THICK FILAMENT MOVEMENT AND ISOMETRIC TENSION IN ACTIVATED SKELETAL MUSCLE

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ABSTRACT Thick filaments can move from the center of the sarcomere to the Z-disc while the isometric tension remains stable in skinned rabbit psoas fibers activated for several minutes (Horowits and Podolsky, 1987). Using the active and resting tension-length relations and the force-velocity relation, we calculated the time course and mechanical consequences of thick filament movement in the presence and absence of the elastic titin filaments, which link the ends of the thick filaments to the Z-discs and give rise to the resting tension. The calculated time course of thick filament movement exhibits a lag phase, during which the velocity and extent of movement are extremely small. This lag phase is dependent only on the properties of the cross-bridges and the initial position of the thick filament. The time course of thick filament movement in skinned rabbit psoas fibers at 7°C is well fit assuming a small initial thick filament displacement away from the center of the sarcomere; this leads to a lag of ~80 s before any significant thick filament movement occurs. In the model incorporating titin filaments, this lag is followed by a phase of slow, steady motion during which isometric tension is stable. The model excluding titin filaments predicts a phase of acceleration accompanied by a 50% decrease in tension. The observed time course of movement and tension are consistent with the model incorporating titin filaments. The long lag phase suggests that in vivo, significant movement of thick filaments is unlikely to occur during a single contraction. Therefore, the primary physiological function of titin filaments may be to keep the thick filaments centered during passive stretch and to prevent sarcomere asymmetry from accumulating over several contractions by recentering the thick filaments each time the muscle is relaxed.

INTRODUCTION

We have recently demonstrated that thick filaments can move from the center of the sarcomere toward the Z-disc upon activation of skeletal muscle fibers (Horowits and Podolsky, 1987). This occurs because the amount of active force pulling on each end of the thick filament is proportional to the cross-bridge bearing length that overlaps with thin filaments, so that any initial imbalance is amplified as the thick filament is actually pulled toward one end of the sarcomere. The extent of this movement exhibits a dependence on sarcomere length that is easily explained by the dependence of active and resting tensions on sarcomere length, provided that the resting tension comes from stretch of elastic elements connecting the ends of the thick filaments to the Z-discs (Horowits and Podolsky, 1987). The elastic elements in this model were attributed to titin (also called connectin) filaments, which have the required properties: they are elastic (Wang et al., 1985), link thick filaments to Z-discs (Maruyama et al., 1985), and produce the resting tension (Horowits et al., 1986; Yoshioka et al., 1986).

Here we address the dynamic aspects of thick filament movement. Starting with the dependence of active and resting tension on sarcomere length and the steady-state dependence of the velocity of filament sliding on load, we have calculated the time course and mechanical consequences of thick filament movement in the presence and absence of titin filaments. This analysis reveals that, independent of the presence or absence of titin filaments, thick filament movement away from the center of the sarcomere is initially extremely slow. The elastic titin filaments prevent the thick filaments from accelerating to velocities >1% of the maximum unloaded velocity, V_{max}, as the motion continues. The titin filaments also prevent the isometric tension output of the sarcomere from decreasing as the thick filaments approach the Z-disc. These predictions of the model incorporating titin filaments are in good agreement with experimental findings.

METHODS

Experimental Methods

All experimental results were obtained from skinned rabbit psoas muscle at 7°C. Isometric tension was measured using standard techniques, and thick filament movement was measured by electron microscopy. Experimental methods are identical to those previously described (Horowits and Podolsky, 1987).

Modeling Thick Filament Movement

The forces acting on each half of a thick filament consist of passive forces originating in the titin filaments and active forces originating in the

cross-bridges. Throughout this paper the subscript 1 will refer to the side of the thick filament that is moving towards the nearest Z-disc, and subscript 2 will refer to the side that is moving away from the nearest Z-disc (Fig. 1). Then I_1 and I_2 are the Z-disc to thick filament distances on each side of the sarcomere expressed in μm, RT_1 and RT_2 are the resting tensions pulling the thick filament toward sides 1 and 2, respectively, P_1 and P_2 are the active tensions pulling the thick filament toward sides 1 and 2, respectively, and V_1 and V_2 are the velocities with which the thick filament slides past the thin filaments on each side of the sarcomere. The lengths of the thick and thin filaments in rabbit psoas muscle are 1.6 and 1.1 μm, respectively; in addition, the thick filament has a 0.15-μm wide region at its center that is devoid of cross-bridges (Huxley, 1963; Trinick and Elliot, 1979).

