



# A differential equation with state-dependent delay from cell population biology

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## Abstract

We analyze a differential equation, describing the maturation of a stem cell population, with a state-dependent delay, which is implicitly defined via the solution of an ODE. We elaborate smoothness conditions for the model ingredients, in particular vital rates, that guarantee the existence of a local semiflow and allow to specify the linear variational equation. The proofs are based on theoretical results of Hartung et al. combined with implicit function arguments in infinite dimensions. Moreover we elaborate a criterion for global existence for differential equations with state-dependent delay. To prove the result we adapt a theorem by Hale and Lunel to the  $C^1$ -topology and use a result on metric spaces from Diekmann et al.

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### 0. Introduction

In this paper we analyze a class of differential equations of the form

$$w'(t) = q(v(t))w(t), \tag{0.1}$$

$$v'(t) = \frac{\gamma(v(t - \tau(v_t)))g(x_2, v(t))w(t - \tau(v_t))}{g(x_1, v(t - \tau(v_t)))} e^{\int_0^{\tau(v_t)} (d - D_1 g)(y(s, v_t), v(t-s)) ds} - \mu v(t). \tag{0.2}$$

We use the standard notation

$$x_t(s) := x(t + s), \quad s < 0,$$

if a function  $x$  is defined in  $t + s \in \mathbb{R}$ . If  $t$  is fixed, then  $x_t$  is a function describing the history of  $x$  at time  $t$ . Both (0.1) and (0.2) are equations in  $\mathbb{R}$  and all functions are real-valued. Next,  $\tau$  is a nonlinear functional with domain in a space of functions. The functions  $q, \gamma, g$  and  $d$  have real arguments,  $\mu$  is a parameter and  $\gamma, g, d, \tau$  and  $\mu$  take nonnegative values.

The functional  $\tau$  describes the delay and is allowed to depend exactly on the second component  $v_t$  of the state. The delay is in general only implicitly given: For a function  $\psi$  defined on an interval  $[-h, 0]$ , we specify  $\tau = \tau(\psi)$  as the solution of the equation

$$y(\tau, \psi) = x_1, \tag{0.3}$$

where  $y(\cdot, \psi)$  is defined via the ordinary differential equation (ODE)

$$\begin{aligned} y'(s) &= -g(y(s), \psi(-s)), \quad s > 0, \\ y(0) &= x_2, \end{aligned} \tag{0.4}$$

and  $x_1, x_2 \in \mathbb{R}, x_1 < x_2$  are given model parameters, see Fig. 1. We interpret  $s$  as the time to evolve from  $y(s)$  to  $x_2$ , i.e., we define  $y$  going backward in time. This facilitates denoting time dependence in the second argument of  $g$ , given that  $\psi$  is defined on  $[-h, 0]$ . As a consequence  $y(s, v_t)$  is the state at time  $t - s$ , given that  $x_2$  is reached at time  $t$ . The notation allows to express this state, and hence also the delay  $\tau$ , as a function of history  $v_t$  at time  $t$ . Equations (0.1)–(0.4) can be classified as a differential equation with implicitly defined delay with state dependence.

The system describes the maturation process of stem cells. The underlying model is formulated as a partial differential equation (PDE) of transport type in [12]. A special case of the PDE is derived via a limiting argument for related multi-compartment models. In our notation, the PDE formulation is (0.1) along with

$$\begin{aligned} g(x_1, v(t))u(t, x_1) &= \gamma(v(t))w(t), \\ \partial_t u(t, x) + \partial_x g(x, v(t))u(t, x) &= d(x, v(t))u(x, v(t)), \quad x \in (x_1, x_2), \\ v'(t) &= u(t, x_2)g(x_2, v(t)) - \mu v(t). \end{aligned}$$

An integration along the characteristics, similar to the one in Section II 4.1 in [24], yields that  $u(t, x_2)$  is equal to the first summand on the right hand side of (0.2) divided by  $g(x_2, v(t))$ . Filling

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