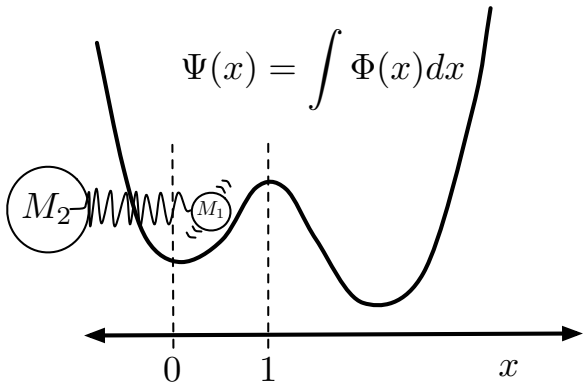
Math 3140 Project - Chemical Reactions, Potential Wells



Introduction

The goal of this project is to understand the behavior of chemical bonds and how they break by modeling the thermal fluctuations of the molecules as stochastic differential equations and PDEs. This approach entails modeling the bond forces that determine how molecules stick to together. Bonds break when random thermal fluctuations impart enough energy to the molecule to surpass the bond potential. Such breaking events are necessarily random, but through analysis of the PDEs that model the bond, we can compute the average time its expected to take for bond breakage. One over the average bond breaking waiting time is the reaction rate.

Model of bond position subject thermal and bond forces

Suppose $x(t)$ represents the position of a molecule with mass M_1 in a one-dimensional space, representing the distance relative to another molecule M_2 which is connected by a chemical bond. The chemical bond creates a restoring force that, in the absence of any other forces, would determine $x(t) = 0$ for all time. We assume that $M_2 \gg M_1$ so that the position of the larger molecule can be considered a stationary anchor for M_1. If M_1 is moved left or right of zero, the bond force restore position to the zero equilibrium. Such forces are experimentally measured using optical “tweezer" techniques that utilize lasers to pull molecules apart in order to carefully measure the nonlinear bond forces.

In addition to the bond force, the surrounding medium contains many particles that collide, perturbing the position of the particle in a random fashion. Finally, there are the standard inertial and viscous (velocity-dependent) forces. This situation is depicted schematically in the above Figure.

The force balance equation is

$$M_1 \frac{d^2x}{dt^2} = \Phi(x) - \tau \frac{dx}{dt} + \sigma\xi(t), \tag{1}$$

where Φ is the bond force, $\tau dx/dt$ is the velocity-dependent friction force with timescale parameter $\tau > 0$, and $\sigma\xi(t)$ is a random (stochastic) noise term. We will assume inertial forces are very small relative to the magnitudes of the other forces ($M_1 \ll \tau dx/dt,\ \sigma\xi, \Phi$), and thus we set it to zero. This results in the first order stochastic ODE:

$$\tau \frac{dx}{dt} = \Phi(x) + \sigma\xi(t). \tag{2}$$

The noise term has a parameter $\sigma > 0$ that determines the strength of the noise and the noise signal itself $\xi(t)$ fluctuates infinitesimally rapidly and randomly. We will skip over many of the hidden details that enable Equation (2) to make sense (It would seem that dx/dt should not equal something that is everywhere discontinuous and that no derivative operation could produce), it suffices to state that the noise fluctuates rapidly enough and randomly, sampled from a normal distribution, so that the value of the noise $\xi(t_1)$ and $\xi(t_2)$ at any two distinct times t_1 and t_2 will not be correlated (knowledge of one will not predict anything about the other).

To numerically simulate (2), one must use a modified Euler method. Let $x_n = x(t_n)$ and $x_{n+1} = x(t_n + \Delta t)$, where Δt is a sufficiently small step size to guarantee desired accuracy. The algorithm, written in Matlab-ese is

$$x_{n+1} = x_n + \frac{1}{\tau}\Phi(x_n)\Delta t + \frac{\sigma}{\tau} randn(1)\sqrt{\Delta t}. \tag{3}$$

Notice that the noise term $\xi(t_n)$ is called as the normally-distributed random number function $randn(1)$ in Matlab. Note also that non-random Euler method multiplies the righthand side by Δt, but the above random algorithm multiplies the noise term by $\sqrt{\Delta t}$. The reason for this is beyond the scope of this write-up, but you may try removing the square-root to verify that it gives the wrong result (see below).

