Modeling Ribosome Motion During Genetic Translation

Habibu AHMAD

Tutor: **Andrea PARMEGGIANI**
Mentor: *Jean-Charles WALTER*

Universite De Montpellier

30/01/2024

Genetic Translation

1. Gene expression is vital for protein synthesis, influencing cellular functions and organism development.
2. The three steps of central dogma are:Replication, Transcription and Translation.
3. Three steps of Translation are: Initiation, elongation and termination Blythe and Evans (2007)

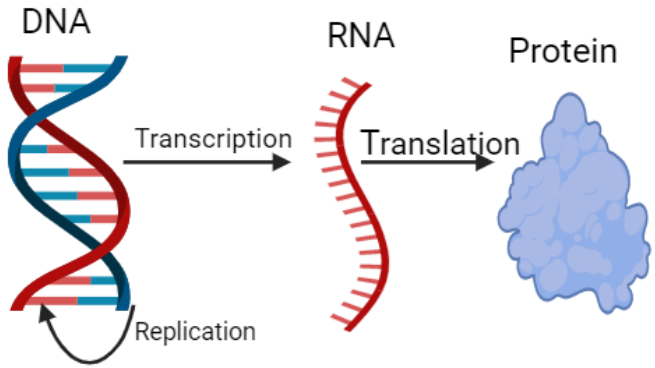

Figure 1: Central Dogma

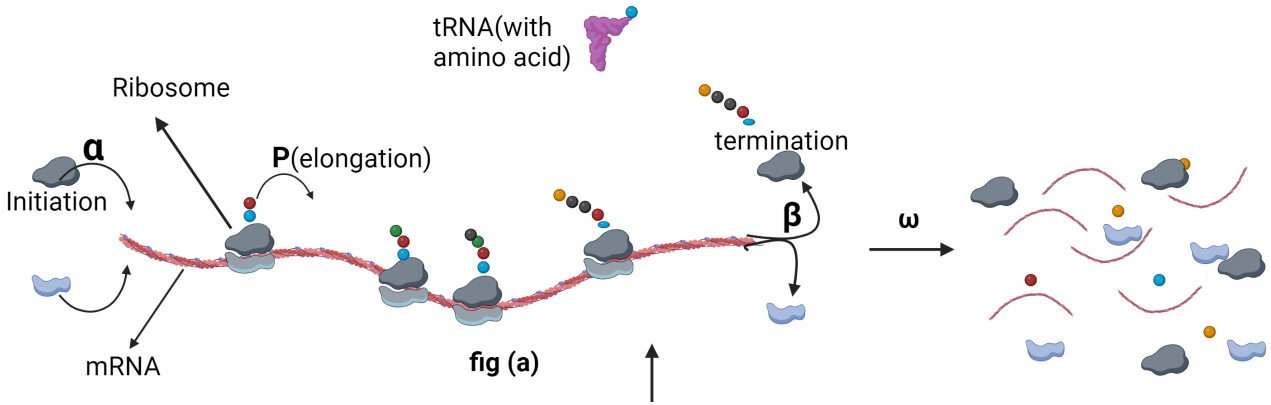

Figure 2: Translation Process

Model Description/Physical transport

A frequently employed model within the category of self-driven diffusive systems is the totally asymmetric simple exclusion process (TASEP) MacDonald et al. (1968)

- Particle enters(exits) the lattice with rate $\alpha(\beta)$
- The particle hops to the nearest empty site on the right with a unit rate
- Obeys hard-core exclusion process

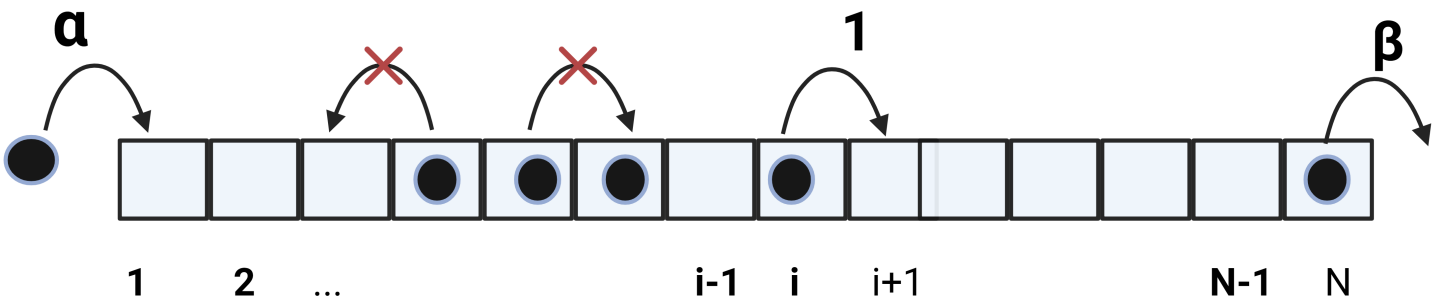

Figure 3: Schematic TASEP Model with open boundary

Master Equation

Let the state of each site for the discrete lattice be denoted by a particle occupation number n_i where each n_i is a binary variable defined as

$$n_i = \begin{cases} 1 & \text{if site } i \text{ is occupied by a particle} \\ 0 & \text{if site } i \text{ is empty} \end{cases} \tag{1}$$

