Length

- Since sarcomeres are arranged in series, the force that a muscle fiber can generate is independent of the number of sarcomeres, i.e. provided that sarcomere length is not changing, the force produced by each sarcomere will be equal. The force produced by the muscle fiber will be equal to the sarcomere force.

- Because the maximum force which can be produced by a sarcomere depends on sarcomere length, the maximum force which can be produced by a muscle fiber will on its length. The relationship between maximum force and muscle fiber length will depend on the number of sarcomeres that make up the fiber.

- Sarcomeres may not be uniform and homogeneous. Sarcomere diameter, myofilament length and myofilament density may vary along the length of the muscle fiber. This will result in different length-tension relations for different sarcomeres.

- When a muscle fiber is stretched beyond a certain point, the structural proteins acting in parallel with contractile proteins begin to be stretched. The force produced by these parallel elastic structures then increases rapidly with muscle length. Consequently, the total sarcomere force (active + passive) is generally a monotonically increasing function of length, despite the fact that myofilament overlap decreases at long lengths.

- Although all sarcomeres must generate equal tension during isometric contraction, they will generally not all be the same length. This will result in different amounts of overlap between actin and myosin filaments for different sarcomeres (Fig. 1.5).

- The sarcomeres with the greatest overlap will be able to generate the required tension at the shortest lengths. Those with the least overlap will be stretched until sufficient passive tension is generated by parallel elastic structures to make the total force equal to that of the shorter sarcomeres. The shorter sarcomeres are, therefore, considered stronger than the longer sarcomeres. Note that the maximum force that can be supported by a muscle fiber will be equal to that of its weakest sarcomere.

Velocity

- When a muscle fiber is activated to produce a steady force while being held isometric and is then stretched at constant velocity, the resulting force is greater than the isometric force (Fig. 2.1). For low velocities of stretch the force increases with velocity, but as the velocity increases further the force levels off or drops slightly, reaching a maximum of between 1.2-1.8 times the isometric force (Fig 2.3).

  - The increase in force with muscle lengthening velocity is probably largely due to stretching of attached cross-bridges (Fig. 1.6). Cross-bridges, which are being stretched,
will generate a greater average force during their period of attachment than cross-bridges which are isometric. The higher the lengthening velocity, the greater the amount of stretch that will occur during the period of attachment and hence, the greater the average force during the period of cross-bridge attachment. When the lengthening velocity becomes too high, cross-bridges are stretched beyond the limits that can be supported by the binding force between actin and myosin, resulting in forcible detachment. This limits the maximum force during muscle lengthening.

• When a muscle fiber is held isometric and is then released and allowed to shorten at a constant velocity, the contractile force produced by the muscle fiber drops to a lower relatively constant value. The higher the shortening velocity the lower the force (Fig. 2.2). Conversely, by decreasing the load on a muscle fiber, its shortening velocity can be increased.

• If contractile force is plotted against shortening velocity a hyperbolic relation is obtained where force is inversely proportional to velocity, decreasing continuously from its isometric value to zero at maximum shortening velocity (Fig. 2.3).

• There are several possible reasons why muscle force drops as the velocity of shortening increases.

  - First, there are fewer cross-bridges attached during shortening and their number decreases as the velocity of shortening increases. It has been suggested that this is a consequence of an increase in the rate of cross-bridge detachment during muscle shortening and a decrease in the rate of attachment. Both of these rates may be functions of velocity.

  - Second, shortening likely reduces the tension in attached myosin cross-bridges (Fig. 1.6). Cross-bridges, which are shortening, will generate a smaller average force during their period of attachment than cross-bridges which are isometric. The higher the shortening velocity, the greater the amount of shortening that will occur during the period of attachment and hence, the lower the average force during the period of cross-bridge attachment.

  - Third, some cross-bridges may be compressed as the result of shortening before they detach. These cross-bridges would generate negative force, thereby reducing the overall tension developed by the fiber. The higher the shortening velocity the more quickly cross-bridges would compress, resulting in a greater number of cross-bridges generating negative force before detachment.

• The maximum velocity of muscle fiber shortening occurs when there is no load on the muscle fiber. Conversely, when the muscle fiber is shortening at maximum velocity it does not generate any contractile force. Although the maximum shortening velocity of a muscle fiber does not seem to depend on the activation level of the muscle fiber, it does depend on the number of sarcomeres that make up the muscle fiber and their average length.
The velocity of muscle fiber shortening is the sum of the shortening velocities of the individual sarcomeres. Each sarcomere has a maximum shortening velocity. Therefore, the maximum shortening velocity of the muscle fiber will be equal to the sum of the maximum shortening velocities of the sarcomeres. The greater the number of sarcomeres the higher the maximum velocity.

