A continuous semiflow on a space of Lipschitz functions for a differential equation with state-dependent delay from cell biology

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Abstract

We analyze a system of differential equations with state-dependent delay (SD-DDE) from cell biology, in which the delay is implicitly defined as the time when the solution of an ODE, parametrized by the SD-DDE state, meets a threshold. We show that the system is well-posed and that the solutions define a continuous semiflow on a state space of Lipschitz functions. Moreover we establish for an associated system a convex and compact set that is invariant under the time-t-map for a finite time. It is known that, due to the state dependence of the delay, necessary and sufficient conditions for well-posedness can be related to functionals being almost locally Lips-

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chitz, which roughly means locally Lipschitz on the restriction of the domain to Lipschitz functions, and our methodology involves such conditions. To achieve transparency and wider applicability, we elaborate a general class of two component functional differential equation systems, that contains the SD-DDE from cell biology and formulate our results also for this class.

Keywords:
Delay differential equation, State-dependent delay, Well-posedness, Invariant compact set, Almost locally Lipschitz, Stem cell model

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Contents

1. Introduction

In this paper we analyze a system of delay differential equations (DDE) from cell biology of the form

$$w'(t) = q(v(t))w(t), \tag{1.1}$$

$$v'(t) = \frac{\gamma(v(t-\tau(v_t)))}{g(x_1, v(t-\tau(v_t)))} g(x_2, v(t)) w(t-\tau(v_t)) e^{\int_0^{\tau(v_t)} [d-D_1 g](y(s,v_t), v(t-s))ds} - \mu v(t), \tag{1.2}$$

with $y = y(\cdot, \psi)$ and $\tau = \tau(\psi)$ defined via

$$y'(s) = -g(y(s), \psi(-s)), \; s > 0, \;\; y(0) = x_2 \;\text{ and} \tag{1.3}$$

$$y(\tau, \psi) = x_1, \tag{1.4}$$

where $x_1 < x_2$ are given parameters. As common in DDE, we introduce $x_t(s) := x(t+s)$, $s < 0$, for functions x defined in $t+s \in \mathbb{R}$. Next, $D_1 g$ denotes the derivative of g with respect to the first argument and all values of γ, g and τ are nonnegative. Precise conditions for all functions and parameters will be given in Section 4.

The following mathematical difficulties make the analysis challenging. If we fix a time t, in (1.1–1.2) appear both, a point delay τ and a distributed delay s, which is an integration variable. The delay τ is implicitly defined via (1.4) as the time, when the solution y of the external nonlinear ordinary differential equation (ODE) (1.3) meets a lower threshold x_1. This ODE is parametrized by a function ψ, which in (1.1–1.2) is specified as the second state variable v_t of the DDE system, hence also the solution of the ODE y and the delay τ have a functional or history dependence on ψ. In summary we have a system of DDE with a state-dependent delay (SD-DDE), which is implicitly defined via a threshold condition, and an additional distributed delay.

A difficulty we will encounter when analyzing the invariance of bounded sets under the solution operator is the special type of coupling. Whereas we can often assume that the functions in (1.1–1.2) decrease in v, the right hand sides increase in w and the equation (1.1) has no self-regulatory mechanism.

The system describes the dynamics of a stem cell population, whose size at time t is denoted by $w(t)$, regulated by the mature cell population, similarly denoted by $v(t)$. The equations have been deduced via integration along the characteristics from a partial differential equation describing the "transport" of a density $n(t,x)$ over the progenitor cell maturity $x \in [x_1, x_2]$. See [7] and references therein for the latter and modeling background and [6] for biological background. We will refer to (1.1–1.4) as the cell SD-DDE.

Let us introduce the space $\mathcal{C} := C([-h,0], \mathbb{R}^n)$, where $h \in (0,\infty)$ will be related to the maximum delay, endowed with the usual sup-norm denoted by $\|\cdot\|$. For discussion of the results we will also refer to $\mathcal{C}^1 := C^1([-h,0], \mathbb{R}^n)$, endowed with its standard norm defined by $\|\phi\|_1 := \|\phi\| + \|\phi'\|$. In [7] the authors have elaborated conditions to guarantee, via application of results of [13, 21], that the cell SD-DDE is well-posed and the solutions define, for $n = 2$, a semiflow on the *solution manifold*, a continuously differentiable submanifold of $\mathcal{C}^1$, and that the semiflow is differentiable in the $\mathcal{C}^1$-topology. For general SD-DDE differentiability of the semiflow in the $\mathcal{C}^1$-topology implies a linearized stability theorem, see [13] and [19] for a criterion for, respectively, stability and instability of a supposed equilibrium.

The cell SD-DDE (1.1–1.4) may feature a unique positive equilibrium emerging from the zero equilibrium in a transcritical bifurcation: q may decrease to a negative value and $q(0)$ should increase from negative to positive upon variation of the bifurcation parameter, see [6, 8]. A combination of the discussed results of [13, 19, 7] facilitated a local stability analysis of equilibria for the cell SD-DDE in [8].

The paper [8] contains numerical and analytical evidence that the interior equilibrium is stable upon emergence and destabilizes in a Hopf bifurcation. The latter motivates also analytical research for periodic solutions for the cell SD-DDE. One way to prove the existence of periodic solutions in general is to establish their correspondence with fixed points of an operator and to apply fixed point theory. This is done for a certain class of SD-DDE in [14]. As in many fixed point arguments, also in [14] convexity and compactness of the domain is used, properties the solution manifold in general does not have.

In [11] the existence of non-continuable and global solutions is established for systems of DDE defined by functionals that are continuous on domains that are open in the $\mathcal{C}$-topology ($\mathcal{C}$-open). Continuous dependence on initial values is shown under the precondition that the solution is unique. Uniqueness of solutions is shown if the functional is Lipschitz on compact subsets of a $\mathcal{C}$-open domain. A known problem is that, in general, for SD-DDE the functional is not locally Lipschitz, if its domain includes functions that are not locally Lipschitz, see e.g. [15, Section 1].

In [15] the above mentioned uniqueness problem is overcome by restricting initial conditions to Lipschitz functions and using that for SD-DDE the functional often is *almost locally Lipschitz*, which roughly means locally Lipschitz on a domain of Lipschitz functions. Then, a combination with the discussed results in [11] yields existence and uniqueness on a domain of Lipschitz functions. The equation in [15] features two feedback conditions, one from above, at A, and one from below, at $-B$, that guarantee that solutions remain in a bounded domain of the form $C([-h,0],[-B,A])$. The feedback conditions for the bounded domain firstly facilitate the proof of global existence. Moreover, they lead to the intersection, of this set with a set of functions that share a finite Lipschitz constant, being mapped into itself by the time-t-map. By the Arzelà-Ascoli theorem, a set of functions that share the same finite bound and finite Lipschitz constant is compact in $\mathcal{C}$. In this way in [15] a convex and compact set that is invariant under the time-t-map could be established.

Whereas in [15] a scalar equation is treated, the cell SD-DDE is a two-dimensional system (here and below *dimension* often refers to the *range* space of the functional defining the equation). We will show that it preserves non-negativity, such that feedback from below, at zero, is granted. Regarding feedback from above, however, the following problem arises. If a solution $(w, v)(t)$ of the cell SD-DDE through (φ, ψ) exists, then

$$w(t) = \begin{cases} \varphi(t), & t \in [-h, 0], \\ \varphi(0)e^{\int_0^t q(v(s))ds}, & t > 0. \end{cases} \tag{1.5}$$

Now, q may take positive values for small arguments, see [6], and (1.5) shows that for such q the set of all Lipschitz functions of $C([-h, 0], [0, A_1] \times [0, A_2])$ is not mapped into itself. This leads to the fact that an invariant compact set cannot be established by a straightforward generalization of the approach of [15]. For similar reasons (see the proof of Theorem 3.8 (a) below) we cannot expect this for the set of R-Lipschitz functions, where $R > 0$ is a fixed given number, either. Moreover, due to the missing of the feedback from above it seems necessary to use a more general criterion for global existence than the one used for the equation in [15].

The first main result of this paper is the proof that the cell SD-DDE is well-posed and the solutions define a continuous semiflow on a state-space of Lipschitz functions. In comparison to the solution manifold established in [7], the new set of admissible initial conditions is much larger and, other than the former, convex. Moreover, whereas the $\mathcal{C}^1$-differentiability established in [7] requires convergence of a sequence of initial functions in $\mathcal{C}^1$ for concluding convergence of the sequence of solutions (in $\mathcal{C}^1$) the $\mathcal{C}$-continuity shown here requires only $\mathcal{C}$-convergence of the initial functions. An application that we will discuss is that convergence of a solution to a constant in $\mathbb{R}$ is sufficient to conclude that the constant is an equilibrium solution. This conclusion can not be drawn from the differentiability result in [7]. We also show that a criterion for global existence similar to the one in [11], and more general than the one used in [15], can be formulated for a general class of SD-DDE.

To establish the above results for the cell SD-DDE, we first show that solutions of a general class of DDE define a semiflow on a state space defined by all functions that have a finite (but not necessarily the same) Lipschitz constant and belong to $\mathcal{C}^+ := C([-h, 0], \mathbb{R}^n_+)$, where $\mathbb{R}_+ := [0, \infty)$. This is essentially a specific combination of (variants of) arguments of [15], [11] and [4].

We then elaborate conditions for the above results to be transferable to the cell SD-DDE. Conditions for local, global and unique existence may differ and may be equation specific. To reach more transparence, we here try to separate the corresponding assumptions. Moreover, we head for assumptions that are both general and easy to check. It turns out that continuity of the functions defining the cell SD-DDE guarantees continuity and boundedness properties of the functional, the first of which yields local existence. Added boundedness of functions allows to add boundedness of orbits on finite times, which together with the boundedness properties of the functional yields global existence. Local Lipschitzian functions lead to almost local Lipschitzian functionals and these to uniqueness. To prove the above we develop some techniques regarding Lipschitz properties of integral-, evaluation- and implicitly defined operators acting on Lipschitz subsets of continuous functions.

The discussion on (1.5) motivates that in order to establish invariance for the cell SD-DDE, it seems helpful to first consider the v-component: One can fill (1.5) into (1.2) to obtain an equation in v parametrized by the initial condition φ for w and analyze invariance for the latter equation. It will turn out that this approach can be adapted to a more general system of the form

$$w'(t) = m(w_t, v_t),\ v'(t) = j(w_t, v_t) - \mu v(t) \tag{1.6}$$

in combination with linear boundedness conditions for m and j.

Our second main result is then the establishment of a compact and convex set that is invariant for finite times under the v-component of the time t-map. The result is elaborated for both, (1.6) and the cell SD-DDE. We are not aware of previous results in this direction that are applicable in the absence of component-wise feedback conditions from above.

To establish the invariant set for (1.6) we first combine a linear boundedness condition with a monotonicity argument to derive an exponential estimate for w that, for the specific case $m(\varphi, \psi) := q(\psi(0))\varphi(0)$, one could also derive from (1.5). Then we will apply the variation of constants formula to the second equation of (1.6) along with the exponential estimate for w. The resulting bound for v will be estimated further using two alternative linear boundedness conditions for j. Whereas the first will be more general, the second is a translation of the fact, that in the cell SD-DDE the delay functional has a lower bound $\underline{\tau}$ which is positive, to a more specific linear boundedness condition for j. This condition then yields a minimum invariance time $\underline{\tau} > 0$ that in a sense is uniform with respect to initial conditions. Somewhat tedious though perhaps elementary estimation techniques employing monotonicity arguments complete this analysis.

The remainder of the paper is structured top down: In Section 2 we consider general DDE, but with an approach tailored to SD-DDE. Section 3 contains results for the class of two-dimensional DDE (1.6) and in Section 4 we analyze the cell SD-DDE. Finally, Section 5 contains a discussion of our results and an outlook on future research.

2. A continuous semiflow for DDE on a space of Lipschitz functions

We start with a well-known definition of solutions for DDE.