The observed dependence of resting tension on sarcomere length is illustrated in Fig. 2 *A*. For our model the resting tension was assumed to arise only from the titin filaments; it was fit to a straight line at lengths >2.73 μm, and was taken to be 0 at shorter lengths. From this data and the lengths of the thick and thin filaments:

$$\text{for } I_1 \geq 0.566\ \mu\text{m}, RT_1 = (1.71I_1 - 0.968)P_o \text{ and for } I_1 \leq 0.566\ \mu\text{m}, RT_1 = 0 \quad (1)$$

$$\text{for } I_2 \geq 0.566\ \mu\text{m}, RT_2 = (1.71I_2 - 0.968)P_o \text{ and for } I_2 \leq 0.566\ \mu\text{m}, RT_2 = 0, \quad (2)$$

where P_o is defined as the active isometric tension at full filament overlap with centered thick filaments. Note that this formulation assumes no resistance to compression of the titin filaments. Since

$$I_2 = L - I_1 - 1.6\ \mu\text{m}, \quad (3)$$

where L is sarcomere length, both RT_1 and RT_2 are simple functions of I_1, i.e., $RT_1(I_1)$ and $RT_2(I_1)$.

The active isometric tensions on each half of the thick filament, P_{o1} and P_{o2}, are taken to be proportional to the length of thick filament which overlaps with thin filaments, allowing myosin cross-bridges of the proper polarity to interact with actin (Gordon et al., 1966). With the thick filaments centered, the active isometric tension decreases linearly with increasing sarcomere length, as illustrated in Fig. 2 *A*. For sarcomeres on the descending limb of the active tension-length relation (i.e., $L \geq 2.35$ μm, the sarcomere length corresponding to maximum overlap between thick and thin filaments), scaling P_{o1} and P_{o2} for filament overlap yields the following:

$$\text{for } I_1 \geq 0.375\ \mu\text{m}, P_{o1} = P_o(1.1 - I_1)/0.725 \text{ and for } I_1 \leq 0.375\ \mu\text{m}, P_{o1} = P_o \quad (4)$$

$$\text{for } I_2 \leq 1.1\ \mu\text{m}, P_{o2} = P_o(1.1 - I_2)/0.725 \text{ and for } I_2 \geq 1.1\ \mu\text{m}, P_{o2} = 0. \quad (5)$$

The active tensions during thick filament movement, P_1 and P_2, are specified by applying Hill's equation relating force and velocity to each half of the thick filament (Hill, 1939). For side 1, the thick filament slides past the thin filament in the same direction as it does during shortening, so:

$$P_1/P_{o1} = (1 - V_1/V_{max})/(1 + CV_1/V_{max}), \quad (6)$$

where C is a constant specifying the curvature of the force-velocity relation. For rabbit psoas muscle at 10°C, Cooke and Pate (1985) report that V_{max} = 1.22 muscle lengths/s. Since muscle length was measured at a sarcomere length of 2.4 μm and shortening occurs due to filament sliding in both halves of the sarcomere, this corresponds to a maximum velocity of 1.46 μm/s for the relative sliding of thick and thin filaments. From the data of Cooke and Pate (1985), we calculate C = 9.5. These values of V_{max} and C were used in all calculations except where noted.

For side 2 of the thick filament, sliding occurs in the same direction as it does during lengthening. It has been found that, below a critical velocity of V_c, activated muscle lengthens several times slower than predicted by Eq. 6 (Katz, 1939). Since $V_2 = -V_1$, appropriately modifying Eq. 6 yields:

$$P_2/P_{o2} = (1 + FV_1/V_{max})/(1 - FCV_1/V_{max}) \quad \text{for } |V_1| \leq |V_c|, \quad (7)$$

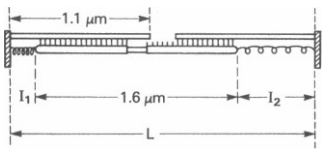

FIGURE 1 Schematic model of the sarcomere. The thick filament is displaced from the center and is moving to the left. Elastic elements representing titin filaments link each end of the thick filament to the nearest Z-line.

