INTEGRATED SKELETAL MUSCLE FUNCTION[1]

Summary: The events of isometric and isotonic twitches and tetany in skeletal muscles are discussed with special attention on the role of the series elastic elements. A summary over-view of EC coupling is given. Muscle and motor unit fiber types and recruitment during different types of activity are viewed with an eye towards understanding fatigue.

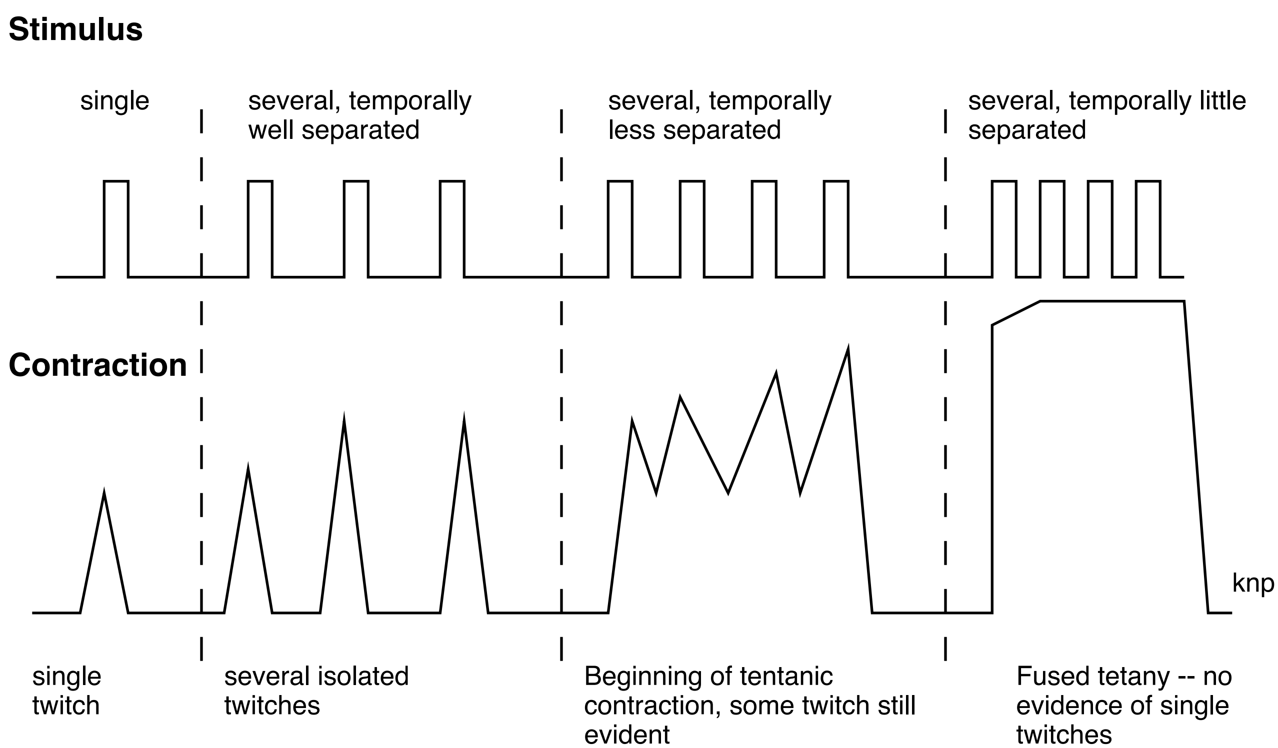
I. Biophysics of Skeletal Muscles, continued

A. In order to further investigate the effects of the SEE and PEE and to better understand EC coupling, we will now look at what happens when **A SERIES OF CLOSELY SPACED STIMULI ARE APPLIED TO A MUSCLE**

1. So far we have only considered single twitches. However, most muscles do not contract only in single twitches. Instead a rapid series of stimuli are given to result in one overall contraction called at tetanic contraction:

a. Pictured below are the forces measured with respect to time when a series of closely spaced (in time) single stimuli are administered. For comparison, a single twitch is also shown:

