Stochastic gene expression in a fluctuating environment
Authors: M. Thattai and A. van Oudenaarden
Genetics **167**, 523 (2004)

Phenotypic diversity, population growth, and information in fluctuating environments
Authors: E. Kussell and S. Leibler
Science **309**, 2075 (2005)

Recommended with a commentary by Mehran Kardar

In the effort to survive in a changing environment, simple bacteria have developed interesting strategies. A population of bacteria can share identical genetic material (genotype), yet the expression of some genes may be on or off in distinct subgroups (phenotypes). These (epigenetic) distinctions arise from possible metastable states (fixed points) of autocatalytic loops of proteins controlling gene expression. The corresponding traits are heritable and may persist over several generations, but the unavoidable fluctuations due to the small number of proteins in the cell may cause a stochastic switch to a different state.

As the distinct phenotypes grow at different rates, there is a "diversity cost" associated with carrying along sub-populations of less fit individuals. The payoff comes when there is a change in the environment which modifies the relative fitness of the phenotypes. For example a small sub-population of slow-dividing but antibiotic- resistant bacteria can help the organism survive exposure to penicillin. This strategy is similar to bet-hedging or diversifying a stock portfolio.

The two articles above attempt to quantify the advantages of stochastic switching: The key parameter is the Lyapunov exponent governing the exponential growth (in time) of the overall population size as it passes through many episodes of environmental change. The state of the colony at any time is represented by the vector of the relative numbers in each phenotype. The change in size of each sub- population is related to its fitness in the current environment, as well as the switching rates between the phenotypes. The mathematical complexity is reminiscent of finding the decay rate of a quantum state in a time-varying potential, or the localization length of an electron along a disordered wire. Thattai et al compute the growth rate by numerical means, while the method of Kussell et al is similar to the "sudden approximation" from quantum mechanics. Not surprisingly, both groups find that maximal growth occurs when the stochastic switching rate is similar to the rate at which the environment changes.

Kussell et al also ask if it is favorable for the organism to develop a sensing mechanism that allows it to switch phenotypes in response to the changing environment. The long-term gain in population from intelligently switching to the fastest growing state must compensate for an overall reduction in growth due to the load of working the sensor. Interestingly, the former is found to depend on the entropy (or information content) of the probability distribution characterizing the stochastic environment. If the environmental changes are slow or predictable enough, it is better to switch by chance than by design.