# Stochastic resonance of ion pumps on cell membranes

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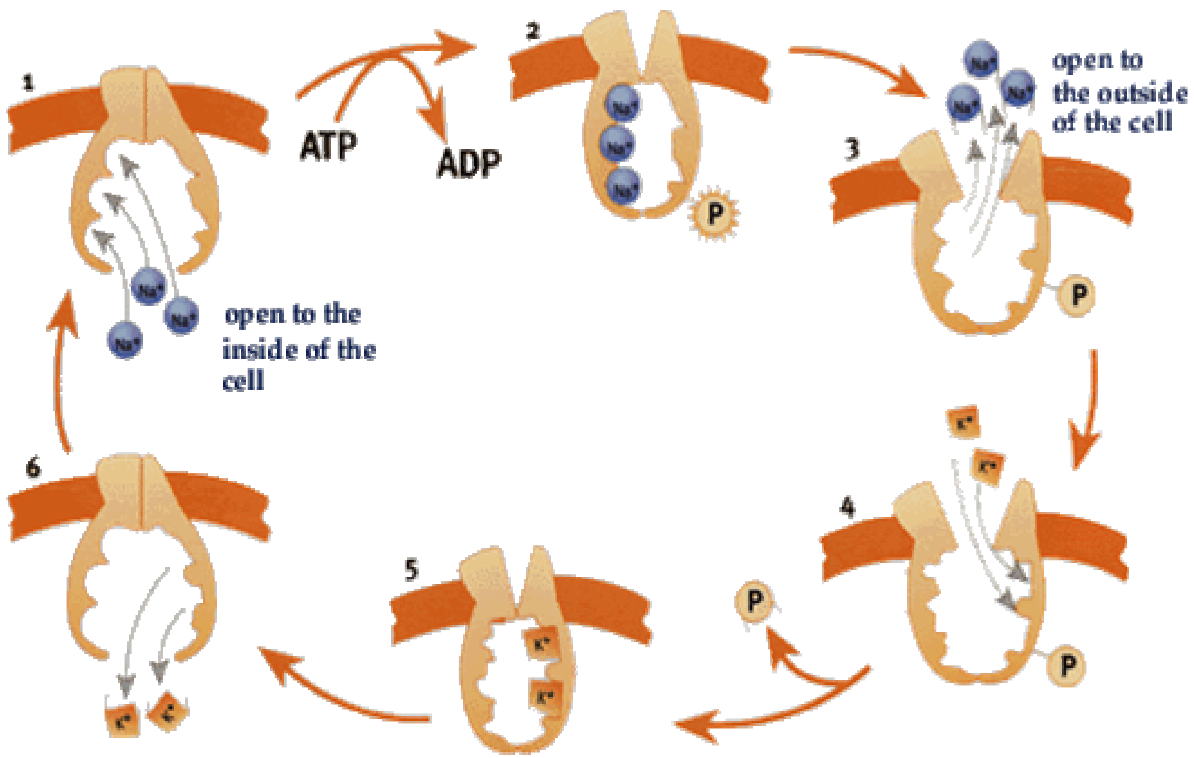
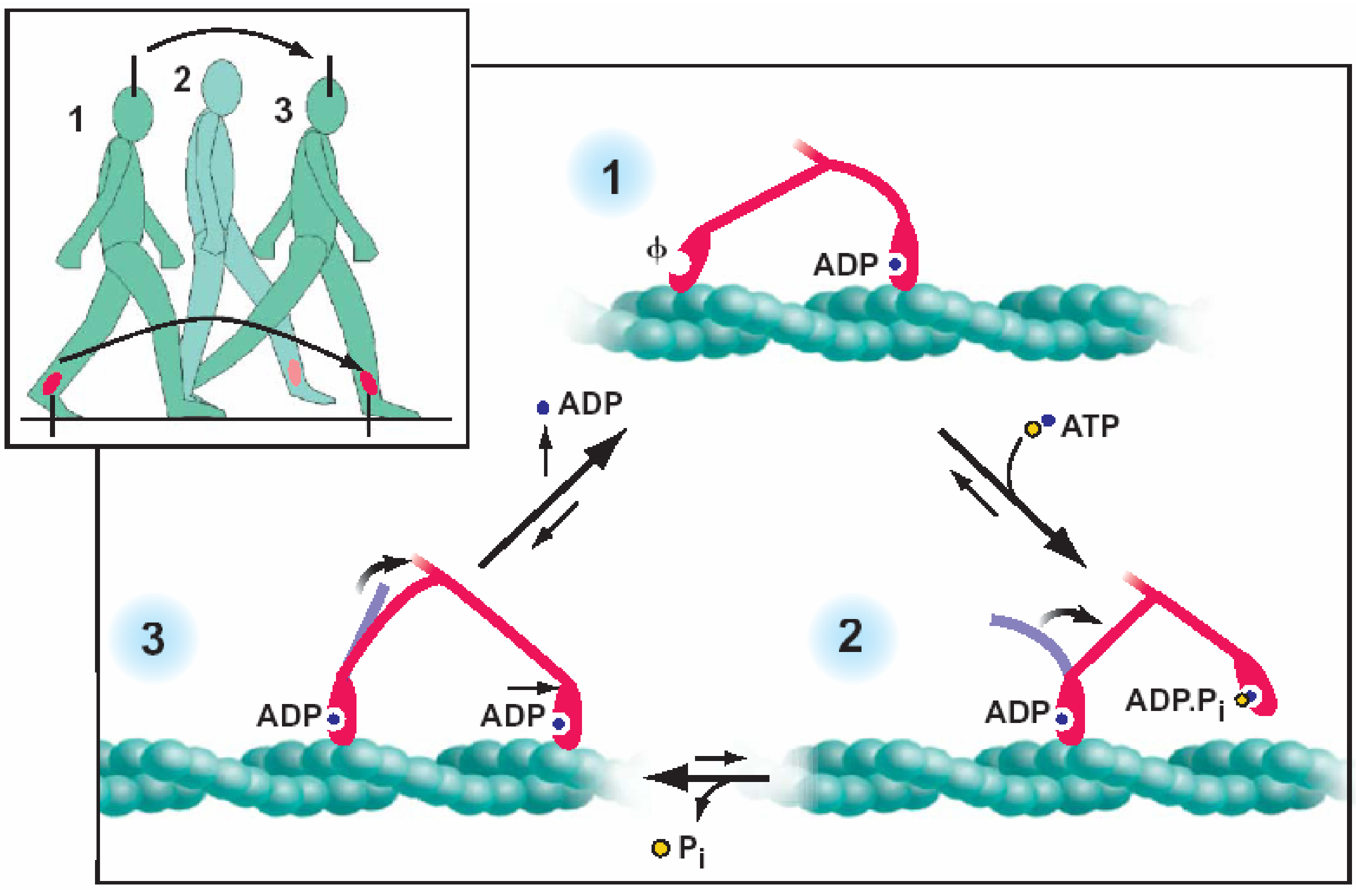
# Examples of biological motors