Twitches and Tetany



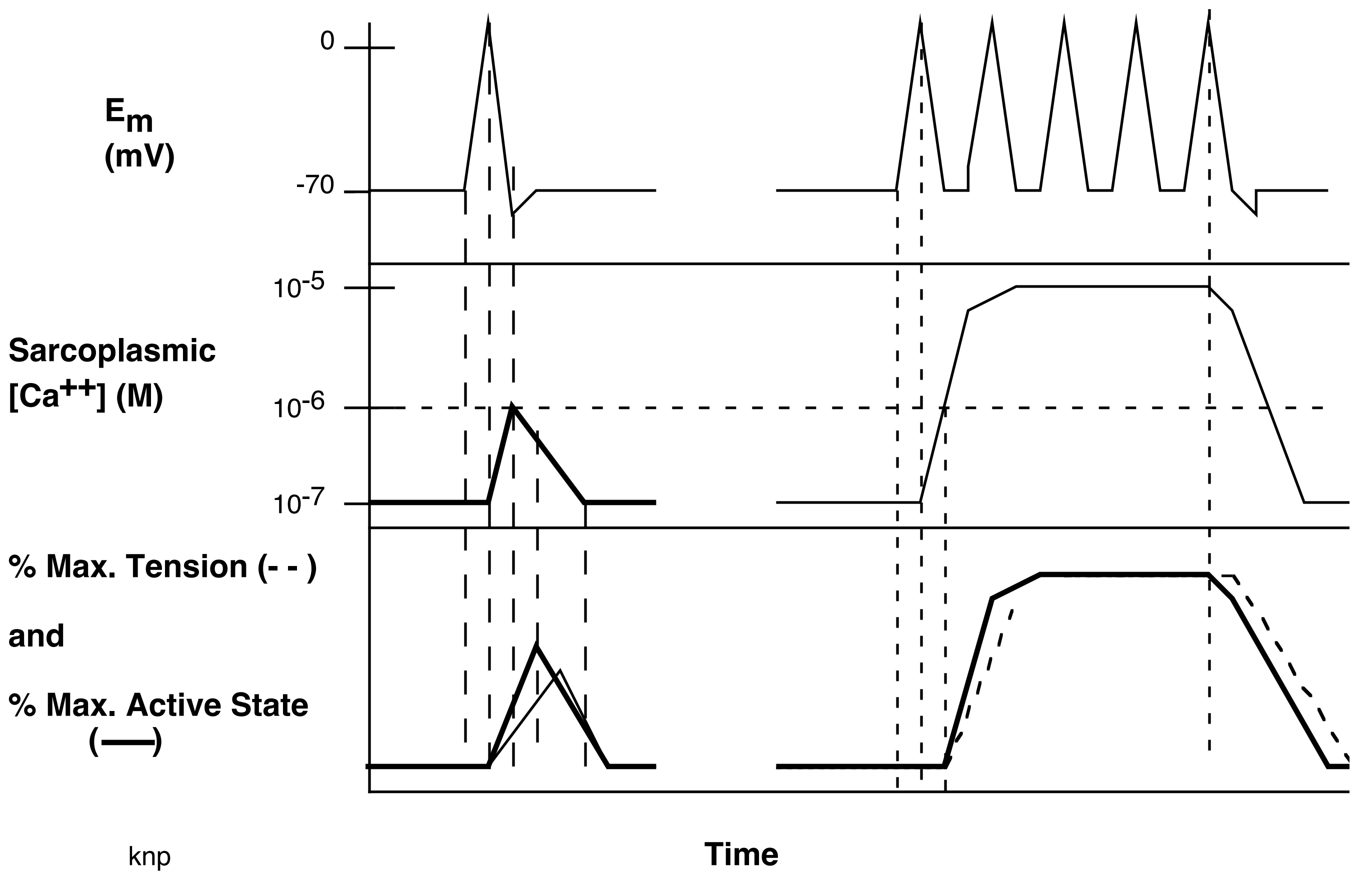
Notice that as the frequency of stimulation increases (the number of discrete stimuli per unit time) a point is reached where the individual contractions start to merge into one (3rd section from left) and eventually merge into a smooth continuous contraction. Notice also that as this happens, the maximum force increases.

b. The total force of contraction increases with the rate of delivery of stimuli until some point where a completely fused maximal contraction called **TETANY** is reached. At this point, single contraction
peaks (twitch peaks) are no longer evident.

1. Note that force develops over time -- the maximal force is not reached until after a few ms. This increase in force, which at low rates of stimulus delivery looks like a staircase is called a **TREPPE**.

2. The ratio of the force developed during tetany as compared to a single twitch is called the **TETANY-TWITCH RATIO**. It is usually greater than 2 and may be as high as 4 or 5.

c. The observations we have made with respect to latent period, twitches, and tetany all need to be rolled in to one all-encompassing theory. This can be done with a simple set of graphs:



1. In a single twitch, the [Ca^{++}] does not get high enough to fully active the maximum number of crossbridges; however, it does get high enough to do so in tetany
. 2. In both single twitches and in tetany, maximal tension takes longer to develop than the full-blown **ACTIVE STATE**.

The **ACTIVE STATE** is the period of time when crossbridges are being actively formed and broken. Thus, a "full-blown" active state is a situation when the maximum number of crossbridges are being cycled per unit time.)

a. Likewise, tension persists at a higher level during relaxation than would be predicted simply by the active state.

b. The **SEE are acting as STORAGE UNITS FOR MUSCULAR FORCE**: some the tension developed during the active state is used to stretch the SEE; this energy is stored and can be released when the active state decays. (Thus, the SEE acts somewhat like a capacitor in an electrical system).

c. The SEE tend to smooth out the contraction.

d. Note that the maximum force is still the same in tetany as it would be if there were no SEE: max. force is released when the SEE is in equilibrium (in terms of force) with the CE and load. In twitch, there is not enough time for equilibrium to be reached if the load is large.

