Core Concepts

Many cellular phenomena are affected by random thermal motion of fluids, e.g., Brownian motion of particles in water

Langevin introduced a stochastic differential equation that contains a wildly fluctuating (random) term representing the fast, short length scale effects of the (watery) environment, and a damping term representing the viscosity of the fluid

Langevin's solution is the basis for Brownian dynamics simulations

Several microscopy techniques use "thermal noise" to measure diffusion and size of cellular objects (proteins, vesicles, nanoparticles, etc)

Cell uses *noise* to do *work*

Homework - natural scales

Before the 2nd lecture: calculate the following quantities from Mass, Length and Time scales given (or the table); and think about what the answer tells you about a cell or the process:

Ex. 1 Cell diameter/membrane thickness (~ 2 * lipid end-to-end length)

Ex. 2 How many vesicles would fit into a single cell? i.e., have the same volume

Ex 3. What is the ratio of the area of all the vesicles in Ex. 2 to the plasma membrane area? How does this value compare to the experimental result that the PM is 2% of all membranes in a cell?

Ex. 4 How long does a lipid take to diffuse its own diameter in the PM due to thermal motion? Assume D ~ 1 micron^2/sec, and area per lipid ~ 0.7 nm^2

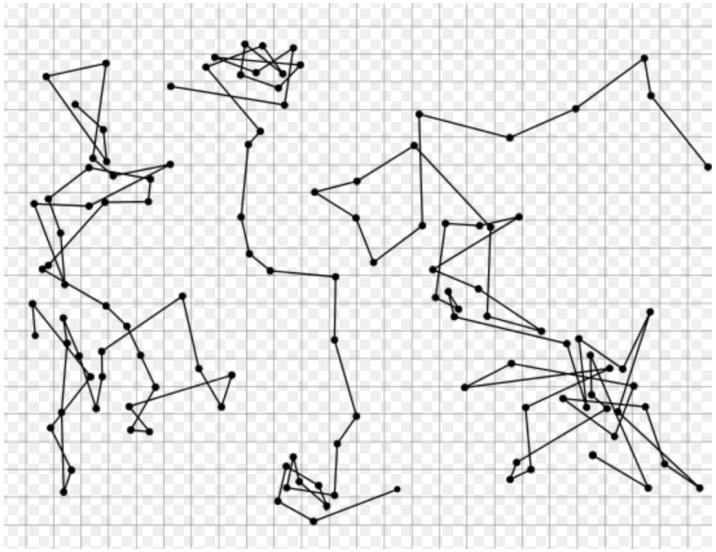
Ex. 5 What is the electrostatic force between a Na and Cl ion on opposite sides of a cell's plasma membrane?

History of Brownian Motion

In1827, Robert Brown observed pollen grains in water, and noticed how they moved continuously and erratically. At first, he thought they were alive….. but pieces of glass and rock also showed similar motion. It was long thought to be an experimental artifact.

In 1908, Perrin and others did experiments with more precision: different materials, size, size distribution, fractionation, counting (Perrin received Nobel Prize, 1926, for this work).

This helped establish the molecular nature of matter which was still controversial at the time.



Jean-Baptiste Perrin, Les Atomes, 1909

P. Langevin Comptes. Rendues 146:530 (1908)

Hypothesis or description?

In Brown's time (1820s) up to late 19th C, the existence of molecules was controversial: they were seen as a *calculational* tool to predict macroscopic thermodynamic quantities like pressure, temperature, etc., but they couldn't be *verified*. (cp. electron spin angular momentum): scientists couldn't measure anything directly related to molecules at that time.

Also note that the 1st law of thermodynamics was not known until ~ 1849 (Joule)

It took a long time before scientists were convinced that Brownian motion was not an effect of external causes (vibrations, temperature differences, illumination, surface tension, microscopic currents, …) but a fundamental physical property of the fluid itself.

Q. How can one exclude that the observed Brownian motion is the result of temperature fluctuations in the fluid, chemical reactions at the particle's surface, microscopic currents, etc.?

1d Discrete Random Walk

A simple, discrete model of a Brownian particle in 1d, that may be symmetric or asymmetric, is the following:

Let a particle start at the origin X = 0, and make a sequence of steps, each of length d, moving right with probability p, and left with 1-p (a symmetric walker has p = 1/2).

What is the **mean position** $\langle X \rangle$ and its **variance** $\langle X^2 \rangle - \langle X \rangle^2$ after N steps?

Note that this is identical to the question: if a fair coin is tossed N times, what is the difference between the numbers of heads and tails as N increases?

(Required Derivation 1 due on 12th March: derive the expressions for $\langle X \rangle$ and $\langle X^2 \rangle$ on the next page, and therefore the variance)

2d, 3d Random Walks

$\langle X \rangle = Nd\,(2p - 1)$

$\langle X^2 \rangle = (Nd)^2\,(2p - 1)^2 + 4\,N\,d^2\,p(1 - p)$

and so $\langle X^2 \rangle - \langle X \rangle^2 = 4\,N\,d^2\,p(1 - p)$

What changes for a Brownian particle in 2d or 3d?

