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Michael Hinczewski is the Warren E. Rupp Assistant Professor in the Department of Physics at Case Western Reserve University. He received his B.S. in Physics at Yale University, followed by Ph.D. work in condensed matter theory at MIT. His current interests include a variety of topics in the statistical mechanics of biological systems, including cell adhesion, signaling, and molecular motors. The common theme through all of these is protein biophysics, which he learned as a postdoc in the lab of Dave Thirumalai at the University of Maryland, College Park.

Steering Evolution: what can pulling proteins teach us about population genetics?

One of the great challenges in modern medicine is the rapid evolution of drug resistant genetic variants, whether in the case of bacterial infections and antibiotics, or metastatic cancer and chemotherapy. There is growing interest in therapeutic strategies that bias the evolutionary trajectories of cellular populations through rationally designed control protocols: for example varying drug dosage levels, drug types, and/or order of application. If chosen correctly, such protocols can guide the population into genetic states that are known to be maximally susceptible to a particular final treatment. The mathematics that describes how the probability distribution of genotypes varies in time during these protocols is strikingly similar to the diffusive dynamics of protein conformations on complex free energy landscapes. Indeed in certain cases changing drug dosage is analogous to applying a force to a protein in a pulling experiment. This talk deals with one particular therapeutic problem that can potentially be addressed using this analogy. Clinical strategies that attempt to bias the evolution of bacterial or tumor systems often assume enough time passes for relaxation to evolutionary equilibrium (for example after each switch of drug type in a sequential treatment), limiting their practicality. We show how a Fokker-Planck description of evolutionary dynamics, on a time-varying fitness landscape, yields a general analytical method to accelerate this equilibration, allowing faster progress toward the desired final distribution. We also discuss ongoing collaborative efforts to implement this theoretical solution in the lab through a morbidostat apparatus, which monitors a bacterial population subject to time-varying drug dosages.