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Special Issue on The Third Filament System
Edited by D. Pette and D. Fürst (Guest Editor)

With 67 Figures and 4 Tables

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Preface

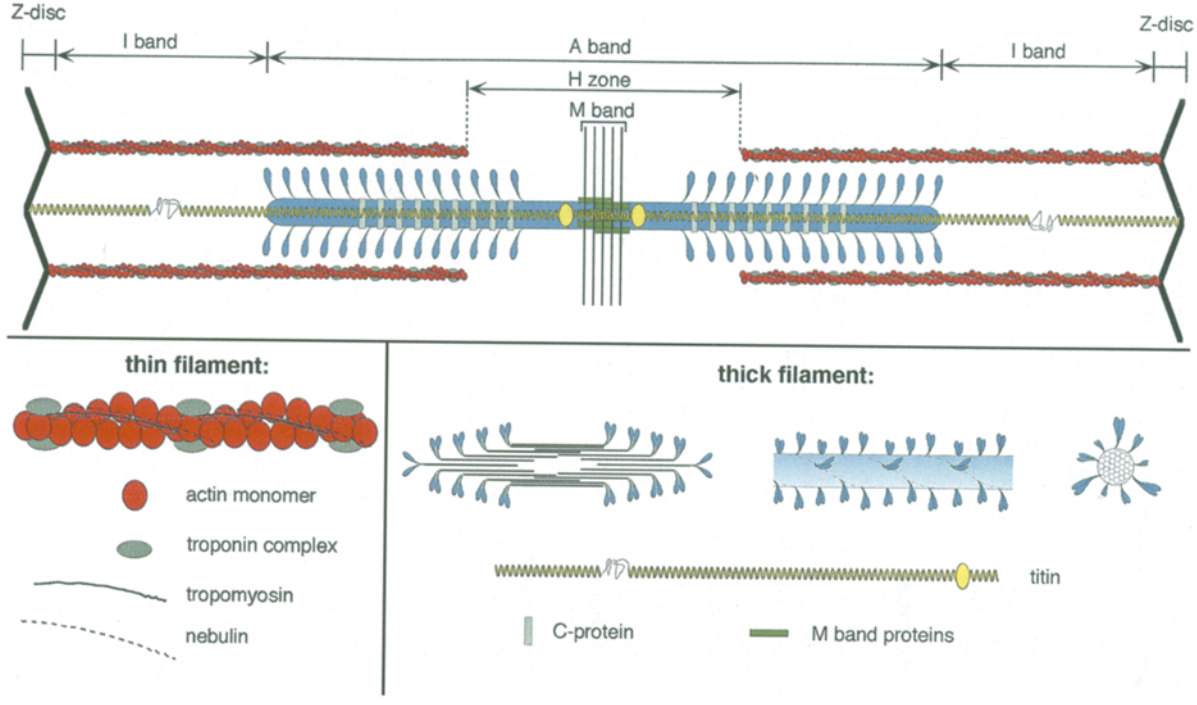
The ability to move is one of the fundamental properties of living organisms. It is based on the existence of two principally different molecular motors, the actomyosin and the microtubular systems. Within the actomyosin system, the regular sarcomeric organization of thick and thin filaments is one of the most fascinating achievements in the evolution of a tissue specialized in performing directed movements. As viewed from the highly ordered structures of thick and thin filaments in the myofibrils of cross-striated muscle, this arrangement can not be explained simply by the molecular properties of its major protein components. This difficulty became evident almost as early as the sliding filament mechanism had been proposed. Several observations pointed to the existence of an as yet unidentified ordering structure, for instance the maintained integrity of ghost fibers after the extraction of myosin (Huxley & Hanson, 1954), the elastic behaviour of those fibers, the strictly defined filament length, the integrity of the sarcomere after extension beyond thin/thick filament overlap (for review see Wang, 1985).

It was the pioneering work of Koscak Maruyama and collaborators which by the discovery of an only badly soluble proteinaceous residue called "connectin" provided for the first time a molecular explanation for these phenomena (Maruyama, 1976). This hitherto unknown gigantic protein, later on renamed as titin (Wang et al., 1979), was shown to be capable of fulfilling the demanded organizing role. Its molecular dimensions, sarcomeric arrangement and multiple functions deciphered since its discovery, justify its distinction as an independent structural element, the so-called third filament, and the notion of the sarcomere as a three-filament system (Fig. 1).

The large body of literature that has accumulated on titin and its associated proteins in the time since its discovery, made it appear timely to bring together the existing knowledge in a comprehensive form. This was the aim of the present volume.

Figure 1. Comprehensive sketch illustrating the so-called "three filament model of the sarcomere". The upper box shows one sarcomere (with Z-discs, I band, A band, H zone, and M band indicated by arrows and brackets), as well as one representative thick filament and four thin filaments. An enlargement of thin filament substructure with an explanation of molecular symbols is shown in the left bottom box. The main features of thick filament structure (assembly of filaments based on myosin molecules, three-dimensional arrangement of myosin heads along the filament, cross section through the filament), and a titin molecule are given in the right bottom box. Note that exclusively titin provides continuity to the sarcomere; on the other hand, this molecule is required to be highly elastic in order not to impede the actin/myosin-based contractile machinery. For further details see the various contributions to this volume.

The history of the discovery of connectin/titin including comparative aspects of the third filament in diverse muscles of vertebrates and invertebrates is summarized in a chapter by K. Maruyama. Fundamental insights into molecular structure/function relationships stem from the meticulous work of Siegfried Labeit's laboratory on the cloning and sequencing studies on titin cDNA and its gene. The results of this work and an outlook on the titin isoform family is presented in chapter 2. Robert Horowits highlights in chapter 3 the physiology of titin by its role in the mechanical properties, as elucidated by selective extractions and direct measurements of segmental elasticity. The complex pattern of titin interactions with other proteins of the myofibrillar apparatus along its length is dealt with by Mathias Gautel and colleagues in chapter 4. This chapter also includes available evidence for the regulation of these interactions by mechanisms under control of different signalling pathways. The role of the third filament as a ruler of the sarcomere during embryonic and in vitro myogenesis is discussed in chapter 5 by Alice Fulton. The interactions of specific titin regions with other protein ligands are described in detail in the following two chapters. Dieter Fürst and collaborators elaborate in chapter 6 interactions of the carboxy terminus of titin with M-band proteins,


Z-disc
I band
A band
H zone
M band
I band
Z-disc
thin filament:
actin monomer
troponin complex
tropomyosin
nebulin
thick filament:
titin
C-protein
M band proteins

both with regard to the structure of the M-band and its assembly. The C-protein, its potential modulatory function on contractility and thick filament formation is dealt with by Pauline Bennett and colleagues in chapter 7. The final chapter of the volume by Guy Benian and colleagues emphasizes comparative aspects and focusses on the genetics and molecular biology of titin-like proteins in invertebrates.

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Dieter Fürst
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