Abstract Submitted
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Role of Multisite Phosphorylation in Timing of a Yeast Cell Cycle Event[1] VOLKAN SEVIM, University of California, San Francisco, XIAOJING YANG, University of California, San Francisco; Peking University, KAI-YEUNG LAU, University of California, San Francisco, CHAO TANG, University of California, San Francisco; Peking University — We study the biochemical network that triggers the S phase in yeast cell cycle. Key components of this network are three proteins: two kinases and an inhibitor. First kinase, Cln1/2-Cdk, acts as an input signal, phosphorylating the inhibitor, Sic1. The second kinase, Clb5/6-Cdk, is sequestered into an inactive complex by Sic1. Clb5/6-Cdk is the output signal of the circuit. Sic1 has nine phosphorylation sites, and phosphorylation of six or more of them causes it to degrade rapidly, leading to a sharp rise of free Clb5/6-Cdk. Our experiments indicate that multisite phosphorylation (MSP) is responsible for the timing robustness of this sharp transition. We study the role of MSP in timing using computer simulations. Preliminary results indicate that, MSP does not bring timing robustness when each kinase can phosphorylate each site with identical specificity. We employ in silico evolution to find the specificity configuration for the phosphorylation sites that leads to most robust timing under extrinsic noise.

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