Escape Problems & Stochastic Resonance

18.S995 - L05

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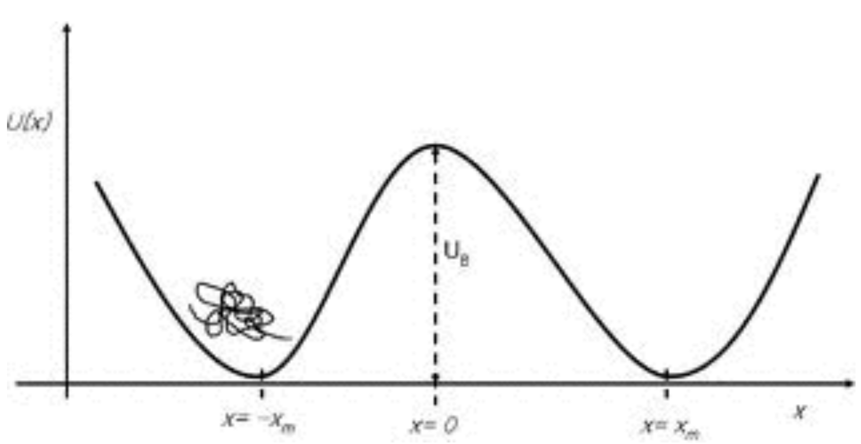
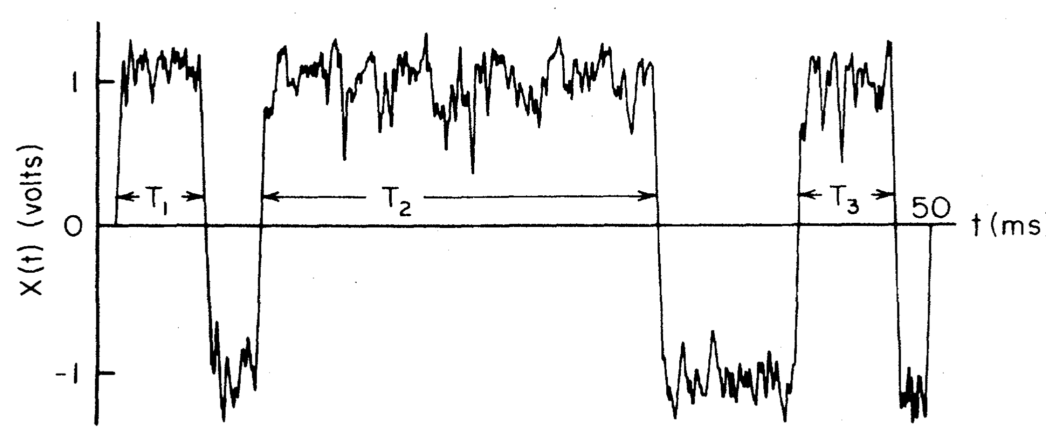
1.4 Escape problem

Escape problems are ubiquitous in biological, biophysical and biochemical processes. Prominent examples include, but are not restricted to,

- unbinding of molecules from receptors,
- chemical reactions,
- transfer of ion through through pores,
- evolutionary transitions between different fitness optima.

Their mathematical treatment typically involves models that are structurally very similar to the one-dimensional examples discussed in this section[13].

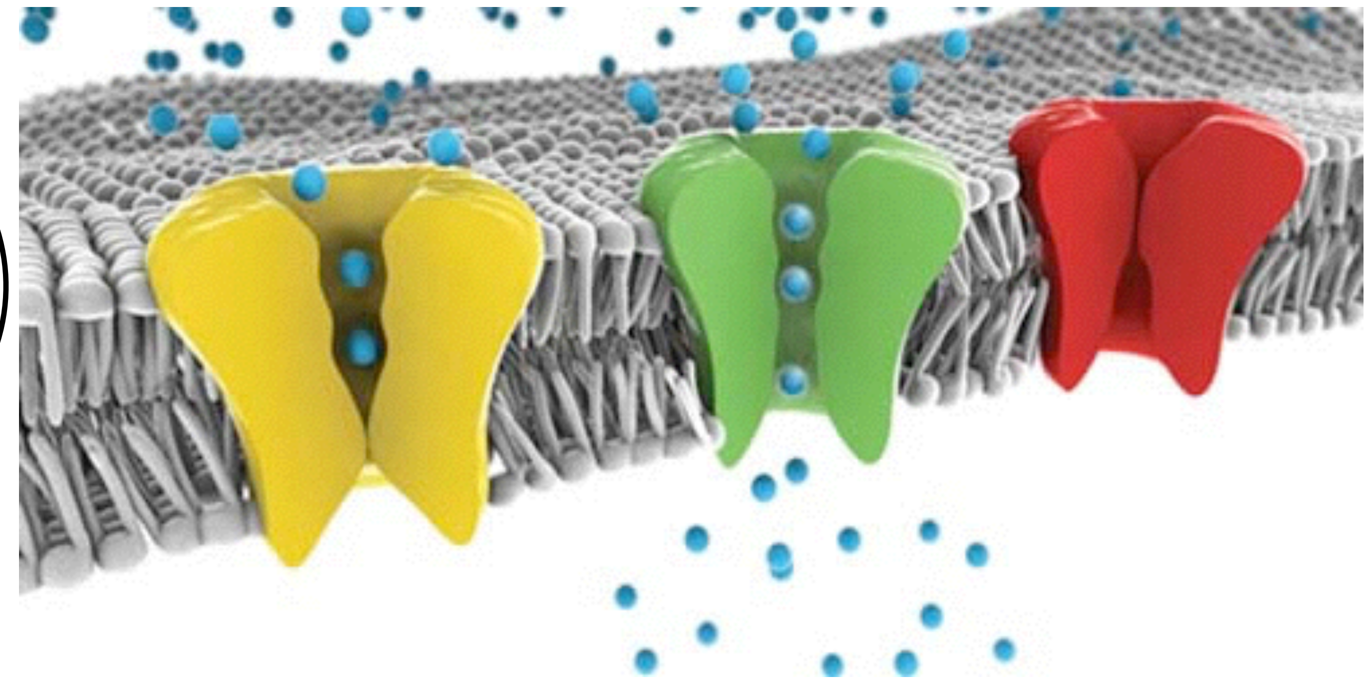


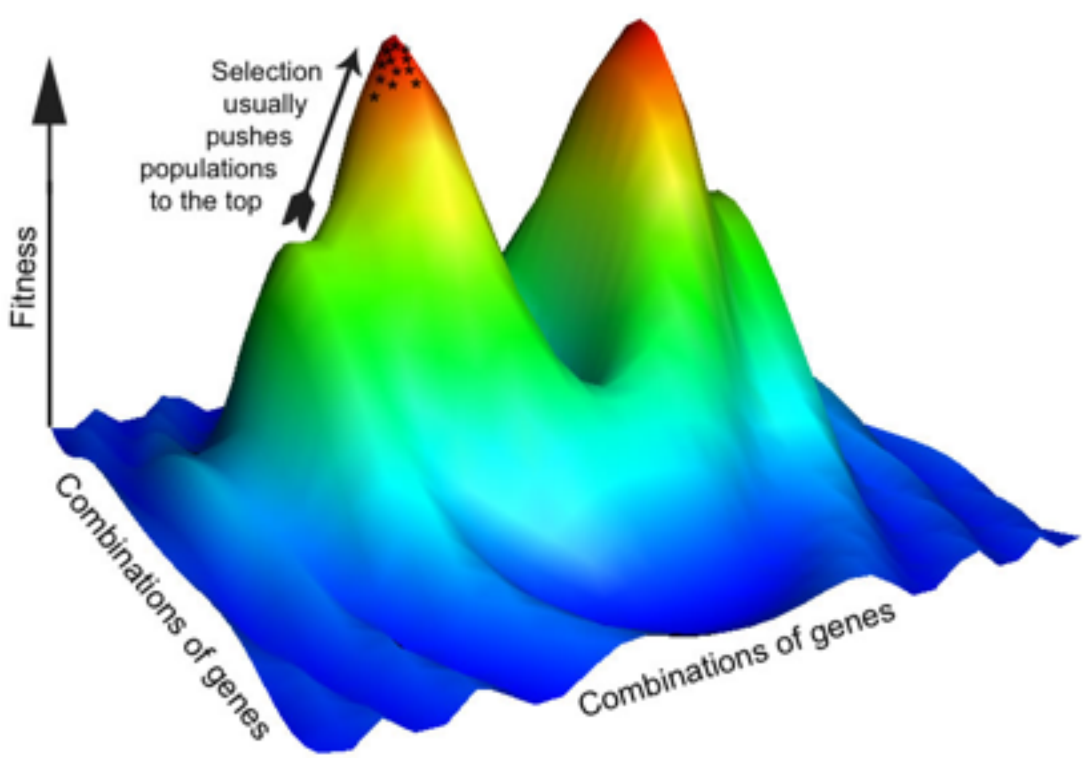


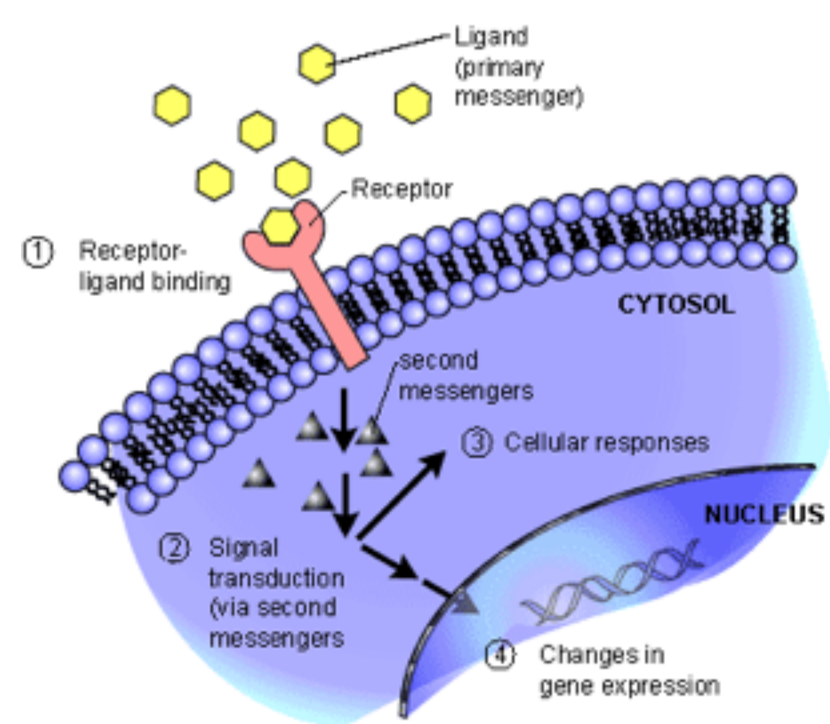
Examples

transport & evolution:
stochastic
escape problems

Illustration by J.P. Cartailler. Copyright 2007, Symmation LLC.







