A Brownian ratchet is a Brownian particle moving in a periodic ratchet (asymmetric) potential, such as the one shown in Fig. 35. It turns out that the mean velocity of the Brownian particle is zero, which implies that such a potential cannot provide a mechanism for the Brownian particle (representing some molecular machine) to do useful work against an applied load. (The result that there is no net motion in a ratchet potential can be counter-intuitive, since one might think that it is more difficult to move backward and cross the steep slope.)

One mechanism for breaking the periodicity is to rectify the motion, as exemplified by polymerization ratchets and translocation ratchets; energy is provided by the binding of a molecule to the polymer or protein. Polymerization ratchets play a major role in cell motility and cell polarization, while the translocation ratchet is used to model the transport of a polymer such as DNA through a membrane pore. On one side of the membrane, proteins known as chaperones, which are too large to pass through the pore, bind the polymer and thus rectify its motion through the pore.

Figure 35: Brownian particle moving in a periodic ratchet potential $V(x)$.

### 13.1 Brownian motion in a periodic potential

Consider the 1D FP equation for a Brownian particle

$$\frac{\partial p}{\partial t} = D_0 \left[ \frac{1}{k_B T} \frac{\partial [V'(x) - F_0]p}{\partial x} + \frac{\partial^2 p}{\partial x^2} \right],$$

where $V(x)$ is an $L$–periodic potential, $V(x + L) = V(x)$ for all $x$, and $F_0$ is a constant external force, see Fig. 36.

In order to solve this equation, we introduce the effective potential or free energy $\mathcal{V}(x) = V(x) - F_0x$ and note that $\mathcal{V}'(x)$ is periodic even though $\mathcal{V}$ is not. Next we define the reduced probability density and currents

$$\hat{p}(x,t) = \sum_{n=-\infty}^{\infty} p(x + nL, t), \quad \hat{J}(x,t) = \sum_{n=-\infty}^{\infty} J(x + nL, t)$$

with

$$J(x,t) = -D_0 \left[ \frac{1}{k_B T} \mathcal{V}'(x)p + \frac{\partial p}{\partial x} \right].$$

It immediately follows that

$$\hat{p}(x + L, t) = \hat{p}(x, t), \quad \int_{0}^{L} \hat{p}(x,t)dx = 1.$$
Brownian ratchets

Figure 36: Brownian particle moving in a periodic potential $V(x)$. In the absence of tilt ($F_0 = 0$) the mean velocity in the long time limit is zero. On the other hand, in the presence of a tilt ($F_0 \neq 0$) the net motion of the particle is in the direction of the force.

condition $\int_{-\infty}^{\infty} p(x,t)dx = 1$.) The principle of superposition for a linear PDE then shows that $\hat{p}$ satisfies the FP equation

$$\frac{\partial \hat{p}(x,t)}{\partial t} + \frac{\partial \hat{J}(x,t)}{\partial x} = 0,$$

with

$$\hat{J}(x,t) = -D_0 \left[ \frac{1}{k_B T} V'(x) \hat{p} + \frac{\partial \hat{p}}{\partial x} \right]$$

and periodic boundary conditions at $x = 0, L$. There exists a stationary solution $\hat{p}_0$ of the reduced FP equation with constant flux $\hat{J}_0$ such that

$$\frac{d}{dx} \left( e^{V(x)/k_B T} \hat{p}_0(x) \right) = -\frac{\hat{J}_0}{D_0} e^{V(x)/k_B T}. \quad (13.6)$$

(The full FP equation does not have a non-trivial steady-state, since $p(x,t) \to 0$ as $t \to \infty$.) Integrating this equation from $x$ to $x + L$ and using periodicity yields the stationary solution

$$\hat{p}_0(x) = \frac{\hat{J}_0 N(x)}{[1 - e^{-F_0 L / k_B T}]}, \quad (13.7)$$

where

$$N(x) = \frac{1}{D_0} e^{-V(x)/k_B T} \int_x^{x+L} e^{V(y)/k_B T} dy. \quad (13.8)$$

Finally, $\hat{J}_0$ is determined by imposing the normalization condition on $\hat{p}_0$.

