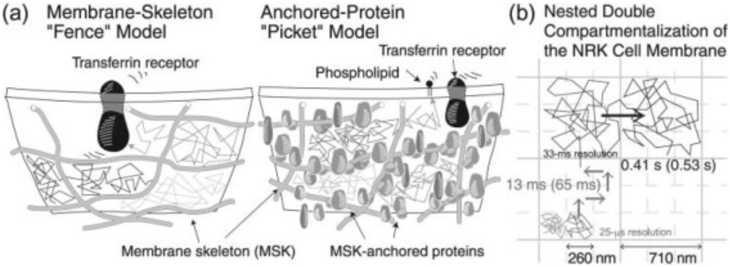
Diffusion through semi-permeable membranes

Aiyan B.

November 26, 2025

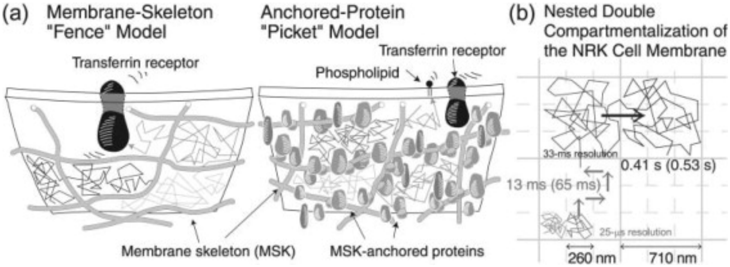
A finer picture of the fence model

- The fence model[1] proposes that the membrane-skeleton (MS) forms "fences" which restrict the motion of transmembrane proteins (TMP) through the plasma membrane (PM)



A finer picture of the fence model

- The fence model[1] proposes that the membrane-skeleton (MS) forms "fences" which restrict the motion of transmembrane proteins (TMP) through the plasma membrane (PM)



- There is no currently microscopic model for how this hop-diffusion occurs: can we build one?

Shortcomings of current models

- MS is a rather non-trivial structure, far from this naive square fence perspective

Shortcomings of current models

- MS is a rather non-trivial structure, far from this naive square fence perspective
- No clear picture as to why long-time high-density regions/ "hot-spots" exist

Shortcomings of current models

- MS is a rather non-trivial structure, far from this naive square fence perspective
- No clear picture as to why long-time high-density regions/ "hot-spots" exist

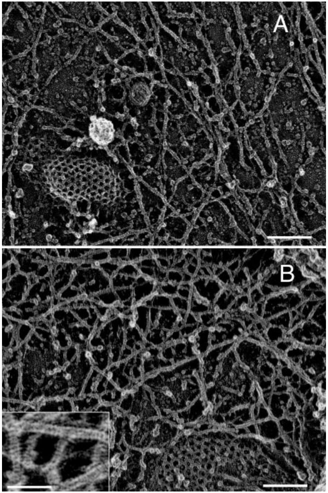


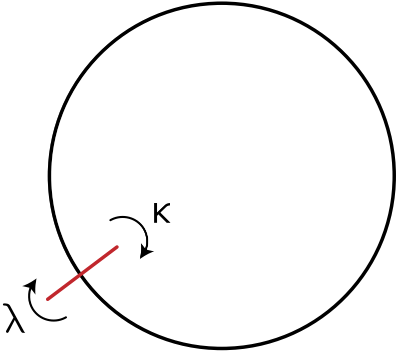
Figure: Taken from Morone et al. (2006)[2]

Diffusion through a semi-permeable membrane

- Consider a particle diffusing on a loop $\mathbb{R} \bmod 2\pi$

Diffusion through a semi-permeable membrane

- Consider a particle diffusing on a loop $\mathbb{R} \bmod 2\pi$
- At some point, there is a highly localized directional and semi-permeable membrane which alters the diffusive nature. In particular, allow crossing from the left with probability $0 \leq \lambda \leq 1$ and from the right with probability $0 \leq \kappa \leq 1$