http://evolutionarysystemsbiology.org/intro/

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Reviews of Modern Physics, Vol. 62, No. 2, April 1990

Reaction-rate theory: fifty years after Kramers

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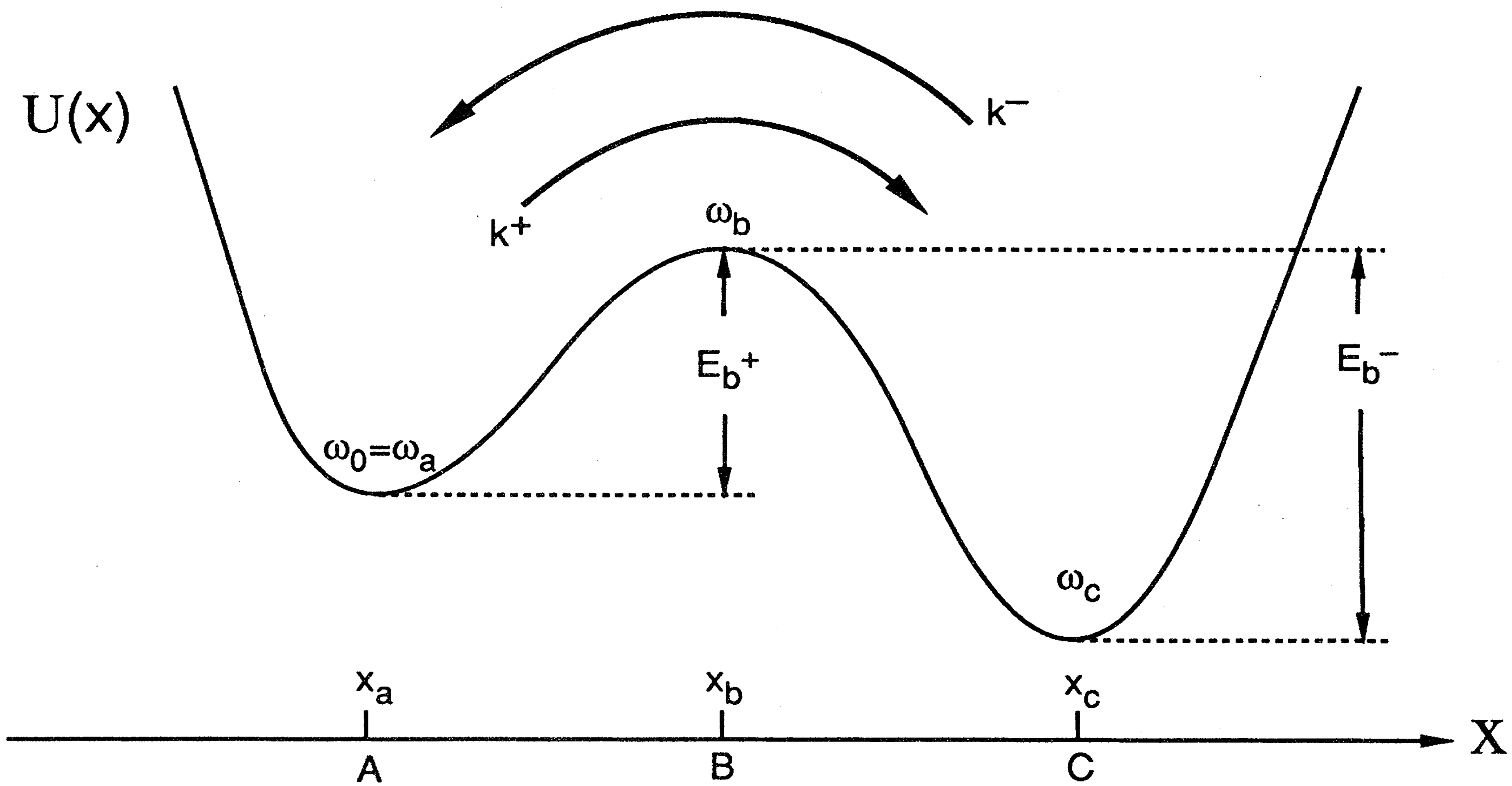

FIG. 3. Potential $U(x)$ with two metastable states A and C. Escape occurs via the forward rate k^+ and the backward rate k^-, respectively, and $E_b^{\pm}$ are the corresponding activation energies.

Arrhenius law

$$k = \nu \exp(-\beta E_b)$$

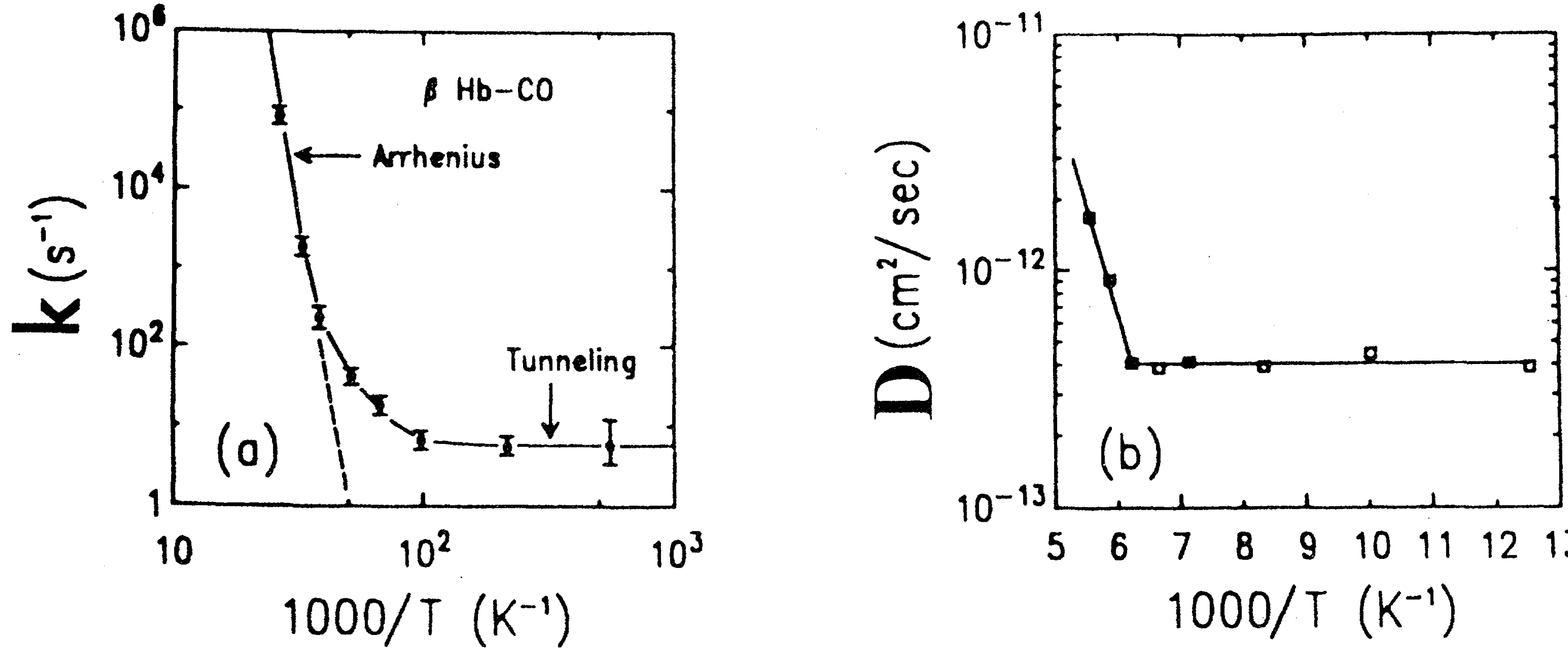

FIG. 2. Van't Hoff-Arrhenius plots of reaction-rate data for two different physical systems in which both thermal activation and tunneling events occur: (a) Rate of CO migration to a separated β chain of hemoglobin (Alberding *et al.*, 1976; Frauenfelder, 1979); (b) diffusion coefficient D of atomic hydrogen moving on the (110) plane of tungsten at a relative H-coverage of 0.1 (data taken from DiFoggio and Gomer, 1982). The diffusion D is directly proportional to the hopping rate k.

