Lecture 28  Diffusion

Announce:

• Sorry no exams until Monday
• Seminar today 3:00 vdW

Outline:

Random Walk
mean displacement
mean square displacement
diffusion
flux
fick’s law
friction & viscosity
solute shape

Review
Collision rate for single particle
\[ z_A = \sigma_A \langle u_A \rangle \rho_A = \sqrt{2} \sigma_A \langle u_A \rangle \rho_A \]
\[ \rho_A = \frac{p}{k_B T} \]
Mean free path
\[ l = \frac{\langle u_A \rangle}{z_A} = \frac{1}{\sqrt{2} \sigma_A \rho_A} = \frac{k_B T}{\sqrt{2} \sigma_A p} \]

at STP  ~ 60 nm

Total collision rate
\[ Z_{AA} = \frac{1}{2} \sigma_A \langle u_A \rangle \rho_A^2 \]
\[ Z_{AB} = \frac{1}{2} \sigma_{AB} \langle u_B \rangle \rho_A \rho_B \]

We are shifting to the related topic of molecular transport (Diffusion)

Random Walk

Consider someone walking on a sidewalk who is unable to decide at each step whether to step forward or back. Each step is therefore random and we would consider this a one-dimensional random walk. Consider the following six random steps:
In this case, the random walker returned to the starting position.

Obviously if we take \( N \) steps and the probability of forward \( (p) \) and backward \( (q) \) steps are the same, then on average the total distance traveled should be zero.

But, if \( N \) is very large, then we don’t expect the number of forward steps \( (m) \) to exactly match the number of backward steps \( (N-m) \). So, individual molecules will drift away from the starting point.

Keep in mind that we are doing this because we can consider the movement of molecules as a three dimensional random walk. Each random step is the direction and distance traveled between collisions (this can be either in a gaseous or liquid medium).

So, what we want to know is the probability that, after \( N \) total steps, we will end up some number of steps \( (m - (N-m) = 2m - N) \) away from where we started.

**What’s the probability we have the sequence \( ffbbbfhfff \)?**

\[
ppqqqpqpppp = p^m q^{N-m}
\]

That is the probability of that sequence. But, of course, any sequence with \( m \) forward and \( N-m \) backward steps has the same probability.

Recall the coin flip problem

\[
P(N, m) = \frac{N!}{m!(N-m)!} \frac{2^N}{2^N} \text{ remember } p=q=\frac{1}{2} \text{ for this case}
\]

more generally

\[
P(N, m) = \frac{N!}{m!(N-m)!} p^m q^{N-m}
\]

**What if we wanted to know the average \( m \)?**  Remember \( \langle x \rangle = \int x f(x) dx \)

\[
\langle m \rangle = \int m P(N, m) dm
\]

but \( m \) is discreet

\[
\langle m \rangle = \sum_{m=0}^{N} m P(N, m)
\]

and \( \langle m^2 \rangle = \sum_{m=0}^{N} m^2 P(N, m) \)
Of course, \( \langle m \rangle = N/2 \) if \( p = q = \frac{1}{2} \)

OK, we really care about the displacement. **How do we connect these?**

\[
d = (m - (N - m))l = (2m - N)l
\]

\[
\langle d \rangle = (2\langle m \rangle - N)l
\]

\[
\langle d \rangle = \left(2 \frac{N}{2} - N\right)l = 0
\]

What about the RMS deviation?

\[
\langle d^2 \rangle = \langle (2m - N)^2 \rangle l^2
\]

\[
\langle d^2 \rangle = \langle 4\langle m^2 \rangle - N^2 \rangle l^2
\]

I won’t derive, but

\[
\langle m^2 \rangle = \frac{N(N+1)}{4}
\]

So,

\[
\langle d^2 \rangle = \left(4 \frac{N^2 + N}{4} - N^2\right) l^2 = NL^2
\]

\[
d_{RMS} = \sqrt{\langle d^2 \rangle} = \sqrt{NL}
\]

What do these results for \( d \) and \( d_{RMS} \) mean?

