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MOLECULAR MOTORS

Power in numbers

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> “…muscle performance … is modulated by the number of myosin motors that are attached to actin.”

No matter how much time is spent at the gym, the force–velocity relationship of muscles ultimately determines their performance. Specifically, the heavier the weight you want to lift, the slower your muscles will shorten. The basis of this relationship was thought to be that each individual muscle-moving molecular motor, such as myosin II, generates a lower force when in motion. However, the force–velocity relationship is actually determined by the number of myosin II motors that are attached to actin when moving high and low loads, report Gabriella Piazzesi and colleagues in *Cell*.

Muscle contraction is driven by superstructures of myosin II motors that emerge from a myosin filament backbone at regular 14.5-nm intervals. During contraction, the N-terminal head domains of myosin II units bind actin, which results in relative sliding of the actin and myosin filaments. Using a combination of X-ray diffraction and mechanical measurements, the authors examined individual myosin motors in intact single cells. For a wide range of shortening velocities, their findings indicated that individual myosin motors apply a force of ~6 pN while pulling actin filaments through a ~6-nm stroke. So, there is minimal variation in the stroke force and distance of myosin II for different loads. Furthermore, the number of motors that are attached to actin during the process of shortening decreases almost linearly with decreasing load.

Given these findings, the authors propose that muscle performance (that is, the combination of shortening velocity and application of force) is modulated by the number of myosin motors that are attached to actin. A calculation of the muscle energetics of this model indicated that it allows individual motors to work at high efficiency, with minimal metabolic cost, against a range of external loads. The authors further suggest that the general features of the myosin II mechanism are likely to be shared by other motor proteins.

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ORIGINAL RESEARCH PAPER Piazzesi, G. *et al.* Skeletal muscle performance determined by modulation of number of myosin motors rather than motor force or stroke size. *Cell* **131**, 784–795 (2007)