Entropy in biology: homework review

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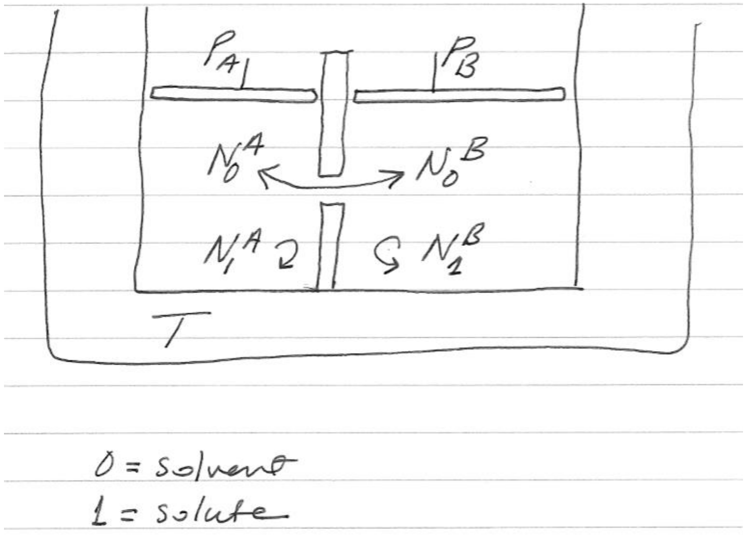
Homework 1: osmotic system

- Osmotic system with finite number of molecules



- Fixed number of solute molecules N_1^A, N_1^B
- $n = N_0^B, N_0^A = N_0 - N_0^B$
- Problem reduces to continuous time Markov chain with a single random variable n (see lecture 2)

Homework 1: simulations

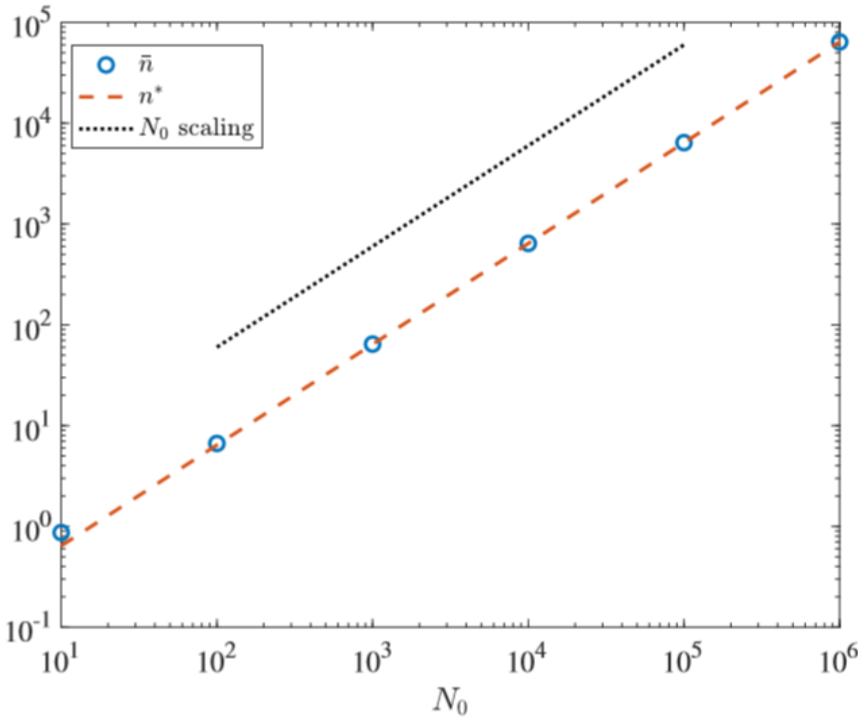
- We determined rate constants for each “reaction”

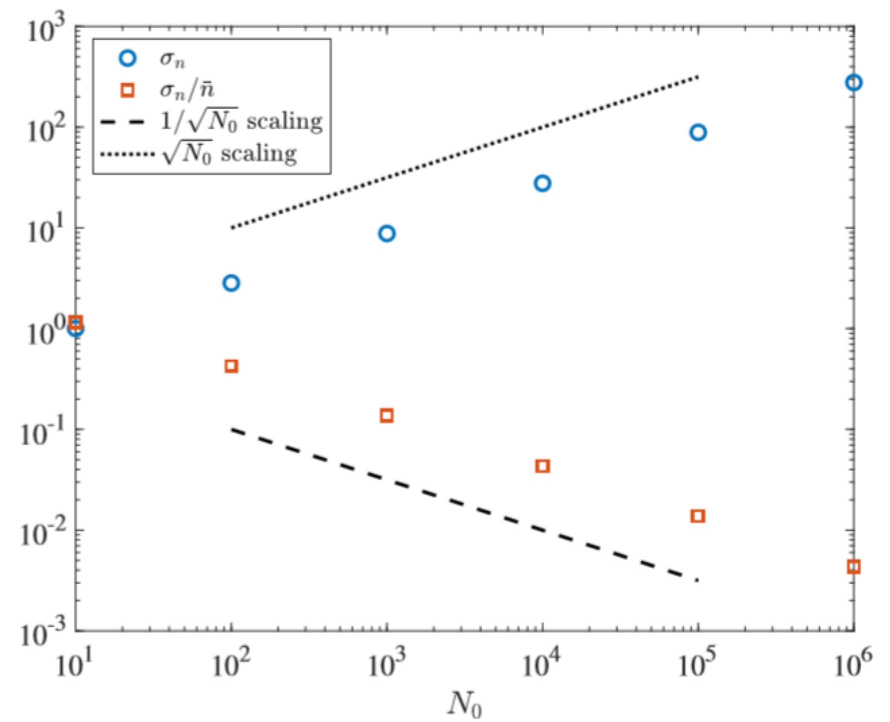
$$\alpha_{n,n+1} = \frac{\gamma\theta_{n,n+1}}{\exp\left(\theta_{n,n+1}\right) - 1} \qquad \alpha_{n,n-1} = \frac{\gamma\theta_{n-1,n}}{1 - \exp\left(-\theta_{n-1,n}\right)}$$

- Transition times are exponentially distributed, choose the first and continue
- Macroscopic equilibrium: osmotic pressure balances pressure difference