Momentum is conserved in each dimension, so the particle experiences independent kicks in each dimension; the particle makes independent random moves in each dimension and the net MSD is the sum of the 3 independent ones:

$\langle R^2 \rangle = \langle x^2 \rangle + \langle y^2 \rangle + \langle z^2 \rangle$

Assuming isotropy of space: $\langle x^2 \rangle = \langle y^2 \rangle = \langle z^2 \rangle = 2.D.t$

$\langle R^2 \rangle = 6.D.t$

so in a d-dimensional isotropic space, the mean-square displacement of a RW at time t is:

$$\langle R^2 \rangle = 2.d.D.t$$

Simple insoluble extension?

A "simple" generalisation of a Brownian particle in 1d is to allow 3 states:

- move right with probability p
- move left with probability q
- remain stationary with probability (1 - p - q)

What is now the mean position and its variance after N steps?

Let the walker take j steps to the right, k steps to the left and (N - j - k) stationary "steps"

$$\langle X \rangle = \sum N! / j! (N-j)!\ \ (N-j)! / (k! (N-j-k)! \left(p^j q^k (1-p-q)^{N-j-k} \right) \left(j.d - k.d + (N-j-k).0 \right)$$

How to solve this?

A simulation would be easy to do (as would a direct summation of all possible states).

Langevin's solution of Brownian Motion

Langevin in 1908 explained Brown's observations starting from the **equipartition theorem** that a particle of mass M in equilibrium should have a mean KE of: $\langle 1/2\ Mv^2 \rangle = 1/2\ k_BT$ (in 1d, and $3/2\ k_BT$ in three-dimensional space).

He assumed two forces act on the particle of mass M in water (where $M >> m_W$):

1) a viscous drag force (Stokes' law) ~ $-6.\pi.\eta.a.dx/dt$

   η = viscosity
   a = particle radius
   dx/dt = particle velocity

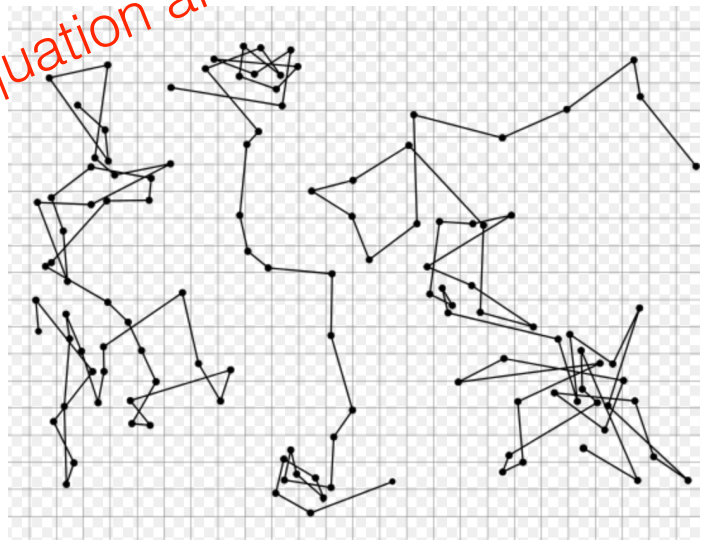
2) a rapidly fluctuating force X(t) subject to:

   $\langle X(t) \rangle = 0$ but $\langle X(t)^2 \rangle \neq 0$

   $\langle x.X(t) \rangle = 0$

Newton's EOM is: $M.d^2x/dt^2 = -6.\pi.\eta.a.dx/dt + X(t)$

Behind an equation are physical assumptions



Langevin's solution of Brownian Motion

Langevin's solution for the mean-square displacement of a particle in solution is:

$$\langle x^2 \rangle - \langle x_0^2 \rangle = (k_B T / 3\pi\eta a)\ t$$

The mean-square displacement (MSD) increases *linearly* with time, so the mean displacement varies with the square-root of time

$$\sqrt{\langle x^2 \rangle} \sim \sqrt{t}$$

Langevin's solution of Brownian Motion

Note that $\langle x^2 \rangle \sim t$ means that the particle's instantaneous velocity is not well defined:

Ballistic motion: $x = v.t$, $\quad v(t) = dx/dt = v$

Brownian motion: $\sqrt{\langle x^2 \rangle} \sim \sqrt{t}$, $\quad v(t) = d/dt \left(\sqrt{\langle x^2 \rangle}\right) = 1/2\ t^{-1/2}$

which caused many problems in the original experiments as they first tried to measure the particles' velocities from graphs of displacement versus time, but eventually used the MSD.

Question: Can one formulate a theory of Brownian motion that does NOT require molecules? i.e., the fluid is continuous. The particle should still exhibit an erratic path but there are no molecules to *kick* the particle. Note that the drag force can have the same form for a continuum fluid, but what causes the random force?

