Grabbing the cat by the tail: Discrete steps by a DNA packaging motor and the inter-subunit coordination in a ring-ATPase

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As part of their infection cycle, many viruses must package their newly replicated genomes inside a protein capsid. Bacteriophage phi29 packages its 6.6 mm long double-stranded DNA into a 42 nm dia. x 54 nm high capsid using a multimeric ring motor that belongs to the ASCE (Additional Strand, Conserved E) superfamily of ATPases. A number of fundamental questions remain as to the coordination of the various subunits in these multimeric rings. The portal motor in bacteriophage phi29 is ideal to investigate these questions and is a remarkable machine that must overcome entropic, electrostatic, and DNA bending energies to package its genome to near-crystalline density inside the capsid. Using optical tweezers, we find that this motor can work against loads of up to ~55 picoNewtons on average, making it one of the strongest molecular motors ever reported. We establish the force-velocity relationship of the motor. Interestingly, the packaging rate decreases as the prohead fills, indicating that an internal pressure builds up due to DNA compression attaining the value of ~6 MegaPascals at the end of the packaging. We show that the chemical energy of ATP is converted into mechanical work during phosphate release. Using ultra-high resolution optical tweezers, we determined the step size of the motor and established the coordination of the polymerases around the ring. We propose a comprehensive model of the operation of this motor.