

II.2 The Cellular Potts Model and Biophysical Properties of Cells, Tissues and Morphogenesis

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Abstract. In this chapter we examine the properties of the Cellular Potts Model (CPM) formalism which make it preeminently suitable for modelling biological cells. The most outstanding feature in which CPM differs from other modelling formalisms, is that a cell is modelled as a deformable object, and takes its shape from a combination of internal and external forces which act upon it. The energy minimisation based CPM formalism enables us to integrate these forces acting at different scales. We map the parameters of the basic CPM formalism to physical and biological properties of cells. We show through those mappings that the modelling formalism is a powerful tool for investigating a large range of biological questions, from those concerning biophysical properties of single cells, cell motion, tissue level properties, all the way up to understanding the full morphogenesis and life-cycle of an organism.

1. Introduction

The CPM is a spatial grid-based formalism that allows for mesoscopic cell description [12]: a cell is defined over a region composed of multiple lattice sites, with constraints acting on its area, while experiencing interactions at its boundary. The dynamics are based on the free energy minimisation principle, and generated by means of Monte Carlo simulations utilising a Metropolis algorithm [33]¹. Effectively, this means that cell motion comes about from the overall minimisation of the energy of deformation and stretching of the membrane through stochastic fluctuations, in which the global and local forces upon a cell edge are resolved [13]. It allows us to study dynamics of biological cells which cannot be (easily) described with other methods that treat cells as unit-pixels or centre-of-mass based (deformable rigid body) entities. This is both due to the intrinsic mesoscopic nature of the CPM, and due to its ability to describe potentially complex (local)

¹We highly recommend to read Chapter II.1 for a more thorough introductory explanation and considerations about energy minimisation and metropolis algorithm. Nevertheless, for the sake of self-consistency, the general implementation procedure is repeated briefly.

deformations of the cell (such as epithelial cells stretching around a blood vessel or the dendritic shape of DCs in lymph nodes). Cell dynamics, both in the CPM and in reality, are due to this entanglement of subcellular cell deformations with cell properties like cell size. Moreover, cells do not displace as fixed units, but by successive subcellular movements, in which at any time a large part of the cell is stationary, connected to other cells or substrate. Essentially, protrusions are being created in the front and dismantling is occurring at the rear, while the centre contacts remain stable, as is the case in the CPM.

The CPM does not explicitly describe effective forces acting upon a cell, in contrast to other model-formalisms (see e.g. [40]). Generally, the force-based approach relies on the main assumption that the movement of the centre of mass of the cell, or of its subdivisions, can be adequately described by a limited number of forces acting upon or between them. This strategy is well suited for describing objects that undergo limited deformation. However, the CPM is a good formalism to adopt for any study in which it becomes relevant to take into account that cells are highly deformable, that the movement of each position depends on the movement of the rest of the cell (e.g. via turgor pressure), that cell membrane dynamics are locally highly correlated, but not fixed to the movement of the centre of mass, and that fluctuations play an important role in the nature of cell protrusion and motility. To represent the above aspects with explicit forces acting on each position of the membrane leads to a huge proliferation of variables, forces, and effects that have to be considered, and is very cumbersome. By computing changes in the Hamiltonian, local forces at the periphery of the cell are described implicitly (via energy gradients with respect to the position of each membrane element). The cell, by energetically exploring its configurational space, is effectively being subjected to forces on a microscopic level, but without them having to be defined explicitly.

In the following sections, we will show how one can relate the “material” properties of individual cells, such as deformability and adhesion, and tissue properties, such as surface tension, to morphogenetic processes. This is a pivotal issue in biology, because it will clarify to what extent developmental processes are emerging from “simple” cell properties, which will lead to a better understanding of the developmental program of organisms.

2. Basic formalism

The implementation of the model is extensively presented in Chapter II.1. Summing up: at each Monte Carlo time step, a random sampling through the lattice is done to determine whether pixels change their state into the state of one of their randomly chosen neighbours. This change (denoted here as “copying”) corresponds to small deformations of the membrane (or any other boundary of a defined structure). To determine whether copying will occur, one calculates the Hamiltonian (\mathcal{H}), which basic structure is of the form

$$\mathcal{H} = \sum_{ij} \sum_{i'j'} J_{\tau(\sigma_{ij}), \tau(\sigma_{i'j'})} \left(1 - \delta_{\sigma_{ij}, \sigma_{i'j'}}\right) + \sum_{\sigma} \lambda (a_{\sigma} - A_{\tau(\sigma)})^2. \quad (1)$$