In the questions below you will be asked to numerically simulate a population of particle paths, each with a unique noise forcing and observe the aggregate behavior. This aggregate behavior can also be described by a probability density function, which we denote by $p(x, t|x_0, 0)$, which expresses the likelihood of observing a particle at position x and time t given a starting position x_0. The idea here is that p represents the time evolution of a whole density of particles, each starting at the same point x_0 but each going its own way. It can be shown that p satisfies the linear PDE:

$$\tau \frac{\partial p}{\partial t} = -\frac{\partial}{\partial x}\Big[\Phi(x)p - \frac{\sigma}{2}\frac{\partial p}{\partial x}\Big], \tag{4}$$

which is termed the Fokker-Planck equation.

$$Flux = \Phi(x)p - \frac{\sigma}{2}\frac{\partial p}{\partial x}, \tag{5}$$

which contains a the standard diffusion-like negative gradient term $-\frac{\sigma}{2}\frac{\partial p}{\partial x}$, but due to the chemical bond non-linear spring-like force, it also contains a position-dependent advection term $\Phi(x)p$.

Your group will employ both numerical and analytical methods to answer the following questions. Also included in this document is reference material, containing derivations of some of the more difficult-to-derive equations you may use if you desire.

Phase one questions

1. Under what conditions on $\Phi(x)$ does the PDE in (4) reduce to the 1D diffusion equation on the real line?

2. Suppose $\Phi(x) = -kx$, where $k > 0$, which models is a linear spring force. Solve the PDE in equilibrium ($p_t = 0$) for $p(x)$, with the conditions that $\lim_{x\pm\infty} p(x) = 0$, $\lim_{x\pm\infty} p_x(x) = 0$, and $\int_{-\infty}^{\infty} p(x)dx = 1$ by using the standard linear first-order ODE solution method of finding an integrating factor. Note that $\Psi(x) = \frac{2}{\sigma}\int \Phi(x)dx$ is termed the potential function. Using technology, plot both the potential function and the solution $p(x)$ on the same axes and discuss at which locations x does one find the state of the molecule to be in and specify how it relates to the potential function.

3. Suppose a particle is at position $x = 1$. What is the probability that in the next small time step Δt that the particle will move to the left? to the right? Using the numerical simulation algorithm in Equation (3) to make your computations. Perform the same computation for $x = 0$ and $x = 2$.

4. With the equation defined that you solved above, numerically simulate the motion of a population of 100 particles over a window of time and create a histogram, divided by 100 so that it represents an approximate probability density, of their final positions (type "help hist" in Matlab to learn more), given they all started initially at $x = 0$. Choose parameters σ and τ to suit your preference and clarity, making sure your Δt step is small enough. Try experimenting with different parameter values and plot results and observations.

5. Derive the Fokker-Planck equation using probability conservation. Use probability conservation to determine the dynamics of the proportion of particles in a small region $[x, x+\Delta x]$ to derive the PDE in (4). As usual, consider the flux of particles at the boundaries of the region x and $x + \Delta x$ and relate it to the time dynamics of the population inside the interval, just as you have for the normal diffusion equation.

6. Set $k = 0$. Show that no equilibrium solution is possible. Can you guess what happens to the particles over time?

Phase two questions

1. Now consider a chemical bond nonlinear force $\Phi(x) = -4x^3 + 9x^2 - 4x$. Find the equilibrium solution $p_{eq}(x)$ of the PDE (4) and provide plots of the solution for a range of σ values. Describe the distribution and how it relates to $\Phi(x)$ and what it means for the typical states of the position of the particle. It may be helpful to recall the first-order linear solution method from 2250. Note that we require $\lim_{x\to\pm\infty} p(x) = 0$, and to be a probability distribution we require $\int_{\mathbb{R}} p dx = 1$.