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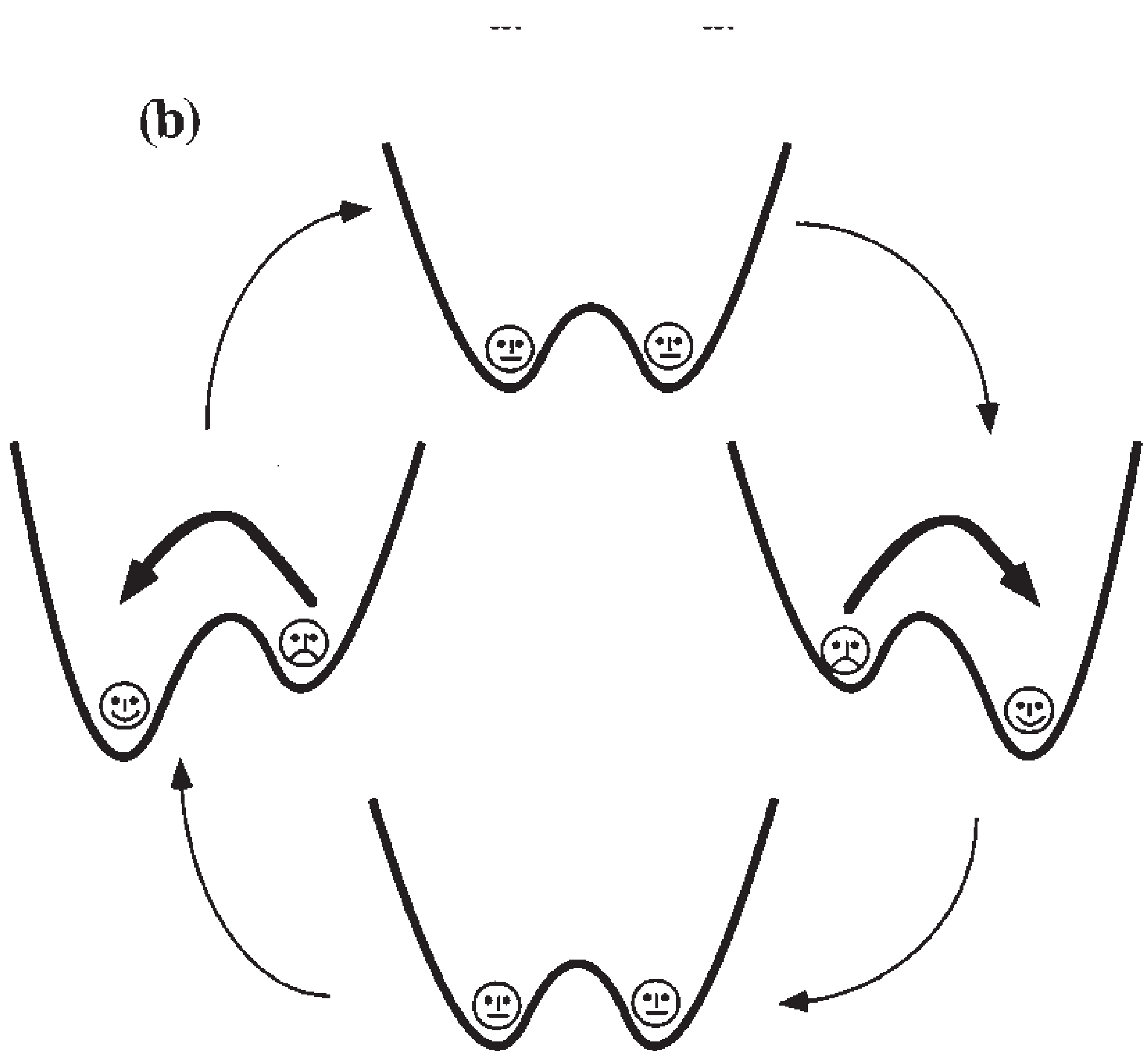
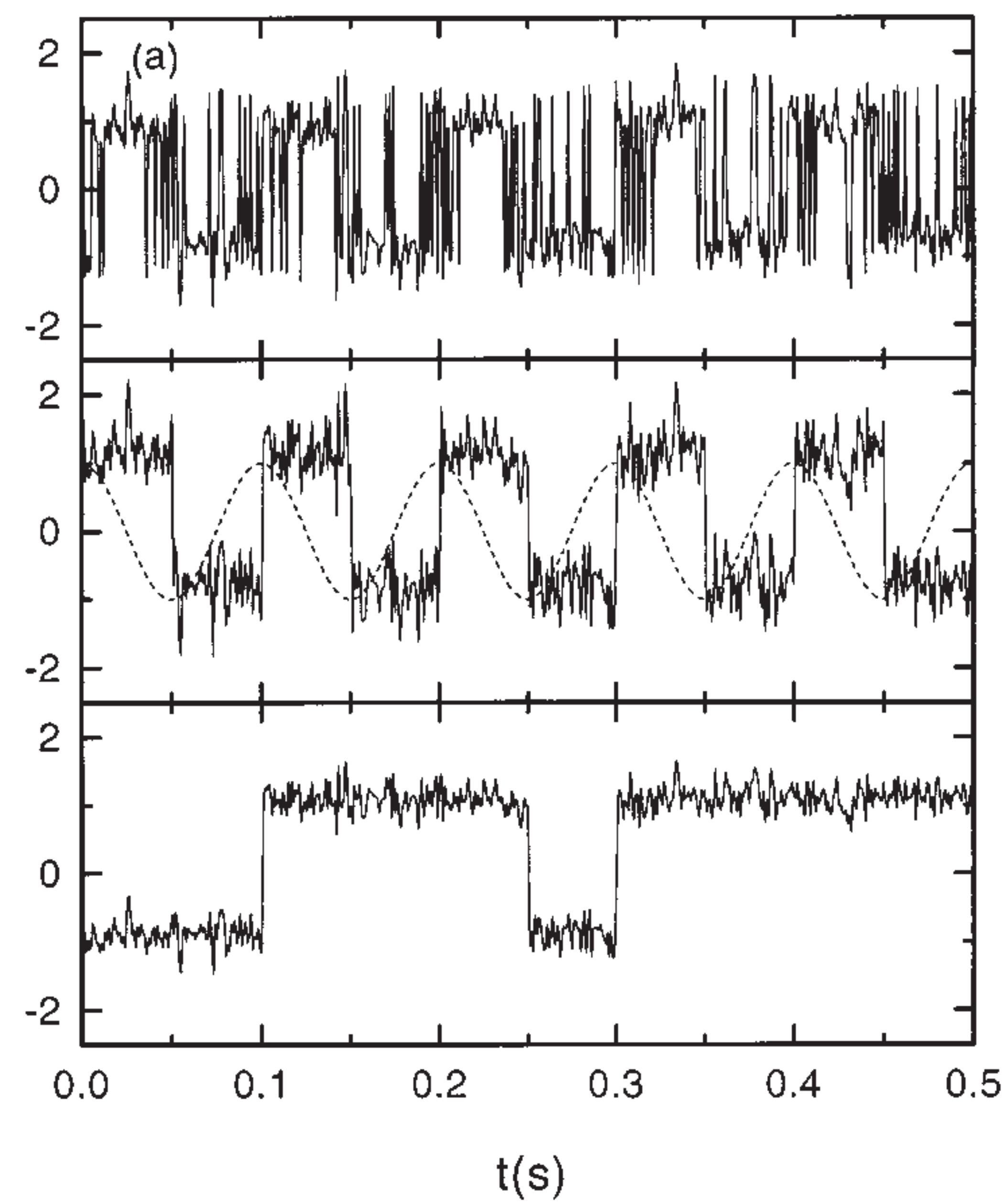
Stochastic resonance





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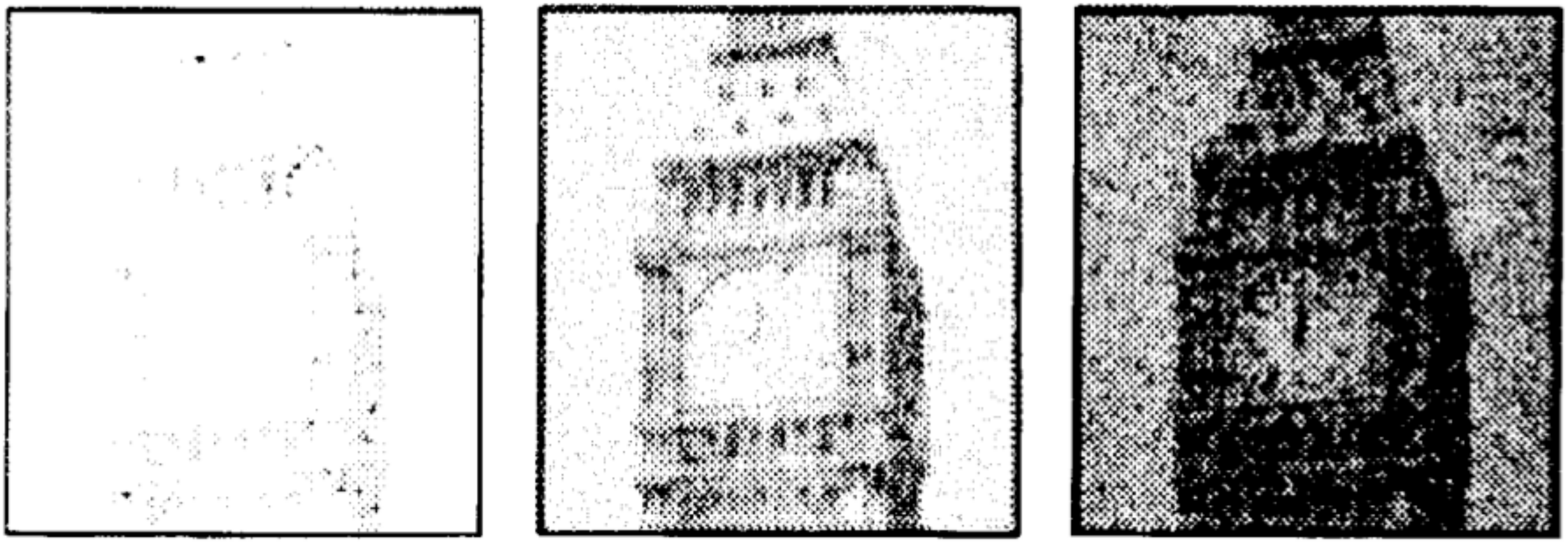
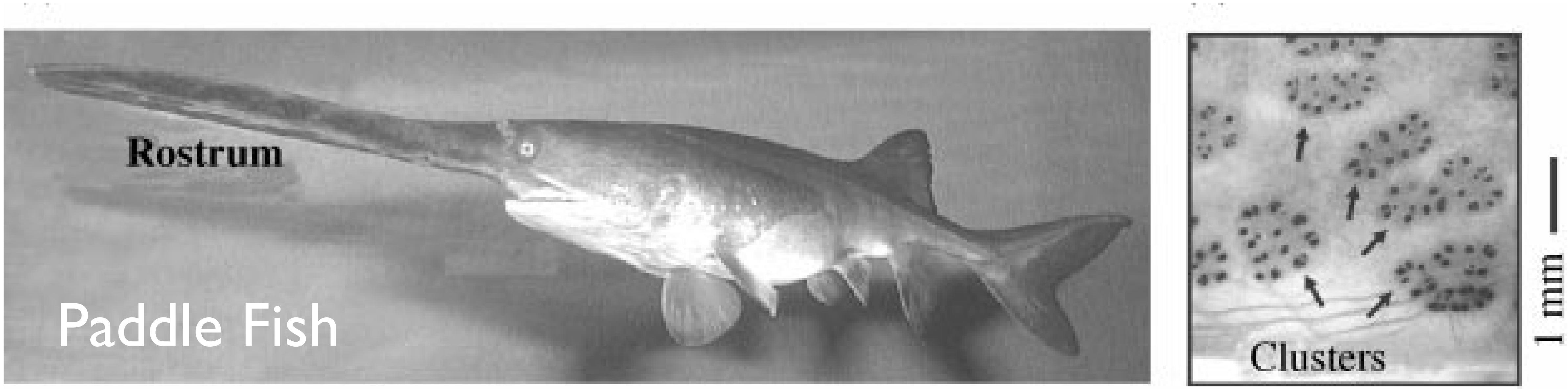
Using fitness landscapes to visualize evolution in action

