>> It's October 10th, 2016. This is Lecture 14 in Physiology. Actually before we go forward, we'll go back just a page. In the concluding moments of Lecture 13, we ran down the molecular basis for muscle shortening. To understand this, first you have to get a sense of how these proteins interdigitate. From anatomy you know that there are more actin than there are myosin, a six to one ration in fact. And therefore creating a tube or a pathway through which the myosin can telescope or travel. So here you see photographs of [inaudible] filaments, first in a relaxed state, and then in a contracted state. As you know what basically happens is the myosin heads, a.k.a. cross-bridges, grab onto the actin therefore pulling it along itself, reducing ultimately the dimension, the distance between one A line and the next. Here's an actual photograph of that, and here's the animation or at least the depiction of the steps that we're about to describe. The sliding filament concept means that myosin literally pulls actin over itself, and it does this by repetitive flexion, extension, flexion, extension. Just as you would do if you were climbing a rope. If there were a rope hanging from the ceiling, how would you get to the ceiling using only using your arms? It would be hand over hand just like that. And in a similar manner, that's what's going on at the molecular level inside a muscle, a repetitive flexion and release of the myosin heads. So here is the chronology, the step-by-step breakdown of what occurs. First in order for our muscle to respond, it has to be stimulated, and that means depolarized, and the creation of a muscle action potential which spreads bilaterally away from the neuro-muscular junction. Then calcium ions which are stored inside the muscle, stored inside sacs called the sarcoplasmic reticula release this calcium and so calcium ions now will flood the vicinity of these proteins. Calcium ions. The calcium ions in turn bind to the troponin molecule which causes the tropomyosin molecule to literally rotate and swing out of the way, exposing the binding sites on the actin. This allows the myosin heads to get a grip and therefore be in a position to pull the actin in the next steps. Before this can happen, we have to attach a molecule of ATP, which of course is available in plentiful supplies. The myosin binds to the – the ATP, I should say, binds to the myosin heads, and the myosin itself serves as an enzyme which splits the ATP into ADP, an inorganic phosphate. Thus the cross-bridges reach out, that is they extend and bind onto the actin-binding sites. This is called the cocked position because essentially it's now ready to fire. The next step follows immediately. Cross-bridges bend – we also use the word flex. This is called the power stroke because this is the effort that's actually being expended and at this time, the byproducts of ADP and inorganic phosphate are released. This happens not once, not twice, but tens of thousands of times in a microsecond. In other words, DEF, DEF, DEF, DEF until, until the myosin molecules are right up against the Z lines. In other words, until they can travel no further. That marks the end of contraction. And so this cycle repeats as long as what's available? What has ignited this was the release of –? So what kills it, what stops it is the removal of that calcium. Where did this calcium come from? Where is it going to? And so it's actively transported back and when that occurs, then of course these regulator proteins are repositioned which denies access to the actin binding sites and forces the myosin heads to disengage. Very

