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A Coarse-Grained Biophysical Model of *E. coli* and Its Application to Perturbation of the rRNA Operon Copy Number[1]

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In this work a biophysical model of *Escherichia coli* is presented that predicts growth rate and an effective cellular composition from an effective, coarse-grained representation of its genome. We assume that *E. coli* is in a state of balanced exponential steady-state growth, growing in a temporally and spatially constant environment, rich in resources. We apply this model to a series of past measurements, where the growth rate and rRNA-to-protein ratio have been measured for seven *E. coli* strains with an rRNA operon copy number ranging from one to seven (the wild-type copy number). These experiments show that growth rate markedly decreases for strains with fewer than six copies. Using the model, we were able to reproduce these measurements. We show that the model that best fits these data suggests that the volume fraction of macromolecules inside *E. coli* is not fixed when the rRNA operon copy number is varied. Moreover, the model predicts that increasing the copy number beyond seven results in a cytoplasm densely packed with ribosomes and proteins. Assuming that under such overcrowded conditions prolonged diffusion times tend to weaken binding affinities, the model predicts that growth rate will not increase substantially beyond the wild-type growth rate, as indicated by other experiments. Our model therefore suggests that changing the rRNA operon copy number of wild-type *E. coli* cells growing in a constant rich environment does not substantially increase their growth rate. Other observations regarding strains with an altered rRNA operon copy number, such as nucleoid compaction and the rRNA operon feedback response, appear to be qualitatively consistent with this model. In addition, we discuss possible design principles suggested by the model and propose further experiments to test its validity.

[1] Joint work of the author and Dr. Tsvi Tlusty, Weizmann Institute