THE CITY UNIVERSITY OF NEW YORK

Computational Modeling of Intracellular Transport

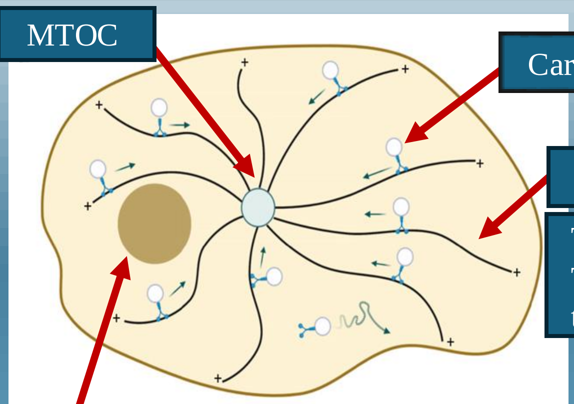
Kevin Bedoya, Department of Computer Science, Dr. Oleg Kogan, Department of Physics

The Department of COMPUTER SCIENCE
Queens College
City University of New York

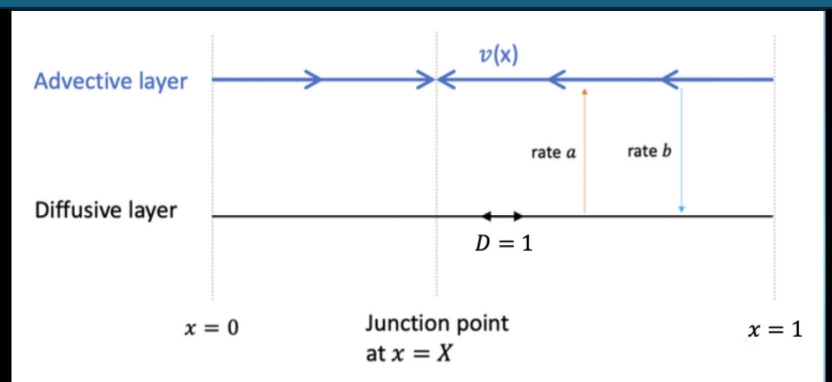
Background

Cells transport cargo using two methods: (i) By diffusion in the cytoplasm and (ii) by carrying it with molecular motor proteins along cytoskeletal filaments. Stiff filaments called microtubules (MT) form one component of the cytoskeleton. A common MT morphology involves multiple MTs converging together at a "microtubule organizing center" or MTOC.

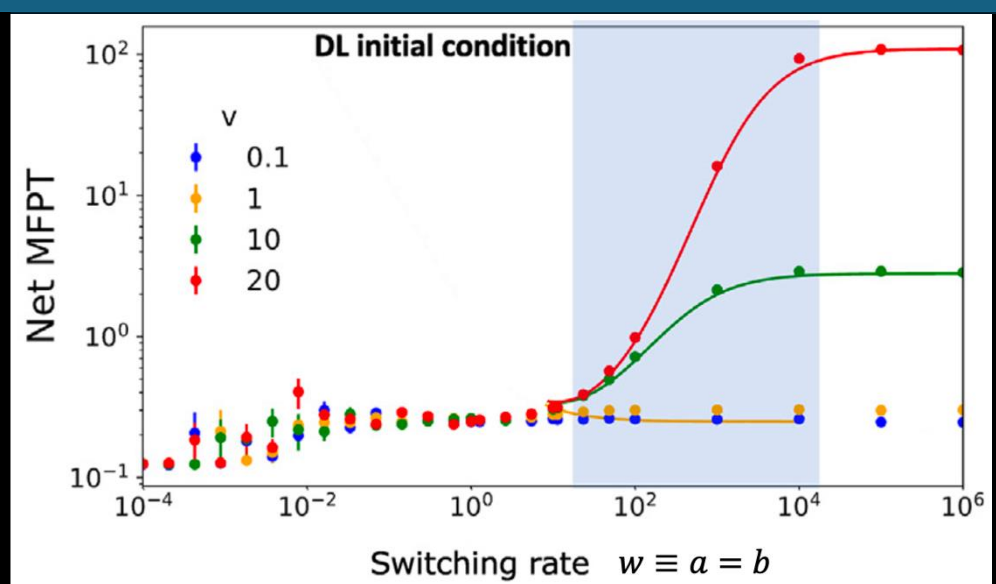
Here's a cartoon of a typical organization of a cell.



