Muscling in on molecular machines

The concept of a “power stroke” - a free-energy releasing shape change of a protein - appears in almost every textbook that deals with the molecular details of muscle, bacterial flagella, and many other bio-molecular machines. Researchers have now shown that the power stroke model is wrong as an explanation of how chemical energy is used by a molecular machine to do mechanical work. Instead the directionality is controlled entirely by the gating of the chemical reaction that provides the fuel for the machine. Achieving directed motion of a molecular machine is much more a problem of molecular recognition than it is of nano-mechanics, as illustrated in Fig. 1 for a schematic molecular machine driven by ATP hydrolysis, the common energy currency in cells.

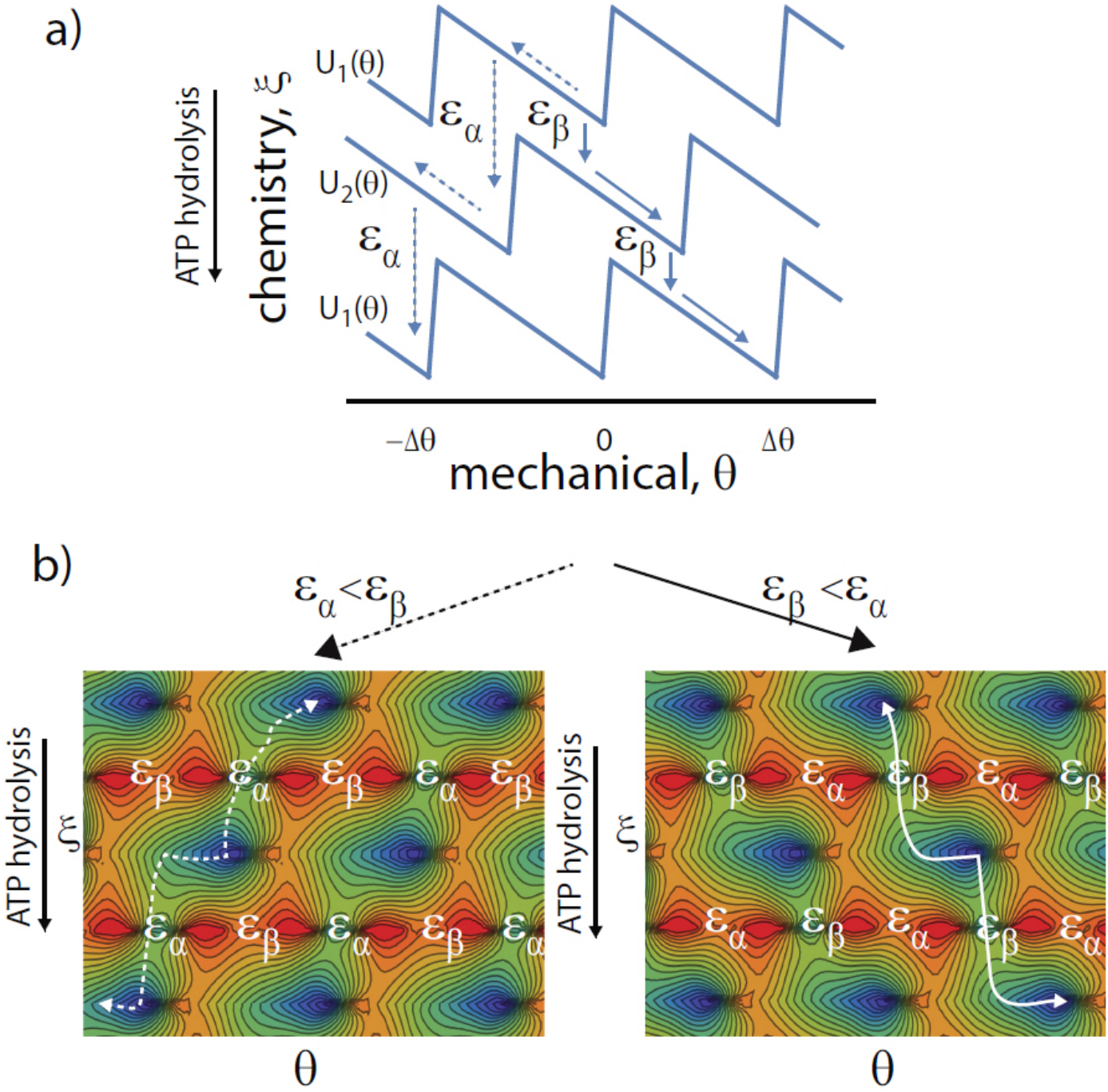

Fig. 1 a) Schematic picture of how a chemical process can drive directed mechanical motion. The mechanism
illustrated with the solid arrows involves two power strokes, downhill “slides” on the slopes of U1 and U2.
The mechanism illustrated by the dashed lines looks impossible from the point of view of macroscopic physics, but when the activation energies for the chemical processes are equal, ?$_?$ = ?$_?$, the mechanism with dashed lines in which the motor steps left is just as likely as the mechanism