At sarcomere lengths that are long enough to stretch the parallel elastic structures of the muscle fiber, passive tension acts as a driving force on the contractile system and increases the speed of shortening above its maximum value at zero load. For very short sarcomere lengths, the maximum shortening velocity decreases in parallel with the isometric tension (Fig. 2.4).

Load

- If a muscle fiber is made to shorten or lengthen while working against a changing load, e.g., a compliant load such as a spring, its velocity will change continuously and will not achieve a constant value. Consequently, the force that it produces will not correspond to the steady-state force-velocity curve.

- If the muscle fiber is activated while being held isometric and then released to shorten against a compliant load instead of a constant load, the velocity initially increases and then decreases to zero. At any given velocity of shortening the force is lower than in the isotonic case. This difference becomes greater as the load becomes less compliant. The less compliant the load, the more slowly the muscle fiber shortens and the lower the force at any given velocity compared to the steady-state force-velocity curve (Fig. 2.6).

- If the muscle fiber is activated while being held isometric and the force is then ramped down from the isometric value to zero, the force at any given shortening velocity is higher than in the isotonic case. The faster the force drops to zero, the higher the force at any given velocity compared to the steady-state force-velocity curve. It also follows that for a given amount of shortening, i.e., at any particular length of the muscle fiber, the faster the rate of shortening, the lower the force (Fig 2.7).

The observations above indicate that the force produced by a muscle fiber depends on its length, the velocity of shortening and the type of load that the fiber is moving. Therefore, it is not surprising that very different length-tension relations are obtained for isometric contraction compared to isotonic contraction, where the muscle fiber shortens to its final length while moving a constant (inertial) load (Fig. 2.5). Clearly, there is an interaction between muscle mechanics and load mechanics which can play an important role in determining how movement and force development proceed under conditions where either the load or the velocity are not constant.
Activation

• The isometric length-tension characteristics of sarcomeres were shown to correlate with the overlap of actin and myosin filaments (Fig. 1.5), i.e., with the number of cross-bridges in position to bind to actin. The length-tension relation was determined under conditions where muscle fibers were maximally activated. When muscle fibers are activated less than maximally, the number of cross-bridges in position to bind to actin will decrease, resulting in less tension for a given sarcomere length. The number of attached cross-bridges will be a function of the level of activation. To account for the effect of activation on sarcomere force, the isometric length-tension curve for maximal activation is often scaled in proportion to the percentage of maximal activation.

• A muscle consists of thousands of muscle fibers organized into motor units. Each motor unit comprises a group of muscle fibers, often several hundred, which are innervated by a single motoneuron. The muscle fibers belonging to one motor unit may be distributed throughout a large region of the muscle, i.e., they need not be adjacent to one another.

• The central nervous system controls tension by specifying the number of active motoneurons (recruitment) and their firing rates (rate coding).
  - A motor unit is activated in an all-or-none fashion by a single action potential, which travels from the motoneuron along the axon to the muscle fibers. The neural action potential leads to an action potential in each muscle fiber innervated by that motoneuron.
  - Motor unit force is a function of the frequency of activation (firing rate) of the innervating motoneuron. Firing rate is defined as number of action potentials per second. The force produced by each muscle fiber, innervated by the motoneuron, increases with firing rate because of the accumulation of intracellular calcium (Ca^{2+}). Each action potential depolarizes the muscle membrane, which results in more Ca^{2+} being released from the terminal cisternae, diffusing through the intracellular space and activating more actin-binding sites.
  - When a muscle is activated voluntarily under isometric conditions, motor units tend to become active in a fixed order. The recruitment order is correlated with the amount of force that a motor unit can produce. Motor unit force is related to the number of muscle fibers and the size of the muscle fibers that it comprises. The motor unit that produces the smallest force is recruited first. It remains active and the next motor unit is recruited as the total muscle force increases. The motor units that produce the largest forces are the last to be recruited. As total muscle force increases, each newly recruited unit contributes an increment in force, which is a similar percentage of the total muscle force. In this way force can be increased smoothly.

