LATTICE-GAS CELLULAR AUTOMATON MODELS FOR THE ANALYSIS OF PATTERN FORMATION IN INTERACTING CELL POPULATIONS*

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Lattice-gas cellular automaton (LGCA) models are introduced as models for the analysis of pattern formation in interacting cell populations. LGCA models are cell-based, computationally efficient, and allow to integrate statistical and biophysical models for different levels of biological knowledge. Moreover, LGCA models permit multiscale analysis of collective phenomena emerging at multiple temporal and spatial scales.

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In the context of multicellular tissue dynamics, various cell-based mechanistic models have been developed to analyse tissue dynamics viewed as collective phenomenon emerging from the interplay of individual biological cells. Since cell-based models represent the biological cell as an individual, variability between cell phenotypes can be captured. This variability can be fundamental for the organization at the tissue level. For example, it has been realized that understanding tumour progression and resistance to treatment requires account for cell-to-cell variabilities [1].

Cell-based models can be classified into lattice and off-lattice or "lattice-free" models depending on if or not the model operates on a fixed lattice (see [2] for references). Lattice models are equivalent to cellular automata. Cellular automata were introduced by J. von Neumann and S. Ulam in the 1950s as models of individual (self-)reproduction [3]. They consist of a regular spatial lattice in which each lattice node can assume a finite, typically small number of discrete states. The next state of a node depends on the states

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in the neighbouring sites and a deterministic or stochastic transition function. Cellular automata provide simple models of self-organising systems in which collective behaviour emerges within an ensemble of many interacting "simple" components — being it molecules, cells or organisms [4–6].

A lattice-gas cellular automaton (LGCA) is a cellular automaton in which each lattice site additionally contains velocity channels. LGCA models were introduced to simulate aspects of fluid dynamics [7], but have also been used successfully to investigate single and collective cell migration, biological pattern formation, and the growth and invasion of tumours [8–21]. LGCA models are cell-based, computationally efficient, and allow to integrate statistical and biophysical models for different levels of biological knowledge [22–25] (Fig. 1). As a cellular automaton, an LGCA is defined

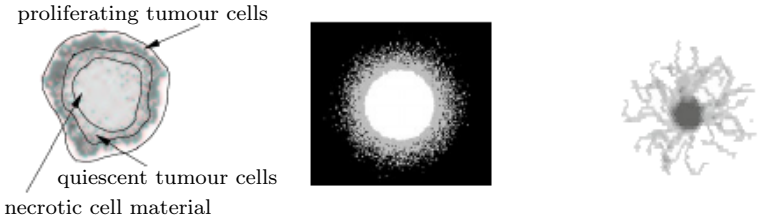

Fig. 1. Applications of LGCA models: avascular cancer growth (left, [8]), invading wave front (middle, [26]), angiogenetic network formation (right, [25]).

on a regular lattice, where the nodes of the lattice take a certain number of discrete states. As a lattice-gas, the state space is related to the lattice geometry. Each node can be occupied by "biological agents", in particular biological cells, characterised by their velocities which are restricted to the unit vectors connecting a node to its nearest neighbours (Fig. 2). Agents move along the links and interact on the nodes of the lattice. This interaction

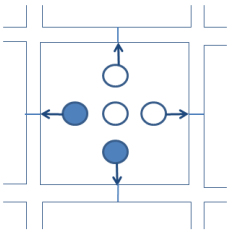

Fig. 2. States in a LGCA: node state is represented by occupation of velocity channels; in the example on the square lattice there are four velocity channels and one rest channel. Filled circles denote the presence of a cell with the respective velocity.

can change the number of agents at individual nodes (birth/death processes) and may depend on the states in neighbouring nodes which allows to model collective effects (Fig. 3).

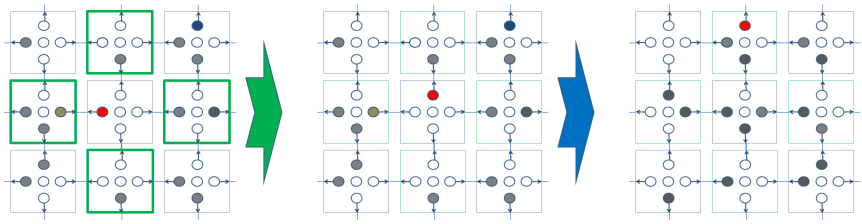

Fig. 3. LGCA: interaction and propagation. Filled circles denote occupied channels and open circles empty channels. Left: part of the lattice before interaction. Black/green squares (von Neumann neighbourhood) denote the nodes that influence the outcome of interaction at the central node. Middle: after interaction: the configuration of the central node has changed due to interaction. Right: after propagation: all cells have moved along the links to their nearest neighbours (the lattice outside the part shown was assumed to be empty, *i.e.* no propagation of cells from "outside").