important: if you listen to Lecture 13 to realize that this process is active in the contractual mode, but in the relaxation mode there's no backpedaling. These cross-bridges don't work in reverse. They simply what? Let go, and the relaxation is just the decompression of the muscle. And so although contraction is very active, relaxation is more or less passive provided what is released – I should say what is returned to the sarcoplasmic reticulum: calcium. So as long as calcium remains in the vicinity, the contraction will remain in force. And this of course is problematic or at least interesting, I suppose, in the case of rigor mortis. If you listened to that lecture, you are aware of something called rigor mortis. That's when the body becomes very stiff. Certainly the individual is not playing any kind of prank here. All the muscles are contracting, and that's because after death, what becomes unavailable is ATP, making it difficult to return calcium back to the –? Therefore the muscle remains in a locked or contracted phase until the muscle just decomposes over the course of many hours. So rigor mortis has no clinical significance because you're dead, but it does have some forensic significance in terms of establishing time of death in a crime scene or in any case of investigation. So essentially then it's the return of calcium which initiates relaxation and until, and unless that happens, the muscle will not relax. This return of calcium back into the SR is not dependent on repolarization, so if the [inaudible] muscular junction fails to repolarize, will the calcium still return? Yes, so that's an important piece of information. So make sure that you don't just memorize this but understand it. And the video that I recommended is a good one because it sort of shows each of these steps in nice graphic three-dimensional imagery. So pretty cool. So now let's turn the page literally and consider what we're going to do with this information. That is how we're going to use it to explain everyday activity and actually study it, for instance, tomorrow in lab. What we're about to talk about is the science of kinesiology which is the study of motion and movement made possible by the action of skeletal muscle. In other words, it's the physics of everyday movement. And when it comes to skeletal muscles, we know naturally that they're attached to the skeleton and move the skeleton or at least stabilize the skeleton and in any endeavor, whether movement or stability, there are opposing forces which are easy to describe and appreciate. First, there's the force generated by the contraction of the muscle itself. And the name of that force is the word tension. Tension, or T is the force exerted by muscles when they contract. And that force is directed against or works in opposition to the load. The load is the force exerted by the mass or weight of something due to gravity. So certainly you could grab some object here and the muscle that's about to move this is generating T. What's that? Tension, and the weight itself represents L, the load. So in any action whether subtle or major, there are these opposing forces. Does the tension always exceed the load? No. Does it have to exceed the load? No. So there are very distinct consequences of this interplay between tension and load. And these go to basic definitions, basic kinds of muscle contraction which are as follows. First, there's a kind of contraction called an isotonic contraction. That word seems to be related to osmosis but it's in a different context in this case. Iso means same. Tonic means tension. So this means

the tension is consistent and constant, and so this type of muscle contraction is also call concentric. In this situation there is actual physical movement of a load through a distance. So it's something you can witness, something you can appreciate, something you can photograph. And of course the reason for this is that the tension is what? What's that symbol there? Greater than the load. Whenever the tension is greater than the load, the load will be moved, and that's demonstrated in many contexts, which is well, doing this. Is this a load? Is it being moved? Therefore the tension generated by my bicep must be greater than the load. And therefore visible shortening occurs, and visible work is appreciated and accomplished. Whether it's moving that thing from point A to point B, or moving your body from point A to point B. Those are all examples of iso what? Isotonic contraction. And never mind the obvious, but what is talking? What is breathing? Are loads being moved there? Talking, breathing all involve isotonic contraction. But what if the load is greater than the tension. Or what if the tension exactly matches the load? If the tension is equal to or less than the load, the load will not be moved. Does this wall represent a load? Can I exert tension on it? Is it likely to move? No. [Laughter] No. Therefore it must be not isotonic, but something called isometric. That means the muscle is contracting, but not able to shorten because the load in this case is immovable. You might think that activity is inferior, inferior to isotonic. But it's very helpful in circumstances such as this. Is this a load? Am I holding it motionless? Is that iso tonic then or isometric? Is this useful? Are there times when we want to do this? Yes. And indeed, as I just stand here apparently motionless, are muscles engaged in contraction? What kind? Isometric. So we want to clear up this presumption that isotonic is good and isometric is somehow bad or inferior. They're both equally important. As you move that pencil across the page, is the movement of that pencil isotonic or isometric? But holding the pencil is what? Isometric. So almost any action that you can perform or imagine is usually a combination of some isometric and some isotonic. One is not better than the other; they're just different. And they're fundamentally different simply by the amount of tension which is applied or not. Can I lift this cup of markers off the table? Doing that's what? Holding it steady is isometric. And so all of these actions contribute to ordinary functions whether writing, walking, and so forth. In fact, it's almost inconceivable to think about daily activity without appreciating the importance of both. That said, which of these would be easier to measure to calculate or otherwise appreciate in a laboratory setting? Isotonic because something's actually moving. Something we can calibrate, measure, photograph, whatever. So in the lab tomorrow, we're actually going to be studying isotonic contraction. And the device that we're going to use looks a little odd, maybe even like a weapon of some kind. It does have a trigger on it, and that trigger is connected to a spring which represents a load. You would place your arm and hand around this handle effect, and grab or otherwise touch the trigger with your finger, and we're going to stimulate the muscles in your forearm. And will that trigger move? Yep. And what kind of contraction will that then be? So tomorrow's effort will involve a stimulator, this device which is called a trigger displacement transducer, and naturally the [inaudible] lab,

