Physics of Molecular Motors:
Swimming in Molasses and Walking in a Hurricane

I. Biasing the random walk of a molecular motor

II. The Unreasonable effectiveness of equilibrium theory for interpreting non-equilibrium experiements

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Text
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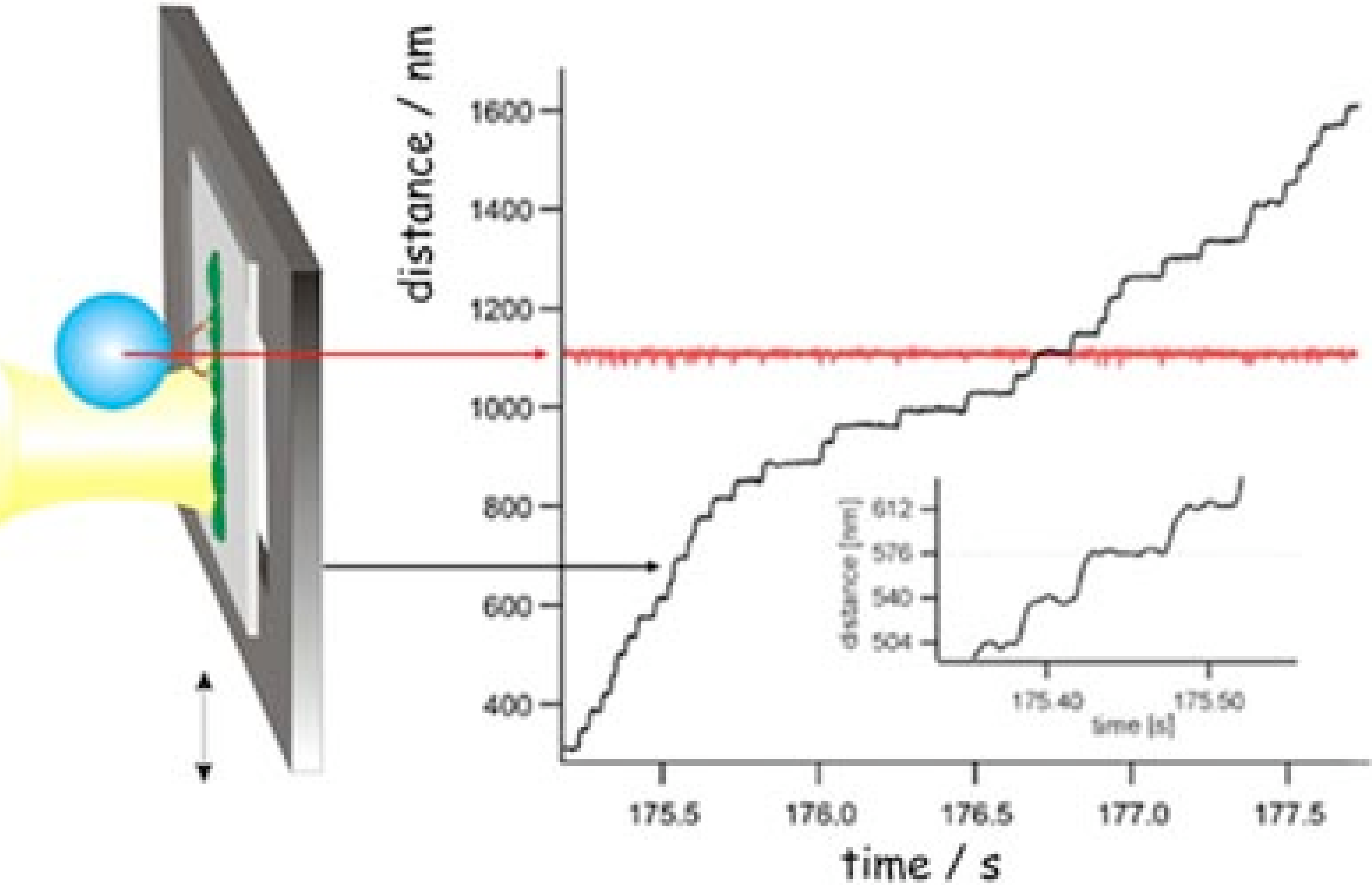
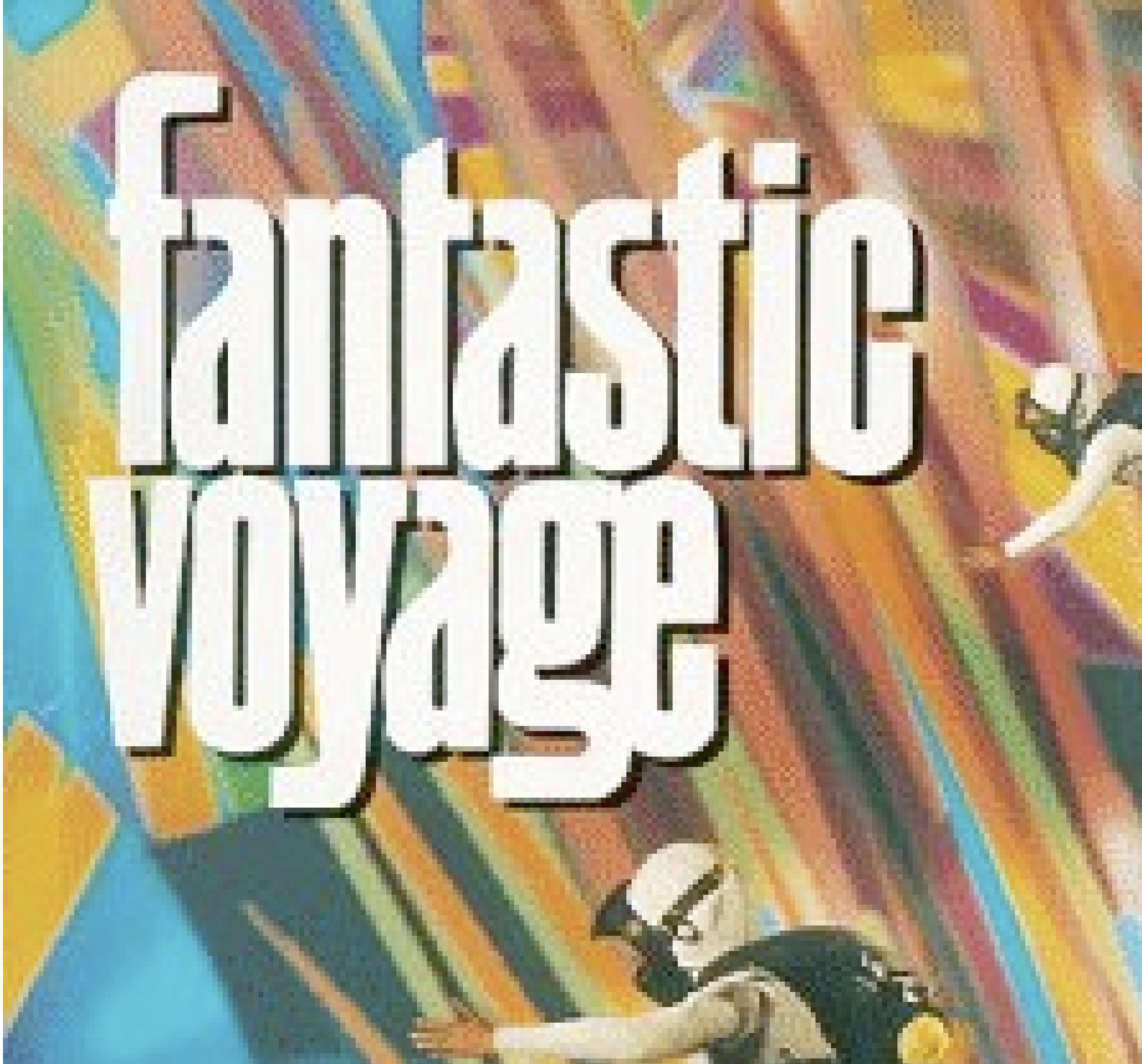


