KMC Project Notes

by Carlos Alas and Trinh Lan Hoa

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I. Problem Description

Here we present a description of the problem, along with the given variables, the master equation, and the transition rates W for our KMC simulations. We follow the notation of reference [1], with simplifications made to deal with only one nanodomain rather than several.

We will look at the phenomenon of monomer emerin proteins freely diffusing through an inhomogenous nuclear membrane surface with spacial varying diffusion rates. Our system will consist of $M = 1600$ total monomer emerin proteins. We wish to track the trajectories of the emerin proteins. The motion of the emerin proteins is governed by diffusion through the membrane lipids. Within the nanodomain, the diffusion coefficient is about an order of magnitude slower ($D_{in} = 250$ nm^2/s) than that outside of it ($D_{out} = 3500$ nm^2/s); the diffusion rate is slower in the nanodomain due to the clustering of emerin proteins there.

We will use a nanodomain in the shape of a square and of area $A_{in} = 12100$ nm^2. The domain of our calculations will be a square patch of area $A = 160000$ nm^2, within which the nanodomain of monomers is contained. Therefore the area outside the nanodomain is $A_{out} = A - A_{in}$. The domain patch will be split into $K = 1600$ uniform lattice square cells with side length $a = 10$ nm, since $a^2 = A/K = 100$ nm. At lattice cell i, for $0 \leq i \leq K-1$, there are N_i emerin proteins. On the four sides of our domain patch, we will enforce periodic boundary conditions, so

$$\sum_{i=0}^{K-1} N_i = M \tag{1}$$

at all times.

We will start the simulations with a uniform distribution of monomers on the domain patch, so $N_0 = N_1 = ... = N_i = ... = N_{K-2} = N_{K-1} = M/K = 1$ at $t = 0$. We will model the monomer protein trajectories as a series of hops as they diffuse through the media. Using a subvolume KMC method described in the reference paper [2], we will simulate, by use of a priority queue (binary min heap), one monomer emerin protein hop at a time. A monomer emerin protein can hop up, down, left, or right to a neighboring lattice cell at each hop. We use a K by 4 array nn to store the nearest neighbors of each lattice cell i in $0 \leq i \leq K-1$, where the 1st column stores the neighbor index above and the remaining neighbors are stored in clockwise order, so up, right, down, and then left, for $j = 0, 1, 2, 3$, respectively. If a protein is inside the nanodomain, the time it must wait to hop is $\tau_{in} = a^2/D_{in}$. Outside the nanodomain, it must wait, to hop, a time $\tau_{out} = a^2/D_{out}$; the hopping rate is slower in the nanodomain due to the clustering of emerin proteins there.

Since we are looking at diffusion in an inhomogenous media, we will reference the paper [1] for the general form of the master equation and transition rates W. In this paper, the notation $\boldsymbol{N} = \{N_i\}$ and $\boldsymbol{m} = \{m_i\}$ represent the state of the system at a time t by its spacial distribution of monomer emerin proteins and the random incremental changes to the spacial distribution due to hopping at each site m_i, respectively. Since we simulate only one emerin protein hopping per iteration, m_i is -1 for a hop out of site i and m_j is $+1$ for the sit j it hops into.

For the kinetic Monte Carlo simulations we require the master equation,

$$\frac{dP}{dt} = \sum_{\boldsymbol{m}} [W(\boldsymbol{N} - \boldsymbol{m}; \boldsymbol{m}) P(\boldsymbol{N} - \boldsymbol{m}, t) - W(\boldsymbol{N}; \boldsymbol{m}) P(\boldsymbol{N}, t)] \tag{2}$$

where $P(\boldsymbol{N}, t)$ is the probability that system is in state $\boldsymbol{N}$ function, where the transition rate

$$W(\boldsymbol{N}; \boldsymbol{m}) = \frac{1}{4} \sum_{i=1}^{K} \frac{N_i}{\tau_i} \delta(m_i + 1) \sum_{jnnofi}^{4} \delta(m_j - 1) \prod_{k \neq i,j}^{K-2} \delta(m_k), \tag{3}$$

and j nn of i are of the four neighboring lattice sites at lattice site i. The first summation over i only gives the term for the protein hopping out, and then the summation over j that remains only the term for where the protein hops into. The product series evaluates to 1 always since $m_k = 0$ for $k \neq i, j$. Note that in the subvolume reference paper [2] they use s in place of W as their notation. So $W_i = (1/4)N_i/\tau_i$.

For the simple case of free diffusion, the master equation can be solved analytically to give the distribution of proteins inside the nanodomain ρ in the systems steady state as

$$\rho = \frac{\tau_{in}}{\tau_{in} + \tau_{out}}. \tag{4}$$

If we plug in the values of the hopping times we use in our simulations, we find that the fraction of proteins in the nanodomain at the systems steady state is $\rho \approx 53\%$.

