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Travelling in a microscopic scale

Abstract

In this essay we compare the effectiveness of the two kinds of transport within cells: the passive and the active one. We do this by computing the average time it takes for a particle to travel a given distance by diffusing and then by moving by the motor protein along a walkway.

1 Introduction

Cells are sometimes called the building blocks of life, since they are the smallest structural and functional units existing on their own. Their functioning has been one of the most interesting field amongst biologists. For example, sometimes some molecules have to be transported from one region to another within the cell. But one can ask, how could a large molecule such as a protein be transported inside the cell? This could be done by two methods, which we are going to examine: the passive diffusion and the active transport.

2 Diffusion

The cell is under collision by other molecules, hence the molecules within the cell are constantly being pushed from random directions. This is the result of the random displacements of its molecules. One of the most analytical method to describe this action is considering the density $F(x, y, z, t)$ of the cell. For randomly diffusing molecules,

$$\frac{\partial F}{\partial t} = D\left(\frac{\partial^2 F}{\partial x^2} + \frac{\partial^2 F}{\partial y^2} + \frac{\partial^2 F}{\partial z^2}\right), \tag{1}$$

where D is a constant. This can be separated for variables x, y, z:

$$\frac{\partial f}{\partial t} = D\frac{\partial^2 f}{\partial x^2}, \tag{2}$$

with similar equations for y and z. Deriving f we get

$$f(x,t) = \frac{1}{2\sqrt{2\pi D t}} e^{-\frac{x^2}{4Dt}} \qquad t > 0, \tag{3}$$

which is the probability of finding a particle at x at time t. One can prove (2) by directly substituting (3) into (2):

$$\frac{\partial f(x,t)}{\partial t} = \frac{\left(\frac{\partial}{\partial t}\left(e^{-\frac{x^2}{4Dt}}\right)\right)(2\sqrt{\pi Dt}) - \left(e^{-\frac{x^2}{4Dt}}\right)\frac{\partial}{\partial t}(2\sqrt{\pi Dt})}{4\pi Dt}$$

$$= \frac{\left(e^{-\frac{x^2}{4Dt}}\right)\left(\frac{x^2}{4Dt}\right)(2\sqrt{\pi Dt}) - \left(e^{-\frac{x^2}{4Dt}}\right)\left(\frac{\pi D}{\sqrt{\pi Dt}}\right)}{4\pi Dt},$$

which if we simplify we get:

$$= \left(e^{-\frac{x^2}{4Dt}}\right)\left(\frac{x^2 - 2Dt}{8Dt^2\sqrt{\pi Dt}}\right) \tag{4}$$

Evaluating the right hand side of (2):

$$D\frac{\partial^2 f}{\partial x^2} = D\frac{\partial}{\partial x}\left(\frac{\partial f}{\partial x}\right)$$

$$= D\frac{\partial}{\partial x}\left(0 + e^{-\frac{x^2}{4Dt}}\frac{-2x}{4Dt}\frac{1}{2\sqrt{\pi Dt}}\right)$$

$$= \frac{-2}{8t\sqrt{\pi Dt}}\frac{\partial}{\partial x}\left(xe^{-\frac{x^2}{4Dt}}\right)$$

$$= \frac{-2}{8t\sqrt{\pi Dt}}\left(\frac{\partial x}{\partial x}e^{-\frac{x^2}{4Dt}} + x\frac{\partial}{\partial x}\left(e^{-\frac{x^2}{4Dt}}\right)\right),$$

$$= e^{-\frac{x^2}{4Dt}}\left(\frac{-1}{4Dt\sqrt{\pi Dt}} + \frac{x^2}{8D^2t^2\sqrt{\pi Dt}}\right),$$

which becomes

$$\left(e^{-\frac{x^2}{4Dt}}\right)\left(\frac{x^2 - 2Dt}{8Dt^2\sqrt{\pi Dt}}\right) \tag{5}$$

after rearranging and simplifying. Clearly, (4) and (5) agree, hence we proved that (3) is a solution for (2).