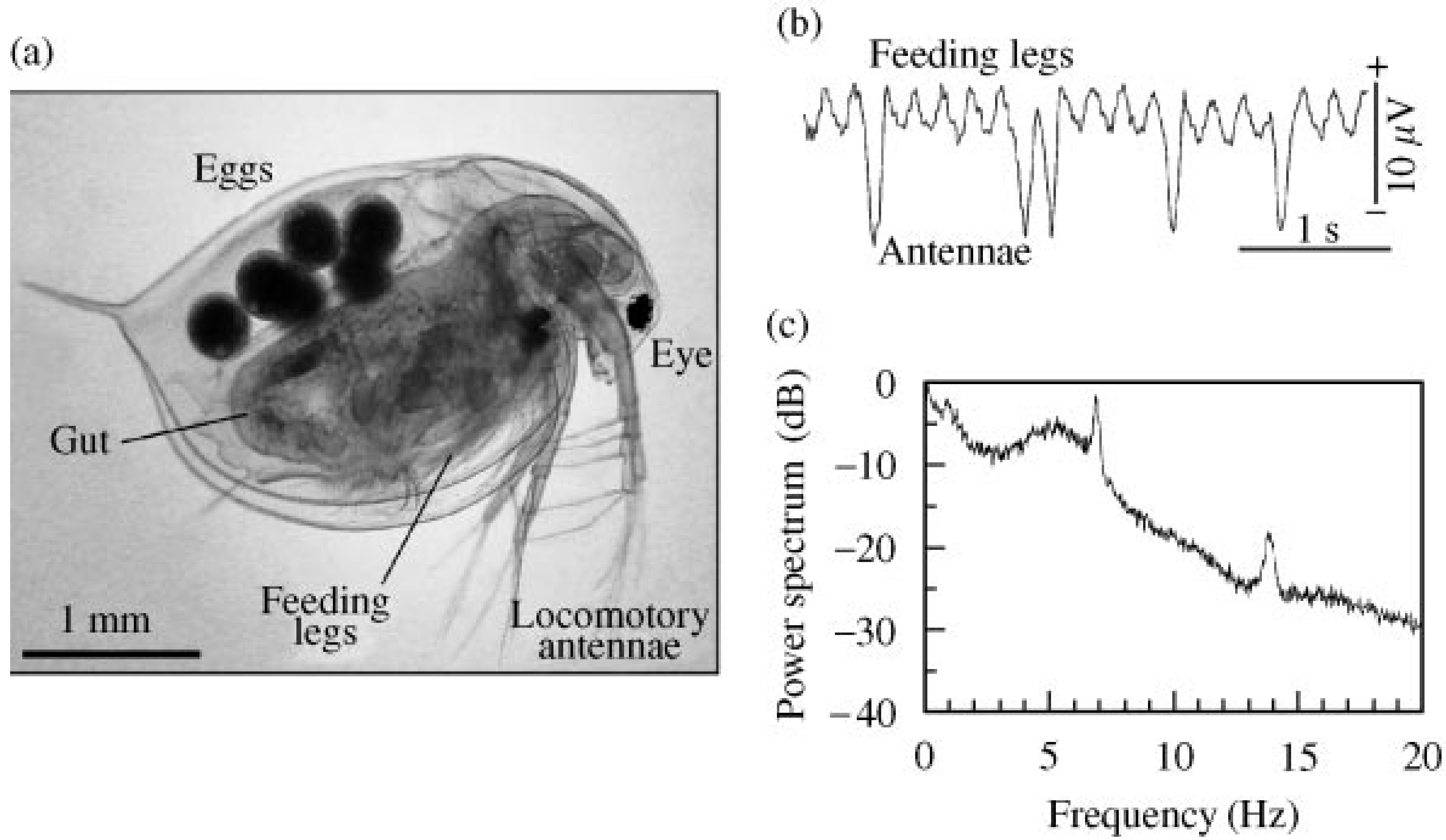
A film by Randy Olson and Bjørn Østman

https://www.youtube.com/watch?v=4pdiAneMMhU



Freund et al (2002) J Theor Biol





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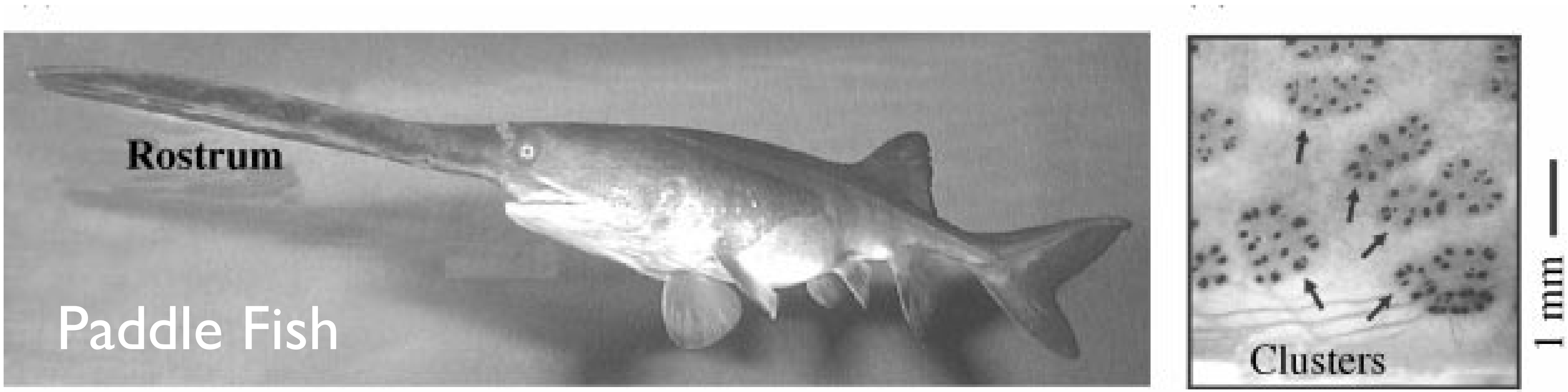
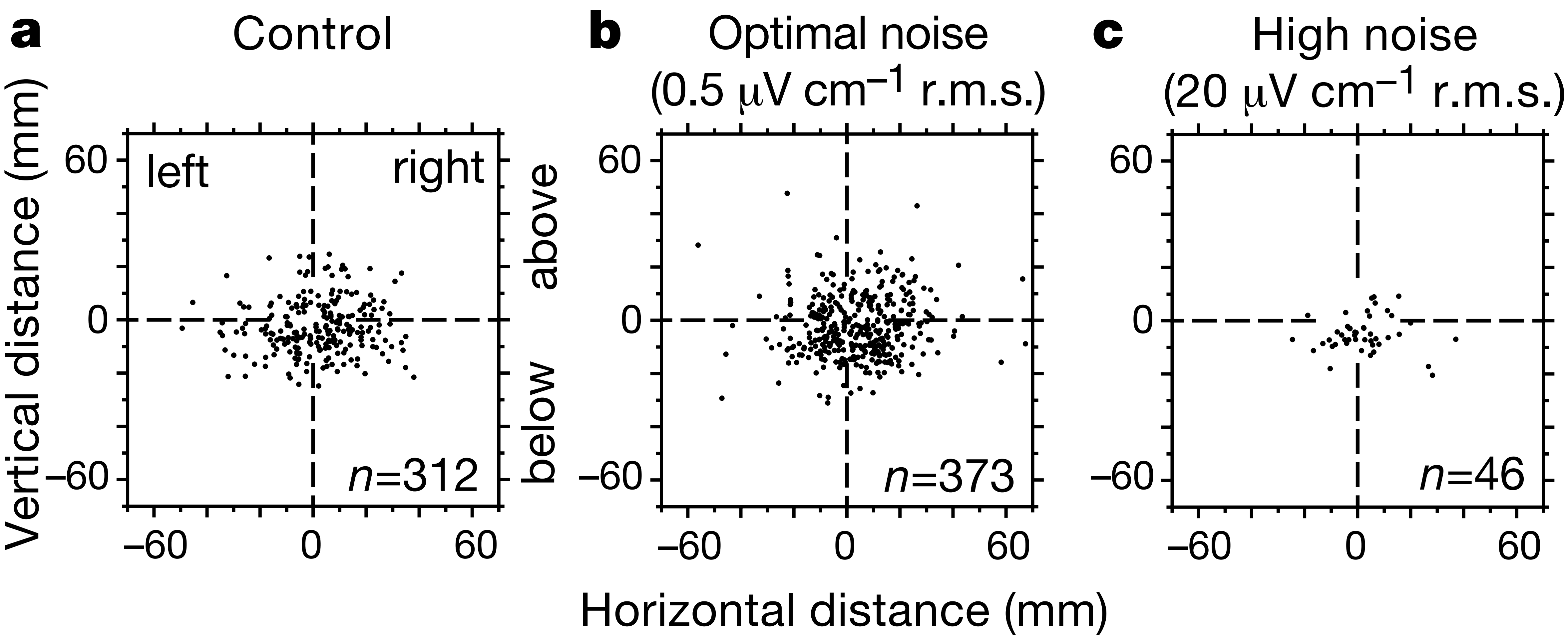
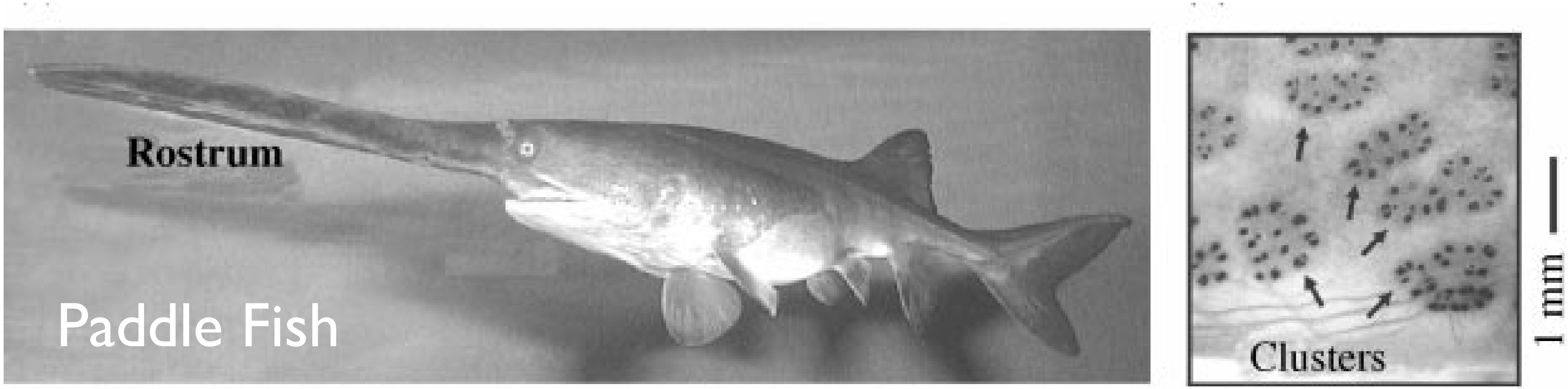