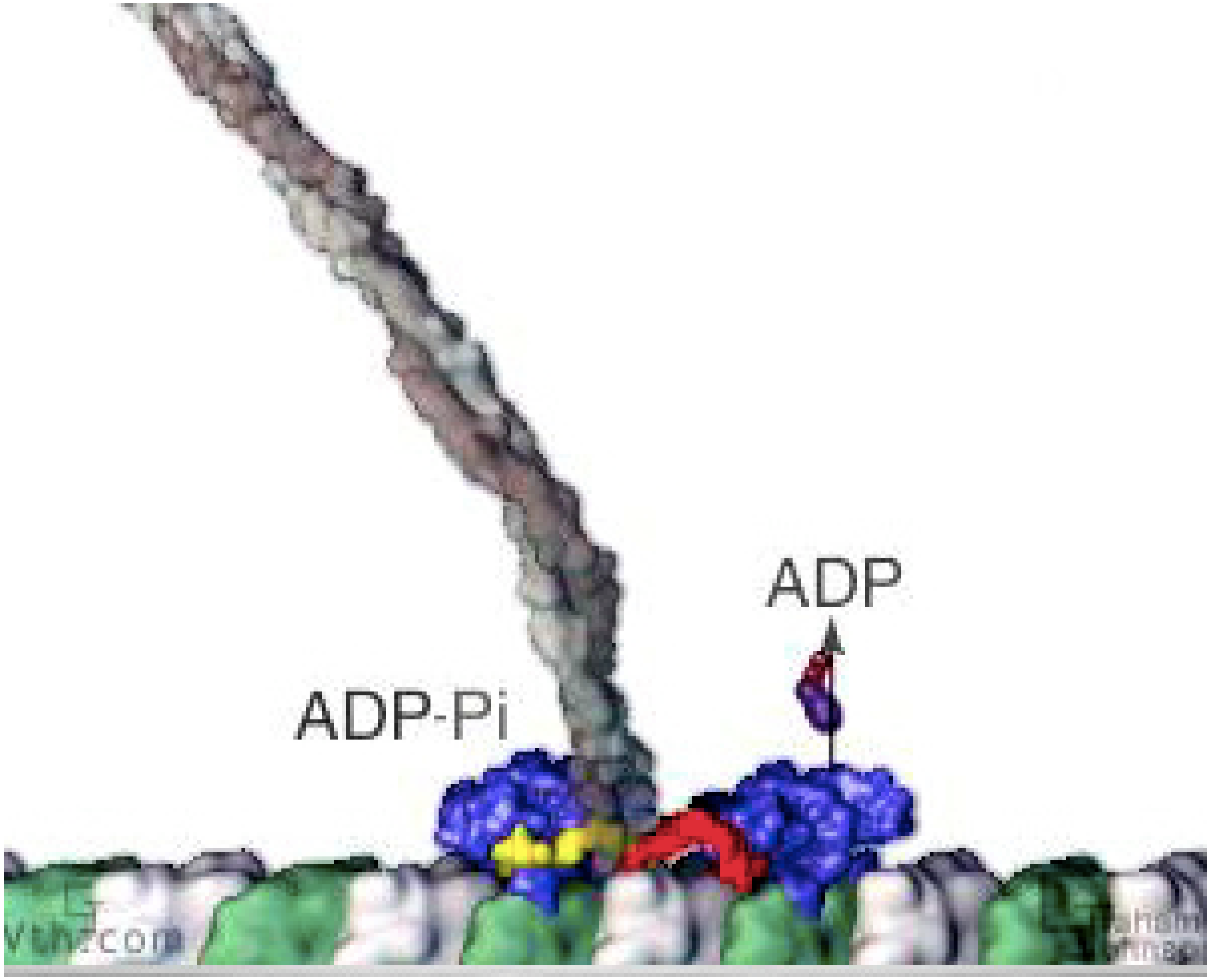
distance / nm
1600
1400
1200
1000
800
600
400
175.5
176.0
176.5
177.0
177.5
time / s
distance [nm]
612
576
540
504
175.40
175.50
time [s]

Take home messages:

I. Thermal noise is so large that nanoscale motions of a protein are best described as a random walk

II. Viscous drag is so large that a protein is in mechanical equilibrium at every instant

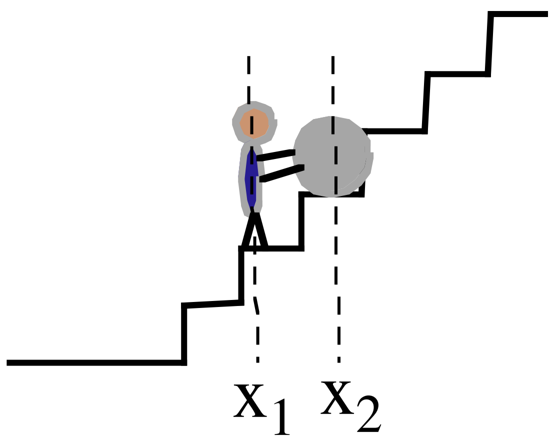

fantastic
voyage

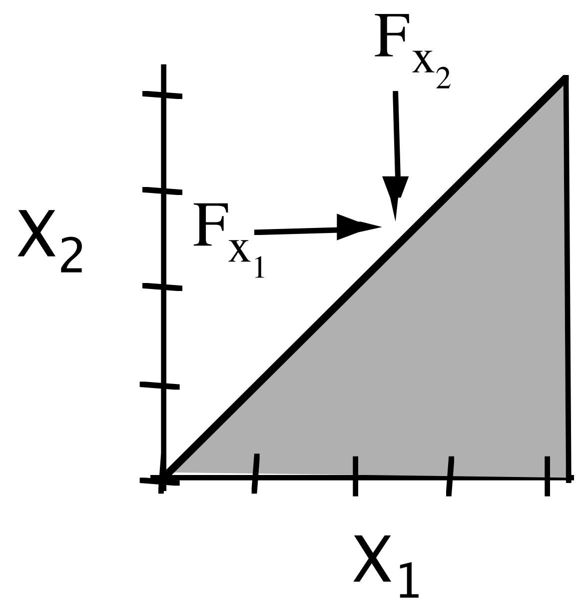

ADP
ADP-Pi

Reduce dimensionality and then use thermal noise to assist motion
In one direction but not another by a brownian ratchet.

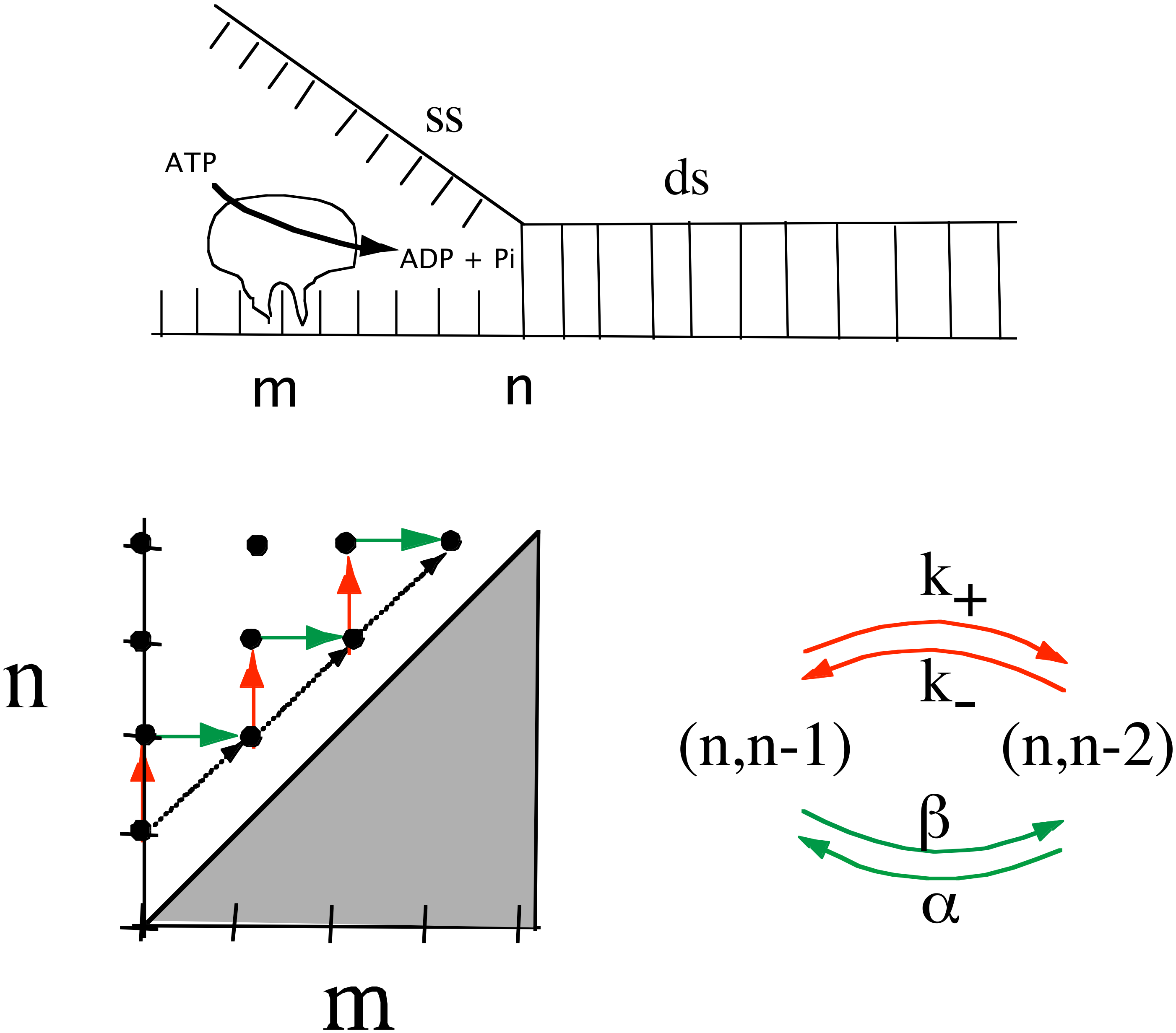
What is a Brownian ratchet?

