

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

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⁵ Summary

⁶ cellular_raza is a cellular agent-based modeling framework which allows researchers to
⁷ construct models from a clean slate. In contrast to other agent-based modeling toolkits,
⁸ cellular_raza was designed to be free of assumptions about the underlying cellular repre-
⁹ sentation. This enables researchers to build up complex models while retaining full control
¹⁰ over every parameter introduced. It comes with predefined building blocks for agents and their
¹¹ physical domain to quickly construct new simulations bottom-up. Furthermore, cellular_raza
¹² can be used with the pyo3 and maturin packages and thus act as a numerical backend to a
¹³ python package.

Statement of Need

¹⁴ 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. In addition, they can describe growth, proliferation,
death and many other cellular processes and should also accurately model cell lineage. These
models live on the mesoscopic scale where the underlying complexity of the problem can often
neither be fully attributed to 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.

²³ State of Field

²⁴ Agent-based models have become popular in cellular biology ([Cess & Finley, 2022](#); [Delile et](#)
²⁵ [al., 2017a, 2017b](#); [Mogilner & Manhart, 2016](#)). While these tools have proven to be effective
²⁶ for targeted research questions, they often lack the ability to be applied more generically.
²⁷ General-purpose ABM toolkits on the other hand are designed without specific applications in
²⁸ mind ([Abar et al., 2017](#); [Datseris et al., 2022](#); [Wilensky, 1999](#)). They are often able to define
²⁹ agents bottom-up and can be a good choice if they allow for the desired cellular representation.
³⁰ However, they lack the explicit forethought to be applied in cellular systems and may not be
³¹ able to describe every cellular aspect. In order to address these issues and construct models
³² from first principles without any assumptions regarding the underlying complexity or abstraction
³³ level, we developed cellular_raza.

³⁴ Cellular Agent-Based Frameworks

³⁵ In our previous efforts ([Pleyer & Fleck, 2023](#)), we assessed the overall state of modelling toolkits
³⁶ for individual-based cellular simulations. These frameworks are designed for specific usages
³⁷ and often require many parameters which are unknown or difficult to determine experimentally.

This poses an inherent problem for their applicability and the ability to properly interpret results. Few modelling frameworks exist that provide a significant degree of flexibility and customization in the definition of cell agents. Chaste (Cooper et al., 2020) allows reuse of individual components , such as ODE and PDE solvers, but is only partially cell-based. Biocellion (Kang et al., 2014) supports different cell shapes such as spheres and cylinders, but admits that their current approach lacks flexibility in the subcellular description. BioDynaMo (Breitwieser et al., 2021) offers some modularity in the choice of components for cellular agents, but cannot deeply customize the cellular representation.

46 **`cellular_raza`**

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

58 **Examples**

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

61 **Cell Sorting**

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

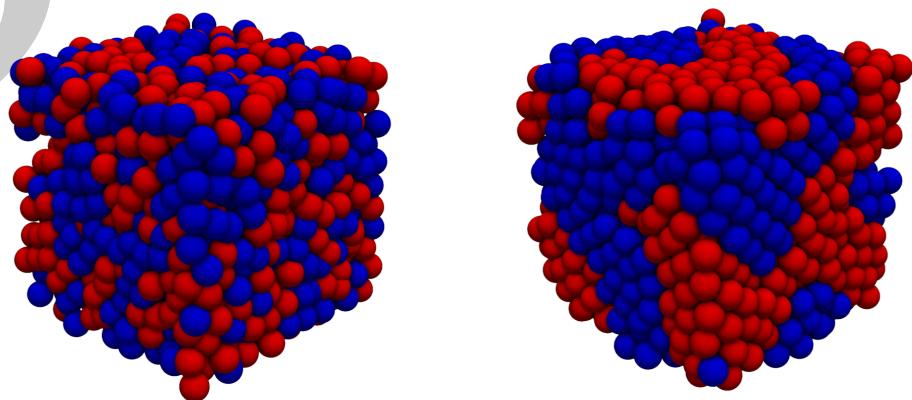


Figure 1: The initial random placement of cells reorders into a phase-separated spatial pattern.

