

# <sup>1</sup> **cellular\_raza: Cellular Agent-based Modeling from a Clean Slate**

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## <sup>5</sup> Summary

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

## <sup>14</sup> Statement of Need

<sup>15</sup> 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  
<sup>16</sup> 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,  
<sup>17</sup> they frequently lack the capacity to be applied more universally. In contrast, general-purpose  
<sup>18</sup> ABM toolkits are not designed with particular applications in mind ([Abar et al., 2017](#); [Datseris](#)  
<sup>19</sup> [et al., 2022](#); [Wilensky, 1999](#)). These toolkits often enable the definition of agents bottom-up  
<sup>20</sup> and can be a suitable choice if they allow for the desired cellular representation. However, they  
<sup>21</sup> lack the explicit forethought necessary for application in cellular systems and may not be able  
<sup>22</sup> to describe every cellular aspect.

<sup>23</sup> In contrast to classical particle simulations, agent-based models (ABMs) treat every cell  
<sup>24</sup> individually. This implies that parameters can vary between agents and that every cell should  
<sup>25</sup> be traceable throughout time and space. Additionally, they can describe growth, proliferation,  
<sup>26</sup> death, and many other cellular processes and should also accurately model cell lineage. These  
<sup>27</sup> models operate on the mesoscopic scale where the underlying complexity of the problem cannot  
<sup>28</sup> be fully attributed to either intracellular or extracellular processes. Their applications include  
<sup>29</sup> modeling of self-organization and emergent phenomena, but they can also be used to introduce  
<sup>30</sup> spatial effects into existing population-based models. To address these issues and construct  
<sup>31</sup> models from first principles without any assumptions regarding the underlying complexity or  
<sup>32</sup> abstraction level, we developed “cellular\_raza.”

## <sup>33</sup> Cellular Agent-Based Frameworks

<sup>34</sup> In our previous efforts ([Pleyer & Fleck, 2023](#)), we assessed the overall state of modelling toolkits  
<sup>35</sup> for individual-based cellular simulations. These frameworks are designed for specific usages  
<sup>36</sup> and often require many parameters which are unknown or difficult to determine experimentally.  
<sup>37</sup> This poses an inherent problem for their applicability and the ability to properly interpret  
<sup>38</sup> results. Few modelling frameworks exist that provide a significant degree of flexibility and

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

## 47 **cellular\_raza**

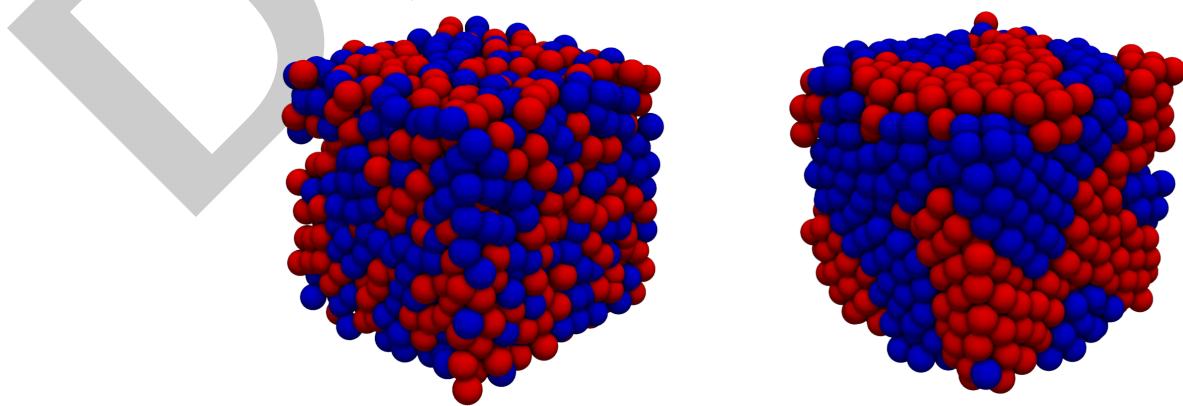
48 We distinguish between different simulation aspects, i.e., mechanics, interaction, or cell cycle.  
 49 These aspects are directly related to the properties of the cells, domain, or other external  
 50 interactions. The user selects a cellular representation, which can be built from pre-existing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

## 59 **Examples**

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

### 62 **Cell Sorting**

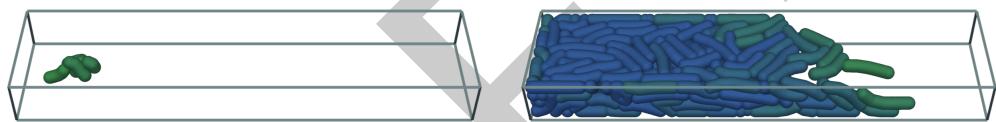
63 Cell sorting is a naturally occurring phenomenon ([Graner & Glazier, 1992](#); [Steinberg, 1963](#)).  
 64 The cellular interaction is specific to their species. We consider two distinct types represented  
 65 by soft spheres. They physically attract each other at close proximity if their species is identical.  
 66 Cells are placed randomly inside a cube with reflective boundary conditions. In the final  
 67 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.

