Computers in Biology and Medicine 76 (2016) 94–112

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

A node-based version of the cellular Potts model

Marco Scianna *, Luigi Preziosi

Department of Mathematical Sciences, Politecnico di Torino, Corso Duca degli Abruzzi 24, 10129 Torino, Italy

ARTICLE INFO

Article history:
Received 21 March 2016
Received in revised form
25 June 2016
Accepted 27 June 2016

Keywords:
Cellular Potts model
Multiscale model
Cell surface rearrangement
Cell membrane node
Domain discretization

ABSTRACT

The cellular Potts model (CPM) is a lattice-based Monte Carlo method that uses an energetic formalism to describe the phenomenological mechanisms underlying the biophysical problem of interest. We here propose a CPM-derived framework that relies on a node-based representation of cell-scale elements. This feature has relevant consequences on the overall simulation environment. First, our model can be implemented on any given domain, provided a proper discretization (which can be regular or irregular, fixed or time evolving). Then, it allowed an explicit representation of cell membranes, whose displacements realistically result in cell movement. Finally, our node-based approach can be easily interfaced with continuous mechanics or fluid dynamics models. The proposed computational environment is here applied to some simple biological phenomena, such as cell sorting and chemotactic migration, also in order to achieve an analysis of the performance of the underlying algorithm. This work is finally equipped with a critical comparison between the advantages and disadvantages of our model with respect to the traditional CPM and to some similar vertex-based approaches.

1. Introduction and motivation

The evolution of biological systems is determined by mechanisms and processes operating at different spatiotemporal scales, *i.e.*, from the microscopic/molecular level to the macroscopic/multicellular level. Each scale can be properly approached with selected mathematical methods. In this respect, individual cell-based models (IBMs) are particularly suitable to describe mesoscopic cell-level dynamics. They in fact allow to preserve the identity of the single component individuals of the system and to capture their behavior and mutual interactions. This family of theoretical approaches can be then classified according to the type of representation given to each cell, which may consist in a material point, an undeformable sphere or ellipsoid or in a deformable polygon or subset of domain elements.

One of the well-known IBMs is the cellular Potts model (CPM, also called the Glazier–Graner–Hogeweg model, see [40–43,64,92] for reviews). The CPM is a grid-based Monte Carlo method, which implements an energy minimization principle to determine the evolution of the simulated system. All CPMs are based on regular numerical lattices as domains, and define a list of discrete objects. They are spatially extended cell-scale elements, which consist of patches of lattice sites sharing the same (integer) identification number. Continuous fields can be included in the modeling environment as well, conferring the CPM a multiscale-hybrid nature. They represent the spatio-temporal evolution of microscopic quantities, such as diffusive ions and molecules. Attributes of discrete individuals and rules for their dynamics and for their interactions with selected fields are described by an effective potential formalism, which results in a system energy given by a *Hamiltonian*. This functional describes indeed the state of the system, whose rearrangements are driven by an algorithm of stochastic minimization, *i.e.*, an iterative Metropolis procedure which accounts for a probabilistic acceptance of random updates of lattice configurations. As long as a biological mechanism can be described with an energetic formalism, it can be included in the CPM framework. In this respect, the CPM is not specific for a given type of biological problems, but it can be rather considered as a framework for model building. For these reasons, the CPM method is becoming an increasingly common technique for the mathematical modeling of a wide range of phenomena.

In this foundational work, we present a new version of the CPM, which is still based on an energy minimization philosophy, but which relies on a vertex-based representation of the discrete cell-scale objects. Besides its intrinsic novelty, our approach has some advantages from a modeling point of view. For instance, it can be employed on every given physical domain (provided a proper discretization): this may be useful for a computational coupling with selected continuum mechanics or fluid dynamics models. Our approach then allows to explicitly represent cell

* Corresponding author.
E-mail addresses: marcosci1@alice.it (M. Scianna), luigi.preziosi@polito.it (L. Preziosi).

