

Measure-transmission metric and stability of structured population models



G. Jamróz*

Institute of Mathematics, Polish Academy of Sciences, Śniadeckich 8, 00-656 Warszawa, Poland

Institute of Applied Mathematics and Mechanics, University of Warsaw, Banacha 2, 02-097 Warszawa, Poland

ARTICLE INFO

Article history:

Received 17 April 2014

Accepted 21 February 2015

Available online 23 March 2015

Keywords:

Transport equation

Measure-valued solutions

Metrics on measures

Structured population models

Cell differentiation

Stability

ABSTRACT

In Gwiazda, et al. (2012) a framework for studying cell differentiation processes based on measure-valued solutions of transport equations was introduced. Under application of the so-called measure-transmission conditions it enabled to describe processes involving both discrete and continuous transitions. This framework, however, admits solutions which lack continuity with respect to initial data. In this paper, we modify the framework from Gwiazda, et al. (2012) by replacing the flat metric, known also as bounded Lipschitz distance, by a new Wasserstein-type metric. We prove, that the new metric provides stability of solutions with respect to perturbations of initial data while preserving their continuity in time. The stability result is important for numerical applications.

© 2015 Elsevier Ltd. All rights reserved.

1. Introduction

Cell differentiation process is a biological phenomenon, in which immature cells of living organisms give rise to more mature, i.e. more specialized, ones, see e.g. [1]. In humans, this process takes place primarily during gestation, childhood and adolescence. During these initial stages of human development a fertilized egg cell, called zygote, divides and differentiates multiple times, eventually giving rise to mature cells of blood, muscles, skin, brain etc. In some tissues, the process of cell differentiation persists during adulthood.

For instance, neural stem cells or neural progenitors, which reside in the part of brain called hippocampus, can differentiate (Fig. 1) to become eventually mature neurons, which has implications for human memory, see e.g. [2,3].

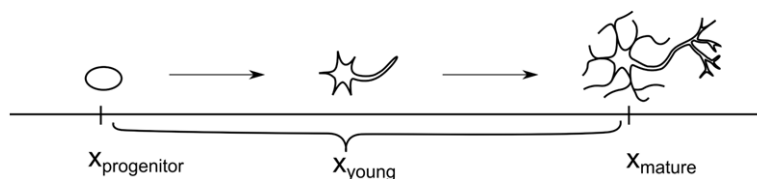


Fig. 1. Schematic drawing of the process of differentiation of neurons in hippocampus. From the discrete state of neural progenitor a cell differentiates to become a young neuron. This continuous phase lasts around four weeks and consists in migration and morphological maturation. Finally, the young neuron reaches the discrete state of maturity.

* Correspondence to: Institute of Mathematics, Polish Academy of Sciences, Śniadeckich 8, 00-656 Warszawa, Poland.
E-mail address: jamroz@mimuw.edu.pl.

Various mathematical models, focusing on different aspects of the process of cell differentiation, and using various mathematical structures, have been proposed in the scientific literature. They include modelling differentiation switches via Markov chains or systems of ordinary differential equations (see [4–6]), modelling the inherent stochasticity via branching processes (see e.g. [7–9]), modelling delays via delay differential equations (see [10–12] and references therein), modelling spatial dynamics via discrete lattice models or reaction–diffusion equations (see [13,14]) and others.

The approach developed in the present paper is called *structured population models*. It consists in tracing populations of cells according to their *maturity level* which is described by a real structure variable $x \in \mathbb{R}$. The order on states x is inherited from \mathbb{R} , which means that state x_2 is *more differentiated* (i.e. more specialized, more mature) than state x_1 iff $x_1 < x_2$. This, in turn, means that a cell from state x_1 can differentiate into a cell in state x_2 yet not vice versa. We distinguish two types of states:

- *discrete states*, in which cells can stay for a positive period of time (e.g. state of stem cell, state of mature cell),
- *continuous states*, which cells pass without halting (e.g. the group of states corresponding to maturing neuron).

Depending on the topology of the state space we distinguish three basic groups of structured population models of cell differentiation:

- discrete models, with state space being a finite subset of \mathbb{R} and composed of discrete states only; the dynamics is based on systems of ODEs, see e.g. [15–18],
- continuous models, with state space being an interval and composed of continuous states only; the evolution of population of cells is then described by a time-dependent density $u(t, x)$ or, more generally, time-dependent positive Radon measure $\mu(t) \in \mathcal{M}(\mathbb{R})$ which evolves according to the transport (balance) equation $\partial_t \mu + \partial_x(g\mu) = p\mu$, see [19–23],
- mixed models, which have both discrete and continuous parts, see [24].