the computer software, and so forth. So the set-up is rather straightforward. We're going to be stimulating the muscles that will cause flexion of the finger. And therefore movement of this trigger, and the result will be a display on the computer screen which reflects the contraction of that trigger, the movement of that trigger representing of course isotonic contraction. Now in dissecting or studying a muscle contraction, there are obviously complex actions versus simple actions. So it would seem appropriate to first look at the simple contractions even if they're not terribly important to day-to-day life. And the simplest kind of contraction that we can study and demonstrate in the lab is something called a single twitch. The word "twitch" implies a brief, momentary contraction and so the definition follows that idea. A twitch, a single twitch, is the mechanical response to a single stimulus. And produces therefore a rather brief, short-lived movement, visible movement. And this will be displayed on the computer. You can print it out for a souvenir and will consist of the following stages or periods within this event. Here on the Y axis is going to be the degree of shortening. And on the X axis will be time in what? What are the units: ms [inaudible] seconds. The stimulus will be applied here at zero. And you would assume and expect that the muscle would contract immediately, but in fact it doesn't. That is there is a delay before movement becomes obvious and measurable. That delay before movement is actually appreciated as a period of time called the latent period. The word latent means to be lagging behind or delayed. Latent period then is the time from when we actually stimulate the muscle to the moment it actually begins to shorten. So that's the definition, but why is there this delay? Remember, we're going to be measuring a single twitch. Is that isometric or isotonic? Isotonic. Is the load going to be exceeded then by the tension? Yes. But does that tension develop immediately or gradually, do you think? And therefore is there a period of time when that tension is still less than the load even though it eventually will overcome that load? Yes. So why is there this delay? Why doesn't the muscle begin to shorten immediately? Because it takes time for that tension to build and overcome what? The load. And so this period of time is not just the latent period, it's also the period of time when the tension is less than the load. And what's the meaning, what's the definition of that? Whenever the tension is less than the load, that's a case of isometric contraction. So this is sometimes called the isometric phase. So in our myelogram, that is in the data that we collect tomorrow, we will stimulate the muscle at point A, but nothing will appear, nothing will happen for this brief period of time. What's that brief period of apparent non-contraction? What's the explanation for it? Is there tension during this time? But it's still less than the? Therefore, there's no movement. Hence the alternative name isometric phase. Once the tension exceeds the load, the load will be moved, yes? And the next phase then is the obvious and striking physical shortening of the muscle. And the name for that is simply the contractual period. It's the time when the tension has exceeded the load, and therefore the load is being physically moved or displaced. And therefore, this is not isometric any longer. It's now isotonic because the tension has exceeded the load. So in our graphic representation, this period of non-contraction is followed by this shortening which will be over