• A single muscle action potential produces a brief contraction of the muscle fiber called a twitch. The duration of the twitch depends on the muscle fiber type. The duration of both the
contraction and relaxation phases of the twitch are longer for slow-twitch (type I) than fast-
twitch (type II) fibers (Fig. 2.8).

- Humans can voluntarily activate motor units briefly at instantaneous firing rates of about 100 Hz during brief forceful contractions. The maximum firing rates that they can sustain during steady contractions are considerably lower and generally do not exceed 30 Hz. However, these rates are sufficiently high that several action potentials can occur before the twitch force from the first action potential has dropped to zero. Whereas the muscle action potential has a duration of less than 10 ms, the twitch duration for skeletal muscle fibers is of the order of 100-200 ms. Action potentials which arrive before the twitch force has dropped to its pre-activation level produce additional force by causing more Ca^{2+} to be released.

- If a motor unit is activated at a steady frequency, the force will initially rise and then oscillate about a new mean value at the frequency of activation, producing what is called an unfused tetanus. Both the mean force and the initial rate of force development will increase as firing rate increases. The higher the firing rate the smaller the oscillation with respect to the mean force (Fig. 2.8). At high firing rates, there is no noticeable oscillation in force. This smooth steady force is called tetanus. Because type I motor units have longer twitch contraction times than type II units they reach tetanus at lower frequencies.

- The transformation of nerve impulses (action potentials) into muscle force illustrates how muscle fibers behave like low-pass filters in converting electrical activity into mechanical activity.

- A filter is a device which takes an input signal and transforms it into an output signal that differs in some way from the input. In general, the amount by which the signal is changed depends on the frequency of the input signal.

- A low-pass filter is a filter which has relatively little effect on low frequency input signals, but attenuates high frequency input signals. It is called low-pass because it allows the low frequency signals to pass without changing them significantly.

- To characterize a filter, the amplitude of the output is measured for input signals of different frequencies. The ratio of the amplitude of the output to the input is called the amplitude response or the gain of the filter. In general, the amplitude response changes as the frequency of the input signal changes. In the case of a low-pass filter, the amplitude response will decrease as the frequency of the input signal increases.

- Figure 2.9 illustrates the results of an experiment in which the input signal was an electrical stimulus to a muscle nerve. The stimulus rate was modulated from 5 to 30 impulses per second (ips). At 5 ips the muscle responded by producing single twitches. As the frequency increased, the twitches began to overlap and finally reached tetanus. At 30 ips the tetanus was completely fused.

- The variation in stimulus rate was modulated through a range of frequencies. For example, in A the rate varied from 5-30 ips at a modulation frequency of 0.11 Hz. This means that it
took approximately 9 s (1/0.11) for one complete cycle, beginning with a stimulus rate of 5 ips, increasing to 30 ips and then decreasing back down to 5 ips. As the modulation frequency increased from 0.11 Hz to 3.6 Hz, there was a marked decrease in the peak-to-peak amplitude of the output signal (muscle force) and the single twitches disappeared.

- Since the amplitude of modulation of the stimulus (input) remained constant throughout (always varying from 5-30 ips), the decrease in peak-to-peak amplitude of the muscle force (output) with increase in input frequency represents a decrease in the output amplitude. This is characteristic of a low-pass filter.

- As the frequency of the input increases there is less time for removal of calcium from the intracellular space. Consequently, there is insufficient time for muscle force to relax completely during the interval between decreasing and increasing stimulus rates. The higher the modulation frequency, the less the drop in force. At very high modulation frequencies the force would remain close to tetanus throughout the entire interval.

- The second experiment illustrated in Fig. 2.9 demonstrates a similar effect when muscle shortening, rather than muscle force was used as the output signal. Significant attenuation of the output signal is already apparent at about 2 Hz. In general, there will be significant attenuation of muscle mechanical output for neural inputs modulated at frequencies higher than 2 or 3 Hz.

- In addition to a decrease in the amplitude response at high frequencies, muscle also exhibits a characteristic lag between changes in the electrical input and the mechanical output that may be from 30-100 ms, depending on the size of the muscle. This time lag occurs because there is a finite time required for the sequence of events that constitute excitation-contraction coupling.

- The intracellular calcium concentration produced by a single action potential, increases and decreases more rapidly than the isometric twitch force. Therefore, the amount of force added by a second action potential occurring immediately after the first will depend on the time interval between them, i.e., on the amount of intracellular calcium at the time of occurrence. The additional force contribution by a second action potential drops steeply as a function of the interval between two successive action potentials (Fig. 2.8).