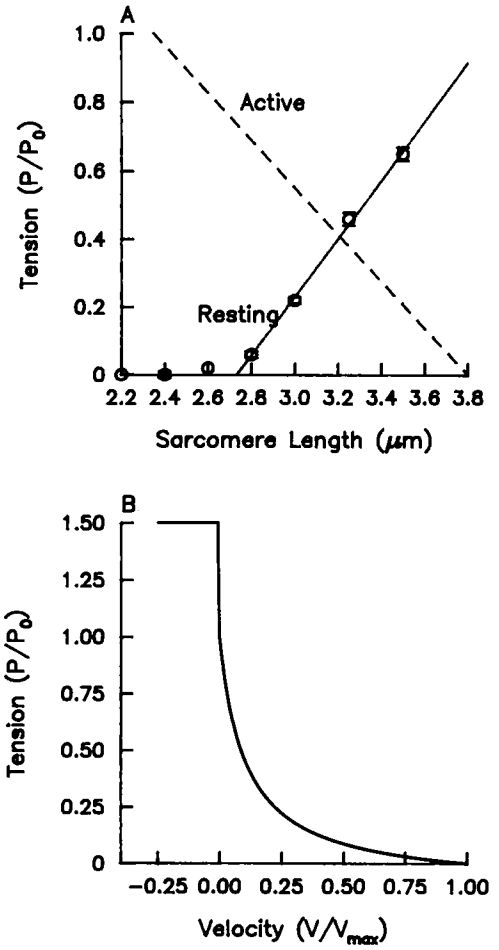

FIGURE 2 Mechanical properties used in modeling thick filament movement. (*A*). Dependence of resting and active tension on sarcomere length. Resting tension was measured 5 min after stretch and normalized to the maximum active tension measured at a sarcomere length of 2.4 μm (P_o) (Horowits and Podolsky, 1987). Each point is the mean resting tension ± SEM for 3 to 6 single fibers. The solid line is fit to the points at $L \geq 2.8$ μm. At $L \leq 2.73$ μm, resting tension is taken as 0. The dashed line is the active tension that is predicted on the basis of filament lengths. (*B*). Dependence of steady state tension on shortening velocity. The curve is specified by Eqs. 6, 7, and 8 with C = 9.5, F = 5, and P_Y = 1.5.

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$$P_2/P_{o2} = (1 + FV_1/V_{max})/(1 - FCV_1/V_{max}) \quad \text{for } |V_1| \leq |V_c|, \quad (7)$$

where F is the factor which accounts for the slowness of the velocity of stretch in excess of that predicted by Eq. 6. In the absence of corresponding data for rabbit psoas muscle, we use the value appropriate for amphibian muscle: $F = 5$ (Katz, 1939), except where noted. At lengthening velocities $> V_c$, the tension output becomes independent of velocity:

$$P_2/P_{o2} = P_Y \text{ for } |V_1| \geq |V_c|. \quad (8)$$

The normalized tension output, P_Y, at these high velocities of lengthening is ~1.5 in amphibian muscle (Flitney and Hirst, 1978), and we use this value in the absence of corresponding data for rabbit psoas muscle, except where noted. V_c can then be calculated from Eq. 7 by taking $P_2/P_{o2} = P_Y$.

Fig. 2 *B* summarizes the relation between tension and velocity, during both shortening and lengthening, that has been used in this formulation. Applying Eqs. 3–8 yields P_1 and P_2 as functions of I_1 and V_1, i.e., $P_1(I_1, V_1)$ and $P_2(I_1, V_1)$. Since the mass of the thick filament and viscous forces are negligibly small, the sum of the active and passive forces acting on each side of the thick filament must be equal, so that:

$$RT_1(I_1) + P_1(I_1, V_1) = RT_2(I_1) + P_2(I_1, V_1). \quad (9)$$

The model with no titin filaments is easily derived by taking $RT_1 = RT_2 = 0$. Substituting the appropriate expressions into Eq. 9 and collecting terms yields a quadratic equation in V_1, which can be solved for V_1 as a function of I_1, i.e., $V_1(I_1)$. (The negative root of the quadratic is chosen, since the positive root can yield $V_1 > V_{max}$.) The velocity of thick filament movement is therefore an analytical function of the position of the thick filament within the sarcomere. Additionally, the net tension output of the sarcomere can be calculated for any I_1 from either side of Eq. 9.