Ultimately energy comes from chemical reaction, but the momentum
Is borrowed from the thermal bath



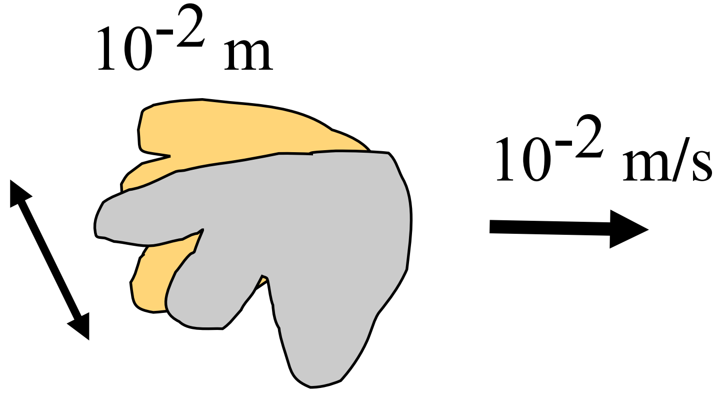


A molecular motor is a molecule that uses chemical energy to move in a preferred direction even if that means increasing the potential energy of a macroscopic system to which it is attached


ss
ATP
ds
ADP + Pi
m
n
n
m
k_+
k_-
(n,n-1)
(n,n-2)
β
α

Bivalves, bacteria, and biomotors

Scallop Theorem - swimming in molasses



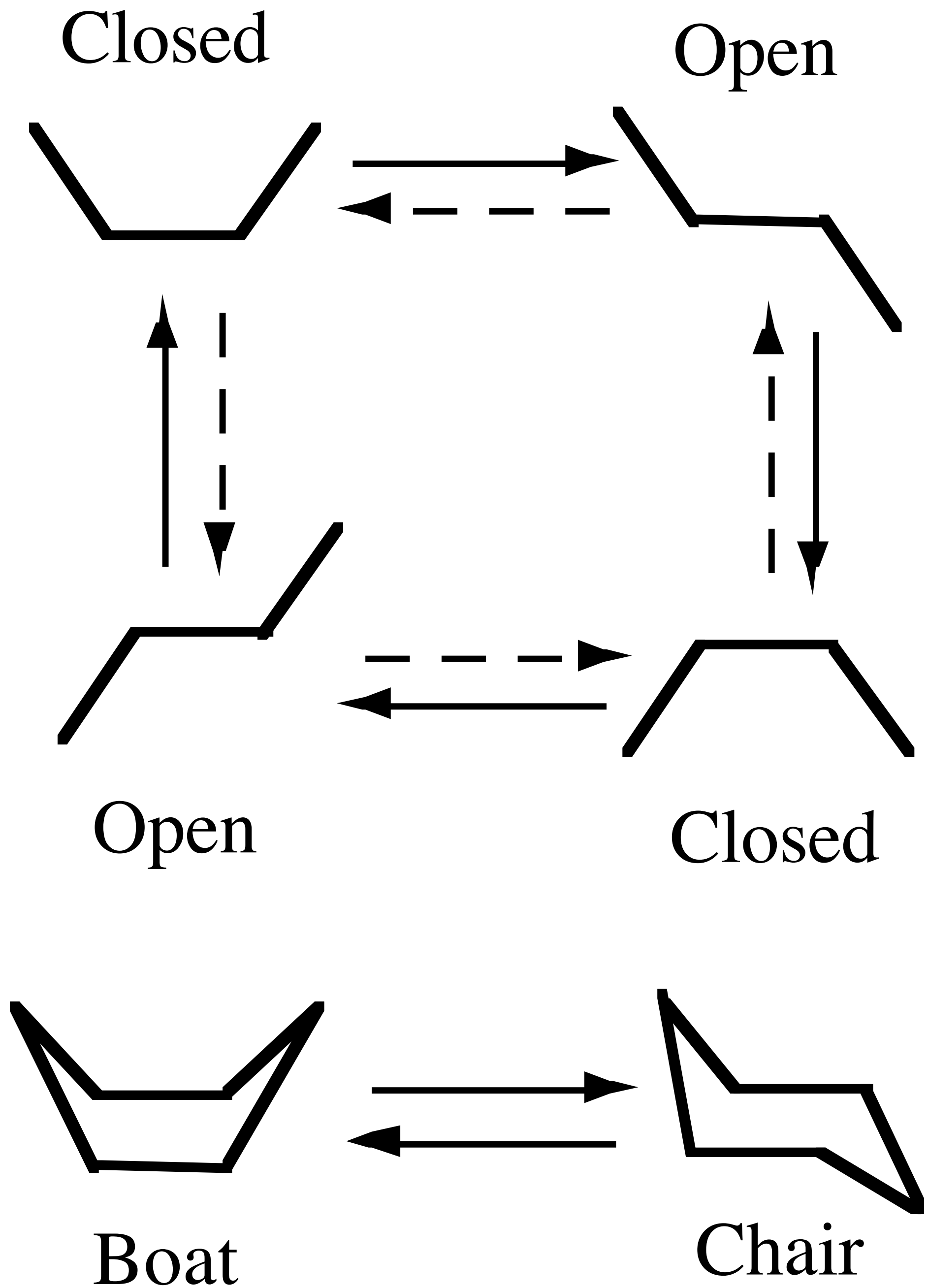
Reynolds number

Inertial force/viscous force

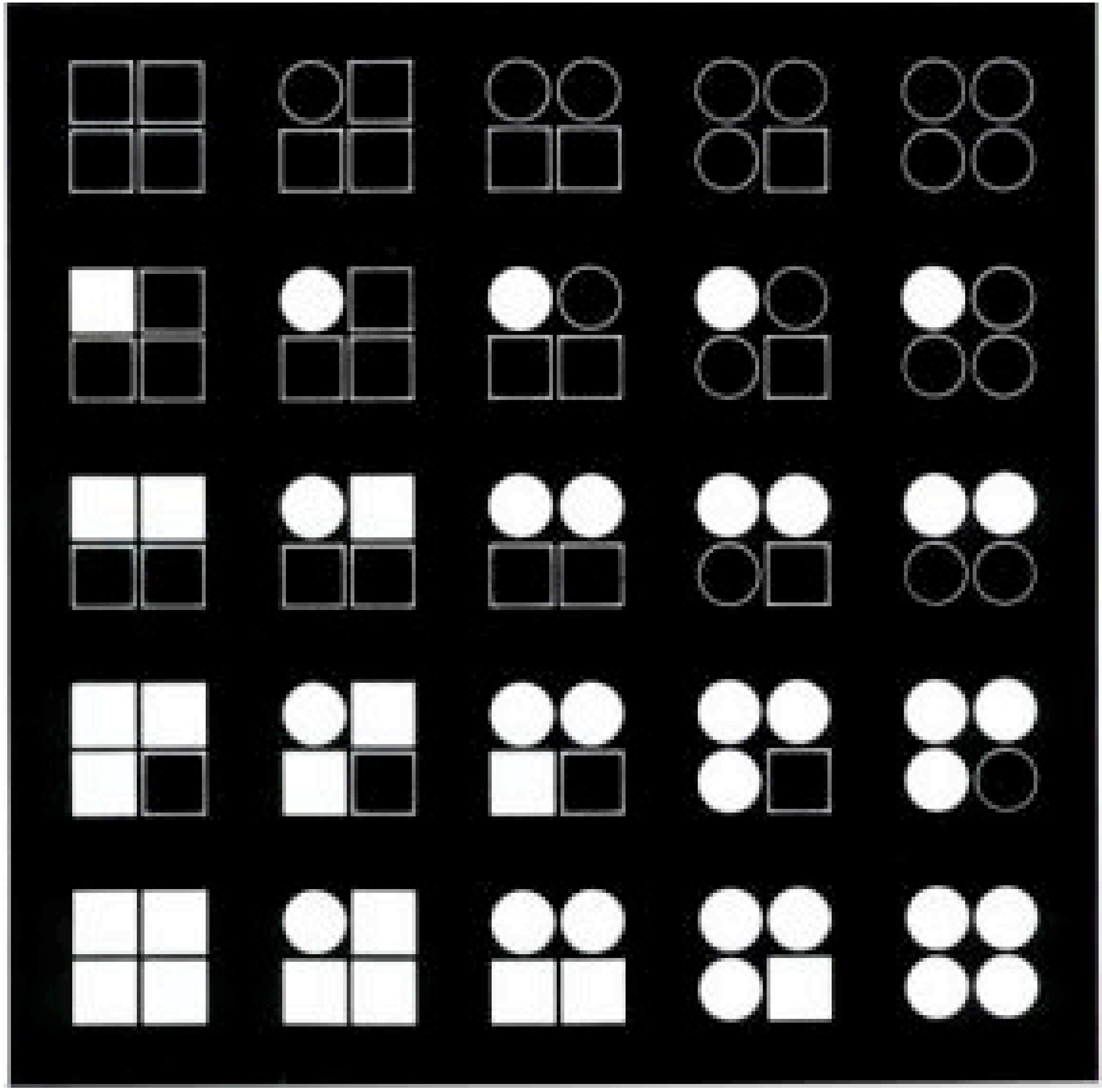
Navier - Stokes:

$$-\nabla p + \eta \nabla^2 \vec{v} = \rho \frac{\partial \vec{v}}{\partial t} + \rho (\vec{v} \cdot \nabla) \vec{v}$$

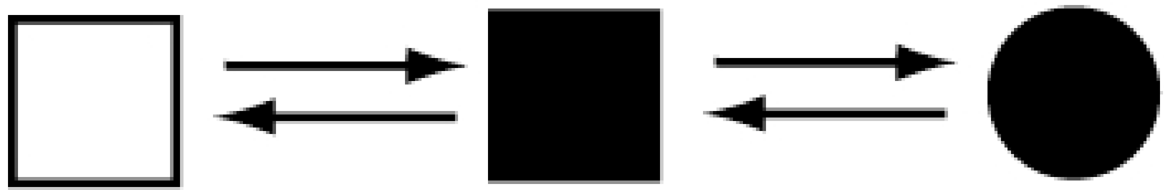
Purcell, AJP 1977



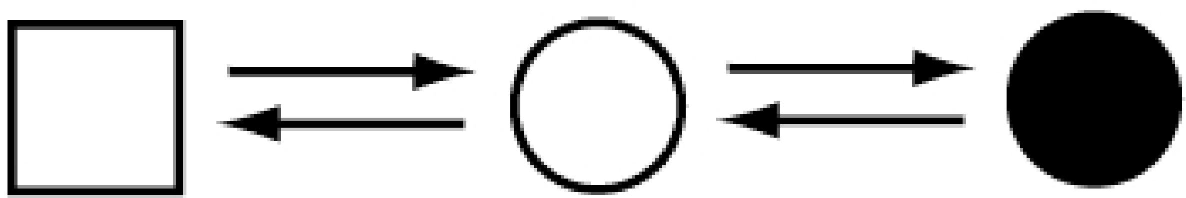
Closed
Open
Open
Closed
Boat
Chair



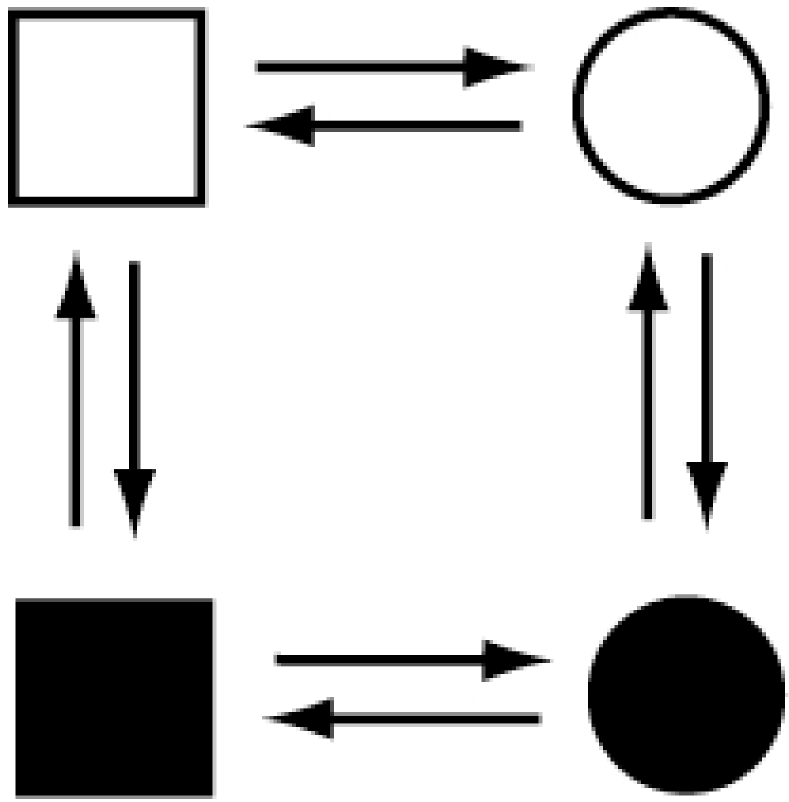
Induced fit

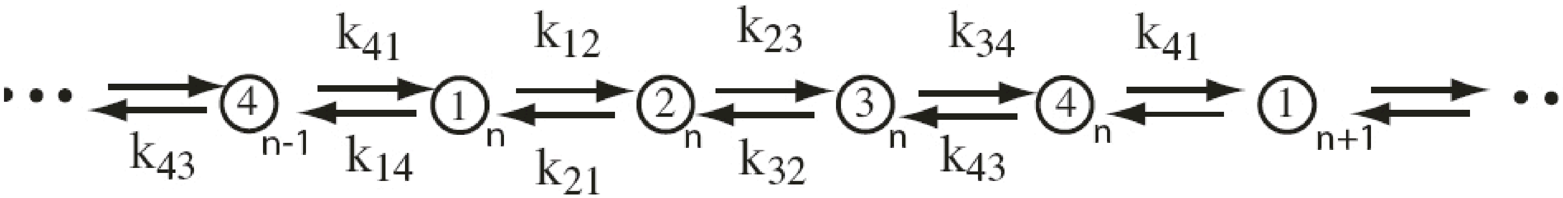


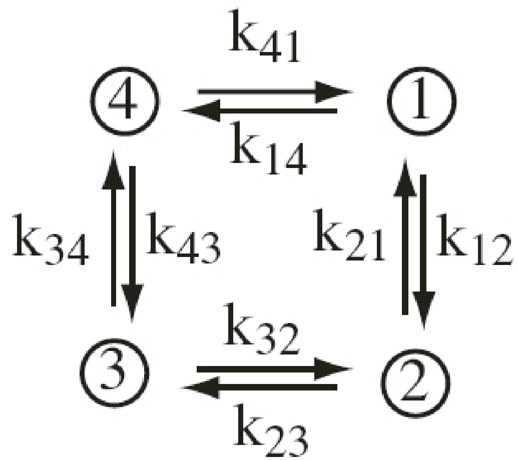
Pre-existing equilibrium



Elementary Brownian Machine

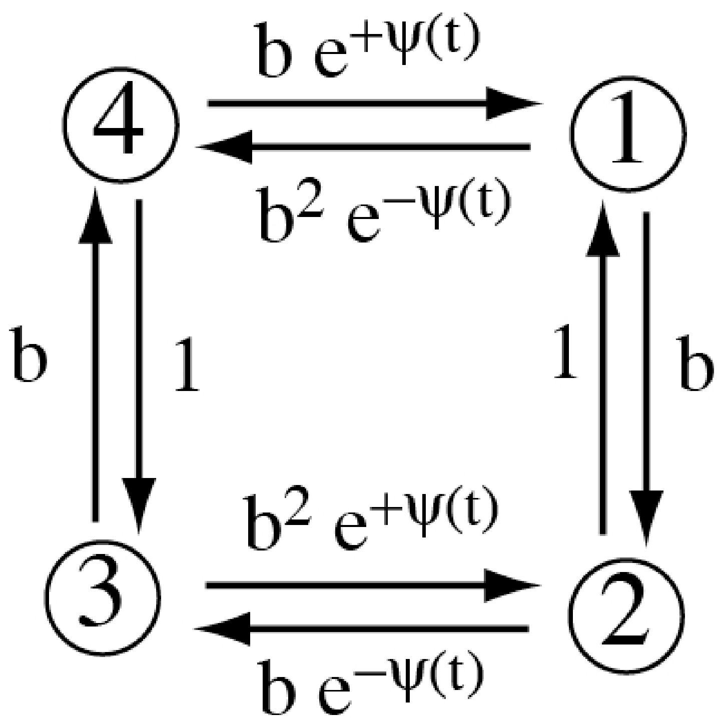