The master equation

- Suppose the membrane occurs at $M \equiv M \bmod N$, where there are N elements on the lattice. The (discrete) master equation for the system reads

$$\frac{\partial p_j(t)}{\partial t} = \frac{1}{\tau}\left[\frac{1}{2}p_{j+1}(t) + \frac{1}{2}p_{j-1}(t) - p_j(t)\right] + \frac{\Delta_\lambda}{\tau}p_M(t)\left(\delta_{M-1,j} - \delta_{M+1,j}\right) + \frac{\Delta_\kappa}{\tau}p_{M+1}(t)\left(\delta_{M+2,j} - \delta_{M,j}\right),$$

where $\Delta_s = \frac{1}{2} - s$ with temporal step size τ

  - If $\lambda = \kappa = 1/2$, $\Delta_\lambda = \Delta_\kappa = 0$ and we recover the random walk

The continuum equation of motion I

- Allow $x_j = ja_0$ for lattice spacing a_0 and take the limit $\tau, a_0 \to 0$
- Dividing the first term by a_0^2 and letting $D = a_0^2/2\tau$ remain fixed in the limit, we find

$$\frac{\partial p(x,t)}{\partial t} = \mathcal{L}(x; x_b) p(x,t), \tag{1}$$

where the generator, to linear order in a_0 is

$$\mathcal{L}(x; x_b) = D\frac{\partial^2}{\partial x^2} + 4D\delta'(x - x_b)\left(\kappa - \lambda - \Delta_\kappa a_0 \left.\frac{\partial}{\partial x}\right|_{x=x_b}\right) \tag{2}$$

The continuum equation of motion I

- Allow $x_j = ja_0$ for lattice spacing a_0 and take the limit $\tau, a_0 \to 0$
- Dividing the first term by a_0^2 and letting $D = a_0^2/2\tau$ remain fixed in the limit, we find

$$\frac{\partial p(x,t)}{\partial t} = \mathcal{L}(x;x_b)p(x,t), \tag{1}$$

where the generator, to linear order in a_0 is

$$\mathcal{L}(x;x_b) = D\frac{\partial^2}{\partial x^2} + 4D\delta'(x-x_b)\left(\kappa - \lambda - \Delta_\kappa a_0 \left.\frac{\partial}{\partial x}\right|_{x=x_b}\right) \tag{2}$$

  - This is a generalization for $\lambda \neq \kappa$ of the continuum limit presented in Kay, T. & Giuggioli, L. (2022)[3]

The continuum equation of motion II

- Define $J(x,t) = -D\partial_x p(x,t)$ as the probability current and let $\Delta_\kappa a_0/\tau \to k$ such that the action of the generator is

$$D\frac{\partial^2 p}{\partial x^2} + 4D\left(\kappa - \lambda\right)\delta'(x - x_b)p + \frac{4\Delta_\kappa^2 D}{k} J(x,t)\delta'(x - x_b) \quad (3)$$

The continuum equation of motion II

- Define $J(x,t) = -D\partial_x p(x,t)$ as the probability current and let $\Delta_\kappa a_0/\tau \to k$ such that the action of the generator is

$$D\frac{\partial^2 p}{\partial x^2} + 4D\left(\kappa - \lambda\right)\delta'(x - x_b)p + \frac{4\Delta_\kappa^2 D}{k} J(x,t)\delta'(x - x_b) \quad (3)$$

- We can interpret these terms as follows – using that the derivative of the Dirac delta acts as $\delta'[\psi] = -\psi'(0)$ –
  1. regular diffusion generator;
  2. local drift due to the directional motion at the barrier;
  3. local drift due to flux generation at barrier

Generalizations

- The generalization to d spatial dimensions is trivial: define a surface $\Gamma \subset \mathbb{R}^d$ along which there is a barrier and modify $\partial_x^2 \to \nabla^2$ such that, for $t \to \tau = Dt$,

$$(\mathcal{L}p)(\mathbf{x}; \mathbf{x}_b) = \nabla^2 p + \delta'(\mathbf{x} - \Gamma)\left[ap + bJ(\mathbf{x}, \tau)\right] = \mathcal{L}_0 p + \mathcal{L}' p, \quad (4)$$

where I have defined $a = 4(\kappa - \lambda)$ and $b = \frac{4\Delta_\kappa^2}{k}$