67 **Bacterial Rods**

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

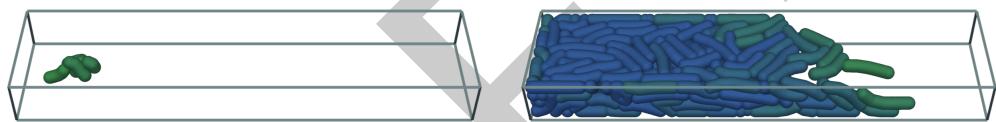


Figure 2: The bacteria extend from the initial placement in the left side towards the right side. Their elongated shape and the confined space favour the orientation facing along the growth direction.

79 **Branching of *Bacillus Subtilis***

80 Spatio-temporal patterns of bacterial growth such as in *Bacillus Subtilis* have been studied for
 81 numerous years ([Kawasaki et al., 1997](#); [Matsushita et al., 1998](#)). Cells are modeled as soft
 82 spheres which take up nutrients from the domain. By consuming intracellular nutrients, the
 83 cell grows continuously and divides upon reaching a threshold. Cells are initially placed inside
 84 a centered square after which they grow outwards into the nutrient-rich area. They are colored
 85 bright purple while they are actively growing and dark when not subject to growth anymore. A
 86 lighter color in the outer domain indicates that more nutrients are available while a dark color
 87 signifies a lack thereof.

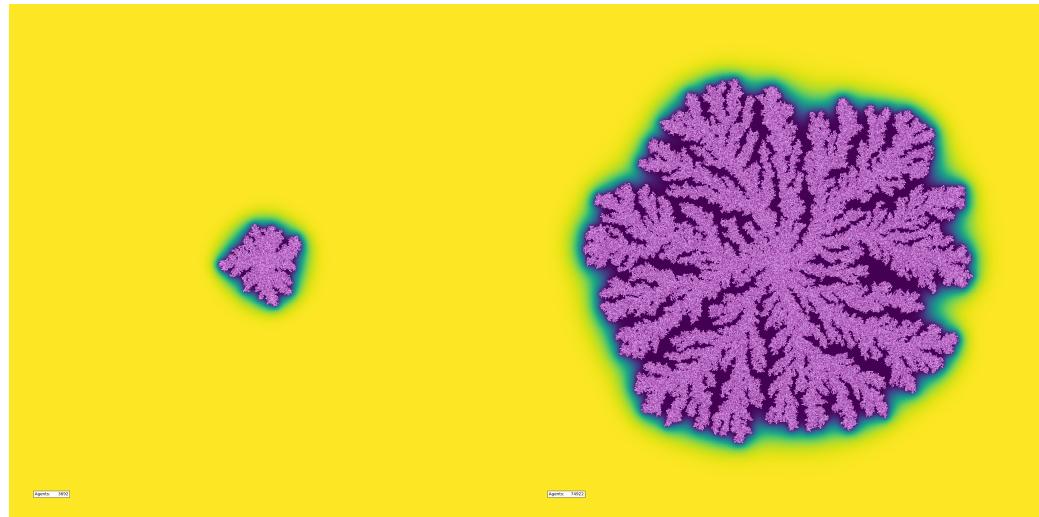


Figure 3: The bacterial colony grows outwards towards the nutrient-rich parts of the domain thus forming branches in the process.

