

Brownian Dynamics

Mutual Diffusion

Suppose that we have two freely diffusing particles with positions r_1 and r_2

$$\partial_t p = (D_1 \nabla_1^2 + D_2 \nabla_2^2) p.$$

where p is now really $p = p(r_1, r_2, t | r_{10}, r_{20}, t_0)$. If we define two new coordinates

$$r = r_2 - r_1 \qquad R = ar_1 + br_2$$

we find that

$$\begin{aligned} \nabla_1^2 &= a^2 \nabla_R^2 + \nabla_r^2 - 2a \nabla_R \nabla_r \\ \nabla_2^2 &= b^2 \nabla_R^2 + \nabla_r^2 - 2b \nabla_R \nabla_r \end{aligned}$$

and the diffusion term becomes

$$D = (D_1 a^2 + D_2 b^2) \nabla_R^2 + (D_1 + D_2) \nabla_r^2 + 2(D_2 b - D_1 a) \nabla_R \nabla_r.$$

If we want r and R to be linearly independent, we choose our constants as

$$a = \sqrt{D_2/D_1} \qquad b = \sqrt{D_1/D_2}$$

so that D becomes

$$D = (D_1 + D_2) \nabla_R^2 + (D_1 + D_2) \nabla_r^2.$$

We are really only interested in the diffusion of the particles with respect to each other (i.e. how r changes), and we can ignore the ∇_R^2 term since it just reflects the drift of the system. With this, our diffusion equation becomes

$$\partial_t p = (D_1 + D_2) \nabla^2 p.$$

The term $D_1 + D_2$ is called the *mutual diffusion coefficient*.

For two interacting particles, we again have a Smoluchowski diffusion equation

$$\partial_t p = (D_1 \nabla_1^2 + D_2 \nabla_2^2 - D_2 \beta \nabla_2 \cdot F + D_1 \beta \nabla_1 \cdot F) p$$

where the force on particle 1 is F and the force on particle 2 is $-F$. Again moving to the set of r and R coordinates, we get

$$\partial_t p = (D \nabla_R^2 + D \nabla \cdot (\nabla - \beta F)) p$$

where we have written $D = D_1 + D_2$. Again, if we ignore the drift in the system, this equation simplifies to

$$\partial_t p = \nabla D \cdot (\nabla - \beta F) p.$$

Once again, if the system adopts a stationary distribution for inter-particle distances r , this means

$$\nabla D \cdot (\nabla - \beta F) p = 0.$$

If we assume that the interactions are only dependent on r , we can again identify the radial current as and we find that the rate at which our particles achieve a separation $r = b$ is

$$J_{tot}(b) = \frac{4\pi c_1 c_2 D}{\int_b^\infty \frac{e^{\beta U(r)}}{r^2} dr} \equiv k c_1 c_2$$

or if we interpret this as a second order rate constant,

$$k = \frac{4\pi D}{\int_b^\infty \frac{e^{\beta U(r)}}{r^2} dr}.$$

This is due to Smoluchowski (1916).

Association Rates

Unfortunately, the interaction between a protein and another ligand or protein are not centrosymmetric, and we actually need to simulate the association of the two molecules. We can, however, use the Smoluchowski result to greatly speed up our simulations. We know how particles perform in centro-symmetric potentials, so we need only simulate in the region where things are not symmetric.

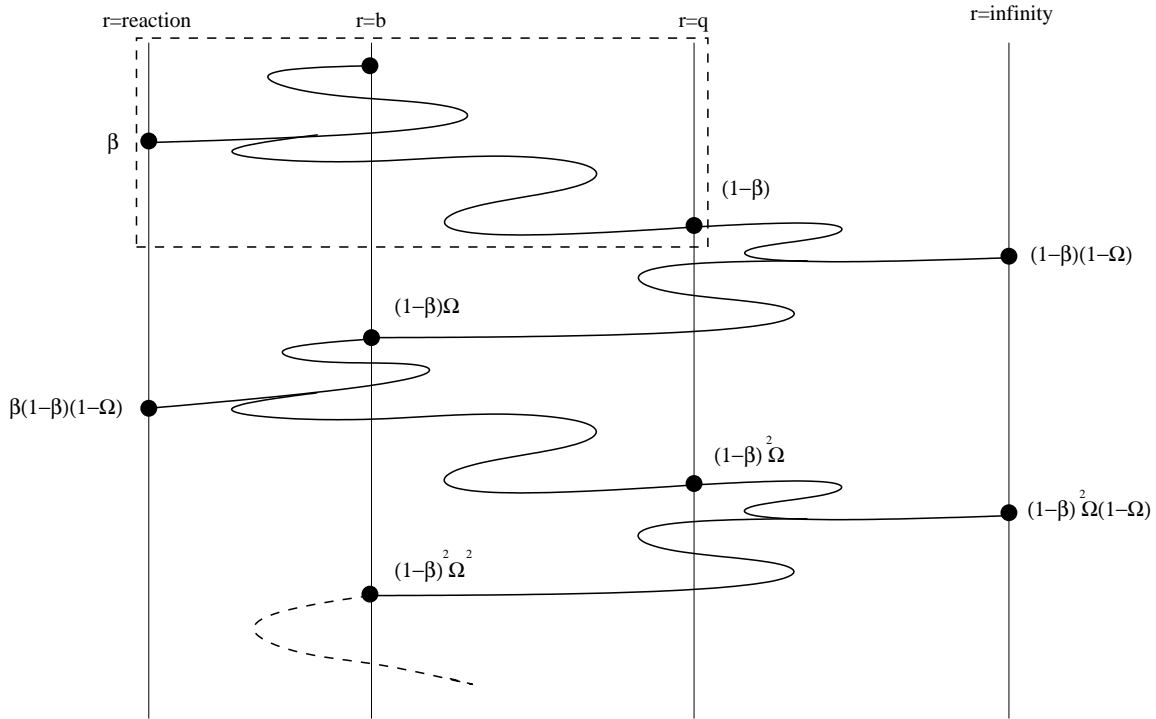
Suppose that the interaction potential between two particles is zero, at least up to a point $r = b$. Since there is no potential up to this point, the rate at which particles achieve a separation b is

$$k(b) = \frac{4\pi D}{\int_b^\infty \frac{dr}{r^2}} = 4\pi D b.$$

If after reaching $r = b$ the proteins have a probability p of interacting, the association rate is

$$k_+ = k(b)p.$$

We will perform Brownian dynamics simulations to find the probability p , starting with the proteins separated by b . If the proteins diffuse away to a distance greater than b , we will be wasting simulation time since there is no interaction at this point. For that reason we introduce an outer radius $q > b$ where we stop our simulations. The following figures depicts how our reaction rates are calculated.



The dashed box in the figure is what we actually simulate, but since we stop our simulations at $r = q$, we do not allow for the possibility that the proteins may again encounter each other before diffusing to infinity. The fraction of particles that turn around before reaching infinity is simply

$$\Omega = \frac{k(b)}{k(q)} = \frac{4\pi D b}{4\pi D q} = \frac{b}{q}.$$

The fraction of successful trajectories is simply the sum of the series

$$p = \beta + \beta(1 - \beta)\Omega + \beta(1 - \beta)^2\Omega^2 + \dots$$

which is just a geometric series yielding

$$p = \frac{\beta}{1 - (1 - \beta)\Omega}$$

and hence

$$k = \frac{k(b)\beta}{1 - (1 - \beta)\frac{k(b)}{k(q)}}.$$