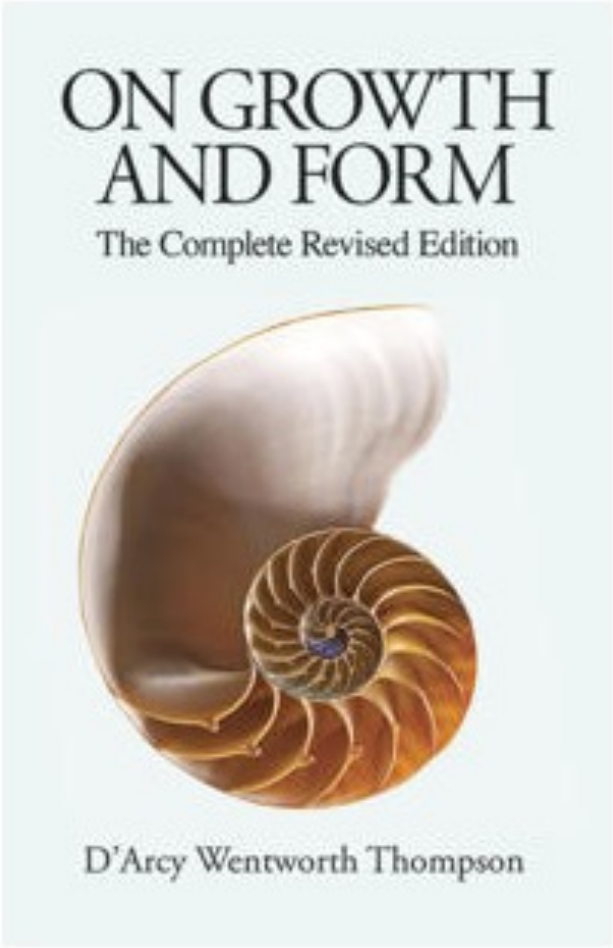
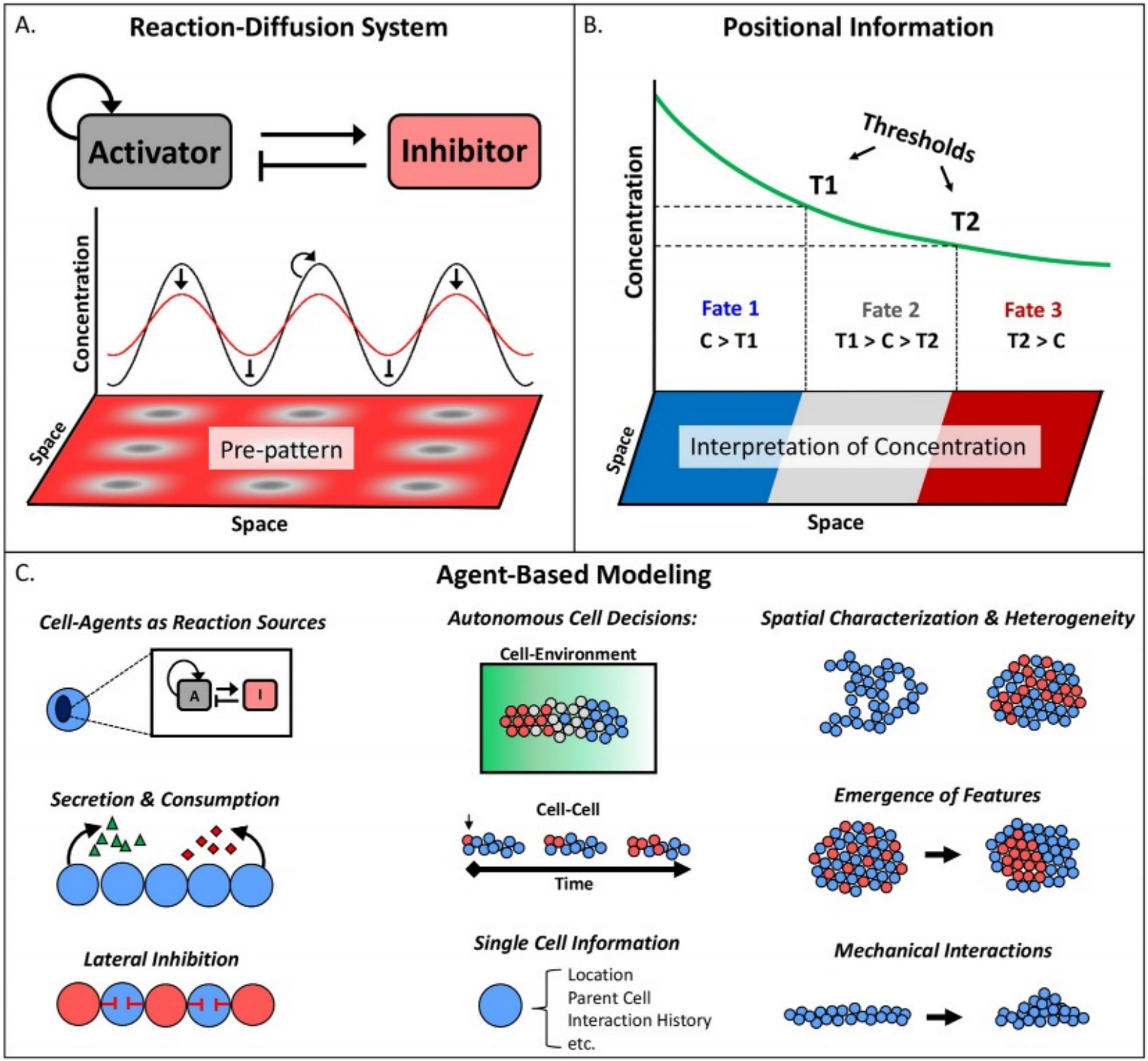
Modelling morphogenesis