### 13.2 Mean velocity

A quantity of particular interest is the mean velocity defined as

$$v = \frac{d \langle X(t) \rangle}{dt} = \frac{d}{dt} \int_{-\infty}^{\infty} p(x,t)dx.$$
Taking the time derivative inside the integral over \( x \) and using the original FP equation shows that, after integration by parts,

\[
v = \int_{-\infty}^{\infty} J(x,t) dx = \int_0^L \tilde{J}(x,t) dx. \tag{13.9}\]

Since \( v = L \tilde{J}_0 \) for constant current, it follows that

\[
v = L \frac{1 - e^{-F_0 L / k_B T}}{\int_0^L \mathcal{N}(x) dx}. \tag{13.10}\]

It can be seen that there is no net motion in a purely periodic potential, since the numerator vanishes when \( F_0 = 0 \). Moreover the net direction of motion for \( F_0 \neq 0 \) is in the direction of the applied force.

### 13.3 Polymerization ratchet

One interesting application of ratchet potentials is to the so-called polymerization ratchet, which is a simplified model of the role of actin polymerization in changing the shape of a cell’s membrane during cell motility. Suppose that a section of cell membrane wall is undergoing Brownian motion in the presence of a resistive force \( F \) due to stretching, see Fig. 37(a). This motion is rectified by the addition of actin monomers to the end of an actin polymer filament, whenever the gap \( x \) between membrane wall and filament is sufficiently large. Assume that in the absence of a load force, actin monomers are added at a rate \( k_+ m \) and lost at a rate \( k_- \), where \( m \) is the background concentration of monomers.

First, consider the limiting case in which the mean time between attachments is sufficiently large so that the Brownian particle reaches thermal equilibrium. This means that the probability density

\[V(x)
\]

\[\Delta G
\]

\[x
\]

![Figure 37](image-url) (a) Cartoon of polymerization ratchet model. (b) Simplified ratchet model
for a gap of size $x$ is given by the Boltzmann-Gibbs distribution (lecture 1)

$$p(x) = \frac{F}{k_B T} e^{-Fx/k_B T}.$$ 

An estimate of the mean polymerization velocity is then

$$v = a [k_+ m P(x > a) - k_-]$$

where $a$ is the size of a monomer and

$$P(x > a) = \int_a^\infty p(x) dx = e^{-Fa/k_B T},$$

Finally, using the equilibrium law of mass action

$$\frac{k_+ m}{k_-} = e^{\Delta G/k_B T},$$

where $\Delta G$ is the binding energy, we have

$$v = ak_- \left[ e^{[\Delta G - Fa]/k_B T} - 1 \right],$$  \hspace{1cm} (13.11)

which suggests that growth stops when the resistive force $F$ becomes sufficiently large such that $F \geq F_S$, where the stall force $F_S = \Delta G/a$. A sketch of the velocity-load curve for typical values of $k_+, m, k_-$ and $a$ is shown in Fig. 38.

Let us now turn to the diffusion limited case, which can be analyzed using diffusion in a ratchet potential, see Fig. 37(b). This is obtained by ignoring spontaneous unbinding of monomers ($k_- = 0$) and assuming that as soon as the distance between the polymer and the wall is equal to $a$, a new monomer is immediately inserted, resulting in a sudden drop in energy by an amount $\Delta G$. However, it is possible to reverse direction by jumping over a free energy barrier of height $\Delta G$ - this represents the dislodging of a monomer due to wall motion.

The analysis of the reduced model proceeds along similar lines to the general motion of a Brownian particle in a tilted potential with

$$\mathcal{V}(x) = Fx - n\Delta G, \hspace{0.5cm} na < x < (n+1)a.$$
However, one now needs to take into account the discontinuities in $V(x)$ at the points $x = na$, integer $n$. Thus, equation (13.6) still holds, but care must be taken when integrating this equation with respect to $x \in (0, a]$. That is, it is necessary to introduce the matching condition

$$\lim_{x \to a^+} \hat{p}_0(x)e^{V(x)} = \lim_{x \to a^-} \hat{p}_0(x)e^{V(x)}$$

One finds that

$$v = \frac{2D_0}{a} \frac{\omega^2/2}{\mathcal{A}(1 - e^{-\omega}) - \omega}, \quad \omega = \frac{Fa}{k_BT}$$

with

$$\mathcal{A} = \frac{e^{\Delta G/k_BT} - 1}{e^{(\Delta G - Fa)/k_BT} - 1}.$$  \hspace{1cm} (13.13)

Note that $v \to 0$ as $Fa \to \Delta G$, since $\mathcal{A} \to \infty$. On the other hand, in the regime $\Delta G \gg Fa$ and $k_BT \gg Fa$,

$$v \approx \frac{2D_0}{a}.$$  

This latter result can be understood as follows: in the absence of a force $F$, the mean time for a diffusive displacement of size $a$ is $T = a^2/2D_0$ so that the mean speed is $v = a/T$.