- When the interval between two successive action potentials is very short, the isometric force can more than double in response to the second action potential. However, the mechanism responsible for this force enhancement saturates rapidly so that a third equally spaced action potential contributes much less additional force than the second. In fact, the third action potential will contribute more additional force if it occurs slightly later. Thus, there is an optimum interval between each action potential in a series, which determines the maximum rate of force development. The rate of force development depends not only on the frequency of activation, but is also sensitive to the pattern of activation (Fig. 2.8).

- If firing rate is constant the mean isometric force will reach a steady value. This force is dependent on the activation history of the muscle though, i.e., the magnitude of the force will depend on the pattern of activation used to achieve it.
This dependence on activation pattern is clearly illustrated by the catch property of muscle. If a motor unit is active at a steady frequency and a single additional action potential is then added immediately prior to or following one of the action potentials in the regular train, producing one very short interval, the isometric force will suddenly jump to a higher level and subsequently remain at the new level. But, if a single action potential is omitted from the train, producing one long interval, the force will suddenly drop and thereafter remain at the lower level (Fig. 2.10).

The force enhancement produced by catch varies in magnitude with the frequency of the underlying regular train. It is maximal when the intervals are between one and two times the twitch contraction time (time to peak twitch force). Furthermore, it is more dramatic in type I than type II muscle fibers since the force enhancement is not sustained in the latter. Although it is possible to produce the catch phenomenon experimentally, it is not known whether it ever occurs in normal voluntary muscle contraction.

- At lower frequencies of activation (intervals longer than twice the twitch contraction time) there is a gradual drop in isometric muscle force, which is greater in type II than type I fibers. This property is known as sag (Fig. 2.11).

- After prolonged activation at moderate frequencies (unfused tetanus) and high frequencies (tetanus) there is a potentiation of the isometric twitch force. One of the consequences of this potentiation is to reduce the effects of catch and sag (Fig. 2.11).

- During prolonged muscle activation there is a reduction in the force producing capacity of a muscle fiber known as fatigue. Force reduction has been attributed to reduced Ca\(^{2+}\) release from the sarcoplasmic reticulum, reduced Ca\(^{2+}\) sensitivity of myofilaments and reduced maximum Ca\(^{2+}\)-activated tension (regulated by troponin). These changes are thought to be linked to reduction in intracellular pH and increase in intracellular phosphate as a result of increased metabolism.

- While peak twitch amplitude declines with fatigue, twitch duration increases as the result of an increase in the duration of twitch relaxation time. Consequently, tetanus occurs at lower frequencies as a muscle fiber fatigues.

- In general, muscle force decreases and its response slows with fatigue. The muscle takes longer to relax after contraction and its maximum velocity of shortening slows.
**Figure 2.1** Force enhancement produced by stretching muscle fiber after activation. Left: response to slow stretches of three different velocities. The fiber was first tetanized isometrically and then stretched from 2.6 μm sarcomere length to 2.75 μm in 0.8 s (a), 1.6 s (b), and 2.4 s (c). Traces d and e are the force records of isometric tetanus at 2.6 and 2.75 μm sarcomere lengths, respectively. Right: response to stretches of different amounts. The fiber was first tetanized isometrically and then stretched from sarcomere length 2.4 to 2.5 μm in 1 s (a) and from sarcomere length 2.4 to 2.6 μm in 2 s (b). Traces c and d are the force records of isometric tetanus at 2.5 and 2.6 μm sarcomere lengths, respectively.

**Figure 2.2** Force decrement produced by shortening muscle fiber after activation. Left: response to slow shortening of two different velocities. The fiber was first tetanized isometrically and then released from 2.6 μm sarcomere length to 2.4 μm in 2 s (b) and in 4 s (c) Trace a is the force at sarcomere length 2.4 μm. Right: response to shortening of different amounts. The fiber was first tetanized isometrically and then released from 2.55 μm sarcomere length to 2.4 μm in 1.5 s (b) and from sarcomere length 2.7 to 2.4 μm in 3 s (c). Trace a is the force record of isometric tetanus at sarcomere length 2.4 μm.
Figure 2.3 Force-velocity relation for muscle fiber shortening (positive velocity) and muscle fiber lengthening (negative velocity). Force, $P$, is normalized to maximum isometric force, $P_0$. Velocity, $V$, is normalized to maximum shortening velocity, $V_{max}$.