Definition 2.1. Let $\mathcal{D}$ be an arbitrary subset of $\mathcal{C}$ and suppose that $\phi \in \mathcal{D}$ and $f : \mathcal{D} \longrightarrow \mathbb{R}^n$. By a *solution* of

$$x'(t) = f(x_t), \quad t \geq 0, \tag{2.1}$$
$$x_0 = \phi, \tag{2.2}$$

or a *solution of (2.1) through* ϕ, we mean a continuous function

$$x^\phi : [-h, \alpha] \longrightarrow \mathbb{R}^n$$

for some $\alpha > 0$, that is such that for $t \in [0, \alpha]$ one has that $x_t^\phi \in \mathcal{D}$ and on $[0, \alpha]$ the function x^ϕ is differentiable and satisfies (2.1–2.2).

Continuity of a solution implies continuity of $[0, \alpha] \to \mathcal{D};\ t \mapsto x_t$ and, if f is continuous, the latter and (2.1) imply continuity of x' and thus continuous differentiability of x^ϕ on $[0, \alpha]$. Solutions on half-open intervals $[-h, \alpha)$ for $\alpha \in (0, \infty]$ are defined analogously. We shall sometimes write x instead of x^ϕ.

2.1. Functionals defined on $\mathcal{C}$

Non-continuable and global solutions

We refer to [11] for the standard definition of a non-continuable solution.

Theorem 2.2. *Suppose that* $F : \mathcal{C} \longrightarrow \mathbb{R}^n$ *is continuous and* $\phi \in \mathcal{C}$.

(a) There exists some $c = c(\phi) \in (0, \infty]$ *and a non-continuable solution* $x^\phi : [-h, c) \longrightarrow \mathbb{R}^n$ *of*

$$x'(t) = F(x_t),\ t \geq 0,\ \ x_0 = \phi. \tag{2.3}$$

If additionally $F(U)$ is bounded whenever $U \subset \mathcal{C}$ is closed and bounded then the following hold:

(b) If $c < \infty$ then for any closed and bounded $U \subset \mathcal{C}$ there exists some $t_U \in (0,c)$ such that $x_t^\phi \notin U$ for all $t \in [t_U, c)$.

(c) If $\{x_t^\phi : t \in [0,\alpha)\} \subset \mathcal{C}$ is bounded, whenever $\alpha \in (0,\infty)$ and x^ϕ is defined on $[0,\alpha)$, then $c = \infty$, i.e., the solution is global.

The existence of a solution $x^\phi : [-h,\alpha] \longrightarrow \mathbb{R}^n$ for some $\alpha > 0$ follows from [11, Theorem 2.2.1] and the statement in (a) is concluded in [11, Section 2.3] from Zorn's lemma. Note that since the non-continuable solution need not be unique, also $c(\phi)$ need not be unique. Next, (b) follows from [11, Theorem 2.3.2] and (c) directly from (b).

Uniqueness

To guarantee uniqueness, the notion of almost local Lipschitzian functionals for $n = 1$ from [15] can be generalized to arbitrary finite dimensions in a straightforward way. Define for any $\phi \in \mathcal{C}$

$$\text{lip } \phi := \sup \left\{ \frac{|\phi(s) - \phi(t)|}{|s-t|} : \; s,t \in [-h,0], \; s \neq t \right\} \in [0,\infty]$$

and $B_\delta(x_0) := \{x : \; \|x - x_0\| < \delta\}$, where $\delta > 0$, $|\cdot|$ denotes a norm in $\mathbb{R}^n$ with n depending on context and the choice of norm $\|\cdot\|$ in $B_\delta(x_0)$ should also be clear from the context, e.g., the choice of x_0. In the following, however, we denote by $\|\cdot\|$ the sup-norm in $\mathcal{C}$. Then, a function ϕ is Lipschitz with Lipschitz constant k (we will write *k-Lipschitz*) whenever $\infty > k \geq \text{lip } \phi$. For each $\phi_0 \in \mathcal{C}$, $\delta > 0$, $R > 0$ define

$$V(\phi_0; \delta, R) := \{\phi \in \overline{B}_\delta(\phi_0) : \; \text{lip } \phi \leq R\}.$$

Definition 2.3. A functional $f : \mathcal{D} \subset \mathcal{C} = C([-h,0],\mathbb{R}^n) \longrightarrow \mathbb{R}^m$ is called *almost locally Lipschitz* if f is continuous and for all $\phi_0 \in \mathcal{D}$, $R > 0$ there exist some $\delta = \delta(\phi_0, R) > 0$ and $k = k(\phi_0, R, \delta) \geq 0$ such that for all $\varphi, \psi \in V(\phi_0; \delta, R) \cap \mathcal{D}$

$$|f(\varphi) - f(\psi)| \leq k\|\varphi - \psi\|.$$

We next prove some general facts that will be relevant in the following sections.

Lemma 2.4. *(a) Suppose that $f, g : \mathcal{D} \subset \mathcal{C} \longrightarrow \mathbb{R}$ are arbitrary almost locally Lipschitz functions. Then so are fg, (f, g) and $f + g$.*
(b) Let $f : \mathcal{D} \subset \mathcal{C} \longrightarrow \mathbb{R}$ be almost locally Lipschitz and $g : f(\mathcal{D}) \subset \mathbb{R} \longrightarrow \mathbb{R}$ be locally Lipschitz, then $g \circ f : \mathcal{D} \longrightarrow \mathbb{R}$ is almost locally Lipschitz.

Proof. Since (a) is fairly standard, we only prove (b). First, clearly $g \circ f$ is continuous. Next, let $\phi_0 \in \mathcal{D}$, $R > 0$, choose ε, k_1 such that g is k_1-Lipschitz on $B_\varepsilon(f(\phi_0))$. Choose, δ, k_2 such that f is k_2-Lipschitz on $V(\phi_0; \delta, R)$ and $f(\overline{B}_\delta(\phi_0)) \subset B_\varepsilon(f(\phi_0))$. Let $\varphi, \psi \in V(\phi_0; \delta, R)$. Then the following estimate implies the statement:

$$|g(f(\varphi)) - g(f(\psi))| \leq k_1 |f(\varphi) - f(\psi)| \leq k_1 k_2 \|\varphi - \psi\|.$$

□

The following theorem is proven as [15, Theorem 1.2] for the case $n = 1$. The proof for general n is analogous and we omit it. For $\mathcal{D} \subset \mathcal{C}$, define $V_\mathcal{D} := \{\phi \in \mathcal{D} : \operatorname{lip} \phi < \infty\}$. Note that if $\mathcal{D}$ is convex, so is $V_\mathcal{D}$.

Theorem 2.5. *Suppose that $F : \mathcal{C} \longrightarrow \mathbb{R}^n$ is almost locally Lipschitz and let $\phi \in V_\mathcal{C}$. If $\alpha > 0$ and $y, z : [-h, \alpha] \longrightarrow \mathbb{R}^n$ are both solutions of (2.3), then $y(t) = z(t)$ for all $t \in [0, \alpha]$.*

Continuous dependence on initial values

The next result follows directly from [11, Theorem 2.2.2] and the above uniqueness result.

Theorem 2.6. *Suppose that $F : \mathcal{C} \longrightarrow \mathbb{R}^n$ is almost locally Lipschitz, $\phi \in V_\mathcal{C}$ and that a solution x^ϕ of (2.3) through ϕ exists on $[-h, \alpha]$ for some $\alpha > 0$. Let $(\phi^k) \in (V_\mathcal{C})^\mathbb{N}$ with $\phi^k \longrightarrow \phi$, as $k \to \infty$. Then x^ϕ is the unique solution on $[-h, \alpha]$, for some $k_0 \in \mathbb{N}$ there exist unique solutions x^k through ϕ^k on $[-h, \alpha]$ for all $k \geq k_0$, $k \in \mathbb{N}$ and $x^k \longrightarrow x^\phi$ uniformly on $[-h, \alpha]$.*

2.2. Retractions and functionals with specific domains

Recall that a *retraction* is a continuous map of a topological space into a subset that on the subset equals the identity. It is remarked in [15] (without proof) that the following result holds in case $n = 1$ and the map g, additionally to satisfying the properties stated below, is a retraction. The proof of our result is analogous and we present it for completeness.

Lemma 2.7. *Let $\mathcal{D} \subset \mathcal{C}$, $g : \mathcal{C} \longrightarrow \mathcal{D}$ be locally Lipschitz. Suppose that for all $\phi_0 \in \mathcal{C}$, $\delta > 0$, $R > 0$*

$$\sup\{\text{lip } g(\phi) : \ \phi \in V(\phi_0; \delta, R)\} < \infty.$$

Then, if $f : \mathcal{D} \longrightarrow \mathbb{R}^n$ is almost locally Lipschitz, so is $F : \mathcal{C} \longrightarrow \mathbb{R}^n$; $F := f \circ g$.

Proof. First, F is continuous as a composition of continuous functions. Next, let $\phi_0 \in \mathcal{C}$, $R > 0$. Define $L := \sup\{\text{lip } g(\phi) : \ \phi \in V(\phi_0; 1, R)\} < \infty$. Choose $\varepsilon = \varepsilon(g(\phi_0), L) > 0$, $k = k(g(\phi_0), L) \geq 0$ such that f is k-Lipschitz on $V(g(\phi_0); \varepsilon, L) \cap \mathcal{D}$. Choose $\delta \in (0, 1)$, $l \geq 0$ such that $g(\overline{B}_\delta(\phi_0)) \subset B_\varepsilon(g(\phi_0))$ and g is l-Lipschitz on $\overline{B}_\delta(\phi_0)$. Then for $\varphi, \psi \in V(\phi_0; \delta, R)$, one has

$$|F(\varphi) - F(\psi)| = |f(g(\varphi)) - f(g(\psi))| \leq k|g(\varphi) - g(\psi)| \leq kl\|\varphi - \psi\|.$$

Hence, F is kl-Lipschitz on $V(\phi_0; \delta, R)$ and thus almost locally Lipschitz. □

A specific retraction for a specific domain

For the remainder of the section we will use the following construction (unless specified otherwise). The construction contains a modification of the retraction in [15], the latter of which maps $C([-h, 0], \mathbb{R})$ onto $C([-h, 0], [-B, A])$ with $-\infty < -B < A < \infty$, to a retraction of the space $C([-h, 0], \mathbb{R}^n)$ onto $\mathcal{C}^+ = C([-h, 0], \mathbb{R}^n_+)$. With the result we can work with nonnegative solutions of multi-dimensional equations. Note that $\mathcal{C}^+$ is convex and that, as discussed before, this implies convexity of $V_{\mathcal{C}^+}$. We define a map

$$r : \mathbb{R} \longrightarrow [0, \infty); \ r(u) := \begin{cases} u, & u \in [0, \infty), \\ 0, & u < 0. \end{cases} \tag{2.4}$$

Then r is a retraction and Lipschitz with lip $r \leq 1$. With r we define a map

$$\begin{aligned} &\rho : \mathcal{C} \longrightarrow \mathcal{C}^+, \ \rho = (\rho_1, ..., \rho_n) \\ &\rho_i(\phi)(\theta) := r(\phi_i(\theta)), \ \theta \in [-h, 0], \ i = 1, ..., n. \end{aligned} \tag{2.5}$$

The following results, Lemmas 2.8–2.10, are straightforward modifications of results in [15], from the retraction in the latter to our retraction. We omit the corresponding proofs.

Lemma 2.8. *ρ is a retraction and maps bounded sets into bounded sets.*

The next lemma follows by definition of ρ from r being Lipschitz with $\operatorname{lip} r \leq 1$.

Lemma 2.9. *One has* $\operatorname{lip} \rho(\phi) \leq \operatorname{lip} \phi$*, hence if ϕ is Lipschitz so is $\rho(\phi)$. Moreover, ρ is Lipschitz with* $\operatorname{lip} \rho \leq 1$.

The result implies that $\sup\{\operatorname{lip} \rho(\phi) : \phi \in V(\phi_0; \delta, R)\} \leq R < \infty$ for all $\phi_0 \in \mathcal{C}$, $\delta > 0$ and $R > 0$. The next lemma is a straightforward combination of this result with Lemma 2.7.

Lemma 2.10. *Suppose that $f : \mathcal{C}^+ \longrightarrow \mathbb{R}^n$ is almost locally Lipschitz. Then so is $F := f \circ \rho : \mathcal{C} \longrightarrow \mathbb{R}^n$. Moreover $F|_{\mathcal{C}^+} = f$.*

Non-continuable and global solutions and uniqueness

To guarantee that a solution remains within a domain a feedback condition can be used. The following result is a slight modification of the corresponding result for one dimension, which is [15, Theorem 1.3].

