Discuss the difference between continuum and cell-based modeling methods for multicellular systems. Use examples to illustrate the differences. Do not repeat an example used by a peer and provide references to resources.

Cellular-Automate (CA)
- CA operates on a discrete lattice with simple states (e.g., "alive" or "dead") and rules for state transitions.
- Suited to track individual cells, allows to study of local and individual mechanisms.
- Upon an event or a fixed-time step, the new state of each cell is determined using deterministic or stochastic rules, and its state at the previous time step.
- CA updates depend only on the states of neighboring lattice sites (local interactions), which makes computations parallelizable and efficient. This is particularly advantageous for simulating systems with many cells.
- CA rules are often simplistic and may not capture complex cellular behaviors, such as changes in shape, adhesion, or biochemical signaling, limiting their ability to model intricate biological processes.

Continuum models
- Utilize calculus and partial differential equations (PDE) to model systems at a macroscopic scale by employing averaged or aggregate quantities.
- Represent quantities, such as cell density, temperature, or pressure, using continuous fields.
- Assume that spatial variation is smooth, with local heterogeneity being averaged out.
- Cellular growth is mechanically regulated by gradient pressure or limited by nutrients, focusing on the role of cell-cell interactions.
- This method is generally more efficient for large-scale systems since it does not track individual entities. The computational costs vary based on the complexity of the equations and the resolution of the numerical methods.
- This approach is particularly well-suited for modeling large-scale cell populations where cell and tissue properties change smoothly over several cell diameters.
- It naturally accommodates mathematical analysis and numerical simulations.
- It can be improved using research from cellular automata (CA) or agent-based modeling (ABM) models.

In this paper [1], the authors created individual lattice-based cellular automaton (CA) and continuum models to simulate the growth of cells in vitro. They identified three cell phenotypes based on their growth and migration patterns. For type I cell monolayers, both "off-lattice" and continuum models predict the same growth dynamics: initial exponential growth of the cell population size and cluster diameter (radius of gyration) followed by power-law growth of the population size and linear growth of the diameter. For type II monolayers, the researchers developed a CA model based on the lattice-free agent to derive a continuum model using Fisher–Kolmogorov–Petrovskii– Piskounov (FKPP) equations.

In this paper [2], the scientists present a stochastic individual-based model for the spatial dynamics of multicellular systems whereby cells undergo pressure-driven movement and pressure-dependent proliferation. They showed that nonlinear partial differential equations commonly used to model the spatial dynamics of growing cell populations can be formally derived from the branching random walk that underlies our discrete model. Their comparative study demonstrated that the numerical simulations of nonlinear partial differential equations replicate the individual-based model outcomes.

References

1. Byrne, H. & Drasdo, D. Individual-based and continuum models of growing cell populations: a comparison. *J. Math. Biol.* **58**, 657 (2008).

2. Chaplain, M. A., Lorenzi, T. & Macfarlane, F. R. Bridging the gap between individual-based and continuum models of growing cell populations. *arXiv* (2018) doi:10.48550/arxiv.1812.05872.