## Ion pump (active transport)




*http://nobelprize.org/nobel_prizes/chemistry/laureates/1997/illpres/skou.html*

# Myosin (muscle contraction)



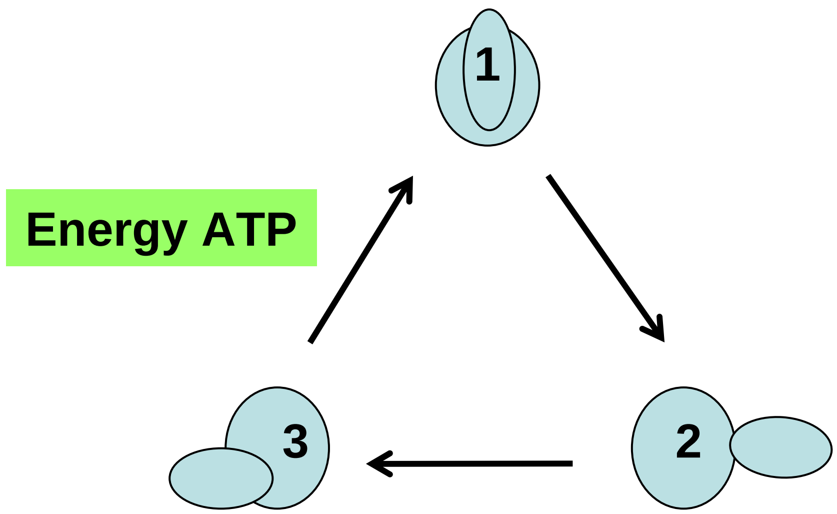

*Justin E. Molloy and Claudia Veigel, Science 300, 2046 (2003)*

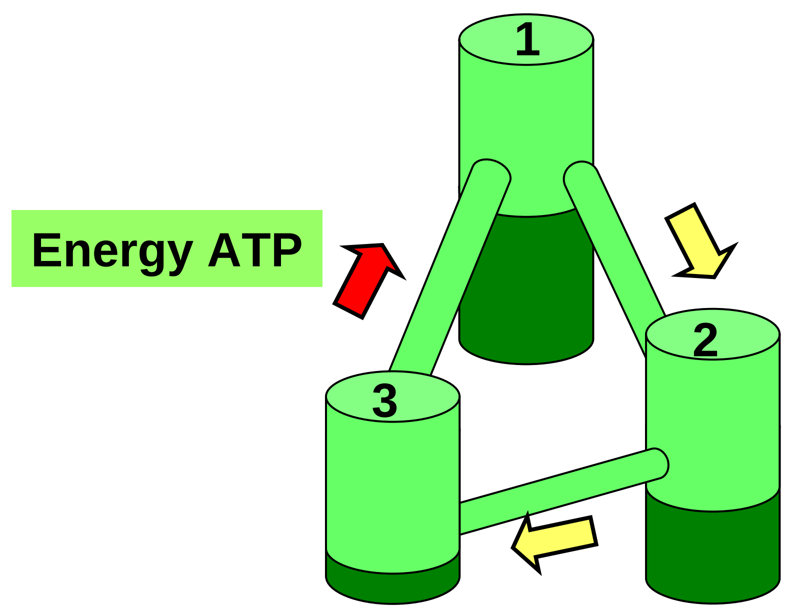
# Working principle in vivo

Free energy: 1 > 2 > 3

**cyclic conformational change**

1 → 2 (automatically)
2 → 3 (automatically)
3 → 1 (add ATP)



# Working principle in vitro

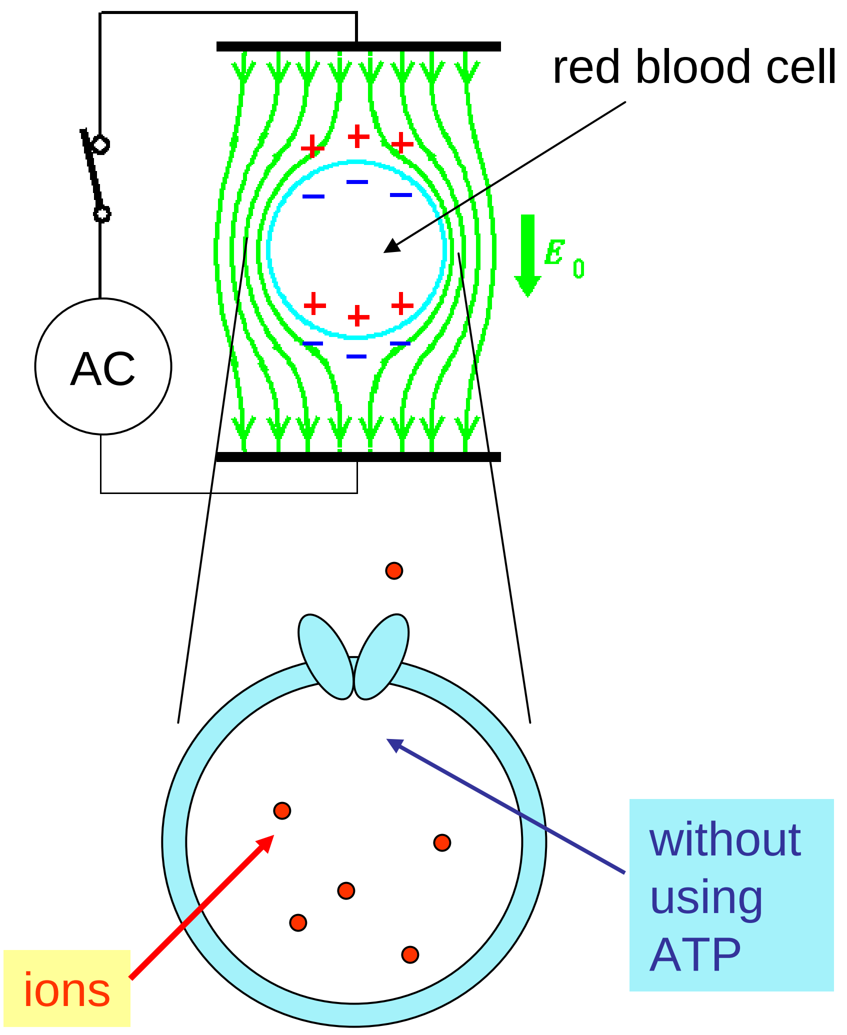
**Example:** Na, K ion pump

(In a living cell it is driven by ATP.)

However, experiments showed that it also can be driven by an AC electric field $E_0$.

