Feast, famine, and microbial persistence

12.S492 Spring 2024 (2-0-4)
Instructors: Tanja Bosak and Daniel Rothman

Overview

Nearly all microbes in the natural environment starve. The reason is quite simple: microbes efficiently consume the energy available to them. Unless their energy source is constantly supplied, typically in the form of organic compounds, most microbes merely persist in starvation conditions. In marine sediments, microbes are known to endure for up to 100 million years. They essentially lie dormant, yet they "wake up" when opportunities for carbon metabolism arise. In the human body, bacterial "persisters" evade antibiotics by becoming dormant; when they wake up, reinfection results. Slow growth or dormancy may be a response to environmental stress. Moreover, the "growth arrest" state appears to be characterized by phenotypic heterogeneity, which may provide a kind of stochastic trigger that makes waking up possible. This seminar explores these and related problems via discussions of recent and classic literature. Experiments, observations, and theoretical models receive roughly equal attention.

Organization

We will meet on Thursdays from 2:30–4:00 in Rm. 4-457. The initial meeting on Thursday, February 8 will be organizational. Interested students with scheduling conflicts should email their schedule to the instructors; we'll make accommodations if we can.

Participation, format, and expectations

Each week we will discuss the assigned readings. Rather than designating discussion leaders, we will each participate in discussions on an equal basis. No one is expected to have any special expertise in any of the subjects; instead, we will all come prepared to learn from each other. Participation is open to all, including undergraduates. Interested students should register (in advance, if possible) for 12.S492. Postdocs, faculty, and research staff are also welcome. All participants will contribute to discussions.

Tentative syllabus

All material will be available on Canvas or obtainable electronically from the MIT Library.

- **February 8:** Introduction, organization, rules.
- **February 15:** Slow life

  Morita, R. Y. (1988). "Bioavailability of energy and its relationship to growth and starvation survival in nature". *Canadian Journal of Microbiology* 34, pp. 436–441.

  Kolter, R., N. Balaban, and T. Julou (2022). "Bacteria grow swiftly and live thriftily". *Current Biology* 32, R599–R605.

- **February 22:** Deep life

  Hoehler, T. M. and B. B. Jørgensen (2013). "Microbial life under extreme energy limitation". *Nature Reviews Microbiology* 11, pp. 83–94.

  Jørgensen, B. B. and I. P. Marshall (2016). "Slow microbial life in the seabed". *Annual Review of Marine Science* 8, pp. 311–332.

- **February 29:** Antibiotic persistence

  Balaban, N. Q., J. Merrin, R. Chait, L. Kowalik, and S. Leibler (2004). "Bacterial persistence as a phenotypic switch". *Science* 305, pp. 1622–1625.

  Pontes, M. H. and E. A. Groisman (2019). "Slow growth determines nonheritable antibiotic resistance in Salmonella enterica". *Science Signaling* 12, eaax3938.

  Optional background reading: Gefen, O. and N. Q. Balaban (2009). "The importance of being persistent: heterogeneity of bacterial populations under antibiotic stress". *FEMS microbiology reviews* 33, pp. 704–717.

- **March 7:** Evolution under starvation (1)

  Finkel, S. E. and R. Kolter (1999). "Evolution of microbial diversity during prolonged starvation". *Proceedings of the National Academy of Sciences* 96, pp. 4023–4027.

  Finkel, S. E. (2006). "Long-term survival during stationary phase: evolution and the GASP phenotype". *Nature Reviews Microbiology* 4, pp. 113–120.

- **March 14:** Evolution under starvation (2)

  Katz, S., S. Avrani, M. Yavneh, S. Hilau, J. Gross, and R. Hershberg (2021). "Dynamics of adaptation during three years of evolution under long-term stationary phase". *Molecular Biology and Evolution* 38, pp. 2778–2790.

  Shoemaker, W. R., S. E. Jones, M. E. Muscarella, M. G. Behringer, B. K. Lehmkuhl, and J. T. Lennon (2021). "Microbial population dynamics and evolutionary outcomes under extreme energy limitation". *Proceedings of the National Academy of Sciences* 118, e2101691118.

- **March 21:** Fluctuation limitation

  Rothman, D. H. (2024). "Slow closure of Earth's carbon cycle". *Proceedings of the National Academy of Sciences* 121. DOI: 10.1073/pnas.2310998121.

- **April 4:** Aging in antibiotic persistence

  Fridman, O., A. Goldberg, I. Ronin, N. Shoresh, and N. Q. Balaban (2014). "Optimization of lag time underlies antibiotic tolerance in evolved bacterial populations". *Nature* 513, pp. 418–421.

  Kaplan, Y., S. Reich, E. Oster, S. Maoz, I. Levin-Reisman, I. Ronin, O. Gefen, O. Agam, and N. Q. Balaban (2021). "Observation of universal ageing dynamics in antibiotic persistence". *Nature* 600, pp. 290–294.

- **April 11:** Physiology of growth arrest

  Bergkessel, M., D. W. Basta, and D. K. Newman (2016). "The physiology of growth arrest: uniting molecular and environmental microbiology". *Nature Reviews Microbiology* 14, pp. 549–562.

- **April 18:** Phenotypic heterogeneity

  Ackermann, M. (2015). "A functional perspective on phenotypic heterogeneity in microorganisms". *Nature Reviews Microbiology* 13, pp. 497–508.

- **April 25:** Stochastic switching

  Acar, M., J. T. Mettetal, and A. Van Oudenaarden (2008). "Stochastic switching as a survival strategy in fluctuating environments". *Nature genetics* 40, pp. 471–475.

  Norman, T. M., N. D. Lord, J. Paulsson, and R. Losick (2015). "Stochastic switching of cell fate in microbes". *Annual review of microbiology* 69, pp. 381–403.

- **May 2:** Evolution beneath the seafloor

  Starnawski, P., T. Bataillon, T. J. Ettema, L. M. Jochum, L. Schreiber, X. Chen, M. A. Lever, M. F. Polz, B. B. Jørgensen, A. Schramm, et al. (2017). "Microbial community assembly and evolution in subseafloor sediment". *Proceedings of the National Academy of Sciences* 114, pp. 2940–2945.

  Becraft, E. D., M. C. Lau Vetter, O. K. Bezuidt, J. M. Brown, J. M. Labonté, K. Kauneckaite-Griguole, R. Salkauskaite, G. Alzbutas, J. D. Sackett, B. R. Kruger, et al. (2021). "Evolutionary stasis of a deep subsurface microbial lineage". *The ISME Journal* 15, pp. 2830–2842.

- **May 9:** Adaptive evolution

  Lenski, R. E. (2017). "Experimental evolution and the dynamics of adaptation and genome evolution in microbial populations". *The ISME journal* 11, pp. 2181–2194.

  Optional background reading: Orr, H. A. (2005). "The genetic theory of adaptation: a brief history". *Nature Reviews Genetics* 6, pp. 119–127.