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

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

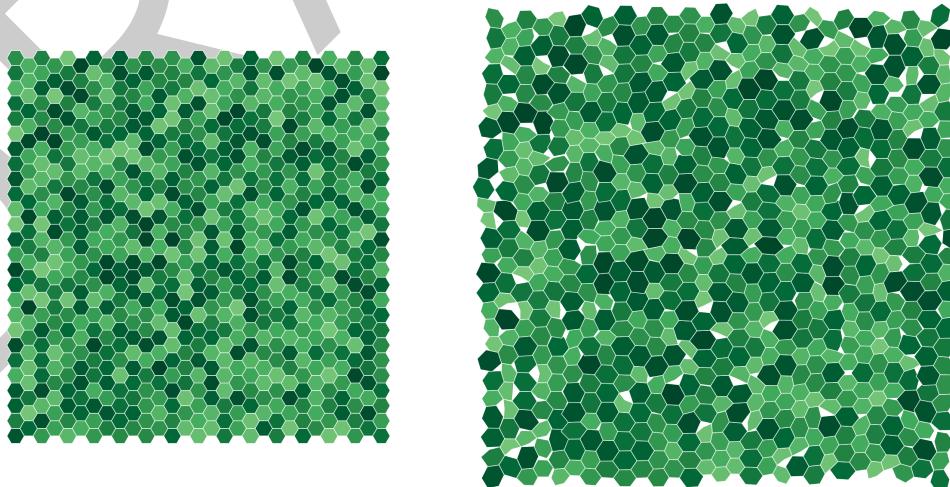


Figure 4: During growth the cells push on each other thus creating small spaces in between them as the collection expands. These forces also lead to deviations in the otherwise perfect hexagonal shape.

96 **Further Information**

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

⁹⁹ pyo3 and maturin konsti (2025) crates.

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¹⁰⁴ References

- ¹⁰⁵ Abar, S., Theodoropoulos, G. K., Lemarinier, P., & O'Hare, G. M. P. (2017). Agent based
¹⁰⁶ modelling and simulation tools: A review of the state-of-art software. *Computer Science
Review*, 24, 13–33. <https://doi.org/10.1016/j.cosrev.2017.03.001>
- ¹⁰⁸ Barton, D. L., Henkes, S., Weijer, C. J., & Sknepnek, R. (2017). Active vertex model for
¹⁰⁹ cell-resolution description of epithelial tissue mechanics. *PLOS Computational Biology*,
¹¹⁰ 13(6), e1005569. <https://doi.org/10.1371/journal.pcbi.1005569>
- ¹¹¹ Billaudieu, C., Chastanet, A., Yao, Z., Cornilleau, C., Mirouze, N., Fromion, V., & Carballido-
¹¹² López, R. (2017). Contrasting mechanisms of growth in two model rod-shaped bacteria.
¹¹³ *Nature Communications*, 8(1). <https://doi.org/10.1038/ncomms15370>
- ¹¹⁴ Breitwieser, L., Hesam, A., Montigny, J. de, Vavourakis, V., Iosif, A., Jennings, J., Kaiser,
¹¹⁵ M., Manca, M., Di Meglio, A., Al-Ars, Z., Rademakers, F., Mutlu, O., & Bauer, R.
¹¹⁶ (2021). BioDynaMo: a modular platform for high-performance agent-based simulation.
¹¹⁷ *Bioinformatics*, 38(2), 453–460. <https://doi.org/10.1093/bioinformatics/btab649>
- ¹¹⁸ Cess, C. G., & Finley, S. D. (2022). Multiscale modeling of tumor adaption and invasion
¹¹⁹ following anti-angiogenic therapy. *Computational and Systems Oncology*, 2(1). <https://doi.org/10.1002/cso2.1032>
- ¹²¹ Cooper, F., Baker, R., Bernabeu, M., Bordas, R., Bowler, L., Bueno-Orovio, A., Byrne, H.,
¹²² Carapella, V., Cardone-Noott, L., Cooper, J., Dutta, S., Evans, B., Fletcher, A., Grogan, J.,
¹²³ Guo, W., Harvey, D., Hendrix, M., Kay, D., Kursawe, J., ... Gavaghan, D. (2020). Chaste:
¹²⁴ Cancer, heart and soft tissue environment. *Journal of Open Source Software*, 5(47), 1848.
¹²⁵ <https://doi.org/10.21105/joss.01848>
- ¹²⁶ Datseris, G., Vahdati, A. R., & DuBois, T. C. (2022). Agents.jl: A performant and
¹²⁷ feature-full agent-based modeling software of minimal code complexity. *SIMULATION*,
¹²⁸ 003754972110688. <https://doi.org/10.1177/00375497211068820>
- ¹²⁹ Delile, J., Herrmann, M., Peyriéras, N., & Doursat, R. (2017a). A cell-based computational
¹³⁰ model of early embryogenesis coupling mechanical behaviour and gene regulation. *Nature
Communications*, 8(1). <https://doi.org/10.1038/ncomms13929>
- ¹³² Delile, J., Herrmann, M., Peyriéras, N., & Doursat, R. (2017b). A cell-based computational
¹³³ model of early embryogenesis coupling mechanical behaviour and gene regulation. In
¹³⁴ *Nature Communications* (No. 1; Vol. 8). Springer Science; Business Media LLC. <https://doi.org/10.1038/ncomms13929>
- ¹³⁶ Fletcher, A. G., Osterfield, M., Baker, R. E., & Shvartsman, S. Y. (2014). Vertex models of
¹³⁷ epithelial morphogenesis. *Biophysical Journal*, 106(11), 2291–2304. <https://doi.org/10.1016/j.bpj.2013.11.4498>
- ¹³⁹ Graner, F., & Glazier, J. A. (1992). Simulation of biological cell sorting using a two-dimensional
¹⁴⁰ extended potts model. *Physical Review Letters*, 69(13), 2013–2016. <https://doi.org/10.1103/physrevlett.69.2013>

