varepsilon \downarrow 0$ the population growth becomes slower and slower and the ratio between the time-scale for convergence of the p-state to its stable distribution, and the time-scale of changes in the total population size, continues to increase. Theorem 3.1 gives sufficient conditions for the quasi-steady-state hypothesis that the population state is *always* in its stable age distribution. The solution $u(t,a)$ is then approximated by $N(t)\phi_0(a)$.

Remark

Instead of $L_1(\Omega)$ it is often biologically speaking more reasonable to take $M(\Omega)$ (which is a dual space Y^*, say) as p-state space for our age-structured population in Theorem 2 and the assumptions preceding it. In that case we do not have that A_0 generates a C_0-semigroup on Y^*, but that A_0 is the weak*-generator of a weak*-semigroup $\{S_0(t)\}$ on Y^*. We then make use of the $(\odot, *)$-formalism of Clément et al. [1,2,3] for the handling of semilinear evolution problems. The perturbation H is then viewed as a mapping from $[0, \varepsilon_0] \times \mathbb{R}^n \times Y^\odot \to Y^*$, where $Y^\odot = L_1(\Omega)$ in our case, and it is defined as that part of Y^* where $\{S_0(t)\}$ *is* strongly continuous. In [1,2,3] it is shown that a mild solution u, i.e. based on a variation of constants formula, to (3.1) exists and is unique. The proof of our original perturbation result Theorem 2.1 only uses this fact, so the proof carries over verbatim to the weak*-continuous case. In the same fashion, the proof of our time-scale argument Theorem 3.1 carries over to the weak*-continuous case.

For applying Theorem 3.1 to simplify 'real' structured population models we have to be able to express the function $Q(N)$ in terms of the basic parameters that relate to the level of the individuals. Actually this calculation can be carried out for a larger class of models than those that satisfy the assumptions of Theorem 3.1. We describe this class and the calculation of Q below.

Assume that we have an i-state space $\Omega \subset \mathbb{R}$, and that all individuals are born with the same i-state, x^0. We regard the following differential operator on $L_1(\Omega)$,

$$(A(E)n)(x) := -\frac{\partial g(x,E)n(x)}{\partial x} - \mu(x,E)n(x), \tag{3.7}$$

with boundary condition

$$g(x^0, E)n(t, x^0) = \int_\Omega \beta(x,E)n(t,x)dx,$$

describing the birth of new individuals. We assume that the environment E is coupled to the population-state as in hypothesis IIa or IIb preceding Theorem 3.1, for some G or K.

The functions $g(\cdot,E), \mu(\cdot,E)$, and $\beta(\cdot,E)$ are elements of $L_\infty(\Omega)$ and describe the rate of change of the i-state x, the death-rate of individuals, and the birth-rate of individuals, respectively.

We introduce a small parameter ε by making the following assumptions on g, μ and β

$$g(x,E) = g_0(x) + \varepsilon g_1(x,E) + o(\varepsilon), \tag{3.8}$$

$$\mu(x,E) = \mu_0(x) + \varepsilon \mu_1(x,E) + o(\varepsilon), \tag{3.9}$$

$$\beta(x,E) = \beta_0(x) + \varepsilon \beta_1(x,E) + o(\varepsilon), \tag{3.10}$$

where the index '0' indicates evaluation of the function at $\varepsilon = 0$, and the index '1' indicates evaluating $\frac{\partial}{\partial \varepsilon}$ of the function at $\varepsilon = 0$. If we write $A_\varepsilon(E)$ for the operator in (3.7) with (3.8) and (3.9) substituted, then $A_\varepsilon(E)n = A_0 n + H_\varepsilon(E)n$ with

$$(A_0 n)(x) = -\frac{\partial g_0(x)n(x)}{\partial x} - \mu_0(x)n(x), \tag{3.11}$$

with boundary condition $g_0(x^0)n(x^0) = \int_\Omega \beta_0(x)n(x)dx$, and

$$\big(H_\varepsilon(E)n\big)(x) = -\varepsilon\frac{\partial g_1(x,E)n(x)}{\partial x} - \varepsilon\mu_1(x,E)n(x) + o(\varepsilon). \tag{3.12}$$

with boundary condition $\varepsilon g_1(x^0,E)n(x^0) = \varepsilon \int_\Omega \beta_1(x,E)n(x)dx + o(\varepsilon)$.