Russel et al (1999) Nature

Freund et al (2002) J Theor Biol



sensory system. However, stochastic resonance requires an external source of electrical noise in order to function. A swarm of plankton, for example *Daphnia*, can provide the required noise. We hypothesize that juvenile paddlefish can detect and attack single *Daphnia* as outliers in the vicinity of the swarm by using noise from the swarm itself. From the power spectral density of the noise plus the weak signal from a single *Daphnia*, we calculate the signal-to-noise ratio, Fisher information and discriminability at the surface of the paddlefish's rostrum. The results predict a specific attack pattern for the paddlefish that appears to be experimentally testable.

1.4.1 Generic minimal model

Consider the over-damped SDE

$$dx(t) = -\partial_x U dt + \sqrt{2D} * dB(t) \tag{1.68a}$$

with a confining potential $U(x)$

$$\lim_{x \to \pm\infty} U(x) \to \infty \tag{1.68b}$$

that has two (or more) minima and maxima. A typical example is the bistable quartile double-well

$$U(x) = -\frac{a}{2}x^2 + \frac{b}{4}x^4 , \qquad a, b > 0 \tag{1.68c}$$

with minima at $\pm\sqrt{a/b}$.

Generally, we are interested in characterizing the transitions between neighboring minima in terms of a rate k (units of time^{-1}) or, equivalently, by the typical time required for escaping from one of the minima. To this end, we shall first dicuss the general structure of the time-dependent solution of the FPE[14] for the corresponding PDF $p(t, x)$, which reads

$$\partial_t p = -\partial_x j , \qquad j(t, x) = -[(\partial_x U)p + D\partial_x p], \tag{1.68d}$$

and has the stationary zero-current ($j \equiv 0$) solution

$$p_s(x) = \frac{e^{-U(x)/D}}{Z} , \qquad Z = \int_{-\infty}^{+\infty} dx\, e^{-U(x)/D}. \tag{1.69}$$

General time-dependent solution

$$\partial_t p = -\partial_x j \ , \qquad j(t,x) = -[(\partial_x U)p + D\partial_x p], \tag{1.68d}$$

To find the time-dependent solution, we can make the ansatz

$$p(t,x) = \varrho(t,x)\, e^{-U(x)/(2D)}, \tag{1.70}$$

which leads to a Schrödinger equation in imaginary time

$$-\partial_t \varrho = \left[-D\partial_x^2 + W(x)\right] \varrho =: \mathcal{H}\varrho, \tag{1.71a}$$

with an effective potential

$$W(x) = \frac{1}{4D}(\partial_x U)^2 - \frac{1}{2}\partial_x^2 U. \tag{1.71b}$$

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Assuming the Hamilton operator $\mathcal{H}$ has a discrete non-degenerate spectrum, $\lambda_0 < \lambda_1 < \ldots$, the general solution $p(t,x)$ may be written as

$$p(t,x) = e^{-U(x)/(2D)} \sum_{n=0}^{\infty} c_n\, \phi_n(x)\, e^{-\lambda_n t}, \tag{1.72a}$$

where the eigenfunctions ϕ_n of $\mathcal{H}$ satisfy

$$\int dx\ \phi_n^*(x)\, \phi_m(x) = \delta_{nm}, \tag{1.72b}$$

and the constants c_n are determined by the initial conditions

$$c_n = \int dx\ \phi_n^*(x)\, e^{U(x)/(2D)}\ p(0,x). \tag{1.72c}$$

General time-dependent solution

$$p(t,x) = e^{-U(x)/(2D)} \sum_{n=0}^{\infty} c_n \, \phi_n(x) \, e^{-\lambda_n t}$$

At large times, $t \to \infty$, the solution (1.72a) must approach the stationary solution (1.69), implying that

$$\lambda_0 = 0 \,, \qquad c_0 = \frac{1}{\sqrt{Z}} \,, \qquad \phi_0(x) = \frac{e^{-U(x)/(2D)}}{\sqrt{Z}} . \tag{1.73}$$

Note that $\lambda_0 = 0$ in particular means that the first non-zero eigenvalue $\lambda_1 > 0$ dominates the relaxation dynamics at large times and, therefore,

$$\tau_* = 1/\lambda_1 \tag{1.74}$$

is a natural measure of the escape time. In practice, the eigenvalue λ_1 can be computed by various standard methods (WKB approximation, Ritz method, techniques exploiting supersymmetry, etc.) depending on the specifics of the effective potential W.

1.4.2 Two-state approximation

We next illustrate a commonly used simplified description of escape problems, which can be related to (1.74). As a specific example, we can again consider the escape of a particle from the left well of a symmetric quartic double well-potential

$$U(x) = -\frac{a}{2}x^2 + \frac{b}{4}x^4 \,, \qquad p(0,x) = \delta(x - x_-) \tag{1.75a}$$