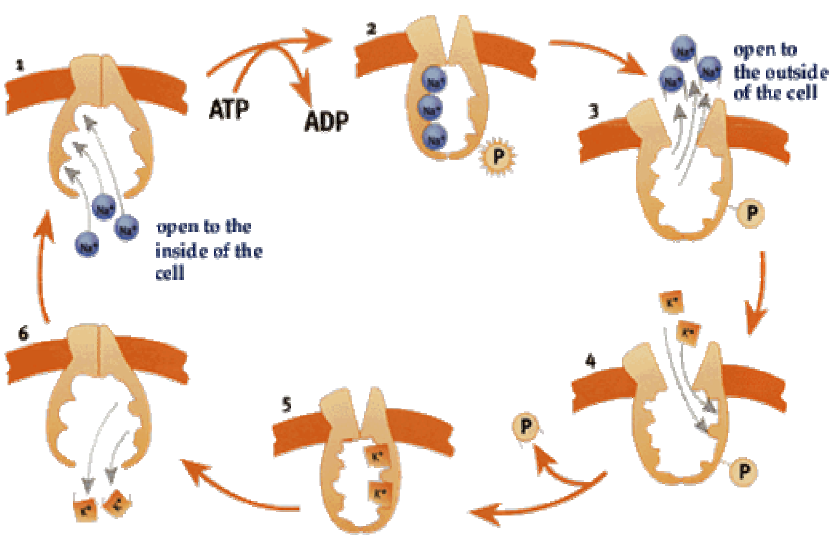
It indicates that this motor has an internal dipole which can response to an external electric field by changing its conformation.

**Question:** how efficient can this motor take this energy source (optimum frequency, …)?

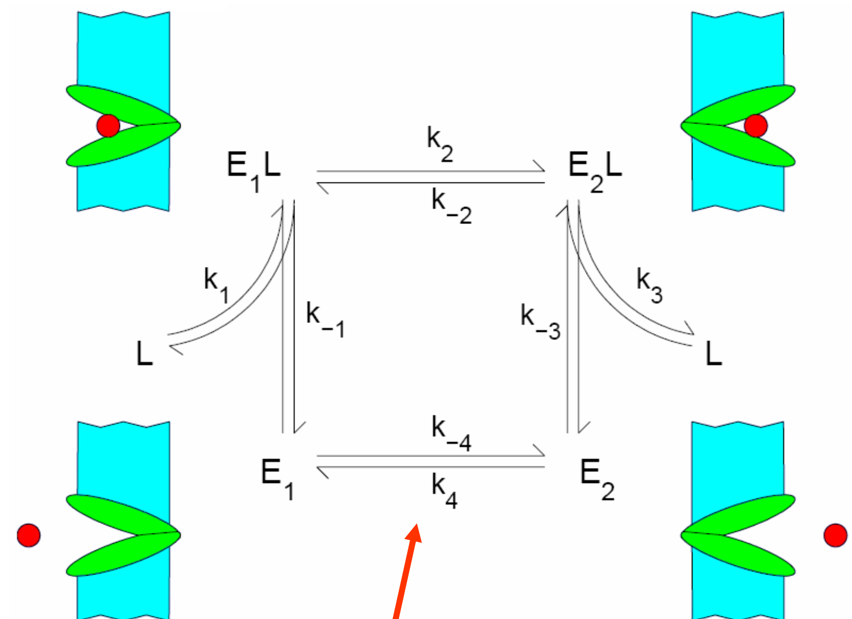


# A 4-state model for the ion pump

Separate a cycle into *n* key states
e.g., *n* = 4




Kinetic equation




Under an external AC electric field the rate constants $k_i$ become time-dependent.

# Kinetic equation for the 4-state model

For the conformation $E_2L$:

$$\begin{aligned} d[E_2L]/dt = \; & k_2[E_1L] + k_{-3}[E_2][L] \quad \text{(flow into } E_2L\text{)} \\ & -k_{-2}[E_2L] - k_3[E_2L] \quad \text{(flow out of } E_2L\text{)} \end{aligned}$$

$[L_1]$ and $[L_3]$:
the concentrations of the ion outside respectively inside the membrane.

$$\frac{d}{dt}V(t) = M(t)V(t),$$

$$M(t) = \begin{pmatrix} -k_3 - k_{-2} & k_2 & k_{-3}[L_3] & 0 \\ k_{-2} & -k_{-1} - k_2 & 0 & k_1[L_1] \\ k_3 & 0 & -k_4 - k_{-3}[L_3] & k_{-4} \\ 0 & k_{-1} & k_4 & -k_{-4} - k_1[L_1] \end{pmatrix}, \qquad V(t) = \begin{pmatrix} [E_2L] \\ [E_1L] \\ [E_2] \\ [E_1] \end{pmatrix}$$

# Time dependent rate constants

$$k_i = h_i \exp[q_i \phi(t) a_i / RT] \qquad i \in \{\pm 1, \pm 2, \pm 3, \pm 4\}$$