The position of the thick filament within the sarcomere is also related to time, t. Since $V_1(I_1) = -dI_1/dt$,

$$t = \int -dI_1/V_1(I_1). \quad (10)$$

RESULTS

Thick Filament Velocity and Positional Stability

It is clear from the above equations that thick filament velocity is a simple function of how far from the center of the sarcomere the thick filament is positioned. This relation is illustrated in Fig. 3. In the absence of titin, the velocity is initially very slow. However, when the thick filament is displaced more than 0.22 μm at a sarcomere length of 2.45 μm (Fig. 3 *A*) or 0.12 μm at a sarcomere length of 2.80 μm (Fig. 3 *B*), the critical velocity of V_c is exceeded. At this point the stretched cross-bridges on side 2 of the sarcomere produce 1.5 times the force that they produce under isometric conditions, and this tension level cannot be increased further by increasing the velocity of thick filament sliding (Fig. 2 *B*). Therefore, as the overlap region on side 2 is further decreased as a consequence of continued thick filament sliding, the velocity increases sharply (Fig. 3). At a sarcomere length of 2.45 μm, the velocity approaches 0.1 V_{max} as the thick filament reaches the Z-disc (Fig. 3 *A*). At a sarcomere length of 2.80 μm, V_{max} is attained before the thick filament reaches the Z-disc due to the complete elimination of the overlap region on side 2 (Fig. 3 *B*).

Fig. 3 also illustrates the thick filament velocities that are predicted when titin filaments are incorporated in the model. At both sarcomere lengths illustrated, the effect of the titin filaments is to slow the movement by providing an additional load on side 2 of the thick filament as it slides to one side. This prevents the thick filament from accelerating to velocities >1% V_{max} as the motion proceeds.

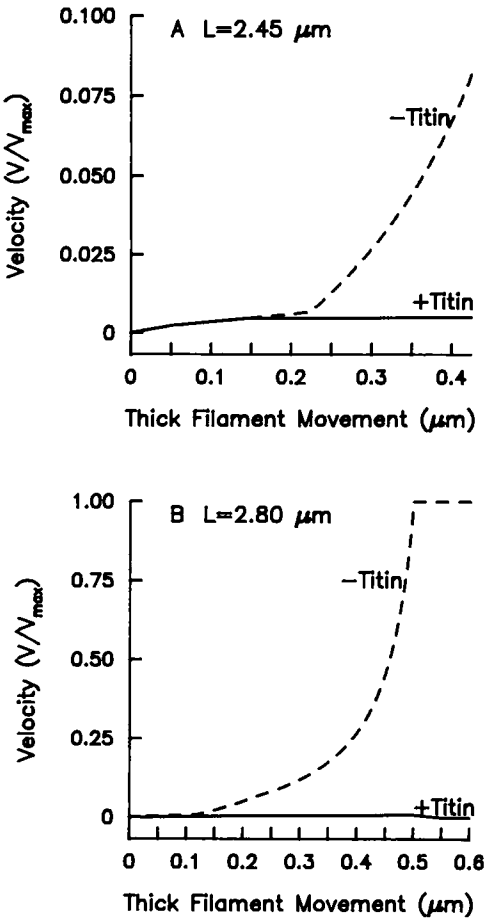

FIGURE 3 Calculated velocity of thick filament movement versus its position in a sarcomere that is 2.45 (*A*) or 2.80 (*B*) μm long. Velocities are shown both for the model incorporating (*solid curves*) or excluding (*dashed curves*) titin filaments.

In the absence of titin filaments, the initial central position of the thick filament is always unstable, i.e., V_1 is positive for all values of thick filament movement >0. This is not the case in the presence of titin filaments. Fig. 4 again illustrates thick filament velocity as a function of its position within the sarcomere in the presence of titin filaments, but on a scale that is expanded relative to that in Fig. 3. At a sarcomere length of 2.45 μm, the velocity is positive for all thick filament positions >0, predicting that the thick filament will move all the way to the Z-disc. However, at a sarcomere length of 2.80 μm, thick filament velocity is negative when the thick filament is located within 0.05 μm of the center of the sarcomere. Therefore, in this region the thick filament should move back toward the center of the sarcomere. This makes its initial position at the center of the sarcomere stable, and no movement toward the Z-disc is predicted.