2. Plot the function $\Psi(x) = \frac{2}{\sigma}\int \Phi(x)dx$, where $\Phi(x) = -4x^3 + 9x^2 - 4x$, which is termed the potential function. What does it indicate about the distribution $p_{eq}(x)$?

3. Numerically simulate the random motion of 1000 particles with $\Phi(x) = -4x^3+9x^2-4x$, each with initial condition $x_0 = 0$. How long roughly does it take for the histogram of all particle's positions to settle down to the equilibrium distribution? Answer this question for a range of different σ-values and make a hypothesis about the rate of equilibration. How does σ relate to the potential function you studied above?

4. Reaction rates: If a molecule starts at position $x_0 = 0$ at time $t = 0$, with $\Phi(x) = -4x^3+ 9x^2 - 4x$, what is the average time $\bar{t}(x_0, 0)$ for the particle to cross the $x = 1$ boundary point? Solve the Backward Fokker Planck Equation that is given in the reference guide.

$$\Phi(x)\frac{\partial \bar{t}}{\partial x} + \frac{\sigma}{2}\frac{\partial^2 \bar{t}}{\partial x^2} = -1$$

with boundary conditions

$$\bar{t}(x = 1) = 0, \quad \frac{\partial \bar{t}}{\partial x}(x = -\infty) = 0$$

to find that

$$\bar{t}(x, 0) = \frac{2}{\sigma}\int_x^1 \Big[exp\Big(-\frac{2}{\sigma}\int_a^s \Phi(u)du\Big)\int_a^s exp\Big(\frac{2}{\sigma}\int_a^z \Phi(q)dq\Big)dz\Big]ds.$$

where we take $a \to -\infty$, or any large-enough negative number so that the liklihood of finding a particle there is effectively zero.

Hint: Let $u(x) = \frac{\partial \bar{t}}{\partial x}$ and note that the DE for $u(x)$ is a linear first order equation with initial condition $u(a) = 0$. After you solve for $u(x)$, integrate again to find $\bar{t}(x, 0)$, but do so from 1 *to* x so that the boundary conditions are satisfied. In each distinct integral, be sure to liberally utilize "dummy" variables of integration so that variables are not equivocated. A MATLAB script attached below will help you plot this result.

Set σ to a intermediate value to make crossing not happen too quickly or too slowly. That is, the noise should not be so strong that it makes the potential insignificant, but not too weak so that the potential well is so tall that particles never get pushed out of it. The reaction rate, for a given level of thermal noise σ, is $1/\bar{t}$. Plot your results and how they depend on σ.

5. Reaction rates using numerical solutions: Simulate 1000 particle paths and when each particle crosses $x = 1$ record the passage times t_i. Take the average of those values $Mean(t_i)$. The inverse average is the reaction rate $k = 1/Mean(t_i)$. Plot reaction rates for a range of σ-values and describe the dependence and compare with the results of the previous problem

6. Find the exact mean reaction time by solving the backward Fokker-Planck equation, see Equation (6) below, for the mean first passage time $\bar{t}(x, t)$ and Φ as defined above. The first passage time to react is computed by specifying the starting position $x = x_0 = 0$ and starting time $t = 0$ (i.e., plug in zeros into the solution $\bar{t}(x, t)$). Plot the reaction rates $k = 1/\bar{t}$ for the same range of values of σ you chose from above.

$$\Phi(x)\frac{\partial \bar{t}}{\partial x} + \frac{\sigma}{2}\frac{\partial^2 \bar{t}}{\partial x^2} = -1 \tag{6}$$

with boundary conditions The backward equation is derived by assuming a particle started at a the bound neutral point $x_0 = 0$ and computes the probability flux through $x = 1$ over all time to come up with a mean reaction time. The details of this derivation are found in the optional appendix. Hint: to solve the backward equation, note that its a first-order linear DE (see Chapter 1 from you book) for the function $y(x) = \frac{\partial \bar{t}}{\partial x}$.

