# A waiting time problem with applications to DNA regulatory sequence evolution, cancer, and the limits of Darwinian evolution

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We consider the population genetics problem: How long does it take before some member of the population has k specified mutations? The case k=2 is relevant to the onset of cancer due to the inactivation of both copies of a tumor suppresor gene. Results of Nowak and collaborators give the waiting time distribution in this case and the time until the mutant phenotype becomes fixed in the population. Here we apply and extend these results to obtain insights into DNA regulatory sequence evolution in Drosophila (fruit flies) and humans. In particular, we examine the waiting time for a pair of mutations, the first of which inactivates an existing transcription factor binding site and the second which creates a new one. Consistent with recent experimental observations for Drosophila, we find that a few million years is sufficient, but for humans with a much smaller effective population size, this type of change would take more than 100 million years. We then discuss models for larger k, which are needed for colon cancer and other diseases where a sequence of mutations leads to cells with uncontrolled growth. Lastly, we'll use these results to expose flaws in some of Michael Behe's arguments concerning mathematical limits to Darwinian evolution.

Bio:

I am a Postdoctoral Fellow at the Mathematical Biosciences Institute (MBI) which is located at The Ohio State University. I spent last year as a postdoc at the Institute for Mathematics and Its Applications (IMA) at the University of Minnesota, immersed in their themed year "Mathematics and Molecular/Cellular Biology". I completed my Ph.D. at the Center for Applied Mathematics at Cornell University in May 2007 under the direction of Rick Durrett. My research interests are in applying probability to problems in population genetics and molecular biology. My Ph.D. research focused on stochastic models of DNA regulatory sequence evolution in different organisms, which is the general topic of my talk at UC Merced. I'm currently working on a few projects at the MBI: a gene regulatory network model of an experimental system with Timothy Newman (Arizona State University) and Vincent Noireaux (University of Minnesota), and a dynamical systems model of microRNA regulation involved in cancer development.