In [25] continuous and mixed models of cell differentiation were embedded into a general framework based on measure-valued solutions of transport equations. We refer to this paper for motivations and further biological background as well as derivation of constituents of the model. Mathematically, framework from [25] reads as follows:

$$\partial_t \mu(t) + \partial_x(g_1(v(t))\mathbf{1}_{x \neq x_i}(x)\mu(t)) = p(v(t), x)\mu(t), \tag{1.1}$$

$$g_1(v(t)) \frac{D\mu(t)}{D\mathcal{L}^1}(x_i^+) = c_i(v(t)) \int_{\{x_i\}} d\mu(t), \quad i = 0, \dots, N \tag{1.2}$$

$$\mu(0) = \mu_0, \tag{1.3}$$

where $t \in \mathbb{R}^+$ and $x \in \mathbb{R}$. $x_0 < x_1 < \dots < x_N$ is a finite collection of points in \mathbb{R} , which correspond to discrete states. $\mathbf{1}_{x \neq x_i}$ is equal to 1 if $x \in (x_0, x_1) \cup (x_1, x_2) \cup \dots \cup (x_{N-1}, x_N)$ and 0 otherwise. $\frac{D\mu}{D\mathcal{L}^1}$ denotes the density of measure μ with respect to the one-dimensional Lebesgue measure and $v(t) := \int_{\{x_N\}} d\mu(t)$ denotes the mass of point x_N . The initial datum μ_0 is a Radon measure supported on the interval $[x_0, x_N]$.

Under certain assumptions on coefficients (see [25, Assumptions 3.2]) it was proven that there exists a unique solution

$$\mu \in C([0, \infty), (\mathcal{M}, \rho_F))$$

of problem (1.1)–(1.3). Here, $\mathcal{M} = \mathcal{M}(\mathbb{R})$ is the space of nonnegative Radon measures on \mathbb{R} (see [26] for an introduction to measure theory) and $C([0, \infty), (\mathcal{M}, \rho_F))$ is the space of continuous functions on $[0, \infty)$ with values in space \mathcal{M} equipped with the flat metric ρ_F , which is an adaptation of Wasserstein metric used in the theory of optimal transport, see [27]. This metric, known also under the name bounded Lipschitz distance, is defined by

$$\rho_F(\mu_1, \mu_2) := \sup_{\psi \in Lip^b(\mathbb{R}), |\psi| \leq 1, Lip(\psi) \leq 1} \int_{\mathbb{R}} \psi d(\mu_1 - \mu_2), \tag{1.4}$$

where $Lip^b(\mathbb{R})$ is the set of bounded Lipschitz continuous functions on \mathbb{R} and $Lip(\psi)$ is the Lipschitz constant of ψ .

The starting point for the present research is the fact that the space $C([0, \infty), (\mathcal{M}, \rho_F))$ is incompatible with the structure of problem (1.1)–(1.3) in the sense highlighted by the following example.

Example 1 (Instability in Flat Metric). Take $N = 2$ and let $g_1 \equiv 1$ and $c_1 \equiv 0$ in (1.1)–(1.3). For initial condition $\mu_0 = \delta_{x_1}$ the unique solution of problem (1.1)–(1.3) in the sense of [25, Definition 3.3] is given by

$$\mu(t) = \delta_{x_1}(dx).$$

Here, $\delta_{x_1}(dx)$ denotes a Dirac mass concentrated in x_1 .

For a perturbed initial condition $\mu_0^\epsilon = \delta_{x_1+\epsilon}$, on the other hand, we have

$$\mu^\epsilon(t) = \delta_{x_1+\epsilon+t}(dx).$$

Using formula (1.4), we obtain $\rho_F(\mu(t), \mu^\epsilon(t)) = t + \epsilon$. This means that

- $\rho_F(\mu_0, \mu_0^\epsilon) = \epsilon \rightarrow 0$ as $\epsilon \rightarrow 0$,
- $\rho_F(\mu(t), \mu^\epsilon(t)) = t + \epsilon \rightarrow t$ as $\epsilon \rightarrow 0$.

Hence, solutions are neither continuous nor stable with respect to initial data.

Download English Version:

<https://daneshyari.com/en/article/837065>

Download Persian Version:

<https://daneshyari.com/article/837065>

[Daneshyari.com](https://daneshyari.com)