

# Modeling Ribosome Motion: Fitting Kinetic Rates from Ribo-seq Experiment Using Ballistic Model

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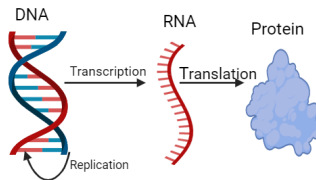
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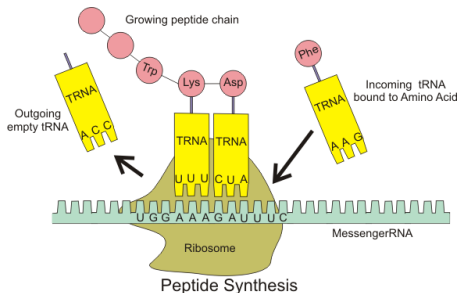


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- 2  $k$ —some density and distribution
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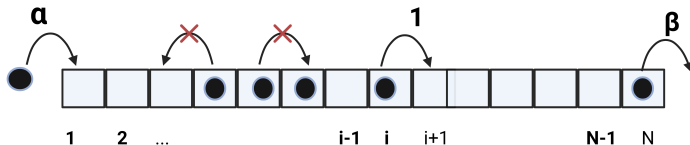
# Genetic Translation



## Central Dogma



# Totally Asymmetric Simple Exclusion

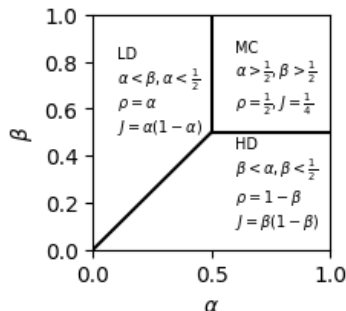


TASEP model

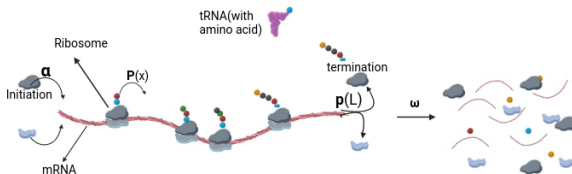
The two major quantities studied in TASEP are density and current expressed as:

$$\rho = \frac{1}{L} \sum_i \rho_i$$

$$J = \rho v = p\rho(1 - \rho) \approx p\rho$$



# Ballistic Model

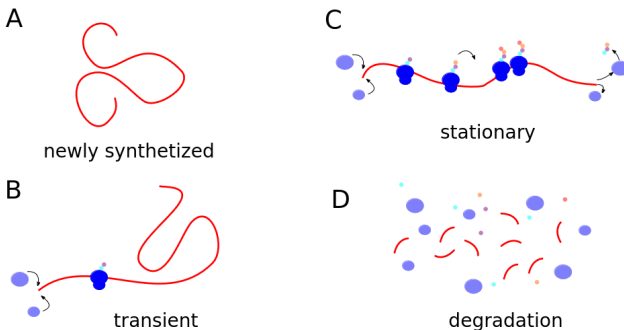


Ballistic model

- Ribosome initiates translation with stochastic rate  $\alpha$ , elongates with deterministic rate  $p(x)$  and terminate the translation with rate  $P(L) = \beta$ , and get degraded with rate  $\omega$
- Low density, neglecting interactions and hence no traffic jam
- 

$$\tilde{\alpha} = \alpha T(L), \quad \tilde{\omega} = \omega T(L), \quad \tilde{p}(x) = p(x) T(L).$$