- Effective charge $q_i$
- Rate constant $h_i$ in zero potential $\Phi(t)=0$
- Gas constant R, temperature T
- Transmembrane potential $\phi(t)$
- Apportionment constant $a_i$,
- $a_j = \delta_j$ and $a_{-j} = -(1-\delta_j)$ for certain $\delta_j$ with j in {1,2,3,4}
- $k_i$ has the simple form $k_i = h_i \exp[d_i\, \psi(t)]$

Example:

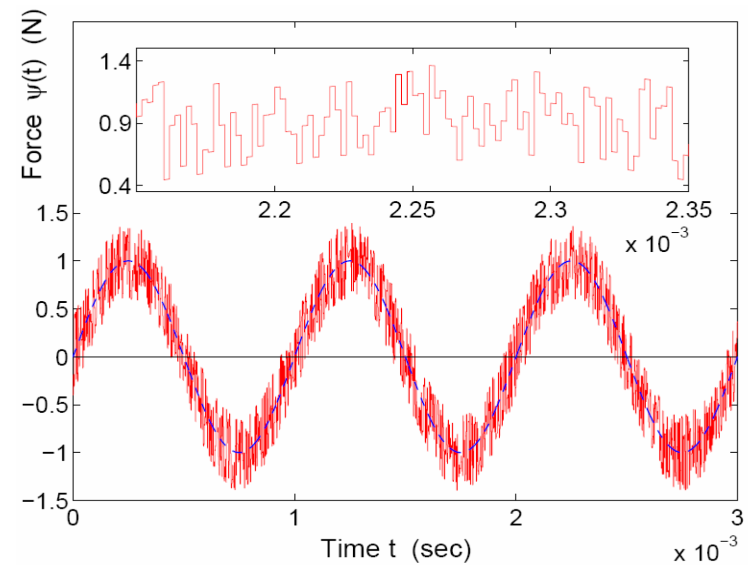
| $i$ | 1 | −1 | 2 | −2 | 3 | −3 | 4 | −4 |
|---|---|---|---|---|---|---|---|---|
| $d_i$ (cm/V) | 0 | 0 | −2 | −3 | 0 | 0 | 4 | −2 |
| $h_i$ ($s^{-1}$) | 40* | 60 | 25700 | 12000 | 70 | 200* | 20 | 10 |

# Energy supply (input)

The ion pump can be driven by an oscillating transmembrance electric field with

$\Psi(t) = A \sin(\omega t) + \xi(t)$

with a dominating signal $A \sin(\omega t)$
and a secondary noise $\xi(t)$
where the noise level is $\eta = \eta_{rms}/A$
with $\eta_{rms} = \sqrt{\int_0^\tau \xi(t)^2\, dt/\tau},$




# Net ion flux (output)

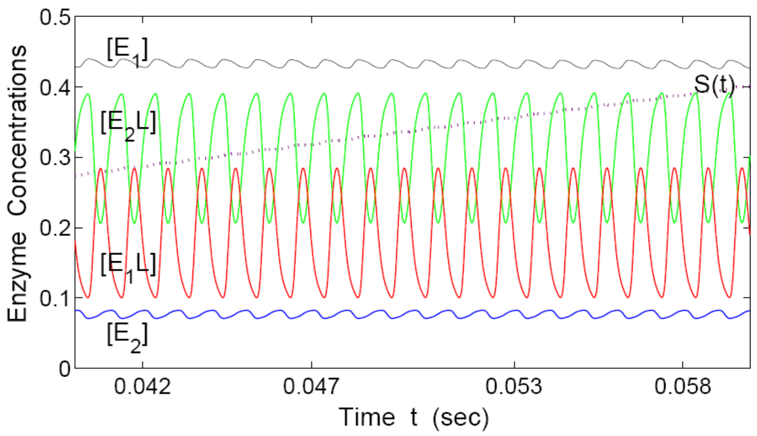
Instantaneous flux

$j(t) = k_3\, [E_2L] - k_{-3}[E_2][L_3]$

Transported amount within time span t:

$S(t) = \int_0^t j(t')\, dt'$

Net flux $J = \lim_{t \to \infty} S(t)/t$



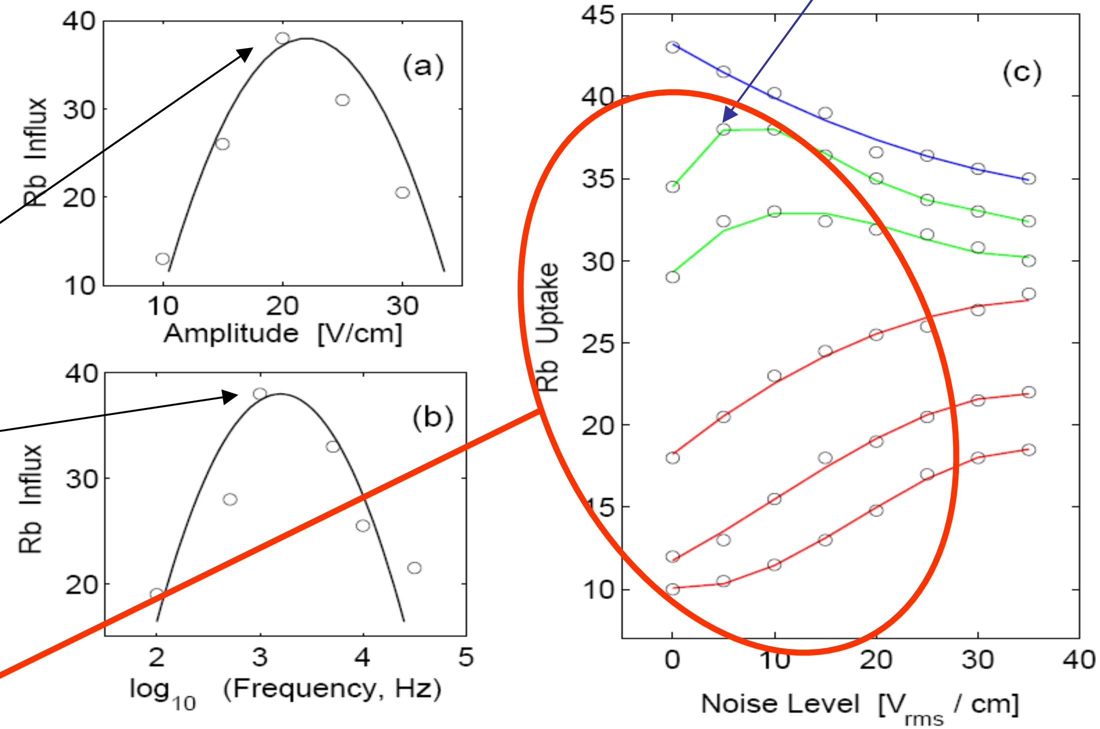
# Experimental results

$J \neq 0$

stochastic resonance

optimal amplitude

optimal frequency



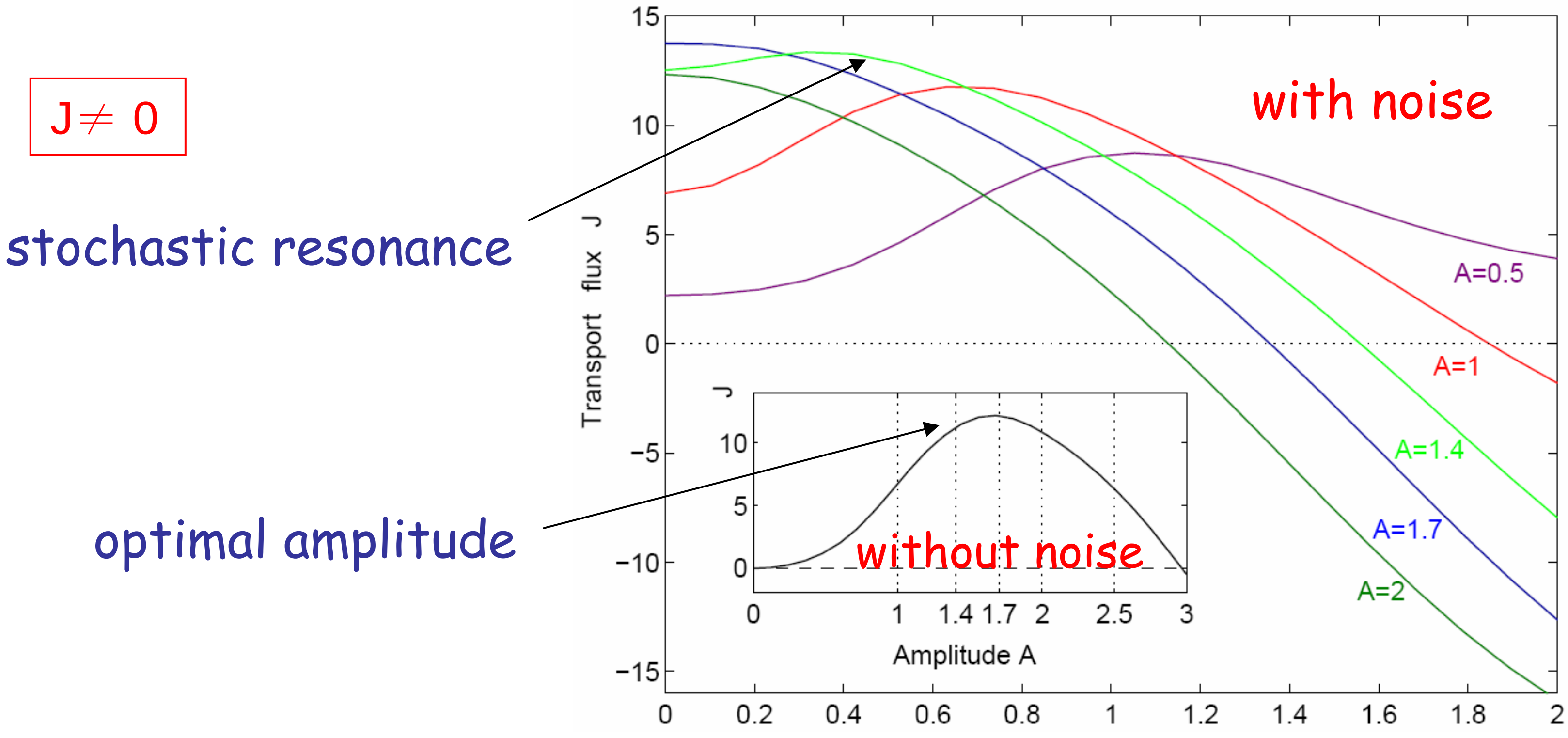

without noise

with noise

Noise is constructive in this regime !!

Electric field induced rubidium pumping of Na, K-ATPase: flux [amole/hour] vs (a) amplitude of the random telegraph fluctuation (RTF) with mean frequency 1 kHz; (b) amplitude of the RTF with amplitude 20 V/cm; (c) noise level $\eta$ under