For the two sites system, we can have the following configuration:

And the master equation is given:

$$\frac{dP(C,t)}{dt} = \sum_{C' \neq C} \underbrace{[W_{C' \to C} P(C',t)]}_{\text{Gain}} - \underbrace{W_{C \to C'} P(C,t)}_{\text{Loss}} \tag{2}$$

$$\frac{d\langle n_i \rangle}{dt} = \begin{cases} \alpha\langle 1 - n_1 \rangle - \langle n_1(1-n_2)\rangle = J_{enter} - J_{1,2} & \text{for } i = 1 \\ \langle n_{i-1}(1-n_i)\rangle - \langle n_i(1-n_{i+1})\rangle = J_{i-1,i} - J_{i,i+1} & \text{For } 1 < i < N \\ \langle n_{N-1}(1-n_N)\rangle - \beta\langle n_N\rangle = J_{N-1,N} - J_{exit} & \text{for } i = N \end{cases} \tag{3}$$

Mean-field approximation

The mean-field approximation ignores the two side correlation, that is,

$$\langle n_i n_j \rangle = \langle n_i \rangle \langle n_j \rangle \text{ where } \langle n_i \rangle = \rho_i \tag{4}$$

And the mean-field equations are:

$$\frac{d\rho_i}{dt} = \begin{cases} \alpha(1-\rho_1) - \rho_1(1-\rho_2) & \text{for } i = 1 \\ \rho_{i-1}(1-\rho_i) - \rho_i(1-\rho_{i+1}) & \text{for } i = 2, 3, \ldots, N-1 \\ \rho_{N-1}(1-\rho_N) - \beta\rho_N & \text{for } i = N \end{cases} \tag{5}$$

taking a continuum limit of the above equations and rescaling time as $t = t/L$, lattice constant $\epsilon = 1/L$, and expanding to the second order, where $x = \frac{i}{N}, 0 < x \leq 1$, we obtained

$$\frac{\partial \rho}{\partial t} = -\frac{\partial}{\partial x}\left(\rho(1-\rho) - \frac{\epsilon}{2}\frac{\partial \rho}{\partial x}\right). \tag{6}$$

And, in the thermodynamic limit, $L \to \infty$ of $(\epsilon \to 0)$, eqn (6)

$$\frac{\partial \rho}{\partial t} + \frac{\partial J}{\partial \rho} = 0 \text{ where } J(\rho) = \rho(1-\rho) \tag{7}$$

The continuity equation above was solved using hydrodynamic

Monte Carlo Simulation

Monte carlo simulation was performed using Random Sequential Update rule which is based on the following dynamicsRubinstein and Kroese (2016)

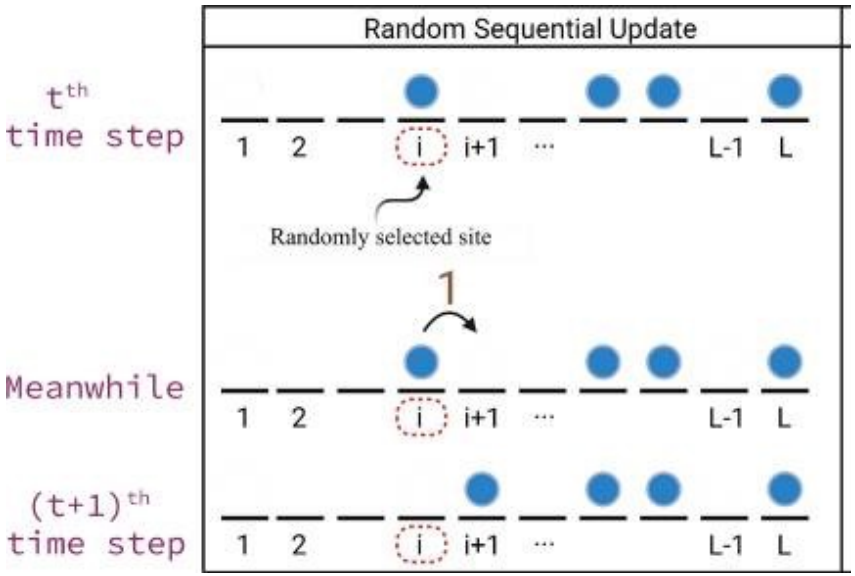

Figure 4: Random sequential update rule

- The simulations are carried out for $L \times 10^5$ time steps and the first 5 percent of the observations are ignored to establish the existence of the stationary state.