Brownian motion and molecules

In Perrin's words (quoted in Haw 2002):

mean kinetic energy of a colloidal granule is thus equal to that of a molecule'. He goes on: '*This is*, established by experiment,... *the theorem of the equipartition of kinetic energies. At the same stroke, the kinetic theory of fluids appears rather fortified, and molecules a little more tangible'*.

Building on these first measurements, as already described, Perrin and his students went on to construct a numerical mountain of experimental data [20–23], all of which gave results consistent with each other and with, for instance, other measures of N and with the molecular–kinetic theory. He and his students also perfected direct measurements of displacements (which had presented Henri and Svedberg with such difficulty) to confirm Einstein's diffusion theory. Experiments at a range of solvent viscosities, with a range of different colloidal materials, and under various external conditions, all combined irrefutably to convert the molecular–kinetic theory from a *hypothesis* to a *description* of matter. Through Perrin's and his students' efforts, the colloidal suspension had demonstrated the molecular nature of reality.

M. D. Haw, J. Phys. Cond. Mat. 14: 7769 (2002)

Langevin's solution is an SDE

Langevin's equation is an example of a stochastic differential equation (SDE), in which there is a rapidly-fluctuating random term X(t).

Each solution of an SDE represents a *different* random trajectory, but their average properties can be calculated if properties of the random function X(t) are defined.

Contrast this with a deterministic differential equation that has a unique solution.

A Langevin equation looks like:

$$dx(t) = x(t + dt) - x(t) = A(x, t)*dt + B(x, t)*X(t)$$

where A(x, t) is called the Drift term, and B(x, t) the diffusion term.

A and B have distinct physical interpretations, and X(t) is a random *noise* term that will be defined more carefully later.

Integrating a Langevin equation

How would we integrate an equation that had X(t) in it on a computer?

Consider the deterministic differential equation:

$$dx/dt = A(x, t)$$

we discretise this for use on a computer:

$$x(t + dt) - x(t) = A(x, t).dt$$

Now consider the corresponding discretised Langevin equation (taking $B(x,t) = \sqrt{D} = \text{const.}$):

$$x(t + dt) - x(t) = A(x).dt + \sqrt{D}.X(t)$$

How would we implement this on a computer?

We have been a bit loose with the function X(t) that represents random solvent collisions.

All we have said is that $\langle X(t) \rangle = 0$, $\langle x.X(t) \rangle = 0$ and $\langle X^2(t) \rangle \neq 0$, but what is X(t)?

It turns out that X(t) has to satisfy some strict conditions to be mathematically sensible - see the Gillespie reference for details.

A *normal* or *Gaussian random variable* X = N(m, σ), with mean m and variance σ^2, is one for which X takes a value x with probability:

$$p(X = x) = 1/\sqrt{(2.\pi.\sigma^2)}.\ \exp(\ -(x - m)^2 / 2.\sigma^2\ )$$

And the *only* well-defined, continuous, memory-less, stochastic process (Langevin equation) is:

$$dx(t) = x(t + dt) - x(t) = A(x).dt + \sqrt{D}.\ N(0, 1).\sqrt{dt}$$

where N(0, 1) is the *unit normal random variable* with mean 0 and variance 1. The square-root of dt is crucial.

D.T. Gillespie, The mathematics of Brownian motion and Johnson noise, Am. J. Phys. 64:225 (1996)

Implementing a Langevin equation

Our original noise term must therefore have the form:

$$X(t) = N(0, 1)\sqrt{dt}$$

and the Langevin equation that we can implement on a computer is:

$$dx(t) = x(t + dt) - x(t) = A(x).dt + \sqrt{D}.\, N(0, 1).\sqrt{dt}$$

where N(0, 1) is a Gaussian random variable with zero mean and unit variance that we sample at each time step to find the next point.

Note

1) We cannot ignore dt wrt $\sqrt{dt}$ because the term N(0, 1) is equally often positive and negative which reduces the magnitude of the sum of many random samples.

2) The square root is necessary to reproduce $\langle X^2 \rangle \sim D.T$ for a diffusive process. No other power will do. D is the diffusion constant.

3) This equation forms the basis for the Brownian Dynamics simulation technique:

D. L. Ermak, and J. A. McCammon, Brownian Dynamics with Hydrodynamic Interactions, J. Chem. Phys. 69:1352 (1978)

Einstein's solution of Brownian Motion

Earlier, in 1905, Einstein produced a different solution based on similar assumptions to Langevin.

1) each particle's (e.g., pollen grain) motion is independent of the others and is caused by frequent impacts on the particle of the constantly moving water molecules in which the particle is suspended; its motion in different time intervals are independent provided these intervals are not too small

2) consider a time interval τ that is short compared to observation times but large enough that in successive intervals of τ, the motions executed by the particles are independent of each other

A. Einstein Ann. Phys. 17: 549 (1905)

Einstein's solution of Brownian Motion

Let n particles be suspended in a liquid, and let their X coordinates change by an amount Δ in time τ, where Δ is different for each particle and is equally likely to be positive or negative (we work in 1d for simplicity).

