

¹ `cellular_raza`: Cellular Agent-based Modeling from a ² Clean Slate

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⁶ Summary

⁷ `cellular_raza` is a cellular agent-based modeling framework which allows researchers to
⁸ construct models from a clean slate. In contrast to other agent-based modeling toolkits,
⁹ `cellular_raza` was designed to be free of assumptions about the underlying cellular repre-
¹⁰ sentation. This enables researchers to build up complex models while retaining full control
¹¹ over every parameter introduced. It comes with predefined building blocks for agents and their
¹² physical domain to quickly construct new simulations bottom-up. Furthermore, `cellular_raza`
¹³ can be used with the `pyo3` and `maturin` packages and thus act as a numerical backend to a
¹⁴ Python package.

¹⁵ Statement of Need

Agent-based models have become increasingly prevalent in the field of cellular biology ([Cess & Finley, 2022](#); [Delile et al., 2017a, 2017b](#); [Mogilner & Manhart, 2016](#)). Numerous tools have been developed that can delineate cellular systems with great precision ([Abar et al., 2017](#); [Pleyer & Fleck, 2023](#)). While these tools have proven effective for specific research inquiries, they frequently lack the capacity to be applied more universally. In contrast, general-purpose ABM toolkits are not designed with particular applications in mind ([Abar et al., 2017](#); [Datseris et al., 2022](#); [Wilensky, 1999](#)). These toolkits often enable the definition of agents bottom-up and can be a suitable choice if they allow for the desired cellular representation. However, they lack the explicit forethought necessary for application in cellular systems and may not be able to describe every cellular aspect.

In contrast to classical particle simulations, agent-based models (ABMs) treat every cell individually. This implies that parameters can vary between agents and that every cell should be traceable throughout time and space. Additionally, they can describe growth, proliferation, death, and many other cellular processes and should also accurately model cell lineage. These models operate on the mesoscopic scale where the underlying complexity of the problem cannot be fully attributed to either intracellular or extracellular processes. Their applications include modeling of self-organization and emergent phenomena, but they can also be used to introduce spatial effects into existing population-based models. To address these issues and construct models from first principles without any assumptions regarding the underlying complexity or abstraction level, we developed “`cellular_raza`.”

³⁶ Cellular Agent-Based Frameworks

³⁷ In our previous efforts ([Pleyer & Fleck, 2023](#)), we assessed the overall state of modeling toolkits
³⁸ for individual-based cellular simulations. These frameworks are designed for specific usages
³⁹ and often require many parameters which are unknown or difficult to determine experimentally.
⁴⁰ This poses an inherent problem for their applicability and the ability to properly interpret

41 results. Few modeling frameworks exist that provide a significant degree of flexibility and
 42 customization in the definition of cell agents. Chaste (Cooper et al., 2020) allows reuse
 43 of individual components, such as ODE and PDE solvers, but is only partially cell-based.
 44 Biocellion (Kang et al., 2014) supports different cell shapes such as spheres and cylinders, but
 45 admits that their current approach lacks flexibility in the subcellular description. BioDynaMo
 46 (Breitwieser et al., 2021) offers some modularity in the choice of components for cellular agents,
 47 but cannot deeply customize the cellular representation.

48 **cellular_raza**

49 We distinguish between different simulation aspects, i.e., mechanics, interaction, or cell cycle.
 50 These aspects are directly related to the properties of the cells, domain, or other external
 51 interactions. The user selects a cellular representation, which can be built from pre-existing
 52 building blocks or fully customized bottom-up. `cellular_raza` utilizes macros to generate
 53 code contingent on the simulation aspects. It makes extensive use of generics and provides
 54 abstract numerical solvers. `cellular_raza` encapsulates the inherent complexity of the code
 55 generation process, yet enables users to modify the specifics of the simulation through the use
 56 of additional keyword arguments. Consequently, users are able to fully and deeply customize
 57 the representation and behavior of the agents. Each simulation aspect is abstractly formulated
 58 as a trait in Rust's type system. The getting-started guide provides a good entry point and
 59 explains every step from building to running and visualizing.