Lemma 2.11. *Suppose that $f : \mathcal{C}^+ \longrightarrow \mathbb{R}^n$ satisfies*

$$f_i(\phi) \geq 0, \text{ if } \phi_i(0) = 0, \ \phi = (\phi_1, ..., \phi_n) \in \mathcal{C}^+, \ i = 1, ..., n. \tag{F}$$

Now fix $\phi \in \mathcal{C}^+$ and assume that x is a solution of $x'(t) = f(\rho(x_t))$ through ϕ on some interval $[-h, \alpha]$. Then $x_t \in \mathcal{C}^+$ and thus $\rho(x_t) = x_t$ for all $t \in [0, \alpha]$ and hence x is a solution of (2.1–2.2) on $[0, \alpha]$.

To prove the result one can directly apply the non-autonomous [17, Proposition 1.2] to the domain $\Omega := \mathbb{R} \times \mathcal{C}$, the map $g : \Omega \to R^n; g(t, \phi) := f(\rho(\phi))$ and $t_0 := 0$. In the next theorem we combine earlier arguments of existence, uniqueness and invariance with the criterion for global existence of Theorem 2.2.

Theorem 2.12. *Suppose that $f : \mathcal{C}^+ \longrightarrow \mathbb{R}^n$ is continuous and satisfies (F). Then the following hold.*

(a) For every $\phi \in \mathcal{C}^+$ there exists some $c = c(\phi) \in (0, \infty]$ and a non-continuable solution x^ϕ on $[-h, c)$ of (2.1–2.2).

(b) If $f(U)$ is bounded, whenever $U \subset \mathcal{C}^+$ is bounded, and if for some $\phi \in \mathcal{C}^+$ the set $\{x_t^\phi :\ t \in [0,\alpha)\} \subset \mathcal{C}^+$ is bounded, whenever $\alpha \in (0,\infty)$ and x^ϕ is a solution defined on $[0,\alpha)$, then $c=\infty$, i.e., the solution is global.

(c) If f is almost locally Lipschitz and $\phi \in V_{\mathcal{C}^+}$, then x^ϕ is the unique solution (on whatever interval it is defined).

Proof. Since $F := f \circ \rho$ is continuous, by Theorem 2.2 (a) there exists a non-continuable solution x^ϕ on $[t_0-h, t_0+c)$ of (2.3) for this F. Next, suppose that $U \subset \mathcal{C}$ is bounded. Then, as remarked, $\rho(U) \subset \mathcal{C}^+$ is bounded and hence by the assumption of (b) also $F(U) = f(\rho(U))$ is bounded. Thus by Theorem 2.2 (c) we have shown that if $\{x_t^\phi : t \in [0,\alpha)\} \subset \mathcal{C}$ is bounded, whenever $\alpha < \infty$ and x^ϕ is defined on $[0,\alpha)$, then $c=\infty$. If f is almost locally Lipschitz, then by Lemma 2.10 so is F and thus by Theorem 2.5 we get uniqueness. To complete the proof note that (F) guarantees via Lemma 2.11 that $\{x_t^\phi : t \in [0,\alpha)\} \subset \mathcal{C}$ and that x^ϕ is a solution of (2.1–2.2). □

Note that by definition of a solution, we have that $x_t \in \mathcal{C}^+$, such that all components of x are nonnegative functions.

Remark 2.13. If f would map only the closed and bounded sets on bounded sets, we could not guarantee that $F(U) = (f \circ \rho)(U)$ is bounded if U is closed and bounded, which was required in Theorem 2.2: the above defined retraction ρ maps bounded on bounded, but in general does not map closed and bounded on closed sets. To see the latter, consider e.g. $\mathcal{C} := C([0,2],\mathbb{R})$, $\mathcal{C}^+ := \{x \in \mathcal{C} : x(t) \geq 0,\ \forall\, t \in [0,2]\}$ and r and ρ defined as above, but for $n=1$ and the modified $\mathcal{C}$ and $\mathcal{C}^+$. Define $U := \{x_n :\ n \geq 2\} \subset \mathcal{C}$, where

$$x_n(t) := \begin{cases} \frac{1}{n}, & t < 1-\frac{1}{n}, \\ 1-t, & 1-\frac{1}{n} \leq t < 1, \\ -n(t-1), & 1 \leq t < 1+\frac{1}{n}, \\ -1, & 1+\frac{1}{n} \leq t \leq 2. \end{cases}$$

Then clearly U is bounded. Too see that U is closed, suppose that $(y_n) \in U^{\mathbb{N}}$, $y \in \mathcal{C}$, $y_n \longrightarrow y$. Then for all $n \in \mathbb{N}$ there is some $k_n \in \mathbb{N}$ such that $y_n = x_{k_n}$. There can be only two cases. In the first, there exists some $K \in \mathbb{N}$ such that $k_n \leq K$ for all $n \in \mathbb{N}$. Then $\{y_n :\ n \geq 2\}$ is a finite set, hence closed. It follows that $y \in \{y_n :\ n \geq 2\} \subset U$ and thus also U is closed. In the second case there exists some $(n_j) \in \mathbb{N}^{\mathbb{N}}$ such that $k_{n_j} \longrightarrow \infty$ as $j \longrightarrow \infty$. Without loss of generality (n_j) is increasing. Then for all $t \in [0,1)$ one has $x_{k_{n_j}}(t) \longrightarrow 0$ as $j \longrightarrow \infty$. For all $t \in (1,2]$ one has $x_{k_{n_j}}(t) \longrightarrow -1$. On the other hand, for any $t \in [0,2]$ one has $x_{k_{n_j}}(t) = y_{n_j}(t) \longrightarrow y(t)$. It follows that y has a discontinuity at $t = 1$, which is a contradiction. Hence only the first case can be and thus U is closed.

Finally, it is easy to see that

$$\rho(U) = \{x : \ \exists\, n \geq 2, \text{ s.th. } x(t) = x_n(t), \ \forall\, t \in [0,1], \ x(t) = 0, \ \forall\, t \in [1,2]\}.$$

is not closed: Indeed for $(z_n) \in \rho(U)^{\mathbb{N}}$, where

$$z_n(t) := \begin{cases} x_n(t), & t \in [0,1], \\ 0, & t \in (1,2], \end{cases}$$

one has $z_n \longrightarrow 0 \in \mathcal{C} \backslash \rho(U)$.

Continuous dependence on initial values

The negative feedback condition (F) now ensures that the results on continuous dependence can be transferred to solutions of (2.1–2.2) for a functional defined on our specific domain.

Theorem 2.14. *Suppose that $f : \mathcal{C}^+ \longrightarrow \mathbb{R}^n$ is almost locally Lipschitz and satisfies (F), let $\phi \in V_{\mathcal{C}^+}$ and let $\alpha > 0$ be such that the solution x^ϕ of (2.1) through ϕ exists on $[-h, \alpha]$. Let $(\phi^k) \in (V_{\mathcal{C}^+})^{\mathbb{N}}$ with $\phi^k \longrightarrow \phi$. Then for some $k_0 \in \mathbb{N}$ there exist unique solutions x^k through ϕ^k on $[-h, \alpha]$ for all $k \geq k_0$, $k \in \mathbb{N}$, and $x^k \longrightarrow x^\phi$ uniformly on $[-h, \alpha]$.*

Proof. Since x^ϕ is a solution of (2.1–2.2) we have $x_t^\phi \in \mathcal{C}^+$ for all $t \geq 0$. Thus, for $F := f \circ \rho$, one has $F(x_t^\phi) = f(x_t^\phi)$ and x^ϕ is a solution of $x'(t) = F(x_t)$ through ϕ. By Theorem 2.6, x^ϕ is the unique solution of $x'(t) = F(x_t)$ and there exists some k_0, such that for all $k \geq k_0$ there exist unique solutions x^k of $x'(t) = F(x_t)$ through ϕ^k on $[-h, \alpha]$ and $x^k \longrightarrow x^\phi$ uniformly. By Lemma 2.11 the x^k solve also (2.1–2.2). □

Semiflow and asymptotic properties

If f satisfies the assumptions for global existence and uniqueness, we can use some standard dynamical systems theory, see e.g. [2, Sections 10, 17]. In the following let X denote a metric space.

Definition 2.15. A map $\Sigma : [0, \infty) \times X \longrightarrow X$ is called a *continuous semiflow* if

(i) $\Sigma(0, x) = x$ for all $x \in X$,

(ii) $\Sigma(t, \Sigma(s, x)) = \Sigma(t + s, x)$ for all $s, t \in [0, \infty)$, $x \in X$,

(iii) Σ is continuous.

For a given semiflow Σ and some $x \in X$ we denote by, respectively,

$$\gamma^+(x) := \{\Sigma(t, x) : \ t \in [0, \infty)\}, \ \ \omega(x) := \bigcap_{t \geq 0} \overline{\gamma^+(\Sigma(t, x))}$$

the *positive orbit* and *ω-limit set* of x under Σ.

Note that

$$\omega(x) = \{y \in X : \ \exists \, t_n \longrightarrow \infty, \ s.th. \ \Sigma(t_n, x) \longrightarrow y \text{ as } n \to \infty\}. \qquad (2.6)$$

To show that the next theorem holds, we combine what we have compiled so far with further results from the literature. Let us specify $X := V_{\mathcal{C}^+}$ endowed with the metric induced by the sup-norm.

Theorem 2.16. *Suppose that $f : \mathcal{C}^+ \longrightarrow \mathbb{R}^n$ is almost locally Lipschitz and satisfies (F), $f(U)$ is bounded whenever $U \subset \mathcal{C}^+$ is bounded and $\{x_t^\phi : \ t \in [0, \alpha)\}$ is bounded whenever $\phi \in V_{\mathcal{C}^+}$, $\alpha \in (0, \infty)$, and a solution x^ϕ of (2.1) is defined on $[0, \alpha)$. Then for any $\phi \in V_{\mathcal{C}^+}$ there exists a unique global solution of (2.1) through ϕ and for all $t \geq 0$ one has $x_t^\phi \in V_{\mathcal{C}^+}$. Hence, we can define a map*

$$S : [0, \infty) \times V_{\mathcal{C}^+} \longrightarrow V_{\mathcal{C}^+}; \ S(t, \phi) := x_t^\phi.$$

This map defines a continuous semiflow on $V_{\mathcal{C}^+}$ with respect to the sup*-norm.*

Proof. First note that existence of a unique global solution for all $\phi \in V_{\mathcal{C}^+}$ follows from Theorem 2.12. To show invariance of the state space $V_{\mathcal{C}^+}$ under the time t-map, one can use continuous differentiability of solutions. Moreover, it is established in [11] (without proof) and in [4, Proposition VII 6.1 (i)] that Definition 2.15 (i-ii) hold, when applied to any continuous initial function. It follows that they hold also for our state space. To see continuity of S, let $(t^k, \phi^k) \in ([0, \infty) \times V_{\mathcal{C}^+})^{\mathbb{N}}$ and $(t, \phi) \in [0, \infty) \times V_{\mathcal{C}^+}$, such that

$(t^k, \phi^k) \to (t, \phi)$. Now, in Theorem 2.14 let $\alpha := t+1$ and choose $k_0 \in \mathbb{N}$ such that $t^k \le t+1$ for all $k \ge k_0$. Then for $k \ge k_0$ and $\theta \in [-h, 0]$

$$\begin{aligned} & |S(t^k,\phi^k)(\theta) - S(t,\phi)(\theta)| = |x^k(t^k+\theta) - x^\phi(t+\theta)| \\ \le \quad & |x^k(t^k+\theta) - x^\phi(t^k+\theta)| + |x^\phi(t^k+\theta) - x^\phi(t+\theta)| =: (I) + (II) \end{aligned}$$

in obvious notation. Let $\varepsilon > 0$. By Theorem 2.14 we can choose $k_1 \ge k_0$, such that $(I) \le \varepsilon/2$ for all $k \ge k_1$, $\theta \in [-h, 0]$. Since x^ϕ is continuous as a solution, it is uniformly continuous on $[-h, t+1]$ and we can choose $k_2 \ge k_1$ such that $(II) \le \varepsilon/2$ for all $k \ge k_2$, $\theta \in [-h, 0]$. It follows that

$$\|S(t^k,\phi^k) - S(t,\phi)\| \le \varepsilon, \ \forall\, k \ge k_2,$$

which concludes the proof. □

Suppose that for the remainder of the section f satisfies the assumptions of Theorem 2.16. A sufficient criterion for relative compactness of the positive orbit for DDE with infinite delay is already established in [9, Lemma 2]. Establishing such a criterion in our setting is similar and easier, because we have finite delay:

Corollary 2.17. *Let $\phi \in V_{\mathcal{C}^+}$ and suppose that $x = x^\phi$ is bounded on $[0, \infty)$. Then $\overline{\gamma^+(\phi)}$ is compact.*

To see that the statement holds, first note that by the boundedness assumption on f also x' is bounded on $[0, \infty)$. Then, similarly to [9, Lemma 2], one can show sequential compactness using the theorem of Arzelà–Ascoli. We omit further details.

