ENTROPY IN BIOLOGY

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Lecture 7: (Continuation of Lecture 6*)

Rotary Motors Driven by Transmembrane Ionic Currents

- Positive definiteness of the mobility matrix
- Boundary conditions for the finite case
- Motor characteristics + efficiency (Homework)
- Ion pump characteristics + efficiency (Homework)
- Fluctuations: Introduction to Brownian dynamics (Homework)

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Notice, too, that the matrix in (37) is positive definite, since its trace is obviously positive, and its determinant is

(38) $$\frac{\bar{f}}{\bar{f} - f_H} - 1 > 0$$

and a 2×2 symmetric matrix with a positive trace and determinant is positive definite. The physical significance of this is that

(39) $$\tau\omega + \bar{E}I$$

is the power per unit length consumed by the motor, and this is positive for any choice of $(\tau, \bar{E})$ other than $(0,0)$.

Up to now we have been considering a motor that is infinitely long, but we can make our model much more realistic and applicable by considering a finite length equal to the membrane thickness, denoted L_m. For simplicity, we assume L_m/L is an integer, where L is the helical period.

Let $z=0$ be the interior face of the membrane, and let $z=L_m$ be the exterior face. Let the ionic species that drives the ~~membrane~~ motor be at concentrations c^{int}, c^{ext} on these two sides of the membrane, and let the voltages on these two sides be denoted v^{int}, v^{ext}.

Within the motor, at the boundaries $z=0$ and $z=L_m$, we have the same charge density of the driving ionic species

$$\sigma = f(\theta+\omega t) \tag{40}$$

This charge density is in contact with the interior and exterior ionic solutions, and in cases of close proximity we may assume thermodynamic equilibrium, even though the system as a whole is not in thermodynamic equilibrium. This gives the following pair of equations:

$$f(\theta+\omega t) = q\, c^{int} K e^{-\frac{q(\phi(\theta,t,0) - v^{int})}{kT}} \tag{41}$$

$$f(\theta+\omega t) = q\, c^{ext} K e^{-\frac{q(\phi(\theta,t,L_m) - v^{ext})}{kT}} \tag{42}$$

Here K is an equilibrium constant with units of length, since it converts charge/volume to charge/area.

Dividing these equations and then taking the logarithm of both sides, we get

(43) $$\phi(\theta,t,L_m) - \phi(\theta,t,0)$$

$$= (v^{ext} - v^{int}) + \frac{kT}{q} \log \frac{c^{ext}}{c^{int}}$$

Since L_m is an integer multiple of the helical period L, we also have

(44) $$\phi(\theta,t,L_m) - \phi(\theta,t,0) = \bar{E} L_m$$

Thus, the parameter $\bar{E}$ is related to the voltages and concentrations on the two sides of the membrane by

(45) $$\bar{E} L_m = (v^{ext} - v^{int}) + \frac{kT}{q} \log \frac{c^{ext}}{c^{int}}$$

By considering equation (41) or equation (42) separately, however, we can also get a boundary condition on ϕ, and this will force us to revise the assumption (29) that we made in the infinite case.

From equation (41), we have

$$(46)\quad \phi(\theta,t,0) = v^{int} - \frac{kT}{q}\log\frac{f(\theta+\omega t)}{q c^{int} K}$$

But we also have

$$(47)\quad \frac{\partial\phi}{\partial z}(\theta,t,z) = E\left(\theta+\omega t + \frac{2\pi}{L}z\right)$$

Combining (46) & (47), we get an explicit formula for ϕ:

$$(48)\quad \phi(\theta,t,z) = v^{int} - \frac{kT}{q}\log\frac{f(\theta+\omega t)}{q c^{int} K} + \int_0^z E\left(\theta+\omega t + \frac{2\pi}{L}z'\right)dz'$$

As the reader can check by subtracting $\bar{E}z$ from both sides, this is <u>not</u> of the form assumed in (29), and therefore, we must revisit the evaluation of torque that was done in the infinite case.