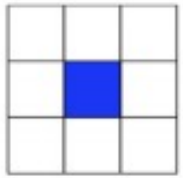


Morphogenetic theories

- D’Arcy Thompson: methods from physical sciences
- Turing: Reaction-Diffusion
- Wolpert: Positional information
- Continuum theories
  - Volumetric & surface growth
  - Elastic instabilities (morpho-elasticity)
  - Mixture theories
  - Morphomechanics
- Mechanotransduction -> Multiscale models



Glen CM, Kemp ML, Voit EO (2019) Agent-based modeling of morphogenetic systems: Advantages and challenges. PLoS Comput Biol 15(3): e1006577

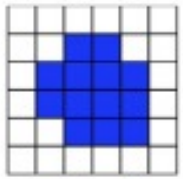


Lattice

Cells are represented as a single grid point on a lattice. For a Euclidean grid, cell movement and interaction are usually constrained to the so-called von Neumann or Moore neighborhoods, which include either four or eight neighbors, as indicated below for the cells shaded in black:



Grids can also be represented as hexagons in 2D or dodecadehedrons in 3D. Although triangles also offer regular tessellations, they are not typically used for ABMs.



Cellular Potts Model (CPM)

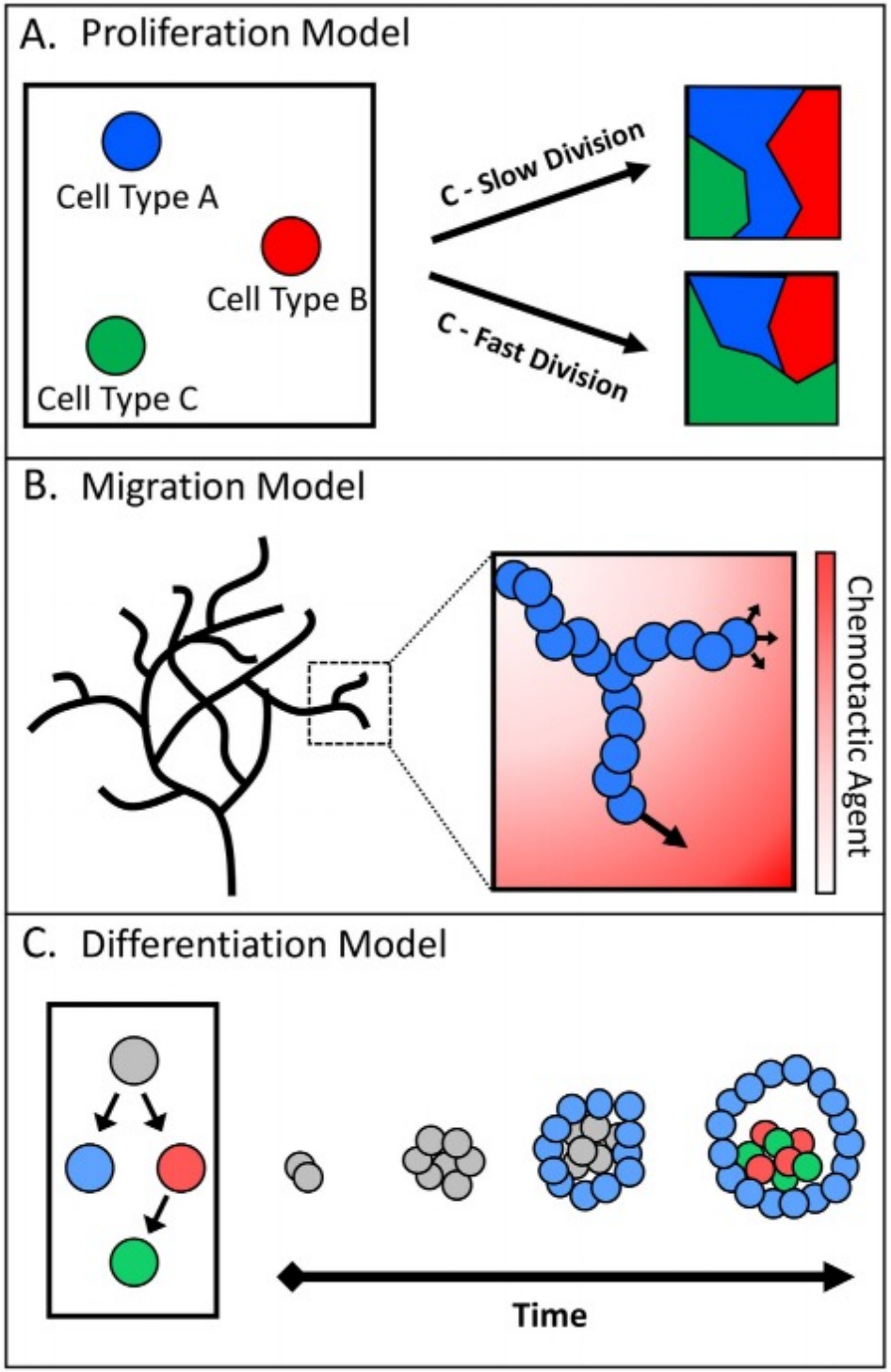
The CPM depicts cells as a cluster of grid points that share the same identifier. Movement and interactions are determined by minimizing the free energy of applied forces. CPM models allow for the realistic representation of cell shape by the division of the cell into subcellular parts.



Lattice-Free

Lattice-free models typically represent cells as incompressible spheres, or centroids, with set radii. Collision detection algorithms allow cells to dynamically move and interact with their environment, while preventing cellular overlap. The lattice-free environment provides unconstrained movement.

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modelling approach	example applications	strengths	limitations