Finally, continuous dependence and Definition 2.15 (ii) can be combined to prove the following result. Recall that for an equilibrium of a (global) semiflow induced by a DDE the corresponding solution is necessarily a constant function on $[-h, \infty)$.

Corollary 2.18. *Suppose that $\phi \in V_{\mathcal{C}^+}$ and $x^\phi(t) \longrightarrow x^* \in \mathbb{R}^n_+$ as $t \to \infty$. Define $\phi^*(\theta) := x^*$ on $[-h, 0]$. Then $\phi^* \in V_{\mathcal{C}^+}$, $S(t,\phi) \longrightarrow \phi^*$ and $S(t,\phi^*) = \phi^*$, hence $x^{\phi^*}(t) = x^*$ for all $t \ge -h$, i.e., x^{ϕ^*} is an equilibrium solution. Moreover $\omega(\phi) = \{\phi^*\}$ and $\overline{\gamma^+(\phi)}$ is compact.*

Proof. Let $(t_k) \in (\mathbb{R}_+)^{\mathbb{N}}$, $t_k \to \infty$. Then $S(t_k, \phi) = x^\phi_{t_k} \longrightarrow \phi^*$ uniformly by our assumption. Fix $t > 0$. Then also $S(t + t_k, \phi) \longrightarrow \phi^*$ as $k \to \infty$. But also $S(t + t_k, \phi) = S(t, S(t_k, \phi)) \longrightarrow S(t, \phi^*)$ by Theorem 2.16. Hence $S(t, \phi^*) = \phi^*$. Thus x^{ϕ^*} is an equilibrium solution. Next, $\omega(\phi) = \{\phi^*\}$ follows trivially from $S(t,\phi) \longrightarrow \phi^*$, (2.6) and $S(t,\phi^*) = \phi^*$. □

3. Semiflow and invariant compact sets for a certain class of two-dimensional DDE

We incorporate the dimension into the notation by introducing $\mathcal{C}_n^+ := C([-h,0],\mathbb{R}_+^n)$ and consider continuous functionals $m : \mathcal{C}_2^+ \longrightarrow \mathbb{R}$, $j : \mathcal{C}_2^+ \longrightarrow \mathbb{R}_+$ and a parameter $\mu > 0$. Next, we specify the functional $f : \mathcal{C}_2^+ \longrightarrow \mathbb{R}^2$;

$$f(\varphi,\psi) := (m(\varphi,\psi), j(\varphi,\psi) - \mu\psi(0))^T, \tag{3.1}$$

such that the general DDE (2.1) can be related to the class of two-dimensional DDE (1.6).

The second component of f features evaluation at zero and a further specification of m and j below will involve more general evaluation operators. We start with a result on smoothness of such operators. Let a and b be such that $b > a \geq 0$ and denote by J and J_i, $i = 1,2,3$ arbitrary subsets of $\mathbb{R}$. We define

$$ev : C([-b,-a],J) \times [-b,-a] \longrightarrow J;\ ev(\varphi,s) := \varphi(s). \tag{3.2}$$

Lemma 3.1. *The operator ev is continuous. For an arbitrary continuous functional $r : C([-b,-a],J_1) \longrightarrow [a,b]$, the functionals*

$$\begin{aligned} &ev \circ (id \times -r) : C([-b,-a],J_1) \longrightarrow J_1;\ \psi \mapsto ev(\psi,-r(\psi)) = \psi(-r(\psi)),\\ &ev \circ (id,-r) : \mathcal{D}_e \longrightarrow J_2;\ (\varphi,\psi) \mapsto ev(\varphi,-r(\psi)) = \varphi(-r(\psi)), \end{aligned} \tag{3.3}$$

where $\mathcal{D}_e := C([-b,-a],J_2 \times J_1)$, are continuous. If r is almost locally Lipschitz, then so are $ev \circ (id \times -r)$ and $ev \circ (id,-r)$. If r is locally Lipschitz, then for all $(\varphi,\psi) \in \mathcal{D}_e$, $R > 0$ there exist $k = k((\varphi,\psi),R)$, $\delta = \delta((\varphi,\psi),R)$, such that $ev \circ (id,-r)$ is k-Lipschitz on $(V(\varphi;\delta,R) \times B_\delta(\psi)) \cap \mathcal{D}_e$. If r is constant, then both functionals are Lipschitz (in fact bounded and linear).

The proof is straightforward and we omit it. The lemma is sharp in the sense that in general neither ev nor the operators defined in the lemma are locally Lipschitz for the given domains, even if r is Lipschitz.

To guarantee existence of solutions in a general way, we define a feedback law and boundedness conditions via

$$m(\varphi,\psi) \geq 0,\ \text{if } \varphi(0) = 0 \text{ and } (\varphi,\psi) \in \mathcal{C}_2^+, \tag{Fm}$$

$$m(U),\ j(U) \text{ bounded, if } U \subset \mathcal{C}_2^+ \text{ bounded}, \tag{Bmj}$$

$$\{(w,v)^{\phi}_t:\ t\in[0,\alpha)\}\subset \mathcal{C}_2^+ \text{ bounded for any solution}$$
$$(w,v)^{\phi}_t \text{ defined on } [0,\alpha),\ \alpha\in(0,\infty). \tag{Bϕ}$$

To establish an invariant bounded set of Lipschitz functions, motivated by (1.1), we define the linear boundedness condition

$$\sup_{(\varphi,\psi)\in\mathcal{C}_2^+,\ \varphi(0)\neq 0}\frac{|m(\varphi,\psi)|}{\varphi(0)}<\infty \tag{lBm}$$

and a second boundedness assumption for j via

$$j(B_1\times B_2)\text{ bounded, if } B_1\times B_2\subset\mathcal{C}_2^+,\ B_1 \text{ bounded.} \tag{sBj}$$

In case (lBm) holds, we define k_m as the supremum and note that by continuity of m one has that $|m(\varphi,\psi)|\le\varphi(0)k_m$ for all $(\varphi,\psi)\in\mathcal{C}_2^+$ and both, (Fm) and the boundedness condition for m in (Bmj) hold. Again, if (lBm) holds, we introduce the nonnegative quantity

$$\overline{q}:=\max\{\sup_{(\varphi,\psi)\in\mathcal{C}_2^+,\ \varphi(0)\neq 0}\frac{m(\varphi,\psi)}{\varphi(0)},0\}$$

and observe that $\overline{q}\le k_m<\infty$. Then, if a solution (w,v) through $(\varphi,\psi)\in\mathcal{C}_2^+$ exists, one has $w'(t)=m(w_t,v_t)\le\overline{q}w(t)$. Under this differential inequality one obtains

$$w(t)\ \le\ \|\varphi\|q_e(t),\ \forall\, t\ge -h,\ \text{ where }\ q_e(t):=\begin{cases}1, & t\in[-h,0],\\ e^{\overline{q}t}, & t>0.\end{cases} \tag{3.4}$$

Note that q_e is continuous, nondecreasing, increasing on $[0,\infty)$ if $\overline{q}>0$, and differentiable on $[-h,0)\cup(0,\infty)$. Moreover, $q_e(t)$ is increasing in $\overline{q}$ for any fixed $t>0$.

Obviously (sBj) implies the boundedness condition for j in (Bmj). We will use the following variation of constants formula. If (w,v) is a solution through (φ,ψ) defined on $[0,t]$, then

$$v(t)=\psi(0)e^{-\mu t}+e^{-\mu t}\int_0^t e^{\mu s}j(w_s,v_s)ds. \tag{VOC}$$

Lemma 3.2. *(a) The functional f is continuous. If (Fm) holds, then f satisfies (F) and for any $\phi\in\mathcal{C}_2^+$ there exists some $c=c(\phi)\in(0,\infty]$ and a*

non-continuable solution $(w,v)^\phi$ *on* $[-h,c)$ *of (1.6) through* ϕ.
(b) If m *and* j *satisfy (Bmj), then* $f(U)$ *is bounded, whenever* $U \subset \mathcal{C}_2^+$ *is bounded. If moreover some* $\phi \in \mathcal{C}_2^+$ *satisfies (B*ϕ*), then any non-continuable solution of (1.6) through* ϕ *is global.*
(c) If m *and* j *are almost locally Lipschitz then so is* f *and a solution is unique where it exists.*
(d) If (lBm) holds, so does (Fm). If moreover (sBj) holds, then so does (Bmj) and for all $\phi \in \mathcal{C}_2^+$ *so does (B*ϕ*).*

Proof. (a) Continuity of f follows from continuity of the functionals m, j, (3.3) for the case $r = 0$ (evaluation at zero) and appropriate projections. Property (F) follows directly from (Fm) and non-negativity of j. Then, application of Theorem 2.12 (a) yields (a) of the lemma.
(b) The first statement is trivial, the second follows by Theorem 2.12 (b).
(c) The Lipschitz property for f can be deduced using Lemmas 2.4 and 3.1. Then, application of Theorem 2.12 (c) yields the second statement.
(d) (Fm) holds by (lBm) as discussed. Regarding the second statement, (sBj) and (lBm) obviously imply (Bmj). To show (Bϕ), we show sufficient properties for each component. Suppose that (w,v) is defined on $[-h,\alpha)$, $\alpha \in (0,\infty)$. Then boundedness of w on $[-h,\alpha)$ follows from (3.4). Boundedness of v on $[0,\alpha)$ can be shown using (VOC), boundedness of the w-component on $[0,\alpha)$ and (sBj). □

Note that, by (a) and (b), (d) provides alternative sufficient conditions for the existence of non-continuable and global solutions, respectively. If m and j are almost locally Lipschitz and, either (Fm), (Bmj) and (Bϕ) on $V_{\mathcal{C}_2^+}$, or (lBm) and (sBj) hold, then, by Theorem 2.16, solutions define a semiflow on $V_{\mathcal{C}_2^+}$.

Proposition 3.3. *Suppose that* m *and* j *are almost locally Lipschitz,* $\mu > 0$ *and that (lBm) holds. Let* A, B, R *and* T *denote positive numbers and let* (w,v) *denote the solution through* $(\varphi,\psi) \in V_{\mathcal{C}_2^+}$. *Choose* A, R *and* T *such that* $k_m A e^{\overline{q}T} \le R$. *Then, if* $\|\varphi\| \le A$ *and* $\operatorname{lip}\varphi \le R$ *one has* $\operatorname{lip} w_t \le R$ *for all* $t \in [0,T]$.