Result

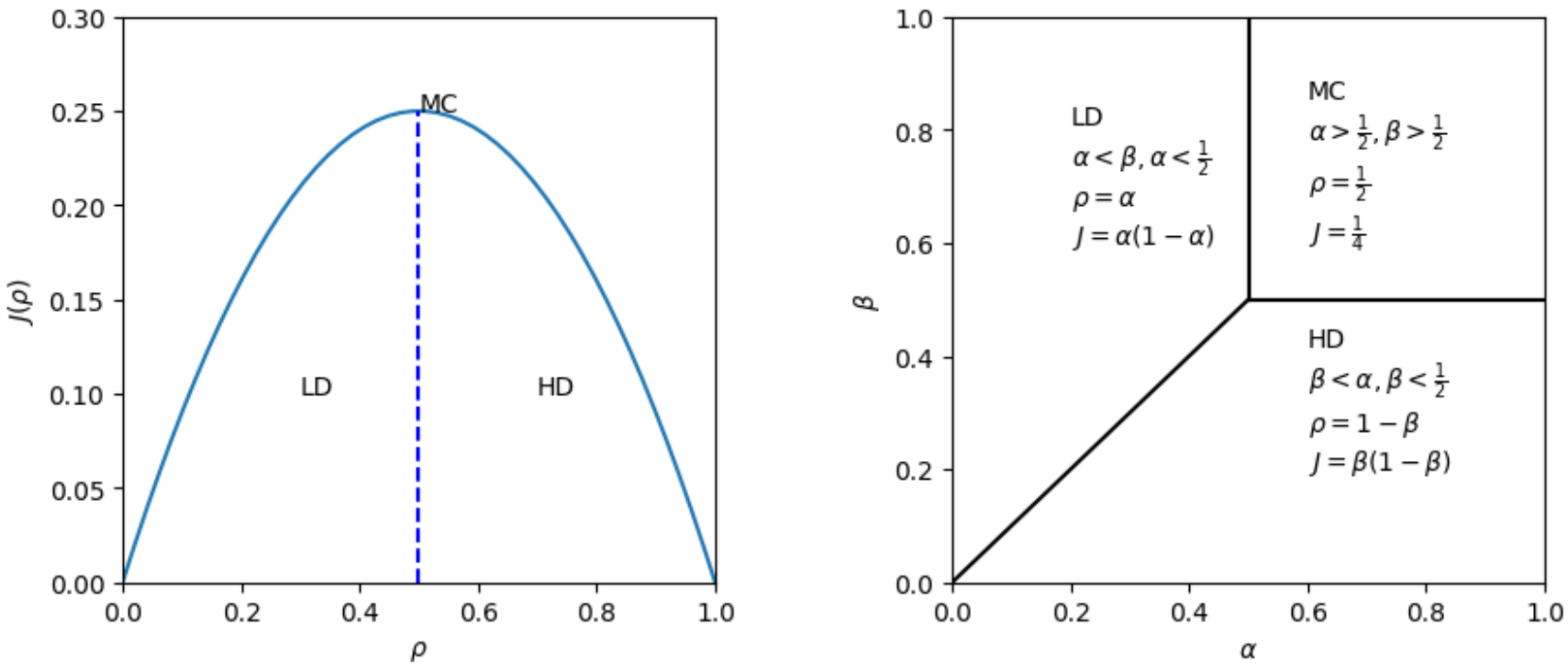

Figure 5: The first figure is a fundamental diagram which gives the current-density relation $J(\rho) = \rho(1 - \rho)$ and the second one is Phase diagram for TASEP with open boundary conditions comprises three distinct phases: LD, HD, and MC