13.4 Tethered ratchet model and cell motility

The growth and shrinkage of actin polymers plays a major role in generating the forces necessary for various forms of cell motility. For example, the movement of crawling cells such as amoeba, keratocytes, fibroblasts and migrating neurons involves the protrusion of lamellipodia and filopodia at the leading edge of the cell, see Fig. 39(a), which requires actin polymerization at the cell membrane boundary. On the other hand, intracellular pathogens such as *Listeria* propel themselves within a host cell by assembling the host cell’s actin into a comet-like tail. The tail consists of oriented cross-linked networks of actin filaments whose growing ends orient toward the bacterial surface, thus thrusting the pathogen forward, see Fig. 39(b). A major challenge is linking the complex biochemical processes regulating actin polymerization with mechanical properties of the cell and the associated forces. In the case of crawling cells, there are contractile forces on the actin cytoskeleton due to the action of myosin motors, traction forces from the drag between the cytoskeleton and surface adhesion complexes, membrane tension resisting the actin polymerization force, viscoelastic stresses arising from deformations of the actin network, and viscous drag between actin filaments and cytosolic fluid flows.

Here we consider a microscopic model of cell protrusion based on an extension of the polymerization ratchet model due to Mogilner and Oster (1996) within the context of the simpler problem of *Listeria* propulsion. Recall that the speed of growth of a polymerization ratchet depends on the diffusion coefficient of membrane Brownian motion. Within the context of bacterial motion, this would imply that the bacterial velocity depends on its diffusion coefficient, and thus on its size. However, such size-dependence has not been observed experimentally, which led Mogilner and Oster to propose an elastic ratchet model, in which thermal bending fluctuations of a semi–stiff actin filament, rather then bacterial diffusion, generates the gap necessary for insertion of an additional monomer, with the resulting growth generating the force to propel the bacterium forward. The elastic ratchet model was itself superseded by the tethered ratchet model, in order to account for a number of additional experimental observations. In particular, Brownian fluctuations are almost completely...
Brownian ratchets

Paul C Bressloff (Spring 2019)

Figure 39: Examples of actin-based cell motility (a) Crawling eukaryotic cell. (b) Pathogen such as *Listeria* propelled by an actin tail assembled from the cytoskeleton of the host cell.

suppressed during *Listeria* propulsion due to the fact that the bacterium is tightly bound to its actin tail. One thus observes smooth particle trajectories that are persistent in both direction and curvature. It is known that the surface of *Listeria* is coated with nucleation promotion factor ActA, which transiently binds the Arp2/3 complex on the sides of attached actin filaments; Arp2/3 is known to mediate nucleation of side-branched filaments. The tethered ratchet model is one way to resolve the dilemma of how the actin tail can be attached to the bacterium, and yet propel the bacterium forward via growth of unattached active filaments. More specifically, it proposes that there are two classes of filament: some are attached, under tension and nucleating rather than growing, while others are unattached and pushing via an elastic ratchet mechanism. In the following, we will describe the tethered ratchet model in more detail.

Suppose that there are $n_a(t)$ unattached filaments and $n_a(t)$ attached filaments at time $t$ and that the bacterium is moving at speed $v$. There are three forces acting on the bacterium, neglecting any elastic recoil forces of the actin tail, see Fig 40: a load force $F_L = \gamma v + F_{\text{ext}}$, where $\gamma$ is a viscous drag coefficient and $F_{\text{ext}}$ represents any experimentally imposed external forces; a tensional force $F_a = n_a f_a$ due to attached filaments, with $f_a$ the force per filament; a pushing force $F_u = n_u f_u$ due to unattached filaments, with $f_u$ the force exerted by a single unattached filament via an elastic ratchet mechanism. The corresponding force-balance equation is

$$F_L + n_a f_a = n_u f_u.$$  \hspace{1cm} (13.14)

