Alfred Nobel Symposium
Energy in Cosmos, Molecules and Life
June 18-22, 2005

F_1-ATPase: A Rotary Motor/Generator

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The protein F_1-ATPase is a rotary motor made of a single molecule. In 1997, we videotaped its motion under an optical microscope [1], as the final proof that its central γ subunit indeed rotates inside a surrounding cylinder made of $\alpha_3\beta_3$ subunits. Since then we have shown, by single-molecule imaging, that (*i*) the rotary torque is nearly independent of the rotation angle [2], (*ii*) 80-90 pN nm of mechanical work can be done per ATP hydrolyzed [3], (*iii*) binding of ATP causes 80-90° rotation [4,5], and (*iv*) release of a hydrolysis product causes further 40-30° rotation [4,5]. Point *ii* implies that the efficiency of chemo-mechanical conversion may reach ~100%, though this statement needs to be qualified [6]. Points *i-iv* allowed us to infer the angle-dependent potential energies for γ rotation for each of chemical intermediates that appear during rotation [4]. On the basis of these potential energies and using a toy model for illustration, we have suggested how the free energy of ATP hydrolysis may be converted to mechanical torque, and more importantly, how the reverse rotation of the motor by an external force may lead to ATP synthesis [6]. The most important aspect is that binding (and release) of a nucleotide, rather than hydrolysis *per se*, is the major source of mechanical output. An equally important corollary is that mechanical motion (rotation) changes the affinity for a nucleotide by orders of magnitude, the essential ingredient of Boyer's binding-change model for ATP synthesis [7]. We have now shown, using magnetic tweezers, that reverse rotation of F_1 indeed produces ATP [8]. Possibly for the first time, energetically uphill chemical synthesis has been accomplished by the action of mechanical force generated by human artifacts (with the aid of the nature's nano machine). If time allows, I will also mention our recent attempts at clarifying precisely how the three catalytic sites in F_1 cooperate to produce rotation.

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