# The Dynamics of Population Growth of *E. coli* as Colonies and in Liquid Culture

Xinxian Shao[1], Andrew Mugler[1], Jason Jeong[2], Justin Kim[2], Bruce Levin[2], Ilya Nemenman[1,2]

*Short Abstract* — In nature, bacterial cells often grow as colonies in physically structured habitats. We lack a comprehensive model for the population growth in such conditions. Based on Monod equation for bacterial growth in liquid culture, we develop a minimal model for bacterial colony growth in 3D, in which a homogeneous colony of cells locally consumes a diffusing nutrient. We test the model experimentally with *E. coli* colonies embedded in soft agar. Our model provides a baseline to which studies of complex growth processes, such as spatially and/or phenotypically heterogeneous colonies, must be compared.

*Keywords* — bacterial colony growth, diffusion limited growth, minimal model

## I.  MOTIVATION

THE well-established the Monod equation [1] models the bacterial growth in well-agitated liquid culture assuming that the planktonic cells have equal access to nutrients, signaling molecules, and toxins like antibiotics.  Instead, in the real world, bacterial infections often develop as colonies or microcolonies, separately or collectively as biofilms in physically structured habitats. In contrast to the conventional Monod model, no comprehensive theory exists for bacterial growth in such conditions. And yet the two growth dynamics can be very different. For example, *E.coli* growing on a surface of hard agar containing limited glucose yields higher stationary cell densities than liquid culture with the same amount of nutrient [2]. It is likely that these differences can be attributed to phenotypic and structural heterogeneity of bacterial colonies, compared to homogeneous growth of planktonic cultures. However, to deduce these mechanisms, one first must have a minimal model of colony growth that incorporates the physical structure of the environment, but not the colony heterogeneity. Building and experimentally verifying such a model is the goal of this work.

## II.  METHODS

Cells in a colony could have geometric heterogeneity and possible physiological heterogeneity [3, 4]. However, for the minimal model, we assume that cells in a colony are homogeneous, having the same growth rate and the same access to nutrients and oxygen. The bacterial colony acts as a sink in the diffusion equation for nutrient molecules, and the sink is proportional to the colony growth rate which is only limited by the local density of nutrient. The colony radius is assumed negligibly small. This model is represented by a set of coupled equations: a PDE that account for nutrient diffusion, and a nonlinear ODE that models the colony growth. Experimentally, the system is studied by monitoring *E. coli* growth in a minimal medium with limited glucose in well-mixed cultures, and embedded into soft agar.

## III.  RESULTS AND DISCUSSION

Analysis and simulations of the mathematical model suggest that, in any number of dimensions, the colony starts growing exponentially until the local nutrients are depleted. Then the colony growth decelerates to a diffusion-limited power-law mode, and finally stops when all nutrients in the plate are exhausted. In the power law regime, the colony size is predicted to be $N \sim (Dt)^{d/2}$, for $d \leq 2$ where $D$ is the nutrient diffusion constant, and $N \sim (Dt)^{\alpha/(\alpha-d+2)}$ for $d \geq 2$, where $\alpha$ depends on the cell packing density (left figure). The experimental data agrees with the model in the exponential region, and the colony growth in agar, indeed, slows down while the liquid cells grow exponentially till the saturation. However, our current experimental data is insufficient to verify if the exponent is the predicted 1, so it is so far impossible to rule out the minimal model prior to saturation. Nonetheless, both the liquid and the colony growth differ from the minimal model at saturation: bacterial density in the liquid culture drops at long times, and structured colony achieves higher bacterial densities than the liquid culture (right figure).
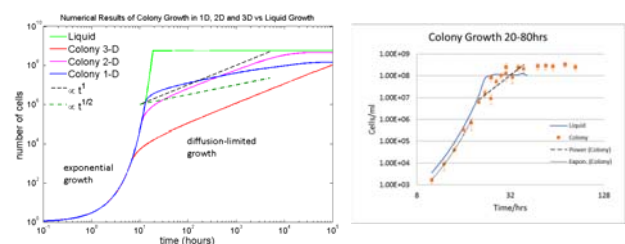
## REFERENCES

[1]  Monod, J. (1949). *Annual Reviews in Microbiology*, *3*(1), 371-394
[2]  Simonsen, L. (1990). *Journal of general microbiology*, *136*(6), 1001-1007
[3]  Landy, J. (2013). *arXiv preprint arXiv:1312.0674*
[4]  Lavrentovich, M. O., Koschwanez, J. H., & Nelson, D. R. (2013). *Physical Review E*, *87*(6), 062703

[1]Department of Physics, Emory University, Atlanta, GA, USA. E-mail: xshao@physics.emory.edu,
[2]Department of Biology, Emory University