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Scientific Abstract: Fast and Processive Linear and Rotary Molecular Motors Made of DNA

Realization of bioinspired molecular machines that can perform complex operations – specifically the development of molecular motors that consume energy and perform work – is a complex task. To make molecular motors that are fast and processive is even harder. Mechanisms for powering the motors, tailored structural and dynamical properties, methods for motor fabrication, and means for characterization of the motors and their operation are major challenges. Not surprisingly, the synthetic molecular motors described thus far have poor performance in comparison to biological motors. Fortunately, recent advances in structural DNA nanotechnology and our ability to program DNA reactions offer promising solutions. Here we propose a clear path for the realization of externally controlled DNA linear and rotary motors that are likely to perform hundreds and possibly thousands of precise steps at high speed, significantly more than demonstrated to date for DNA motors. In recent years, my group has developed and studied a DNA origami-based bipedal motor model system. We recognized two fundamental and general problems that limit the motor processivity and speed. The first problem is the interaction of the motor with redundant energy-providing and commanding DNA strands (called Fuels and Antifuels) that accumulating in the solution. We have solved this problem, possibly in its entirety, by using a microfluidics device to introduce these strands and to insure their removal from the solution surrounding the motor after use. With this system, our bipedal motor performs 32 computer-controlled steps, crossing 370 nm, in 44% yield, which is, to the best of our knowledge, the highest number of operations ever demonstrated for a controlled DNA machine. The second fundamental problem is the consecutive binding of two 'fuel' strands, instead of one, that blocks the attachment of a bipedal leg to the DNA origami track, directly leading to walker dissociation. This mechanism reduces processivity and, unavoidably, speed. Here we propose a conceptually different strategy to operate externally controlled motors and machines. Redesigned fuels will be introduced and the system washed before the leg is lifted, in principle avoiding this problem entirely. Our preliminary results are promising, and a calculation based on reaction rates measured using the microfluidics predicts about two orders of magnitude improvement in processivity and speed over the current system. The operation and dynamics of the bipedal motor will be monitored and studied using a single-molecule FRET system we developed. Furthermore, building on our optimized bipedal walker, we propose to construct an origami-based rotary motor. By attaching the rotor to the motor frame using a single-stranded DNA swivel element, the machine should remain intact in the event of error in the operation. Because the rotor cannot dissociate, the challenge of processivity will be, in principle, solved, and this may allow even faster operation rates. The operation of the rotary motor will be monitored by following the polarization of light scattered from a single gold nanorod attached to the rotor. This technique has much higher resolution then FRET, and it will allow precise real-time determination of the rotor angle over very long time periods. Through this work, we expect to demonstrate that highly reliable, externally controlled DNA motors that can perform hundreds to thousands of precise operation are now in reach. The rotary motor device proposed here can be instrumental in the development of autonomous propulsion mechanism and autonomous rotary motor.