

Shape and flexibility in the titin 11-domain super-repeat

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Introduction

Titin is a giant protein of striated muscle with important roles in the assembly, intracellular signalling and passive mechanical properties of sarcomeres. The molecule consists principally of <300 immunoglobulin and fibronectin domains arranged in a chain more than 1 μm long. The isoform dependent N-terminal part of the molecule forms an elastic connection between the end of the thick filament and the Z-line. The larger, constitutively expressed C-terminal part is bound to the thick filament. Through most of the thick filament part, the immunoglobulin and fibronectin domains are arranged in a repeating pattern of 11 domains termed the 'large super-repeat'. There are 11 contiguous copies of the large super-repeat making up a segment of the molecule nearly 0.5 μm long. We have studied a set of two-domain and three-domain recombinant fragments from the large super-repeat region by electron microscopy, synchrotron X-ray solution scattering and analytical ultracentrifugation, with the goal of reconstructing the overall structure of this part of titin.

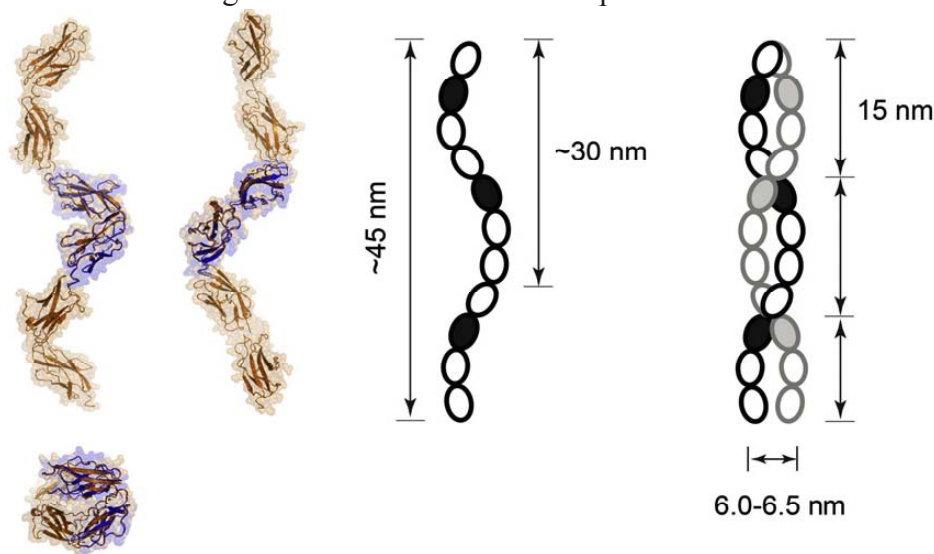


Figure 1: (left panel) Model of the six-domain segment corresponding to the first two subdivisions of the large super-repeat reconstructed from solution scattering models. **(middle and right panels)** Schematic representations of large super-repeat structure in monomeric (middle) and dimerised (right) states. Ig domains are black.

Results

The data illustrate different average conformations in different domain pairs, which correlate with differences in interdomain linker lengths. They also illustrate interdomain bending and flexibility around average conformations. Overall, the data favour a helical conformation in the large super-repeat. They also suggest that this region of titin is dimerised when bound to the thick filament.

Publications

Tskhovrebova, L., Walker, M., Grossmann, G. Khan, G., Baron, A. and Trinick, J. (2010) Shape and flexibility in the titin eleven domain super-repeat. *J Mol Biol* **397**:1092-105.

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Collaborators

Matt L. Walker (Newton Abbott) and J. Gunter Grossmann (Daresbury Laboratory).