and done pretty quick. Because remember, a twitch is the mechanical response to how many stimuli? One. So it's like [boom]. That's it. We stimulated it how many times? And therefore contraction is over rather quickly followed naturally by the return of the muscle to its resting length. And that, that takes a considerable amount of time. Here in green is the period referred to as the relaxation period which is easily double that of the contractual phase simply because it takes time for the muscle to return to its original length. Remember, that phase is passive versus the active effort involved in the contraction. So these are the three phases of a single what? Twitch. And although we've given this some credibility and apparently some importance, in actual life it has almost no importance because are any of your activities the result of a single stimulus to a muscle? No. The only one that I can even think of would be the blinking of your eyelid because that's a very brief response to a single stimulus. Apart from that, everything you do is not a momentary stimulus but a series of stimuli one after another which brings about not immediate relaxation, but sustained contraction. More or less over a period of seconds, minutes, maybe even hours. So what I just said is that a single twitch is interesting maybe, but not very productive, not very useful. It doesn't have day-to-day significance in our lives. But we'll go ahead and do it, that is we'd like to record it and measure these intervals. To repeat, what is obviously the shortest interval in a single twitch? Followed by the? And then the relaxation. Now let's say for argument that this stimulus was sufficiently large. That is the voltage was significantly great to stimulate not one but all the motor units in a bundle. Are there any more than all to be stimulated. So you would assume that if the stimulus was involving all motor units that the contraction would be as great as it could ever be, right? And in fact, what's the name for that voltage when you have recruited or stimulated every single motor unit in that particular bundle? Maximal, maximal stimulus voltage. So for the sake of our discussion, let's say we're using maximal stimulus voltage. How many motor units are involved? All of them. And therefore we would assume that the contraction is now as great as it could ever be. Because can we recruit any more than 100% of the motor units that are there? No. So let's start with that premise. Here with s in mind, these are stimuli, each one now maximal. Again, maximal means the voltage necessary to stimulate all the motor units. So here we would get a single twitch with the familiar periods. Latent contraction, relaxation. Then we do what again? S stands for? We stimulate it exactly the same way, and what would happen? Would be yet another contraction followed then by another contraction. Each of these is isolated. Each of these is independent. Each of these is a single what? Single twitch, single twitch, single twitch. What percentage of the motor units are engaged apparently? Could we ever expect that to produce then a greater degree of shortening? Logically, you would think not. But what we are about to show and do in this lower panel here. Are we changing the voltage? No, we're changing the f word: frequency. So here the frequency is rather low. In the bottom panel, we're going to be stimulating it [taps] quite a bit more frequently. You might say, "Well, okay. What difference would that make?" Notice that here we have a contractual phase followed by the? And then we're

going to do what? S before it has a full chance to [inaudible]? Now some of you might be thinking, "Hold on. That can't be possible because the muscle hasn't repolarized." But let's be clear. This is not repolarization. This phase is called instead relaxation. Has the muscle repolarized even before the end of the latent period? Yes. So can it be stimulated at this time? Yes. And what would be the response? The same, less, or more than previously? The surprising discovery is this next contraction will produce a greater degree of shortening than a single twitch. And if we repeat this over and over again, if we stimulate the muscle before it's had a chance to fully what? Then each contraction is going to be added to the existing one. The name for this is called summation. Because each contraction is added to the one before. And does this produce a significant improvement in shortening? Is this degree of shortening much greater than we got with a single stimulus? Yes. And you can accept that, but you should be skeptical as to why that's even possible. Because it sort of defies our previous expectation. Recall, we're using what voltage? Maximal. What percentage of the motor units are involved? And they're all contracting in an all-or-none fashion. So think of that. If all the motor units are contracting, and they're contracting all or none, how could we possibly ever achieve a greater degree of shortening than what we see with a single stimulus? But yet apparently that happens. So our quest here is to explain how that's possible assuming all the motor units are participating and contraction in an all-or-none fashion. All we can deduce from this information is this: is the single twitch the greatest degree of shortening that that muscle is actually capable of? No. And what apparently has to be done to achieve a greater degree of shortening is not stimulated harder, but more what [pounds on table]? More frequently. But what does that do? How does that enable a greater degree of shortening? The data that we just showed you only tells us this. That the external shortening of the muscle, what we see and photograph and measure, apparently does not have time to develop fully with a single stimulus. But apparently it can develop if we do what [knocks on table]? Stimulate more frequently. That's an observation, not an explanation. So what is the explanation for that observation? There are two reasons for this quite remarkable improvement in contraction. First, let's remember what actually ignited contraction on a molecular level? What was responsible for the engagement of these [inaudible] filaments? It was the release of calcium. And that calcium is not just released but almost immediately brought back through what process? Back into the sarcoplasmic reticulum. So the opportunity for that calcium to work is rather brief if we only stimulate what? One time. The calcium's released, but it's almost immediately what? So does the calcium in that mode have any chance to linger or accumulate? No, it's out and what? [Finger click], back. It's almost like a revolving door at a hotel. You know what I mean? Out, but then right back in or otherwise immediately returned. So the first factor which is responsible in our observation is the calcium levels, calcium ion levels cannot be maintained. They don't have an opportunity to accumulate with what? But if we stimulate repetitively [taps on desk], the calcium's going out, then what? Back, then what? Out, then back. And therefore, it has a chance to linger, to have a prolonged effect and therefore