3. The **LATENT PERIOD** is due to all of these factors plus the time needed for the AP to move along the membrane. In order of importance, the AP transmission and Ca^{++} diffusion are the most important factors in accounting for the latency; SE stretch is the least important.

4. The **TREPPE** is probably due to at least 2 factors:

a. Increases of Ca^{++} with each AP.

b. Heating of the muscle as a result of hydrolysis of ATP and CP (creatine phosphate or other phosphagen).

B. **ISOTONIC CONTRACTIONS**:

1. All of the preceding has, of course, dealt with **ISOMETRIC (constant total muscle length) CONTRACTIONS**. We will now deal with **ISOTONIC (constant force) CONTRACTIONS**.

a. in an **isotonic contraction**, the **muscle shortens against a constant (= iso) load; thus, once shortening begins it exerts a constant force on the load.**

b. the initial part of any isotonic contraction must be isometric: this is because the muscle will not start shortening until the force it generates is greater than the resistive force of the load.

2. WORK, FORCE AND POWER. We need to remind ourselves of what these terms mean, especially in terms of a muscle:

a. **Force** (also sometimes referred to as muscular tension) it is often given simply in terms of the mass moved with the acceleration being implicit as that of gravity. Thus, if someone says a muscle is exerting 1 kg of force, what they really mean is that it is exerting
9.8 N.

b. **Work**: is the product of FORCE and DISTANCE.

1. It should be obvious that any isometrically contracting muscle does no **external** work since it does not shorten. It does do internal work. HOW?

2. Likewise, a muscle that shortens against no external load does no external work. Does it do internal work?

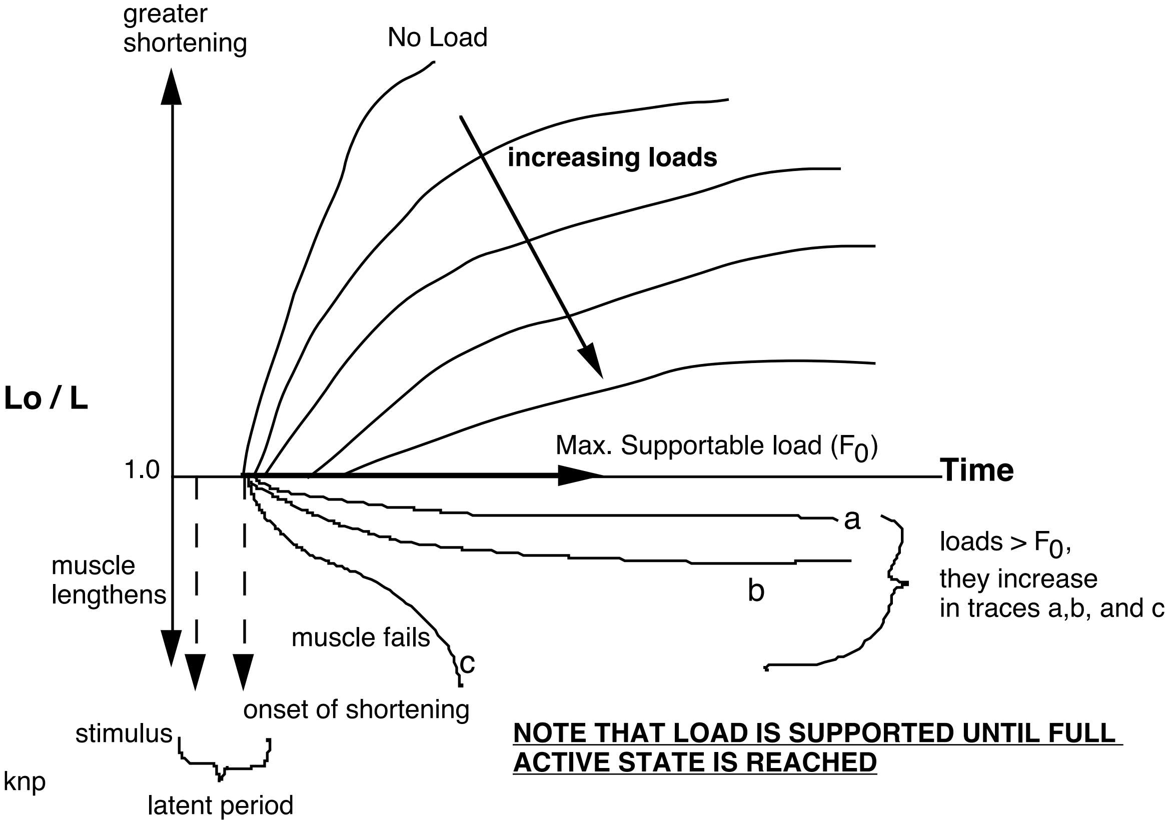
c. **Power**: Since it is work/time, it is the product of Force and Velocity. Once again, an isometrically contracting muscle develops no external power, nor does an isotonically contracting muscle with no external load develop any power.