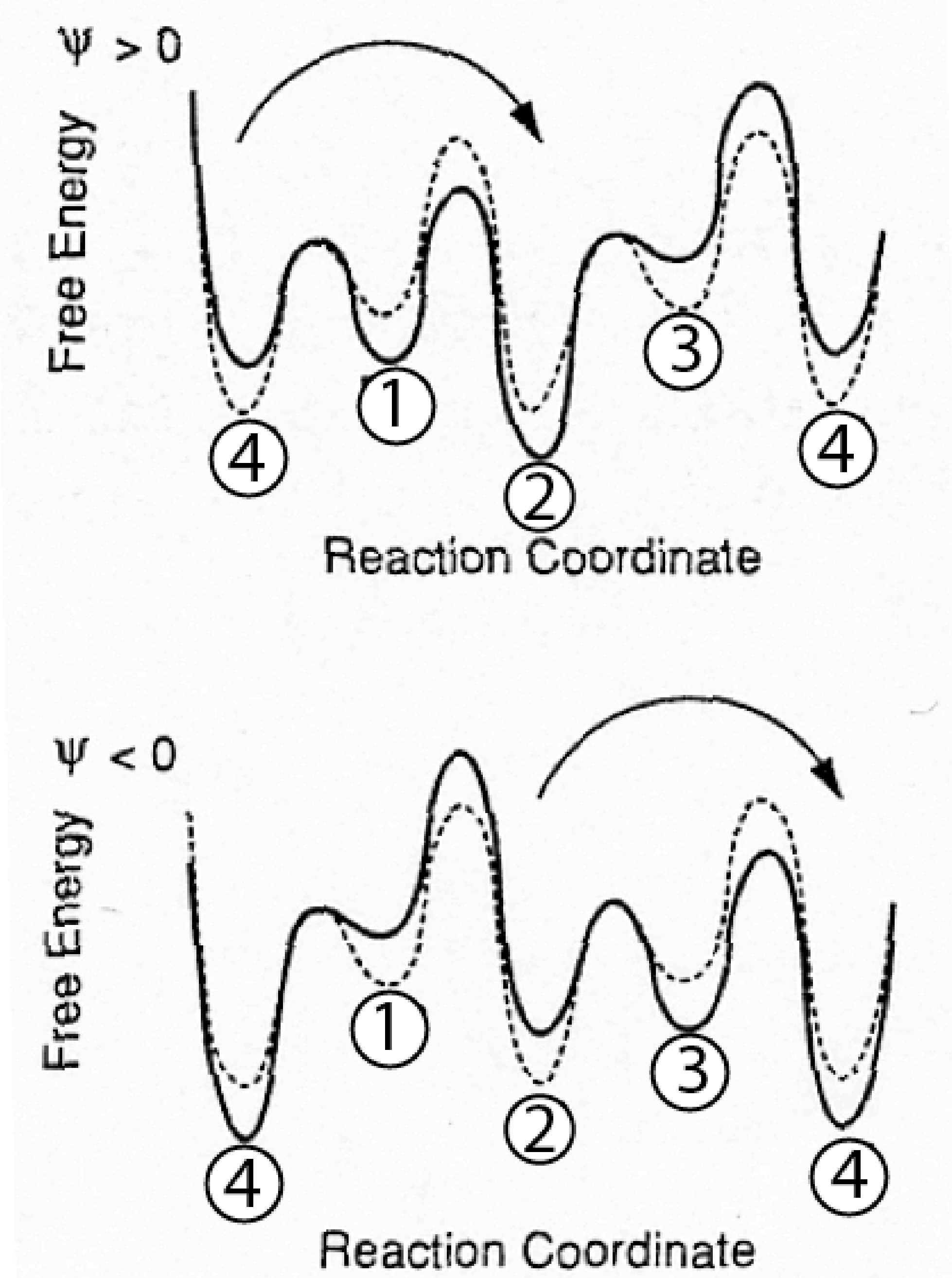


Detailed Balance

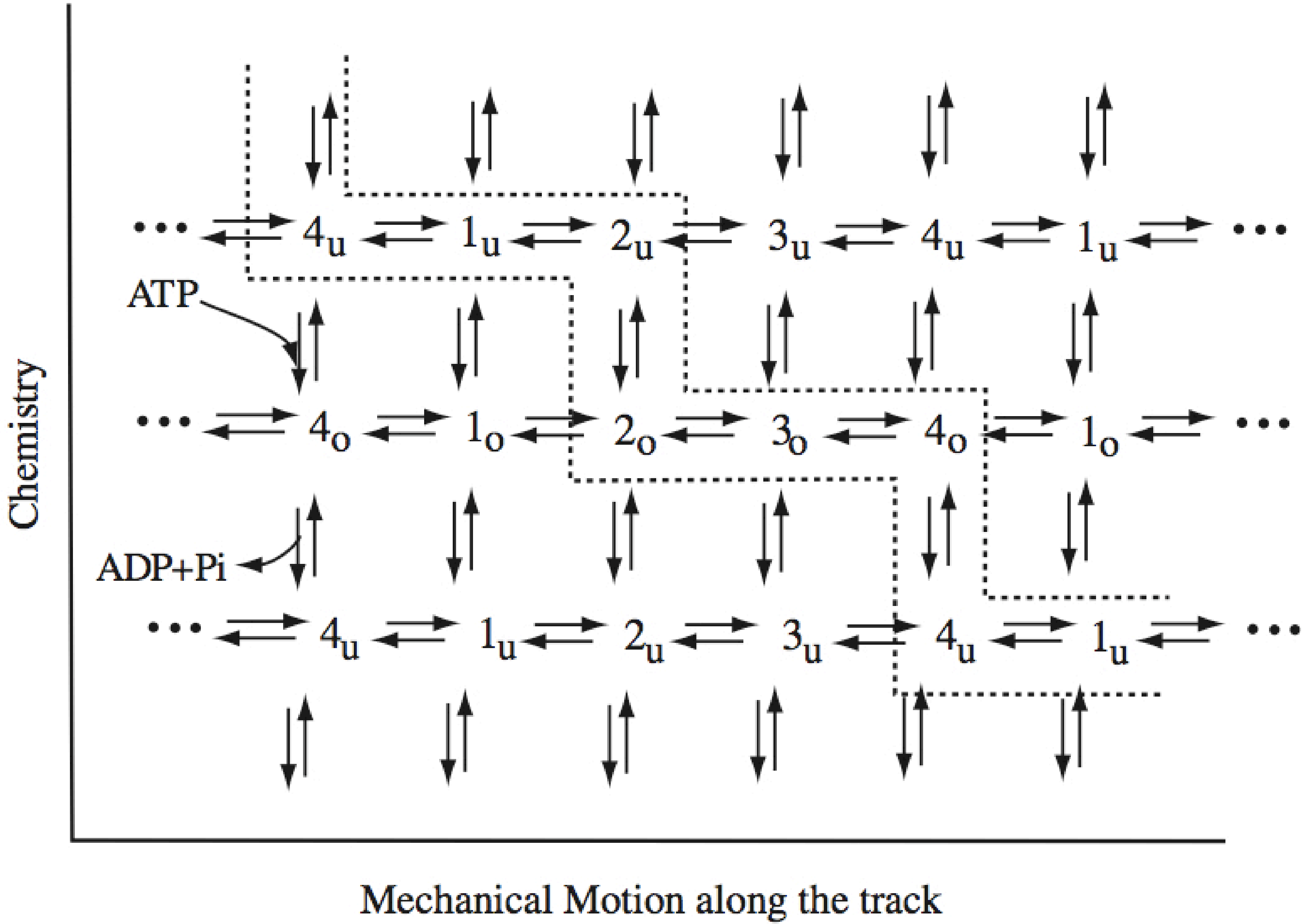
$$
\begin{aligned}
k_{12}\overline{W_1} &= k_{21}\overline{W_2} \\
k_{23}\overline{W_2} &= k_{32}\overline{W_3} \\
k_{34}\overline{W_3} &= k_{43}\overline{W_4} \\
k_{41}\overline{W_4} &= k_{14}\overline{W_1}
\end{aligned}
\quad \Rightarrow \quad
\frac{k_{12}k_{23}k_{34}k_{41}}{k_{14}k_{43}k_{32}k_{21}} = 1
$$



b $e^{+\psi(t)}$
b^2 $e^{-\psi(t)}$
b
1
1
b
b^2 $e^{+\psi(t)}$
b $e^{-\psi(t)}$
4
1
3
2

