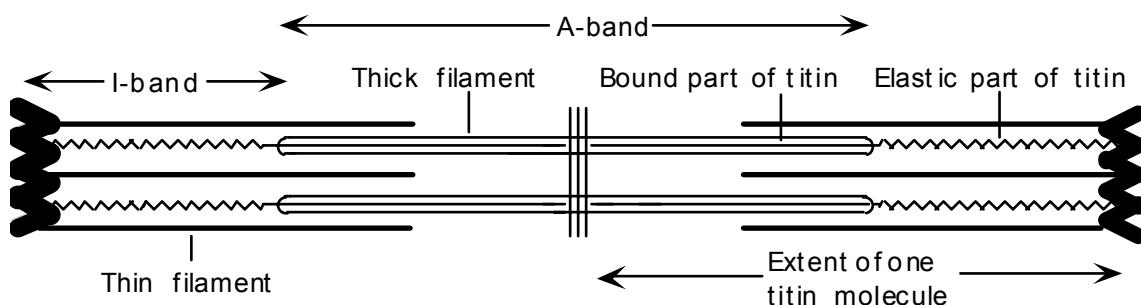


# Titin

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Titin is the largest protein yet described (chain weight 3-3.7 MDa) and the third most abundant protein in muscle. More than half of the titin molecule is bound to muscle thick filaments in the sarcomere, where we have suggested it regulates exact assembly of the 294 myosin molecules known to comprise the filament. The remainder of the titin molecule forms an elastic connection between the end of the thick filament and the Z-line (Fig. 1). These connections are the main source of the passive elasticity of muscle. They also ensure that thick filaments stay in the middle of the sarcomere, which ensures that even forces are developed by myosin in each half of the filament.

Studies of titin elasticity are of considerable interest and have notably been pursued in many single molecule studies (including some by ourselves) using optical tweezers and AFM. It has been tempting to assume that the single molecule data can be scaled to explain directly muscle passive elasticity. However, several factors suggest that such direct extrapolation may not be possible, including interactions of the elastic region of titin *in situ*, both with itself and with other proteins. We have shown that a section of the titin molecule ~100 nm long, located in the elastic region near the end of the myosin, self-associates to form a hexameric assembly. This demonstrates that a substantial fraction of the elastic part of titin does not function as independent single molecules. Effects of molecular crowding and confinement within the lattice of actin (thin) filaments are also under consideration, which would also be expected to modulate the behaviour of the molecule.



**Fig. 1.** Schematic of the location of titin in muscle

## Publication

Tskhovrebova, L. and Trinick, J. (2004). Properties of titin immunoglobulin and fibronectin-3 domains. *J. Biol. Chem.*, 279:46351-46354.

## Funding

This work is funded by the British Heart Foundation.