Differentiating both sides of (48) with respect to θ, we find

$$\frac{\partial \phi}{\partial \theta}(\theta,t,z) = -\frac{kT}{\zeta}\frac{f'(\theta+\omega t)}{f(\theta+\omega t)} + \int_0^z E'\left(\theta+\omega t+\frac{2\pi}{L}z'\right)dz' \tag{49}$$

$$= -\frac{kT}{\zeta}\frac{f'(\theta+\omega t)}{f(\theta+\omega t)} + \frac{L}{2\pi}\left(E\left(\theta+\omega t+\frac{2\pi}{L}z\right) - E(\theta+\omega t)\right)$$

Instead of the torque per unit length, we now need to evaluate the total counterclockwise torque applied by the electric field to the rotor, which is equal to the total clockwise torque that must be applied by an external agent to maintain the steady state. We denote this total torque by T. It is given by

$$(50)\quad T = r\int_0^{2\pi}\int_0^{L_m}\left(-\frac{1}{r}\frac{\partial\phi}{\partial\theta}(\theta,t,z)\right)\left(-f\left(\theta+\omega t+\frac{2\pi}{L}z\right)\right)dz\, r\,d\theta$$

$$= r\int_0^{2\pi}\int_0^{L_m} -\frac{kT}{\delta}\frac{f'(\theta+\omega t)}{f(\theta+\omega t)}\, f\left(\theta+\omega t+\frac{2\pi}{L}z\right)dz\,d\theta$$

$$+\frac{rL}{2\pi}\int_0^{2\pi}\int_0^{L_m} E\left(\theta+\omega t+\frac{2\pi}{L}z\right) f\left(\theta+\omega t+\frac{2\pi}{L}z\right)dz\,d\theta$$

$$-\frac{rL}{2\pi}\int_0^{2\pi}\int_0^{L_m} E(\theta+\omega t)\, f\left(\theta+\omega t+\frac{2\pi}{L}z\right)dz\,d\theta$$

In the first and last term, we can do the integral over z first, with the result

$$(51)\quad \int_0^{L_m} f\left(\theta+\omega t+\frac{2\pi}{L}z\right)dz = L_m\,\bar{f}$$

In the first term, the integral over θ that remains is equal to 0 by periodicity

In the third term, we have

(52) $$\int_0^{2\pi} E(\theta+\omega t)\,d\theta = 2\pi \bar{E}$$

so the third term is equal to

(53) $$-\, r L L_m \bar{f} \bar{E}$$

In the second term, we can change variables in θ to make the integrand be independent of z and t. Thus, equation (50) reduces to

(54) $$T = r L L_m \left(\frac{1}{2\pi} \int_0^{2\pi} E(\theta) f(\theta)\,d\theta \;-\; \bar{E}\bar{f} \right)$$

This indeed has the units of torque, since E and $\bar{E}$ have the units of electric field, and f and $\bar{f}$ have the units of charge per unit area. By some kind of miracle, this is just L_m times the torque per unit length that we calculated previously, even though the assumption that we made about the form of ϕ in the infinite-length case is not applicable to the finite-length case. Thus, we can still use our previous results concerning τ and make the simple translation

$$T = \tau L_m \tag{55}$$

Similarly, let

$$V = \bar{E} L_m = v^{ext} - v^{int} + \frac{kT}{q} \log \frac{c^{ext}}{c^{int}} \tag{56}$$

see (45),
so that V is the electrochemical drive on the motor. Then we can easily translate equation (37) to the finite-length case by multiplying and dividing by L_m on the right-hand side:

$$\begin{pmatrix} \omega \\ \\ I \end{pmatrix} = q \left(\frac{D}{kT}\right)\left(\frac{2\pi}{L L_m}\right) \begin{pmatrix} \frac{1}{rL(\bar{f} - f_H)} & 1 \\ \\ 1 & rL\bar{f} \end{pmatrix} \begin{pmatrix} T \\ \\ V \end{pmatrix} \tag{57}$$