where

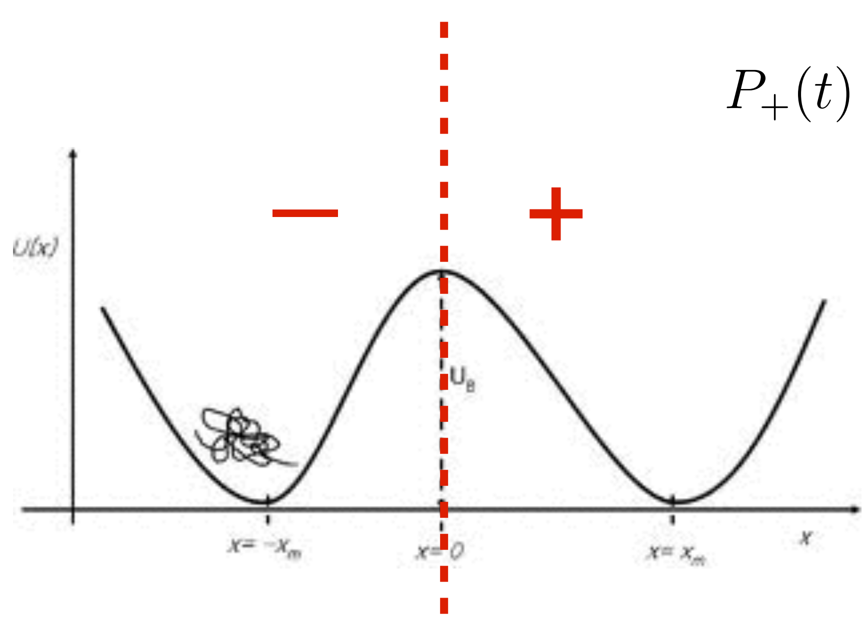
$$x_- = -\sqrt{a/b} \tag{1.75b}$$

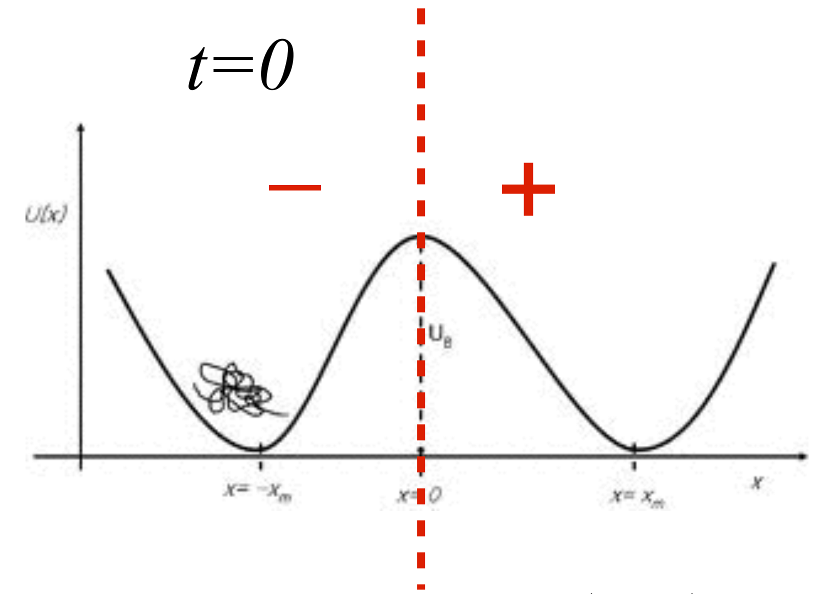
is the location of the left minimum, but the general approach is applicable to other types of potentials as well.

The basic idea of the two-state approximation is to project the full FPE dynamics onto simpler set of master equations by considering the probabilities $P_\pm(t)$ of the coarse-grained particle-states 'left well' $(-)$ and 'right well' $(+)$, defined by

$$P_-(t) = \int_{-\infty}^{0} dx\, p(t,x), \tag{1.76a}$$

$$P_+(t) = \int_{0}^{\infty} dx\, p(t,x). \tag{1.76b}$$





If all particles start in the left well, then

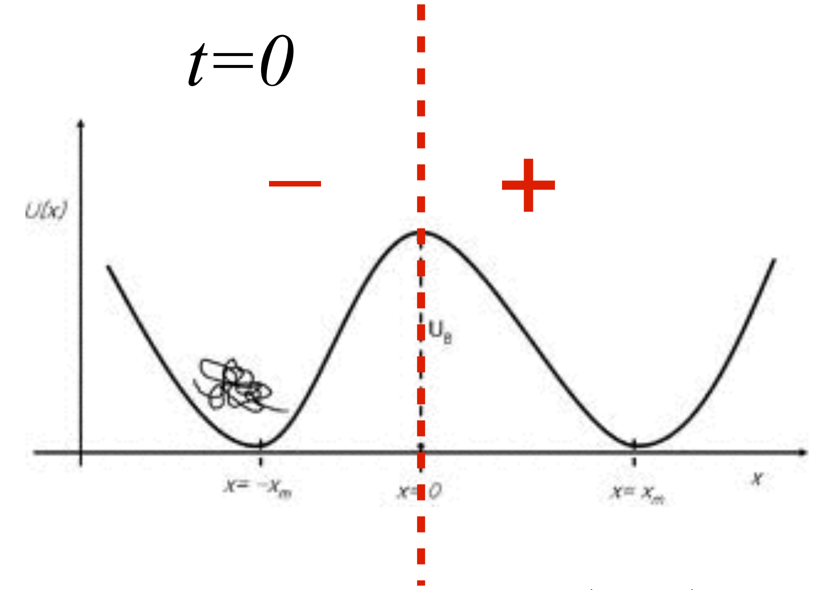
$$P_{-}(0) = 1\ , \qquad P_{+}(0) = 0. \tag{1.77}$$

Whilst the exact dynamics of $P_{\pm}(t)$ is governed by the FPE (1.68d), the two-state approximation assumes that this dynamics can be approximated by the set of master equations[15]

$$\dot{P}_{-} = -k_{+}\, P_{-} + k_{-}\, P_{+}\ , \qquad \dot{P}_{+} = k_{+}\, P_{-} - k_{-}\, P_{+}. \tag{1.78}$$

For a symmetric potential, $U(x) = U(-x)$, forward and backward rates are equal, $k_{+} = k_{-} = k$, and in this case, the solution of Eq. (1.78) is given by

$$P_{\pm}(t) = \frac{1}{2} \mp \frac{1}{2}\, e^{-2k\,t}. \tag{1.79}$$



If all particles start in the left well, then

$$P_-(0) = 1\ , \qquad P_+(0) = 0. \tag{1.77}$$

Whilst the exact dynamics of $P_\pm(t)$ is governed by the FPE (1.68d), the two-state approximation assumes that this dynamics can be approximated by the set of master equations[15]

$$\dot{P}_- = -k_+\,P_- + k_-\,P_+\ , \qquad \dot{P}_+ = k_+\,P_- - k_-\,P_+. \tag{1.78}$$

For a symmetric potential, $U(x) = U(-x)$, forward and backward rates are equal, $k_+ = k_- = k$, and in this case, the solution of Eq. (1.78) is given by

$$P_\pm(t) = \frac{1}{2} \mp \frac{1}{2}\,e^{-2k\,t}. \tag{1.79}$$

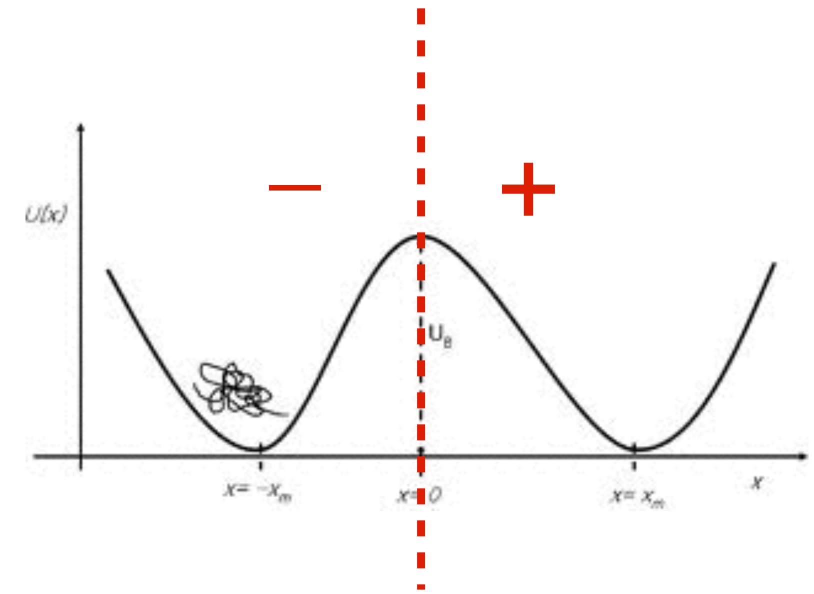
For comparison, from the FPE solution (1.72a), we find in the long-time limit

$$p(t,x) \simeq p_s(x) + c_1 e^{-U(x)/2D}\phi_1(x)\ e^{-\lambda_1 t}, \tag{1.80}$$

Due to the symmetry of $p_s(x)$, we then have

$$P_-(t) \simeq \frac{1}{2} + C_1\,e^{-\lambda_1 t} \tag{1.81a}$$

[15]Note that Eqs. (1.78) conserve the total probability, $P_-(t) + P_-(t) = 1$.



Solution

$$P_-(t) \simeq \frac{1}{2} + C_1\, e^{-\lambda_1 t}$$

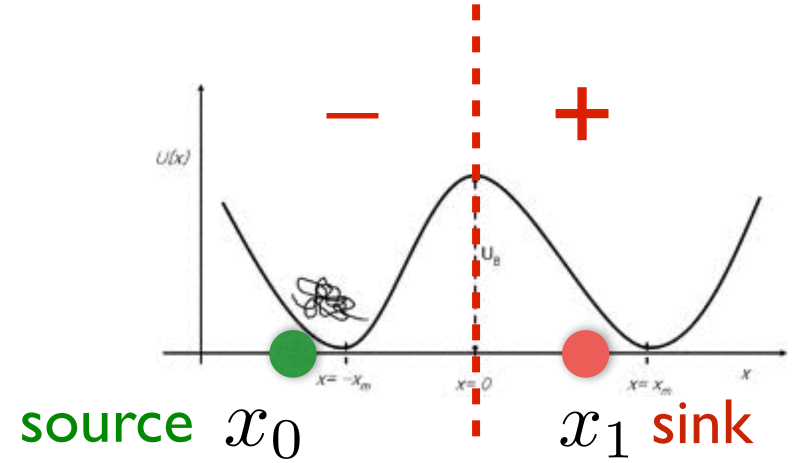
where

$$C_1 = c_1 \int_{-\infty}^{0} e^{-U(x)/2D} \phi_1(x) \;, \qquad c_1 = \phi_1^*(x_-)\, e^{U(x_-)/(2D)}. \tag{1.81b}$$

Since Eq. (1.81a) neglects higher-order eigenfunctions, C_1 is in general not exactly equal but usually close to 1/2. But, by comparing the time-dependence of (1.81a) and (1.79), it is natural to identify

$$k \simeq \frac{\lambda_1}{2} = \frac{1}{2\tau_*}. \tag{1.82}$$

We next discuss, by considering in a slightly different setting, how one can obtain an explicit result for the rate k in terms of the parameters of the potential U.



