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Stochastic waiting times of complex biochemical reactions may exhibit universal behavior B. MUNSKY, G. BEL, N. SINITSYN, I. NEMENMAN, Los Alamos National Lab — To model cell regulatory pathways, one must understand completion times of complex, multistep, often reversible biochemical reactions. As transient properties, these completion (first passage) times are typically unobtainable from stationary behavior, and their distributions are known only for simple homogeneous network topologies. Here, we derive explicit formulas for first passage time distributions of various biological models, such as multi-site phosphorylation, kinetic proofreading, and discrete walks along an inhomogeneous line, and others. In many cases, as system size grows, the system behavior frequently becomes simpler, approaching an unexpected universality. Under many conditions, this limiting behavior is deterministic, under others it is a memoryless Markovian dynamics, and the two results are separated by a phase transition. For example, below a critical parameter, the time to complete a given complex multistep reaction obeys a narrow gamma distribution, and above this threshold, waiting times are exponentially distributed. These findings suggest first that possibilities to coarse-grain cellular networks are immense, and second that the common practice of arbitrarily replacing unknown dynamics with ballistic motion or exponential waiting times may be justified in a wide array of circumstances.

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