PHYS 414 Problem Set 2: No pumping!

Designing a "machine" on the nanometer scale is a formidable task: it has to operate in a violent environment where the energies of thermal fluctuations are comparable to the intrinsic energies of the machine itself. Yet nature has evolved a wide array of so-called motor proteins, molecular systems that convert an external (usually chemical) energy source into motion. This movement is invariably stochastic, but in order for the motor to be a meaningful machine, it has to exhibit a definite bias, i.e. taking more forward steps than backward steps for linear movement (to act as a cargo transporter), or more clockwise rather than counterclockwise motion for a rotary motor (to act as a propeller to generate thrust). Inspired by these natural systems, researchers are attempting to design artificial nanoscale machines, first as proof-of-principle demonstrations, and eventually for technological applications. All these efforts have inspired theoretical work to understand the fundamental physical constraints on the behavior of stochastic machines.

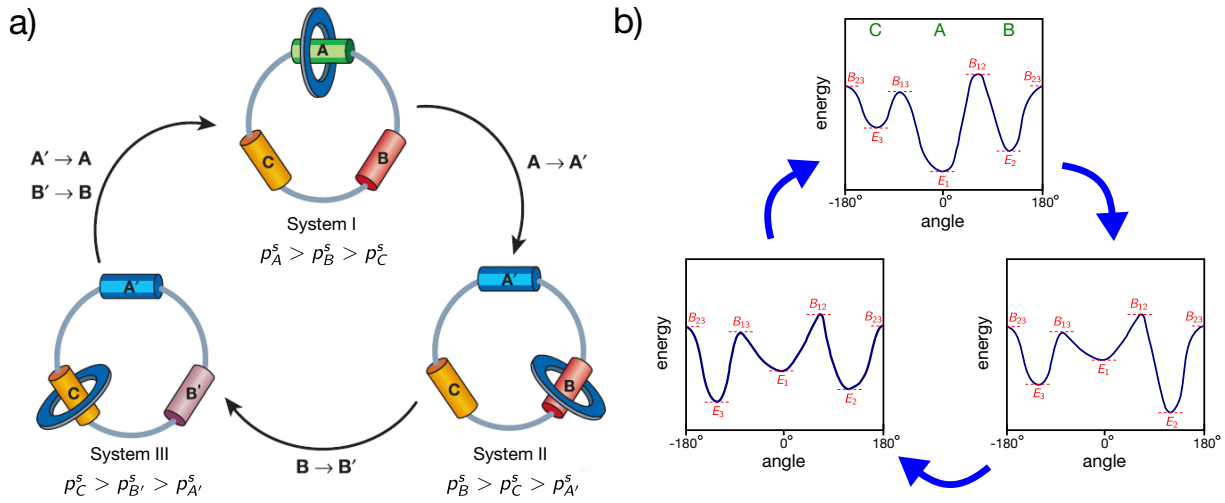

Figure 1: a) Externally imposed cycle driving the experimental [2]catenane system of Leigh *et al.*, Nature **424**, 174 (2003). b) Schematic energy landscapes underlying this cycle (see Problem 2 for notation) where state energies $E_n(t)$ change with time, but the barrier heights B_{mn} stay fixed.

One ingenious experiment [Leigh *et al.*, Nature **424**, 174 (2003)] constructed an artificial motor from an interlocked assembly of one or two small rings moving around a larger ring. Fig. 1a shows a schematic diagram of the [2]catenane, the case of one small ring on a larger ring, which we will analyze in this problem set. The small ring has three possible binding sites (A, B, C) on the larger ring, and the strength of binding can vary between the sites. Using an external stimulus controlled by the experimentalist (in the form of light, heat, or chemicals) one can drive the motor between different conditions (systems I, II, and III), where in each case one binding site is strongest. As shown in the figure, in system I the equilibrium probability p^s_A of being in site A is larger than p^s_B or p^s_C. Though the small ring hops around stochastically, on average it will be on site A more than the others. Modifying A to A' by external stimulus (system I to system II) destabilizes the binding, making $p^s_{A'}$ now the smallest probability. The small ring will on average be mostly bound to site B, which has the largest equilibrium probability. Similarly, modifying

B to B' (system II to system III) makes p_C^s the largest, so the ring will spend more of its time on C. Finally the experimentalist returns the system to its original state, by reverting $A' \to A$ and $B' \to B$ (system III to system I). In principle then we should be able to drive the small ring around the circle through this cycle of external changes, but one question remains: will there be bias in the driving (clockwise vs. counterclockwise)? Can we design a mainly unidirectional motor?