sinusoidal signal with amplitude 20 V/cm and frequency 1 kHz. The curves have signal amplitudes 20, 17.5, 15, 12.5, 10, and 7.5 V/cm from top to bottom.

# Theoretical results (for different amplitudes)

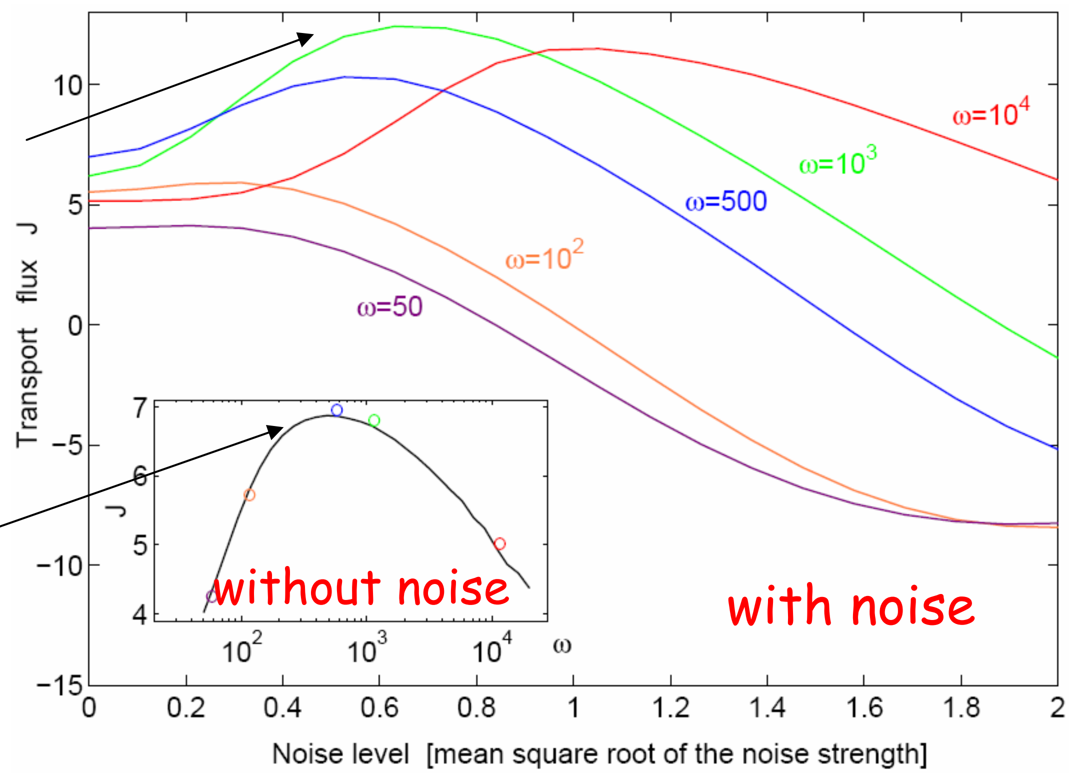



The averaged flux $J$ vs the noise level $\eta$ under five different amplitudes of sinusoidal signal with signal frequency $\omega=10^3$ and $\omega_n/\omega=10^3$, where $A_1=0.5$, $A_2=1$, $A_3=1.4$, $A_4=1.7$, and $A_5=2$. The inset shows the signal amplitude dependence of the averaged flux $J$ without noise.