shown by the solid arrows in which the motor steps right. b) Potential energy profiles for the ratchet mechanism in Fig. 1a) for the cases $?_? > ?_?$ and $?_? > ?_?$. The most likely trajectories are shown by the white solid and dashed curves.

The better understanding of bio-molecular motors provided by the recent research has led to progress in the design of synthetic molecular machines. One specific example involves threading several rings onto a long rod by a “molecular pump” shown in Fig. 2. A key step in the function of this synthetic pump is the oxidation of a recognition site on the rod. In the reduced state (purple) there is an attractive interaction between the ring and the recognition site, but on oxidation (blue) the interaction becomes repulsive. The movement of the ring from the oxidized recognition site to a collecting chain is very reasonably termed a power stroke.

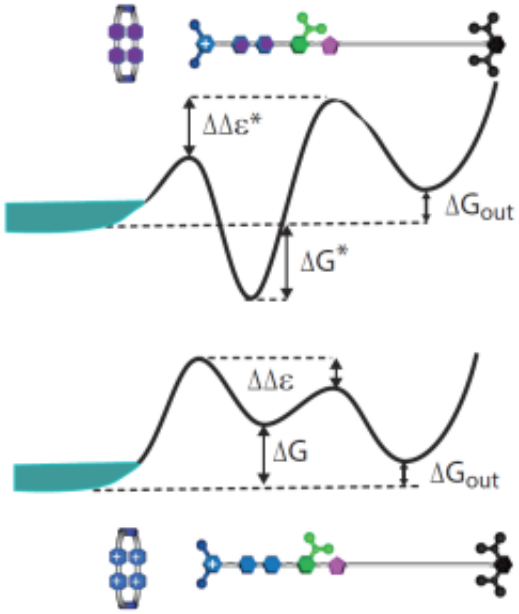

Fig. 2 Molecule that can serve as a molecular pump for a ring compound. Sequential oxidation to the lower state (indicated by blue on the ring and recognition site) and reduction to the upper state (indicated by purple substituents on the ring and recognition site) leads to accumation of rings on the collection site at the left hand of the rod compound.

By repetitively changing the redox potential (and hence the reduction/oxidation of the recognition site) several rings can be pumped onto the collecting chain to form a non-equilibrium complex, a structure that would exist in only negligible amounts in the absence of energy input that is provided by repetitively changing the redox potential. The power stroke for this pump is absolutely essential.

On further consideration, however, it soon became apparent that a power stroke is not sufficient to allow the energy released by chemical catalysis to drive pumping. Even more surprisingly perhaps, the power stroke is not even necessary. The essential requirement is seen to be a mechanism for gating the catalysis such that reaction with substrate is fast and reaction with product slow in one state of the mechanical cycle, and reaction with substrate slow and reaction with product fast in a different state of the mechanical cycle, thus assuring that the mechanical and chemical steps are interleaved with one another, a condition that, combined with energy from the catalyzed reaction, is both necessary and sufficient for pumping of the rings onto the collecting chain. This mechanism has been termed an information ratchet because the essential feature is that the specificity of the catalytic active site is controlled by information about the mechanical state of the motor molecule. Ongoing efforts devoted to the design and construction of synthetic molecular pumps and motors will result both in better understanding of bio-molecular machines, and in the development of tools for harnessing the power of molecule by molecule assembly.

R. Dean Astumian
Dept. of Physics, Univ. of Maine

Publications

Huxley's Model for Muscle Contraction Revisited: The Importance of Microscopic Reversibility.
Astumian RD
Top Curr Chem. 2015

Design and Synthesis of Nonequilibrium Systems.
Cheng C, McGonigal PR, Stoddart JF, Astumian RD
ACS Nano. 2015 Sep 22