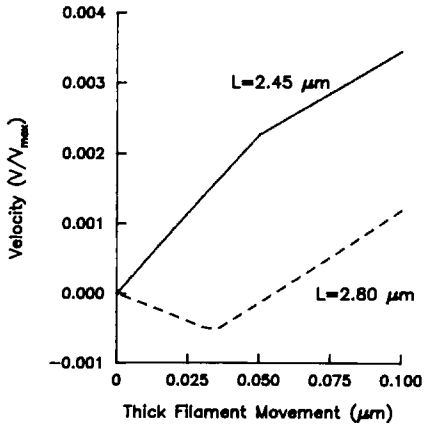

FIGURE 4 Calculated velocity of thick filament movement versus its position for the model incorporating titin filaments. The curves shown are expanded versions of those illustrated in Figs. 3 *A* (*solid curve; L* = 2.45 μm) and 3 *B* (*dashed curve; L* = 2.80 μm).

Fig. 5 illustrates the sarcomere length dependence of the extent of thick filament movement that is calculated from the models with and without titin filaments, along with data previously obtained from a skinned rabbit psoas fiber (Horowits and Podolsky, 1987). Without titin filaments, maximum movement of thick filaments is predicted at all sarcomere lengths. However, when the titin filaments are included in the model, no movement is predicted at sarcomere lengths >2.73 μm, in agreement with the experimental results.

The Modeled Time Course of Thick Filament Movement and Isometric Tension

The time course of thick filament movement is derived from the dependence of the velocity of movement on thick filament position (Eq. 10). We investigated the effect of incorporating or deleting titin filaments, as well as the effect of varying the properties of the cross-bridges, on the time course of thick filament movement predicted at a sarcomere length of 2.45 μm, where the extent of movement is maximum (Fig. 6). In all cases, the time course exhibits an initial lag phase, during which the velocity and extent of thick filament movement are extremely small. This lag phase is independent of the presence or absence of titin filaments. In the presence of titin filaments, the lag phase is followed by a phase of slow, steady motion, while in the absence of titin filaments, the motion exhibits continuing acceleration.

The calculations in Fig. 6 assume that the thick filament is 0.09 nm off-center at time 0. A change in this initial value alters the position of the curves along the time axis without changing their shape. Clearly, some finite initial displacement is needed for thick filament movement to occur.

Decreasing the slope of the force-velocity relation near P_o accelerates the motion. This effect is illustrated by decreasing C, which specifies the overall curvature of the force-velocity relation (Fig. 6 *A*), or by decreasing F, which specifies the resistance to stretch of the cross-bridges in excess of that predicted by Hill's equation (1939) (Fig. 6 *B*). The major effect of each of these changes is a shortening of the lag phase. In contrast, decreasing P_Y, the maximum tension that the cross-bridges can exert during stretch, generally accelerates the final phase of motion, but does not affect the duration of the initial lag phase (Fig. 7 *C*). These results demonstrate that the duration of the initial flat portion of the curve is determined by the properties of the cross-bridges and by the precision with which the thick filament is initially centered.

We calculated the tension output of the sarcomere as a function of thick filament position for the models with and without titin filaments. The time corresponding to a particular thick filament position was determined using the same

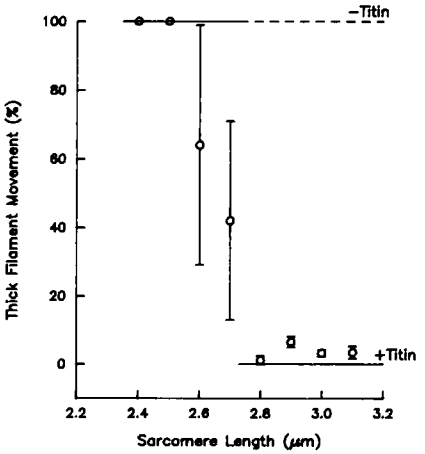

FIGURE 5 Dependence of the extent of thick filament movement on sarcomere length. The values predicted by the models incorporating and excluding titin are shown as solid and dashed lines, respectively. Each point is the mean ± SEM previously measured in a small bundle of skinned fibers activated for 7.5 min (Horowits and Podolsky, 1987).