Generalizations

- The generalization to d spatial dimensions is trivial: define a surface $\Gamma \subset \mathbb{R}^d$ along which there is a barrier and modify $\partial_x^2 \to \nabla^2$ such that, for $t \to \tau = Dt$,

$$(\mathcal{L}p)(\mathbf{x};\mathbf{x}_b) = \nabla^2 p + \delta'(\mathbf{x} - \Gamma)\left[ap + bJ(\mathbf{x},\tau)\right] = \mathcal{L}_0 p + \mathcal{L}' p, \quad (4)$$

where I have defined $a = 4(\kappa - \lambda)$ and $b = \frac{4\Delta_\kappa^2}{k}$

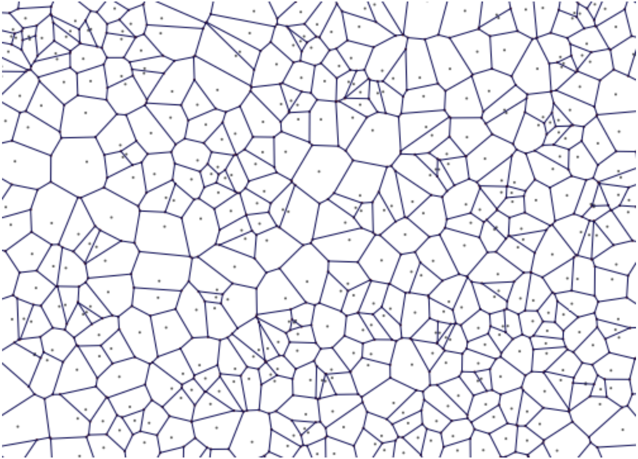
- Also straightforward to generalize Eq. (4) to multiple surfaces/ points by performing a sum over all individual surfaces,

$$(\mathcal{L}p)(x;x_b) = \mathcal{L}_0 + \sum_i \delta'(\mathbf{x} - \Gamma_i)\left[ap + bJ(x,\tau)\right], \quad (5)$$

where Γ_i is the ith semi-permeable barrier

A note on a potential path forward

- Apparent “random” structure of the skeleton suggests it might be useful to define surfaces as the edges of random tessellations



A Green's function solution I

- The non-interacting Green's function solves the problem $(\partial_t - \mathcal{L}_0)G^{(0)} = \delta(\mathbf{x}, \tau)$ and is clearly the heat kernel,

$$G^{(0)}(\mathbf{x}, \tau|\mathbf{x}') = \frac{1}{(4\pi\tau)^{d/2}}\Theta(\tau)\exp\left(-\frac{|\mathbf{x} - \mathbf{x}'|^2}{4\tau}\right) \tag{6}$$

or, more simply, in energy-momentum space,

$$G^{(0)}(\mathbf{k}, \omega) = (i\omega - k^2)^{-1} \tag{7}$$

A Green's function solution II

- To second order in the Dyson series, $\hat{G} = \hat{G}^{(0)} + \hat{G}^{(0)}\hat{\mathcal{L}}'\hat{G}^{(0)}$. We can evaluate this explicitly by understanding the interaction propagator as acting on $G^{(0)}$. Returning to one dimension for simplicity,

$$\frac{G^{(1)}(x,\tau|x')}{G^{(0)}(x,\tau|x')} = 1 + a\frac{x_b - x'}{2\tau} + b\left(\frac{1}{2\tau} - \frac{(x_b - x')^2}{4\tau^2}\right) \tag{8}$$

A Green's function solution II

- To second order in the Dyson series, $\hat{G} = \hat{G}^{(0)} + \hat{G}^{(0)}\hat{\mathcal{L}}'\hat{G}^{(0)}$. We can evaluate this explicitly by understanding the interaction propagator as acting on $G^{(0)}$. Returning to one dimension for simplicity,

$$\frac{G^{(1)}(x,\tau|x')}{G^{(0)}(x,\tau|x')} = 1 + a\frac{x_b - x'}{2\tau} + b\left(\frac{1}{2\tau} - \frac{(x_b - x')^2}{4\tau^2}\right) \tag{8}$$