There is a frequency law for Δ that says the number dn of particles whose X coordinates change by Δ to $\Delta + d\Delta$ in a time τ is

$$dn = n\,\Phi(\Delta)\,d\Delta$$

where $\Phi(\Delta)$ is normalised to unity, symmetric, $\Phi(\Delta) = \Phi(-\Delta)$, and only non-zero for small Δ.

Let f(x, t) dx the number of particles per unit volume at (x, t), then f satisfies:

$$f(x, t + \tau)\,dx = dx \int f(x - \Delta, t)\,\Phi(\Delta)\,d\Delta$$

Einstein's solution of Brownian Motion

The differential equation satisfied by f(x, t) is the Diffusion Equation

$$df / dt = D\, d^2f / dx^2$$

where $D = 1/(2\tau)\int \Delta^2\, \Phi(\Delta)\, d\Delta$ is the diffusion coefficient.

The solution to this equation is well-known:

$$f(x, t) = n /\sqrt{(4\, \pi\, D\, t)}\, \exp(-x^2/4\, D\, t)$$

From this, the mean-square displacement is found to be:

$$\langle x^2 \rangle = 2\, D\, t$$

and by comparing this to Langevin's solution we find the diffusion coefficient is:

$$D = k_B T / 6\, \pi\, \eta\, a$$

This makes the predictions that diffusion a) increases with temperature, b) decreases with increasing particle size, and c) decreases for higher viscosity fluids.

Particle diffusion with drift

The diffusion equation for f(x, t) is translationally invariant in space. How can we introduce a net drift to the particles?

e.g., charged pollen grains in water subject to a weak spatially-varying electric field.

Recall that the frequency law $\Phi(\Delta)$ was assumed to be a symmetric function of Δ.

Suppose we add an anti-symmetric part:

$$\Phi(\Delta) = \Phi_s(\Delta) + \Phi_{as}(\Delta)$$

where $\Phi_s(\Delta) = \Phi_s(-\Delta)$

and $\Phi_{as}(\Delta) = -\Phi_{as}(-\Delta)$

How does this change the solution?

Particle diffusion with drift

The new differential equation satisfied by f(x, t) is:

$$d\,f(x,t)/dt = -d\,(A\,f)/dx + D\,d^2f/dx^2$$

where $A(x) = 1/(\tau)\int \Delta\ \Phi_{as}(\Delta)\ d\Delta$

and as before $D = 1/(2\tau)\int \Delta^2\ \Phi_s(\Delta)\ d\Delta$

This equation has a drift (represented by A(x)) superimposed on the diffusing particles.

A simple case is to choose A(x) = -k.x

$df(x,t)/dt = d(k \times f)/dx + D\,d^2f/dx^2$

This is the Ornstein-Uhlenbeck process which represents a random walk with a "memory" that is quantified by the parameter k.

Stationary State of OU Equation

We can find the stationary state of this equation easily by setting $df(x, t) / dt = 0$

$d(k.x.f) / dx + D.d^2f / dx^2 = 0$

$d/dx\ (k.x.f + D.df/dx) = 0$

$k.x.f + D.df/dx = const$

with solution $f(x) = (k / 2\pi D)^{1/2}.exp(- k\ x^2 / 2D)$

which is a Gaussian with mean 0 and variance D/k. No matter what the initial distribution f(x, t) is, the long-time solution tends to a Gaussian.

Contrast this with the simple Diffusion Equation that has no stationary state: the density everywhere tends to zero as time increases.

Langevin or Einstein?

We now have two apparently different solutions for the same Brownian motion.

The differential equation for the probability function f(x, t) for finding particles at a point (x, t) (which is an example of a Fokker-Planck equation):

$$df(x, t) / dt = -d(A.f) / dx + D.d^2f / dx^2$$

is equivalent to the Langevin equation for the trajectory of a single particle x(t):

$$dx = A(x).dt + \sqrt{D(x)}. X(t)$$

where A(x) is called the *drift* term and D(t) the *diffusion* term, and the random noise term must satisfy: $\langle X \rangle = 0$, $\langle X^2 \rangle = \delta(dt)$, so $X(t) = N(0, 1).\sqrt{dt}$

Depending on how we choose A(x) and D(x) we get different models.

It can be shown that every Langevin equation can be equivalently written as a Fokker-Planck equation, but that is beyond our scope.