Profile Density

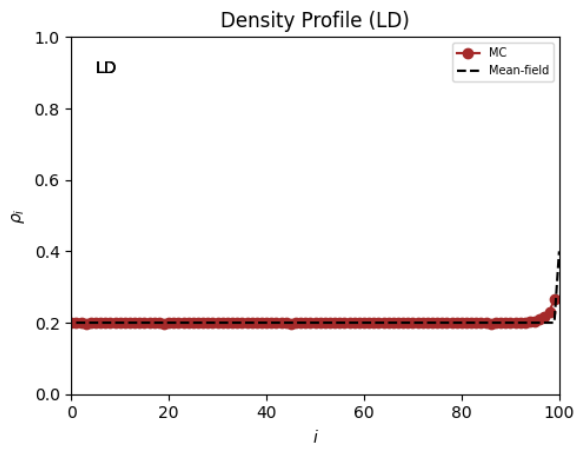

Figure 6: $\alpha = 0.2, \beta = 0.6$

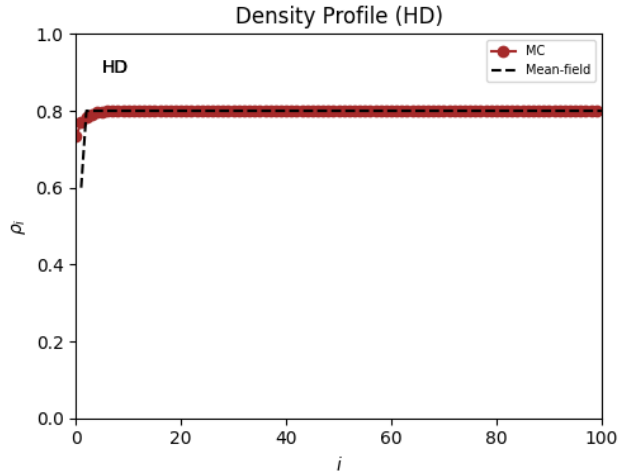

Figure 8: $\alpha = 0.6, \beta = 0.2$

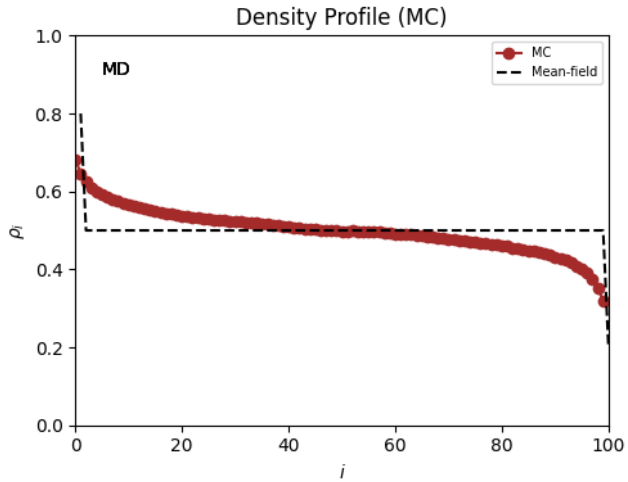

Figure 7: $\alpha = 0.75, \beta = 0.8$

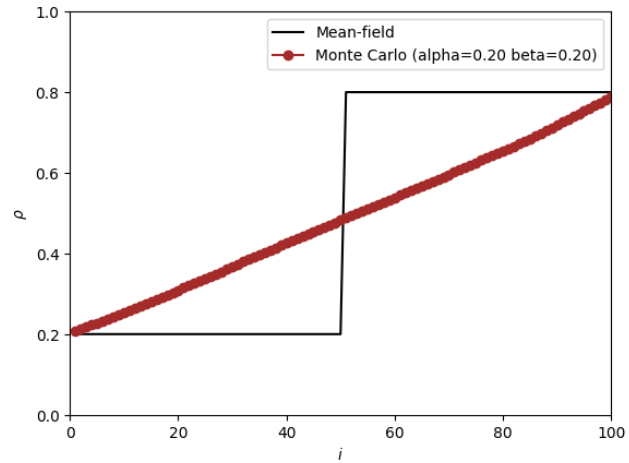

Figure 9: $\alpha = \beta = 0.2$

Conclusion

In this project, the steady states and ribosomal profile densities are analysed using mean-field approximation and then compared with monte-carlo simulation. In this semester, we will generalize the TASEP model and put into account degradation rate. we will also compare our theoretical prediction with ribosome profiling experiment.

References

Blythe, R. A. and Evans, M. R. (2007). Nonequilibrium steady states of matrix-product form: a solver's guide. *Journal of Physics A: Mathematical and Theoretical*, 40(46):R333–R441.

MacDonald, C. T., Gibbs, J. H., and Pipkin, A. C. (1968). Kinetics of biopolymerization on nucleic acid templates. *Biopolymers: Original Research on Biomolecules*, 6(1):1–25.

Rubinstein, R. Y. and Kroese, D. P. (2016). *Simulation and the Monte Carlo method*. John Wiley & Sons.

Thanks!