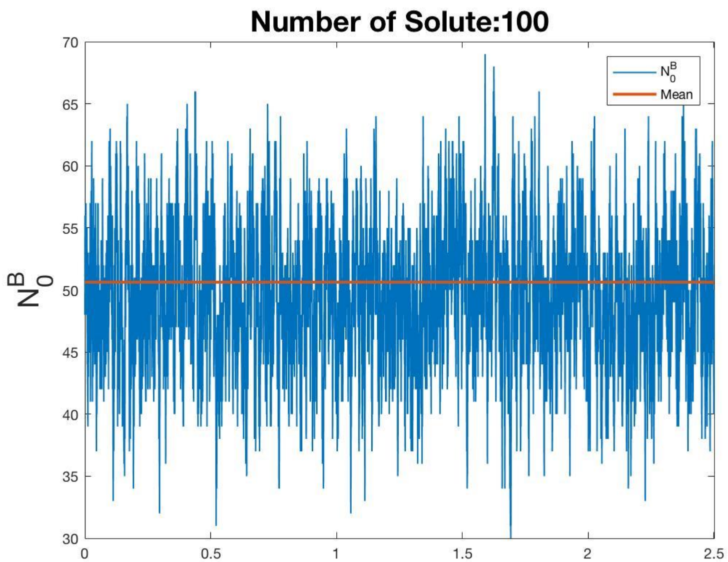
Homework 1: results

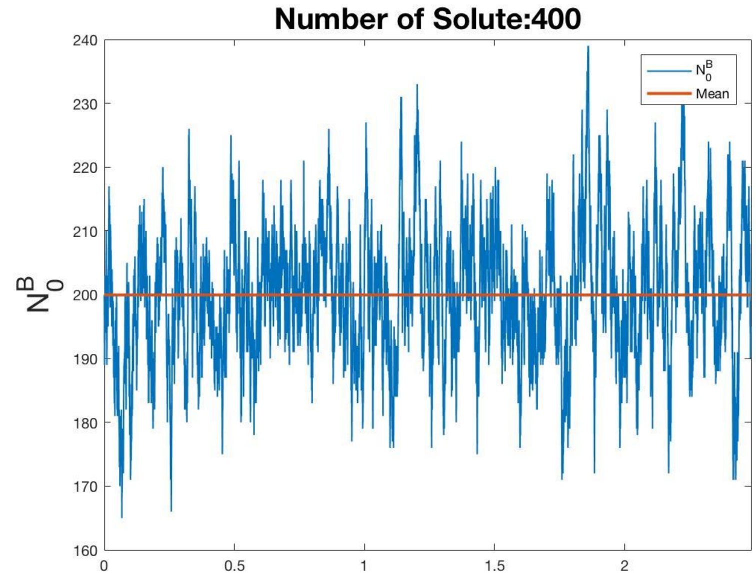
- Mean n converges to macroscopic equilibrium and scales linearly with system size
- Fluctuations: σ_n= standard deviation in n scales as $\sqrt{n}$

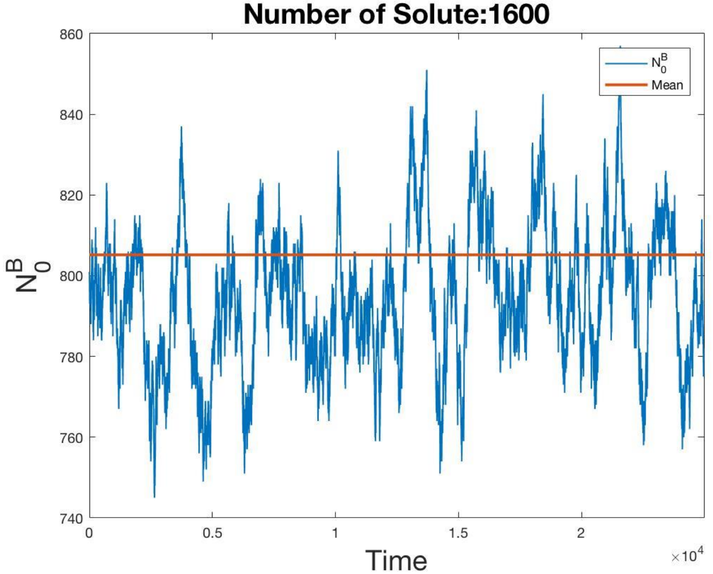


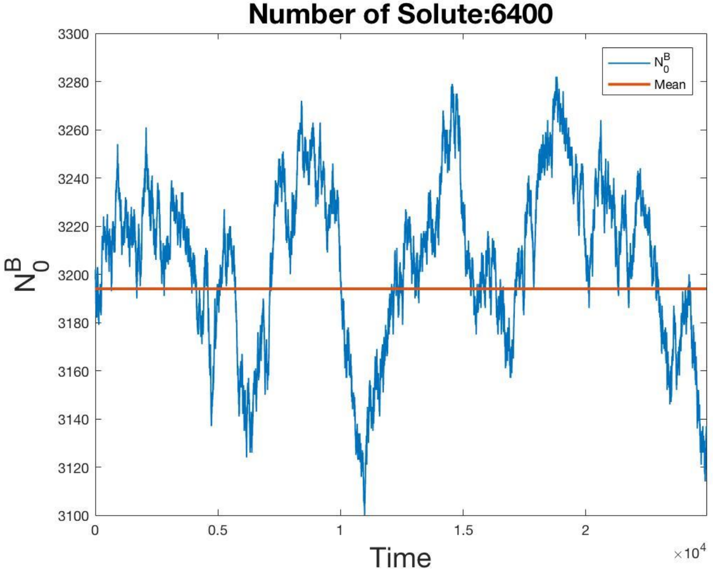


Homework 1: trajectories









Homework 2: 1D Poisson-Boltzmann

We are trying to solve the standard 1D Poisson-Boltzmann equation for dilute solutions

$$-\Delta\phi = \frac{1}{\epsilon}\left(\rho_b(x) + \sum_{i=1}^{n} q z_i c_i(x)\right), \quad \text{where} \tag{1}$$

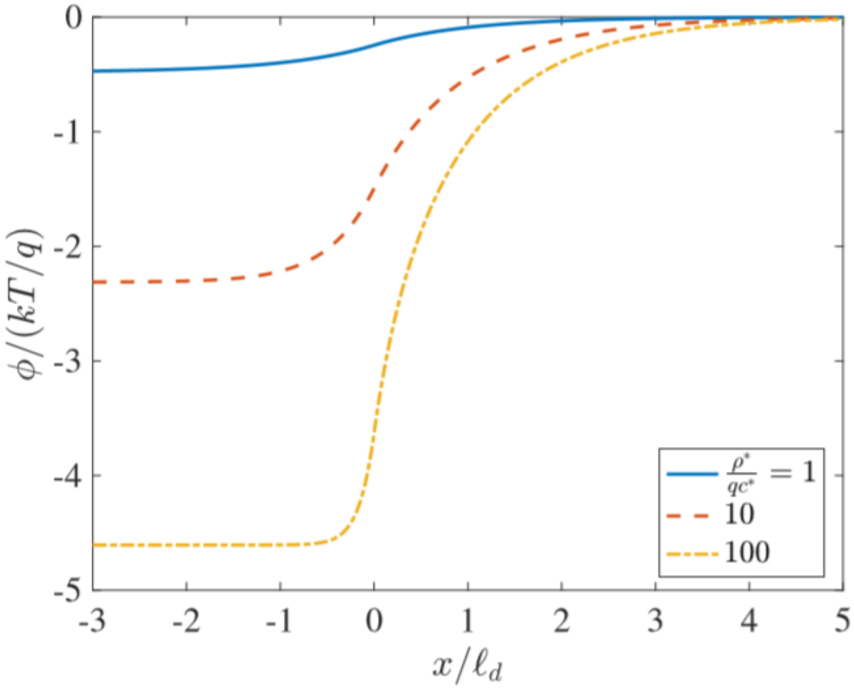
$$c_i(x) = c_i^{\infty} \exp\left(\frac{-q z_i \phi}{kT}\right). \tag{2}$$

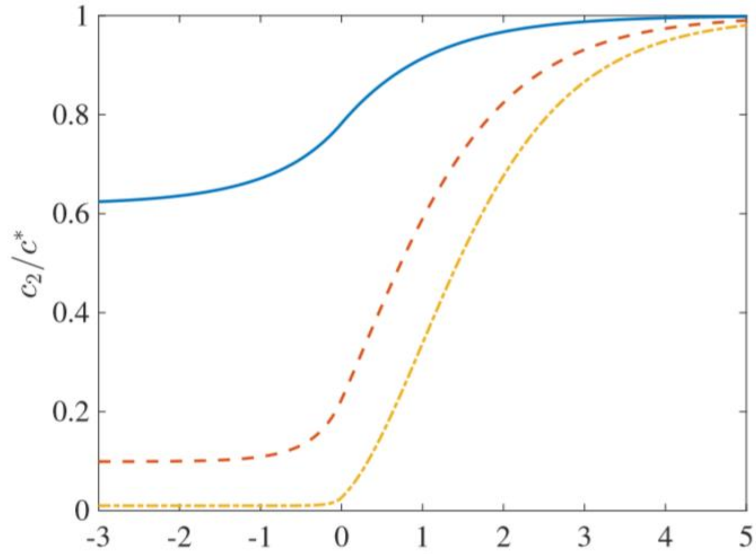
We are considering $n = 2$ ions with $z_1 = 1$ and $z_2 = -1$ with boundary conditions $c_1(\infty) = c_2(\infty) = c^*$ and $\phi(\infty) = 0$. The background charge density is given by

