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In-silico studies of neutral drift for functional protein interaction networks MD ZULFIKAR ALI, Clark University, NED S WINGREEN, Princeton University, RANJAN MUKHOPADHYAY, Clark University — We have developed a minimal physically-motivated model of protein-protein interaction networks. Our system consists of two classes of enzymes, activators (e.g. kinases) and deactivators (e.g. phosphatases), and the enzyme-mediated activation/deactivation rates are determined by sequence-dependent binding strengths between enzymes and their targets. The network is evolved by introducing random point mutations in the binding sequences where we assume that each new mutation is either fixed or entirely lost. We apply this model to studies of neutral drift in networks that yield oscillatory dynamics, where we start, for example, with a relatively simple network and allow it to evolve by adding nodes and connections while requiring that dynamics be conserved. Our studies demonstrate both the importance of employing a sequence-based evolutionary scheme and the relative rapidity (in evolutionary time) for the redistribution of function over new nodes via neutral drift. Surprisingly, in addition to this redistribution time we discovered another much slower timescale for network evolution, reflecting hidden order in sequence space that we interpret in terms of sparsely connected domains.

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