1.4.3 Constant-current solution

Consider a bistable potential as in Eq. (1.75), but now with a particle source at $x_0 < x_- < 0$ and a sink[16] at $x_1 > x_b = 0$. Assuming that particles are injected at x_0 at constant flux $j(t,x) \equiv J = const$, the escape rate can be defined by

$$k := \frac{J}{P_-}, \tag{1.83}$$

with P_- denoting the probability of being in the left well, as defined in Eq. (1.76a) above. To compute the rate from Eq. (1.83), we need to find a stationary constant flux solution $p_J(x)$ of Eq. (1.68d), satisfying $p_J(x_1) = 0$ and

$$J = -(\partial_x U)p_J - D\partial_x p_J \tag{1.84}$$

for some constant J. This solution is given by [HTB90]

$$p_J(x) = \frac{J}{D} e^{-U(x)/D} \int_x^{x_1} dy \; e^{U(y)/D}, \tag{1.85}$$

as one can verify by differentiation

$$\begin{aligned} -(\partial_x U)p_J - D\partial_x p_J &= -(\partial_x U)p_J - D\partial_x \left[\frac{J}{D} e^{-U(x)/D} \int_x^{x_1} dy \; e^{U(y)/D}\right] \\ &= -(\partial_x U)p_J - J\left[-\frac{(\partial_x U)}{D} e^{-U(x)/D} \int_x^{x_1} dy \; e^{U(y)/D} - 1\right] \\ &= J. \end{aligned} \tag{1.86}$$

Therefore, the inverse rate k^{-1} from Eq. (1.83) can be formally expressed as

$$k^{-1} = \frac{P_-}{J} = \frac{1}{D} \int_{-\infty}^{x_1} dx\, e^{-U(x)/D} \int_{x}^{x_1} dy\, e^{U(y)/D}, \tag{1.87}$$

and a partial integration yields the equivalent representation

$$k^{-1} = \frac{1}{D} \int_{-\infty}^{x_1} dx\, e^{U(x)/D} \int_{-\infty}^{x} dy\, e^{-U(y)/D}. \tag{1.88}$$

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Assuming a sufficiently steep barrier, the integrals in Eq. (1.88) may be evaluated by adopting steepest descent approximations near the potential minimum at x_- and near the maximum at the barrier position x_b. More precisely, taking into account that $U'(x_-) = U'(x_b) = 0$, one can replace the potentials in the exponents by the harmonic approximations

$$U(x) \simeq U(x_-) - \frac{1}{2\tau_b}(x - x_-)^2, \tag{1.89a}$$

$$U(y) \simeq U(x_-) + \frac{1}{2\tau_-}(y - x_-)^2, \tag{1.89b}$$

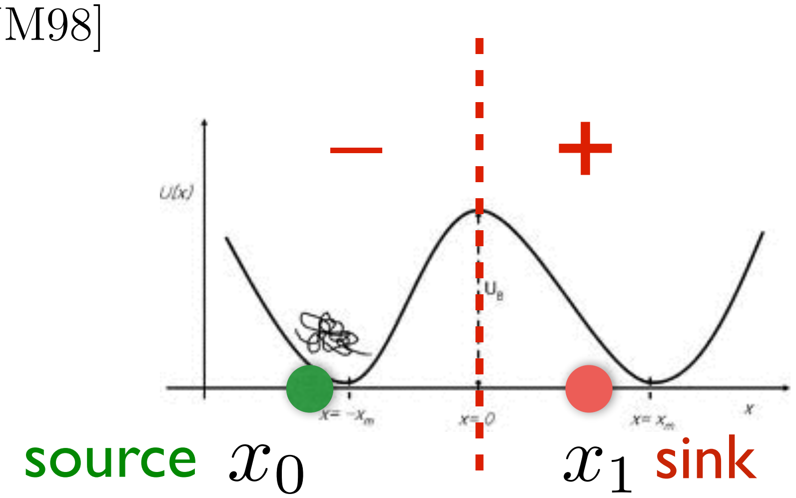
where

$$\tau_- = -U''(x_0) > 0\,, \qquad \tau_b = U''(x_b) > 0 \tag{1.90}$$

carry units of time. Inserting (1.89) into (1.88) and replacing the upper integral boundaries by $+\infty$, one thus obtains the so-called Kramers rate [HTB90, GHJM98]

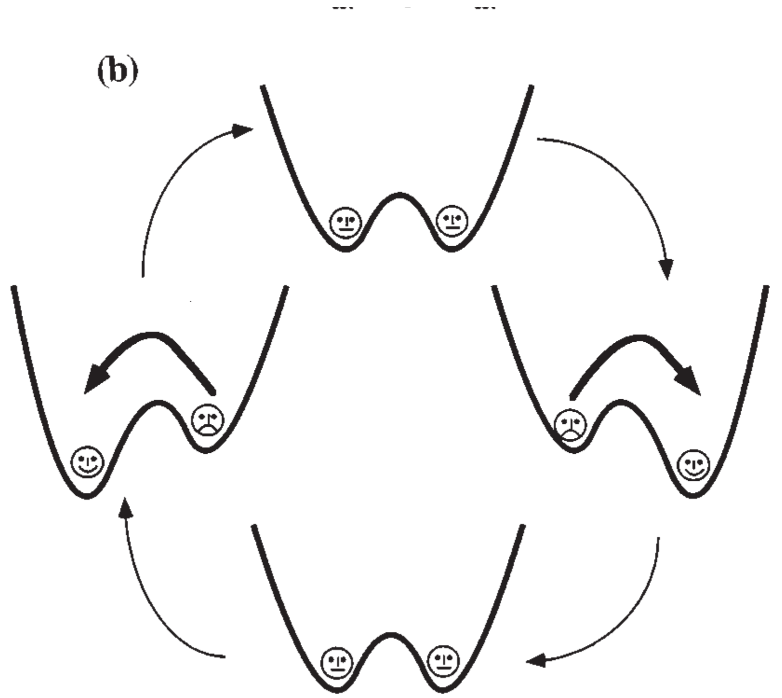
$$k \simeq \frac{e^{-\Delta U/D}}{2\pi\sqrt{\tau_- \tau_b}} =: k_{\mathrm{K}}\,, \qquad \Delta U = U(x_b) - U(x_-).$$

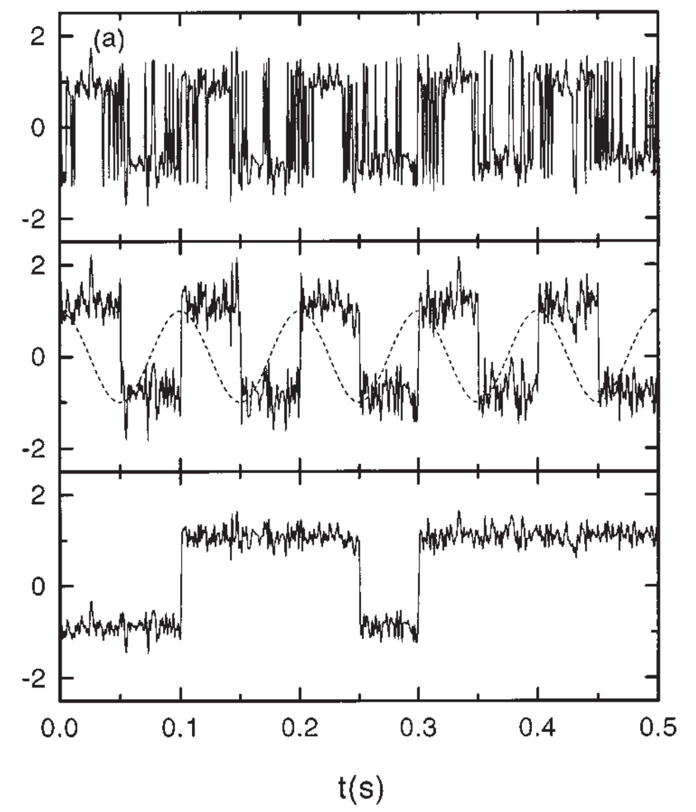
Arrhenius law



Stochastic resonance

1. a nonlinear measurement device[17],
2. a periodic signal weaker than the threshold of measurement device,
3. additional input noise, uncorrelated with the signal of interest.





$$k \simeq \frac{e^{-\Delta U/D}}{2\pi\sqrt{\tau_- \tau_b}} =: k_{\mathrm{K}} \sim \Omega$$

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1.5 Stochastic resonance

1.5.1 Generic model

To illustrate SR more quantitatively, consider the periodically driven SDE

$$dX(t) = -\partial_x U\, dt + A\cos(\Omega t)\, dt + \sqrt{2D} * dB(t), \tag{1.93a}$$

where A is the signal amplitude and

$$U(x) = -\frac{a}{2}x^2 + \frac{b}{4}x^4 \tag{1.93b}$$

a symmetric double-well potential with minima at $\pm x_* = \pm\sqrt{a/b}$ and barrier height $\Delta U = a^2/(4b)$. Introducing rescaled variables

$$x' = x/x_*\ , \qquad t' = at\ , \qquad A' = A/(ax_*)\ , \qquad D' = D/(ax_*^2)\ , \qquad \Omega' = \Omega/a.$$

and dropping primes. we can rewrite (1.93a) in the dimensionless form

$$dX(t) = (x - x^3)\, dt + A\cos(\Omega t)\, dt + \sqrt{2D} * dB(t), \tag{1.93c}$$

with a rescaled barrier height $\Delta U = 1/4$. The associated FPE reads

$$\partial_t p \;=\; -\partial_x\{[-(\partial_x U) + A\cos(\Omega t)]p - D\partial_x p\}. \tag{1.94}$$

For our subsequent discussion, it is useful to rearrange terms on the rhs. as

$$\partial_t p = \partial_x[(\partial_x U)p + D\partial_x p] - A\cos(\Omega t)\partial_x p. \tag{1.95}$$

Perturbation theory

$$\partial_t p = \partial_x[(\partial_x U)p + D\partial_x p] - A\cos(\Omega t)\partial_x p. \tag{1.95}$$