Motor characteristics

Two important properties of the motor are its angular velocity when it is spinning freely ($T=0$), and the torque that is just sufficient to prevent rotation. From (57), these are given by

(58) $$\omega_{free} = q \frac{D}{kT}\left(\frac{2\pi}{L L_m}\right) V$$

(59) $$T_{stall} = - rL\left(\bar{f} - f_H\right) V$$

and the corresponding currents are

(60) $$I_{free} = q\left(\frac{D}{kT}\right)\left(\frac{2\pi}{L L_m}\right) rL \bar{f} V$$

(61) $$I_{stall} = q\left(\frac{D}{kT}\right)\left(\frac{2\pi}{L L_m}\right) rL f_H V$$

Note the opposite dependence on L in ω_{free} and in $-T_{stall}$. To make a motor that turns rapidly in its unloaded condition, we should make the helical wavelength small, and in principle there is no limit to how far we can go in this direction. By doing so, however, we make a motor that is weak; it stalls easily when subjected to the slightest load. To make a motor that can turn against the largest possible load, we should make L as large as possible, i.e., $L = L_m$ (since we have assumed that L_m is an integer multiple of L).

Equation (58) has a simple kinematic interpretation that can be brought out by writing it as

$$L \frac{\omega_{free}}{2\pi} = g \frac{D}{kT}\left(\frac{V}{L_m}\right) \tag{62}$$

On the left-hand side of this equation, we have the velocity of the helical wave when the motor is rotating at the angular velocity ω_{free}.

On the right-hand side we have the drift velocity of the ions in the mean electric field $V/L_M = \bar{E}$. Thus, the torque-free state is one in which the ions are surfing the helical wave.

Note that in the expressions for I_{free} and I_{stall}, the parameter L cancels out. Also the expressions for I_{free} and I_{stall} are identical except that I_{free} is proportional to $\bar{f}$ and I_{stall} is proportional to f_H. Since $\bar{f} > f_H$ the motor allows more

current to flow through it when it is spinning freely than when it is stalled.

(This is opposite to the behavior of electric motors involving magnetic fields generated by current flowing through inductors. There, a stalled motor is in a short-circuit condition and draws a large and dangerous current.)

Homework:

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

$$T = -\beta \omega \tag{63}$$

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

$$\lim_{\beta \to 0} \omega \quad , \quad \lim_{\beta \to 0} I$$

$$\lim_{\beta \to \infty} T \quad , \quad \lim_{\beta \to \infty} I$$

(ii) The efficiency of the motor can be defined as

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

(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 $\mathcal{E}_m$, 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:

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

Hint: It may help in this problem to think of T as the independent variable rather than β.

Ion pump characteristics

Although I don't know whether this ever happens in nature, our motor can be run in reverse by applying a positive torque to it and thereby driving an ionic current against an electrochemical potential difference.

From the second equation of (57), the current-voltage relation is then

(65) $$I = \delta\left(\frac{D}{kT}\right)\left(\frac{2\pi}{LL_m}\right)\left(T + rL\bar{f}\,V\right)$$

In particular,

(66) $$I_{V=0} = \delta\left(\frac{D}{kT}\right)\left(\frac{2\pi}{LL_m}\right)T$$

(67) $$V_{I=0} = -\frac{T}{rL\bar{f}}$$

Here we do not see the same kind of tradeoff concerning the parameter L as before. Both the short-circuit current ($I_{V=0}$) and the open-circuit voltage ($V_{I=0}$) are inversely proportional to L, so to make them large for a given applied torque T, we should make L as small as possible, i.e., use a tightly-wound helix. The explanation for this effect, however, is that the angular velocity has an even stronger dependence on L:

(68) $$\omega_{V=0} = g\left(\frac{D}{kT}\right)\left(\frac{2\pi}{L L_m}\right)\frac{T}{rL}\left(\frac{1}{\bar{f}-f_H}\right)$$

(69) $$\omega_{I=0} = g\left(\frac{D}{kT}\right)\left(\frac{2\pi}{L L_m}\right)\frac{T}{rL}\left(\frac{1}{\bar{f}-f_H} - \frac{1}{\bar{f}}\right)$$

so the input power requirement will increase faster than the power generated as $L \to 0$, see Homework, below. From (68) & (69), note that the ion pump spins faster when it is electrically unloaded than when there is a load sufficient to stop the flow of current.