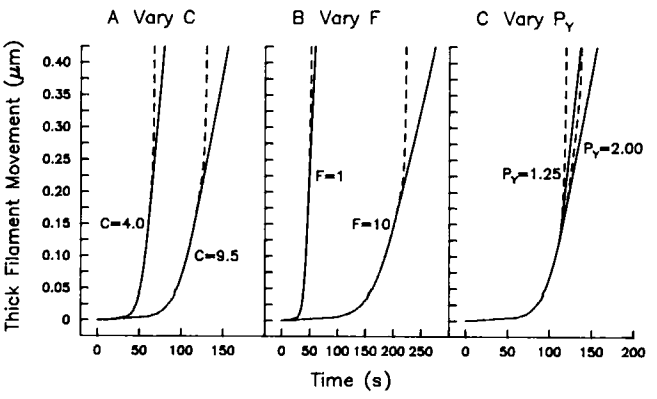

FIGURE 6 Effect of varying cross-bridge parameters on the time course of thick filament movement calculated from the models incorporating (*solid curves*) or excluding (*dashed curves*) titin filaments. The sarcomere length is 2.45 μm, and an initial displacement of 0.09 nm was assumed. *A*, *B*, and *C* illustrate the effect of independently varying C (the curvature of the force-velocity relation), F (the slowness of the velocity of stretch), or P_Y (the maximum tension output during stretch), respectively.

initial conditions as in Fig. 6, and the tension output plotted as a function of time for the model without titin filaments (Fig. 7). In all cases, the tension remains nearly constant until the final rapid phase of motion, when the tension abruptly decreases.

Fig. 7 illustrates the effects of varying the cross-bridge properties on isometric tension during thick filament movement in the absence of titin filaments. Decreasing C or F accelerates the time course of movement (Figs. 6 *A* and 6 *B*), but does not alter the major changes in tension predicted during movement in the absence of titin filaments (Fig. 7 *A* and *B*). Decreasing P_Y accelerates the final phase of movement (Fig. 6 *C*), and in the absence of titin filaments leads to a larger decrease in isometric tension as the thick filament approaches the Z-disc (Fig. 7 *C*).

In contrast to the large decrease in isometric tension that is predicted in the absence of titin filaments, the calculated tension in the presence of titin changes <10% during thick filament movement under all conditions investigated (calculations not shown). The calculations illustrate that the titin filaments help preserve isometric tension in the face of thick filament movement by contributing to the tension output on side 2 of the sarcomere.

Comparison of the Modeled Time Course of Thick Filament Movement and Isometric Tension with Experimental Results

Using skinned rabbit psoas fibers, we measured the time course of thick filament movement in sarcomeres ranging from 2.4 to 2.5 μm long, where the extent of movement is maximum. Fig. 8 *A* illustrates experimental results (open circles), along with the time course of thick filament movement calculated from the models with (solid curve) and without (dashed curve) titin filaments using parameters appropriate for skinned rabbit psoas fibers, as detailed in the Methods section.

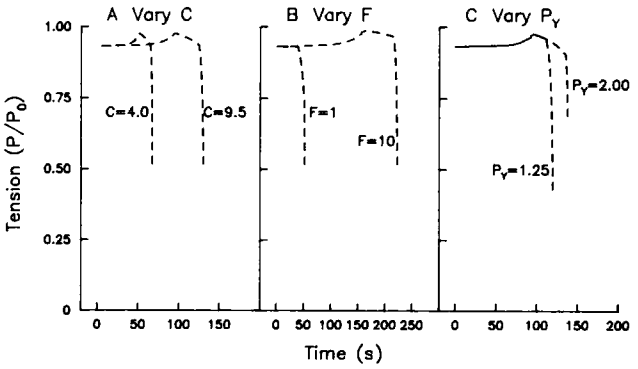

FIGURE 7 Effect of varying cross-bridge parameters on the time course of tension during thick filament movement in the model excluding titin filaments. The sarcomere length and initial conditions are the same as in Fig. 6. *A*, *B*, and *C* illustrate the effect of independently varying C, F, or P_Y, respectively. Note that the curves terminate at the time when the thick filament hits the Z-line. After the motion ends, the tension output from the cross-bridges on side 2 of the thick filament decreases; the steady tension level after the completion of thick filament movement is 0.34 P_o in all cases.