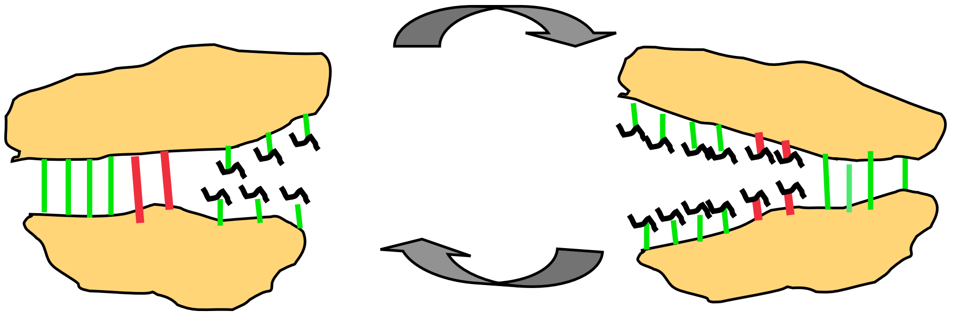


ψ > 0
Free Energy
Reaction Coordinate
ψ < 0
Free Energy
Reaction Coordinate
4
1
2
3
4



Chemistry
ATP
ADP+Pi
4u 1u 2u 3u 4u 1u
4o 1o 2o 3o 4o 1o
4u 1u 2u 3u 4u 1u
Mechanical Motion along the track