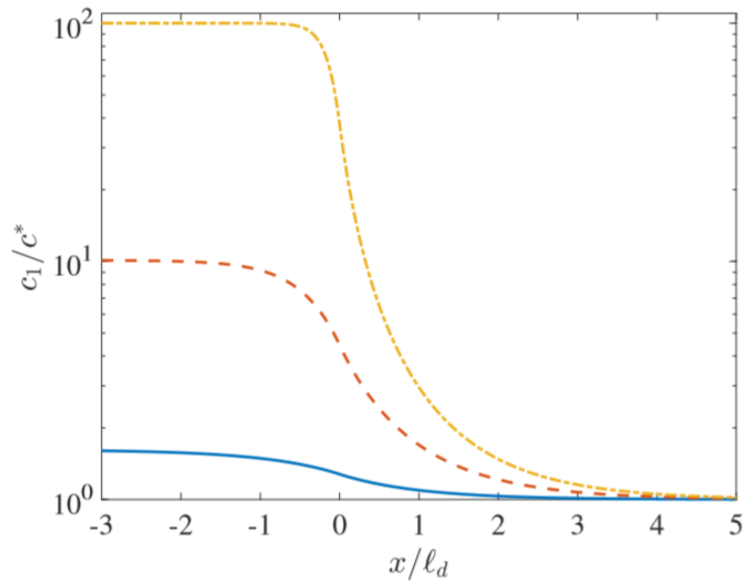
$$\rho_b(x) = \begin{cases} -\rho^* & x < 0 \\ 0 & x > 0 \end{cases}. \tag{3}$$

Homework 2: solution

- See [lecture 4] for formulas, plots below







Homework 3: Cell volume control

Ionic fluxes: in class we derived the flux law

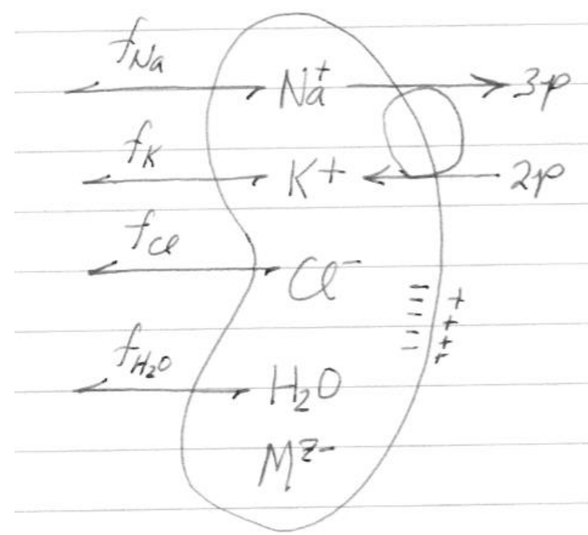
$$f\left(c^{int}, c^{ext}, \phi\right)$$

By considering 3 assumptions: mass action, thermodynamics, and Ohm's law

$$f(c_1, c_2, \phi) = c_1 f_1(\phi) - c_2 f_2(\phi)$$

$$f\left(c e^{-\frac{qz\phi}{kT}}, c, \phi\right) = 0$$

$$f(c, c, \phi) = \gamma c \phi q z$$



Homework 3: new flux derivation

- Deriving the flux law in lecture 5 by diffusion & drift in a cylinder

$$\frac{dF}{dx} = 0 \qquad \text{with} \qquad F = -D\frac{dc}{dx} + \mu\frac{qz\phi}{\ell_m}c. \tag{1}$$

The ODE we need to solve for $c(x)$ is therefore,

$$-D\frac{d^2c}{dx^2} + \mu\frac{qz\phi}{\ell_m}\frac{dc}{dx} = 0. \tag{2}$$

The general solution to this is given by

$$c(x) = c_0 + c_1 \exp\left(kx/\ell_m\right), \quad \text{where} \quad k = \frac{qz\phi\mu}{D} \tag{3}$$

with c_0 and c_1 unknown constants to be determined from the boundary conditions

$$c(0) = c^{\text{int}} \qquad c(\ell_m) = c^{\text{ext}}. \tag{4}$$

Notice we have introduced a k that is different from Boltzmann's constant, which we will refer to as k_B. Solving for c_0 and c_1, we have

$$c_0 = \frac{c^{\text{ext}} - e^k c^{\text{int}}}{1 - e^k} \qquad c_1 = \frac{c^{\text{int}} - c^{\text{ext}}}{1 - e^k}. \tag{5}$$

The flux is then given by

$$F(x) = -\frac{kDc_1}{\ell_m}\exp\left(kx/\ell_m\right) + \frac{Dk}{\ell_m}\left(c_0 + c_1\exp\left(kx/\ell_m\right)\right) \tag{6}$$

$$= \frac{Dkc_0}{\ell_m} \tag{7}$$

Homework 3: new flux derivation

For $F(x) = 0$, we need $c_0 = 0$. Using our notation, the zero flux condition is that $F(x) = 0$ when $c^{\text{int}} = c^{\text{ext}} \exp\left(-\frac{Dk}{\mu k_B T}\right)$. Plugging this into Eq. (5), we have that

$$c_0 = c^{\text{ext}} \frac{1 - \exp\left(k\left(1 - \frac{D}{\mu k_B T}\right)\right)}{1 - e^{-k}} \tag{8}$$

$$1 = \frac{D}{\mu k_B T} \rightarrow D = \mu k_B T. \tag{9}$$

Eq. (9) is the Einstein relation as desired. Substituting this into the expression for k in Eq. (3), we have $k = \frac{qz\phi}{k_B T}$. If we multiply c_0 by $-e^k / -e^k$, we obtain a formula for the flux,

$$F = \frac{qz\phi\mu}{\ell_m}\left(\frac{c^{\text{int}} - \exp\left(-\frac{qz\phi}{k_B T}\right)c^{\text{ext}}}{1 - \exp\left(-\frac{qz\phi}{k_B T}\right)}\right). \tag{10}$$

Comparing to (14) in the notes, we have

$$\frac{f}{F} = \frac{\gamma \ell_m}{\mu} = \frac{\alpha D}{\mu k T} = \alpha. \tag{11}$$

So the ratio of the two fluxes is just the ratio of the length of channel to the length of membrane, and we derived the same (Goldman-Hodgkin-Katz) flux law.

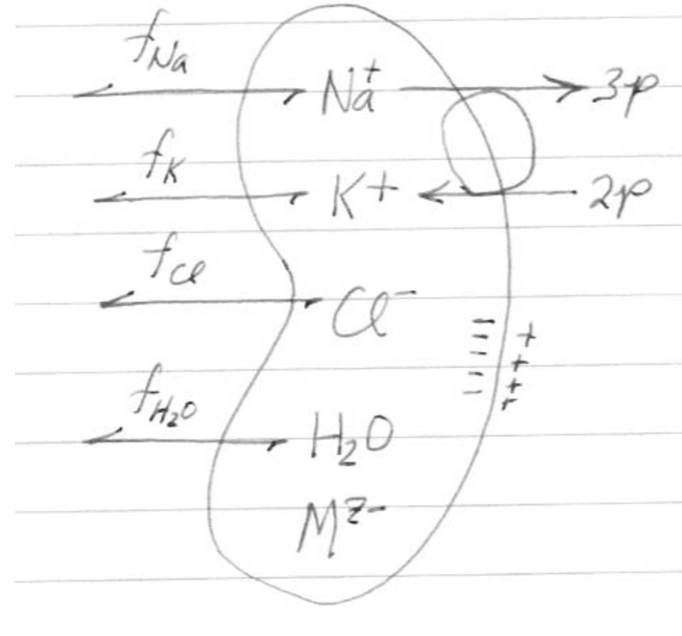
Homework 3: steady state

$$f_{Na^+} + 3p = 0$$

$$f_{K^+} - 2p = 0$$

$$f_{Cl^-} = 0$$

$$f_{H_2O} = 0$$



- Fifth equation: intracellular electroneutrality
- Plug in fluxes from prior part, get 5 equations in 5 unknowns: $[Na^+]^{int}, [K^+]^{int}, [Cl^-]^{int}, \phi^{int}, V$