2.1 Average time

Next we want to determine the average time it takes for such a particle to cover a distance (x) while diffusing in the cell. The average distance $< x >$ travelled by the particle in the cell

why is <x>=0?

is 0. However it does move about, thus we are looking for $< x^2 >$, the average value of x^2, in order to calculate the mean time t. One can calculate $< x^2 >$ by evaluating

$$\int_{-\infty}^{\infty} x^2 f(x,t)dx, \tag{6}$$

given that

$$N(t) = \int_{-\infty}^{\infty} f(x,t)dx = 1, \tag{7}$$

where $N(t)$ is the area under the graph of the probability distribution function $f(x,t)$. To start with, let $\lambda = \frac{1}{4Dt}$, then from (3) we have

$$f(x,\lambda) = \sqrt{\frac{\lambda}{\pi}}\ e^{-\lambda x^2}. \tag{8}$$

Then combining (8) and (7) one can see that

$$\int_{-\infty}^{\infty} \sqrt{\frac{\lambda}{\pi}}\ e^{-\lambda x^2} dx = 1,$$

which is

$$\int_{-\infty}^{\infty} e^{-\lambda x^2} dx = \sqrt{\frac{\pi}{\lambda}} \tag{9}$$

after rearrangements. By partially differentiating both sides with respect to λ, we get

$$\int_{-\infty}^{\infty} -x^2 e^{-\lambda x^2} dx = -\frac{1}{2}\sqrt{\frac{\pi}{\lambda^3}}$$
$$= \int_{-\infty}^{\infty} -x^2 e^{-\frac{x^2}{4Dt}} dx = -\frac{1}{2}\sqrt{\pi(4Dt)^3} \tag{10}$$

Our aim is to get the left hand side of (10) in the form of (6), hence multiply both sides with $-\frac{1}{2\sqrt{2\pi Dt}}$:

$$\int_{-\infty}^{\infty} x^2 \frac{1}{2\sqrt{2\pi Dt}} e^{-\frac{x^2}{4Dt}} dx = \frac{1}{2\sqrt{2\pi Dt}} \frac{1}{2}\sqrt{\pi(4Dt)^3}. \tag{11}$$

The left hand side of (11) clearly equals to (6), while the right hand side is $2Dt$ after simplifying it, hence

$$< x^2 > = 2Dt \tag{12}$$

and

$$d = < x^2 > = \sqrt{2Dt}, \quad (13)$$

where d is the distance travelled by the diffusing particle. To move on in the process of determining the time needed to diffuse, we have to calculate D for a given particle:

$$D = \frac{k_b T}{6\pi\eta r}, \quad (14)$$

where k_b is the Boltzmann constant, T is the temperature of the system in Kelvin, η is the viscosity of the fluid in the cell, and r is the radius of the diffusing particle.

2.2 Examples

For example the tubulin protein with radius $r = 3nm$ at temperature $T = 300K$ and with $\eta = 2 * 10^{-3}\ Pa\ s$ has a $D = 3.66 * 10^{-11}\ m^2/s$, and hence the average time t to travel a distance $d = 50\mu m$ is $t = 34.15\ s$ according to (13).

Vacuoles are tiny spheres made out of oil and are stored and shipped to different parts of the cell, in addition, they have significant role in the life of the cell. Consider a vacuole with $r = 50nm$ under the same conditions as before. Then one can determine the time it takes for the vacuole to travel the distance $d = 50\mu m$ using (14) and (13), and get $t = 569.22\ s$.

To illustrate that the time can be extremely large for long distance, consider a tubulin protein with $r = 3nm$, and calculate the time it takes for it to freely diffuse from the top in our brain to the bottom in our toe, in which case d is approximately 2m, leaving the conditions the same as in the previous examples. Substituting the parameters into (14) and (13) we derive that it takes $t = 5.46 * 10^{10}\ s \approx 1732\ years$.

Can you conclude anyything from this?

2.3 Displacement of particle

All in all, solving the diffusion equation is relatively simple, however one of its weakness is that it only gives us probability distribution of the particle, and does not describe very well how the particle behaves at that point. To illustrate the displacement of a particle in one dimension at a given time, we write a program which performs simulations using random numbers, and plots the results in a histogram(green) with the theoretical values(red) alongside, which were calculated by (3).

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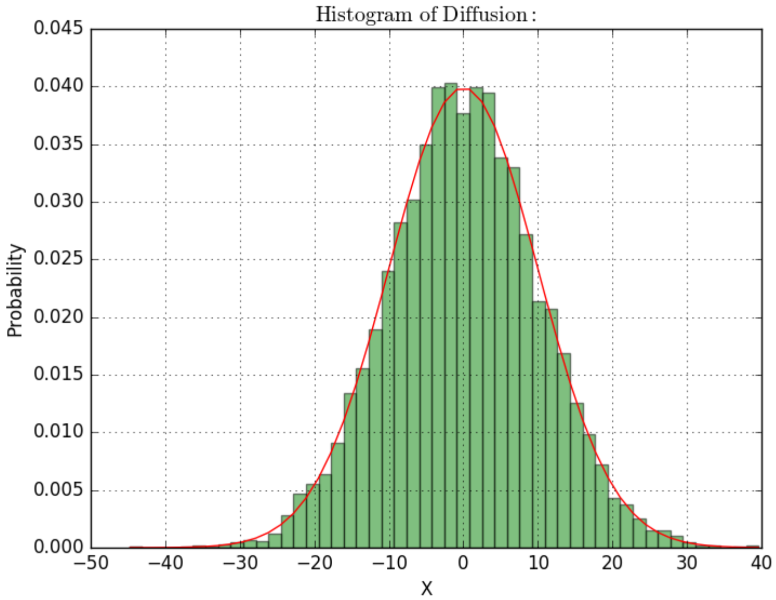