? EXPLAIN THE CONCEPTS OF EXTERNAL AND INTERNAL WORK AS THEY APPLY TO MUSCLES. YOU NEED TO FIGURE THIS ONE OUT FOR YOURSELF.
? Do isometrically and isotonically contracting muscles consume power? EXPLAIN!

d. It is possible to generate two types of curves that are especially useful in discussions dealing with isotonic contractions:

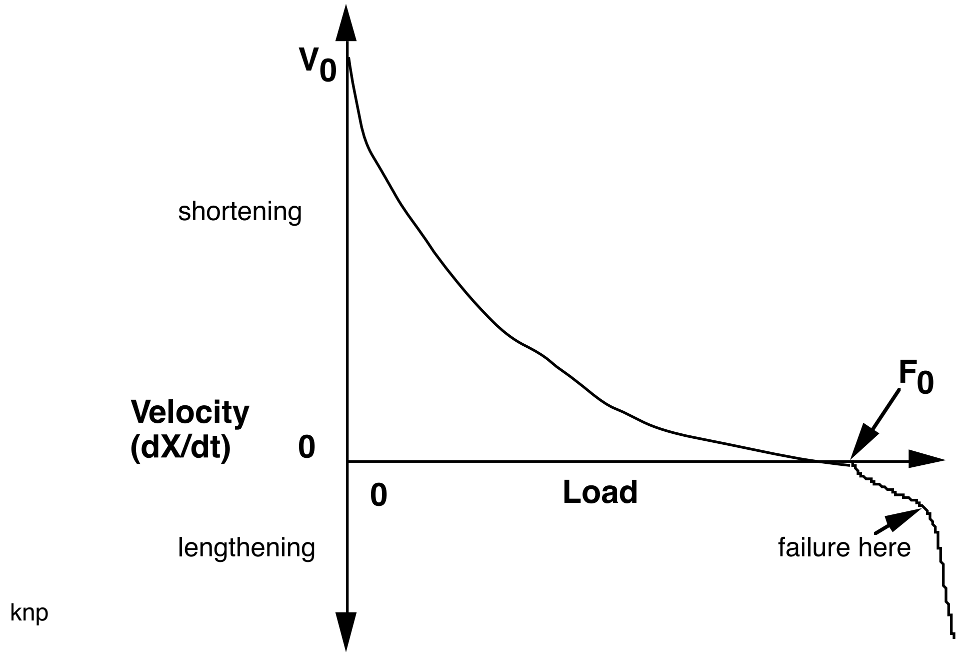
1. **Velocity**: the muscle is allowed to contract against a series of different loads. The result is a series of curves, one for each load:

The Effect of Load on Skeletal Muscle Contraction



As load increases from unloaded to the maximum load that a muscle can support without lengthening (F_0), the distance that a muscle can shorten decreases as does the velocity with which it shortens.
The latent period (time between the stimulus and the onset of movement) increases. Beyond F0, the muscle lengthens even though contracting maximally; at some load (C) the muscle fails elastically.
These data are idealized and are not from a real experiment done under cnsistent conditions-- for all loads assume the load is hung and that it is supported until maximal crossbridges are formed.

The slope of each of these curves (for a certain range of lengths) is the velocity ($\Delta X/\Delta t$). Each velocity is plotted against the appropriate load and the result is:



An idealized relationship between velocity and load for a skeletal muscle. V_0 is the maximum velocity of contraction and occurs in an unloaded muscle, at F_0, the maximum force that the muscle can support, the contraction becomes totally isometric (the muscle does not change length).

a. We can see from these curves, that as expected, for heavier loads the movement of a given muscle is slower.

b. Additionally, note that as larger and larger loads are applied to the muscle, shortening eventually stops and then the muscle actually elongates (that is, elastic elements lengthen and/or the crossbridges are broken by the load). If a large enough load is placed on the muscle, it completely fails (rapid lengthening).