Homework 3: steady state

$$R = \frac{Q_M}{q V 2 [Cl^-]^{ext}}$$

- Solve for R in terms of known quantities

$$[Na^+]^{int}\left[(1-R)\left(1-\frac{3\gamma_{K^+}}{2\gamma_{Na^+}}\right)\right] = [Na^+]^{ext} - \frac{3\gamma_{K^+}}{2\gamma_{Na^+}}\left(\left([Na^+]^{ext}+[K^+]^{ext}\right)(1-R^2) - [K^+]^{ext}\right)$$

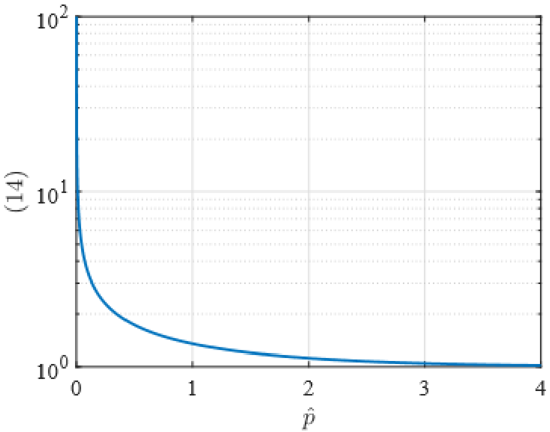
- Set $[Na^+]_{int} = 0$ and solve for R

$$R_{\max} = \sqrt{q\left(1-\frac{2r}{3}\right)}, \quad \text{where} \quad q = \frac{[\mathrm{Na}^+]^{\mathrm{ext}}}{[\mathrm{Na}^+]^{\mathrm{ext}} + [\mathrm{K}^+]^{\mathrm{ext}}} \quad \text{and} \quad r = \frac{\gamma_{\mathrm{Na}^+}}{\gamma_{\mathrm{K}^+}}.$$

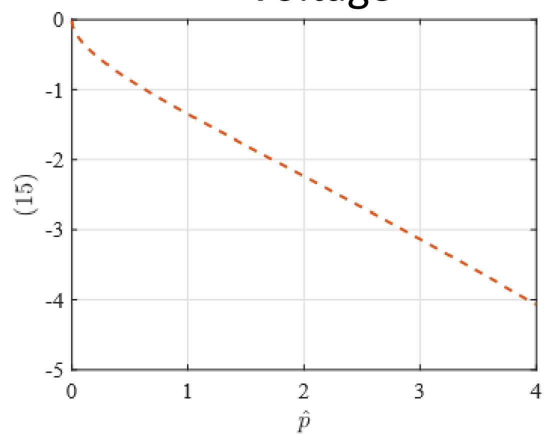
Homework 3: steady state plots

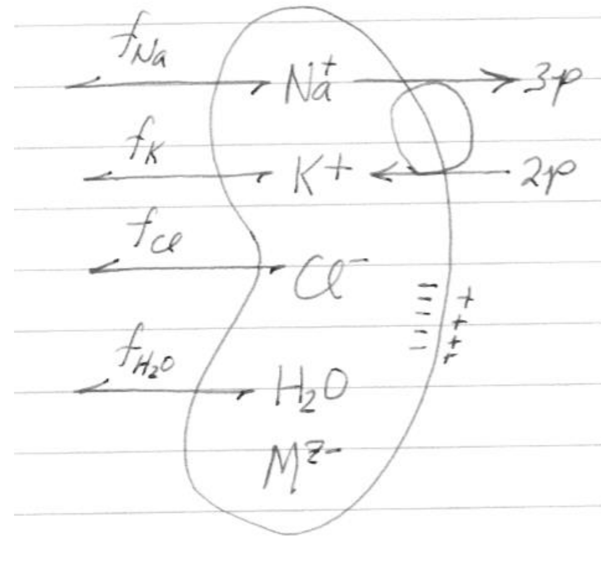
- $\hat{p}$ is the pump rate

Volume



Voltage



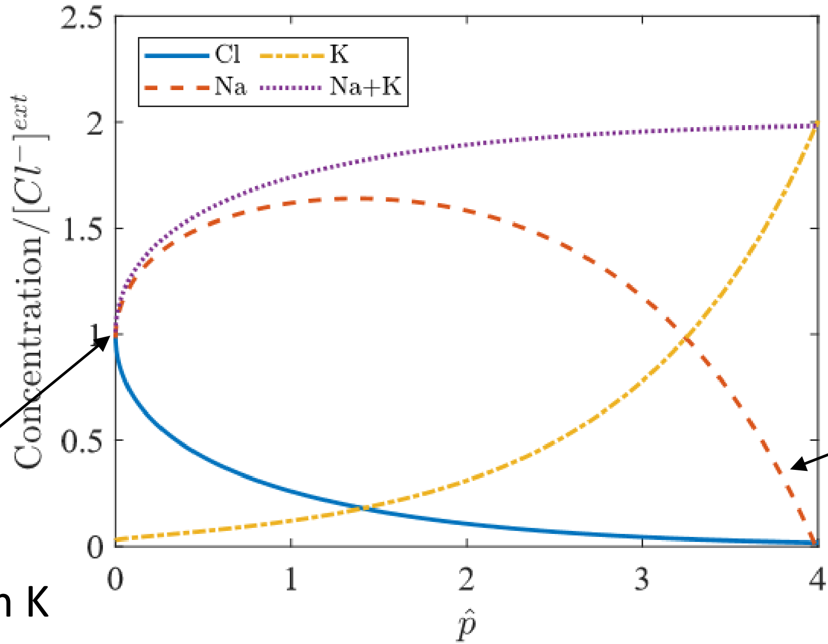


$$\hat{p}(R) = R \log\left(\frac{1}{1-R}\right)$$

$$\frac{V}{\frac{Q_M/q}{2[\mathrm{Cl}^-]^{\mathrm{ext}}}} = \frac{1}{R}$$

$$\frac{\phi^{\mathrm{int}}}{\frac{kT}{q}} = \log(1-R).$$

Homework 3: steady state plots



No pumping, cell doesn't know Na from K

Na is pumped OUT, goes to 0 as p grows

$$\hat{p}(R) = R \log\left(\frac{1}{1-R}\right)$$

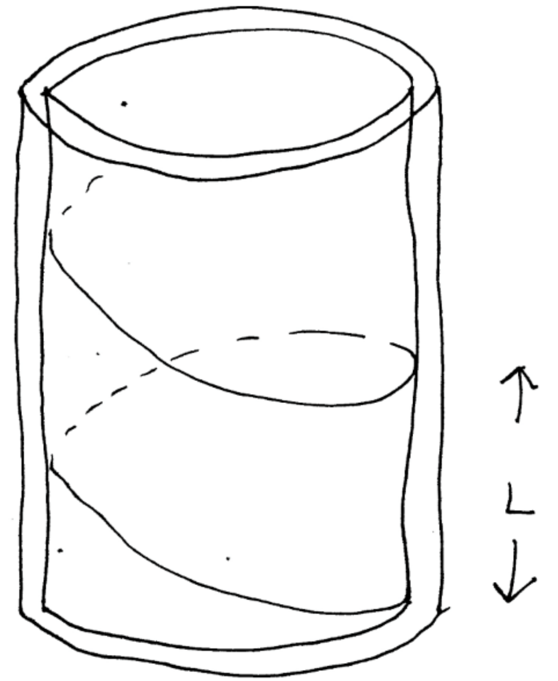
$$\frac{[\mathrm{Na}^+]^{\mathrm{int}} + [\mathrm{K}^+]^{\mathrm{int}}}{[\mathrm{Cl}^-]^{\mathrm{ext}}} = 1 + R$$

$$\frac{[\mathrm{Cl}^-]^{\mathrm{int}}}{[\mathrm{Cl}^-]^{\mathrm{ext}}} = 1 - R.$$

