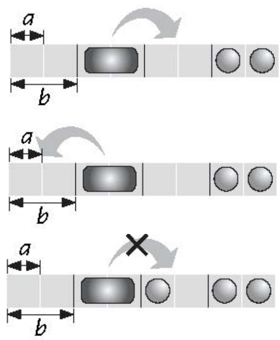
Exercise 04 - Solutions

1. Diffusion and crowding

(a) This is a general case for the Chapter 14.3.2 Diffusion in Crowded Environments.
Possible trajectories of the tracer molecule are a step of length b in the positive x-direction, a step in the negative x-direction, or staying put. The probabilities of each of these trajectories is $1/2(1-\phi)^r$, $1/2(1-\phi)^r$, and $1-(1-\phi)^r$. The first two are calculated as the probability of a step (1/2), times the probability that the adjacent site is unoccupied ($(1-\phi)^r$), thus allowing for a step. An adjacent site of size b is considered unoccupied if all the r=b/a sites of size a that are part of it are unoccupied by crowding molecules. The fraction a a-size sites that are occupied is ϕ, which is also the probability of occupancy of one of these sites by a crowding molecule.



TRAJECTORY	PROBABILITY	DISPLACEMENT X
1	$(1/2)\,(1-\varphi)^r$	+b
2	$(1/2)(1-\varphi)^r$	-b
3	$1-(1-\varphi)^r$	0

Taking all the trajectories and their probabilities into account, the average of the square of the displacement of the tracer particle after one step is

$$\langle x^2\rangle_1 = b^2(1-\varphi)^r \qquad (1)$$

Since every step is independent of every other step, and all the steps are identically distributed random variables, the average displacement squared after N = t/τ steps is

$$\langle x^2\rangle = Nb^2(1-\varphi)^r = 2Dt \qquad (2)$$

The diffusion constant is given by

$$D = D_0(1-\varphi)^r \qquad (3)$$

where $D_0 = b^2/2\tau$ is the diffusion constant of tracer particles in the absence of crowding molecules.

(b) The table below provides the molecular mass of each crowding molecule used in the experiments. From this we can compute the relative sizes *r* of the tracer molecule (adolase) to the crowding agents, by taking the third root of the ratio of the two masses. This assumes that all the molecules used in the experiment can be treated as balls of equal density. The molecular mass and *r* for all molecules used in the experiment are given in the table below.

Molecular species	M_W [Da]	r
ribonuclease	13,700	2.3
ovalbumin	45,000	1.5
BSA	66,430	1.3
adolase	160,000	1

To compare with the experiments shown in Fig. 2, we plot the concentration dependence of the diffusion constant for different crowding agents. The concentration of crowding molecules c is related to the volume fraction in eq. 3 as $\phi = c/1300$, where c is in units of grams per litre (1300g/l is the assumed density of protein [≈ 1.3 x Water concentration]).
The general trends observed in the experimental data are reproduced by the model (Eq. 3), but it clearly underestimates the effect of crowding on the diffusion constant.