60 Examples

61 In the following, we present four different examples of how to use `cellular_raza` (see cellular-raza.com/showcase).
 62

63 Cell Sorting

64 Cell sorting is a naturally occurring phenomenon (Graner & Glazier, 1992; Steinberg, 1963),
 65 where the cellular interaction is species-specific. We consider two distinct types represented by
 66 soft spheres. They physically attract each other at close proximity if their species is identical.
 67 Cells are placed randomly inside a cube with reflective boundary conditions. In the final
 68 snapshot, we can clearly see the phase-separation between the different species.

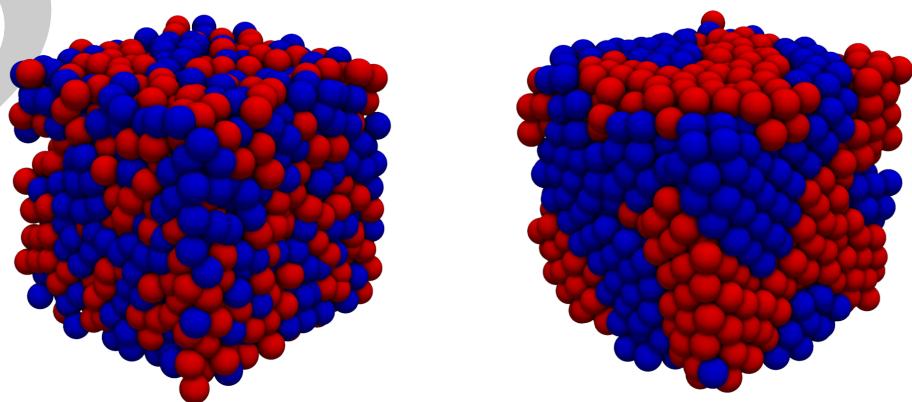


Figure 1: The initial random placement of cells reorders into a phase-separated spatial pattern.

69 Bacterial Rods

70 Bacteria come in various forms ([Young, 2006](#); [Zapun et al., 2008](#)) such as elongated shapes
 71 ([Billaudeau et al., 2017](#)) which grow asymmetrically in the direction of elongation. Our model
 72 describes the physical mechanics of one cell as a collection of multiple vertices \vec{v}_i which
 73 are connected by springs. Their relative angle α at each connecting vertex introduces a
 74 curvature force proportional to $2 \tan(\alpha/2)$. Cells interact via a soft-sphere force potential
 75 with short-ranged attraction. Multiple contributions are calculated between every vertex and
 76 the closest point on the other cells edges. In addition, the cell cycle introduces growth of
 77 the bacteria until it divides in the middle into two new cells. This growth is downregulated
 78 by an increasing number of neighboring cells. Cells are placed inside the left-hand side of
 79 an elongated box with reflective boundary conditions. Their colors range from green for fast
 80 growth to blue for dormant cells.

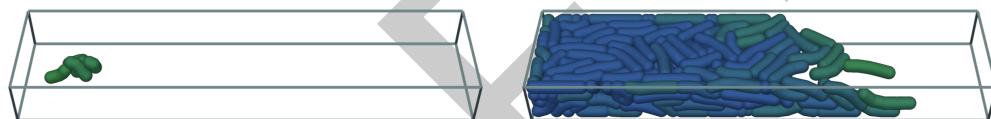


Figure 2: The bacteria extend from the initial placement in the left side towards the right side. Their elongated shape and the confined space favour the orientation facing along the growth direction.

81 Branching of *Bacillus Subtilis*

82 Spatio-temporal patterns of bacterial growth such as in *Bacillus Subtilis* have been studied for
 83 numerous years ([Kawasaki et al., 1997](#); [Matsushita et al., 1998](#)). Cells are modeled as soft
 84 spheres which take up nutrients from the domain. By consuming intracellular nutrients, the
 85 cell grows continuously and divides upon reaching a threshold. Cells are initially placed inside
 86 a centered square after which they grow outwards into the nutrient-rich area. They are colored
 87 by the size of their radii from dark purple right after the division event to bright. A lighter
 88 color in the outer domain indicates that more nutrients are available while a dark color signifies
 89 a lack thereof.