Proof. Since $\operatorname{lip}\varphi \le R$, it remains to show that $\operatorname{lip} w|_{[0,T]} \le R$. This follows since on $[0,T]$ by (lBm) and (3.4) one has

$$|w'(t)| = |m(w_t,v_t)| \le k_m w(t) \le k_m \|\varphi\| e^{\overline{q}t} \le k_m A e^{\overline{q}t} \le R.$$

□

Next, we will establish an invariant set for the v-component of the time-t-map. For given $B > 0$ and $R > 0$ this set will be of the form

$$C_{B,R} := \{\chi \in C([-h, 0], [0, B]),\ \mathrm{lip}\ \chi \leq R\}. \tag{3.5}$$

Note that $C_{B,R}$ is convex and, by the Arzelà–Ascoli theorem, compact. Recall that solutions of (1.6) are nonnegative. For further invariance analysis and motivated by the expression on the right hand side of (1.2) we introduce two new boundedness conditions for j via

$$\exists\ k_j > 0,\ s.th.\ j(\varphi, \psi) \leq k_j \|\varphi\|,\ \forall\ (\varphi, \psi) \in \mathcal{C}_2^+, \tag{lBj}$$

$$\exists\ k_j > 0,\ s.th.\ j(\varphi, \psi) \leq k_j \varphi(-\tau(\psi)),\ \forall\ (\varphi, \psi) \in \mathcal{C}_2^+, \tag{τBj}$$

where $\tau : \mathcal{C}_1^+ \longrightarrow [\underline{\tau}, h]$ for some $\underline{\tau} \in [0, h)$. Obviously (lBj) is a weaker requirement than (τBj) and any of the two implies (sBj). On the other hand, as we will see, (τBj) may lead to better results while still applicable to the cell SD-DDE.

Suppose that for the remainder of the section (lBm) and either (lBj) or (τBj) hold. A combination of (VOC) with (lBj–τBj) and then (3.4) leads to the following lemma.

Lemma 3.4. *For any given solution (w, v) through $(\varphi, \psi) \in \mathcal{C}_2^+$ one has*

$$v(t) \quad \leq \quad \begin{cases} e^{-\mu t}\psi(0) + \|\varphi\| f_l(t), & \text{if (lBj) holds,} \\ e^{-\mu t}\psi(0) + \|\varphi\| f_\tau(t), & \text{if (τBj) holds,} \end{cases} \quad \forall\ t \geq 0, \tag{3.6}$$

introducing $f_l, f_\tau : \mathbb{R}_+ \longrightarrow \mathbb{R}_+$;

$$f_l(t) := k_j e^{-\mu t} \int_0^t e^{(\mu+\overline{q})s} ds,\ f_\tau(t) := e^{-\mu t} k_j \int_0^t e^{\mu s} q_e(s - \underline{\tau}) ds. \tag{3.7}$$

Under the respective assumptions, one has

$$f_l(t) \quad = \quad \frac{k_j}{\mu + \overline{q}} (e^{\overline{q}t} - e^{-\mu t}), \tag{3.8}$$

$$f_\tau(t) \quad = \quad \begin{cases} \frac{k_j}{\mu}(1 - e^{-\mu t}), & \text{if } t \leq \underline{\tau} \\ k_j \frac{\overline{q}(e^{-\mu(t-\underline{\tau})} - e^{-\mu t}) + \mu(e^{\overline{q}(t-\underline{\tau})} - e^{-\mu t})}{\mu(\mu+\overline{q})}, & \text{if } t > \underline{\tau}. \end{cases} \tag{3.9}$$

Proof. If (lBj) holds, the second addend in (VOC) can be estimated with (3.4) as

$$e^{-\mu t}\int_0^t e^{\mu s} j(w_s, v_s)ds \le k_j e^{-\mu t}\int_0^t e^{\mu s}\|w_s\|ds \le \|\varphi\| k_j e^{-\mu t}\int_0^t e^{(\mu+\overline{q})s}ds.$$

If one uses the definition of f_l in (3.7), the previous estimation yields the first estimate in (3.6) and a straightforward integration of that expression leads to (3.8).

If (τBj) holds, then similarly

$$\begin{aligned} & e^{-\mu t}\int_0^t e^{\mu s} j(w_s, v_s)ds \le e^{-\mu t} k_j \int_0^t e^{\mu s} w(s-\tau(v_s))ds \\ \le \;& e^{-\mu t} k_j \|\varphi\| \int_0^t e^{\mu s} q_e(s-\tau(v_s))ds \le \|\varphi\| e^{-\mu t} k_j \int_0^t e^{\mu s} q_e(s-\underline{\tau})ds, \end{aligned}$$

which proves the second estimate in (3.6). Another straightforward integration yields (3.9). □

When writing about f_l or f_τ we agree that from now on, respectively, (lBj) or (τBj), holds.

Lemma 3.5. *Both, f_l and f_τ, are zero in zero. If $\overline{q} = 0$, then*

$$f_l(t) = f_\tau(t) = \frac{k_j}{\mu}(1 - e^{-\mu t}).$$

If $\overline{q} > 0$ the following hold. If $\underline{\tau} = 0$, then $f_l = f_\tau$ and if $\underline{\tau} > 0$, then for each fixed $t > 0$, one has $f_l(t) > f_\tau(t)$, the image $f_l(t)$ is increasing in $\overline{q}$ and the image $f_\tau(t)$ is nondecreasing in $\overline{q}$ if $t \le \underline{\tau}$ and increasing in $\overline{q}$ if $t > \underline{\tau}$. Both, f_l and f_τ, tend to ∞ at ∞, are increasing and continuously differentiable. One has

$$\lim_{t\to 0^+} \frac{f_i(t)}{1 - e^{-\mu t}} = \frac{k_j}{\mu},\; i \in \{l, \tau\}.$$

The functions g_l and g_τ defined by

$$g_i : \mathbb{R}_+ \longrightarrow \mathbb{R};\; g_i(t) := \frac{f_i(t)}{1 - e^{-\mu t}},\; i \in \{l, \tau\},$$

respectively, increase from k_j/μ to infinity on $\mathbb{R}_+$, equal k_j/μ on $[0, \underline{\tau}]$ and increase to infinity on $[\underline{\tau}, \infty)$.

Proof. The statements related to being zero in zero and the cases $\overline{q} = 0$ and $\underline{\tau} = 0$ are obvious. Let now $\overline{q} > 0$ and $\underline{\tau} > 0$. Monotonicity in $\overline{q}$ as stated follows from (3.7) and the fact that $\exp(\overline{q}s)$ and $q_e(s-\underline{\tau})$ have related monotonicity properties. To understand that $f_l(t) > f_\tau(t)$ it is sufficient to compare the two functions given in the previous sentence. We omit further details on these statements. Now, note that by the rule of l'Hôpital (case "0/0") and (3.8) we have

$$\lim_{t\to 0^+} g_l(t) = \lim_{t\to 0^+} \frac{f_l(t)}{1-e^{-\mu t}} = \lim_{t\to 0^+} \frac{f_l'(t)}{\mu e^{-\mu t}} = \frac{k_j}{\mu}. \tag{3.10}$$

For f_τ the limit statement follows directly from (3.9). Next, by (3.8)

$$\operatorname{sgn}\frac{d}{dt}g_l(t) = \operatorname{sgn} g(t), \text{ where } g(t) := \overline{q}e^{\overline{q}t} - (\overline{q}+\mu)e^{(\overline{q}-\mu)t} + \mu e^{-\mu t}.$$

Then $g(0) = 0$ and $g'(t) = \overline{q}^2 e^{\overline{q}t}(1-e^{-\mu t}) + \mu^2 e^{-\mu t}(e^{\overline{q}t}-1) > 0$. Thus $g(t) > 0$ for all $t > 0$ and hence g_l is increasing.

To show that g_τ is increasing, we prove that

$$g(t) := \frac{\overline{q}(e^{-\mu(t-\underline{\tau})} - e^{-\mu t}) + \mu(e^{\overline{q}(t-\underline{\tau})} - e^{-\mu t})}{1-e^{-\mu t}}$$

is increasing for $t > \underline{\tau}$. Using positivity of the sign of both, the denominator of g' and μ, it is straightforward to compute that $\operatorname{sgn} g'(t) = \operatorname{sgn} h(\overline{q})$ where

$$h(\overline{q}) := \overline{q}e^{\overline{q}(t-\underline{\tau})}(1-e^{-\mu t}) - \mu e^{\overline{q}(t-\underline{\tau})-\mu t} + \overline{q}e^{-\mu t}(1-e^{\mu\underline{\tau}}) + \mu e^{-\mu t}.$$

Then $h(0) = 0$. Next, similarly

$$\begin{aligned} h'(\overline{q}) &= e^{\overline{q}(t-\underline{\tau})}\{\overline{q}(t-\underline{\tau})(1-e^{-\mu t}) - t\mu e^{-\mu t} + (\underline{\tau}\mu - 1)e^{-\mu t} + 1\} \\ &\quad + e^{-\mu t}(1-e^{\mu\underline{\tau}}), \\ h'(0) &= j(t), \text{ where } j(t) := 1 - e^{-\mu(t-\underline{\tau})} - \mu(t-\underline{\tau})e^{-\mu t}. \end{aligned}$$

Then $j'(t) = \mu e^{-\mu t}[e^{\mu\underline{\tau}} - 1 + \mu(t-\underline{\tau})] > 0$, hence $h'(0) = j(t) > j(\underline{\tau}) = 0$. Now,

$$\begin{aligned} h''(\overline{q}) &= (t-\underline{\tau})e^{\overline{q}(t-\underline{\tau})}k(\overline{q}), \text{ defining} \\ k(\overline{q}) &:= \overline{q}(t-\underline{\tau})(1-e^{-\mu t}) - t\mu e^{-\mu t} + (\underline{\tau}\mu - 2)e^{-\mu t} + 2. \end{aligned}$$

Then, applying $e^x \geq 1 + x$ to $x = \mu(t - \underline{\tau})$, one gets

$$\begin{aligned} k(0) &= 2 - [2 + \mu(t - \underline{\tau})]e^{-\mu t} \geq 1 - e^{-\mu t} + 1 - e^{-\mu \underline{\tau}} > 0, \\ k'(\overline{q}) &= (t - \underline{\tau})(1 - e^{-\mu t}) > 0. \end{aligned}$$

Hence, k is positive for $\overline{q} > 0$, thus so is h'', hence so is h', thus so is h, hence so is sgn g'. We have shown that g_τ is increasing. Monotonicity of f_l follows from monotonicity of g_l and the same conclusion holds for f_τ. Using that $(1 - e^{-\mu t})^{-1}$ converges to one at infinity the remaining statements are straightforward to deduce. □

Lemma 3.6. *Assume that, respectively, (lBj) or (τBj) holds and that A, B and T are such that $Ag_l(T) \leq B$ or $Ag_\tau(T) \leq B$. Then, if $\|\varphi\| \leq A$ and $|\psi(0)| \leq B$, one has that $v(t) \leq B$ for all $t \in [-h, T]$.*

Proof. We prove the statement for (lBj) only, since the proof for (τBj) is similar. By (3.6) one has $v(t) \leq Be^{-\mu t} + Af_l(t)$ for $t \in (0, T]$. Hence $v(t) \leq B$ if $Ag_l(t) \leq B$ and the latter follows by assumption and Lemma 3.5. □

An elaboration of the maximum in the following lemma will be carried out further down.

Lemma 3.7. *Let $\|\varphi\| \leq A$ and $|\psi(0)| \leq B$. Let $T > 0$ and choose*

$$R \geq \begin{cases} \max_{t \in [T-h,T] \cap [0,\infty)} \max\{k_j q_e(t) A, \mu(e^{-\mu t} B + A f_l(t))\}, \\ \text{if } (lBj) \text{ holds}, \\ \max_{t \in [T-h,T] \cap [0,\infty)} \max\{k_j q_e(t - \underline{\tau}) A, \mu(e^{-\mu t} B + A f_\tau(t))\}, \\ \text{if } (\tau Bj) \text{ holds}. \end{cases}$$

Then, if lip $\psi \leq R$ *and (w, v) is a solution through (φ, ψ), also* lip $v_T \leq R$.