If we have many particles, their average position will be zero, but each of the particles are moving. Any individual particle on average will move by \( \sqrt{N} \).

2 particles starting at zero

●

●

have moved, but avg. still zero

●

●
For example:

<table>
<thead>
<tr>
<th># steps</th>
<th>sequence</th>
<th>result</th>
<th>$\langle d \rangle$</th>
<th>$\sqrt{\langle d^2 \rangle}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L R</td>
<td>+1</td>
<td>0 = 0</td>
<td>$\sqrt{1}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>LL LR,RL RR</td>
<td>+2</td>
<td>0 = 0</td>
<td>$\sqrt{2}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>LLL LLR,LRL,RL RRL,RLR,LRR RRR</td>
<td>+3</td>
<td>0 = 0</td>
<td>$\sqrt{3}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

To connect these random walk results to real life:

- **Replace the number of steps per second by** the collision rate, $z_A$
- **Replace average step size** by the mean free path, $\lambda$

So, for $N_2$ at STP

- $\lambda = 60 \text{ nm}$
- $z_A = 7 \times 10^9 \text{ s}^{-1}$

\[
d_{\text{RMS}} = \sqrt{1 \text{sec} \cdot 7 \times 10^9 \text{ sec}^{-1} \cdot 60 \times 10^{-9} = 0.56cm} \text{ in one second}
\]

Remember that $\langle u \rangle = 474 \text{ m/s}$

So, $d_{\text{RMS}}$ is small, not because the particles aren’t moving quickly, but because all the collisions keep reversing direction (roughly), remember 3 dimensions.

Diffusion is NOT efficient transport over macroscopic scales, but it is efficient over microscopic scales, such as the cellular level.

We now know about diffusion at the molecular level – let’s look at macroscopic level.

Consider a box partitioned by a door.

\[ C_1 \quad \begin{array}{c} \text{C_2} \end{array} \]

\[ x \]
If \( C_1 > C_2 \), what happens when door opens? concentrations will eventually equalize. 
In terms of diffusion, matter is flowing in \(+x\) direction. This is simply because there are more particles with the opportunity to move \(+x\) than \( -x \).

**Flux** is a measure of the net flow through the doorway -- # ptcls/unit time

Clearly the direction of flow is opposite the concentration gradient. It seems sensible that the net flux depends on the disparity in concentrations. This is expressed by Fick’s first law of diffusion:

\[
J_x(t) = -D \frac{\partial C(t, x)}{\partial x}
\]

\( D \) is the diffusion coefficient

Calculating the diffusion constant is a big deal -- very complicated. We can hand wave and say that \( D \propto \langle u \rangle \lambda \)

As \( T \uparrow, u \uparrow, \) so \( D \uparrow \)

as \( p \uparrow, \lambda \downarrow, \) so \( D \downarrow \) many collisions make it hard to move far

as molecule gets smaller, \( \lambda \uparrow \) and \( u \uparrow, \) so \( D \uparrow \)

Also Fick’s second law of diffusion:

\[
\left( \frac{\partial C}{\partial t} \right)_x = D \left( \frac{\partial^2 C}{\partial x^2} \right)_x
\]

This says that you have to be near a change in concentration (in space) in order for the concentration to change in time.

What if we start with all our matter at one spot?
The solution to Fick’s second law for the initial condition above:

\[ C(x) = \frac{C_0}{2\sqrt{\pi Dt}} e^{-\frac{x^2}{4Dt}} \]

**What shape is this?** Gaussian

This is the same as a probability distribution for how far particles might be from zero, as a function of time. We can solve for the average squared displacement as before:

\[ \langle x^2 \rangle = \int x^2 C(x) \]

\[ \langle x^2 \rangle = \langle d^2 \rangle = 2Dt \quad \text{or} \quad D = \frac{\langle d^2 \rangle}{2t} \]

For N₂: recall that \(d_{\text{rms}} = 0.56 \text{ cm}\)

\[ D_{\text{N}_2} = (0.56 \text{ cm})^2 / (2 \times 1 \text{ sec}) = 1.5 \times 10^{-1} \text{ cm}^2 \text{s}^{-1} \]