- 142 Kang, S., Kahan, S., McDermott, J., Flann, N., & Shmulevich, I. (2014). Biocellion :
143 Accelerating computer simulation of multicellular biological system models. *Bioinformatics*,
144 30(21), 3101–3108. <https://doi.org/10.1093/bioinformatics/btu498>
- 145 Kawasaki, K., Mochizuki, A., Matsushita, M., Umeda, T., & Shigesada, N. (1997). *Modeling*
146 *Spatio-Temporal Patterns Generated by Bacillus subtilis*. <https://doi.org/10.1006/jtbi.1997.0462>
- 148 konsti. (2025). *maturin: Build and publish crates with pyo3, cffi and uniffi bindings as well as*
149 *rust binaries as python packages* (Version 1.8.2). <https://github.com/pyo3/maturin>
- 150 Matsushita, M., Wakita, J., Itoh, H., Ràfols, I., Matsuyama, T., Sakaguchi, H., & Mimura, M.
151 (1998). *Interface growth and pattern formation in bacterial colonies*. [https://doi.org/10.1016/S0378-4371\(97\)00511-6](https://doi.org/10.1016/S0378-4371(97)00511-6)
- 153 Merks, R. M. H., Guravage, M., Inzé, D., & Beemster, G. T. S. (2011). VirtualLeaf: An
154 open-source framework for cell-based modeling of plant tissue growth and development.
155 *Plant Physiology*, 155(2), 656–666. <https://doi.org/10.1104/pp.110.167619>
- 156 Mogilner, A., & Manhart, A. (2016). Agent-based modeling: Case study in cleavage furrow
157 models. *Molecular Biology of the Cell*, 27(22), 3379–3384. <https://doi.org/10.1091/mbc.e16-01-0013>
- 159 Pleyer, J., & Fleck, C. (2023). Agent-based models in cellular systems. *Frontiers in Physics*,
160 10. <https://doi.org/10.3389/fphy.2022.968409>
- 161 PyO3 Project and Contributors. (n.d.). *PyO3*.
- 162 Steinberg, M. S. (1963). Reconstruction of tissues by dissociated cells: Some morphogenetic
163 tissue movements and the sorting out of embryonic cells may have a common explanation.
164 *Science*, 141(3579), 401–408. <https://doi.org/10.1126/science.141.3579.401>
- 165 Wilensky, U. (1999). *NetLogo* [Http://ccl.northwestern.edu/netlogo/]. Center for Connected
166 Learning; Computer-Based Modeling. <http://ccl.northwestern.edu/netlogo/>
- 167 Young, K. D. (2006). The selective value of bacterial shape. *Microbiology and Molecular*
168 *Biology Reviews*, 70(3), 660–703. <https://doi.org/10.1128/mmbr.00001-06>
- 169 Zapun, A., Vernet, T., & Pinho, M. G. (2008). The different shapes of cocci. *FEMS*
170 *Microbiology Reviews*, 32(2), 345–360. <https://doi.org/10.1111/j.1574-6976.2007.00098.x>