It is assumed that the two filament populations evolve according to the simple kinetic equations

$$\frac{dn_a}{dt} = \sigma - k n_a, \quad \frac{dn_u}{dt} = k n_a - \kappa n_u,$$  \hspace{1cm} (13.15)

where $\sigma$ is the nucleation rate of side branches, $k$ is the rate of detachment, and $\kappa$ is the rate of capping of unattached filaments which can then no longer polymerize and push on the bacterium’s surface. It remains to specify the dependence of the forces $f_a, f_u$ and the detachment rate $k$ on the bacterium velocity $v$. The force-velocity relation for a single polymerizing filament is taken to from the polymerization ratchet model (see equation (13.11)):

$$v = v_+ e^{-f_u l / k_B T} - v_-,$$  \hspace{1cm} (13.16)

where $v_+ = k_{\text{on}} l M$ is the polymerization velocity and $v_- = k_{\text{off}} l$ is the depolymerization velocity. Here $k_{\text{on}}$ and $k_{\text{off}}$ are the rates of monomer assembly and disassembly, $M$ is the concentration of...
monomers available for polymerization, and $l$ is the effective increase in filament length due to addition of one monomer.

In order to estimate the average attachment force $f_a$, it is assumed that an attached filament acts like a Hookean spring. Suppose that the filament binds to an ActA complex at time $t = 0$. The force acting on the resulting bond is given by $f(t) = \eta vt$, where $\eta$ is the effective spring constant. Using the basic theory of chemical bond breaking, the rate of detachment takes the velocity-dependent form

$$k(v, t) = k_0 e^{\eta vt/l},$$  

where $x_b = f_b/\eta$ can be interpreted as bond length at which the bond breaks sharply. The probability $p(t)dt$ of the bond first breaking in the time interval $(t, t + dt)$ is given by the product of no failure in the interval $(0, t)$ times the probability of subsequent failure within the interval $(t, t + dt)$. Hence,

$$p(t) = k(v, t)e^{-\int_0^t k(v, s)ds}.$$  

Set $v_0 = f_bk_0/\eta$, which can be interpreted as the velocity at which the bond stretches to the critical length $x_b$ over the characteristic bond lifetime $1/k_0$. Rescaling velocity and time according to $\mu = v/v_0$ and $\tau = k_0t$, we have

$$p(\tau) = \exp \left( \mu \tau + \frac{1}{\mu} \right).$$

It follows that the mean attachment time of a filament (for constant $v$) is

$$\langle t \rangle = \frac{1}{k_0} \int_0^\infty \tau p(\tau)d\tau = \frac{1}{k_0} w(\mu),$$  

with

$$w(\mu) = \int_0^\infty \tau \exp \left( \mu \tau + \frac{1-e^{-\mu \tau}}{\mu} \right)d\tau.$$
Figure 41: The load-velocity curve for the tethered ratchet model of Mogilner and Oster (2003). The solid curve is generated from equation (13.20) using the following parameter values: monomer size \( l = 2.2 \text{nm} \), polymerization velocity \( v_+ = 500 \text{nm/s} \), depolymerization velocity \( v_- = 2.2 \text{nm/s} \), nucleation rate \( \sigma = 10 \text{s}^{-1} \), capping rate \( \kappa = 0.5 \text{s}^{-1} \), free detachment rate \( k_0 = 0.5 \text{s}^{-1} \), thermal energy \( k_B T = 4.1 \text{pN nm} \), effective length of bond \( x_b = 0.4 \text{nm} \), effective strength of bond \( f_b = 10 \text{pN} \), and spring coefficient \( \eta = 1 \text{pN/nm} \). The dashed curve is obtained by introducing a threefold increase in the nucleation rate \( \sigma \), and illustrates the effect of filament density on the load-velocity behavior. Finally, the squares represent data from stochastic model simulations with a reduced polymerization velocity \( v_+ = 240 \text{nm/s} \).

We now identify the mean detachment rate as \( k = 1/\langle t \rangle \) and take the average force \( f_a \) exerted by a single attached filament to be \( f_a = \eta v \langle t \rangle \). Thus,

\[
k(\mu) = \frac{k_0}{w(\mu)}, \quad f_a = f_b \mu w(\mu). \quad (13.19)
\]

Note that the function \( w(\mu) \) has the following properties:

1. If \( \mu \ll 1 \) then \( w(\mu) \approx 1 \), which implies that for sufficiently slow movement (\( v \ll v_0 \)) the effective detachment rate is equal to the force-free rate (\( k \approx k_0 \)) and \( f_a \approx f_b v/v_0 \).

