Physical Principles in Biology
Biology 3550
Spring 2024

Lecture 36

Molecular Motors and the Brownian Ratchet

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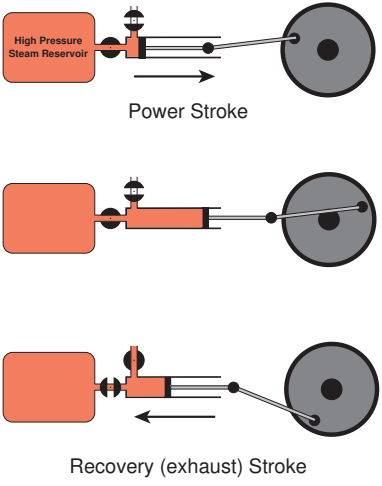
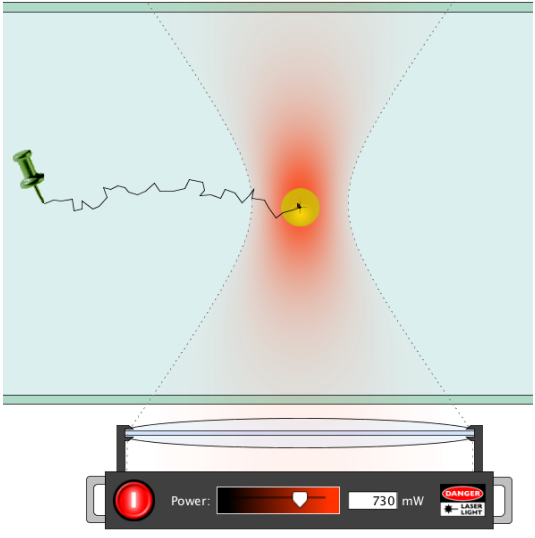
A Simple Steam Engine



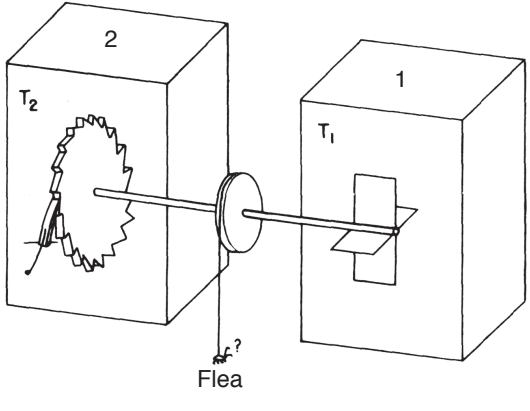
- Similar requirements for a molecular motor:
  - Loss of free energy (*e.g.,* ATP hydrolysis) must be coupled to mechanical work.
  - Motor must operate cyclically.
  - Individual steps in cycle must be regulated.
- Important differences for a molecular motor:
  - No temperature differences at the molecular scale.
  - No momentum at the molecular scale.

Stretching DNA with Optical Tweezers



- Thermal motion of solvent molecules generates a force.
- Force increases as DNA ends are moved further apart.
- Force is entropic in nature: There are more possible conformations with the ends closer together.
- Bead and DNA must rapidly equilibrate among the many possible configurations in order for the force to be exerted.
- Could a force like this be used as a molecular motor?

A “Brownian Ratchet”

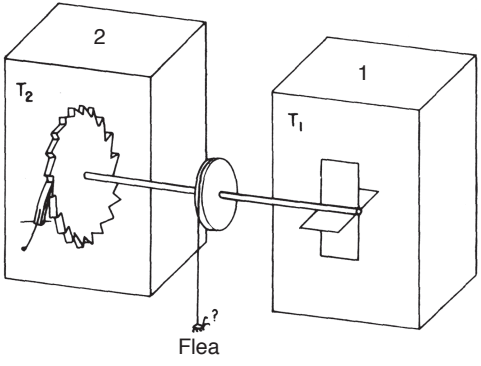


- Thermal motions of gas molecules in compartment 1 make paddle wheel jiggle back and forth.
- Ratchet mechanism in compartment 2 allows motion in only one direction.
- String is wound onto the pulley and the flea is slowly lifted.
- Will this work?

Feynman, R. P., Leighton, R. B. & Sands, M. (2013). *The Feynman Lectures on Physics*, volume I, chapter 46. Basic Books
http://www.feynmanlectures.caltech.edu/I_46.html

Clicker Question #2

Will the Brownian ratchet lift the flea?



A) Yes

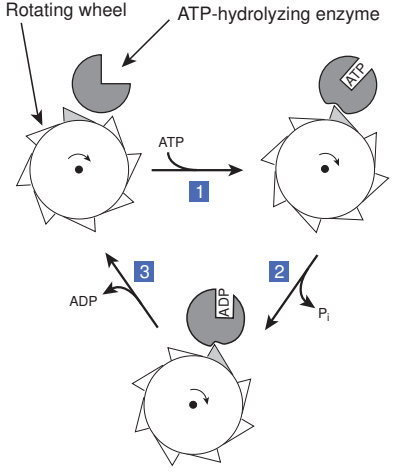
B) Only if the temperature of compartment 1 is greater than that of 2.

C) Only if the temperature of compartment 2 is greater than that of 1.

D) No way!

In the absence of a temperature difference (or other source of free energy), thermal motion can generate a force and directional motion, but cannot drive a cyclic motor.

A Hypothetical ATPase Ratchet



- Enzyme changes conformation during catalytic cycle.
- Changes in enzyme conformation control motion of the wheel.
- microscopic motions are random.
- Steps in the cycle
  1. Enzyme binds ATP and changes conformation.
     Wheel rotates clockwise.
  2. ATP is hydrolyzed, phosphate ion is released and enzyme changes conformation
     Wheel rotates clockwise.
  3. ADP is released and enzyme returns to its original conformation.
     Wheel rotates clockwise.