BEH. 410 - 02/10/2003
L # 2

Outline :
- energy scales : $k_B T$ is our "ruler"
- molecular interactions
- thermal forces

Readings :
- Mahadevan ch. 3
- Daune ch. 2
- Dill & Bromberg ch. 6, 8, 10

▸ length scales in biology $10^{-9} \rightarrow 10^{1}$ m
central dogma : DNA → RNA → proteins → organelles → → cells → tissues → organs

✣ Central problem : characterize mechanical interactions (chemical) from nm to m

<u>Molecular mechanics</u> :
- conformation of macromolecules (DNA, proteins ...)
- apply forces ⇒ change conformations
- things are "noisy" at the molecular level
- mechanochemistry

▪ <u>Energy scales in biology</u>

. Thermal energy : $E_{th} \sim k_B T$ (k_B: Boltzmann constant $k_B = 1.38 \cdot 10^{-23}$ J.K^{-1}; T: temperature)

$$\boxed{\begin{array}{l} k_B T \simeq 4 \cdot 10^{-21} \text{ J} \\ RT = N k_B T = 25 \text{ kJ.mol}^{-1} \end{array}}$$

at room temperature 298 K
in terms of moles

. Comparison of energies ($\times 10^{-21}$ J)

E_{th}	kT	4.1	
ATP hydrolysis	ΔG	~ 100	
electron transport	eV	~ 29	(for 180 mV)
covalent bond	C - H	~ 660	
non-covalent interactions		~ 0.1 - 60	

↳ hydrogen bonds, hydrophobic interaction, screened Coulombic interaction of ionic bonds

▷ many weak interactions together ≡ strong, hence importance & stability
transient / statistical behaviors
can lead to specific structures in self-assembled peptides (hydrophobicity)

▫ Forces in mechanics

$E_{th} \sim 4 \cdot 10^{-21}$ J ≡ force . distance
over typical distance of nanometer (10^{-9} m)
hence typical thermal force $= 4 \cdot 10^{-12}$ N
$= 4$ pN

- measurements

thermal force	pN
optical tweezer	0.1 - 100 pN
magnetic tweezer	0.01 - 100 pN
AFM	10 - 10,000 pN

▫ Case of thermal forces - modeling of DNA in solution - effect of kT

Thermal forces & diffusion

- Brownian motion (Brown 1827) in "simple" fluids (water)
Jean Perrin quantified these observations (1900's)

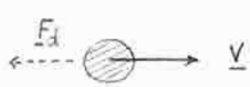
$\langle r \rangle = 0$ (ensemble average)
$\langle \underline{r} \cdot \underline{r} \rangle$ linear in time $= 4\, D\, t$ — diffusion coefficient
$= \langle x^2 + y^2 \rangle$ in 2 dimensions

- what comes into D? "guess" using dimensional analysis:
Fourier 1780: a physical equation must be { dimensionally consistent; consistent in order (scalar, vector) }

e.g. $\underset{L/T}{A} = \underset{L\ T^{-1}}{BC}$

{ dimensions: tell us about what we are meaning (length, velocity ...)
units: a mean to measure dimension (meters, meters per second ...)

Postulate that D related to { the drag coefficient ξ; the thermal energy E_{Th} ($k_B T$) }



drag force $\underline{F_d} = -\xi\, \underline{v}$

body in fluid $\xi = 6\pi\, \mu\, a$ (for sphere of radius a fluid of viscosity μ)

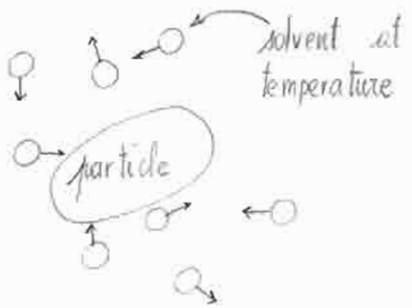
dimensions: $\left.\begin{array}{ll} D: & \dfrac{L^2}{t} \\ \xi: & \dfrac{M}{t} \\ E_{th}: & \dfrac{ML^2}{t} \end{array}\right\}$ The dimensionally correct coefficient is

$$\boxed{D \sim \frac{k_B T}{\xi}}$$

never get coefficients from this approach

$$\langle x^2 \rangle \sim D t$$

- Brownian forces & the Langevin equation



model $\longrightarrow$ solvent collisions on particle described by thermal force $\underline{f}$