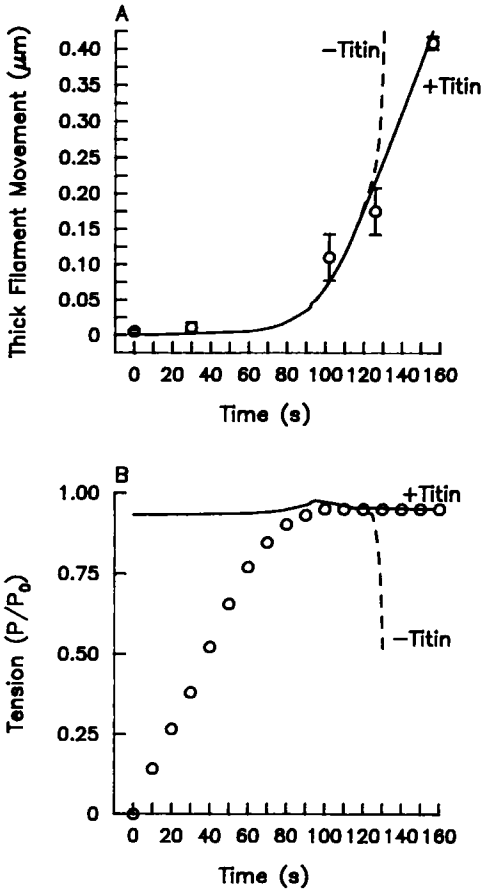

FIGURE 8 Time course of thick filament movement (*A*) and isometric tension (*B*) in skinned rabbit psoas fibers. Continuous curves were calculated from the models incorporating (*solid curves*) or excluding (*dashed curves*) titin filaments, with a sarcomere length of 2.45 μm and an initial thick filament displacement of 0.09 nm. Each point in *A* represents the mean ± SEM for sarcomeres fixed at the indicated time after activation; complications resulting from the heterogeneity in sarcomere length that occurs after activation were eliminated by selecting only those sarcomeres between 2.4 and 2.5 μm long. The points in *B* are taken from a tension record of a small bundle of skinned fibers immersed in activating solution at time 0. After 7.5 min of activation, the tension in this preparation had decreased <5%. Electron microscopy at this time showed that the mean sarcomere length was 2.5 μm and that 66% of the sarcomeres had A-bands adjacent to one Z-disc. Some of the experimental data shown have been previously published in different form (Horowits and Podolsky, 1987).

As discussed above, the calculated time course could be shifted along the time axis by varying the starting position of the thick filament. The calculations in Fig. 8 *A*, as in the previous figures, assume that the thick filament is 0.09 nm off-center at time 0. With this assumption the observed time course is reasonably well fit by the model incorporating titin filaments. In contrast, the model without titin filaments predicts a phase of acceleration that can not be made to fit the experimentally measured time course.

Fig. 8 *B* illustrates the tension output predicted for rabbit psoas fibers during thick filament movement in the

presence (*solid curve*) or absence (*dashed curve*) of titin filaments. Also shown in Fig. 8 *B* is the time course of tension observed in a typical small bundle of skinned rabbit psoas fibers activated by immersion in a solution containing a high concentration of free calcium (*open circles*). Experimentally, tension remains high as the thick filaments move completely to one side of the sarcomere, in agreement with the values calculated from the model that includes titin filaments.