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

(70) $$-\frac{T}{rLf} < V < 0$$

The efficiency of the ion pump can be defined as

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

i) Prove that $\mathcal{E}_p \in (0, 1)$

ii) Evaluate V^* and $\mathcal{E}_p^*$, where V^* maximizes $\mathcal{E}_p$ and $\mathcal{E}_p^*$ is the maximum value.

iii) Choose L to make $\mathcal{E}_p^*$ as large as possible, recalling that the possible values of L are $L_m, L_m/2, L_m/3, \ldots$

Fluctuations

Since our motor (or ion pump) exists in a thermal environment, it is subject to fluctuations. To simulate these fluctuations, we can use Brownian dynamics (which is the zero-mass limit of Langevin dynamics). For warmups, we consider the scalar case.

Consider a particle that moves in one dimension along the x-axis, and let $X(t)$ be the position of the particle at time t. The particle is connected to the origin by a spring of stiffness a and zero rest length. It is also subject to a drag force $-\gamma \frac{dX}{dt}$

and to a random force $r(t)$. Our goal is to choose $r(t)$ to simulate the thermal environment. (More precisely, it is the combination of the drag force with $r(t)$ that simulates the thermal environment.)

Since we are neglecting mass, the equation of motion of our particle is

(72) $$0 = -\rho \frac{dx}{dt} - ax + r(t)$$

We assume that $r(t)$ and $x(t)$ are stationary stochastic processes, i.e., that their statistical properties are independent of time.

Also we assume that

(73) $$E[r(t)] = 0$$

and it follows that

(74) $$E[x(t)] = 0$$

We rewrite (72) as

(75) $$\frac{dx}{dt} + \rho^{-1} a x = \rho^{-1} r$$

Now we multiply both sides by $e^{\rho^{-1} a t}$, integrate over $(-\infty, t)$ and then divide both sides by $e^{\mathfrak{f}^{-1}at}$. This gives

(76) $$x(t) = \int_{-\infty}^{t} e^{-\mathfrak{f}^{-1}a(t-t')}\,\mathfrak{f}^{-1}r(t')\,dt'$$

The potential energy of the spring is given by

(77) $$\frac{1}{2}ax^2(t) = \frac{1}{2}a\iint_{-\infty}^{t} e^{-\mathfrak{f}^{-1}a(t-t')}e^{-\mathfrak{f}^{-1}a(t-t'')}$$
$$\mathfrak{f}^{-2}\,r(t')\,r(t'')\,dt'dt''$$

Now we make the assumption that

(78) $$E[r(t')r(t'')] = c\,\delta(t'-t'')$$

where c is a constant that remains to be determined. Then

(79) $$E\left[\frac{1}{2}ax^2(t)\right] = \frac{c}{2}a\mathfrak{f}^{-2}\int_{-\infty}^{t} e^{-2\mathfrak{f}^{-1}a(t-t')}\,dt'$$
$$= \frac{c}{4}\mathfrak{f}^{-1}$$

From statistical mechanics, the stationary probability density for $x(t)$ should be