Naively, one would think that the small ring would generally take the shortest route to its preferred binding site, so the cycle in Fig. 1a would create a net clockwise motion, since the preferred site is moved clockwise. Surprisingly, the experiments revealed that actually there is *no bias* in this cycle: on average, the small ring is just as likely to move counterclockwise as clockwise to its preferred site. The full theoretical explanation for this came several years later, when Saar Rahav, Jordan Horowitz and Christopher Jarzynski proved a general *no-pumping theorem* [Phys. Rev. Lett. **101**, 140602 (2008)], describing under what circumstances it is impossible to "pump" (generate biased motion) in a stochastic system with a periodic cycle of external driving. It turns out that pumping requires a very particular kind of driving, which is not satisfied in the [2]catenane experiment, no matter what cycle the experimentalist constructs. For this system, the resolution turned out to be adding another small ring and four binding sites, making it a [3]catenane (see Fig. 5 of the *Nature* article). The repulsive interaction between the two small rings (the rings cannot penetrate through each other) created conditions where pumping is allowed.

The many-body case of two small rings is rather complex, so we will not delve into it. But the impossibility of pumping for one small ring by varying the binding site strengths periodically over time can be shown to be a consequence of detailed balance, using elementary master equation techniques. We will divide the task into two parts: in Problem 1 we will explore the stationary state of a master equation under periodic driving; in Problem 2 we will build on these results to derive the no pumping theorem for the [2]catenane system. The combination of experimental results and theory highlights the non-trivial achievement of functioning molecular machines: it is no simple matter to get anything done with a nano-engine!

Problem 1: Master equation under periodic driving

External changes in the environmental parameters are very simple to incorporate into the master equation framework: the transition rates W_{mn} between states n and m in the system become time-dependent functions $W_{mn}(t)$, which reflect some fixed protocol controlled by the experimentalist. Note that at each instant in time the probabilities of each transition out of n over the interval δt have to still sum to one, $\sum_m W_{mn}(t)\delta t = 1$. Following the derivation in class, the form of the master equation remains the same:

$$\frac{dp_m(t)}{dt} = \sum_n \left[W_{mn}(t)p_n(t) - W_{nm}(t)p_m(t)\right] \tag{1}$$

For an arbitrary $W_{mn}(t)$, this master equation is not easy to manipulate, but we are interested in a specific class of external stimulus which has the form of a cycle: in other words, $W_{mn}(t)$ is periodic, $W_{mn}(t+T) = W_{mn}(t)$, with some period T. In this problem we will show that an ergodic system under these circumstances will go to a periodic state in the long-time limit, $p_n(t+T) = p_n(t)$ for any n as $t \to \infty$.

For a driven system, it turns out to be easier to work at the level of discrete time steps δt. The discrete time version of Eq. (1), the initial form we used earlier in the course, is just:

$$\mathbf{p}(t+\delta t) = \delta t\, W(t)\mathbf{p}(t) \tag{2}$$

where $\mathbf{p}(t)$ is a vector with components $p_m(t)$, and $W(t)$ is a matrix with components $W_{mn}(t)$.

a) Let us first focus on times t that are integer multiples of the period, $t = jT$ for $j = 0, 1, 2, \ldots$. (We can also assume that $T = \tau\delta t$ is an integer multiple of δt for some $\tau > 0$.) By iterating Eq. (2) and using the periodicity $W(t+T) = W(t)$, show that $\mathbf{p}(jT+T)$ can be related to $\mathbf{p}(jT)$ as:

$$\mathbf{p}(jT+T) = T\hat{W}\mathbf{p}(jT), \tag{3}$$

where $\hat{W}$ is a matrix independent of j. Find $\hat{W}$ in terms of products of the $W(t)$ matrices, and show that $\hat{W}$ has the standard property of a transition matrix, namely $\sum_m \hat{W}_{mn}T = 1$.