C. W. Gardiner, handbook of Stochastic Methods, 2nd ed. Springer, 1997

Where do RWs appear in a cell

Now we have a model for RWs, we can see them everywhere

Bulk diffusion in cytoplasm (3d)

Lipid and protein diffusion in membranes (2d)

Ion diffusion through channel proteins (1d)

Actin monomers diffuse and bind to form filaments (3d)

Motor protein diffusion along filaments (1d)

DNA binding proteins, transcription and translation (1d)

(Reaction coordinate in chemical reactions, 1d)

(Membrane potential on a neuron, 1d)

Other Random Walks

We have viewed the RW as the track of a particle moving in space, but there are many other applications. We can use it to represent, e.g., the membrane voltage u(t) of a "noisy neuron".

The membrane voltage for a *leaky integrate-and-fire* neuron is:

$\tau \, du(t)/dt = -u(t) + R \, I(t)$

where τ is the "time constant" (or memory), R membrane resistance, I(t) current. The voltage u(t) varies and when it crosses a threshold a "spike" is generated and u(t) reset.

We can add noise to the voltage equation to get the Langevin equation:

$\tau \, du(t)/dt = -u(t) + R \, I(t) + \Gamma(t)$

where the white noise term is formally defined by: $\Gamma(t) = \text{Lim } (dt \rightarrow 0) \; N(0, 1) / \sqrt{dt}$

$< \Gamma(t) > = 0$
$< \Gamma(t) \, . \, \Gamma(t') > = \delta(t - t')$

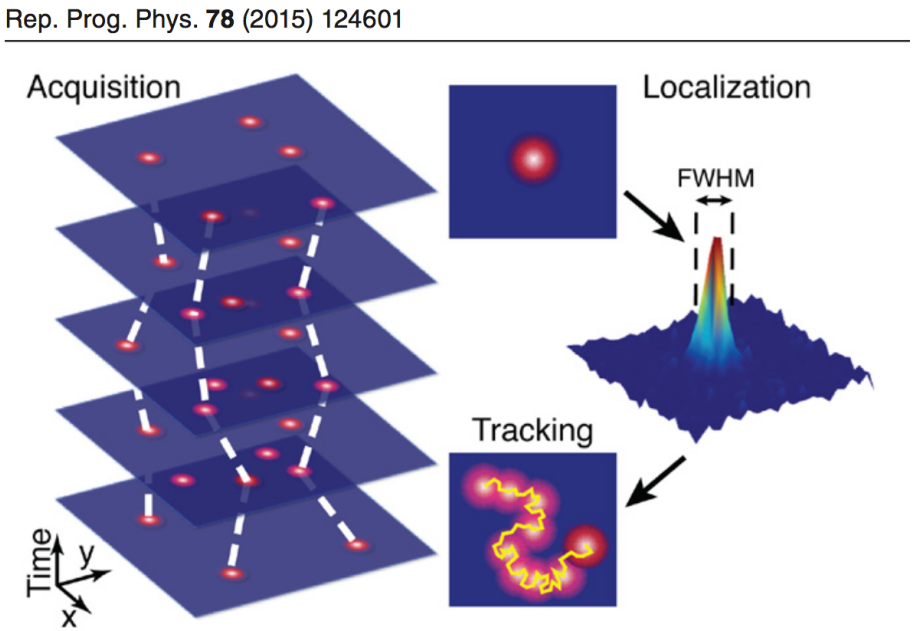
Sect. 5.5, W. Gerstner and W. Kistler, Spiking Neuron Models, Cambridge University Press (2002)

Measuring Brownian motion

Brown used light microscopy to measure the diffusion of single particles; what experimental techniques are available now?

1) SPT - single particle tracking

Updated version of Brown's method that uses light microscopy to track a single fluorescently-labelled particle, e.g., a quantum dot, as it diffuses in space or on a cell's surface