(80) $$p_x(\xi) = \frac{e^{-\frac{1}{2}\frac{a\xi^2}{kT}}}{\int_{-\infty}^{\infty} e^{-\frac{1}{2}\frac{a\eta^2}{kT}}\,d\eta}$$

and from this we have

(81) $$E\left[\tfrac{1}{2}a x^2(t)\right] = \frac{\frac{1}{2}\int_{-\infty}^{\infty} a\xi^2 e^{-\frac{1}{2}\frac{a\xi^2}{kT}}\,d\xi}{\int_{-\infty}^{\infty} e^{-\frac{1}{2}\frac{a\xi^2}{kT}}\,d\xi}$$

$$= \frac{kT}{2}\,\frac{\int_{-\infty}^{\infty} u^2 e^{-\frac{1}{2}u^2}\,du}{\int_{-\infty}^{\infty} e^{-\frac{1}{2}u^2}\,du} = \frac{kT}{2}$$

From (79) & (81)

(82) $$c = 2kTf$$

so (78) becomes

(83) $$E[r(t')r(t'')] = \delta(t'-t'')\, 2kT f$$

The random force that we need is thus characterized by (73) & (83). Note that it does not depend at all upon the conservative force, $-ax$, that was applied to the system. We needed such a force, and it had to be linear, for the above argument to go through, but once we know the properties of the random force $r(t)$, we can use it in more general situations, i.e., in the presence of a nonlinear force, or a constant force, or no force at all.

We now seek to generalize the foregoing to systems, in which a and f are symmetric, positive definite $n \times n$ matrices, and $X(t)$ and $r(t)$ are column vectors of length n.

Through equation (76), everything is the same as before. The next step is to evaluate

(84) $$x(t)\, x^T(t) =$$

$$\iint_{-\infty}^{t} e^{-\rho^{-1} a (t-t')} \rho^{-1} r(t') r^T(t'') \rho^{-1} e^{-a\rho^{-1}(t-t'')} dt' dt''$$

Now suppose $r(t)$ satisfies the matrix generalization of (83), which is

(85) $$E[r(t') r^T(t'')] = \delta(t'-t'')\, 2kT\rho$$

Then

(86) $$E[x(t) x^T(t)] = 2kT \int_{-\infty}^{t} e^{-\rho^{-1} a (t-t')} \rho^{-1} e^{-a\rho^{-1}(t-t')} dt'$$

$$= 2kT \int_0^{\infty} e^{-\rho^{-1} a t''} \rho^{-1} e^{-a\rho^{-1} t''} dt''$$

But

(87) $$\int_0^\infty e^{-\gamma^{-1} a t''}\, \gamma^{-1}\, e^{-a\gamma^{-1} t''}\, dt''$$

$$= -\int_0^\infty \frac{d}{dt''}\left(e^{-\gamma^{-1} a t''}\right) a^{-1}\, e^{-a\gamma^{-1} t''}$$

and in exactly the same way, the left-hand side of (87) is also equal to

(88) $$-\int_0^\infty e^{-\gamma^{-1} a t''}\, a^{-1}\, \frac{d}{dt''}\left(e^{-a\gamma^{-1} t''}\right) dt''$$

Adding these two results, we get (since a^{-1} is independent of time)

(89) $$2\int_0^\infty e^{-\gamma^{-1} a t''}\, \gamma^{-1}\, e^{-a\gamma^{-1} t''}\, dt''$$

$$= -\int_0^\infty \frac{d}{dt''}\left(e^{-\gamma^{-1} a t''}\, a^{-1}\, e^{-a\gamma^{-1} t''}\right)$$

$$= a^{-1}$$

Substituting this result into (86) gives

(90) $$E[x(t)\,x^T(t)] = kT\,a^{-1}$$

Now we multiply both sides by a (from the left or right) take the trace of both sides, divide by 2, and use the cyclic property of trace. Since a is deterministic and trace is linear, both of them can be brought inside the expectation. In this way, we reach the conclusion that

(91) $$E\left[\tfrac{1}{2}\,x^T(t)\,a\,x(t)\right] = \tfrac{1}{2}kTn,$$

since trace $(I)=n$, the dimension of the system. We leave it as an exercise for the reader to show that the same conclusion follows from the stationary probability density function