Note that Eq. (3) has the same form as Eq. (2), but with δt replaced by T and $W(t)$ replaced by the time-independent $\hat{W}$. Thus it describes time evolution of the probability $\mathbf{p}$ over time intervals equal to T. We will assume $\hat{W}$ corresponds to a strongly connected network, so that as $t \to \infty$ (or equivalently $j \to \infty$) the probability $\mathbf{p}(jT) \to \mathbf{v}$, where $\mathbf{v}$ is some time-independent vector.

b) The final step is to find $\mathbf{p}(t)$ for some time t that is an integer multiple of δt, but not necessarily an integer multiple of T. Using Eqs. (2) and (3), show that you can write:

$$\mathbf{p}(t) = A(t \bmod T)\mathbf{p}\left(\lfloor t/T \rfloor T\right), \tag{4}$$

where $A(t \bmod T)$ is a matrix depending on $t \bmod T \equiv t - \lfloor t/T \rfloor T$, and $\lfloor x \rfloor$ is the floor of x (the largest integer smaller or equal to x). Find an expression for $A(t \bmod T)$, and argue that as $t \to \infty$, the probability becomes periodic in T, namely $\mathbf{p}(t+T) = \mathbf{p}(t)$.

This is the main result that will help us with analyzing the motor cycle. Under periodic driving, $\mathbf{p}(t)$ does not go to a stationary state in the strict sense, since $\mathbf{p}(t)$ still varies over small time intervals δt. We will denote it instead as a *periodic state*, and write $\mathbf{p}(t \to \infty) = \mathbf{p}^{ps}(t)$, where $\mathbf{p}^{ps}(t+T) = \mathbf{p}^{ps}(t)$.

Problem 2: The no-pumping theorem

Rather than deriving the original proof [Rahav *et al.*, Phys. Rev. Lett. **101**, 140602 (2008)], we will follow a simpler line of argument to get to the no-pumping theorem, outlined by Dibyendu Mandal and Christopher Jarzynski [J. Stat. Mech. P10006 (2011)].

The main constraint of the transition rates $W_{nm}(t)$ in the motor cycle is that they must always respect detailed balance at *every time instant*. To understand this further, let us do a thought experiment. Imagine we drive the motor from time zero to t, and $W(t)$ is the rate matrix at time t. If we suddenly stopped varying the rates after time t, so that $W(t') = W(t)$ for $t' \geq t$, then the system should just relax to an equilibrium stationary state $\mathbf{p}(t' \to \infty) = \mathbf{p}^s(t)$. Note the somewhat strange notation here: normally we write the equilbrium probability $\mathbf{p}^s$ without

a time subscript. But here it depends on what the rate matrix $W(t)$ was at the moment we stopped varying the rates. The value of this rate matrix will determine exactly what equilibrium distribution we end up at through the detailed balance condition:

$$\frac{W_{nm}(t)}{W_{mn}(t)} = \frac{p_n^s(t)}{p_m^s(t)}. \tag{5}$$

Thus for every matrix $W(t)$ at different times t there exists a corresponding $\mathbf{p}^s(t)$ which is the equilibrium probability which would be achieved if the rates became frozen at t. Since detailed balance assumes an ergodic system, $p_n^s(t) > 0$ for all states n.

Of course in the real motor cycle we never freeze the rates, but continue to vary them periodically with $W(t+T) = W(t)$. In this case the system never relaxes to any $\mathbf{p}^s(t)$, but rather goes to a periodic state $\mathbf{p}^{ps}(t)$ as shown in Problem 1. However we can still treat the $\mathbf{p}^s(t)$ as mathematical functions associated with $W(t)$.

a) Since $p_n^s(t) > 0$ for all n, we can write it in the form $p_n^s(t) = \exp(-E_n(t))$ for some real function $E_n(t)$. From our point of view $E_n(t)$ is just a number, but the natural thermodynamic interpretation (which will be evident when we cover the canonical ensemble in class) is that $E_n(t)$ is the energy of the nth state, measured in units where k_BT. Similarly for those $W_{nm}(t)$ that are non-zero, we can write them in a specific form, $W_{nm}(t) = w_0 \exp(-B_{nm}(t) + E_m(t))$, where $B_{nm}(t)$ is another real function and w_0 is a constant with units of inverse time. Show that detailed balance, Eq. (5), implies that the matrix $B(t)$ is symmetric: $B_{nm}(t) = B_{mn}(t)$. Since $B_{nm}(t)$ controls how quickly the system can transition between m and n, it can be interpreted as the height of the energy barrier between the two states, in units of k_BT (we will verify this intuition in our later discussion of the Arrhenius law, where we will also see that w_0 sets the scale of how fast diffusion occurs on the energy landscape). See Fig. 1b for a schematic energy landscape picture of the [2]catenane system.