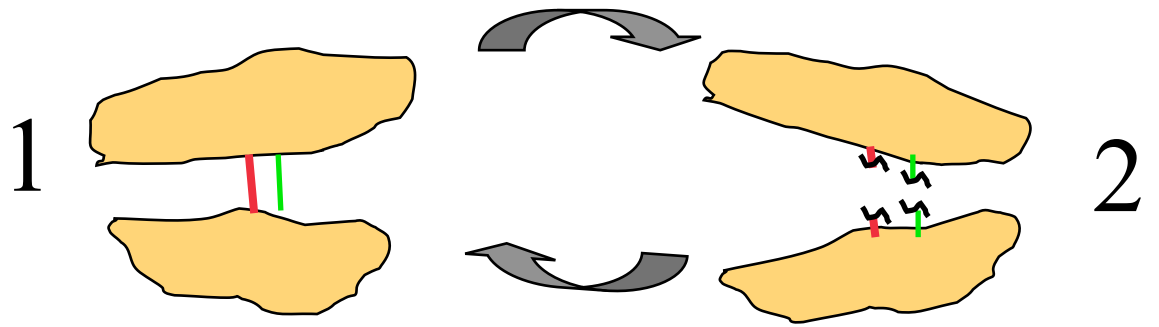
Energetics - Stability vs. Lability

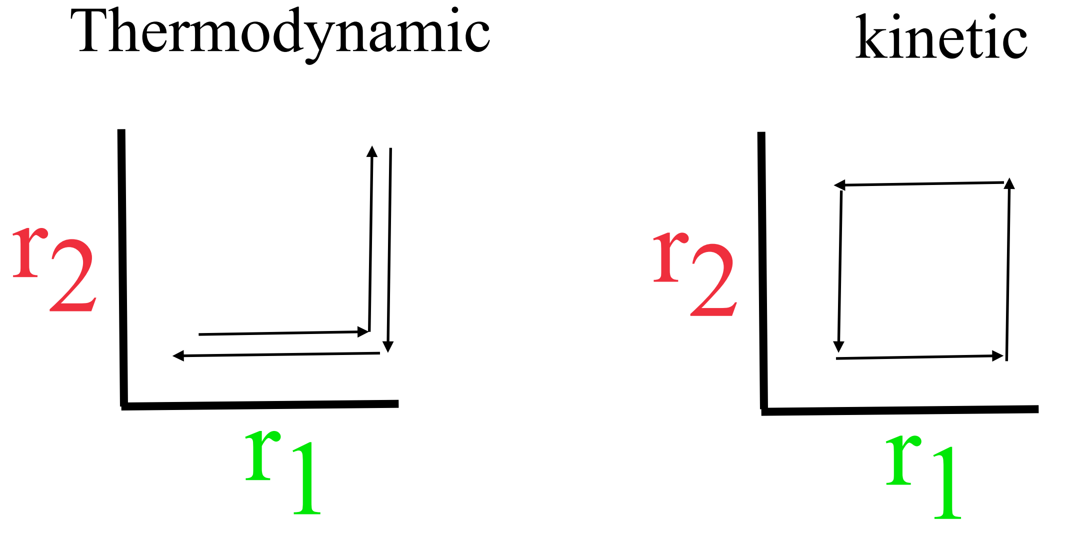


First formed last broken; thermodynamic control

First formed first broken; kinetic control

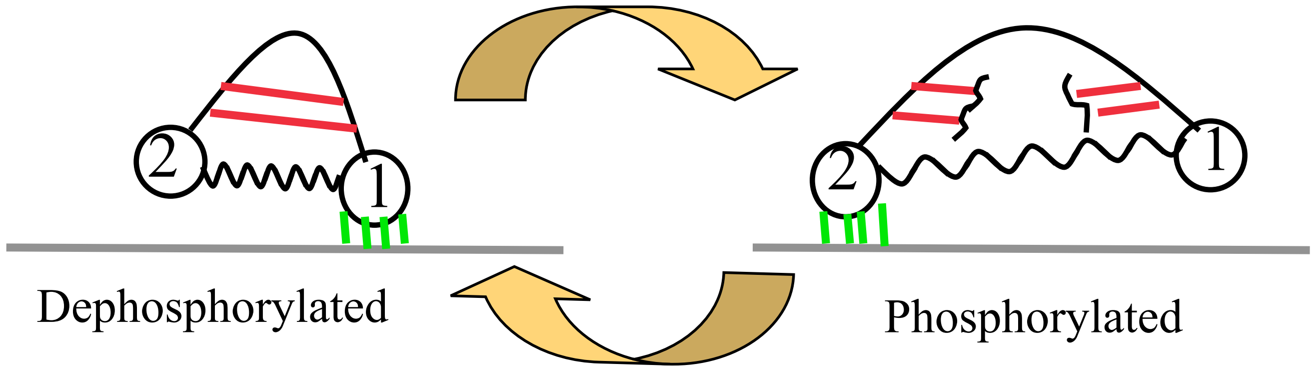
Trajectory

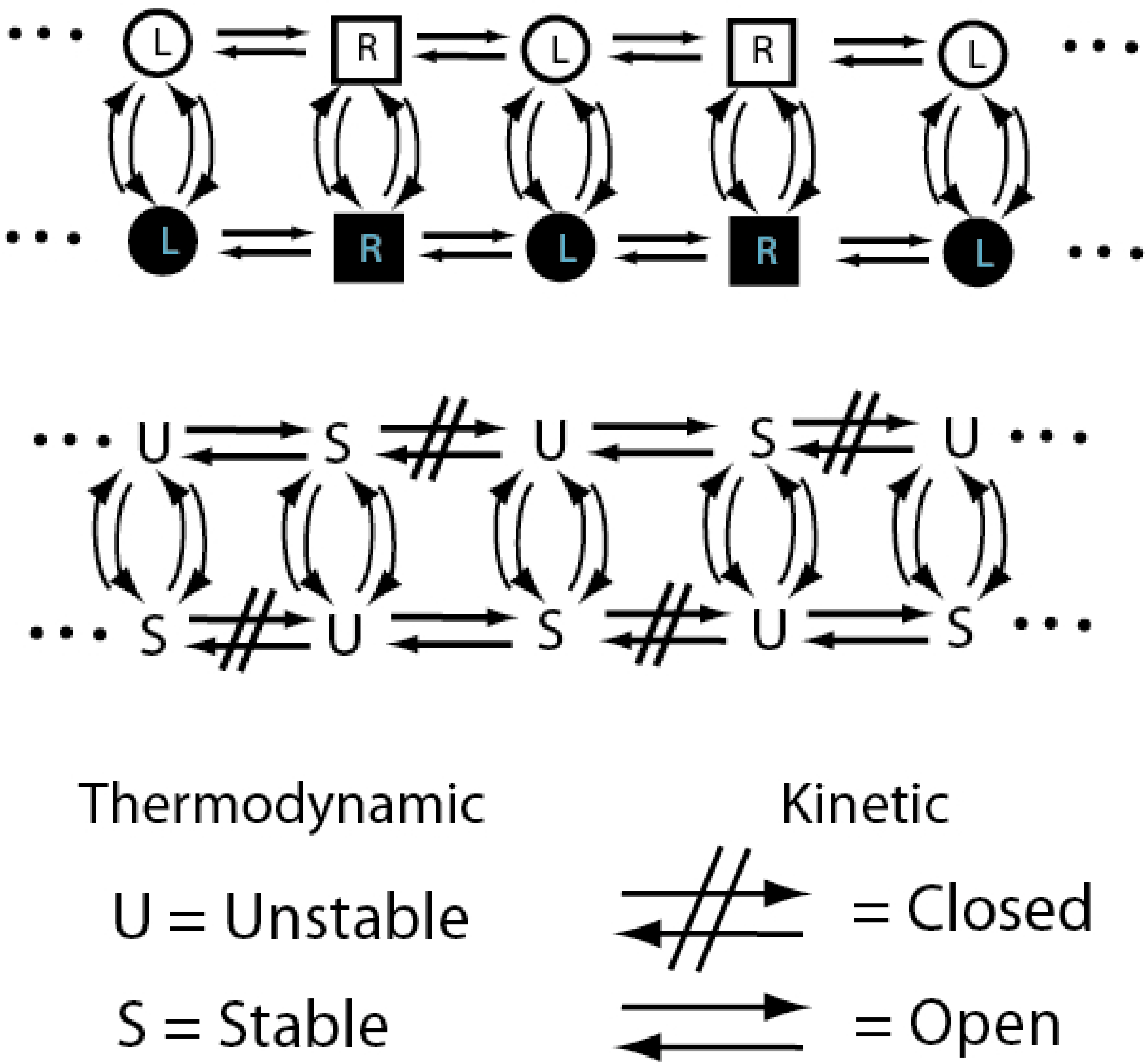


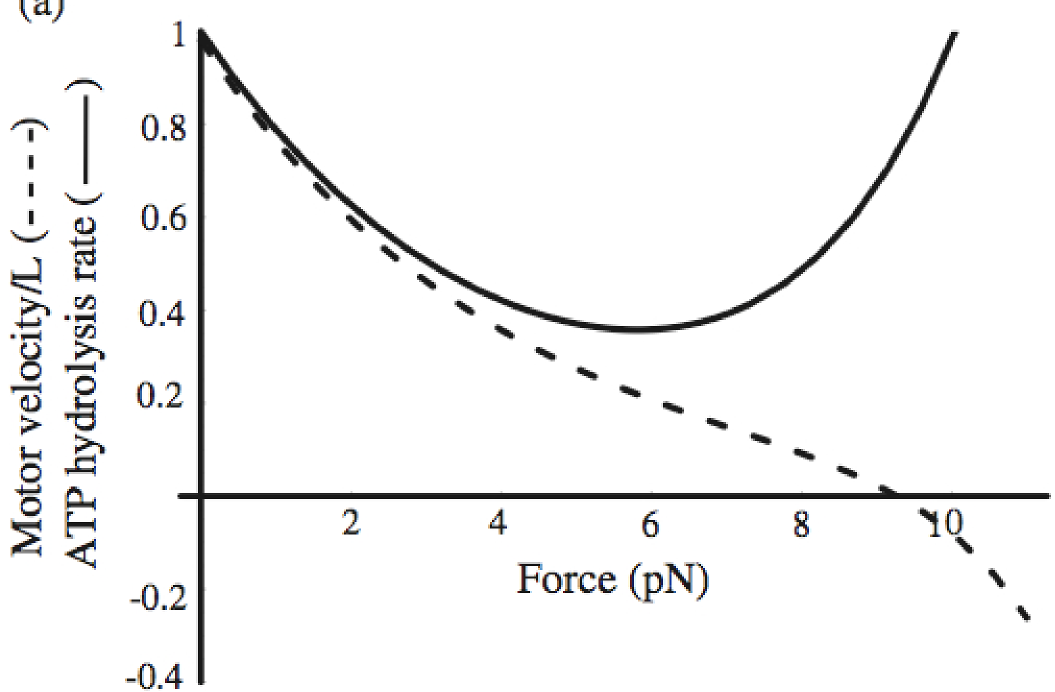


Three two-state processes

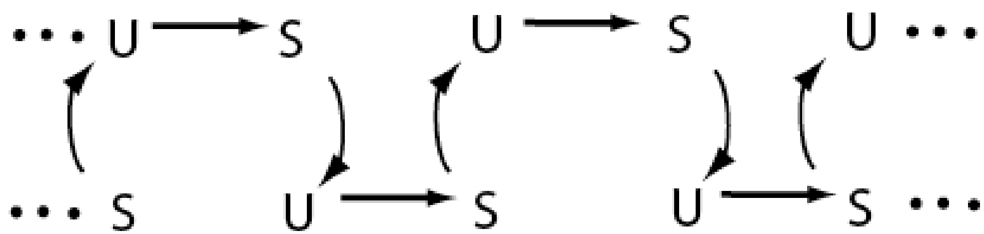
Head one/two bound
Spring contracted/extended
Protein phosphorylated/dephosphorylated



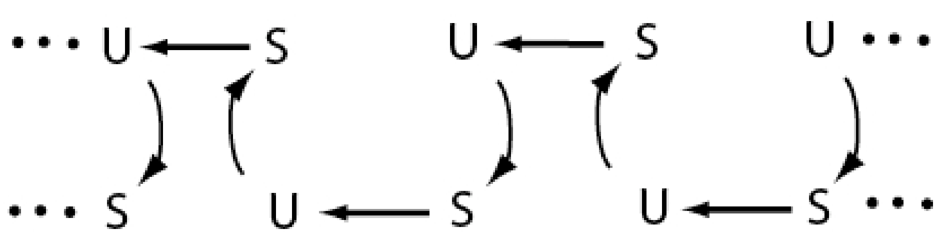

L
R
L
R
L
L
R
L
R
L
U
S
U
S
U
S
U
S
U
S
Thermodynamic
U = Unstable
S = Stable
Kinetic
= Closed
= Open



Small applied load



Large applied load



Principles of directed motion of molecular motors and pumps

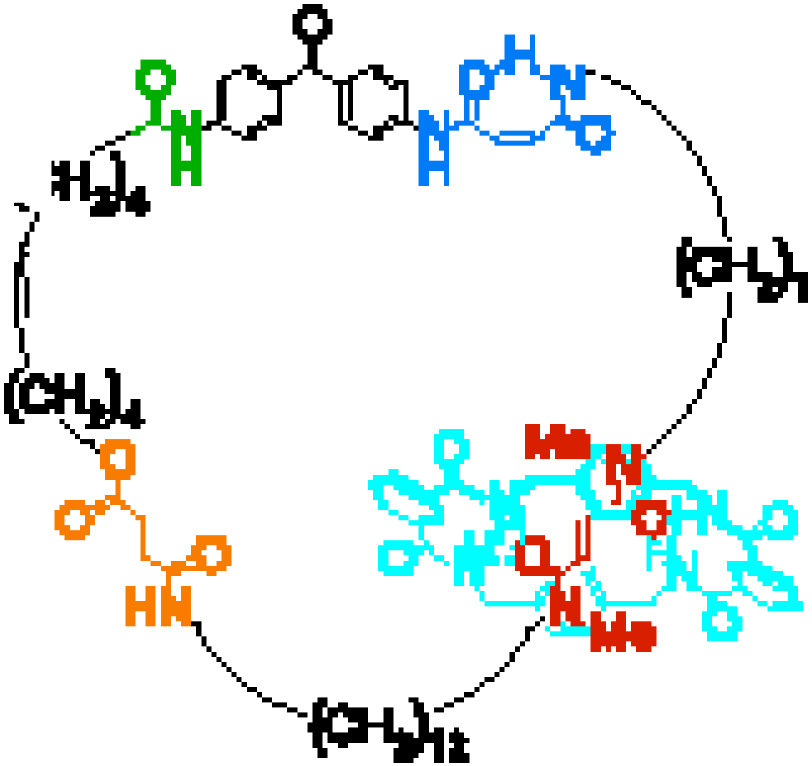
Molecular motors operate in an environment where viscosity dominates
Inertia, and hence where velocity if proportional to force. Analogies
With electric circuits and chemical networks are much more appropriate
Than models based on cars, turbines, judo throws, and the like.

