Gambling with evolution: bet hedging in fluctuating environments

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For the last 150 years the theory of evolution has radically changed our view of life. This powerful framework underpins our understanding of all Biology, yet there remain many open questions about the principles and laws that shape the evolutionary processes. These questions range from the evolution of human language and society to the fast adaptation of pathogenic bacteria that are resistant to multiple antibiotics. Deducing these principles is particularly challenging because evolution is a stochastic and highly dynamic process. Moreover, interactions within and between populations and the environment can give rise to non-intuitive properties, such as cooperation and altruistic behavior. Given the inherent complexity and the long temporal scale of evolutionary processes, mathematical models and computer simulations are essential tools to study evolution. With these tools, we can evolve simple organisms within a computer, allowing us to study the principles of evolution through thousands of generations, which would be impossible by experimental and observational approaches.

A critical open question in evolutionary theory is how organisms deal with the uncertainty of a fluctuating environment, where a population needs to efficiently adapt over and over to new conditions to escape extinction. While classic evolutionary theory predicts that selection of random beneficial mutations (*i.e.* genetic adaptation) would allow organisms to adapt to an environmental change, other mechanisms have been observed in living organisms, including bet hedging through stochastic epigenetic switches. An epigenetic switch is a system capable of stochastically alternating between multiple stable phenotypes which can be inherited without DNA mutation. This bet hedging mechanism could maximize the chances that a population survives over the long-term, but it also imposes a cost to the population, reducing its average fitness. To discern the specific evolutionary pressures that favor epigenetic switches over genetic adaptation, we simulated the evolution of a self-activating genetic circuit, which can both adapt genetically and exhibit epigenetic switching, in a fluctuating environment. Unlike laboratory evolution experiments, this *in silico* experiment was replicated many times over a range of evolutionary parameters and under different biological assumptions to uncover statistical regularities in the evolutionary histories. As might be expected from the timescales of the different adaptation mechanisms, we showed that genetic adaptation (slower) is superior when the environment fluctuates slowly, whereas epigenetic switching (faster) has the advantage when the environment fluctuates rapidly. Less intuitively, we demonstrated that the balance between genetic adaptation and epigenetic switching arises from a trade-off between minimizing the adaptation time after each environmental transition and increasing the robustness of the phenotype while the environment stays constant (between transitions). A key insight was that epigenetic switching becomes accessible by the selection of high nonlinearity and faster genetic adaptation. Finally, we demonstrated that epigenetic switching allows for quick adaptation while still constraining the biochemical noise level, providing a clear evolutionary advantage as a bet-hedging mechanism.[1]

The evolutionary mechanisms that lead to the appearance and persistence of complexity remain elusive. I believe these mechanisms can only be elucidated by understanding both the molecular dynamics of gene regulation, and the effect of natural selection on these systems. My work integrated the study of gene circuit dynamics and the role of biochemical noise with evolutionary theory, paving the way towards understanding how emergent properties of gene networks appear, spread and persist through evolution.

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[1] M. Gómez-Schiavon, N. E. Buchler, Evolutionary dynamics of an epigenetic switch in a fluctuating environment. *bioRxiv* (2016). doi:10.1101/072199