Homework 4: rotary motors

- Surface charge density on rotor surface

$$\sigma_0 = -f\left(\theta + \omega t + 2\pi \frac{z}{L}\right)$$



- Symmetric matrix for relationship between rotation rate & current and torque and voltage (electric field x length) – see [lecture 7]

$$\begin{pmatrix} \omega \\ I \end{pmatrix} = q\left(\frac{D}{kT}\right)\left(\frac{2\pi}{L L_m}\right)\begin{pmatrix} \frac{1}{rL(\bar{f} - f_H)} & 1 \\ 1 & rL\bar{f} \end{pmatrix}\begin{pmatrix} T \\ V \end{pmatrix}$$

Homework 4: turning flagella

Assume that the motor is turning a load (like a bacterial flagellum) in a viscous fluid, so that

$$T = -\beta \omega$$

where β is a constant that is characteristic of the load

(i) Evaluate $\bar{\omega}$, T, and I as functions of β. As a check evaluate

$$\begin{pmatrix} \omega \\ I \end{pmatrix} = q\left(\frac{D}{kT}\right)\left(\frac{2\pi}{LL_m}\right)\begin{pmatrix} \frac{1}{rL(\bar{f}-f_H)} & 1 \\ 1 & rL\bar{f} \end{pmatrix}\begin{pmatrix} T \\ V \end{pmatrix}$$

with $V = v^{ext} - v^{int} + \frac{kT}{q}\log\left(\frac{c^{ext}}{c^{int}}\right)$ given

(i) We first assume that

$$T = -\beta\omega \rightarrow \omega = -T/\beta \quad (1)$$

Let $a = \frac{1}{rL(\bar{f}-f_H)}$, $b = rL\bar{f}$, where $ab - 1 > 0$

and $c = q\left(\frac{D}{kT}\right)\left(\frac{2\pi}{LL_m}\right)$. $(*)$

then

$$\omega = c(aT + V) \quad (1)$$

$$I = c(T + bV) \quad (2)$$

Using assumption (1)

$$-T/\beta = c(aT + V) \longrightarrow cV = -T\left(\frac{1}{\beta} + ca\right)$$

$$\boxed{T = \frac{-cV}{\frac{1}{\beta} + ca}} \longrightarrow \boxed{\lim_{\beta\to\infty} T = -V/a = T_{stall}}$$

$$\omega = -T/\beta = \boxed{\frac{cV}{1 + ca\beta} = \omega} \rightarrow \boxed{\lim_{\beta\to 0} \omega = cV = \omega_{free}}$$

$$I = cT + cbV$$

$$\boxed{I = \frac{-c^2V}{\frac{1}{\beta} + ca} + cbV} \longrightarrow \boxed{\begin{aligned} &\lim_{\beta\to 0} I = cbV = I_{free} \\ &\lim_{\beta\to\infty} I = -\frac{cV}{a} + cbV = I_{stall} \end{aligned}}$$

$$\mathcal{E}_m = \frac{-T\omega}{VI}$$

(ii.1) Prove that $\mathcal{E}_m \in (0, 1)$ for any $\beta \in (0, \infty)$.

(ii.2) Evaluate $\mathcal{E}_m$ as a function of β

(ii.3) Let β^* be the value of β that maximizes $\mathcal{E}$, and let $\mathcal{E}_m^* = \mathcal{E}_m(\beta^*)$. Evaluate β^* and $\mathcal{E}_m^*$.

(ii.4) With all other parameters constant, How should L be chosen to maximize $\mathcal{E}_m^*$. Recall that the possible values of L are discrete:

$$L = L_m,\ L_m/2,\ L_m/3,\ \cdots$$

(ii) Using (1) and (2), we have

$$\varepsilon_m = -\frac{cT(aT+V)}{cV(T+bV)} = -\frac{T}{V}\left(\frac{aT+V}{T+bV}\right)$$

(ii.1)

$$aT+V = -\frac{caV}{\frac{1}{\beta}+ca} + \frac{caV+V/\beta}{\frac{1}{\beta}+ca} = \frac{V/\beta}{\frac{1}{\beta}+ca} = \frac{V}{1+ca\beta}$$

$$T+bV = \frac{-cV}{\frac{1}{\beta}+ca} + \frac{\frac{bV}{\beta}+bacV}{\frac{1}{\beta}+ca} = \frac{cV(ab-1)}{\frac{1}{\beta}+ca} + \frac{bV}{1+ca\beta}$$

So

$$\frac{aT+V}{T+bV} = \frac{V}{cV\beta(ab-1)+bV} = \frac{1}{c\beta(ab-1)+b}$$

and

$$\varepsilon_m = -\frac{T}{V}\left(\frac{1}{c\beta(ab-1)+b}\right)$$

$$\varepsilon_m = \frac{c\beta}{1+\beta ca}\left(\frac{1}{c\beta(ab-1)+b}\right)$$

Since $ab>1$, $\varepsilon_m > 0$ since $a,b,c>0$ and $\beta>0$.

Further

$$\varepsilon_m = \frac{c\beta}{c\beta(2ab-1)+\underbrace{b+(\beta c)^2 a(ab-1)}_{>0}}$$

(expanding the denominator).

So since $ab>1$, $\dfrac{c\beta}{c\beta(2ab-1)} < 1$, so $\varepsilon_m < 1$.

(since the rest of the denominator is >0).

(ii.2) From the previous part,

$$\boxed{\varepsilon_m = \frac{c\beta}{1+c\beta a}\left(\frac{1}{c\beta(ab-1)+b}\right)}$$

where a, b, c are defined in (*)

(ii.3) $\dfrac{d\mathcal{E}_m}{d\beta} = \dfrac{c(-ba^2\beta^2c^2 + a\beta^2c^2 + b)}{((a\beta c+1)^2(b-\beta c + ab\beta c)^2)} = 0.$ (Set derivative to 0 to maximize $\mathcal{E}_m$)

So $-ba^2\beta^2c^2 + a\beta^2c^2 + b = 0$

$$\beta^2(ac^2 - a^2bc^2) = -b$$

$$\beta^2 = \frac{b}{ac^2(ab-1)}$$

$$\boxed{\beta^* = \sqrt{\frac{b}{ac^2(ab-1)}}}$$

$$\mathcal{E}_m^* = \mathcal{E}_m(\beta^*) = \frac{c}{\left(\frac{1}{\beta^*} + ca\right)}\left(\frac{1}{c(ab-1)\beta^* + b}\right)$$

$$\mathcal{E}_m^* = \frac{c}{c(ab-1) + \sqrt{bac^2(ab-1)} + \sqrt{bac^2(ab-1)} + abc}$$

$$\boxed{\mathcal{E}_m^* = \frac{c}{\left(\sqrt{c(ab-1)} + \sqrt{abc}\right)^2} = \frac{1}{\left(\sqrt{ab-1} + \sqrt{ab}\right)^2}}$$

Let $L = \frac{L_m}{m}$. then

$$c = g\left(\frac{D}{kT}\right)\left(\frac{m\,2\pi}{L_m^2}\right) \qquad a = \frac{m}{rL_m(\bar{f} - f_H)} \qquad b = \frac{rL_m\bar{f}}{m}$$