maintain the tension, maintain the contraction of these myofilaments. The second factor that contributes quite a bit is the anatomy, the microanatomy of a muscle because the myofilament tension which is generated by the myofilaments doesn't reach the tendons immediately without first having to pass through some rather sloppy components collectively called what? Here it is. Series elastic components. We'll abbreviate from now on. We'll call these the SEC. So to understand, we need to make a quick sketch. It's very diagrammatic. Here's a muscle. Let's call it the bicep that connects your scapula with your radius, et cetera. Two tendons on both ends, right? In here we have muscle cells, yes? I've blown one up. That's a muscle cell. It's part of the unit called the motor unit. And inside this muscle cell naturally the proteins that you know are actin and myosin. Where is the tension being generated? Right there. But does that tension which results in the shortening of that muscle, does that tension reach or have a chance of traveling through all of this tissue at the same moment that it's occurring at the molecular level, or is there some sort of delay or inertia in reaching these points? The answer's yes. Because each of these muscle cells is basically connected to others which are ultimately linked to something I'll show as just a spring. All of these things which don't look like that at all are called the what? S-E-C. Component means part. Elastic means what? Here's a rubber band. Is it elastic or rigid? Right. Series elastic components are all of the tissues which are in line with this axis of contraction and it is these components that the tension has to spread through before it will ever be felt or seen or have an action on the bone. So here's an attempt to show that. Here's a load, which is just a water bottle, and I've attached a cord to it, okay? Let's pretend that I'm now going to represent the contraction of a single cell. Does this contract quickly? All or none? But does that tension travel through something rather inelastic or something very elastic? If the material between here and here were inelastic, then a contraction here would be seen immediately in the what? The movement of that? But it's not that way. Because the tissues that transmit this tension – what's the E word? Much like this right here, right? So if I bring about some movement here, is that movement immediately seen in the displacement of that bottle? No, it takes time for that tension to spread through the what? Which now represent the SEC. And so when we stimulate a muscle once, does this cell contract in its usual all-or-none fashion? Is that tension immediately seen or delivered to the tendon? No. Because it has to travel through the? So how can we get this contraction to manifest itself, that is produce its full potential out here. We have to do two things. First we have to keep this in what state? And therefore allow time for what? Time for this tension to move through the series elastic components. How can we do that? Is more voltage going to solve the problem? More voltage will not recruit anymore muscles because we've agreed already that we're using maximal stimulus voltage. The other way that we can get this muscle to achieve more shortening then is not by stimulating it harder, but stimulating it more frequently allowing these cells to remain in what state? How are they able to remain in one state? What ion is held in place and therefore – yes, calcium. And if the calcium is maintained, then so will the contraction be maintained. Therefore allowing time for what? T, what?

Tension, to travel through the –? And therefore finally have its full effect on tendons, on the muscle. It takes not more voltage. More what? Frequency. And that's what we saw in this previous image. What were the differences in these two tests? Well, we're stimulating the same voltage. Here it's more what? And therefore the tension was maintained having time to spread what? Through the series elastic components. The name of this phenomenon is summation, a word which we've already used. But a more sophisticated term is a tetanic contraction. Now let's be clear on the spelling because some people want to call that the titanic contraction. Let me make that clear. That's a ship that sunk at the bottom of the sea. This is not titanic, it's what? And if it has any familiarity, it's probably because you've been inoculated for a condition, a pathological disease called tetanus. Also known as lock jaw, yes? A tetanic contraction at least in terms of normal activity is not to be feared, but rather to be welcomed. Titanic contractions – tetanic contractions [laughter] part of everyday actions. And incidentally, important for isometric as well as isotonic movements. So by definition, a tetanic condition is a sustained contraction meaning a prolonged contraction which is created not by one, but what?