LGCA models allow multiscale analysis of behaviours emerging at multiple temporal and spatial scales. In particular, one can distinguish microscopic and macroscopic spatial scales, where the microscopic scale is much smaller than the typical cell size and is not explicitly considered in LGCA models. The macroscopic scale is much larger than the cell size and refers to the behaviour of the cell population. An LGCA operates at a mesoscopic scale between the microscopic and the macroscopic scale: the mesoscopic scale coarse-grains microscopic properties but distinguishes individual cells. LGCA as "mesoscopic" models can be regarded either as coarse-grained microscopic models, or discretised macroscopic models. The LGCA framework facilitates theoretical analysis of emergent, tissue-scale (macroscopic) behaviours. In many cases, the macroscopic behaviour of the mesoscopic LGCA can be analysed very well with a spatial mean-field description based on a partial differential equation [7, 9, 27, 28].

For simulations see: `https://imc.zih.tu-dresden.de//biolgca/`

REFERENCES

[1] F. Bertaux, S. Stoma, D. Drasdo, G. Batt, *PLOS Comput. Biol.* **10**, e1003893 (2014).

[2] P. Van Liedekerke, M.M. Palm, N. Jagiella, D. Drasdo, *Comp. Part. Mech.* **2**, 401 (2015).

[3] A.W. Burks, *Essays on Cellular Automata*, University of Illinois Press, Urbana IL, 1970.

[4] J.L. Casti, *Alternate Realities*, John Wiley, New York 1989.

[5] B. Chopard, M. Droz, *Cellular Automata Modeling of Physical Systems*, Cambridge University Press, New York 1998.

[6] S. Wolfram, *A New Kind of Science*, Wolfram Media Inc., 2002.

[7] U. Frisch, B. Hasslacher, Y. Pomeau, *Phys. Rev. Lett.* **56**, 1505 (1986).

[8] S. Dormann, A. Deutsch, *In Silico Biol.* **2**, 393 (2002).

[9] A. Deutsch, S. Dormann, *Cellular Automaton Modeling of Biological Pattern Formation: Characterization, Examples, and Analysis*, Birkhauser, Boston 2018.

[10] K. Böttger *et al.*, *PLOS Comput. Biol.* **11**, e1004366 (2015).

[11] H. Hatzikirou, K. Böttger, A. Deutsch, *Math. Model. Nat. Phenom.* **10**, 94 (2015).

[12] K. Böttger, H. Hatzikirou, A. Chauviere, A. Deutsch, *Math. Model. Nat. Phenom.* **7**, 105 (2012).

[13] C. Mente *et al.*, *Acta Phys. Pol. B Proc. Suppl.* **5**, 99 (2012).

[14] S. de Franciscis, H. Hatzikirou, A. Deutsch, *Acta Phys. Pol. B Proc. Suppl.* **4**, 167 (2011).

[15] M. Tektonidis *et al.*, *J. Theor. Biol.* **287**, 131 (2011).

[16] B. Chopard *et al.*, *Acta Biotheor.* **58**, 329 (2010).

[17] H. Hatzikirou, A. Deutsch, *Curr. Top. Dev. Biol.* **81**, 401 (2008).

[18] S. Dormann, A. Deutsch, A.T. Lawniczak, *Future Gener. Comput. Syst.* **17**, 901 (2001).

[19] A. Deutsch, *Math. Comput. Model.* **31**, 35 (2000).

[20] H. Bussemaker, A. Deutsch, E. Geigant, *Phys. Rev. Lett.* **78**, 5018 (1997).

[21] A. Deutsch, *J. Biol. Syst.* **3**, 947 (1995).

[22] J.M. Nava-Sedeño, H. Hatzikirou, R. Klages, A. Deutsch, *Sci. Rep.* **7**, 16952 (2017).

[23] J.M. Nava-Sedeño, H. Hatzikirou, F. Peruani, A. Deutsch, *J. Math. Biol.* **75**, 1075 (2017).

[24] H. Hatzikirou, L. Brusch, A. Deutsch, *Acta Phys. Pol. B Proc. Suppl.* **3**, 399 (2010).

[25] C. Mente *et al.*, *J. Math. Biol.* **63**, 173 (2010).

[26] H. Hatzikirou *et al.*, *Comput. Math. Appl.* **59**, 2326 (2010).

[27] D.A. Wolf-Gladrow, *Lattice-Gas Cellular Automata and Lattice Boltzmann Models: an Introduction*, Springer, New York 2000.

[28] S. Wolfram, *Cellular Automata and Complexity — Collected Papers*, Addison-Wesley, 1994.