Stochastic Models of Cell Cycle Regulation in Eukaryotes

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THE DNA replication-division cycle in eukaryotic cells is controlled by a complex network of regulatory proteins (called cyclin-dependent kinases, Cdk's) and their activators and inhibitors (Tyson & Novak, 2008). Chen et al. (2004) have proposed a comprehensive deterministic model of Cdk regulation in budding yeast that accurately accounts for the average phenotypic properties of wild-type cells and 150^+ mutant strains. However, the deterministic model cannot account for the considerable variabilities in cell cycle properties that have been observed among genetically identical cells. These variabilities are due in large part to small numbers of molecules in yeast cells: 1 copy of each gene, 5-10 copies of each specific mRNA species, and 100's – 1000's of molecules of each specific protein per haploid yeast cell. How can the cell cycle function reliably in the face of the large intrinsic molecular fluctuations implied by such numbers (Kar et al., 2009)? We have addressed this question by constructing a realistic model of Cdk regulation in budding yeast (Barik et al., 2010) that is suitable for exact stochastic simulation by Gillepie's algorithm. The results of this model compare favorably to the extensive statistical properties of budding yeast cell cycle progression collected recently in Fred Cross's laboratory (Di Talia et al., 2007; Skotheim et al., 2008; Di Talia et al., 2009).

References: Chen et al. (2004) Mol Biol Cell 15:3841; Di Talia et al. (2007) Nature 448:947; Skotheim et al. (2008) Nature 454:291; Tyson & Novak (2008) Curr Biol 18:R759; Di Talia et al. (2009) PLoS Biology, 7:e1000221; Kar et al. (2009) PNAS 106:6471; Barik et al. (2010) Mol Syst Biol, in press.