Recently one us studied a one-dimensional model. It included two layers: the advective layer (AL) that represents MTs and the diffusive layer(DL) that represents the cytoplasm.



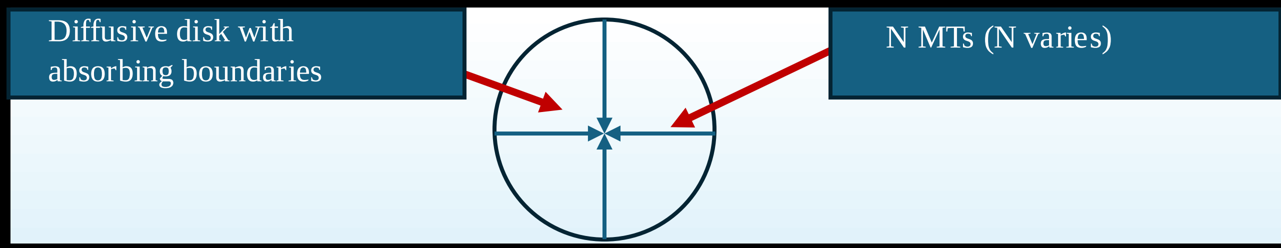
This model predicts the evolution of the probability to find cargo-motor complex in each layer, starting with some initial location. It also computes the mean first passage time MFPT – a time to exit through the membrane as a function of parameters.



This model predicted a dramatic rise in the MFPT in a window of interlayer switching rates. This rise takes place over the range of w that matches in-vivo values. From Biophysical Reports 4(3), 100171 (2024).

Question: Will these results hold in a 2-D model? (A more realistic model in most situations)

Two-Dimensional Model



The probability densities in the diffusive layer $\boldsymbol{\phi(r,\theta,t)}$ and one each MT $\rho(r,t)$ evolve according to the following equations:

$$\frac{\partial \phi}{\partial t} = \nabla^2 \phi + a\rho_i - b\phi$$

$$\frac{\partial \rho_i}{\partial t} = \vec{v} \cdot \vec{\nabla} \rho_i - a\rho_i + b\phi$$

Here the diffusion coefficient has a value 1 due to a change in units. Additionally, the radius of the disk is also 1 in our units. Also, $i = 1, 2, \dots N$.

We implement these equations numerically by discretizing the disk into a circular grid.

Numerical implementaton

Figure 1

Figure 1

The following figure is an example of how our discretized space is modeled in our computational analysis. Note, we choose the number of rings (3) and the number of rays (8) arbitrarily for the sake of demonstration. Furthermore, green dots across the space denote positions of particle density indexed by (m,n): m=some patch(s) across a radius, and n= an angle on the patch. Also, particle densities across the last ring are all set to zero to conform to the absorbing boundary condition.

Figure 2

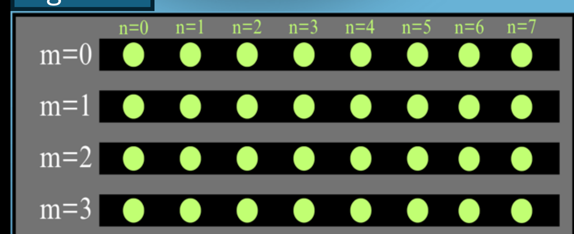


Figure 2

We translate points indexed by (m,n) from our model into a table of particle densities, formally referred to as an *array* within our code. The density in the central patch is stored separately (not shown).

Figure 3 (In general, N MTs are laid along some of the rays)

MTs (in green) are laid over some angles, collectively forming the AL in our discretized model. MTs extend from the first ring until the absorbing boundary (last ring). Each MT is divided into the same number of segments as the number of rings (here, 3). ρ, represents the density in MTs, which is different from the density in the DL (green dots) represented by ϕ.

