304a Genome-Scale Analysis of Translation in S. Cerevisiae: Insights into System Response and Regulation

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The genetic information in the DNA is transcribed to mRNA which is further translated to proteins, which form the building blocks of life. Translation or protein synthesis is thus a central cellular process in every living organism. Translation and its regulation lead to several interesting and important biological phenomena like circadian rhythms and cell cycle oscillations and several common antibiotics work by inhibiting translation. Hence, understanding the protein synthesis machinery from a mechanistic and systems perspective is a very important problem in systems biology. With the recent advances in genomics, microarray technology, and proteomics, it is now possible to measure simultaneously the changes in the levels of every mRNA and protein species in a cell subject to an environmental and/or genetic perturbation. Mathematical modeling and computational studies is the key to the integration and interpretation of quantitative information from such large networks.

We have developed a genome-scale mechanistic model for the translation machinery, which accounts for all the expressed genes in a cell and all the proteins they code for. Such a global model is essential because translation is a competitive process where the mRNAs in the cell compete for other cellular components like ribosomes and transfer RNAs. Utilizing our mathematical framework, we have performed studies on genome-scale translation networks to quantify the effects of parameters and conditions on system behavior. High throughput data from S. cerevisiae has been used to estimate the kinetic parameters of its protein synthesis machinery and provide insights into the regulation of its protein expression. Our results have implications in design of rational protein production systems, wherein quantitative knowledge of responses of protein expression to changes in the cellular environment, can be used to optimize a cellular system towards the production of a protein of interest.