DISCUSSION

We previously demonstrated that thick filaments can move from the center of the sarcomere to the Z-disc upon prolonged activation of skinned rabbit psoas fibers; the extent of this movement was shown to depend on sarcomere length in a manner consistent with the localization of titin filaments as elastic links between the thick filaments and Z-discs (Horowits and Podolsky, 1987). However, the individual contributions of the cross-bridges and of the titin filaments in determining the time course of thick filament movement and the accompanying tension output of the sarcomere were not completely understood. The present results demonstrate that the cross-bridges control the initial phase of movement, while the titin filaments slow the thick filaments as they approach the Z-disc (Fig. 8 *A*). The titin filaments also help maintain isometric tension at a high level during this final phase of movement (Fig. 8 *B*). As the thick filament nears the Z-disc, the tension output on side 2 of the thick filament is divided nearly equally between the cross-bridges and the titin filaments. When the thick filaments reach the Z-disc and movement stops, the total tension output should decrease by ~10% due to a decrease in tension from the cross-bridges on side 2. We observe that active tension declines by ~5% during an isometric contraction lasting several minutes longer than needed for the thick filaments to reach the Z-disc (Horowits and Podolsky, 1987).

The present results also provide additional evidence that the titin filaments can account for the observed dependence of the extent of thick filament movement on sarcomere length (Fig. 5). The experimentally observed dependence of the extent of thick filament movement on sarcomere length, the observed time course of the movement, and the observed constancy of tension during the movement were all found to be consistent with the model of the sarcomere in which the titin filaments are elastic structures that link the thick filaments to the Z-discs and give rise to the resting tension; none of these observations could be explained by a mechanical model that excludes these structures. Furthermore, the models on which these conclusions are based utilize parameters that have been determined in independent experiments defining the force-velocity and resting tension-sarcomere length relations. Since the initial position of the thick filaments could not be determined with the precision required, it was allowed to vary in order to fit the observed time course of thick filament movement. It should be noted that the estimate of the initial position so obtained is not accurate because it is sensitive to small changes in F, which was measured only in amphibian muscle; for example, if F is 10 for rabbit muscle instead of 5 as for amphibian muscle, an initial displacement of 10 nm instead of 0.1 nm must be assumed in order to fit the observed time course. Even with this uncertainty, it is evident that the observed time course of thick filament movement can be fit only by assuming that the thick filaments are initially positioned extremely close to the center of the sarcomere, as experimentally observed in relaxed muscle fibers.

The time course of thick filament movement is useful in evaluating its physiological significance. Thick filament movement toward the Z-disc is biphasic: it starts slowly and, after a lag phase, begins to accelerate. The lag phase depends only on the properties of the cross-bridges (see Fig. 6) and on the initial position of the thick filaments. Almost no thick filament movement is predicted for the first 80 s of activation in rabbit psoas fibers at 7°C, both with and without titin filaments (Fig. 8 *A*). Even if V_{max}, and hence thick filament movement, were 10 to 20 times faster at a body temperature of 37°C, the muscle fiber would have to be activated for more than 5 s for significant movement to occur. In humans, individual fast-twitch motor units are activated continuously only for much shorter periods (Warmolts and Engel, 1972; Hannerz, 1974; Grimby and Hannerz, 1977). Under these conditions, significant movement of thick filaments is unlikely to occur during a single contraction. This is also likely to be the case in slow-twitch fibers. Although in vivo activations of individual slow-twitch motor units can be several times longer than those of fast-twitch fibers (Warmolts and Engel, 1972; Hannerz, 1974; Grimby and Hannerz, 1977), the slower V_{max} in these fibers is expected to lead to a two to threefold longer lag phase. Significant movement of thick filaments is thus unlikely to occur during a single contraction of physiological duration in either slow or fast-twitch muscle fibers. Therefore, the primary function of the titin filaments in vivo may be to keep the thick filaments centered during passive stretch and to prevent sarcomere asymmetry from accumulating over several contractions by recentering the thick filaments each time the muscle is relaxed.

The time needed to recenter the thick filament upon relaxation should depend on the stiffness of the titin filaments. Taking into account the effect of fluid viscosity and the curvelinear nature of the actual data relating resting tension to sarcomere length (Fig. 2 *A*), we estimate that the total recentering time will vary between 1 and 10 ms as resting tension varies between the measured values (Fig. 2 *A*) and a 10-fold decrease. Since these times are short relative to the intervals between contractions in vivo (Warmolts and Engel, 1972; Hannerz, 1974; Grimby and Hannerz, 1977), the resting tension of different muscles is probably free to vary over a wide range, according to local

anatomical and physiological requirements, without risk of impairing active contractile function due to inappropriate positioning of the A-band.

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