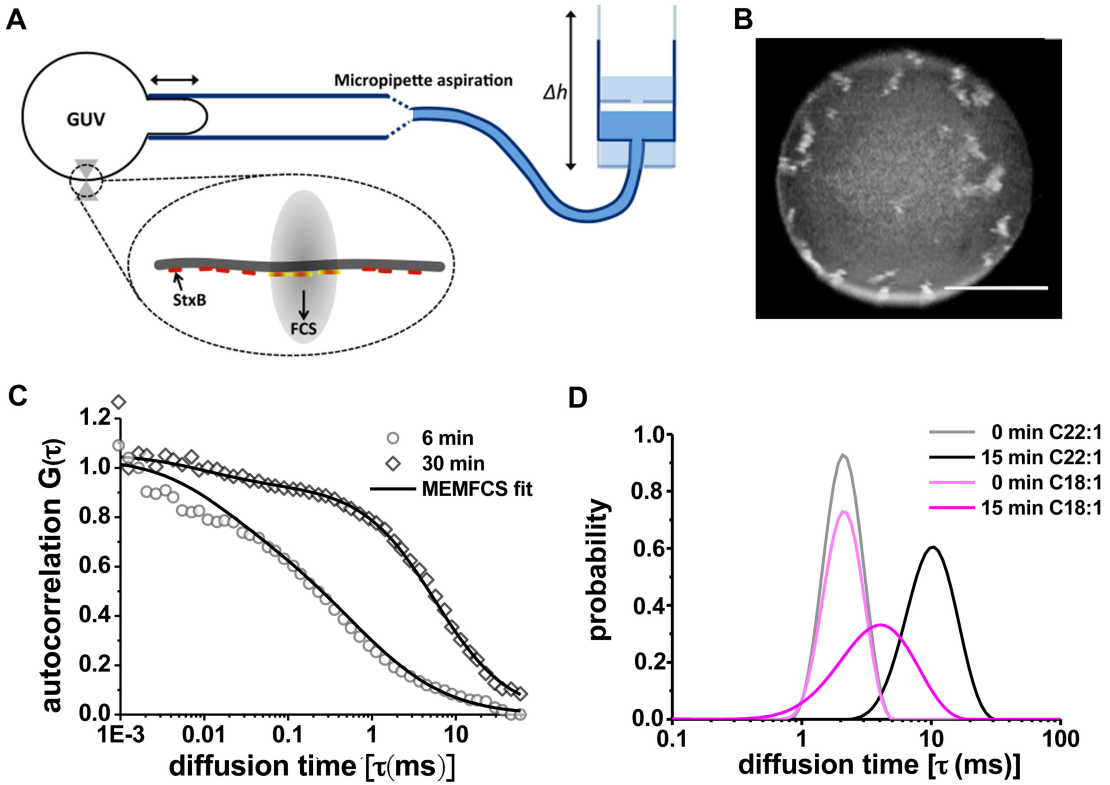
Pros	Cons
complete trajectory	tracks may reflect distinct processes; localisation errors (stuck particle ~ small D), diffusion and sub-diffusion mixed
no ensemble averaging	signal is inherently noisy
	optical resolution
	tracks may have gaps especially for blinking QDs

C. Manzo and M. F. Garcia-Parajo, A Review of progress in single particle tracking; from methods to biophysical insights. Rep. Prog. Phys. 78:124601 (2015)

Measuring Brownian motion

2) FCS - fluorescence correlation spectroscopy

Laser light is focussed on a spot, and the scattered intensity from the (dilute) fluorescing particles is measured as a function of time and the two-time correlation function is analysed to extract the diffusion coefficient of the particles.



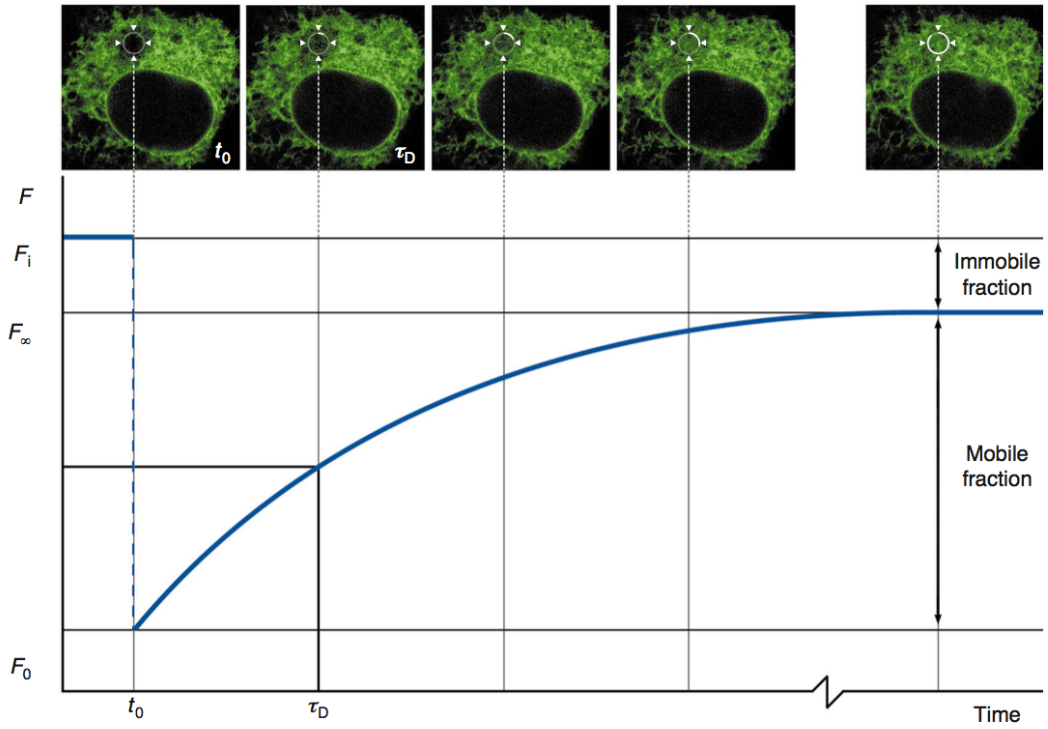
Pros	Cons
Good statistics	Needs a (complex) model to extract diffusion constants
	needs a dilute system