(92) $$\rho_x(\xi) = \frac{e^{-\frac{1}{2}\frac{\xi^T a \xi}{kT}}}{\displaystyle\int_{\mathbb{R}^n} e^{-\frac{1}{2}\frac{\eta^T a \eta}{kT}}\,d\eta_1\cdots d\eta_n}$$

Now we are ready to state a numerical scheme to simulate the stochastic process described above. First, we generalize the foregoing by considering any applied force of the form $f(x(t), t)$ instead of $-ax$. The equation of motion is then as follows

(93) $$\gamma \frac{dx}{dt} = f(x(t), t) + r(t)$$

where γ is a symmetric, positive-definite $n \times n$ matrix, and where

(94) $$E[r(t)] = 0$$

(95) $$E[r(t') r^T(t'')] = \delta(t' - t'') \, 2kT\gamma$$

Letting m be the time-step index, we discretize (93) by Euler's method

(96) $$\gamma \frac{x^{m+1} - x^m}{\Delta t} = f(x^m, m\Delta t) + r^m$$

and the discretizations of (94) & (95) are

$$E[r^m] = 0 \tag{97}$$

$$E[r^m (r^{m'})^T] = \frac{\delta_{mm'}}{\Delta t} 2kT \mathcal{S} \tag{98}$$

Note in particular the important factor $1/\Delta t$ in (98). To realize (98) for $m \neq m'$, we simply choose r^m independently for different m, and then because of (97), (98) is automatically satisfied for $m \neq m'$. For $m = m'$, (98) becomes

$$E[r^m (r^m)^T] = \frac{2kT}{\Delta t} \mathcal{S} \tag{99}$$

To achieve (97) & (99), we first choose W^m (independently for different m), and such that

$$E[W^m] = 0, \quad E[W^m (W^m)^T] = I \tag{100}$$

and then we set

$$r^m = \left(\frac{2kT}{\Delta t}\right)^{1/2} \mathcal{S}^{1/2} W^m \tag{101}$$

where $\mathcal{S}^{1/2}$ is any square root of the symmetric positive-definite matrix $\mathcal{S}$. It is easy to check that (100) & (101) imply (97) & (99). When (100) is written in components, it reads

(102) $$E[W_i^m] = 0 \quad , \quad E[W_i^m W_j^m] = \delta_{ij}$$

and this can be achieved by choosing the components of W^m independently with mean zero and variance 1. For example, in Matlab

(103) $$W = \text{randn}(n, 1)$$

which generates a column of n independent Gaussian random numbers, each with mean zero and variance 1.

Putting everything together, we have the following scheme:

(104) $$\begin{aligned} X^{m+1} = X^m &+ (\Delta t)\mathcal{S}^{-1} f(X^m, m\Delta t) \\ &+ (2kT\Delta t)^{1/2} \mathcal{S}^{-1/2} W^m \end{aligned}$$

In applying the foregoing to our rotary motor / ion pump, we have

$$x = \begin{pmatrix} -\theta \\ Q \end{pmatrix} = \begin{pmatrix} \int_0^t \omega dt \\ \int_0^t I dt \end{pmatrix} \tag{105}$$

$$f = \begin{pmatrix} T \\ V \end{pmatrix} \tag{106}$$

$$\varphi^{-1} = q\left(\frac{D}{kT}\right)\left(\frac{2\pi}{L L_m}\right)\begin{pmatrix} \frac{1}{rL(\bar{f}-f_H)} & 1 \\ 1 & rL\bar{f} \end{pmatrix} \tag{107}$$

and of course matlab can evaluate the square root of a matrix, but be sure you are getting the matrix square root instead of the square root of each element!

Homework: Give this a try, and plot some sample paths of $-\theta(t)$ and $Q(t)$, preferably aligned in t to see how they relate.

I suggest considering these two cases:

$$\left(T=0,\ V=3\frac{kT}{\xi}\right) \text{ and } \left(T=T_{stall},\ V=3\frac{kT}{\xi}\right)$$

see equations (58-59). Look for dimensionless combinations of parameters to reduce the number of arbitrary choices that you have to make.