[Taps on Table]

Repetitive depolarization, repolarization, depolarization, and repolarization. In very rapid succession. To understand and present this in a graphic form, let's overlay two very different perspectives of a tetanic contraction. First, the internal contraction which we cannot see, and second, the external contraction which we can see and appreciate. Once again, let's start with a stimulus delivered right here at the intersection or the x and y axis. That stimulus is going to release what ion from what location? And that calcium will flood the vicinity of the myofilaments. Will the cross-bridges engage? And this shortening, which we can't see but we can nevertheless graph, we're going to call it the internal contraction. Which means the microscopic contraction basically the result of myosin moving along actin. That contraction occurs almost immediately, and maxes out. Why does it max out? Why can't it go any higher? What stops that contraction from traveling anymore? The myosin has moved as far along as possible and basically hits the Z lines. Now remember, this is the internal contraction, the result of how many stimuli? Once. So as soon as that calcium is released, what happens to it? Actively returned. And therefore what does that force to occur as far as these myofilaments. Once the calcium's gone, they are forced to? And therefore the muscle relaxes almost as quickly as it contracted. Contracts and what? And that event, that contraction and relaxation is over and done within 20 ms. That's a millisecond. This is something we can't see. This is the what? What we see and appreciate is not the internal but the external contraction. And here it is in blue. First, as you recall, there's a period where nothing's happening at all. What is that delay or point of hesitation there? And then the muscle finally starts to contract, yes? But why does it not reach its full potential? What's happening internally is that the internal contraction is already on its way what? And therefore that forces this to immediately begin to relax even though it could have contracted quite a bit more.

Again, why is there this delay? What were the two reasons for this inability to achieve this contraction that we know it is capable of? First, the calcium is not being maintained, and second of all, the contraction has to travel through these things. What are those? And does that take time? How can we overcome both of those limitations? Not by stimulating harder, but more? And so if we do that, if we stimulate, stimulate, stimulate, stimulate, stimulate, stimulate, then the internal contraction never really subsides. The internal contraction remains fully contracted. And therefore this gives time, this gives opportunity for this tension to be carried through the what? SEC, and therefore manifest in a significant degree of shortening. This then is called summation, but in the end it produces a smooth, steady contraction for as long as the stimulus exists, and the name of that is tetanus, or tetanic contraction. Achieved by what? High frequency simulation. Tetanic contraction, not to be feared, is actually the way we conduct business whether it's isometric or isotonic. Tetanus can be demonstrated both isometrically and what? Isotonically. Back to this. I'm holding this weight motionless. Is that a sustained contraction? So are the frequency of stimuli rapid? Yes. And not only is this a sustained contraction, but the tension has been calculated to keep this motionless. So it's a case of tetanus. What kind of tetanus? Isometric. Then when I move it, it's no longer isometric, it's iso – but this is still tetanus. Yes, because it's sustained muscle contraction. There are actually though two types of tetanus that you'll demonstrate tomorrow in lab and that are contingent on the degree, the frequency of stimulation. If the stimulation is infrequent, if it were infrequent, that would allow each of these contractions to relax more before being stimulated again. That would produce very undesirable effects. Something like what? Something like this. Which would be twitching or tremors and so forth. When that occurs, and it's usually certainly not welcome or desirable, it's called incomplete tetanus. Also known as unfused. It's unfused because each contraction is followed by a visible period of short relaxation, and then builds again and builds again. So it's essentially an on again, off again and very, very jerky kind of effect. What's it called? And how do you convert that into something that's sustained and motionless and steady? By changing the frequency, by increasing the frequency. And that produces a kind of contraction called fused tetanic contraction. A fused tetanic contraction is one that's smooth, uninterrupted with no relaxation. These are the contractions that we what? That we typically endeavor to use because they are graceful. They are controlled. They bring about movement which is purposeful and productive. If I want to bring a cup of coffee up to my lips, is that going to require isotonic movement? Yes. Do we want this to be fused or unfused? Fused looks like this. Unfused looks like this. And does that happen in pathological conditions? Parkinson's disease and other conditions of tremor. So let's be clear – tetanus is a normal, natural, desirable means of contracting muscles. Tetanus can be isometric or it can be isotonic, but it is always, or at least desirably what kind? It' complete or fused unless there's some explanation or some complication. So tomorrow lab. We're going to measure a single twitch? Yes, where we measure also tetanus. Both kinds? Yes. And how do we convert unfused to fused? Increase the frequency. And right before your eyes

