

The role of ribosome recycling, diffusion, and mRNA loop formation in translational regulation

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ABSTRACT

The rate of protein production needs to be constantly regulated for all life processes. Genetic expression, protein production, post-translational modification, as well as transport and activation are all processes that can regulate the amount of active protein/enzymes in a cell. Although much recent research has focussed on the biochemical steps regulating the switching of genes and rates of transcription, translational control mechanisms, post-translational processing, and macromolecular transport are also important [2].

Individual protein translation events start at an initiation site upon binding of the appropriate enzymes and cofactors. After elongation and detachment from the mRNA at the termination site, parts of this machinery can diffuse back to the initiation site, especially if it is held nearby (such as in a loop [2, 3]), thereby enhancing overall translation rates. We consider the physical mechanisms and balance the rates of all relevant steps in this scenario for ribosome “recycling.” The diffusion of ribosome parts is treated in the steady state approximation with the initiation and termination sites represented by a sink and a source, respectively. The elongation steps of the attached ribosome along the mRNA is modeled using exact asymptotic results of the asymmetric exclusion process (TASEP) [1]. Since the injection rates of the TASEP depend on the local concentrations at the initiation end, diffusion from the termination end is included to obtain a self-consistent set of equations.

The probability distribution of the distance between the initiation and termination sites is found using simple worm-like and freely jointed chain models with ends that bind to each other. These three ingredients are represented by self-consistent equations that determine which of the density, current, and hence ribosome throughput regimes hold under certain parameter sets. We map the rates of protein production as a function of circularization probability and bulk ribosome concentration.

REFERENCES

- [1] B. Derrida, M. R. Evans, V. Hakim, and V. Pasquier. Exact solution of a 1d asymmetric exclusion model using a matrix formulation. *J. Phys. A*, 26:1493–1517, 1993.

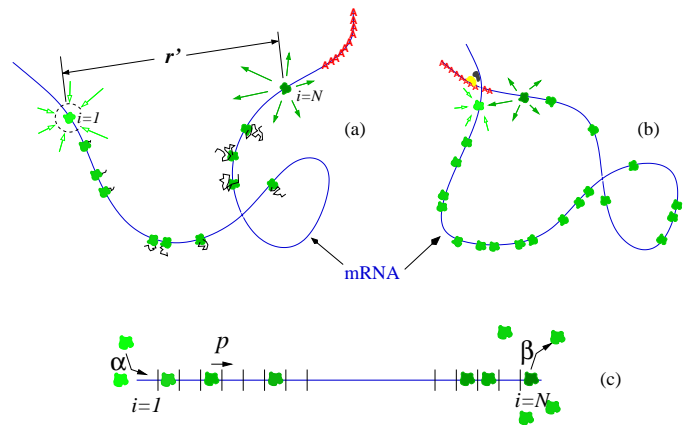


Figure 1: A cartoon of translation in eukaryotes. Many intermediary proteins and cofactors have been neglected. (a) A random mRNA chain loaded with ribosomes (green), in various stages of protein (black) production. Ribosomal components as well as other components such as tRNA exist at a uniform background concentration. The initiation and termination sites are additional sinks (light green) and sources (dark green), respectively, of ribosomes. (b) Binding factors (yellow and dark grey) can increase the probability of loop formation or “circularization,” which brings the poly(A) tail (red) in better proximity to the initiation site. This may enhance ribosome recycling and enhance translation. Protein is not shown here. (c) Schematic of the associated TASEP.

- [2] J. W. B. Hershey, M. B. Mathews, and N. Sonenberg. *Translational Control*. Cold Spring Laboratory Press, Cold Spring Harbor, 1996.
- [3] S. E. Wells, P. E. Hillner, R. D. Vale, and A. B. Sachs. Circularization of mRNA by eukaryotic translation initiation factors. *Molecular Cell*, 2:135–140, 1998.