http://dx.doi.org/10.1016/j.compbiomed.2016.06.027
0010-4825/

membrane, with its extended protrusions (*e.g.*, filopodia, pseudopodia), and to avoid the introduction of a generalized medium element when it is not necessary. Such main model features will be presented in Section 2. In particular, we will describe the Metropolis algorithm underlying our approach and propose some possible Hamiltonians that can be implemented in the resulting computational framework. We will further indicate some procedures to implement more complex cell dynamics (*i.e.*, division, compartmentalization). Section 3 will be instead focused on sample applications, dealing with single cell and multicellular dynamics. Such simulation outcomes will allow also to achieve a qualitative relationship between variations in some relevant model parameters and the resulting system evolution. An analysis of the computational efficiency of our method, compared with the traditional version of the CPM, will be instead provided in Section 4. This work will be finally equipped by a detailed discussion, where the advantages and the disadvantages of the proposed model with respect to both classical CPM approaches and similar vertex-based models will be commented.

2. Proposed mathematical model

As traditional Potts models, our approach includes both discrete cell-scale elements and continuous fields, while the evolution of the system comes from an iterative and stochastic minimization of its free energy.

The domain of our method can be any physical region $\Omega \subset \mathbb{R}^2$, equipped by a proper discretization, that can be regular (*e.g.*, in the case of triangular or square grid elements) or irregular (*e.g.*, in the case of Voronoi tessellations), fixed or adaptative according to the system dynamics (see Fig. 1(A)). This is the first relevant difference with respect to classical CPMs which can be only employed on rigid lattices formed by equivalent (square or hexagonal) sites. Let us then define with

$$\overline{\Omega} = \left\{ \mathbf{x}_j \in \mathbb{R}^2 : j = 1, \ldots, J \right\} \tag{1}$$

the set of the spatial locations of the vertices of the domain discretization, where the integers $j = 1, \ldots, J$ their tracking numbers. The first-nearer neighborhood of a given mesh vertex j is then identified with

$$\overline{\Omega}_j = \left\{ \mathbf{x}_k \in \overline{\Omega} : k \neq j \text{ and } k \text{ belongs to the same grid element as } j \right\}, \tag{2}$$

as represented in Fig. 1(B).

We then consider a system formed by N_c cells (or cell-scale elements). Each cell $c = 1, \ldots, N_c$ is assumed to be defined by a given set of *numerically ordered* membrane nodes i, where $i = 1, \ldots, V_c$ (V_c indicates the total number of nodes characterizing the c-th individual). $\mathbf{x}_{c,i}(t)$ then indicates the actual location within the domain of node i of cell c. In this respect, if, for instance, the node $i=9$ of the cell $c=3$ coincides, at a given time step t, with the grid vertex $j=23$, we can write $\mathbf{x}_{3,9}(t) = \mathbf{x}_{23}$. Indeed, each cell c is defined, at a given time step t, by the following subdomain:

$$\overline{\Omega}^c(t) = \left\{ \mathbf{x}_j \in \overline{\Omega} : \mathbf{x}_j = \mathbf{x}_{c,i}(t), \text{ with } i = 1, \ldots, V_c \right\}. \tag{3}$$

Remark. For the sake of clarity, we underline that the term "vertex" is used to indicate the junctions between domain grid elements. The term "node" instead denotes the punctual "hotspots" that identify each cell and that might be thought also as clusters of adhesive molecules, as we will see in the following.

The membrane of a cell c can be defined, in general, by any close un-knotted curve connecting *in the right order* the component nodes