at a low frequency, this trigger will be doing this [rapid tapping sound]. And when we increase the frequency, it'll become one single smooth motion. Fun to watch. Not so much fun to be stimulated that way. Because obviously we're not going to allow you to do this. We're going to have a stimulator do it for you. And will that produce some sensation that might be a little disturbing? Yes. But you guys can handle it, and all of us will get to watch. We'll enjoy as you grip this to death here with that higher frequency. Now before we're done today, we have to go further into the source of tension. The tension is the force generated by essentially the muscle. And we know that that tension comes from the gripping of the myosin heads pulling the actin along. Okay, fine. That is the obvious and more important source of tension. But it turns out there are two very independent sources of muscle tension. One more important than the other. The obvious and most significant source is MT; MT stands for myofilament tension. This is basically the result of active cross-bridge gripping. Is therefore a function of the number of myofibrils in a cell. It's also a function of the number of motor units that are engaged and so forth. When you say active, we know that means there's energy being expended. And this tension is not just a function of cross-bridge gripping. But also the degree of cross-bridge overlap, and the number of myofibrils in the particular cell. I had a model in here which I bet is gone. I have so much junk. Oh, no, it's here. Okay, cool! So I know – this is kind of funny. I got this actually at Big Lots. These are actually gold clubs for toddlers. Isn't that great? Okay. But I looked at that and said, "Oh, myosin heads." [Laughter] So I just duct taped it all together. Doesn't this look like the end of a myosin molecule? These are the cross-bridges. This piece of pipe can stand in for the actin. And of course there are how many of these for each of these? Alright, so you get that analogy, right? These are capable of F-word: flexing, and therefore pulling the actin along. Okay, that's all stuff we've talked about. What is this notion of cross-bridge overlap? When a muscle's in a relaxed state, the cross-bridges are fully over lapped. That means in contact with the actin. Therefore able to reach it, therefore able to pull it. Yes? But what if we took a muscle, any muscle, and stretched it? What would happen at the molecular level if we went too far? Down at the protein level these molecules would be [beeping sounds]. They wouldn't make that sound, but okay. Now some of these cross-bridges are not [inaudible] and therefore not in a position to grab the? Does this generate more or less tension in this mode? There are fewer oars in the water, yes? So to speak? So what's my point? This is optimum overlap. This is less overlap. And because there are fewer cross-bridges in contact with the actin, will this generate less tension? Yes. Take it to an extreme. What if we kept stretching that muscle? Eventually the myosin would disengage from the actin altogether and therefore these oars are entirely out of the water, so to speak. That is not able to do anything at all. What's this concept called? Cross-bridge overlap. Optimally, there should be good overlap, that is normal contact of the cross-bridges with the actin molecule. And so let's just look at this graphic decay of MT. What is MT? Myofilament tension. When a muscle's in its natural, relaxed state, are the cross-bridges ready to go? Are they in a position to grab onto the actin? Yes. That's called optimum or normal overlap.