2. If we multiply the velocity of shortening by the load, we can convert the graph shown above into one for **power**:

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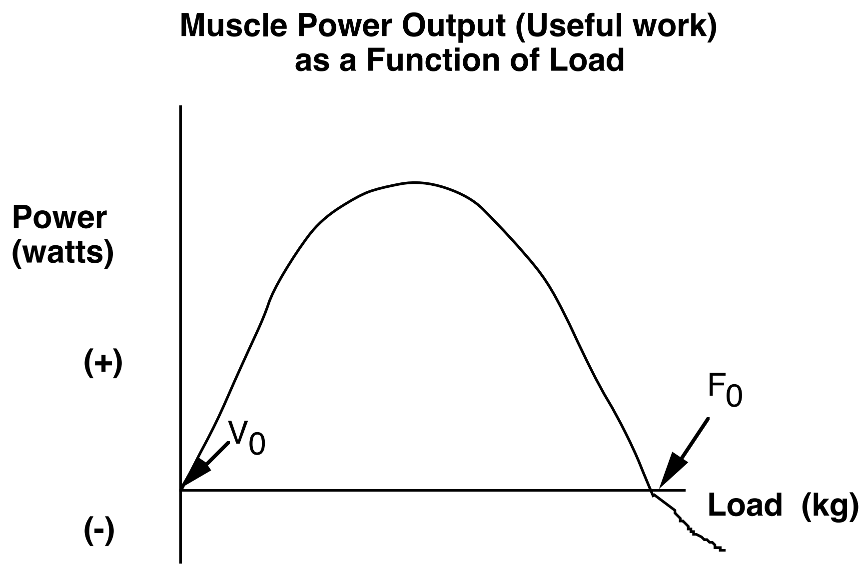


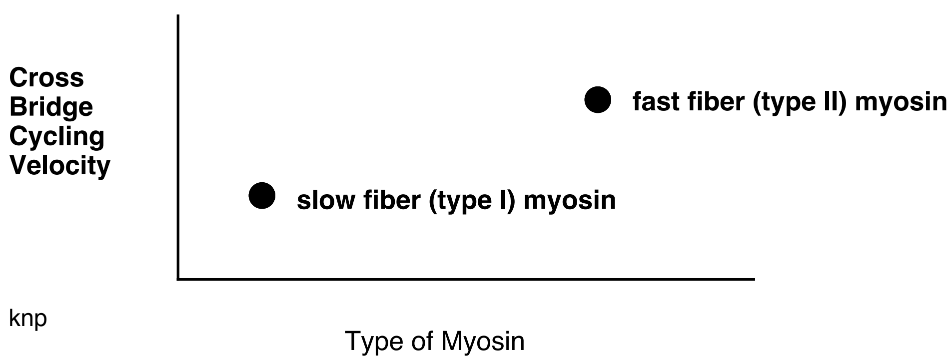
*This graph is derived from the velocity plot by simply multiplying the load (mass * acceleration due to gravity) by the velocity. Note that at both V_0 and F_0 the useful power output is zero; maximum power is transfered from the muscle to the load at some intermediate load value.*

knp

a. This curve is very interesting because it implies that there is an optimum load for a given muscle in terms of its ability to produce external power. At both lighter and heavier loads the power output (**P_o**) diminishes.

b. This implies that muscles cannot contract at proportionately faster and faster rates as the load is reduced: if they could, one would expect a high P_o at low and intermediate loads instead of just at intermediate loads. Further, different muscles will give P_o curves that are oriented differently on the graph.

3. One corollary of this is the observation that different types of muscles have myosin ATPases that cycle at different rates: myosins from fibers that are normally slow in contracting (so called "slow" fibers) have slow rates of cycling when compared to myosins from fast fibers.



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The difference is attributable to the presence of several varieties of myosin in different muscle cells. Interestingly, the myosins are apparently all produced by the same gene, but they are modified in different ways in different cells.

C. Skeletal Muscle Fiber Types

1. For vertebrate skeletal muscle, a number of different types of fibers are recognized. There are a large number of ways that different types of fibers can be distinguished from each other, but the most important relate to the **SPEED OF CONTRACTION** and **METHOD OF PRODUCING ~P**.

a. the old (and still useful) way of distinguishing muscles is to talk about "red" and "white" muscle.

1. The only problem with this method is that there are clearly many gradations of each of these two categories. Nevertheless, as a simplistic description of muscles you can equate red muscle with oxidative and slow twitch fibers and white with glycolytic (anaerobic), fast-twitch fibers.

2. The color difference between these two types is due to MYOGLOBIN and LARGE NUMBERS OF MITOCHONDRIA in the red (oxidative) type of fibers.