Due to the placement of the initial particle density (at the center of the model), there is an outflow of density from the center at the DL. Conversely at the AL, particle density is re-channelled toward the center. (As shown by the arrows in figure 3)

Figure 3

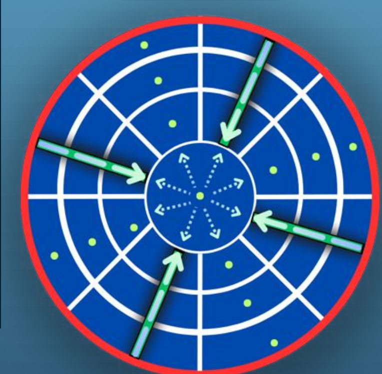


Figure 4

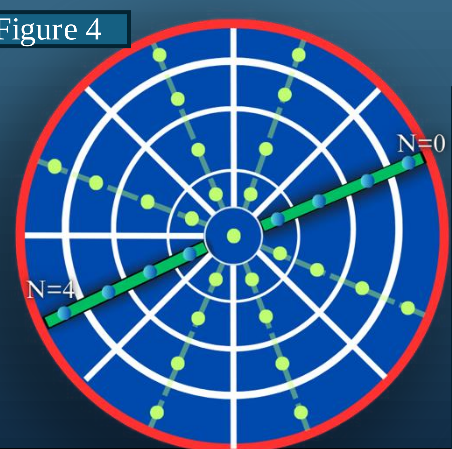


Figure 4

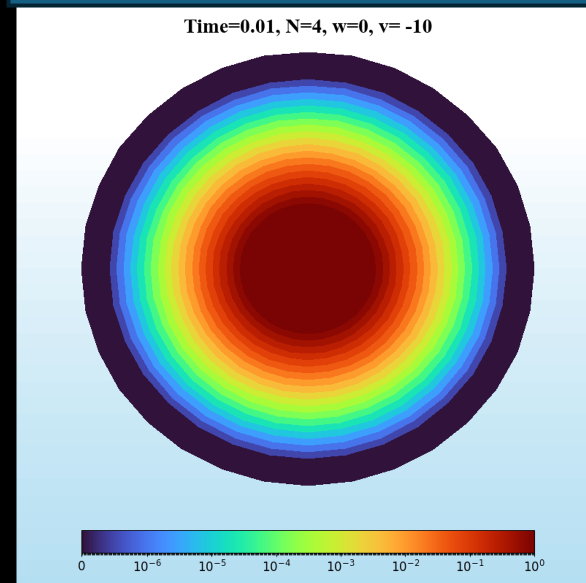
(Our parameters are chosen arbitrarily for demonstration)

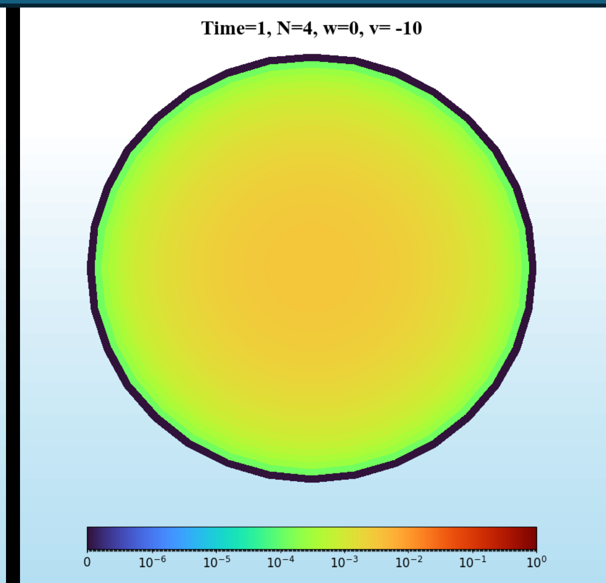
Microtubule positions are specified by an angle denoted by n. In the figure there are two, N=0 and N=4.

The points labeled (in blue) across MTs (green rectangles) represent positions of particle density at the AL, which are located at the same radii as particle positions at the DL.

