1

Life from a physics perspective

1.12.1 *One E. coli bacterium divides in 30 minutes, if the temperature is good and food is plentiful. One bacterium fills a volume of* $1\,\mu m^3$*. How long would it take for one E. coli to reach the volume of the Earth (which has the radius of* $\sim$ *6.000 km)? Repeat the calculation for human replication (each having a volume of about 0.1* m^3*), assuming a doubling time of 30 years.*

Answer After n generations, the descendants of one bacterium could expand to a volume of:

$$V = 2^n \cdot 1\,\mu\mathrm{m}^3 = 2^n \cdot 10^{-18}\,\mathrm{m}^3$$

This volume reaches the volume of the Earth when:

$$\begin{aligned}\frac{4\pi}{3}(6\,000\,000\,\mathrm{m})^3 = 2^n 10^{-18}\,\mathrm{m}^3 \Rightarrow \\ n = \log\left(\frac{4\pi}{3}(6\,000\,000)^3 \cdot 10^{18}\right)/\log(2) \\ = \log(10^{39})/\log(2) = 39/\log_{10}(2) = 129\end{aligned}$$

This takes only about 65 hours.

Repeating the above for a human with 0.1 m^3 volume gives:

$$\begin{aligned}n &= \log\left(\frac{4\pi}{3}(6\ 000\ 000)^3 \cdot 10\right)/\log(2) \\ &= \log(10^{22})/\log(2) = 22/\log_{10}(2) = 73\end{aligned}$$

generations, which takes 2200 years.

1.12.2 *There are* 10^{14} *cells in a human body and every day* 10^{11} *cells die. How much information needs to be re-generated inside a human to keep it functional over a lifetime of 80 years (human DNA contains* 3×10^9 *base pairs)? There is damage to DNA* $\sim 10^5$ *times per cell per day in humans, every one of which could lead to cancer. How many damages need to be repaired during human lifetime?*

Answer The total number of cells that need to be regenerated is:

$$N = 10^{11} \cdot 365 \cdot 80 \sim 3 \cdot 10^{15} \tag{1.1}$$

a number that is about 30 times the number of cells in our body. As each cell has $3 \cdot 10^9$ different base pairs in two chromosome copies, the necessary information processing is:

$$N_{\mathrm{I}} = 6 \cdot 10^9 \cdot N = 2 \cdot 10^{25} \tag{1.2}$$

base pairs, with each base pair having two bits of information. Thus in total one needs to generate $4 \cdot 10^{25}$ bits of information due to cell death during a lifetime.

DNA damage requires a total repair of:

$$N_{\mathrm{I\ damage}} = 10^{14} \cdot 10^5 \cdot 365 \cdot 80 = 3 \cdot 10^{23} \tag{1.3}$$

1.12.3 *Life is highly specific. Assume that you need to say hello to everybody in a city with* 10^6 *people. How long would this take if saying hello takes 1 second? What is the maximum time unit allocated to non-specific binding between pairs of random proteins in a* E. coli *cell, if any particular pair meets at least once within the 30 minutes generation time of an E. coli cell. There are of the order of 3 000 000 proteins in* E. coli.

Answer Assigning 1 sec to each hello, the total time would be 10^6 s or $10^6/3600 \sim 300$ hours.
The visit time for each protein should then be $2000\,\mathrm{s}/3\,000\,000 = 0.0007$ s or about 1 ms.

1.12.4 *Consider the four-step cycle of a molecular motor modeled in terms of two variables* $\varphi_1 = 0, 1$ *and* $\varphi_2 = 0, 1$ *and an energy function:*

$$H \;=\; A \;\cdot (\varphi_1 + \varphi_1 \varphi_2) \cdot \tag{1.4}$$

where the degeneracy $g = 10$ *of the* $\varphi_i = 0$ *states is larger than that of the unique* $\varphi_i = 1$ *states implying that* $\varphi_i = 0$ *is 10 times more likely than* $\varphi_i = 1$ *when* $A = 0$*. Let* A *alternate between 0 and 1. For* $A = 0$*, the state (0,0) is by far the most likely, and the (1,1) state will decay to the (0,0) situation. For* $A = -1$*, on the other hand, the (1,1) state is favored. Define motion* $x \to x + 1$ *respective to* $x \to x - 1$ *in terms of the sequence of shifts in these variables, and show that directed motion can be possible [43].*

Answer The two φ variables are controlled through one external variable A, which may take the values $A = 0$ or $A = -1$, and is associated with the hydrolysis state of the motor. The control is enforced through the total energy function:

$$H = A\,(\varphi_1 + \varphi_1\varphi_2) \tag{1.5}$$

As there are more non-specific states than specific (bound) ones, the degeneracy of the $\varphi = 0$ states is larger than that of the $\varphi = 1$ states. In the model we typically set the degeneracy of the $\varphi_1 = 0$ and the $\varphi_2 = 1$ states to be $g = 10$, whereas we assume only one specific state for $\varphi_1 = 1$ and $\varphi_2 = 1$. The states and associated steps are illustrated in Fig. 1.1.

For each value of A and starting conditions for (φ_1, φ_2) one may consider the trajectory for (φ_1, φ_2). Starting at (0,0) we have the options:

(a) Forward motion $x \to x + 1$ is associated with the sequence of events where binding is followed by stroke: $(0,0) \to (1,0) \to (1,1)$

(b) Backward motion $x \to x - 1$ is associated with the sequence where stroke is happens before binding: $(0,0) \to (0,1) \to (1,1)$

Further, in case of reversal $(1,1) \to (0,0)$, backtracking a given path implies that one reverses the corresponding x move.