3. **MYOGLOBIN** is a protein that is related to hemoglobin but is found only in certain types of muscles. Its main function is to assist in moving oxygen into the muscle cells. **It is NOT an important store of oxygen in the muscles when compared to stores in the blood**.

b. The table below is a good basic classification of skeletal muscles. You should know it. Its only limitation is that there is much evidence that there are really more types of fibers than are shown here; so realize that this table is simplistic:

	Type I: slow oxidative (red)	**Type IIB: fast glycolytic (white)**	**Type IIA: fast oxidative (red)**
Myosin isoenzyme (ATPase velocity)	slow	Fast	Fast
SR Ca^{++} pumping capac	Moderate	High	High
Diameter (diffusion dist	Moderate	Large	Small
Oxidative capacity: mitochondrial content, capillary density, myogl	High	Low	Very High
Glycolytic capacity	Moderate	High	High

(source: Berne and Levy, *Physiology* , Mosby, 1983)

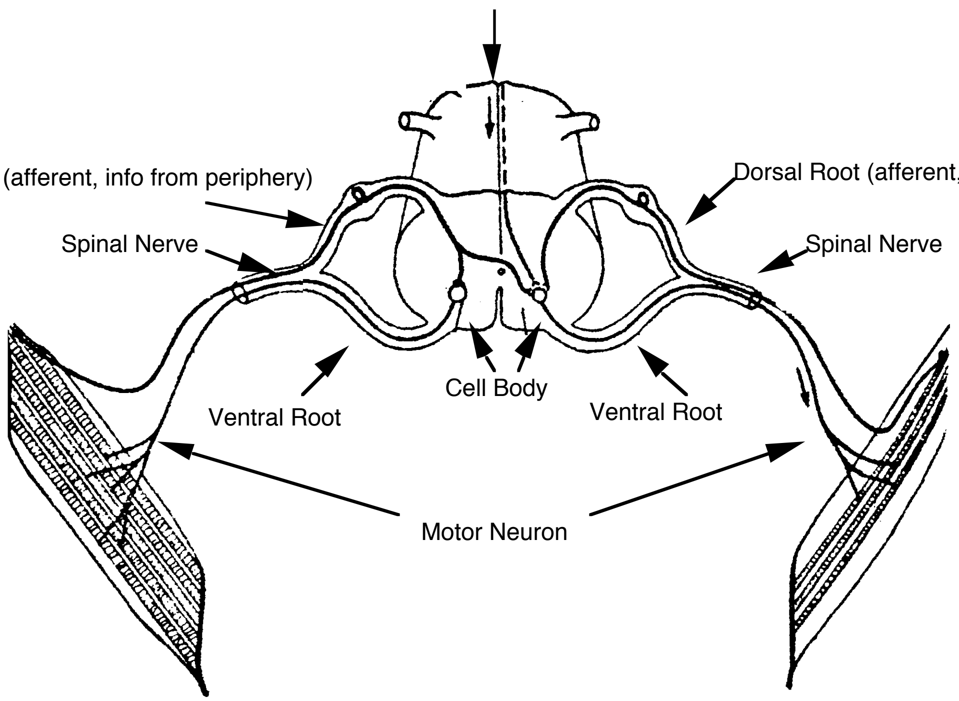
! Note that type IIA fibers are generally rare in humans (and other primates). Our muscles are mostly type I and type IIB.

2. Skeletal muscles can also be distinguished by their innervation. In this case, we are referring to the entire **MOTOR UNIT, that is the NEURON + ALL MUSCLE FIBERS THAT IT INNERVATES**. Innervation ratios vary from as low as 1 or 2 (i.e., one neuron only innervates one or two fibers) to several hundred.

a. The picture and table shown below give the characteristics of type 1 and II motor units (Note: in the table the number of fibers refers to the typical range of innervation ratios -- it tends to be low for type 1 units).

? What does the innervation ratio indicate about possible fineness of control of movement and about force in a movement?

Anatomy of Spinal Nerves and Information on Motor Units



Large motor unit	**Properties**	**Small motor unit**
large, fast conducting, relatively inexcitable	AXON	small, slow conducting, relatively excitable
Many, type II (large, fast, glycolytic)	MUSCLE FIBERS	few, type I , (smaller, slow, oixidative)
recruited infrequently in forceful contractions	FUNCTIONS	recruited first, frequently active

Note that each spinal nerve has both afferent fibers (dorsal root) that bring sensory information into the CNS (e.g., position, stretch, touch, pain, temperature, etc.) and efferent fibers to control the action of skeletal muscles (ventral root). Note also that the cell bodies for efferent spinal nerves are located in the spinal cord; those for the afferent pathways are located at or near the receptor (peripherally). The interesting thing to note is that for the pectoral and pelvic regions, single axons run along nerves over long distances -- several feet in the case of some neurons in the legs.

Please note that there is no left righ correspondance between large and small motor units -- they are found on each side of the nervous system.

(This diagram was taken from Berne and Levy, *Physiology,* Mosby, 1983, and modified by knp).