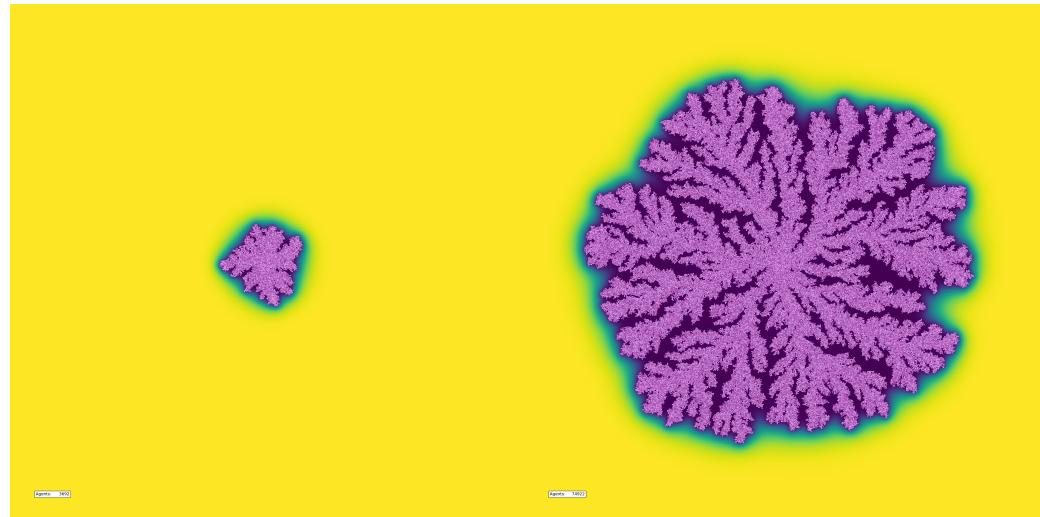


Figure 3: The bacterial colony grows outwards towards the nutrient-rich parts of the domain thus forming branches in the process.

90 **Semi-Vertex Model for Epithelial and Plant Cells**

91 Vertex models are actively being used to describe mechanical properties of plant cells (Merks
 92 et al., 2011) or organoid structures of epithelial cells (Barton et al., 2017; Fletcher et al.,
 93 2014). We represent cells by a polygonal collection of vertices connected by springs. An inside
 94 pressure pushes vertices outwards, creating perfect hexagonal cells. Cells are attracting each
 95 other but whenever two polygons overlap, a repulsive force acts. They are placed in a perfect
 96 hexagonal grid such that edges and vertices align and assigned growth rates from a uniform
 97 distribution.

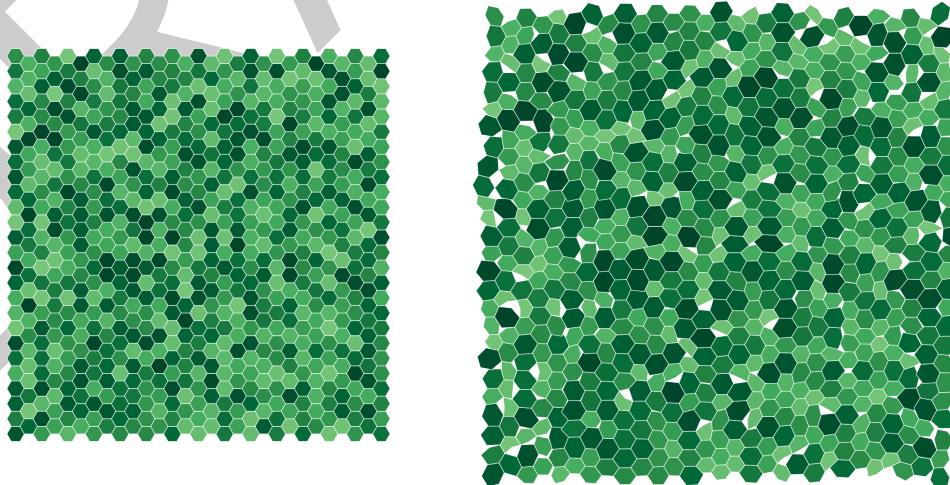


Figure 4: During growth the cells push on each other thus creating small spaces in between them as the collection expands. These forces also lead to deviations in the otherwise perfect hexagonal shape.

98 **Further Information**

99 The full documentation including guides, all examples from above and more is available at
 100 cellular-raza.com. cellular_raza can also be used as a numerical backend together with the

¹⁰¹ pyo3 and maturin konsti (2025) crates.

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