Proof. We should show that lip $v|_{[T-h,T]} \leq R$. First,

$$\text{lip } v|_{[T-h,T] \cap [-h,0]} = \text{lip } \psi|_{[T-h,T] \cap [-h,0]} \leq R.$$

Next, if (lBj) holds, we get $v'(t) \leq j(w_t, v_t) \leq k_j \|w_t\| \leq k_j q_e(t) \|\varphi\|$. If ($\tau$Bj) holds, then $v'(t) \leq k_j w(t - \tau(v_t)) \leq k_j q_e(t - \tau(v_t)) \|\varphi\| \leq k_j q_e(t - \underline{\tau}) \|\varphi\|$. Moreover, in the respective cases,

$$v'(t) \geq -\mu v(t) \geq \begin{cases} -\mu(e^{-\mu t} |\psi(0)| + \|\varphi\| f_l(t)), \\ -\mu(e^{-\mu t} |\psi(0)| + \|\varphi\| f_\tau(t)) \end{cases}$$

and thus for $t > 0$

$$|v'(t)| \leq \begin{cases} \max\{k_j q_e(t)\|\varphi\|, \mu(|\psi(0)|e^{-\mu t} + \|\varphi\| f_l(t))\}, \\ \max\{k_j q_e(t-\underline{\tau})\|\varphi\|, \mu(|\psi(0)|e^{-\mu t} + \|\varphi\| f_\tau(t))\}. \end{cases}$$

Hence, in either case, $\operatorname{lip} v|_{[T-h,T]\cap[0,\infty)} \leq \max_{t\in[T-h,T]\cap[0,\infty)} |v'(t)| \leq R.$ □

We can summarize our results on invariance.

Theorem 3.8. *Suppose that m and j are almost locally Lipschitz, $\mu > 0$, (lBm) holds and so does (lBj) or (τBj). Denote by (w, v) the solution through $(\varphi, \psi) \in V_{\mathcal{C}_2^+}$ and let A, B, R and T denote positive numbers such that $\psi(0) \leq B$ and $\operatorname{lip} \psi \leq R$, both of which follow if $\psi \in C_{B,R}$, and $\|\varphi\| \leq A$.*

(a) If (lBj) holds, $Ag_l(T) \leq B$ and $R \geq \max\{\mu B, k_j A e^{\overline{q}T}\}$, then one has $v_t \in C_{B,R}$ for all $t \in [0, T]$.

(b) If (τBj) holds, $Ag_\tau(T) \leq B$ and

$$R \geq \max\{\mu B, k_j A q_e(T - \underline{\tau})\},$$

then, again $v_t \in C_{B,R}$ for all $t \in [0, T]$.

Proof. (a) Let $\tilde{T} \in [0, T]$. Then

$$e^{\overline{q}T} \geq \max_{t\in[\tilde{T}-h,\tilde{T}]\cap[0,\infty)} q_e(t).$$

Moreover

$$\max_{t\in[0,\tilde{T}]} (e^{-\mu t} B + A f_l(t)) = B$$

since $e^{-\mu t} B + A f_l(t)|_{t=0} = B$ and $e^{-\mu t} B + A f_l(t) \leq B$ for all $t \in (0, \tilde{T}]$ since $Ag_l(t) \leq B$ for all $t \in (0, \tilde{T}]$ by the assumptions and monotonicity of g_l. Hence, by the assumptions

$$\begin{aligned} R &\geq \max\{\mu B, A k_j e^{\overline{q}T}\} \\ &\geq \max\{\max_{t\in[\tilde{T}-h,\tilde{T}]\cap[0,\infty)} \mu(e^{-\mu t} B + A f_l(t)), \max_{t\in[\tilde{T}-h,\tilde{T}]\cap[0,\infty)} A k_j q_e(t)\} \\ &= \max_{t\in[\tilde{T}-h,\tilde{T}]\cap[0,\infty)} \max\{\mu(e^{-\mu t} B + A f_l(t)), A k_j q_e(t)\}. \end{aligned}$$

Then, by Lemma 3.7 applied to $T := \tilde{T}$ one has lip $v_{\tilde{T}} \leq R$. As $\tilde{T}$ was chosen arbitrarily, one has lip $v_t \leq R$ for all $t \in [0, T]$. The boundedness property follows by Lemma 3.6.
(b) By the assumption and the monotonicity of g_τ, shown in Lemma 3.5, one has that $B \geq Ag_\tau(t)$. Then by Lemma 3.4

$$\begin{aligned} v(t) &\leq Be^{-\mu t} + Af_\tau(t) \leq B, \ \forall\, t \in [0, T] \text{ and} \\ R &\geq \max\{Ak_j q_e(T - \underline{\tau}), \mu B\} \\ &\geq \max_{t \in [0,T]} \max\{Ak_j q_e(t - \underline{\tau}), \mu(Be^{-\mu t} + Af_\tau(t))\}. \end{aligned}$$

Hence the Lipschitz-property follows by Lemma 3.7. □

For further discussion we state some technical results.

Lemma 3.9. *For all $t > 0$ one has $\frac{k_j e^{\overline{q}t}}{\mu} \geq g_l(t)$ and $k_j q_e(t - \underline{\tau}) \geq \mu g_\tau(t)$. If $\overline{q} > 0$, the corresponding strict inequalities hold and, if $\overline{q} = 0$, equalities hold.*

Proof. The case $\overline{q} = 0$ is trivial. We present the case $\overline{q} > 0$. For $t > s \geq 0$ one has

$$e^{\overline{q}(t-s)} > \frac{\overline{q}(e^{-\mu(t-s)} - e^{-\mu t}) + \mu(e^{\overline{q}(t-s)} - e^{-\mu t})}{(\mu + \overline{q})(1 - e^{-\mu t})} \tag{3.11}$$

$$\Leftrightarrow e^{\overline{q}(t-s)} f(t) > 0, \text{ where}$$
$$f(t) := \overline{q} + (\mu + \overline{q})e^{-\overline{q}(t-s) - \mu t} - (\mu + \overline{q})e^{-\mu t} - \overline{q}e^{-(\overline{q}+\mu)(t-s)}.$$

Then $\lim_{t \downarrow s} f(t) = 0$ and

$$f'(t) = (\mu + \overline{q})e^{-\mu t}[\overline{q}e^{-\overline{q}(t-s)}(e^{\mu s} - 1) + \mu(1 - e^{-\overline{q}(t-s)})] > 0.$$

Hence $f(t) > 0$ for all $t > s$ and (3.11) holds. Setting $s = 0$ shows the first inequality and setting $s = \underline{\tau}$ shows the second inequality for $t \geq \underline{\tau}$. The second inequality for $t < \underline{\tau}$ follows directly by definition of q_e and f_τ. □

By the lemma, to guarantee the preconditions in Theorem 3.8 (a) and (b), it would be sufficient to have

$$R \geq \mu B \geq \begin{cases} k_j A e^{\overline{q}T}, & \text{respectively,} \\ k_j A q_e(T - \underline{\tau}), & \end{cases}$$

which is stronger but easier to check than the present assumptions. In particular, if $\overline{q}=0$, the preconditions in (a) and (b) are satisfied for any A, B, and R with $R \geq \mu B \geq Ak_j$ and arbitrary T.

Recall that if $\underline{\tau}=0$ then $f_\tau = f_l$. Then it becomes obvious that also in Theorem 3.8 and Lemma 3.9 the cases (lBj) and (τBj) coincide.

If $\underline{\tau}>0$ and $\overline{q}>0$, through (b) a lower bound, a lower Lipschitz constant and a larger invariance time than through (a) can be achieved. We formulate this more precisely in obvious notation without proof:

Corollary 3.10. *Fix positive numbers A and T. Then*

$$\begin{aligned} B_a &:= Ag_l(T) > Ag_\tau(T) =: B_b, \\ R_a &:= \max\{\mu B_a, k_j A e^{\overline{q}T}\} > \max\{\mu B_b, k_j A q_e(T-\underline{\tau})\} =: R_b. \end{aligned}$$

Now, fix A, B and R such that $R \geq \mu B > Ak_j > 0$ and define $t_a := \min\{t_{a1}, t_{a2}\}$ and $t_b := \min\{t_{b1}, t_{b2}\}$, with t_{ij} defined via

$$\begin{aligned} &Ag_l(t_{a1}) = B,\ Ag_\tau(t_{b1}) = B, \\ &R = \max\{\mu B, Ak_j e^{\overline{q}t_{a2}}\},\ R = \max\{\mu B, Ak_j q_e(t_{b2}-\underline{\tau})\}. \end{aligned}$$

Then $t_{aj} < t_{bj}$, $j=1,2$, hence $t_a < t_b$.

Theorem 3.11. *Suppose that m and j are almost locally Lipschitz, $\mu > 0$, (lBm) holds, so does (τBj) and denote by $(w,v) = (w,v)^{\varphi,\psi}$ the solution through $(\varphi,\psi) \in V_{\mathcal{C}_2^+}$. Let A, B and R denote positive numbers, such that $Ak_j < B\mu \leq R$. If $\overline{q}>0$, choose $\delta > 0$ such that $Ak_j e^{\overline{q}\delta} = \mu B$, and if $\overline{q}=0$, choose any $\delta > 0$. Then, if $|\psi(0)| \leq B$ and $\operatorname{lip}\psi \leq R$, so in particular if $\psi \in C_{B,R}$, and $\|\varphi\| \leq A$ one has $v_t \in C_{B,R}$ for all $t \in [0, \underline{\tau}+\delta]$.*

The result can be concluded from Theorem 3.8 (b): To prove this for $\overline{q}>0$, define $T=\underline{\tau}+\delta$ in (b), and apply the second estimate of Lemma 3.9 with $t=T$. We omit further details.

Note that, if (τBj) holds and additionally $\underline{\tau}>0$, then by Theorem 3.11 the positive time $\underline{\tau}$ for which invariance holds is uniform for all A, B satisfying $Ak_j/\mu < B$. If merely (lBj) holds and $\overline{q}>0$, we cannot get such a lower bound on invariance time through Theorem 3.8 (a).

Remark 3.12. Recall that $\overline{q} \leq k_m$, and that $q_e(t)$, $f_l(t)$ and $f_\tau(t)$ are either nondecreasing or increasing in $\overline{q}$. Then it is easy to see that our statements essentially remain true, if one replaces $\overline{q}$ by k_m, in particular in these functions, but become weaker. Hence $\overline{q}$ is the more suitable quantity here.

Remark 3.13. Define

$$\tilde{q} := \sup_{(\varphi,\psi)\in\mathcal{C}_2^+,\ \varphi(0)\neq 0} \frac{m(\varphi,\psi)}{\varphi(0)}.$$

If $\tilde{q} \leq 0$, then $\overline{q} = 0$ and A and B can be chosen such that we obtain invariant sets for arbitrary times. In this sense the analysis of this case is ahead of the analysis of the case $\tilde{q} > 0$. If $\tilde{q} < 0$, the estimates could probably still be improved if one would use functions defined in terms of $\tilde{q}$ instead of $\overline{q}$. However, this would be at the expense of a more involved notation. On the other hand the case $\tilde{q} < 0$ can be related to extinction and the absence of both, positive equilibria and oscillations, which makes it mathematically simpler in many senses.

4. Semiflow and invariant compact sets for the cell SD-DDE

We specify the functionals m, j and τ introduced in Section 3 such that the two-dimensional DDE (1.6) becomes the cell SD-DDE (1.1–1.4). We will guarantee that the functionals m and j have smoothness properties that are such that the results of Section 3 can be applied.

Consider a function $g : \mathcal{D}_g \longrightarrow [0, K]$, where $\mathcal{D}_g := \overline{B}_b(x_2) \times \mathbb{R}_+$ and $b, x_2, K \in \mathbb{R}$ are given parameters with $b > 0$, $K > 0$. Define $h := b/K > 0$. The following result contains an application of the Picard–Lindelöf theorem.

Lemma 4.1. *Suppose that g is continuous on $\mathcal{D}_g$ and Lipschitz in the first argument, uniformly on compact intervals of $\mathbb{R}_+$ with respect to the second. Then for $\psi \in \mathcal{C}_1^+$ there exists a unique solution $y = y(\cdot, \psi)$ on $[0, h]$ of (1.3).*

Proof. Fix ψ. Define $f_\psi : [0, h] \times \overline{B}_b(x_2) \longrightarrow \mathbb{R}$; $f_\psi(s, y) := -g(y, \psi(-s))$ and with f_ψ a non-autonomous ODE $y'(s) = f_\psi(s, y(s))$. Then f_ψ satisfies the conditions of the Picard–Lindelöf Theorem, e.g. [12, Theorem II.1.1], which guarantees that there exists a unique solution y on $[0, h]$, since we defined $h := b/K$. □

Next, we show that the Gronwall inequality leads to the following result. In the proof of part (b) of Lemma 4.2 below we will need, additionally to the assumptions of Lemma 4.1, that g is locally Lipschitz in the second argument, uniformly with respect to the first. Note that the two together are equivalent to g being locally Lipschitz.