Characteristics	Type I Motor Unit	Type II Motor Unit
Properties of the neuron		
Cell diameter	small	large
Conduction Velocity	fast	very fast
Excitability	high	low
Properties of the muscle cell		
Number of fibers	few	many
Fiber diameter	moderate	large
Force of unit	low	high
Metabolic profile	oxidative	glycolytic
Contraction velocity	moderate	fast
Fatigability	low	high

source: Berne and Levy, *Physiology* , Mosby, 1983

D. Grading of Contractile Response of Skeletal Muscles

1. The first motor neurons to fire normally are the small, type 1 fibers. These fibers will remain active for the entire activity cycle -- that is they will continue firing and their muscle fibers contract as long as there is any activity in the muscle. This fits in well with the fact that these tend to be very oxidative, slow contracting muscles.

2. With greater and greater excitation, the type II units become involved in increasing numbers. These activate much more rapidly moving and powerful muscle fibers. As more powerful contractions are needed, even more and more of the type II fibers become involved.

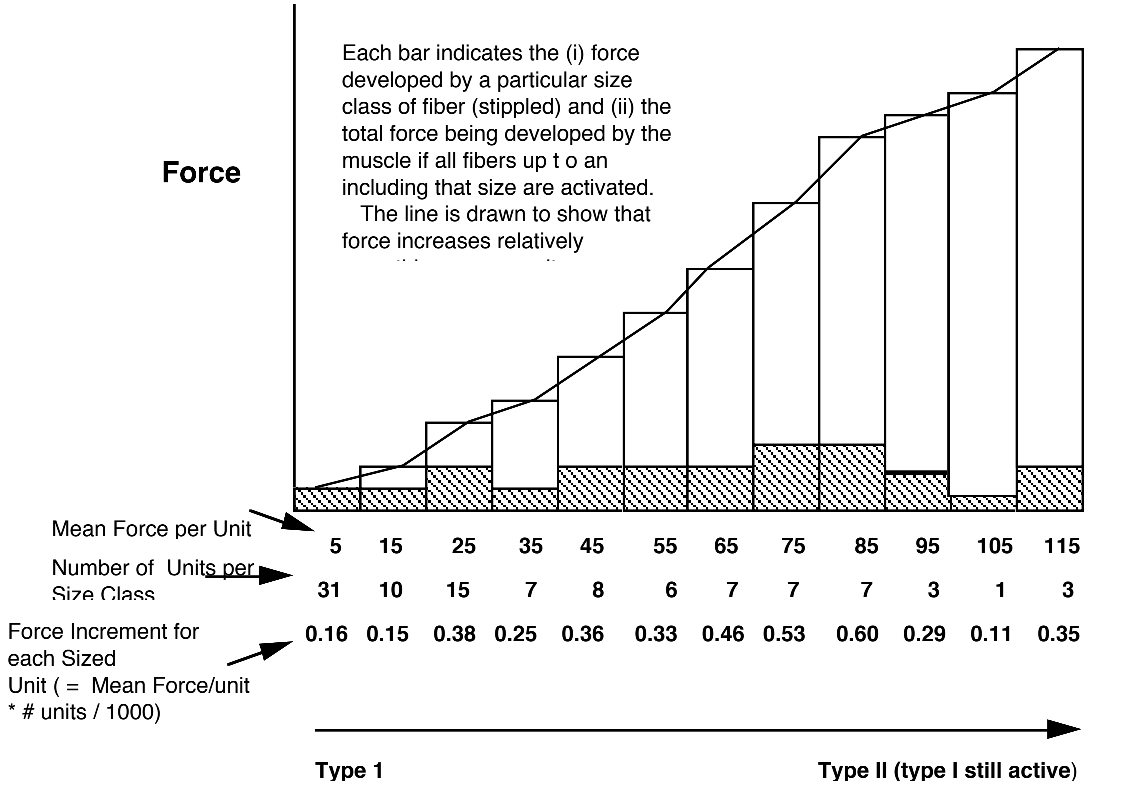
3. The force does not increase in a jerky manner as more and more groups are **RECRUITED** since the larger motor fibers are not brought into action until the muscle is already developing a large amount of force. Thus, any additional force by these units is proportionally small to the total force being developed.

? Why would the increments in force be jerky if this were not true?

4. When relaxation begins, it tends to work oppositely to the order of recruitment: the large fibers of type II units relax first followed by the type I.

5. Thus, the large, powerful, anaerobic fibers found in type II units are only used for a short part of the contraction cycle. They will fatigue rapidly if forced to remain active for long periods of time. Thus, heavy exercise, which must increasingly involve these fibers is eventually limited by the fact that they fatigue. Any exercise that recruits large portions of type II units frequently will be limited by fatigue processes.

Recruitment in Skeletal Muscles



The numbers below each bar indicate the mean force produced by each **motor unit** of a particular size class (for instance, 5 N for the first group; the second set of numbers indicates the actual number o f motor units of a particular force found in the muscle under study (31 for the first group) and the final row of values gives the force increment for for the entire muscle if all of the motor units of a certain class are activated.