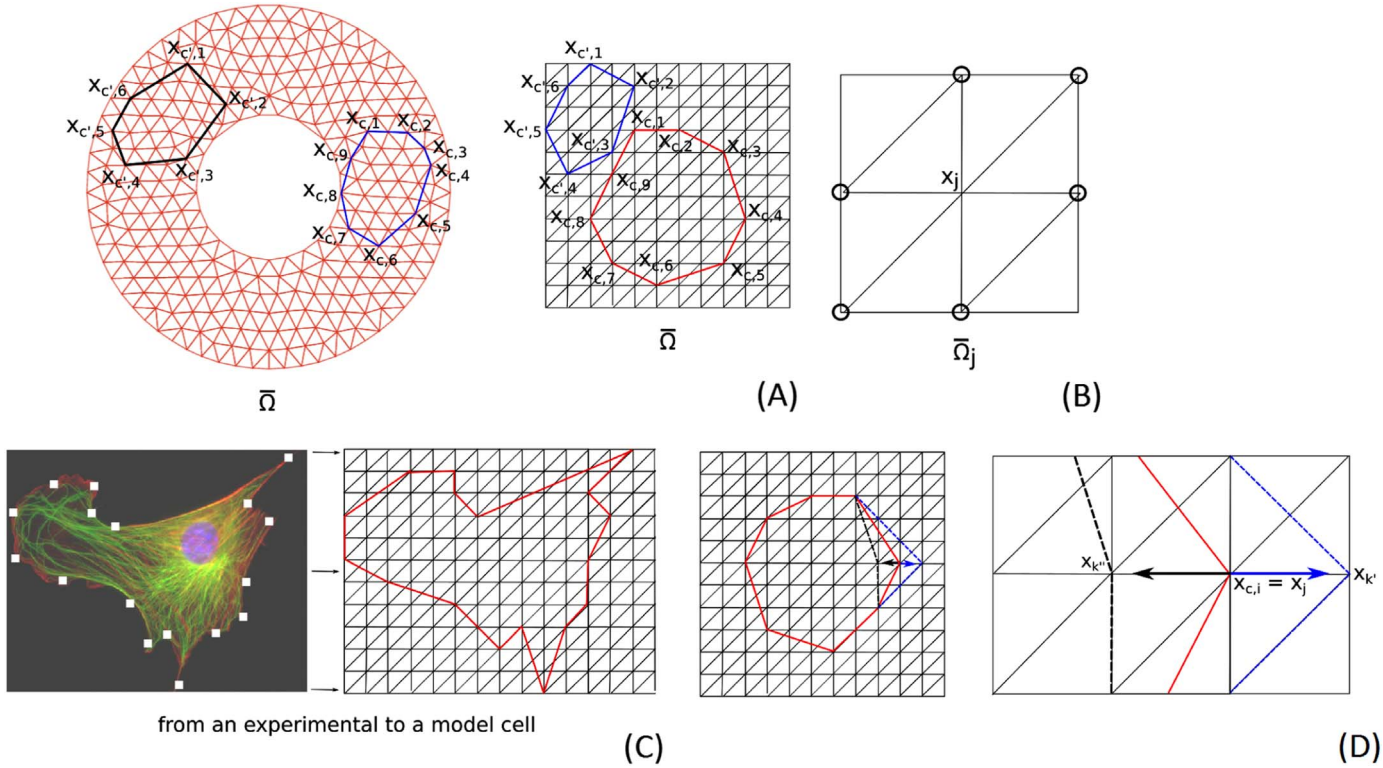

Fig. 1. (A) Examples of 2D discretized domains $\overline{\Omega}$ containing two representative cells, c (defined by $V_c=9$ membrane nodes) and c' (defined by $V_{c'} = 6$ membrane nodes). (B) First-nearer neighborhood $\overline{\Omega}_j$ of a generic grid vertex j, which is composed of the set of manually encircled grid vertices. (C) Sample procedure to properly reproduce in the model a complex cell shape (see the text for details). (D) Basic Monte Carlo Step (MCS) of the Metropolis algorithm. A membrane node i of a cell c, which actually coincides with grid vertex j (*i.e.*, $\mathbf{x}_{c,i}(t) = \mathbf{x}_j$), is selected at random and attempts move to one of the free neighboring grid vertex locations $\mathbf{x}_k \in \overline{\Omega}_j$. In particular, if the target grid vertex is within the cell (say, k''), c is retracting (see the dark-dashed line). Otherwise, if the target grid vertex is outside the cell (say, k'), c is protruding (see the blue-dashed line). (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this paper.)