We proceed with describing how Q can be expressed in the parameters of (3.7). As a preliminary step we consider the age-representation of the i-state for the case of a fixed environment $\hat{E}$. Switching to this representation is allowed because everybody is born equal (see [8]). Introduce an auxilliary function $X(a,\hat{E})$ that is the solution of the ODE

$$\frac{dX}{da} = g(X,\hat{E}), \quad X(0,\hat{E}) = x^0,$$

that describes the changes in the i-state variable x with the increasing age of the individual. Let furthermore

$$\mathcal{F}(a,\hat{E}) = e^{-\int_0^a \mu(X(\alpha,\hat{E}),\hat{E})d\alpha},$$

which is the probability that, in environment $\hat{E}$, the individual is still alive at age a. The basic reproduction ratio, i.e. the expected number of future offspring produced by a newborn individual, can then be calculated as

$$R(\varepsilon,\hat{E}) = \int_0^\infty \beta(X(a,\hat{E}),\hat{E})\mathcal{F}(a,\hat{E})da.$$

and the average age at childbearing as

$$m(\varepsilon,\hat{E}) = \frac{1}{R(\varepsilon,\hat{E})}\int_0^\infty a\beta(X(a,\hat{E}),\hat{E})\mathcal{F}(a,\hat{E})da. \tag{3.13}$$

As in (3.8-3.10) we write $X = X_0 + \varepsilon X_1 + o(\varepsilon)$ then X_0 is the solution of

$$\frac{dX_0}{da} = g_0(X_0), \tag{3.14}$$

and X_1 is the solution of

$$\frac{dX_1}{da} = \frac{d}{dX}(g_0(X_0))X_1 + g_1(X_0, \hat{E}). \tag{3.15}$$

Furthermore we write $R(\varepsilon, \hat{E}) = R_0 + \varepsilon R_1(\hat{E}) + o(\varepsilon)$ and $m(\varepsilon, \hat{E}) = m_0 + O(\varepsilon)$. Then R_0, R_1 and m_0 can be calculated in a straight forward way in terms of X_0, X_1 and the parameters. We find $R_0 = \int_0^\infty \beta_0(X_0(a))\mathcal{F}_0(a)da$, where $\mathcal{F}_0(a) = \exp(-\int_0^a \mu_0(X_0(\alpha)d\alpha)$ and

$$m_0 = \int_0^\infty a\mathcal{F}_0(a)\beta_0(X_0(a))da, \tag{3.16}$$

and for R_1

$$R_1(\hat{E}) = \int_0^\infty \mathcal{F}_0(a)\Big[\frac{d}{dX}(\beta_0(X_0(a)))X_1(a, \hat{E}) - \beta_1(X_0(a), \hat{E}) \tag{3.17}$$
$$- \beta_0(X_0(a)) \int_0^a \frac{d}{dX}(\mu_0(X_0(\alpha)))X_1(\alpha, \hat{E})d\alpha - \mu_1(X_0(\alpha), \hat{E})d\alpha\Big] da.$$

We now have all the ingredients to determine Q. We first show that Q describes the growth of the population on the slow time-scale. We assume that, for $\varepsilon = 0$, the individuals on average only replace themselves in the population, i.e. $R_0 = 1$. This implies that A_0 has dominant eigenvalue zero. Let ϕ_0 and ϕ_0^* be the eigenvectors of A_0 and A_0^* corresponding to zero, with $\langle \phi_0, \phi_0^* \rangle = 1$, and $\|\phi_0\| = 1$. We expand the dominant eigenvalue of $A_\varepsilon(\hat{E})$ in ε as above, i.e. we write formally $\lambda_d(\varepsilon, \hat{E}) = \varepsilon\lambda_1(\hat{E}) + o(\varepsilon)$ ($\lambda_0 = 0$, by assumption). The term $\lambda_1(\hat{E})$ describes the growth of the population, in dependence of the environment, on the slow time-scale.