E. L. Elson, Fluorescence Correlation Spectroscopy: Past, Present and Future. Biophys. J. 101:2855 (2011)

Measuring Brownian motion

3) FRAP - fluorescence recovery after photobleaching

A region of membrane containing diffusing dye molecules is irreversibly bleached by intense light, and the gradual recovery of the fluorescence as unbleached dye diffuses back into the region carries information about the particles' diffusion coefficient



Pros

Measure the mobile fraction and diffusion constant

Measures diffusion, reactions, conformational changes

Cons

2D unless complex model used

E. A. J. Reits and J. J. Neefjes, From fixed to FRAP: measuring protein mobility and activity in living cells. Nature Cell Biology 3:E145 (2001).

What use is noise in a cell?

Noise = random thermal motion = unlimited source of energy

Do we have perpetual motion?

In a way, except that it is undirected motion that cannot do useful work without constraints

The cell uses the random thermal noise to create structures of use and to *search* states of interacting particles, or explore (short-distance) space by diffusion, e.g.,

- membranes form spontaneously from amphiphilic lipids diffusing in water
- ions flow through a channel in a membrane to do work (but a pump maintains the gradient)
- filaments spontaneously *assemble* but to *disassemble* them requires energy consumption;
- motor proteins pull vesicles along filaments, but ATP is required to make the motion directed
- two chemical reactants will randomly explore possible binding conformations, but to separate them requires expenditure of ATP
- noise allows systems to jump over energy barriers

A cell also needs energy to keep things constant (membrane potential, chemical gradient, etc).

Conservation and transport in a cell

The cellular cytoplasm is a *fluid*, so we might expect molecules and aggregates to diffuse around until there are no gradients. Unconstrained diffusion would be a problem for a cell as it would lead to high entropy and complete mixing.

Equilibrium = Death

Fortunately,

cell is an active body - energy is expended to create gradients or keep things separate, e.g., neuron membrane potential maintained by Na-K pump.

cell contains organelles that separate constituents and maintain unequal concentrations, e.g., mitochondria that generate ATP. These organelles *spontaneously* assemble their membranes so random thermal motion leads both to mixing and to segregation!

Conservation is related to transport: continuity equation:

$$d\rho/dt + \text{div}\,(\rho.\mathbf{v}) = 0$$

The simplest way to keep things separate (i.e, a gradient in concentration) is to segregate inside membrane-bounded organelles.

Conservation and transport in a cell

Cellular cytoplasm is a fluid: but what kind of fluid?

Do we underestimate the importance of water in cell biology?
M Chaplin, Nature Reviews Mol. Cell Biol. 7:861 (2006)

Abstract | Liquid water is a highly versatile material. Although it is formed from the tiniest of molecules, it can shape and control biomolecules. The hydrogen-bonding properties of water are crucial to this versatility, as they allow water to execute an intricate three-dimensional 'ballet', exchanging partners while retaining complex order and enduring effects. Water can generate small active clusters and macroscopic assemblies, which can both transmit information on different scales.

As well as the membrane-bounded organelles, there are non-membrane bounded organelles - nucleolus, Cajal bodies, pot-synaptic density in synapses, etc. These are distinct from the cytoplasm in their composition and phase, but continuous with it.

As the cell uses random thermal motion to move things around, it may use the physical state or phase of the cytoplasm to influence or control cellular functions?

This has led to the study of liquid liquid phase separation, we'll return to it in a later lecture.

Break

10 mins.

Exercise

1) Install Paraview / VMD on laptops for visualisation.

2) Create a linear polymer in water and measure its equilibrium properties:

Steps involved:

Specifying multiple polymers in a DPD simulation

Defining bonds to connect beads into polymers

Specifying the polymer "shape" and concentration

Setting the a_{ij} parameters between beads

3) How does the end-to-end length of a polymer respond to an applied force?

Paraview is am open-source data analysis and visualization programme
http://www.paraview.org

VMD is another option - beautiful graphics/movies, but harder to use

1) Go to: https://www.ks.uiuc.edu/Development/Download/download.cgi

2) Select your platform (linux, Mac OS X, windows)

3) Create a user/pw and agree to license, downdload the VMD bundle

4) (or get make-gro.sh, pov2vmd.sh, xtc.zip, and rod9.vmd files from moodle)

5) Unzip xtc.zip, and compile povtoxtc on your platform with one of the following commands (or use the executable provided):

linux: compile.sh
mac OS X: comac.sh

6) Place the resulting pov2xtc executable in your path along with make-gro.sh and pov2vmd.sh from step 6

7) Given a set of dmpccs.runid.*.pov files, convert them to runid.gro, runid.xtc with the command:

make-gro.sh. runid 10

NB The number of time-steps between snapshots is hardwired to 1000, so you can only convert multiples of 1000. The example above assumes you saved them at 10,000 step intervals:

8) Invoke vmd on the gro/xtc files:

vmd -e ~/path-to-scripts/rod9.vmd runid.gro

Converting Povray to VMD scripts

Given a simulation input file dmpci.runid, and the associated pov files saved every n thousand steps, we create the runid.gro, runid.xtc files as follows:

make-gro.sh $1 = runid $2 = multiple of 1000

```
nt=$(ls dmpccs.$1.*.pov|wc -l)

echo "${nt}"

~/your_path_to_scripts/pov2vmd.sh $1 1 "${nt}"  $2
```

pov2vmd.sh $1 = runid $2 = first $3 = last $4 = multiple of 1000

```
~/your_path_to_scripts/pov2xtc  -id $1  -b $2  -e $3  -j $4

mv output.gro  $1.gro
mv output.xtc  $1.xtc
```

2) Polymer end-to-end length

(see dmpci.ex2 on moodle)

```
Bead  W
0.5
25
4.5

Bead  B
0.5
30    25
4.5   4.5

Bond  B B 128.0  0.5
```

Each new bead type needs a value of a_{ij} for all preceding types and itself (the second line is the dissipative parameter which is always left at 4.5, see Groot and Warren 1997 for why).

This results in a lower-diagonal matrix of a_{ij} in which the final value for each bead type is its self-interaction

Hookean springs are used to tie beads together into polymers. The parameters are:

Names of the two beads to connect (B B)
Strength of the bond (128)
Unstretched length (usually left as 0.5)

```
Polymer    Water    0.9995    " (W) "
Polymer.   PEG      0.0005    " (B (6 B) B) "
```

Instead of writing out B B B B B B one can use the shorthand (6 B) to create 6 B beads in a line. But the first and last beads MUST be explicitly named.

Groot and Warren, J. Chem. Phys. 107:4423 (1997)

Where is the polymer end-to-end length?

Use second analysis period

Mean

dmpcas.nnn

```
47  Time = 10000
48  Temperature
49  1.0104773       0.0073156424
50
51  Pressure
52  23.715989       0.081562143
53
54  CM Mom
55  -4.0262336e-17  2.7442685e-17
56  4.8555382e-17   2.0268539e-17
57  5.8985819e-17   2.74477e-17
58  9.4523236e-17   2.0991814e-17
59
60  CM Pos
61  8.0002684       0.015473779
62  7.9990433       0.013561895
63  8.0003785       0.015066759
64  13.856242       0.015803866
65
66  <more stuff here>
67
68  Bond Length
69  0.56147655      0.016740266
70
71  BB bond length
72  0.56147655      0.016740266
73
74  Water EE distance
75  0               0
76
77  PEG EE distance
78  2.5119539       1.0980165
79
80
```

Std. dev.

Ignore these for now

Mean / Std. dev

2) Stretching a polymer

To Do:

1. Set a box size of 30 x 10 x 10; adjust the number fractions to have 1 polymer of type (BH (14 B) BT), i.e., distinct head and tail beads so they can be selected.
2. Turn force on at T = 1000 steps. How long should you keep it on?
3. How can you measure the extension?How does Lee change if you make the polymer longer?
4. How does it change if you raise the temperature?

Discuss this first

5. Now change the backbone to contain a new bead type that is "sticky". Try (BH B B B S S S S B B B BT), and give S the same interactions as B except for its self interaction that is reduced to make it sticky. Vary number of S beads.

Questions to answer

What is the stress/strain relation F(L) for the "molecular spring"?

Does it have different regimes for F(L) under different tensions? Why?

With sticky beads there are two new parameters: the number of sticky beads and their self-interaction. How can you select sensible values for these?

(see dmpci.ex1 on moodle, entropic spring input file)

```
Polymer Water    0.9998   " (W) "
Polymer Spring   0.0002   " (BH (14 B) BT) "

Box          30  10  10       1  1  1
Density      3
Temp         1
RNGSeed      -4436
Lambda       0.5
Step         0.01
Time         6000
SamplePeriod     10
AnalysisPeriod   6000
DensityPeriod    6000
DisplayPeriod    100
RestartPeriod    6000
Grid         1  1  1


Command ToggleBeadDisplay             1    W
Command SetCurrentStateCamera         1    0.5 -1.0 -0.5  0.5 0.5 0.5
Command SetCurrentStateDefaultFormat  1    Paraview

Command SelectBeadTypeInSimBox        1  head  BH
Command SelectBeadTypeInSimBox        1  tail  BT

Command ConstantForceOnTarget         1000  head  fh   1 0 0   1.0
Command ConstantForceOnTarget         1000  tail  ft   1 0 0   -1.0

Command RemoveCommandTargetActivity   5000   fh
Command RemoveCommandTargetActivity   5000   ft
```

Use unique bead names so a force can be applied to them independently

Select each end of polymer as a "Command Target"

Apply a force to the targets

Turn the force off