Notice that $ab = \frac{\bar{f}}{\bar{f} - f_H}$ does not depend on m. So

at β^*, L is irrelevant to $\mathcal{E}_m^*$.
L can be chosen arbitrarily

Homework 4: will skip this

Homework

Assume that the ion pump is driven by a fixed torque $T > 0$, and that it is opposed by an electrochemical potential difference V such that

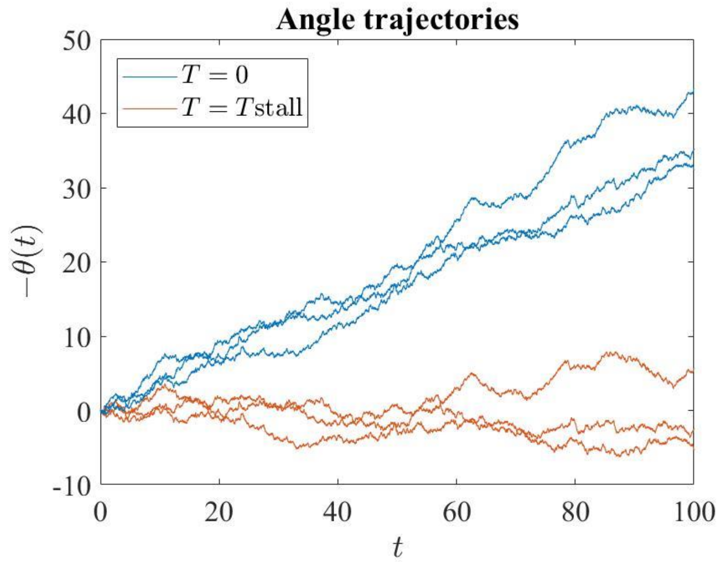
$$-\frac{T}{rL\bar{f}} < V < 0$$

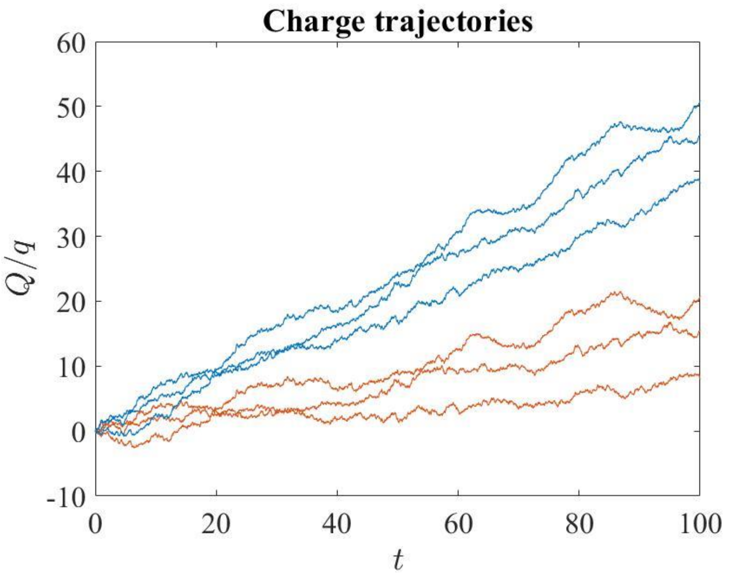
The efficiency of the ion pump can be defined as

$$\mathcal{E}_p = \frac{-VI}{T\omega}$$

Homework 4: Brownian dynamics

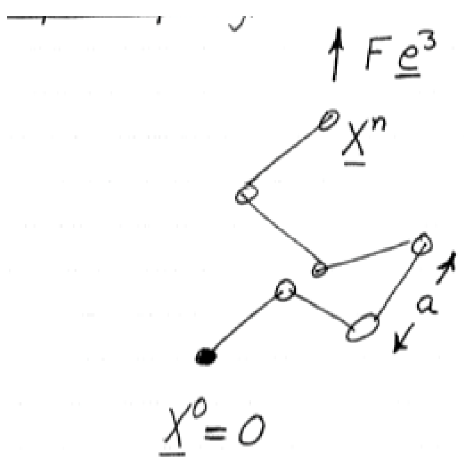
- $T = 0$ (motor freely rotating) or $T = T_{stall}$ (motor stalled)
- Without noise: θ increases linearly in time for free motor, slope $q\left(\frac{D}{kT}\right)\left(\frac{2\pi}{LL_m}\right)V \approx 0.38$
- Charge increases linearly in time in both cases, faster for free motor

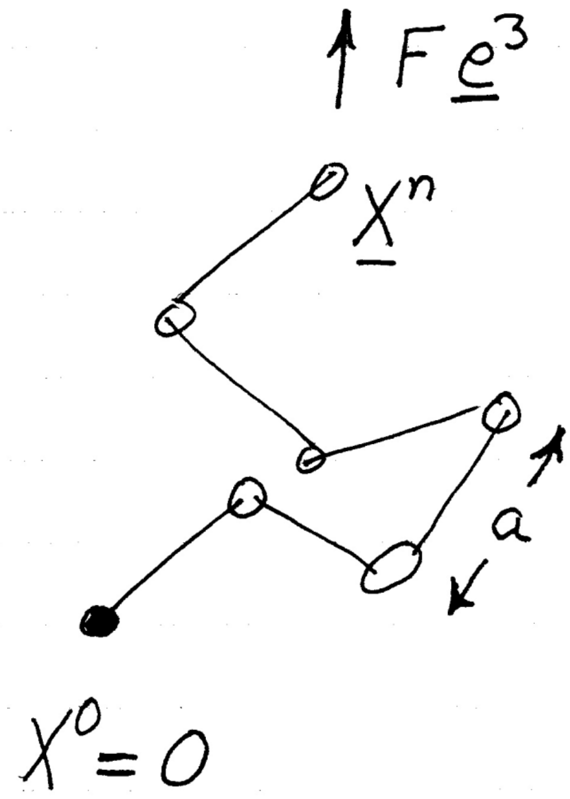




Homework 5: entropic spring

- Freely jointed chain with force at the end
- See lecture 8

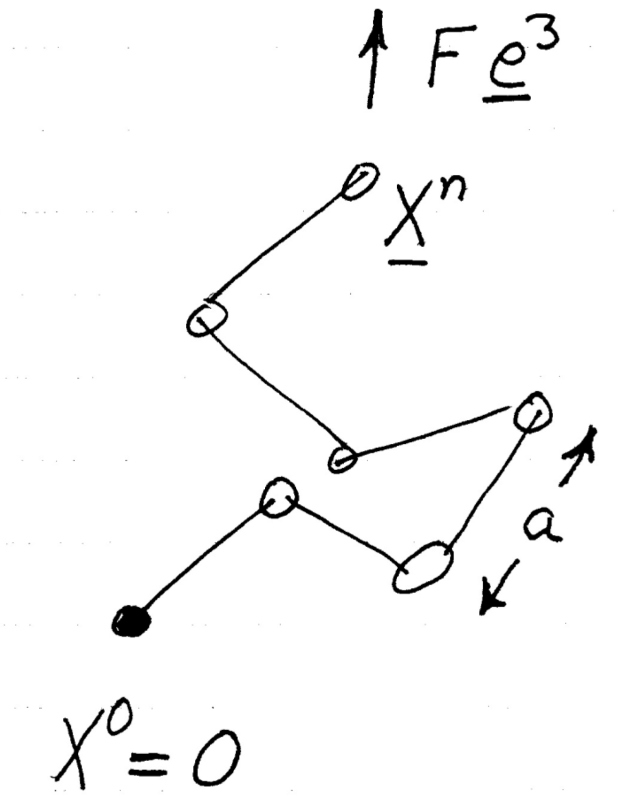




Our model

- n chain of links of length a
- Nodes at position $\boldsymbol{X}^{i}$
- Node 0 is fixed at 0 and we pull on the last node with force $F\boldsymbol{e}^{3}$
- Let $\boldsymbol{D}^{i} = \boldsymbol{X}^{i} - \boldsymbol{X}^{i-1}$
- The potential energy is

$$U = -F\boldsymbol{e}^{3} \cdot \boldsymbol{X}^{n} = -F\sum_{i=0}^{n} D_3^i$$



Our model

- At temperature T
- The equilibrium distribution is

$$\rho(\boldsymbol{D}^{\boldsymbol{0}}, \dots, \boldsymbol{D}^{\boldsymbol{n}}) = Z^{-1} \exp\left(\frac{U}{kT}\right)$$

$$= Z^{-1} \exp\left(\frac{F \sum_{i=0}^{n} D_3^i}{kT}\right)$$

$$= \prod_{i=0}^{n} Z_D^{-1} \exp\left(\frac{F D_3^i}{kT}\right) = \prod_{i=0}^{n} \rho_D(\boldsymbol{D}^{\boldsymbol{i}})$$