2. If \( \mu \gg 1 \) then \( w(\mu) \approx \mu^{-1} \ln \mu \).

Consider the case of constant propulsion speed \( v \). The steady–state numbers of attached and detached filaments are then

\[
n_a = \sigma/k, \quad n_u = \sigma/\kappa.
\]

Substituting the force-balance equation (13.14) into the velocity equation (13.16) gives

\[
v = v_+ \exp \left[ -l (n_a f_a/n_u + F_l/n_u)/k_B T \right] - v_-.
\]

Since \( n_a/n_u = \kappa/k = w(\mu) \kappa/k_0 \) and \( f_a = f_b \mu w(\mu) \), the velocity satisfies the implicit equation

\[
v = v_+ \exp \left[ -l \left( \frac{f_b k_0}{\kappa v_0} w^2 (v/v_0) + \frac{F_L \kappa}{\sigma} \right)/k_B T \right] - v_- \quad (13.20)
\]
Using biophysically based estimates for the various parameters, Mogilner and Oster numerically solved the equation for $v$ and obtained speeds of the order 10nm/s, which is consistent with experimental data, see Fig. 41. They also showed that the load-velocity relation exhibits biphasic behavior, whereby the velocity decreases rapidly with $F_L$ at low load forces and decreases more slowly at high load forces. This is a consequence of the modeling assumptions regarding chemical bond breaking. At high velocities increasing the external load helps the attached filaments to hold on longer, thus increasing the resistive force $F_a$ which itself slows the bacterium further. On the other hand, at sufficiently slow velocities the external load has a minor effect on the resistive force $F_a$ and the velocity decreases more slowly.

13.5 Translocation ratchet

Following gene expression, many proteins have to translocate into or across a cellular membrane. Examples include translocation through nuclear pores and through pores in the endoplasmic reticulum. It has been suggested that translocation may be driven by a brownian ratchet. The basic mechanism is illustrated in Fig. 42. Once the protein chain enters a pore, thermal fluctuations causes it to diffuse back and forth through the pore without any net displacement. However, suppose that the protein has ratchet sites that are equally spaced along the chain with nearest neighbor separation $\delta$. In the case of a perfect ratchet, it is assumed that once a ratchet site has passed through the pore it cannot re-enter the pore, that is, it is reflected. On the other hand, for an imperfect ratchet there is a certain probability $\pi$ of reflection. The latter could be due to the binding of a macromolecule (chaperonin) to the ratchet site on the distal side of the pore.

Consider a translocation ratchet and let $p(x, t)$ be the probability density that $X(t) = x$, where $X(t), 0 < X(t) < \delta$, is the position of the first ratchet site to the right of the pore exit. Let $F$ be the net force resisting translocation of the protein. The corresponding FP equation takes the form

$$\frac{\partial p}{\partial t} + \frac{\partial J}{\partial x} = 0, \quad J = -\frac{DF}{k_BT}p - D\frac{\partial p}{\partial x}. \quad (13.21)$$

The boundary conditions for a perfect ratchet are

$$J(0, t) = J(\delta, t), \quad p(\delta, t) = 0. \quad (13.22)$$

The periodic flux condition expresses the fact that as soon as one ratchet site crosses $x = \delta$, another site appears at $x = 0$, with $x = \delta$ treated as an absorbing boundary. The steady-state solution

![Figure 42: Cartoon of a translocation ratchet.](image-url)
satisfies the constant flux condition
\[ -\frac{DF}{k_B T}p - D \frac{\partial p}{\partial x} = J_0. \]

Multiplying both sides by \( D^{-1} e^{Fx/k_B T} \), integrating from \( x \) to \( \delta \), and using the absorbing boundary condition yields
\[ p(x) = \frac{k_B T J_0}{DF} \left[ e^{F(\delta-x)/k_B T} - 1 \right]. \]

Imposing the normalization condition \( \int_0^1 p(x) dx = 1 \) then determines \( J_0 \) according to
\[ 1 = \frac{J_0 \delta^2}{D} \frac{1}{\omega} \left[ e^\omega - 1 \right], \quad \omega = \frac{F\delta}{k_B T}. \]

It follows that the average speed of the perfect translocation ratchet is
\[ v = \delta J_0 = \frac{2D}{\delta} \frac{\omega^2}{e^\omega - 1 - \omega}. \quad (13.23) \]

Note that one major simplification of the above model is that it treats the translocating polymer as rigid. However, a polymer such as a protein or DNA tends to be highly coiled (small persistence length) so that one has to take into account an effective entropic force, reflecting the fact that a free polymer has many more configurational states than one that is threaded through a pore.