![Graph showing force-velocity relation](image)

Figure 2.4 Effect of sarcomere length on maximum velocity of shortening. Sarcomere length-tension relation is shown for comparison.

![Graph showing sarcomere length-tension relation](image)
Figure 2.5 Effect of load and shortening velocity on final force.

$P$-$F$ curves obtained during auxotonic shortening preceded by isometric tetanus. Inset, length and force records of auxotonic shortening following quick releases (4% of $L_a$) under three different compliances, together with those during the isometric force redevelopment (interrupted lines). Curves $A$, $B$ and $C$ were obtained under the compliances of 1.2 (records $a-a'$), 3.5 ($b-b'$) and 5.9% $L_a$/$P_o$ ($c-c'$) respectively.

Figure 2.6 Effect of load compliance on instantaneous force and shortening velocity.
$P-V$ curves obtained during ramp decreases in load. Inset, length and force records during ramp decreases in load form $P_o$ to zero at four different rates. Curves A, B, C, and D were obtained at the rates of 38 (records $a-a'$), 21 (b-b'), 10 (c-c') and 6 $P_o$/s (d-d'), respectively.

Figure 2.7 Effect of rate of change of load on instantaneous force and shortening velocity.
Figure 2.8 Twitch and tetanus of fast and slow motor units. Numbers to the right of each trace indicate the time interval in ms, between successive action potentials. At low stimulation rates (long intervals between action potentials) tetanus is unfused.
Tension responses of cat triceps surae muscle when responding to stimuli applied on its motor nerve at impulse rate varying sinusoidally from 5 to 30 pulse/sec. Frequency of cyclic variation of stimulus rate: A: 0.11 cycle/sec, B: 0.37 cycle/sec, C: 0.9 cycle/sec, D: 3.6 cycle/sec. Note variability of successive cycles in D, resulting from granularity effects in stimulus pattern.

Dynamic effects of modulated stimulation. A: time graphs of response of load moving by cat triceps surae muscle driven with a sinusoidally modulated stimulus rate, 5-25 pulses/s, and at modulation frequencies marked on graphs. Amplitude of modulation was constant, but response amplitude changed with frequency of modulation. B: change in movement amplitude with frequency of modulation cycle. All stimulus cycles ranged from 5 to 35 pulses/s. Although the gravity part of loads was constant, each line represents a different load inertia, spanning a 28-fold variation within the physiological range (394).

Figure 2.9 Low-pass filtering of electrical activation by muscle to produce mechanical output.
The “catch” effect in a type S muscle unit from cat medial gastrocnemius (MG). Superimposed traces of 3 isometric responses to pulse trains with average frequencies of about 12.5 pulses/s but different interval structures (diagrams a–c below). The addition of a single extra pulse (arrow) within 10 ms of the 1st pulse in the basic train (pattern a) produced marked and persistent enhancement of force output (record a) even though the basic train rate is unchanged. Widening one interval slightly during this catch enhancement (pattern b) caused a drop in output force that was then “caught” again at a new force level (record b). A modest shortening of a single interval (pattern c; arrow) produced an equivalently modest catch enhancement (record c). [From Burke et al. (115). Copyright 1970 by the American Association for the Advancement of Science.]

Figure 2.10 Catch property in slow-twitch motor unit.
Effect of posttetanic potentiation (PTP) on mechanical responses of a type F muscle unit in cat medial gastrocnemius (MG). Top records are superimposed traces of a single twitch and a fused tetanus before (A) and after (C) repeated high-frequency (200 Hz) tetanization. Note that there is a marked increase in twitch force and duration and more rapid rising phases of the twitch and tetanus after PTP, but that there is no change in fused-tetanus plateau force. Lower records illustrate unfused tetanic responses to low-frequency (approximately 20 Hz) stimulation with (larger response) and without a single extra pulse within 10 ms of the 1st (a "doublet," to illustrate the catch effect; see Fig. 32). In contrast to the S unit in Fig. 32, catch enhancement is not sustained (record C); instead, force output decays with a time course similar to that of the "sag" of tension in the basic tetanus. After PTP the initial doublet produces much less catch enhancement, and the tetani with and without the extra pulse converge within 200 ms. [From data of Burke et al. (116).]

Figure 2.11 Twitch, tetanus and catch property before and after tetanus in fast-twitch motor unit, illustrating the effect of posttetanic potentiation.