To solve Eq. (1.95) perturbatively, we insert the series ansatz

$$p(t,x) = \sum_{n=0}^{\infty} A^n p_n(t,x), \tag{1.96}$$

which gives

$$\sum_{n=0}^{\infty} A^n \partial_t p_n = \sum_{n=0}^{\infty} \left\{ A^n \partial_x[(\partial_x U)p_n + D\partial_x p_n] - A^{n+1}\cos(\Omega t)\partial_x p_n \right\} \tag{1.97}$$

Perturbation theory

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Focussing on the liner response regime, corresponding to powers A^0 and A^1, we find

$$\partial_t p_0 = \partial_x[(\partial_x U)p_0 + D\partial_x p_0] \tag{1.98a}$$

$$\partial_t p_1 = \partial_x[(\partial_x U)p_1 + D\partial_x p_1] - \cos(\Omega t)\partial_x p_0 \tag{1.98b}$$

Perturbation theory

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$$\partial_t p_0 \quad = \quad \partial_x[(\partial_x U)p_0 + D\partial_x p_0] \tag{1.98a}$$

$$\partial_t p_1 \quad = \quad \partial_x[(\partial_x U)p_1 + D\partial_x p_1] - \cos(\Omega t)\partial_x p_0 \tag{1.98b}$$

Equation (1.98a) is just an ordinary time-independent FPE, and we know its stationary solution is just the Boltzmann distribution

$$p_0(x) = \frac{e^{-U(x)/D}}{Z_0}\,, \qquad Z_0 = \int dx\, e^{-U(x)/D} \tag{1.99}$$

First-order correction

$$\partial_t p_1 \quad = \quad \partial_x[(\partial_x U)p_1 + D\partial_x p_1] - \cos(\Omega t)\partial_x p_0 \qquad (1.98b)$$

To obtain a formal solution to Eq. (1.98b), we make use of the following ansatz

$$p_1(t,x) = e^{-U(x)/(2D)} \sum_{m=1}^{\infty} a_{1m}(t)\, \phi_m(x), \qquad (1.100)$$

where $\phi_m(x)$ are the eigenfunctions of the unperturbed effective Hamiltonian, cf. Eq. (1.71),

$$\mathcal{H}_0 = -D\partial_x^2 + \frac{1}{4D}(\partial_x U)^2 - \frac{1}{2}\partial_x^2 U. \qquad (1.101)$$

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Inserting (1.100) into Eq. (1.98b) gives

$$\sum_{m=1}^{\infty} \dot{a}_{1m}\phi_m = -\sum_{m=1}^{\infty} \lambda_m a_{1m}\,\phi_m - \cos(\Omega t)\; e^{U(x)/(2D)}\;\partial_x p_0. \qquad (1.102)$$

Multiplying this equation by $\phi_n(x)$, and integrating from $-\infty$ to $+\infty$ while exploiting the orthonormality of the system $\{\phi_m\}$, we obtain the coupled ODEs

$$\dot{a}_{1m} = -\lambda_m a_{1m} - M_{m0}\cos(\Omega t), \qquad (1.103)$$

with 'transition matrix' elements

$$M_{m0} = \int dx\;\phi_m\, e^{U(x)/(2D)}\partial_x p_0. \qquad (1.104)$$

First-order correction

$$\dot{a}_{1m} = -\lambda_m a_{1m} - M_{m0} \cos(\Omega t), \tag{1.103}$$

with 'transition matrix' elements

$$M_{m0} = \int dx \; \phi_m \, e^{U(x)/(2D)} \partial_x p_0. \tag{1.104}$$

The asymptotic solution of Eq. (1.103) reads

$$a_{1m}(t) = -M_{m0} \left[\frac{\Omega}{\lambda_m^2 + \Omega^2} \sin(\Omega t) + \frac{\lambda_m}{\lambda_m^2 + \Omega^2} \cos(\Omega t) \right]. \tag{1.105}$$

Note that, because $\partial_x p_0$ is an antisymmetric function, the matrix elements M_{m0} vanish[18] for even values $m = 0, 2, 4, \ldots$, so that only the contributions from odd values $m = 1, 3, 5 \ldots$ are asymptotically relevant.

Linear response

Focussing on the leading order contribution, $m = 1$, and noting that $p_0(x) = p_0(-x)$, we can estimate the position mean value

$$\mathbb{E}[X(t)] = \int dx\, p(t,x)\, x \tag{1.106}$$

from

$$\begin{aligned}
\mathbb{E}[X(t)] &\simeq A \int dx\, p_1(t,x)\, x \\
&\simeq A \int dx\, e^{-U(x)/(2D)}\, a_{11}(t)\, \phi_1(x)\, x \\
&= -AM_{10} \left[\frac{\Omega}{\lambda_1^2 + \Omega^2} \sin(\Omega t) + \frac{\lambda_1}{\lambda_1^2 + \Omega^2} \cos(\Omega t) \right] \int dx\, e^{-U(x)/(2D)}\, \phi_1(x)\, x
\end{aligned}$$

Using $\lambda_1 = 2k_{\mathrm{K}}$, where k_{K} is the Kramers rate from Eq. (1.91), we can rewrite this more compactly as

$$\mathbb{E}[X(t)] = \overline{X} \cos(\Omega t - \overline{\varphi}) \tag{1.107a}$$

with phase shift

$$\overline{\varphi} = \arctan\left(\frac{\Omega}{2k_{\mathrm{K}}} \right) \tag{1.107b}$$

and amplitude

$$\overline{X} = -A \frac{M_{10}}{(4k_{\mathrm{K}}^2 + \Omega^2)^{1/2}} \int dx\, e^{-U(x)/(2D)}\, \phi_1(x)\, x. \tag{1.107c}$$

Linear response

$$\overline{X} = -A \frac{M_{10}}{(4k_{\mathrm{K}}^2 + \Omega^2)^{1/2}} \int dx \, e^{-U(x)/(2D)} \, \phi_1(x) \, x. \tag{1.107c}$$

The amplitude $\overline{X}$ depends on the noise strength D through k_{K}, through the integral factor and also through the matrix element

$$M_{10} \quad = \quad \int dx \; \phi_1 \, e^{U(x)/(2D)} \partial_x p_0. \tag{1.108}$$

To compute $\overline{X}$, one first needs to determine the eigenfunction ϕ_1 of $\mathcal{H}_0$ as defined in Eq. (1.101). For the quartic double-well potential (1.93b), this cannot be done analytically but there exist standard techniques (e.g., Ritz method) for approximating ϕ_1 by functions that are orthogonal to $\phi_0 = \sqrt{p_0/Z_0}$. Depending on the method employed, analytical estimates for $\overline{X}$ may vary quantitatively but always show a non-monotonic dependence on the noise strength D for fixed potential-parameters (a, b). As discussed in [GHJM98], a reasonably accurate estimate for $\overline{X}$ is given by

$$\overline{X} \simeq \frac{Aa}{Db} \left(\frac{4k_{\mathrm{K}}^2}{4k_{\mathrm{K}}^2 + \Omega^2} \right)^{1/2}, \tag{1.109}$$

which exhibits a maximum for a critical value D_* determined by

$$4k_{\mathrm{K}}^2 = \Omega^2 \left(\frac{\Delta U}{D_*} - 1 \right). \tag{1.110}$$

That is, the value D_* corresponds to the optimal noise strength, for which the mean value $\mathbb{E}[X(t)]$ shows maximal response to the underlying periodic signal – hence the name ‘stochastic resonance’ (SR).

1.5.2 Master equation approach

Similar to the case of the escape problem, one can obtain an alternative description of SR by projecting the full FPE dynamics onto a simpler set of master equations for the probabilities $P_\pm(t)$ of the coarse-grained particle-states 'left well' ($-$) and 'right well' ($+$), as defined by Eq. (1.76). This approach leads to the following two-state master equations with time-dependent rates

$$\dot{P}_-(t) \quad = \quad -k_+(t)\,P_- + k_-(t)\,P_+, \tag{1.111a}$$

$$\dot{P}_+(t) \quad = \quad k_+(t)\,P_- - k_-(t)\,P_+. \tag{1.111b}$$

The general solution of this pair of ODEs is given by [GHJM98]

$$P_\pm(t) \quad = \quad g(t)\left[P_\pm(t_0) + \int_{t_0}^{t} ds\,\frac{k_\pm(s)}{g(s)}\right] \tag{1.112a}$$

where

$$g(t) \quad = \quad \exp\left\{-\int_{t_0}^{t} ds\,[k_+(s) + k_-(s)]\right\}. \tag{1.112b}$$

To discuss SR within this framework, it is plausible to postulate time-dependent Arrhenius-type rates,

$$k_\pm(t) = k_{\mathrm{K}}\exp\left[\pm\frac{Ax_*}{D}\cos(\Omega t)\right]. \tag{1.113}$$

Adopting these rates and considering the asymptotic limit $t_0 \to -\infty$, one can Taylor-expand the exact solution (1.112) for $Ax_* \ll D$ to obtain

$$P_\pm(t) = k_\mathrm{K}\left[1 \pm \frac{Ax_*}{D}\cos(\Omega t) + \left(\frac{Ax_*}{D}\right)^2\cos^2(\Omega t) \pm \ldots\right]. \tag{1.114}$$

These approximations are valid for slow driving (adiabatic regime), and they allow us to compute expectation values to leading order in Ax_*/D. In particular, one then finds for the mean position the asymptotic linear response result [GHJM98]

$$\mathbb{E}[X(t)] = \overline{X}\cos(\Omega t - \overline{\varphi}) \tag{1.115a}$$

where

$$\overline{X} = \frac{Ax_*^2}{D}\left(\frac{4k_\mathrm{K}^2}{4k_\mathrm{K}^2 + \Omega^2}\right)^{1/2}, \qquad \overline{\varphi} = \arctan\left(\frac{\Omega}{2k_\mathrm{K}}\right) \tag{1.115b}$$

with k_K denoting Kramers rate as defined in Eq. (1.91). Note that Eqs. (1.115) are consistent with our earlier result (1.107).