continuum models	brain cortical folding [18] cephalic furrow formation [19] ventral furrow formation [20]	strong mathematical foundation; typically few parameters; well placed to study buckling and folding phenomena	difficult to incorporate cell-level heterogeneity or subcellular processes
lattice-based models (CA, CPM)	epiboly [23] branching morphogenesis [22]	computationally cheap; straightforward to simulate many cells	risk of lattice anisotropies and cell fragmentation; difficult to relate parameters to experimentally accessible quantities
off-lattice cell-centre models	*C. elegans* germ line [29]	more physically motivated and easily parametrized than lattice-based models	more computationally costly than lattice-based models Lack explicit description of cell shape dynamics
vertex models	tissue size regulation [30,31] germband extension [32,33]	explicitly incorporate cell neighbour rearrangements; straightforward to generate experimentally testable summary statistics	typically neglect cell–matrix adhesion, medial actomyosin contractility, active cytoskeletal remodelling
viscoelastic models	ventral furrow formation [34–36] cell sorting [37] germband retraction [38]	include active cytoskeletal remodelling	like vertex models, require cells to be in confluent tissues
'multi-node'/curved edge models	gastrulation [39] cell sorting [40]	detailed description of cell shape dynamics	more computationally costly than vertex and 'finite-element' models
IBM	limb bud morphogenesis [41] Turing patterns [42]	do not require confluent tissues; allow detailed modelling of regulated growth and death processes; straightforward to incorporate subcellular structures	unclear how to estimate 'fluid' properties from biological data; require sophisticated numerical solvers to avoid fluid 'leakage'
SEM	primitive streak formation [43]	allow detailed and emergent cell shape changes in response to mechanical stimuli	computationally intensive; difficult to associate interactions functions directly with particular cytoskeletal components