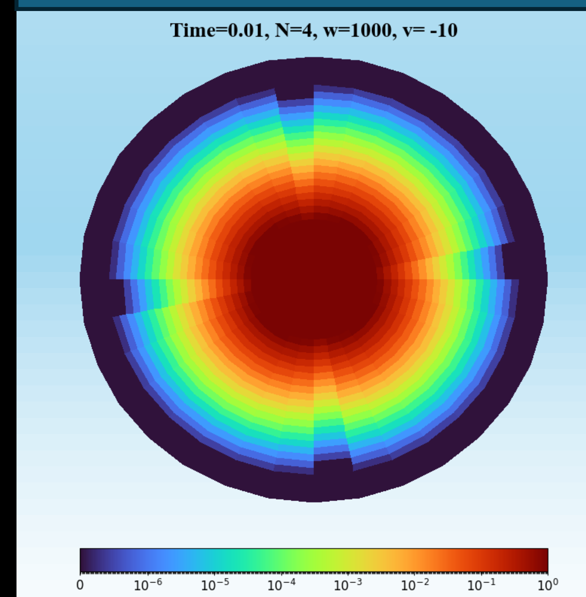
Results

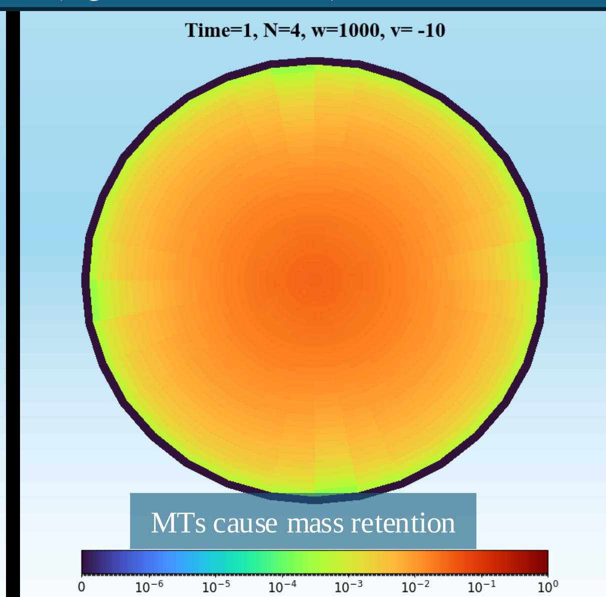
The initial density was $\phi = \frac{1}{\pi \Delta r^2}$ in the center of the DL and 0 everywhere else. Also, $\rho = 0$ everywhere. The parameters are: v = speed of the motors on the MT, N = number of MTs, w = rate of switching between layers (w=a=b). When w = 0, we get just diffusive spread. The following "heat maps" present diffusive particle density at the DL.



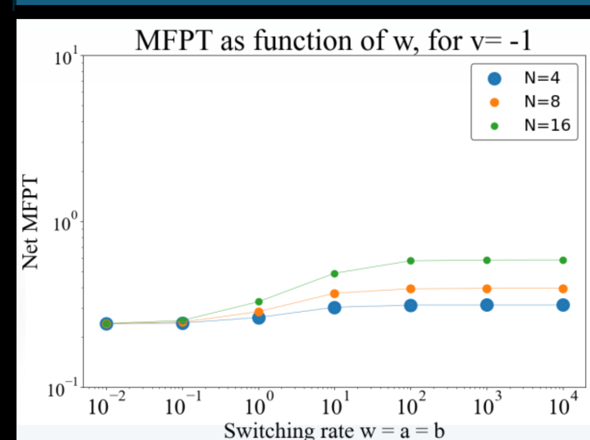


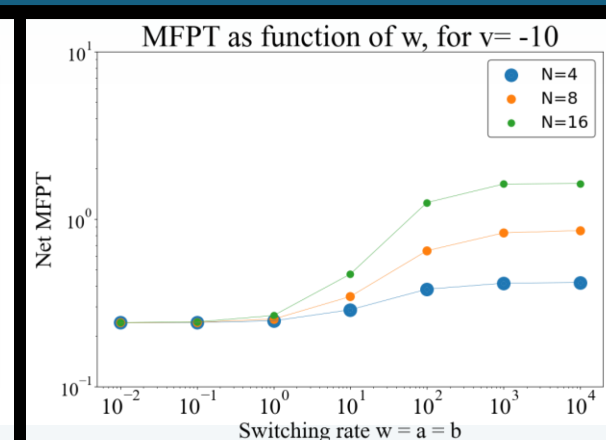
We now show results for non-zero w. (Again within the DL)





(Preliminary Results on MFPT in 2D) **lines on the plots are only for visual guidance**





Conclusion: It appears that the qualitative features of 1-D results are preserved. Moreover, the crossover from low to high plateaus also takes place over a similar range of *w*s. However, the magnitude of the increaase of MFPT at larger *w* depends on the number of MTs. The quantitative dependence of the rise in MFPT on N is yet to be investigated.

We acknowledge the SURP program at Queens College for their support.

Scan the QR code to view the source code developed in this study. (Documentation supplied as well)

GitHub