# Theoretical results (for different frequencies)

stochastic resonance

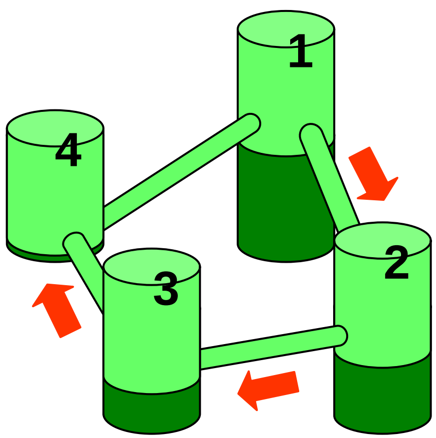
optimal frequency

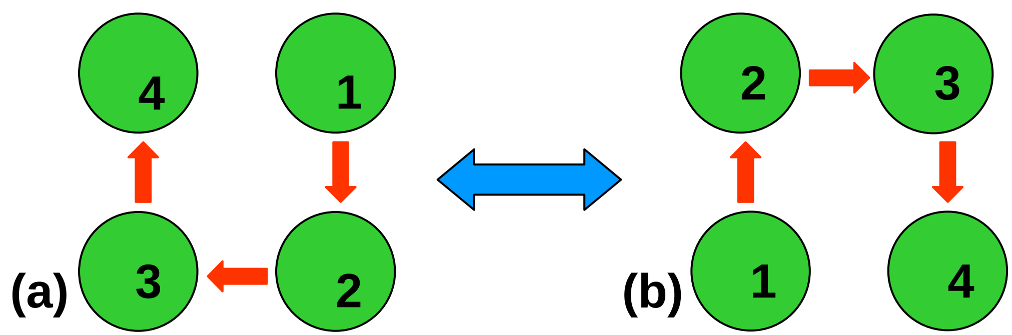



The averaged flux *J* vs the noise level $\eta$ under five different signal frequencies $\omega$'s with signal amplitudes A = 1 and $\omega_n / \omega = 10^3$, where $\omega_1$=50, $\omega_2$=$10^2$, $\omega_3$=500, $\omega_4$=$10^3$, and $\omega_5$=$10^4$. The inset shows the frequency dependence of the averaged flux *J* without noise.

# Condition for net ion transport

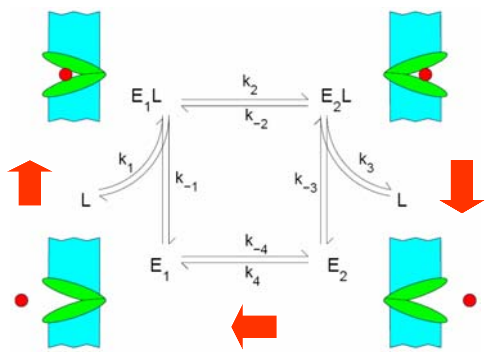
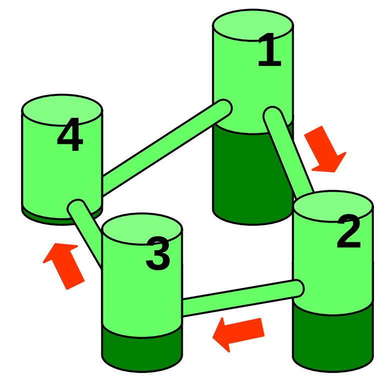
Under the oscillating external field, suppose the free energies of the four states $E_1L$, $E_2L$, $E_2$, $E_1$ have the magnitude arrangement for t = 0 in (a) and for t = $\pi$ in (b):




Then a clockwise net transport (following the red arrows) will occur, when switching between (a) and (b) [thermal ratchet effect].

# Comparison between different energy inputs

| Energy input |  |  |
|---|---|---|
| AC field | All $k_i$ change simultaneously. | All pipes change slop. |
| ATP | Only two $k_i$ change, say $k_2$ and $k_{-2}$. | Only one pipe changes slop. |

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