  - As $\tau \to \infty$, we approach the same steady state as in the regular heat equation (cannot be the reason for confinement)
  - As $\tau \to 0^+$, observe convergence in $G^{(1)}(x,\tau|x')$ to zero
  - At short times, $\tau \sim 0$, increasingly large contributions from higher-order factors to compensate for starting near x_b'
  - When $\lambda = \kappa$, $a = 0$

References

[1] A. Kusumi, C. Nakada, K. Ritchie, K. Murase, K. Suzuki, H. Murakoshi, R. S. Kasai, J. Kondo, and T. Fujiwara, Annual Review of Biophysics **34**, 351 (2005).

[2] N. Morone, T. Fujiwara, K. Murase, R. S. Kasai, H. Ike, S. Yuasa, J. Usukura, and A. Kusumi, Journal of Cell Biology **174**, 851 (2006).

[3] T. Kay and L. Giuggioli, Phys. Rev. Res. **4**, L032039 (2022).

Continuum limit I (details)

- Formally, the discrete-to-continuum mapping is given by the following relationship $\sum_i \to \frac{1}{a_0} \int dx$
- Hence $\delta_{M,j} \to a_0 \delta(x - x_b)$ where x_b is the location of the barrier
- To this end, the first difference of deltas can be written

$$\delta_{M-1,j} - \delta_{M+1,j} \to a_0 \left[\delta(x - (x_b - a_0)) - \delta(x - (x_b + a_0))\right] \quad (9)$$

- Taylor expanding in the delta functions,

$$\delta(x - (x_b \pm a_0)) = \delta(x - x_b) \mp a_0 \delta'(x - x_b) + \mathcal{O}(a_0^3) \quad (10)$$

and substituting into the Kronecker delta mapping,

$$\delta_{M-1,j} - \delta_{M+1,j} \to 2a_0^2 \delta'(x - x_b) + \mathcal{O}(a_0^4) \quad (11)$$

Continuum limit II (details)

- In a similar manner, the second difference of delta functions can be mapped

$$\delta_{M+2,j} - \delta_{M,j} \to a_0 \left[\delta(x - (x_b + 2a_0)) - \delta(x - x_b)\right] \tag{12}$$

and so, following a series expansion,

$$\delta_{M+2,j} - \delta_{M,j} \to -2a_0^2 \delta'(x - x_b) + \mathcal{O}(a_0^4) \tag{13}$$

- We now return to the inhomogeneous term and note that $p_{M+1}(t) = p(x_b + a_0, t) = p(x_b, t) + a_0 \left.\frac{dp}{dx}\right|_{x=x_b} + \mathcal{O}(a_0^2)$. So, to first order in a_0,

$$\frac{2\Delta_\lambda a_0^2}{\tau} p(x_b, t)\delta'(x - x_b) - \frac{2\Delta_\kappa a_0^2}{\tau}\delta'(x - x_b)\left(p(x_b, t) + a_0 \left.\frac{dp}{dx}\right|_{x=x_b}\right) \tag{14}$$

Continuum limit III (details)

- Reorganizing and using the definitions $\Delta_s = \frac{1}{2} - s$ and $D = a_0^2/2\tau$,

$$4D\left(\kappa - \lambda\right) p(x,t)\delta'(x - x_b) + 4\Delta_\kappa a_0 \delta'(x - x_b) J(x,t) \quad (15)$$

- We now suppose that $\Delta_\kappa a_0/\tau \to k$ and remains finite in the limit such that

$$4D\left(\kappa - \lambda\right) p(x,t)\delta'(x - x_b) + \frac{4D\Delta_\kappa^2}{k}\delta'(x - x_b) J(x,t) \quad (16)$$

Energy-momentum space

- It is convenient to define the Fourier transform as

$$G(\mathbf{x}, t) = \int \frac{d^d k}{(2\pi)^d} \frac{d\omega}{2\pi} \, e^{i\mathbf{k}\cdot\mathbf{x} - i\omega t} G(\mathbf{k}, \omega) \tag{17}$$

  such that we get a pole in the upper half of the plane