If $A = 0$, the two options (a,b) are equally likely, and x makes a random step. If $A = -1$, the forward step (a) is most likely, because it is associated with an energy gradient on both steps along the path. That is, a first move along step (b) may easily be reversed ($(0,0) \to (0,1) \to (0,0)$) because this costs no energy. Thus for $A = -1$ there will be a bias toward forward motion.

The steps (a,b) define what happens from (0,0) to (1,1), and we saw a tendency to forward step when starting at (0,0), imposing the switch $A = 0 \to A = -1$. To complete the cycle we must let $A = -1 \to A = 0$. Thus we retrace what happens with (φ_1, φ_2) from state (1,1) in the absence of forces.

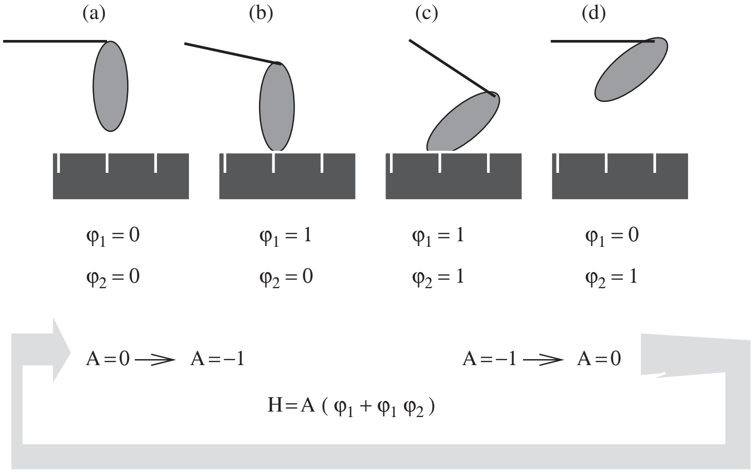

Figure 1.1 Schematic view of some states during one cycle of the discrete ratchet model discussed in the text. Below the four states, which are labelled as in the earlier figure, we show the parameterization of the states in terms of two binary variables. By making movement of φ_2 dependent on the state of φ_1, as shown by the energy function H, one can drive the cycle of states into a directed motion by externally changing the potential through the parameter A. As was the case with the continuous ratchet, this model is also at a maximum 50% effective, because state (1,1) can go to states (1,0) and (0,1) with equal probability when $A = 0$. In the first case, $(1,1) \to (1,0)$, one is back in state (b), and has not performed any motion. (c) is the rigor state and the $A = -1 \to A = 0$ transition corresponds to the ATP binding transition.

In this case any of the two variables may relax first. If they retrace through the reverse of path (a), then $x \to x - 1$ and there is no net motion. However if they retrace as the reverse of path, (b) then the system in fact progresses even further. The $A = -1 \to A = 0$ change induces a move from (1,1) to (0,0) that makes no average motion.

To study the dynamics in a discrete simulation, we shift between the $A = 0$ and the $A = -1$ cases. For each A, the model is simulated in a metropolis-like algorithm, where at each update one selects randomly either φ_1 or φ_2 and tries to change it. The factor $g > 1$ in degeneracy of the $\varphi = 0$ states means that for zero energy difference a transition $0 \to 0$, or $1 \to 0$ is g times more likely than a transition $0 \to 1$ or $1 \to 1$. When imposing $A = -1$, then any move where the energy is increased is penalized by a

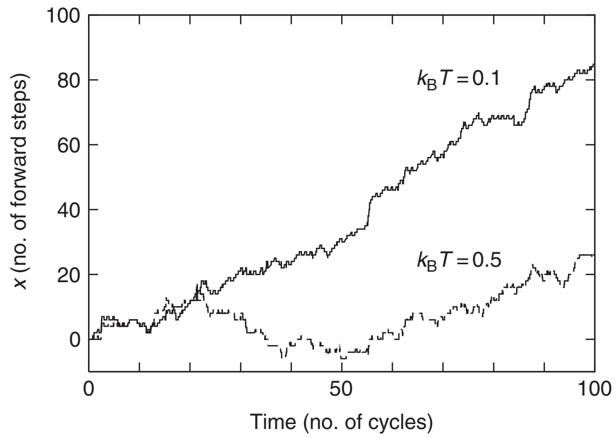

Figure 1.2 Movement in the discrete ratchet of Fig. 1.1, $H = A(\varphi_1 + \varphi_1\varphi_2)\mathcal{E}_0$ for A cycling between 0 and -1 and a degeneracy factor $g = 10$ for the detached state ($\varphi = 0$). When the temperature increases, the state $\varphi_1, \varphi_2 = 1, 1$ becomes thermodynamically suppressed, even when $A = -1$, and the "motor" performs a random walk (any trajectory between the (0,0) and the (1,1) states becomes equally likely). $k_\mathrm{B}T$ is measured in units of $\mathcal{E}_0$.

factor $\mathrm{e}^{-\mathcal{E}_0/k_\mathrm{B}T}$. Therefore the reversal in path (a) is suppressed, whereas reversal in path (b) is not. Figure 1.2 shows the simulated movement of x for two different temperatures. For the high temperature the motion stops, because the free energy of the (1,1) state always stays higher than that of the (0,0) state.