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Biophysical Models of Evolution: Application to Transcription Factor Binding Sites in Yeast MICHAEL MANHART, ALLAN HALDANE, ALEXANDRE MOROZOV, Rutgers University — There has been growing interest in understanding the physical driving forces of evolution at the molecular scale, in particular how biophysics determines the fitness landscapes that shape the evolution of DNA and proteins. To that end we study a model of molecular evolution that explicitly incorporates the underlying biophysics. Using population genetics, we derive a steady-state distribution of monomorphic populations evolving on an arbitrary fitness landscape. Compared to previous studies, we find this result is universal for a large class of population models and fully incorporates both stochastic effects and strong natural selection. This distribution can then be used to infer the underlying fitness landscape from genomic data. This model can be applied to a variety of systems, but we focus on transcription factor binding sites, which play a crucial role in gene regulatory networks. Since these sites must be bound for successful gene regulation, we consider a simple thermodynamic model of fitness as a function of the free energy for binding a transcription factor at the site. Using empirical energy matrices and genome-wide sets of binding sites from the yeast *Saccharomyces cerevisiae*, we use this model to infer the role of DNA-protein interaction physics in evolution.

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