The three filament model of muscle contraction and its implications for human movement, health and performance

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Muscle contraction occurs through the interaction of the two contractile filaments actin and myosin. Muscle contraction has been described for the past half century using the sliding filament [1, 2] and the cross-bridge theory [3]. Andrew Huxley was the first to describe the cross-bridge theory mathematically, thereby allowing for quantitative predictions of the theory. From the very beginning, Huxley was aware that the theory predicted the forces, stiffness and energetics of muscle contraction well for isometric and concentric muscle actions, but could not predict these mechanical variables accurately for eccentric muscle action [4]. Specifically, his initial theory vastly overestimated the forces and metabolic cost of eccentric muscle action, and later revised versions of the theory were never able to predict the residual force enhancement associated with eccentric muscle action [4, 5].

In 2002, we discovered that the residual force enhancement property was caused (at least in part) by passive structural elements [6], rather than by cross-bridges or the development of sarcomere length non-uniformities, as had been assumed up until then. We then identified that residual force enhancement is a sarcomeric property [7, 8] that was associated with the structural spring molecule titin [9]. We identified that titin increases its stiffness upon activation by binding calcium to specific sites on titin [10] and by shortening its spring length (likely by binding to actin upon activation and muscle stretching [11]).

These discoveries led to the formulation of a mathematical model consisting of three sarcomeric proteins (actin, myosin and titin) for force regulation in active muscles [12]. Possible implications for human movement, disease and athletic performance will be discussed in the context of this new model of muscle contraction (e.g.[13]).

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