

A single-cell based modeling approach to bacterial colony growth

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Abstract

The emergence of improved microfluidic devices together with automated microscopy, where the behavior of individual cells can be monitored under controlled conditions over time, has provided us with tools to answer many long standing questions [1]. We can now address questions concerning heterogeneities in cell populations and how individual properties of a cell such as size and growth rate affect the overall behavior of cell colonies or tissues. In order to answer such questions and to test hypotheses quantitatively it will be absolutely crucial to have good models describing the systems at hand, taking into account both mechanical interactions as well as biochemical interactions and gene regulatory networks.

Here we present a detailed model of *Escherichia coli* where growth, cell division and cell-cell interactions are modeled explicitly and where genetic networks and protein-protein interactions are incorporated at the level of individual cells (see Fig. 1). Thanks to the detailed mechanical description we can monitor how cells interact mechanically with its environment, follow how stress builds up in growing cell colonies and how individual cell properties such as length affects global colony properties such as directional correlation between cells [2].



Figure 1: Model simulation of a bacterial colony growing under uniform conditions

Moreover we can investigate how cells interact biochemically with their surroundings by incorporate biochemical networks into the models. For example we study the biochemical network responsible for bacterial chemotaxis which allows cells to sense temporal gradients of chemical ligands in their vicinity. The bacterium moves in a series of smooth runs followed by tumbling events, where the bacterium chooses a new random direction for the next run. By adjusting the tumbling frequency a bacterium can swim towards a nutrition source by performing a biased random walk [3, 4]. Here we incorporate the chemotactic network explicitly in each individual cell together with our mechanical description. This allows us to investigate how growing cell colonies behave in non-uniform environments and how param-

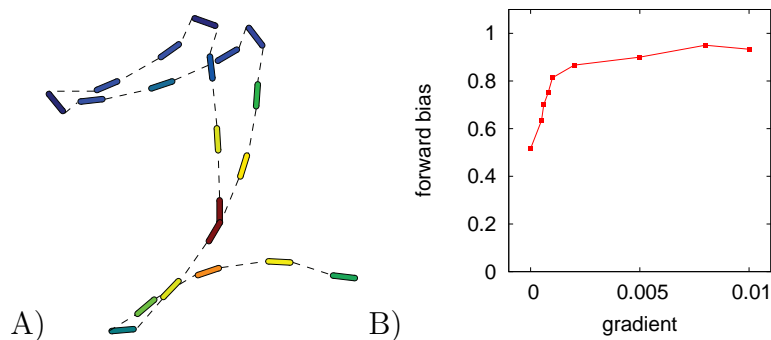


Figure 2: A) Model of a cell moving around a nutrition source. The color coding refers to the nutrition concentration sensed by the cell where red means high concentration and blue means a low concentration. B) The forward bias, percentage of cells leaving a chamber in the direction of the gradient, as function of the steepness of the gradient.

eters of the model affect the behavior of individual cells as well as the collective behavior of the cell population (see Fig. 2).

Finally it is also possible to investigate how heterogeneities within a cell population affect the faith of the colony as a whole. This is a challenging prospect since it is known that heterogeneities in cell populations are important, e.g. response to antibiotic treatment [5]. These are properties that cannot be described by models that do not treat cells as individual entities, and which is why we believe that models at the level of individual cells will become an increasingly important tool for the challenges facing Systems Biology in the years to come.

References

- [1] Groisman, A., Lobo, C., Cho, H., Campbell, J.K., Dufour, Y.S., Stevens, A.M. & Levchenko A. *Nature Methods* **2**, 685–689 (2005).
- [2] Cho, H., Jönsson, H., Campbell, J.K., Melke, P., Williams, J.W., Jedynak, B., Stevens, A.M., Groisman, A. & Levchenko A. (submitted).
- [3] Berg, H.C. & Brown, D.A. *Nature* **239**, 500–504 (1972).
- [4] Barkai, N. & Leibler, S. *Nature* **387**, 913–917 (1997).
- [5] Balaban, N.Q., Merrin, J., Chait, R., Kowalik, L. & Leibler, S. *Science* **305**, 1622–1625 (2004).

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