Question 1: Expected Chain Length

- Let $R^2 = \|\boldsymbol{X^n}\|^2$. We wish to compute $\mathbb{E}[R^2]$. To this we expand:
    - $R^2 = \left\|\sum_{i=1}^n \boldsymbol{D^i}\right\|^2 = \sum_{i,j=1}^n \boldsymbol{D^i} \cdot \boldsymbol{D^j}$
- $\mathbb{E}[R^2] = \sum_{i,j=1}^n \mathbb{E}\left[\boldsymbol{D^i} \cdot \boldsymbol{D^j}\right]$
- $= \sum_{i=1}^n \mathbb{E}\left[\boldsymbol{D^i} \cdot \boldsymbol{D^i}\right] + \sum_{\substack{i,j=1 \\ i \neq j}}^n \mathbb{E}\left[\boldsymbol{D^i} \cdot \boldsymbol{D^j}\right]$
- $= \sum_{i=1}^n \mathbb{E}\left[\left\|\boldsymbol{D^i}\right\|^{\boldsymbol{2}}\right] + \sum_{\substack{i,j=1 \\ i \neq j}}^n \mathbb{E}\left[\boldsymbol{D^i}\right] \cdot \mathbb{E}\left[\boldsymbol{D^j}\right]$
- Now recall that $\boldsymbol{D^i}$ are i.i.d., have length a and are distributed according to
- $\rho_D\left(\boldsymbol{D^i}\right) = Z_D^{-1} \exp\left(\frac{F D_3^i}{kT}\right)$, so
- $\mathbb{E}\left[D_1^i\right] = \mathbb{E}\left[D_2^i\right] = 0.$

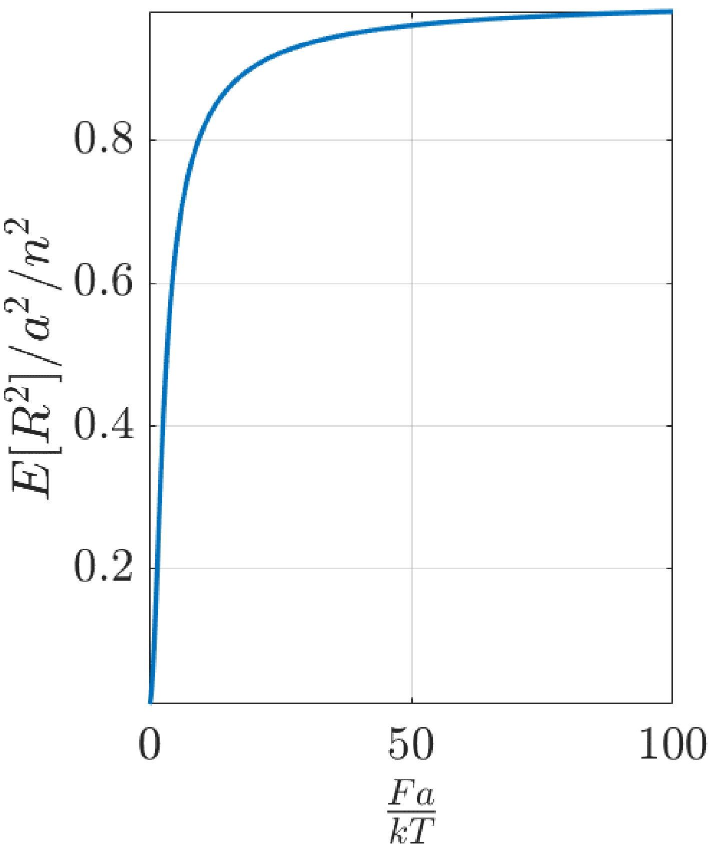
Question 1 (cont.)

$$\mathbb{E}[R^2] = \sum_{i=1}^{n} \mathbb{E}\left[\left\|\boldsymbol{D^i}\right\|^2\right] + \sum_{\substack{i,j=1 \\ i\neq j}}^{n} \mathbb{E}[\boldsymbol{D^i}] \cdot \mathbb{E}[\boldsymbol{D^j}]$$

$$= \sum_{i=1}^{n} a^2 + \sum_{\substack{i,j=1 \\ i\neq j}}^{n} \mathbb{E}[D_3^i]\mathbb{E}\left[D_3^j\right]$$

$$= na^2 + n(n-1)\mathbb{E}[D_3^1]^2$$

$$= na^2 + n(n-1)a^2\left(\coth\left(\frac{Fa}{kT}\right) - \left(\frac{Fa}{kT}\right)^{-1}\right)^2$$

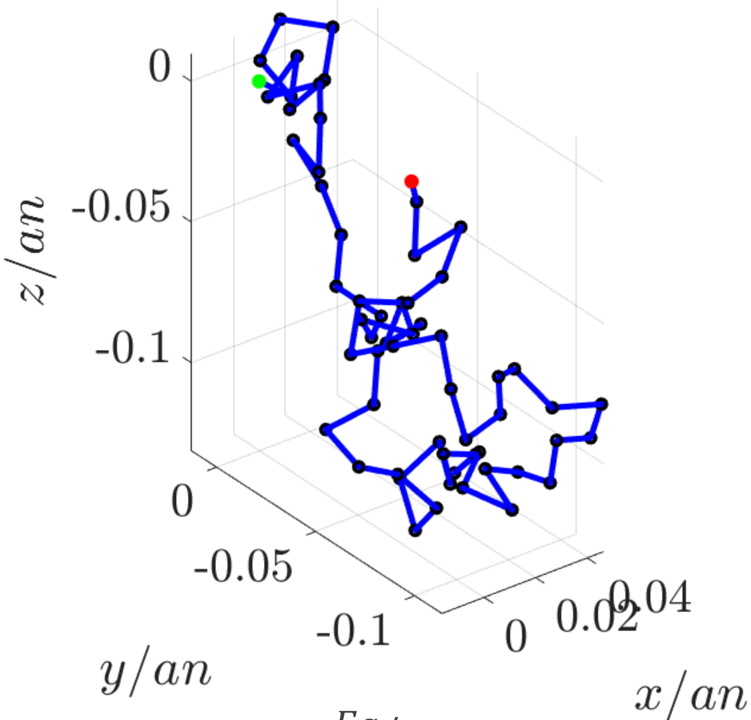


Question 2: Simulated Chains

We wish to draw sample chains from the equilibrium distribution.

$\boldsymbol{D}^{\boldsymbol{i}}$ are independent, so we separately generate then add.