The figure shows that contractions always start with type I fibers and gradually add more and more fibers to produce a more forceful total contraction (tops of bars). Notice that:
(i) the force per motor unit increases as one moves through the continuum from type I to type II motor units;
(ii) there are many more fatigue resistant type I motor units in this particular muscle than there are fatigue prone type II units -- this is typical for mammals but not for all muscles in other types of animals.
(iii) Note that more units are added to the ones that were already active -- thus the term recruitment.
(This figure was re-drawn from Berne and Levy, *Physiology,* 1983, Mosby, p 392. The data are from Henneman and Olson, 1968, J. Neurophysiology, 28:581-598. **Please note that due to the accuracy of my draw program the bars are only of approximate height** -- their actual values are given below (third row for stippled values, total of present and all previous for the open bar).

E. Muscle Dimensions: Speed and Force

1. Obviously, force is mainly a function of the cross-sectional area of the muscle. The greater the thickness, the more myofibrils and the more force generated. Thus, force is largely determined by the number of elements in Parallel: one way to envision this is to think of the force required to break bonds in a muscle, like a thick rope, a thick muscle has more crossbridges per area, thus the load is spread over a greater area and less along one contractile fiber and therefore it is less-likely any fiber will break.

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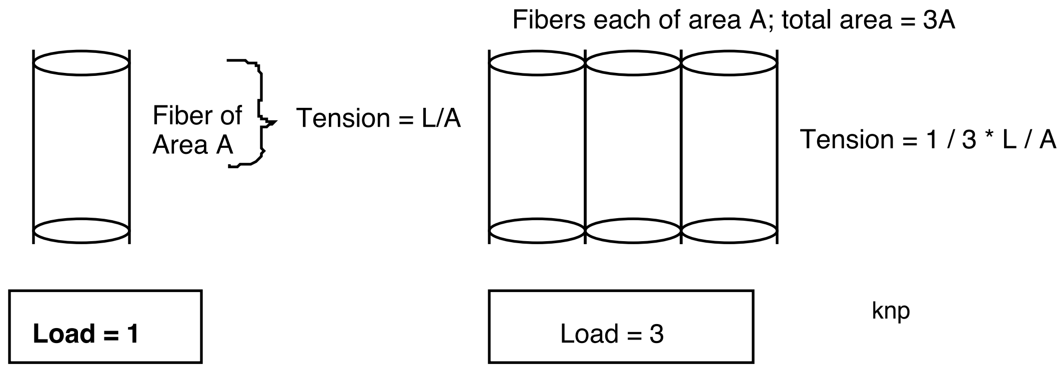
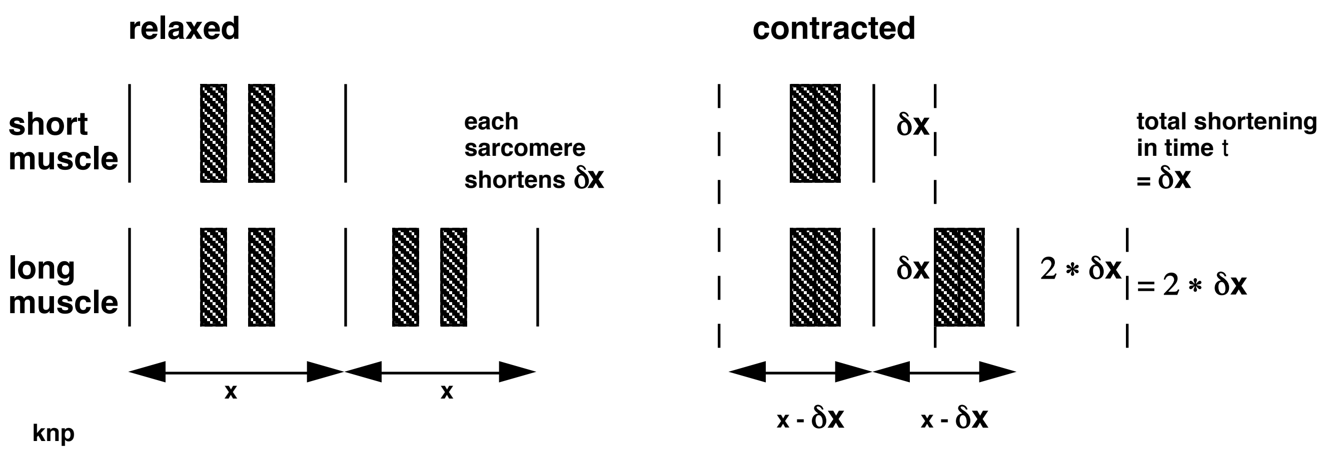


2. Speed is to a large degree a function of muscle length. The more sarcomeres is SERIES the greater the displacement that occurs when all move at the same time.



3. Obviously, if there is much of a load on a muscle, the total strength will also be important in determining speed.