# Different stages of mRNA

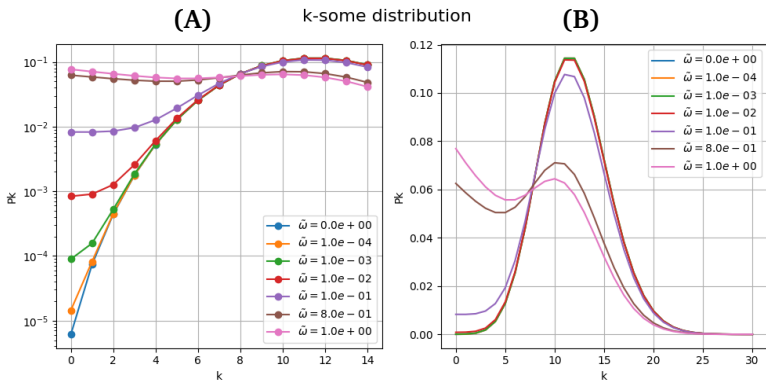


Some possible stages mRNA undergoes from its synthesis to degradation

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# k-some Distribution

$$P_k = \frac{\tilde{\omega}}{\tilde{\alpha} + \tilde{\omega}} \left( \frac{\tilde{\alpha}}{\tilde{\alpha} + \tilde{\omega}} \right)^k \frac{\gamma(k+1, \tilde{\alpha} + \tilde{\omega})}{k!} + \frac{\tilde{\alpha}^k}{k!} e^{-(\tilde{\alpha} + \tilde{\omega})}, \quad (1)$$

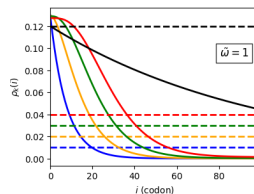
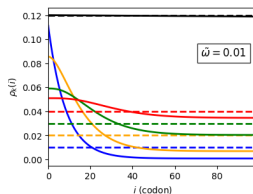
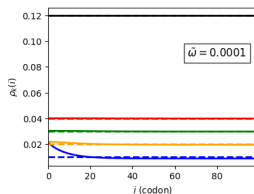


The distribution  $P_k$  for  $\tilde{\omega}$  from 0 to 1, with parameters fixed at  $T(L) = 200$  s,  $L = 100$  codons, and  $\alpha = 0.06 \text{ s}^{-1}$  (A) In the lin-log graph (B) In the lin-lin



# *K*-some Density

$$\rho_k(x) = \frac{\tilde{\alpha}}{P_k P(\tilde{x})} \frac{e^{-(\tilde{\alpha} + \tilde{\omega})}}{(k-1)!} + \frac{\tilde{\omega}}{P_k P(\tilde{x})} \left( \frac{\tilde{\alpha}}{\tilde{\alpha} + \tilde{\omega}} \right)^k \frac{\gamma(k, \tilde{\alpha} + \tilde{\omega}) - \gamma(k, (\tilde{\alpha} + \tilde{\omega})(\tau(x)))}{(k-1)!}$$



Plot of *k*-some densities  $\rho_k$  for  $k = 1$  to  $4$  against the genomic coordinate  $x$  with  $\alpha = 0.06$ ,  $p = 0.5$  and  $L = 100$ . The black curve is for polysome density, and the dashed lines are for infinite lifetime;  $\tilde{\omega} = 0$

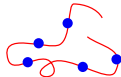
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# Ribo-seq experiment procedure