Reference materials: Derivation of the backward Fokker-Planck equation for first passage time problem

Here we derive the backward Fokker-Planck equation for the first passage time problem. We start with the standard (forward) Fokker-Planck equation defined as follows:

- The function of interest is the probability density of x at time t given a starting position x_0 at time $t = 0$: $p(x, t|x_0, 0)$.
- The forward Fokker-Planck PDE: $p_t = -Lp$, where $L = \frac{\partial}{\partial x}\left[\Phi(x) - \frac{\sigma}{2}\frac{\partial}{\partial x}\right]$.
- Initial condition $p(x, 0|x_0, 0) = \delta(x - x_0)$, where δ is the Dirac delta functional.
- Boundary condition $p(x = 1, t|0) = 0$. This is called an absorbing boundary condition.
- We want the time t_1 to pass $x = 1$. The above PDE is looking forward from a known starting point $(x_0, 0)$. The idea behind a backward equation is to ask if we observe a particle cross the $x = 1$ boundary at time t_1, find an equation for p in terms of the initial starting point x_0? To do this, we need to lay some groundwork:
- With p, we can compute the probability function that the particle is still in the interval $(-\infty, 1)$ and NOT crossed the boundary as a function of time:

  $$G[x(t) \in (-\infty, 1), t] = \int_{-\infty}^{1} p(x, t|0, 0)dx.$$

  We shorten to $G(t)$ for simplicity. This function starts out 1—100% of particles are in the domain—and decays to zero as all particles eventually leave the interval at the absorbing boundary.
- The probability density for the passage times is $g(t) = -G_t(t)$.
- The mean passage time is the first moment of g: $\bar{t} = \int_0^\infty sg(s)ds$.
- The first moment can also be expressed as follows by using integration by parts

  $$\bar{t}(x_0) = -\int_0^\infty sG'(s)ds = \int_0^\infty G(s)ds = \int_0^\infty \int_{-\infty}^{1} p(\xi, s|x_0, 0)d\xi ds.$$

  where the mean passage time can be parameterized by the starting position x_0.
- How do we find g and p? We must use a property of some random systems that exact knowledge of prior events (density at a previous point in time) help determine likely present states, but knowledge states at a time prior to the prior state is irrelevant.

That is, only immediately preceding states are relevant. This is called a Markov random system. Let $t_1 > t > 0$ be three ordered times. We will define t_1 as the unknown future time when the particle passes the boundary $x = 1$ The Chapman-Kolmogorov equation states how the known likely states at time t can determine the likely future at t_1:

$$p(x, t_1|0, 0) = \int_{-\infty}^{1} p(x, t_1|\xi, t)p(\xi, t|0, 0)d\xi, \tag{7}$$

where the future state is $p(x, t_1|0, 0)$, the present state is $p(\xi, t|0, 0)$, and $p(x, t_1|\xi, t)$ is the likelihood that a state ξ at time t will become $x = 1$ in the future t_1. Any knowledge of states $p(\xi, \eta|0, 0)$ for $0 < \eta < t$ has no influence on the future. Equation (7) expresses an essential structural fact about how future states are determined. That is, we must include this as a constraint (just like we include boundary constraints when solving other PDEs) to solve the PDE.

- Another important property of these random systems is stationarity. The probabilities of outcomes should not change if we shift our system in time by t. We can express this as

$$p(x, t_1|x_0, t_0) = p(x, t_1 + t|x_0, t_0 + t), \tag{8}$$

which will be useful in a later calculation.

- Now, as usual with deriving PDEs, we take the time derivative of (7) with respect to t (not t_1):

$$p(x, t_1|0, 0)_t = 0 = \int_{-\infty}^{1} p(x, t_1|\xi, t)p(\xi, t|0, 0)d\xi \tag{9}$$

$$= \int_{-\infty}^{1} \frac{\partial}{\partial t}[p(x, t_1|\xi, t)]p(\xi, t|0, 0) + p(x, t_1|\xi, t)\frac{\partial}{\partial t}[p(\xi, t|0, 0)]d\xi \tag{10}$$

$$= \int_{-\infty}^{1} \frac{\partial}{\partial t}[p(x, t_1|\xi, t)]p(\xi, t|0, 0) - p(x, t_1|\xi, t)L[p(\xi, t|0, 0)]d\xi \tag{11}$$

- The integral in the final line above are actually two inner products:

$$\langle \frac{\partial}{\partial t}p(x, t_1|\xi, t), p(\xi, t|0, 0)\rangle = \langle p(x, t_1|\xi, t), Lp(\xi, t|0, 0)\rangle \tag{12}$$

The right side contains the forward Fokker-Planck linear operator. Linear operators and inner products have a very nice relationship as they define a companion operator to L called the operator adjoint L^T. We use the “transpose" notation because if we were in a finite dimensional vector space such adjoint operators are merely the matrix transpose.