Let’s compare this value to diffusion in liquid media:

<table>
<thead>
<tr>
<th>Diffusion Type</th>
<th>Diffusion Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>diffusion of N₂ in N₂ (air)</td>
<td>1.5 x 10^{-1} cm² s⁻¹</td>
</tr>
<tr>
<td>self diffusion of liquid water</td>
<td>2.26 x 10^{-5} cm² s⁻¹ slower in liquid</td>
</tr>
<tr>
<td>diffusion of protein myoglobin in water</td>
<td>1.13 x 10^{-6} cm² s⁻¹</td>
</tr>
</tbody>
</table>

We can also rearrange the above equation to see how long it takes a particle (on average) to diffuse a certain distance:

\[ t = \frac{d^2}{2D} \]

(If you were Einstein, you could prove such a thing from first principles.)
So, it takes ~ 0.5 s to diffuse 10 microns (approx. cell diameter)

Important questions: How do we actually determine $D$ and what does this tell us about the size and shape of complex molecules?

Driving force for diffusion is thermal kinetic energy working against friction.

Again Einstein can show:

$$D = \frac{k_B T}{f}$$

Usually, $D$ is measured, allowing calculation of the friction, $f_{\text{EXP}}$.

$$f_{\text{EXP}} = \frac{k_B T}{D}$$

Theoretically,

$$f_{\text{THEO}} = 6\pi \eta r$$

$h$ is viscosity coefficient

$$r = \left( \frac{3V}{4\pi} \right)^{\frac{1}{3}}$$ (for sphere)

Comparing these two frictions, usually $f_{\text{EXP}} > f_{\text{THEO}}$

**Why?** solvent sticks to diffusing particle making it larger.

Also, particle not spherical – makes $r$ effectively larger

In simplest sense, $V = \text{mass/density} = \text{mass} \times \text{specific volume}$

So, for bare particle

$$V = \frac{M \nu_2}{N_A}$$

$\nu_2$ is specific volume of bare particle (cm$^3$/g)

(same as $f_{\text{THEO}}$ given above)

If we want to include the solvent sticking effect:

$$V = \frac{M (\nu_2 + \delta \nu_1)}{N_A}$$

$\nu_1$ = specific volume of the free solvent (cm$^3$ g$^{-1}$) - inverse of density

$\nu_2$ = partial specific volume of the macromolecule (cm$^3$ g$^{-1}$) - dependent on pH, salt concentration, etc. (shape of macromolecule can respond to many parameters).

$\delta_1$ = hydration (unitless) - weight of solvent bound per weight of molecule

If we solve this for radius
\[ r = \left( \frac{3M(v_2 + \delta_1 \nu_1)}{4\pi N_A} \right)^{\frac{1}{3}} \]

**Typical values:**
- **Proteins**
  - \( \nu_2 = 0.70 - 0.75 \text{ cm}^3 \text{ g}^{-1} \)
  - \( \delta_1 = 0.2 - 0.6 \) (g of water per g of protein)
- **DNA**
  - \( \nu_2 = 0.40 - 0.50 \text{ cm}^3 \text{ g}^{-1} \)
  - \( \delta_1 = 0.4 - 0.5 \) (g of water per g of nucleic acid)

From these parameters, we can see that DNA interacts more strongly (and is more dense) with the solvent than proteins do. Typically, hydration increases the frictional coefficient by 10-20% (slows down diffusional transport).

Frictional coefficients can be calculated for any shape. **Show Tinoco 6.8** Notice that the frictional coefficient increases as the object becomes more non-spherical \( \left( \frac{f_{\text{exp}}}{f_{\text{theor}}} \right) \)

Why is diffusion an important thing to know in biochemistry?

1) the measurement of diffusion coefficients can be used to infer the **size and shape of macromolecules**. \( \left( \frac{f_{\text{exp}}}{f_{\text{theor}}} \right) \) determines shape

2) since many biochemical reaction rates are limited by how fast molecules can be transported between active centers, the diffusion rate can also be predictive of the **rate of biochemical processes**.