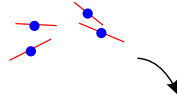
1. Liquid culture



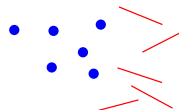
2. Chemical cross-links



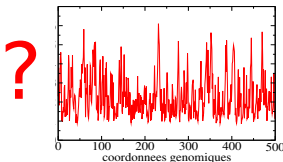
3. Sonication



4. Reverse cross-links of protected fragments

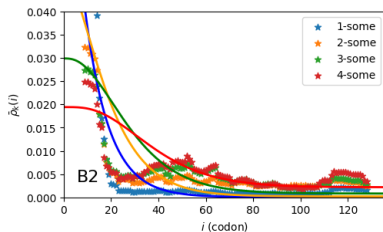
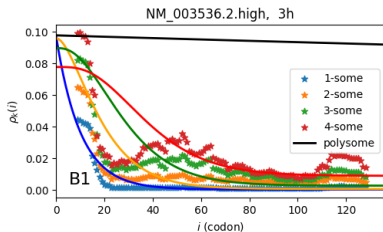
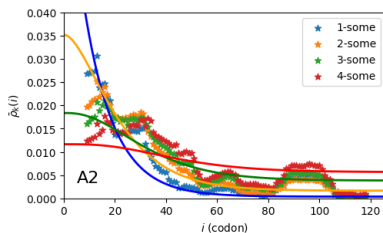
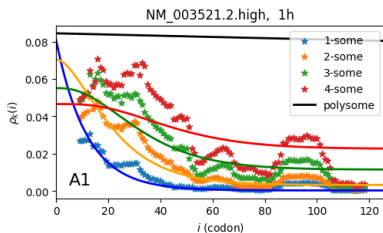


5. sequencing

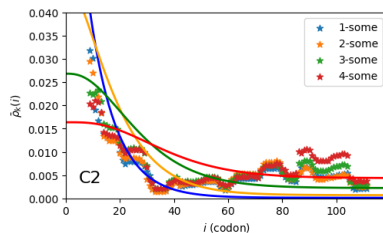
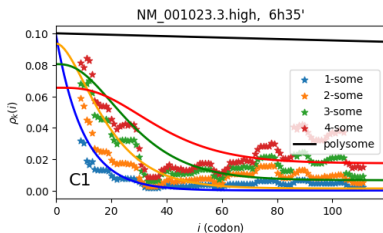


Experimental Observations During Genetic Translation

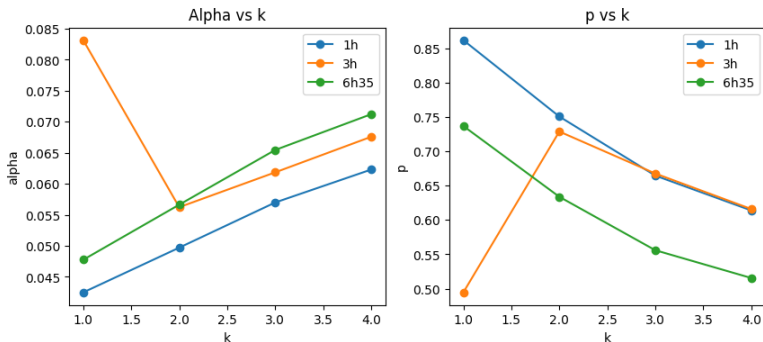
# Experiment vs Ballistic model



# Cont..

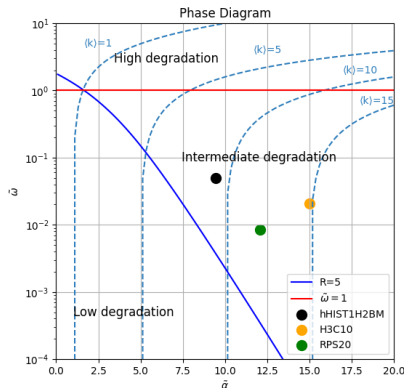


# Fitted Parameters vs $k$



Fitted parameters  $\alpha$  (left) and  $p$  (right) versus  $k$  for three genes: histone gene HIST1H2BM (blue), histone gene H3C10 (orange), and ribosomal protein RPS20 (green)

# Phase Diagram



Phase diagram of the  $(\tilde{\alpha}, \tilde{\omega})$  plane showing the three phases of the ballistic model: low degradation (LD), intermediate degradation (ID), and high degradation (HD) separated by  $\tilde{\omega} = 1 \sim o(1)$  and  $R(0)_1 = 5 \sim o(1)$ . The positions of the analyzed genes HIST1H2BM (black dot), H3C10 (orange), and RPS20 (green) indicate their relevance to the intermediate degradation phase.

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# Conclusion

- The ballistic model is solved analytically, and the  $k$ -some distribution and density profiles are obtained, showing the effect of finite lifetime on  $k$ -some density.
- From the ribo-seq data, the kinetic parameters  $\alpha$  and  $p$  are fitted, and the variation with  $k$  - the number of ribosomes - is visualized.

**Thank You for Your  
Attention!**