How was the simulation perfor

Fig 1: comparing the results generated from random numbers(green) with the theoretical ones(red)

One can see from Fig 1 that the results of the two kind agree, so the probability of a particle to be at x at a given time t can be determined in either way.

2.3 The average time

Previously we calculated the typical time it takes for a particle to cover a given distance, however to calculate the average time it takes for a particle to cover such a distance we write another program, which computes the average time at 5 different distances d and 3 different values of D. The table with the results is show below:

d	$t: computed$	D	$t: theoretical$
1.	1.02451706	0.5	1
2.	4.08794975	0.5	4
3.	9.04598808	0.5	9
4.	16.07076073	0.5	16
5.	25.23965454	0.5	25
1.	0.51667798	1.	0.5
2.	2.01035976	1.	2
3.	4.64023256	1.	4.5
4.	8.08319187	1.	8
5.	12.47505665	1.	12.5
1.	0.25744841	2.	0.25
2.	1.03250539	2.	1
3.	2.31130123	2.	2.25
4.	4.12027836	2.	4
5.	6.44544792	2.	6.25

Fig 2: results for average time at various distances and values of D

The expression for the average time (t: $computed$) is obtained by running the program 10000 times and taking the mean of the results at every given d and D, thus we get 15 results. From the table in Fig 2 we conclude that the computed values of average t agree with the theoretical ones within an error of 0.1 in most cases.

3 Motor

The other type of transport is called the active transport, which is faster and more effective than the diffusion. In this case, the motor proteins are attached to their cargo on one end, and to the walkway (microtubules or actin filaments) on the other end, and they "walk" on the walkway and hence moving the cargo (Fig 3). However, they can also get detached from the walkway or the cargo. The time between the steps and the detachment are both random, and both given by the Boltzmann distribution characterised by different rates. Nonetheless, the two events are independent of each other.

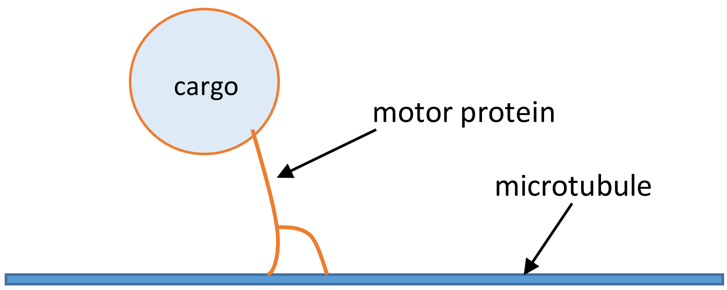

Fig 3: illustration of the movement of the motor protein

We then write a program which illustrate the movement of the motor until it detaches.