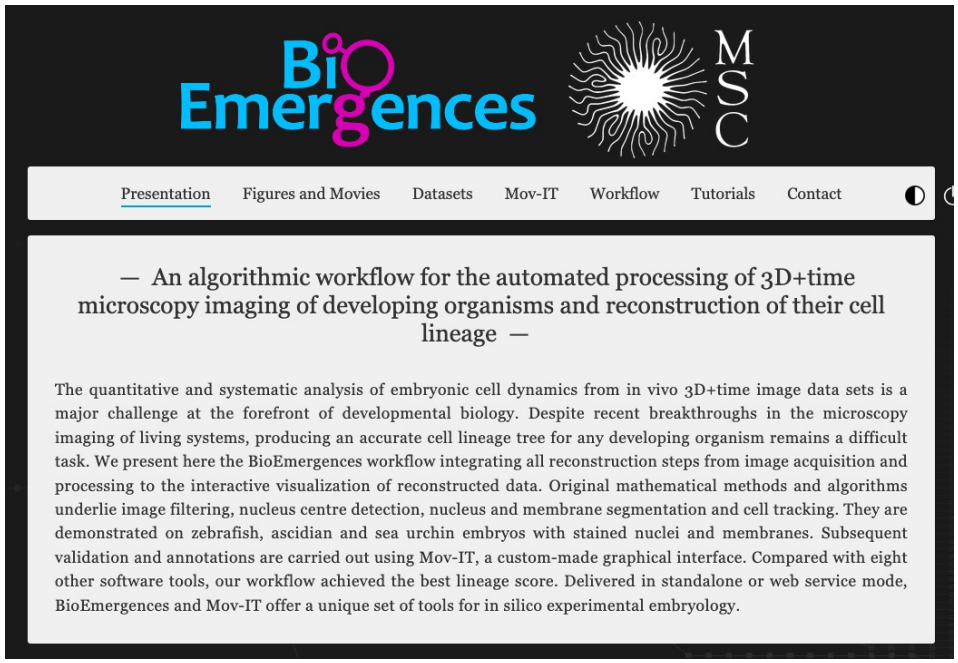
Summary of applications to date of different modelling approaches for epithelial tissue morphogenesis. CA, Cellular automata; CPM, cellular Potts

model; IBM, immersed boundary method; SEM, subcellular element model.

Fletcher AG, Cooper F, Baker, RE. (2017) Mechanocellular models of epithelial morphogenesis. Phil. Trans. R. Soc. B 372: 20150519

Follow the cell

Digital reconstruction of cell trajectories in a zebrafish embryo. (A) Three-dimensional (3D) rendering of cell nuclei (blue) in raw data and selection of cells (yellow) in the dorsal line, performed at 10.7 h-post-fertilization and backtracked to 7 hpf. From left to right, each panel shows a different spatial orientation (animal pole, lateral and ventral). (B) Detected cell nuclei (red) and cell selection as in (A) (yellow), shown in a spatial slice over the orthoslice of the raw data channel (gray). Same time step and view angles as in (A). (C) 3D rendering of cell nuclei (blue) and selection of cells of the dorsal line at 10.7 hpf (yellow). (D) Cell detection (red) and cell selection (yellow) in the same slice as (B). (E) Left: Two cell selections (green and yellow) over nuclei detection domains at 7 hpf. Middle: forward tracking (yellow to red colormap indicates time advancement) of the two selected cell domains. Right: forward tracking of the two cell selections from a lateral point of view. (F) Cell selections (green and yellow) at 10.7 hpf. Cell backward tracking (yellow to purple colormap) in same view angles than (E).



Pastor-Escuredo (2020)