The master equation equation for any driven system can be written as:

$$\frac{dp_m}{dt} = \sum_n J_{mn}(t), \qquad J_{mn}(t) \equiv W_{mn}(t)p_n(t) - W_{nm}(t)p_m(t), \tag{6}$$

where $J_{mn}(t)$ is the net probability flux from n to m. To evaluate pumping in the system, we will look at the long time limit $t \to \infty$, where we know from Problem 1 that $p_n(t) \to p_n^{ps}(t)$ under periodic driving. Then $J_{mn}(t) \to J_{mn}^{ps}(t)$ as $t \to \infty$. Note that $J_{mn}^{ps}(t+T) = J_{mn}^{ps}(t)$. Let us define the integrated flux over one period in the long-time limit as:

$$\Psi_{mn}^{ps} \equiv \int_t^{t+T} dt'\, J_{mn}^{ps}(t') \tag{7}$$

The integrated flux is a measure of directed motion in the cycle: if $\Psi_{mn}^{ps} > 0$ for some states m and n, that means that on average more probability flows $n \to m$ than $m \to n$ over the course of one cycle in the long-time limit. This would mean the driving is successfully pumping the system between n and m, generating biased movement.

The *no-pumping theorem* states that $\Psi_{mn}^{ps} = 0$ for all m and n if either of the following is true:

1. If the state energies $E_n(t) = E_n$ are fixed in time, but the barrier heights $B_{nm}(t)$ are allowed to vary in time.

2. If the state energies $E_n(t)$ vary in time, but the barrier heights $B_{nm}(t) = B_{nm}$ are fixed in time.

Thus you have to vary *both* $E_n(t)$ and $B_{nm}(t)$ in time in order to get pumping, $\Psi^{ps}_{nm} \neq 0$. The [2]catenane experiment corresponds to case 2 above, since the external stimulus only affects $p_n(t)$ (or equivalently $E_n(t)$). Hence no pumping will occur, regardless of how the experimentalist changes $p_n(t)$.

b) Prove $\Psi^{ps}_{nm} = 0$ for any m and n in case 1 above. *Hint:* For this case note that the rates $W_{mn}(t)$ vary with time (because $B_{nm}(t)$ is time-dependent) but the ratios $W_{nm}(t)/W_{mn}(t) = \exp(E_m - E_n)$ are time-independent. Show that as a result the time-independent solution $p_n(t) = \exp(-E_n)$ for all n satisfies the master equation, Eq. (6). Thus in this special case the periodic state $p^{ps}_n(t)$ in the long-time limit is the same as the stationary state, $p^{ps}_n(t) = p^s_n = \exp(-E_n)$, which is of course trivially periodic.

c) Prove $\Psi^{ps}_{nm} = 0$ for any m and n in case 2 above. To make the proof tractable, focus on the three-state cyclic kinetic network of the [2]catenane system, where $n = 1$, 2, or 3 correspond to the small ring binding at positions A, B, or C. The transformations shown in Fig. 1a correspond to time-dependent driving of $E_n(t)$. (Note that even when only one $E_n(t)$ is changed, all energies are affected, in order to preserve the normalization $\sum_n p^s_n(t) = \sum_n \exp(-E_n(t)) = 1$.) Assume the barrier heights B_{nm} are fixed in time, and the only allowed transitions are $W_{12}(t)$, $W_{21}(t)$, $W_{23}(t)$, $W_{32}(t)$, $W_{13}(t)$, and $W_{31}(t)$. *Hint:* The proof requires two ingredients. The first is integrating the master equations for various n in Eq. (6) over one period in the long-time limit. The second part comes from looking at the quantity $G_{ij}(t) \equiv J_{ij}(t)e^{B_{ij}}$. Show that the sum of $G_{ij}(t)$ over a cycle in the network is zero, $G_{21}(t) + G_{32}(t) + G_{13}(t) = 0$. Then integrate this equation over one period in the long-time limit.

Extra credit for the foolhardy: Can you figure out why the [3]catenane system, with two small rings hopping around four binding sites [Fig. 5 of Leigh *et al.*, Nature **424**, 174 (2003)], does not fall under either of the two cases where the no-pumping theorem holds?