Langevin equation: $\underline{F} = m\,\underline{a}$, $\underline{r}(t)$ = position

$$m \frac{d^2 \underline{r}(t)}{dt^2} = \underbrace{-\xi \frac{d\underline{r}(t)}{dt}}_{\text{drag}} + \underbrace{\underline{f}(t)}_{\text{thermal}} + \underbrace{\underline{G}(t)}_{\text{others: electric field, magnetic field}}$$

Thermal (Brownian) forces
- fluctuate rapidly ($\sim 10^{-13}$ s in water)
- cannot be represented by a simple functional form

$\rightarrow$ use stochastic (statistical) model for $\underline{f}$

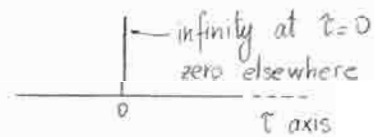
random in direction $\langle \underline{f} \rangle = 0$

uncorrelated on the time scale of particle motion

$$\langle \underline{f}(t) \cdot \underline{r}(t) \rangle = \langle \underline{f}(t) \rangle \langle \underline{r}(t) \rangle = 0$$

$$\begin{cases} \langle \underline{f} \rangle = 0 \\ \langle \underline{f}(t)\, \underline{f}(t+\tau) \rangle = \underset{\substack{\downarrow \\ \text{unknown tensor}}}{\underline{\underline{F}}}\ \delta(\tau) \end{cases}$$

$\delta(\tau)$ $\rightarrow$ delta function



$$\int_{-\infty}^{+\infty} \delta(\tau)\, d\tau = 1$$

$$\int_{-\infty}^{+\infty} \delta(t)\, g(t)\, dt = g(0)$$

Manipulate equations with $\dot{\underline{r}} = \dfrac{d\underline{r}}{dt}$

$$m \frac{d\dot{\underline{r}}}{dt} - \xi \dot{\underline{r}} + \underline{f} = 0$$

multiply by $\underline{r}$ and take ensemble average.

$$m\left(\frac{d}{dt}\langle \underline{r}\,\dot{\underline{r}}\rangle - \langle \dot{\underline{r}}\,\dot{\underline{r}}\rangle\right) = -\xi \langle \underline{r}\,\dot{\underline{r}}\rangle + \underbrace{\langle \underline{r}(t)\,\underline{f}(t)\rangle}_{=0}$$

* equipartition theorem

$$\frac{1}{2} m \langle \underline{\dot{r}}\, \underline{\dot{r}} \rangle = \frac{1}{2} k_B T \, \underline{\underline{\delta}} \qquad \text{where} \quad \underline{\underline{\delta}} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

* $m \dfrac{d}{dt} \langle \underline{r}\, \underline{\dot{r}} \rangle + \xi \langle \underline{r}\, \underline{\dot{r}} \rangle = k T \, \underline{\underline{\delta}}$

solve and use boundary conditions $r(0) = 0$

$$\frac{d}{dt} \langle \underline{r}\, \underline{r} \rangle = \frac{2kT}{\xi} \underline{\underline{\delta}} \left(1 - \exp\left(- \frac{\xi}{m} t\right)\right)$$

integrate and use BC $r(0) = 0$

$$\boxed{\langle \underline{r}\, \underline{r} \rangle = \frac{2kT}{\xi} \underline{\underline{\delta}} \left\{ t + \frac{m}{\xi} \left[\exp\left(- \frac{\xi}{m} t\right) - 1 \right] \right\}}$$

▷ 2 limiting cases

- $t \ll \dfrac{m}{\xi}$ very short time scale

$$\exp(- \xi t / m) \simeq 1 - \frac{\xi}{m} t + \frac{1}{2} \left(\frac{\xi}{m}\right)^2 t^2 \ldots$$

$$\langle \underline{r}\, \underline{r} \rangle = \frac{kT}{m} \underline{\underline{\delta}}\, t^2 \quad \text{ballistic-like motion}$$

- $t \gg \dfrac{m}{\xi}$ very long time scale

$$\langle \underline{r}\, \underline{r} \rangle = \frac{2kT}{\xi} \underline{\underline{\delta}}\, t \quad \text{diffusive motion}$$

▷ Some numbers :

- globular protein: molecular weight 100 kDa

$m = 170 \cdot 10^{-24}$ kg

$\xi \simeq 6\pi \mu a$

$a \simeq 3$ nm

$\mu_{water} \simeq 10^{-3}$ Pa.s

- characteristic time $\dfrac{m}{\xi} \simeq 3.10^{-12}$ s
- how far does it travel in time m/ξ ?

distance $\simeq 10^{-11}$ m $= 10^{-2}$ nm

then diffusion Perrin model