II. Subvolume KMC method

The subvolume KMC method allows only one protein to hop at a time. The transition rates are assigned respecting the diffustion rates inside the nanodomain and outside of it. We begin with a uniform distribution. We assign the hopping events in lattice cells event times and sort them with a min binary heap. We begin the simulation by having the protein in the lattice cell of the event time at the top of the min binary heap hop randomly to one of its neighbors. We then update the transition rates of the lattice cell from which the protein hops out of and in the lattice cell it hops into. Then we assign new subsequent event times to both of these lattice cell and re-sort the min binary heap. We do this over and over again until the simulated time reaching a little over 4 hours.

III. Results

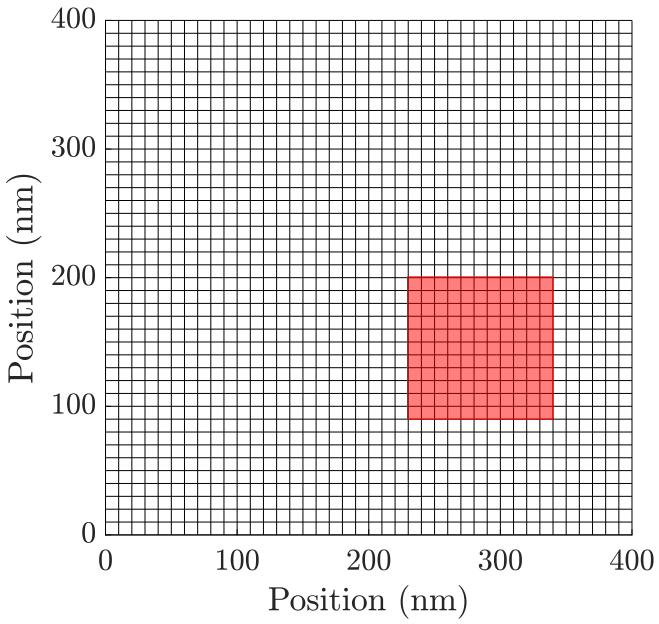

Figure 1. We ran the subvolume KMC method of reference paper [2] using the parameters discussed in the main text of these notes above. Here we show the lattice decomposition in our system domain. The red shaded area is the nanodomain area.

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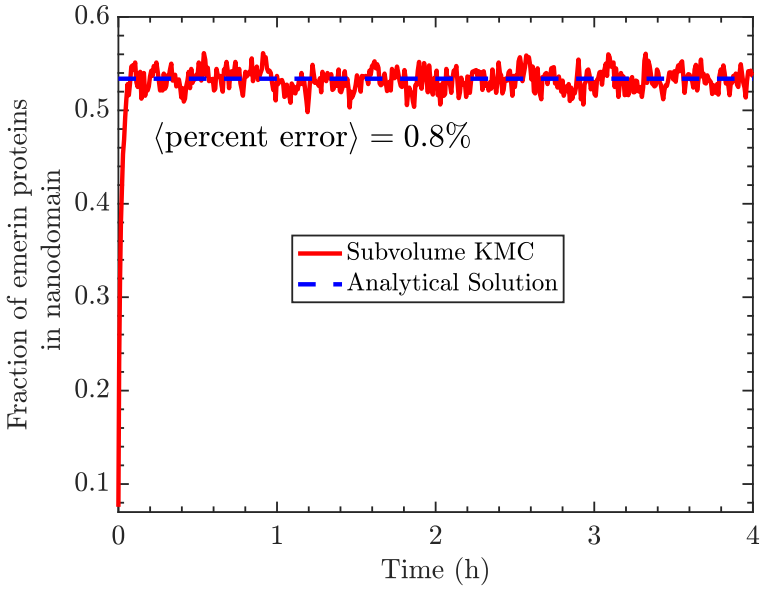

Figure 2. We ran the subvolume KMC method of reference paper [2] using the parameters discussed in the main text of these notes above. The red line is the KMC simulation of the concentration of monomoer emerin proteins in the nanodomain. The blue dashed line is the analytical solution of eqn. (4). The average percent error of the KMC simulation from the analytical solution throughout the entire run is about 0.8%

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Bibliography

[1] Yiwei Li, Osman Kahraman, and Christoph A. Haselwandter. Distribution of randomly diffusing particles in inhomogeneous media. *Physical Review E*, 96(3), Sep 2017.

[2] Johan Elf, Andreas Doncic, and Mans Ehrenberg. Mesoscopic reaction-diffusion in intracellular signaling. In Sergey M. Bezrukov, Hans Frauenfelder, and Frank Moss, editors, *Fluctuations and Noise in Biological, Biophysical, and Biomedical Systems*. SPIE, May 2003.