Lemma 4.2. *(a) Under the assumptions of Lemma 4.1, the map* $Y : \mathcal{C}_1^+ \longrightarrow C([0,h], \overline{B}_b(x_2))$; $Y(\psi)(t) := y(t,\psi)$ *is continuous.*
(b) If g *is locally Lipschitz, then* Y *is locally Lipschitz.*

Proof. Fix $\overline{\psi} \in \mathcal{C}_1^+$ and define $A := \{\psi(-s) : \ s \in [0,h], \ \psi \in \mathcal{C}_1^+ \cap \overline{B}_1(\overline{\psi})\}$. Note that

$$A = [\max\{\min_{s\in[0,h]} \overline{\psi}(-s) - 1, 0\}, \max_{s\in[0,h]} \overline{\psi}(-s) + 1].$$

Hence, A is a compact subinterval of $\mathbb{R}_+$. Choose $L = L(\overline{\psi})$, such that g is L-Lipschitz in the first argument, uniformly with respect to the second on A. Let $\psi, \chi \in \mathcal{C}_1^+ \cap \overline{B}_1(\overline{\psi})$ and $t \in [0,h]$. Then

$$\begin{aligned} |y(t,\psi) - y(t,\chi)| &\leq \int_0^t |g(y(s,\psi),\psi(-s)) - g(y(s,\chi),\chi(-s))| ds \\ &\leq \int_0^t |g(y(s,\psi),\psi(-s)) - g(y(s,\chi),\psi(-s))| ds \\ &\quad + \int_0^t |g(y(s,\chi),\psi(-s)) - g(y(s,\chi),\chi(-s))| ds \\ &\leq L \int_0^t |y(s,\psi) - y(s,\chi)| ds \\ &\quad + \int_0^h |g(y(s,\chi),\psi(-s)) - g(y(s,\chi),\chi(-s))| ds. \end{aligned}$$

Then, by Gronwall's inequality, see e.g. [10, Corollary I 6.6] one has

$$|y(t,\psi) - y(t,\chi)| \leq e^{Lh} \int_0^h |g(y(s,\chi),\psi(-s)) - g(y(s,\chi),\chi(-s))| ds \quad (4.1)$$

for all $\psi, \chi \in \mathcal{C}_1^+ \cap \overline{B}_1(\overline{\psi})$ and $t \in [0,h]$.

To prove (a) first note that (4.1) holds for $\chi := \overline{\psi}$. Then continuity of Y at $\overline{\psi}$ can be deduced using (4.1) and uniform continuity of g on the compact set $\overline{B}_b(x_2) \times A$. To prove (b), note that, since g is locally Lipschitz in the second argument, uniformly with respect to the first, by compactness of A, g is Lipschitz on A in the second argument, uniformly with respect to the first argument, i.e., there exists some K_A, such that

$$|g(y,z_1) - g(y,z_2)| \leq K_A |z_1 - z_2|, \ \forall \ y \in \overline{B}_b(x_2), \ z_1, z_2 \in A. \quad (4.2)$$

The proof can be completed, using (4.1) and (4.2). □

Remark 4.3. Note that the smoothness formulated in the previous lemma can be formulated as smoothness of solutions with respect to variation of a parameter in a Banach space in a non-autonomous ODE. We refer to the discussion section in [7] for details and a discussion of literature. Somewhat similar, the conclusion of Lemma 4.2 (a) is a special case of the conclusion of [11, Theorem 2.2.2], if one considers in the latter only continuous dependence with respect to the functional for a non-autonomous functional differential equation. The preconditions in [11, Theorem 2.2.2], however, are somewhat different. Openness of both components of the domain of the functional is required and existence and uniqueness of solutions are assumed. On the other hand rather than Lipschitz assumptions, mere continuity of the functional is required. Here we proved (a) at little extra cost with respect to the proof of (b).

Lemma 4.4. *Suppose that additionally to the assumptions of Lemma 4.1 there are parameters $x_1, \varepsilon \in \mathbb{R}$, such that $0 < \varepsilon < K$ and $x_2 - x_1 \in (0, b\varepsilon/K)$ and suppose that $g(y,z) \geq \varepsilon$ for all $(y,z) \in \mathcal{D}_g$. Then $x_1 \in \overline{B}_b(x_2)$ and there exists a unique*

$$\tau = \tau(\psi) \in [\frac{x_2 - x_1}{K}, \frac{x_2 - x_1}{\varepsilon}] \subset (0, h]$$

solving (1.4).

Proof. Fix ψ and denote by $y = y(\cdot, \psi)$ the solution of (1.3) and by $\tau = \tau(\cdot, \psi)$ possible solutions of (1.4). Then y is decreasing by (1.3) since $g > 0$ which shows that there can be at most one τ solving (1.4). By the fundamental theorem of calculus applied to (1.3) and using that $\varepsilon \leq g(y,z) \leq K$ for all $(y,z) \in \mathcal{D}_g$, one can show that $y((x_2 - x_1)/K) \geq x_1 \geq y((x_2 - x_1)/\varepsilon)$. By the intermediate value theorem there exists some τ in the stated interval solving (1.4). The remaining statements follow by our assumptions on parameters. □

In the setting of the previous lemma, we can now define a functional

$$\tau : \mathcal{C}_1^+ \longrightarrow [0, h], \text{ with } \tau(\mathcal{C}_1^+) \subset [\underline{\tau}, h), \text{ where } \underline{\tau} := (x_2 - x_1)/K > 0.$$

Smoothness of Y is inherited by τ in the following sense.

Lemma 4.5. *Suppose that the assumptions of Lemma 4.4 hold. Then the functional $\tau : \mathcal{C}_1^+ \longrightarrow [0, h]$ is continuous. If additionally to the stated assumptions g is locally Lipschitz, then so is τ.*

Proof. Let $\overline{\psi}, \psi \in \mathcal{C}_1^+$. By definition of $\tau(\psi)$ and $\tau(\overline{\psi})$ one has

$$y(\tau(\psi), \psi) = y(\tau(\overline{\psi}), \overline{\psi}) \ \ (= x_1).$$

Hence,

$$|y(\tau(\psi), \psi) - y(\tau(\psi), \overline{\psi})| = |y(\tau(\psi), \overline{\psi}) - y(\tau(\overline{\psi}), \overline{\psi})|.$$

The left hand side is dominated by $\|Y(\psi) - Y(\overline{\psi})\|$. By the mean value theorem, there exists some $t \in [0, h]$, such that the right hand side equals

$$\begin{aligned} & |D_1 y(t, \overline{\psi})||\tau(\psi) - \tau(\overline{\psi})| \\ = \ & |g(y(t, \overline{\psi}), \overline{\psi}(-t))||\tau(\psi) - \tau(\overline{\psi})| \geq \varepsilon|\tau(\psi) - \tau(\overline{\psi})|. \end{aligned}$$

Thus $|\tau(\psi) - \tau(\overline{\psi})| \leq \frac{1}{\varepsilon}|Y(\psi) - Y(\overline{\psi})|$ and the proof is completed by applying Lemma 4.2. □

Next, we introduce functions $q : \mathbb{R}_+ \longrightarrow \mathbb{R}$, $\gamma : \mathbb{R}_+ \longrightarrow \mathbb{R}_+$ and $d : \mathcal{D}_g \longrightarrow \mathbb{R}$. Define

$$m : \mathcal{C}_2^+ \longrightarrow \mathbb{R};\ m(\varphi, \psi) := q(\psi(0))\varphi(0).$$

If the assumptions of Lemma 4.4 (and Lemma 4.1) hold and moreover g is partially differentiable in the first argument and $D_1 g$ and d are continuous, we can define $j : \mathcal{C}_2^+ \longrightarrow \mathbb{R}_+$ via

$$j(\varphi, \psi) \ \ := \ \ \frac{\gamma(\psi(-\tau(\psi)))}{g(x_1, \psi(-\tau(\psi)))} g(x_2, \psi(0))\varphi(-\tau(\psi)) e^{\int_0^{\tau(\psi)} [d - D_1 g](y(s,\psi), \psi(-s)) ds}. \tag{4.3}$$

Note that continuity of the partial derivative of g implies the Lipschitz property required in Lemma 4.1. To guarantee smoothness of j, it is useful to introduce a notation that summarizes ingredients with the same type of delay. We will use below that j is a special case of the functional defined in the following corollary.

Corollary 4.6. *Let $\beta : \mathbb{R}_+ \longrightarrow \mathbb{R}_+$, $r : \mathcal{C}_1^+ \longrightarrow [0, h]$ and $\mathcal{G} : \mathcal{C}_1^+ \longrightarrow \mathbb{R}$ be continuous maps and suppose that $g(x_2, \cdot)$ is continuous. Then the functional $\mathcal{C}_2^+ \longrightarrow \mathbb{R}_+$;*

$$(\varphi, \psi) \longmapsto \beta(\psi(-r(\psi)))g(x_2, \psi(0))\varphi(-r(\psi))e^{\mathcal{G}(\psi)} \tag{4.4}$$

is continuous. If β and $g(x_2, \cdot)$ are locally Lipschitz and r and $\mathcal{G}$ are almost locally Lipschitz, it is almost locally Lipschitz.

The result is a straightforward application of Lemma 3.1 and discussed or straightforward rules. We omit further details. Below we will apply the corollary to even locally Lipschitz r and $\mathcal{G}$. However, Lemma 3.1 and the discussion below it should make clear that assuming locally Lipschitz r and $\mathcal{G}$ does not allow to sharpen the second statement of the corollary to "locally Lipschitz".

Lemma 4.7. *Consider arbitrary continuous operators*

$$\begin{aligned}&Q:\mathcal{D}_Q\longrightarrow\mathcal{R}_Q,\ r:\mathcal{D}_Q\longrightarrow[a,b],\ G:\mathcal{D}_G:=\mathcal{D}_Q\times\mathcal{R}_Q\longrightarrow\mathcal{R}_G,\ \text{where}\\ &\mathcal{D}_Q:=C([-b,-a],J_1),\ \mathcal{R}_Q:=C([a,b],J_2),\ \mathcal{R}_G:=C([a,b],J_3),\end{aligned}$$

$a,b\in\mathbb{R}$ *with* $a<b$ *and* J_1, J_2 *and* J_3 *are nonempty subsets of* $\mathbb{R}$. *Define*

$$\mathcal{G}:\mathcal{D}_Q\longrightarrow J_3;\ \mathcal{G}(\psi):=G(\psi,Q(\psi))(r(\psi)).$$

Then $\mathcal{G}$ *is continuous. If* G, Q *and* r *are locally Lipschitz and moreover*

$$\forall\, x_0\in\mathcal{D}_G\ \exists\, k=k(x_0),\ \delta=\delta(x_0),\ s.th.\ \sup_{x\in\mathcal{D}_G\cap B_\delta(x_0)}\operatorname{lip}G(x)\le k,\tag{4.5}$$

then $\mathcal{G}$ *is locally Lipschitz.*

Proof. First, we decompose $\mathcal{G}$ as

$$\begin{aligned}&\psi\xmapsto{(id\times Q)\times r}((\psi,Q(\psi)),r(\psi))\xmapsto{(G,id)}(G(\psi,Q(\psi)),r(\psi))\\ &\xmapsto{ev}G(\psi,Q(\psi))(r(\psi)).\end{aligned}$$

As the involved maps are continuous, the decomposition shows that so is $\mathcal{G}$. To prove the second statement, first, by similar arguments, $\psi\mapsto G(\psi,Q(\psi))$ is locally Lipschitz as a composition. Next, in notation similar to the one in Lemma 3.1, we can write $\mathcal{G}(\psi)=ev\circ(id,r)(G(\psi,Q(\psi)),\psi)$. Then the remainder of the proof is similar to showing the last statement of Lemma 3.1, if one uses that functions in the first argument of $ev\circ(id,r)$ lie in $\mathcal{R}_G$ and thus are Lipschitz by (4.5). □

The following lemma will be helpful to apply G of the previous lemma to the integral term appearing in the exponent of j.