Proposition 3.2 *For the differential operator $A_\varepsilon(\hat{E})$ with A_0 and $H_\varepsilon(\hat{E})$ defined by (3.11) and (3.12) respectively, the following holds*

$$\lambda_1(\hat{E}) = \lim_{\varepsilon \downarrow 0} \frac{1}{\varepsilon}\lambda_d(\varepsilon, \hat{E}) = \lim_{\varepsilon \downarrow 0} \frac{1}{\varepsilon}\langle H_\varepsilon(\hat{E})\phi_0, \phi_0^* \rangle = Q(N).$$

Proof: We expand the dominant eigenvector $\phi_d(\varepsilon, \hat{E})$ of $A_\varepsilon(\hat{E})$ formally as $\phi_d(\varepsilon, \hat{E}) = \phi_0 + \varepsilon\phi_1(\hat{E}) + o(\varepsilon)$. Furthermore we write $H_\varepsilon(\hat{E}) = \varepsilon H(\hat{E}) + o(\varepsilon)$ as suggested by (3.12). Then $A_\varepsilon(\hat{E})\phi_d(\varepsilon, \hat{E}) = \lambda_d(\varepsilon, \hat{E})\phi_d(\varepsilon, \hat{E})$ can be written as

$$\big(A_0 + \varepsilon H(\hat{E})\big)\big(\phi_0 + \varepsilon\phi_1(\hat{E})\big) = \varepsilon\lambda_1(\hat{E})\big(\phi_0 + \varepsilon\phi_1(\hat{E})\big) + o(\varepsilon),$$

which leads to

$$A_0\phi_0 + \varepsilon A_0\phi_1(\hat{E}) + \varepsilon H(\hat{E})\phi_0 = \varepsilon\lambda_1(\hat{E})\phi_0 + o(\varepsilon).$$

Taking the duality pairing on both sides with ϕ_0^* and using $A_0\phi_0 = 0 = A_0^*\phi_0^*$ we finally find

$$\langle H(\hat{E})\phi_0, \phi_0^* \rangle = \lambda_1(\hat{E}) + o(\varepsilon)$$

which gives the desired result. ◊

Since $\dim \Omega = 1$, the characteristic equation of $A(\hat{E})$ is then a scalar equation. If $A_\varepsilon(\hat{E})$ satisfies the assumptions of Theorem 3.1 then we can calculate $\lambda_d(\varepsilon, \hat{E})$ from the characteristic equation. However, if we try the same for the more general situation of (3.11-3.12) we run into trouble. The characteristic equation is given by

$$1 = \int_{\Omega} \frac{\beta(x,\hat{E})}{g(x,\hat{E})} e^{-\int_{x^0}^{x} \frac{\mu(\xi,\hat{E})+\lambda}{g(\xi,\hat{E})} d\xi} dx, \tag{3.18}$$

which has only one real solution. To obtain an approximation of λ one could substitute (3.8)-(3.10) and then write λ explicitly. However, if we let $\varepsilon \downarrow 0$ the domain of integration can change! If x, for example, means 'size', then it may well be that there is a maximal size x^m such that $\Omega = [x^o, x^m]$, and that the value of x^m is influenced by the environment which changes as we let $\varepsilon \to 0$. In the more general situation we therefore have to calculate λ_d in another way.

Proposition 3.3 *Let* $\dim \Omega = 1$, *assume* $R_0 = 1$ *and write* $\lambda_d(\varepsilon, \hat{E}) = \varepsilon\lambda_1(\hat{E}) + o(\varepsilon)$ *for the dominant eigenvalue of* $A(\hat{E})$ *from (3.7). Then the following holds*

$$\lambda_1 = \frac{R_1(\hat{E})}{m_0}$$

where $R_1(\hat{E})$ *is given by (3.17) and* m_0 *given by (3.16).*

Proof: First of all we switch to an age-representation in the characteristic equation (3.18) by substituting $x \to X(a, \hat{E})$. This leads to

$$\begin{aligned} 1 &= R(\varepsilon,\hat{E}) \int_0^\infty \frac{1}{R(\varepsilon,\hat{E})} \beta(X(a,\hat{E}),\hat{E}) e^{-\int_0^a \mu(X(\alpha,\hat{E}),\hat{E}) d\alpha} e^{-\lambda a} da \\ &=: R(\varepsilon,\hat{E}) \int_0^\infty m(a,\varepsilon,\hat{E}) e^{-\lambda a} da, \end{aligned}$$