- Study the right hand side of the above by performing integration by parts to achieve the adjoint:

$$\langle p(x, t_1|\xi, t), Lp(\xi, t|0, 0)\rangle \tag{13}$$
$$= \int_{-\infty}^{1} p(x, t_1|\xi, t) Lp(\xi, t|0, 0) d\xi \tag{14}$$
$$= \int_{-\infty}^{1} L^T p(x, t_1|\xi, t) p(\xi, t|0, 0) d\xi, \tag{15}$$
$$= \langle L^T p(x, t_1|\xi, t), Lp(\xi, t|0, 0)\rangle \tag{16}$$

  where the adjoint is

$$L^T = -\Phi(x)\frac{\partial}{\partial x} - \frac{\sigma}{2}\frac{\partial^2}{\partial x^2} \tag{17}$$

  Thus, we infer from the first entries of the equivalent inner products the backward Fokker-Planck:

$$\frac{\partial}{\partial t} p(\xi, t_1|x, t) = L^T p(\xi, t_1|x, t). \tag{18}$$

- Recall that $\bar{t}(x, t)$ is the mean time of passage starting from (x, t), equal to $\int_0^\infty \int_{-\infty}^1 p(\xi, s|x_0, t) d\xi ds$. The above backward equation (19) only operates on the conditioned variables x, t left of the $|$-symbol. Hence, we can integrate (19) with respect to ξ and t_1 to get a PDE for $\bar{t}(x, t)$:

$$\frac{\partial}{\partial t}\bar{t}(x, t) = L^T \bar{t}(x, t) \tag{19}$$
$$= \int_0^\infty \int_{-\infty}^1 \frac{\partial}{\partial t} p(\xi, t_1|x_0, t) d\xi dt_1 \tag{20}$$
$$= \int_0^\infty \int_{-\infty}^1 \frac{\partial}{\partial t} p(\xi, t_1 - t|x_0, 0) d\xi dt_1 \tag{21}$$
$$\text{let } w = s - t, \quad dw = -dt_1 \tag{22}$$
$$= -\int_0^\infty \int_{-\infty}^1 \frac{\partial}{\partial w} p(\xi, w|x_0, 0) d\xi dw \tag{23}$$
$$= -\int_0^\infty \frac{\partial}{\partial w} G(w|x_0, 0) dw \tag{24}$$
$$= -G(w|x_0, 0)|_0^\infty = 1. \tag{25}$$

  Hence, the PDE for the mean first passage time $\bar{t}(x, t)$, given starting position $(x, 0)$ is

$$L^T \bar{t}(x, t) = 1 \tag{26}$$
$$\implies \Phi(x)\frac{\partial \bar{t}}{\partial x} + \frac{\sigma}{2}\frac{\partial^2 \bar{t}}{\partial x^2} = -1 \tag{27}$$

With boundary condition

$$\bar{t}(1, t) = 0.$$

You can use an integrating factor to solve (27).

Reference matlab code

```
a = -1;
b = 1;
n = 1000;
sig = .01;
s = linspace(a,b,n);
x = s;
p = -(-x.^4+3*x.^3-2*x.^2);
for i=1:n-1
    tp(i) = trapz(s(1:i),exp((-p(1:i)+p(i))*2/sig));
end
tp(n)=0;
mfpt(1) = 0;
%% outer integral
for i=1:(n-1)
    mfpt(i) = 2/sig*trapz(s(i:end),tp(i:end));
end
mfpt(n) = 0;
figure(1)
plot(x,mfpt)
```