Directed motion and pumping arises by a cycling through parameter
space

> The role of chemical free energy is to assure that the order
> of breaking and making bonds when "substrate" binds is
> not the microscopic reverse of the order of breaking and
> making bonds when product is released

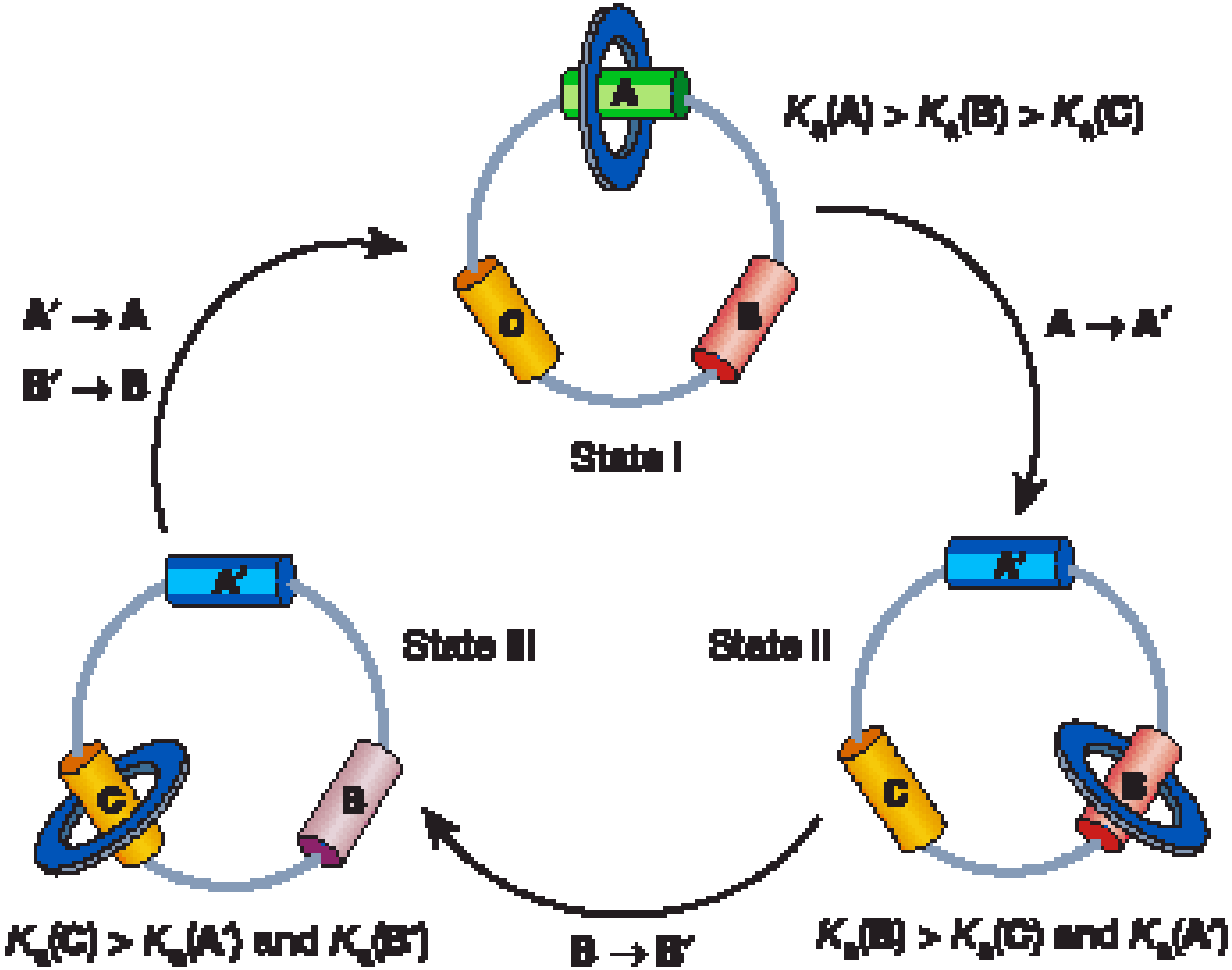
Strong coupling and effective motion in the face of thermal noise
Is attained by reduction of dimensionality.

Time scales are determined by depth of energy wells and height of
Barriers. Moving between wells occurs by thermal activation over
Barriers.



Unidirectional rotation in a mechanically interlocked molecular rotor

Leigh et al., Nature 424: 174 (2003)



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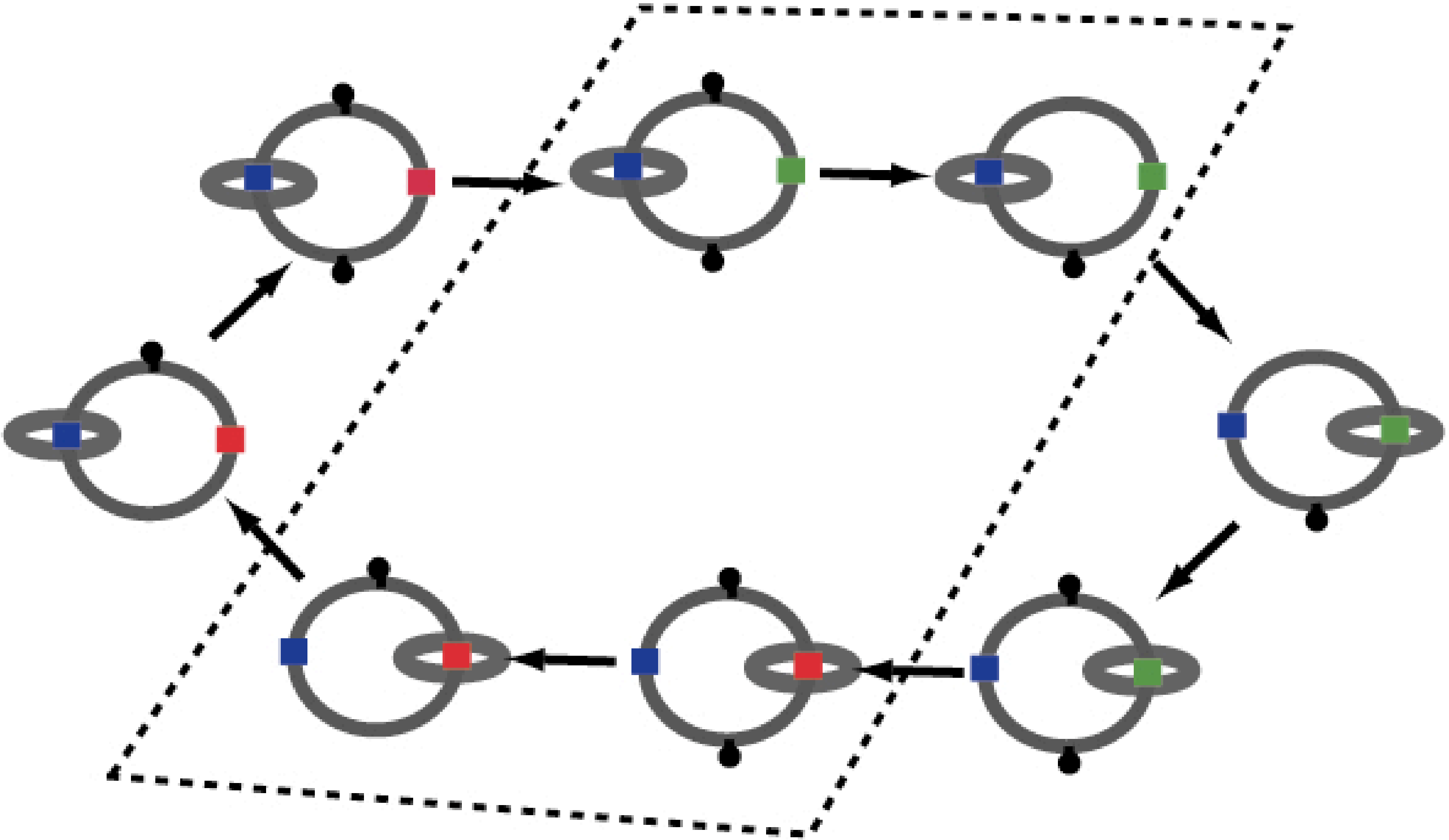

Conclusions:

A very general framework for biological energy transduction takes advantage of the linearity of many processes including low Reynolds number motion.

Velocities depend on time only through the parameters so the distance transported per cycle of modulation can be expressed as a loop integral.

The direction of motion is controlled by the trajectory of the transitions between the "equilibrium" states, and NOT by their structure.

Electrical analogies are more appropriate than automotive ones