Lemma 4.8. *Let J_1 and J_2 be nonempty subsets of $\mathbb{R}$ and let $a, b \in \mathbb{R}$, $a < b$. Suppose that $l : J_2 \times J_1 \longrightarrow \mathbb{R}$ is continuous. Define*

$$H : \mathcal{D}_H := C([a,b], J_2 \times J_1) \longrightarrow C([a,b], \mathbb{R});\ H(\chi)(t) := \int_a^t l(\chi(s))ds.$$

Then H is continuous. If l is locally Lipschitz, then so is H.

Proof. First note that for any $\xi, \chi \in \mathcal{D}_H$ a standard estimation yields

$$\|H(\xi) - H(\chi)\| \leq (b-a) \max_{s \in [a,b]} |l(\xi(s)) - l(\chi(s))|. \tag{4.6}$$

To prove continuity in an arbitrary $\chi \in \mathcal{D}_H$, fix $\varepsilon > 0$. First note that $\chi([a,b]) \subset J_2 \times J_1$ is compact. Hence we can choose a neighborhood U of $\chi([a,b])$ in R^2 such that $K := \overline{U \cap (J_2 \times J_1)}$ is a compact subset of $J_2 \times J_1$. Next, we can choose $\delta > 0$ such that both, $\xi \in \mathcal{D}_H$ and $\|\xi - \chi\| < \delta$ implies $\xi(s) \in K$ for all $s \in [a,b]$ and, by uniform continuity of l on K, one has

$$|l(y) - l(z)| \leq \frac{\varepsilon}{(b-a)},\ \text{if } |y - z| \leq \delta,\ y, z \in K. \tag{4.7}$$

Combining the last argument with (4.6) yields that

$$\|H(\xi) - H(\chi)\| \leq \varepsilon \text{ if } \xi \in \mathcal{D}_H,\ \|\xi - \chi\| < \delta.$$

This proves the continuity statement.

In the following we show that H is locally Lipschitz in $\phi \in \mathcal{D}_H$. Similar as above, we can choose a neighborhood U of $\phi([a,b])$ in R^2 such that $K := \overline{U \cap (J_2 \times J_1)}$ is a compact subset of $J_2 \times J_1$. Since l is locally Lipschitz, it is L-Lipschitz on K for some constant L. Next, we can choose $\delta > 0$ such that $\xi, \chi \in \mathcal{D}_H \cap B_\delta(\phi)$ implies $\xi(s), \chi(s) \in K$ for all $s \in [a,b]$. Hence we can use (4.6) and the Lipschitz property for l so see that H is $L(b-a)$-Lipschitz on $B_\delta(\phi)$, which completes the proof. □

See also [3] for details on smoothness properties of related Nemytskii-operators. Note that in Lemmas 4.7 and 4.8 we obtain locally Lipschitz operators, whereas in Corollary 4.6 only almost locally Lipschitz operators are required. However, in Lemma 4.8 it is fairly natural to assume that the kernel l is locally Lipschitz and, if one would state on a merely almost locally Lipschitz integral operator, it is not clear how to formulate a weaker natural precondition for the kernel. It should become clear below that similar considerations apply to Q and r. We are now ready to establish smoothness of m and j.

Lemma 4.9. *(a) If q is continuous, then the functional m is continuous and $m(U)$ is bounded, whenever $U \subset \mathcal{C}_2^+$ is bounded. If q is locally Lipschitz, then so is m.*
(b) If the assumptions of Lemma 4.4 (and Lemma 4.1) hold, g is partially differentiable in the first argument and $D_1 g$, d and γ are continuous, then the functional j is continuous and $j(U)$ is bounded, whenever $U \subset \mathcal{C}_2^+$ is bounded. If additionally g is locally Lipschitz and $D_1 g$, γ and d are locally Lipschitz, then j is almost locally Lipschitz.

Proof. We prove only (b), since (a) does not involve additional arguments. In the notation of Lemma 4.7 define $a := 0$, $b := h$, $J_1 := \mathbb{R}_+$, $J_2 := \overline{B}_b(x_2)$, $J_3 := \mathbb{R}$, $\beta := \gamma(\cdot)/g(x_1, \cdot)$, $Q := Y$, $r := \tau$,

$$G : \mathcal{C}_1^+ \times C([0,h], \overline{B}_b(x_2)) \longrightarrow C([0,h], \mathbb{R});$$
$$G(\psi, z)(t) := \int_0^t [d - D_1 g](z(s), \psi(-s)) ds$$

and with these ingredients $\mathcal{G}$ and (4.4). To see the first statement, by Corollary 4.6 it is sufficient to show that β, r and $\mathcal{G}$ are continuous. Continuity of β follows from continuity of γ and g. Continuity of $r = \tau$ was shown in Lemma 4.5. Continuity of $\mathcal{G}$ follows from Lemma 4.7, provided we show that G is continuous. To see this, first apply Lemma 4.8 to the case $l := d - D_1 g$ and then observe that $G = H \circ \Phi$, introducing the Lipschitz map

$$\Phi : \mathcal{C}_1^+ \times C([0,h], \overline{B}_b(x_2)) \longrightarrow C([0,h], \mathcal{D}_g); \; \Phi(\psi, z)(s) := (z(s), \psi(-s)).$$

To see that the statement on boundedness holds, let $B_1 \times B_2 \subset \mathcal{C}_2^+$ be bounded. Then $\{\psi(-\tau(\psi)) : \psi \in B_2\}$, $\{\varphi(-\tau(\psi)) : (\varphi, \psi) \in B_1 \times B_2\}$ and $\{(y(s,\psi), \psi(-s)) : \psi \in B_2 \; s \in [0,h]\}$ are bounded. Each of the functions γ, $g(x_2, \cdot)$, $id|_{\mathbb{R}_+}$, d and $D_1 g$ has closed domain that contains the corresponding (see definition of j) of the above sets. Hence for each function the domain contains also the closure of the set. Since each function is continuous and any such closure compact, the functions are bounded on the closures of the sets, thus also on the sets themselves. Finally note that $g(x_1, \cdot) \geq \varepsilon$ on its domain. Then boundedness of j on $B_1 \times B_2$ should be obvious. To see that j is almost locally Lipschitz, similarly as above, it is sufficient to show that β, r and $\mathcal{G}$ are locally Lipschitz. The map β is locally Lipschitz since γ and $g(x_1, \cdot)$ are. The functional $r = \tau$ is locally Lipschitz by Lemma 4.5. Next, similarly as we showed continuity of G above, it follows by Lemma 4.8 that under the corresponding assumptions G is also locally Lipschitz. To see that (4.5) holds, one can use boundedness of l on a suitable compact set, which follows from continuity of l with an argument similarly as above. Then, by Lemma 4.7, also $\mathcal{G}$ is locally Lipschitz. □

Lemma 4.9 refers to conditions under which (1.3–1.4) can be solved and m and j can be defined. Under these conditions (1.6) is equivalent to the cell SD-DDE.

Recall that we can achieve global existence via the results of Section 3 if we guarantee (lBm) and (sBj). If we add to the assumptions that γ, d and $D_1 g$ are bounded it is easy to see that (τBj) and thus in particular (sBj) holds. For our specification of m, (lBm) holds if and only if q is bounded. In this case, in the notation of Section 3

$$\overline{q} = \max\{\sup_{z \in \mathbb{R}_+} q(z), 0\} < \infty.$$

With the results established in this subsection for m and j we can now apply the results of Section 3 on (1.6) to conclude well-posedness and invariance properties for the cell SD-DDE. For better overview, we repeat the main assumptions.

Theorem 4.10. *Consider parameters $x_1, x_2, b, \varepsilon, K$ with $b > 0$, $0 < \varepsilon < K$ and $x_2 - x_1 \in (0, b\varepsilon/K)$. Suppose that for $\mathcal{D}_g := \overline{B}_b(x_2) \times \mathbb{R}_+$ and $g : \mathcal{D}_g \longrightarrow [\varepsilon, K]$ one has that g is partially differentiable in the first argument and g and $\mathcal{D}_1 g$ are continuous and define $h := b/K > 0$. Suppose that moreover $\gamma : \mathbb{R}_+ \longrightarrow \mathbb{R}_+$, $d : \mathcal{D}_g \longrightarrow \mathbb{R}$ and $q : \mathbb{R}_+ \longrightarrow \mathbb{R}$, are continuous. Then the following hold.*
(a) For all $\phi \in \mathcal{C}_2^+$ there exists some $c = c(\phi)$ and a non-continuable solution $(w, v)^\phi$ of the cell SD-DDE (1.1–1.4) on $[-h, c)$ through ϕ.
(b) If g, $D_1 g$, γ, d and q are locally Lipschitz, then for any $\phi \in V_{\mathcal{C}_2^+}$ there exists a unique $c = c(\phi)$ and a unique non-continuable solution on $[-h, c)$ through ϕ.
(c) If $D_1 g$, γ, d and q are bounded, then for any $\phi \in \mathcal{C}_2^+$ there exists a global solution through ϕ.
(d) If the preconditions of both, (b) and (c), hold then for any $\phi \in V_{\mathcal{C}_2^+}$ there exists a unique global solution through ϕ. The solutions define a continuous semiflow in the sense of Theorem 2.16 and with g_τ as in Section 3 satisfy the invariance properties in Proposition 3.3, Theorem 3.8 (b) and Theorem 3.11.

Finally, $\underline{\tau} > 0$, i.e., there exists a positive invariance time which is uniform in the sense discussed in Section 3.

Proof. (a) It is trivial that (Fm) holds. By Lemma 4.9, m and j are continuous. Then the statement follows by Lemma 3.2 (a).
(b) By Lemma 4.9, m is locally Lipschitz and j is almost locally Lipschitz and the statement follows by Lemma 3.2 (c)
(c) The statement follows by Lemma 3.2 (d) and by what we have discussed.
(d) Existence of a unique global solution follows trivially from (b) and (c). Next, by the conditions of (b) and by Lemma 4.9 the functionals m and j are almost locally Lipschitz. Moreover, we have discussed, that (lBm) and (sBj) hold. Then by Lemma 3.2 (e) solutions define a continuous semiflow. The invariance properties follow by Theorem 3.8 (d). □

5. Discussion and outlook

In Section 4 we have elaborated conditions on the functions q, γ, g and d and the positive parameter μ that guarantee well-posedness of the cell SD-DDE and invariance properties. For a further specification of these functions we refer to [6, 5, 16]. The functions introduced in this paper are essentially generalizations of these specifications. We also remark that the exact nature of the cellular and sub-cellular processes related to these ingredients is subject to current research, see e.g. [20].

To establish existence of periodic solutions for a certain class of DDE with state-dependent delay, in [14] the authors include the assumption that the initial function should be at equilibrium value at time zero in their definition of the invariant set. In future analysis of the cell SD-DDE one could include such assumptions and try to investigate convex and compact sets that are invariant under the original untransformed system (1.1–1.4), i.e., sets that are invariant for both components of the state. Motivated by the fact that (global) existence of periodic solutions often can be concluded from behavior in a finite time interval, we also have some hope that the invariance for finite time, as established here, may be sufficient to obtain results on the existence of periodic solutions.

In population dynamics, ultimate boundedness and dissipativity, apart from being interesting on their own, often can be used to conclude population persistence [18] and these topics are essentially open problems for the cell

SD-DDE. In relation to the absence of feedback from above (see the Introduction), in ongoing research on these problems, the authors reencountered some of the discussed challenges they found in the invariance analysis of this manuscript. In this sense there is hope that future research may benefit from the research in this manuscript. The authors are also involved in ongoing research on global stability of equilibria for the cell SD-DDE. Should results be achieved in any of these areas, they may be formulated for the enlarged set of initial conditions established in this manuscript.

Corollary 2.18 is an example for how asymptotic behavior in terms of convergence in $\mathbb{R}$ can be concluded from continuous dependence of the solution on the initial value in the $\mathcal{C}$-topology. Using continuous dependence of the solution on the initial value in $\mathcal{C}^1$, as established in [7], one could possibly prove similarly that the limit is an equilibrium, if the convergence of the solution to the constant is in $\mathcal{C}^1$. The latter, however, is a stronger prerequisite and may be too strong in applications.

Section 4 shows that it is feasible to guarantee that a functional appearing in a real world application is almost locally Lipschitz, but that this should be taken care of by the mathematical rather than by the modelling community and we hope to provide some more generally applicable ideas on how this can be done.

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