where we have multiplied by $R(\varepsilon, \hat{E})$ and its inverse. We write λ_d for the unique real solution. By taking logarithms on both sides we obtain

$$0 = \log R(\varepsilon,\hat{E}) + \log\Big(\int_0^\infty m(a,\varepsilon,\hat{E}) e^{-\lambda_d a} da\Big),$$

and after expanding $e^{\lambda_d a}$ in λ_d

$$\begin{aligned} 0 &= \log R(\varepsilon,\hat{E}) + \log\Big(\int_0^\infty m(a,\varepsilon,\hat{E}) da - \lambda_d \int_0^\infty a m(a,\varepsilon,\hat{E}) da + o(\lambda_d)\Big) \\ &= \log R(\varepsilon,\hat{E}) + \log\Big(1 - \lambda_d(\varepsilon,\hat{E}) m(\varepsilon,\hat{E}) + o(\lambda_d)\Big) \\ &= \log R(\varepsilon,\hat{E}) - \lambda_d(\varepsilon,\hat{E}) m(\varepsilon,\hat{E}) + o(\lambda_d), \end{aligned}$$

where $m(\varepsilon, \hat{E})$ is defined by (3.13). We proceed with expanding $R(\varepsilon, \hat{E})$, $\lambda_d(\varepsilon, \hat{E})$ and $m(\varepsilon, \hat{E})$ in ε

$$0 = \log\Big(1 + \varepsilon R_1(\hat{E}) + o(\varepsilon)\Big) + \Big(\varepsilon\lambda_1(\hat{E}) + o(\varepsilon)\Big) \log(m_0 + O(\varepsilon)) + O(\varepsilon)$$

which leads to

$$0 = \varepsilon R_1(\hat{E}) + \varepsilon\lambda_1(\hat{E}) m_0 + o(\varepsilon).$$

This relation should hold for all $\varepsilon \in [0, \varepsilon_0]$ and therefore we finally find

$$\lambda_1(\hat{E}) = \frac{R_1(\hat{E})}{m_0}$$

where $R_1(\hat{E})$ is given by (3.17). ◊

It follows from propositions 3.2 and 3.3 that $Q(N)$ can be expressed in the basic parameters of the individual level as

$$Q(N) = \frac{R_1(\hat{E})}{m_0}. \tag{3.19}$$

We summarize the above in the following recipe: Fix the environment in an arbitrary $\hat{E}$; calculate X_0 and X_1 from (3.14) and (3.15), respectively; calculate m_0 from (3.16) and $R_1(\hat{E})$ from (3.17); finally calculate $Q(N)$ from (3.19). On the *slow time-scale* then the environment, and therefore $Q(N)$, changes according to some feedback mechanism specified in the assumptions.

In general our differential operator defined by (3.11-3.12) will not satisfy the assumptions of Theorem 3.1. In general, the operator $H_\varepsilon(E)$ will become unbounded. We conjecture however, that for the operator $A_\varepsilon(E) = A_0 + H_\varepsilon(E)$ with A_0 and $H_\varepsilon(E)$ given by (3.11) and (3.12) respectively, with ε small, Theorem 3.1 still holds, i.e. the solutions are approximated by $\phi_0(x)N(t)$ where N is the solution of $dN/dt = Q(N)N$ with Q given by (3.19).

Furthermore, in (3.19) we do not need the one-dimensionality of the individual state space Ω (in the expression for $R_1(\hat{E})$ (3.17) we only integrate along orbits of the i-state variable) we conjecture that (3.19) also holds in the case that $\dim \Omega > 1$ (of course, the operators in (3.11) and (3.12) have to be re-defined in terms of divergences).

We conclude that from a biological as well as from a mathematical point of view the future aim is to attempt to extend the Tikhonov result Theorem 2.1 to operators of the kind described above. The above discussion about the calculation of the dominant eigenvalue suggests that we should perhaps not work with the differential operator itself but more in the vein of [4] with an integrated version of it.

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