## 68 Bacterial Rods

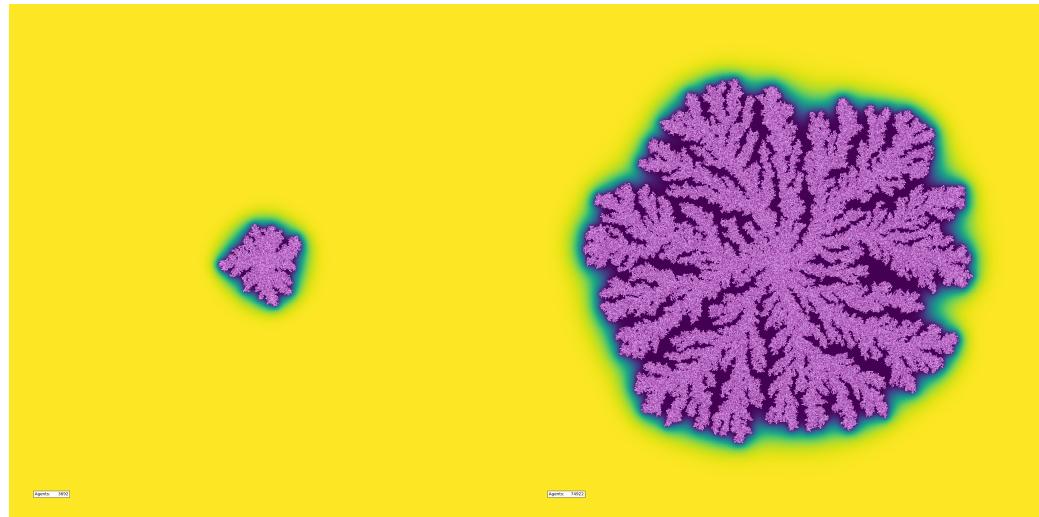
69 Bacteria come in various forms ([Young, 2006](#); [Zapun et al., 2008](#)) such as elongated shapes  
 70 ([Billaudeau et al., 2017](#)) which grow asymmetrically in the direction of elongation. Our model  
 71 describes the physical mechanics of one cell as a collection of multiple vertices  $\vec{v}_i$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

## 80 Branching of *Bacillus Subtilis*

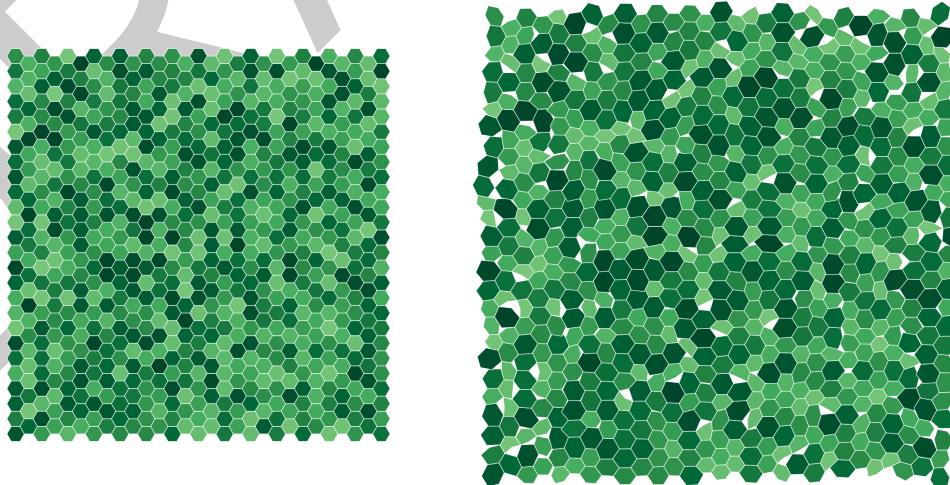
81 Spatio-temporal patterns of bacterial growth such as in *Bacillus Subtilis* have been studied for  
 82 numerous years ([Kawasaki et al., 1997](#); [Matsushita et al., 1998](#)). Cells are modeled as soft  
 83 spheres which take up nutrients from the domain. By consuming intracellular nutrients, the  
 84 cell grows continuously and divides upon reaching a threshold. Cells are initially placed inside  
 85 a centered square after which they grow outwards into the nutrient-rich area. They are colored  
 86 bright purple while they are actively growing and dark when not subject to growth anymore. A  
 87 lighter color in the outer domain indicates that more nutrients are available while a dark color  
 88 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.

### 89    **Semi-Vertex Model for Epithelial and Plant Cells**

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

### 97    **Further Information**

98    The full documentation including guides, all examples from above and more is available at  
 99    [cellular-raza.com](http://cellular-raza.com). cellular\_raza can also be used as a numerical backend together with the

<sup>100</sup> pyo3 and maturin konsti (2025) crates.

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