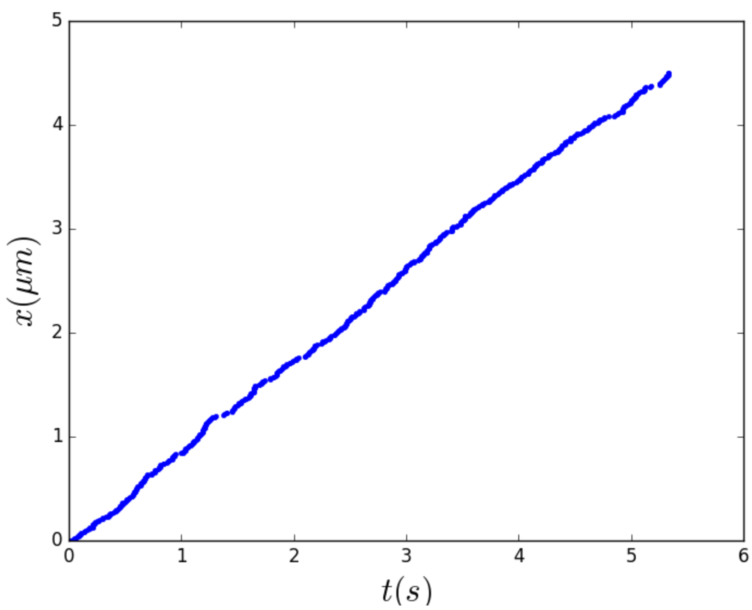

Fig 4: a typical trajectory of a motor protein until it detaches

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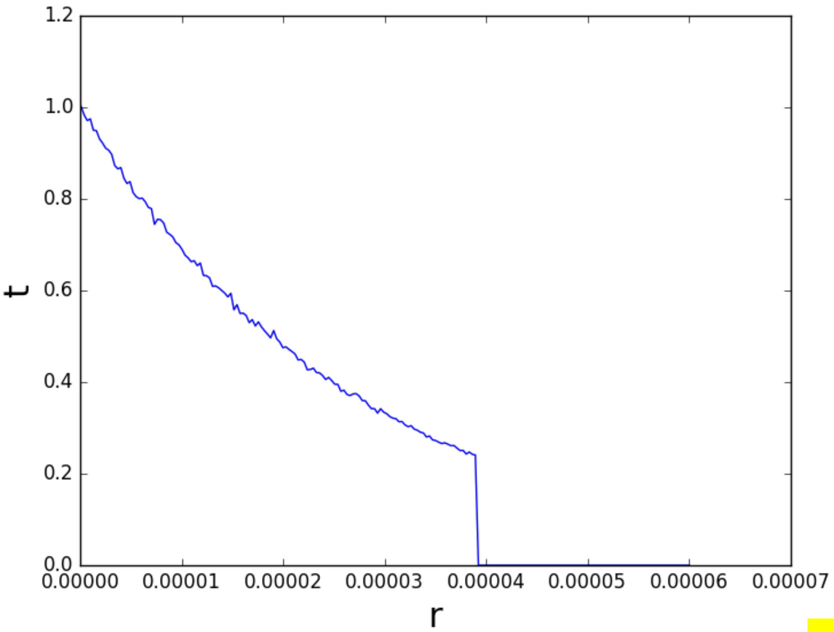
3.1 Average time and displacement as a function of cargo radius

To trace the movement of the motor from another point of view, we examine the average time and the average displacement as a function of cargo radius:



use um as units

Fig 5: the average time the cargo travels until
it detaches as a function of cargo radius

It is clear from Fig 5 that after a point the radius of the cargo is too big for the motor to keep walking on the microtubule.

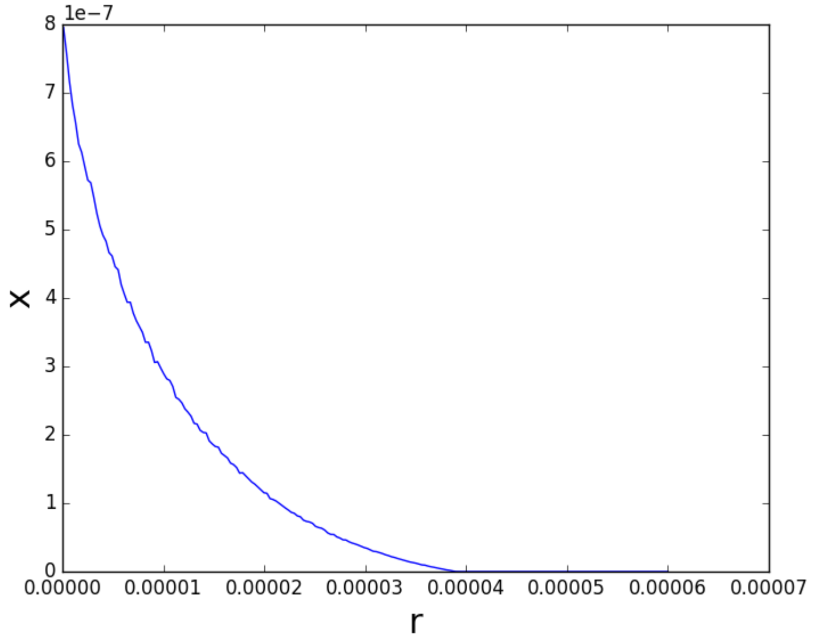


Fig 6: the average displacement of the cargo
as a function of its radius until it detaches

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Comparing Fig 6 and Fig 5 shows that the displacement becomes 0 at the same time when the time drops to 0, hence the motor detaches at that value of r.

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