Each $\boldsymbol{D}^{\boldsymbol{i}}$ is distributed on the sphere of radius a according to $\rho_D(\xi) = Z_D^{-1} \exp\left(\frac{F\xi}{kT}\right)$



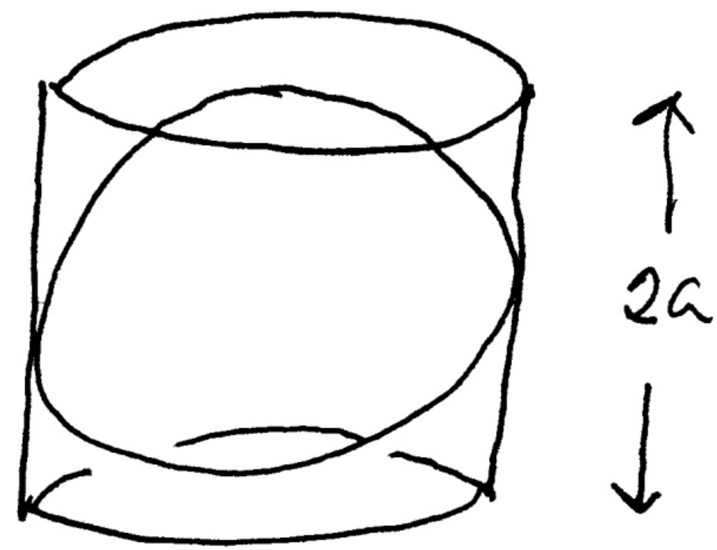
$^{Fa}/_{kT} = 0.2$

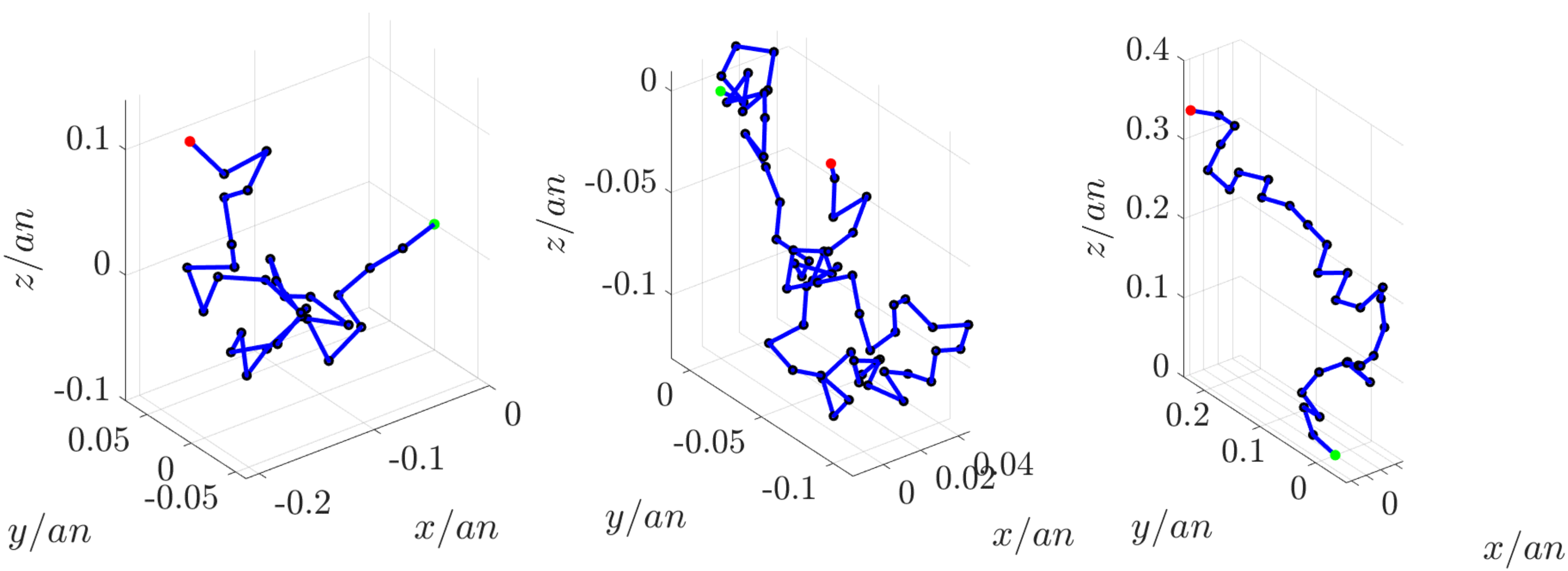
Question 2: Simulated Chains

We generate $\boldsymbol{D}^{\boldsymbol{i}}$ using the rejection method.

To do this we generate samples uniformly on the sphere of radius a using the Archimedes method.

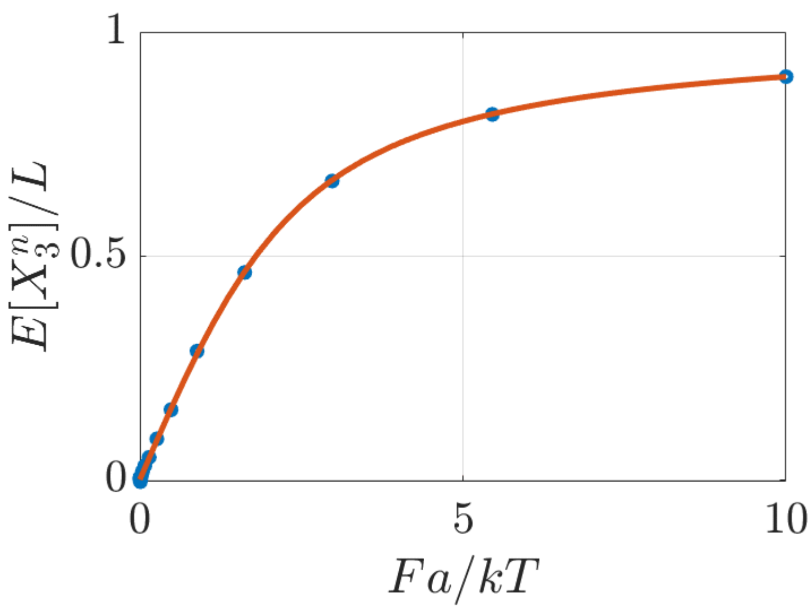
- D_3^i is uniformly distributed between $-a$ and a
- $\left(D_1^i, D_2^i\right)$ is uniformly distributed on the circle of radius $\sqrt{a^2 - (D_3^i)^2}$

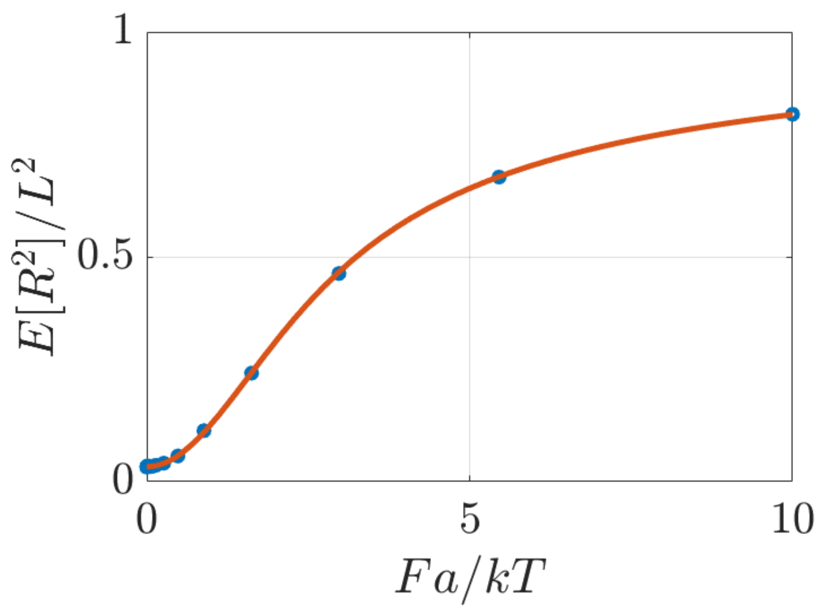




$Fa/_{kT} = 0$ $Fa/_{kT} = 0.2$ $Fa/_{kT} = 1$

Computed values vs. analytical ones





Chain of length 30. Averages computed over 900 trials