And will we get a great degree of muscle tension in that setting? Sure. But what if we stretch the muscle artificially? What if we elongate it or otherwise stretch it? At the molecular level, these filaments are being pulled apart, yes? And in the extreme, the myosin's going to be totally disengaged from the actin. Does that produce any tension? So tension falls to the big zero. So as a muscle is stretched, does this help or actually reduce MT? It reduces MT. Myofilament tension is dependent on the number of myofibrils that are working. But it's also dependent on cross-bridge overlap. One other thing that's obvious is that this requires energy, and therefore is ATP dependent. But this information makes it seem, and certainly at this level it is true that stretch is good or bad for a muscle? Seems to be bad. Because as we elongate a muscle, ultimately we would dislocate the actin from the myosin and therefore make it impossible for it to generate any tension at all. But hold on. What degree of stretch is apparently necessary to achieve that extreme end? This is 100%, that means normal resting length. This is a hundred and what? This is a hundred and –? Think about the muscle that we've been spotlighting, the biceps. Can that be stretched to 160% of its length in normal anatomical settings? The muscle goes from here to here. What would it take to move it 160? You'd have to disengage it from the bones, right? Is that likely to happen? Can you do that? No. Even though this is experimentally demonstrable, it doesn't happen in life. Because is your skeleton, are your joints protecting from this stretch, this degree of stretch, yes? So this is just a theoretical outcome, meaning that stretching a muscle does serious damage to the cross-bridge overlap and rapidly, rapidly reduces MT. What's that? Myofilament tension. So before we move on, MT is myofilament tension. The result of cross-bridge gripping of the actin. Certainly depends on ATP, and also the degree of overlap. Less overlap, less what? Therefore less overall performance of the muscle. But what does it take to reduce overlap? You have to stretch a muscle. And is that easy of hard to do in anatomical states? You can do it to some degree, but certainly not to this degree, not to 130, not to 160. So the loss of MT due to stretch, due to less cross-bridge overlap is really not significant in normal, healthy skeletal context. Alright, let's finish with this because there are two sources of tension. The next contributor has nothing to do with actin, nothing to do with myosin. It's called ET which is not extraterrestrial. ER stands for what? And that's exactly what it is. It's tension as a result of elasticity. Here's a rubber band. Is it elastic? Right now in this mode, is it exerting any tension? No, come on, do something. No, I'm kicking it around, nothing. In order to get any recoil from this, I first have to what? And then the more I do stretch, is there a corresponding recoil that is proportional to that degree of stretch? Yes. The more I stretch, more what? More tension. This is called elastic tension. Where does it come from? Not from the muscle cell, but from the elastic tissue that encapsulates all of these cells. From anatomy, you might recall the superficial fascia, the epimysium inside the perimysium. And so forth. Not to mention the tendons. Are these stretchable to a degree? Yes. And anything that's stretchable will exert a recoil effort which is called what? Elastic tension. To get elastic tension, to benefit from elastic tension, you first have to what? So this is seemingly sug-

gesting that stretch is good whereas previously we suggested that stretch was not good. Stretch is not good to what? It's not good for the MT, but it is good and necessary for ET which comes from the elastic tissues of the muscle itself. So ET is passive recoil of connective tissue, fascia, tendon, sarcolemma, et cetera. And can only be a factor, can only be a contributing factor when the muscle's what? When it's stretched. When a muscle is not stretched, there is no ET. Therefore, this bonus, if you want to call it, is obviously a function of pre stretch, that is stretching the muscle before it contracts, and increases with the degree of that stretch. Now here's an image that you don't have. I obviously got it off the internet, and this is track and field where of course these individuals are engaged in sprinting, right? And you've seen a sprint race. They just don't stand there with their arms folded and say, "Okay, tell me when to run." No, they're down here in this position, yes? And these aluminum things here, these are called the blocks, b-l-o-c-k-s. And this position is not just a policy, but it's designed to take advantage of this bonus which we've described as what? ET. Now where the muscles that are primarily involved in plantar flexing are the foot. Plantar flexing is when you do this, right? And what are these guys back here? Sorry to spring this on you, but these are familiar enough.

[Inaudible]

They're attached to the [inaudible], yes? And when these muscles contract, the foot does that, right? Is that important to get that burst of speed in the first second of this event? And then to sustain it later, yes. So why is this position? This position, the foot is dorsiflexed a bit, therefore putting tension on what tendon that's back here? That tendon that attaches to you calcaneus, the calcaneal tendon, better known perhaps as the Achilles tendon. If we dorsiflex this a bit, will there be tension here? Yes. And so maybe use this rubber band. Is this being stretched back here? Yes, because this is dorsiflexed. Is that an advantage, or will that be an advantage once the gun fires? Because now this has been S-word, stretched. Therefore going to contribute what? And therefore will that help this muscle in the first moments of this event known as a sprint? Yes. So ET will add to what? Add to MT, and therefore produce more TT. What's TT? [Laughter] Think about it. Total tension, right? So it's a simple formula. TT is what? Which is adding together what? MT versus ET. Do all activities involve or benefit or even have ET? No, because the muscle has to be what? Has to be stretched by the load prior to contraction. This is an example of taking advantage of ET. Another case in point: there's this effort that you've seen called a chin-up. I've heard it described. And basically there's this bar above you, okay? And you grab onto the bar which is higher than you can reach, so you have to jump up to it, right? You get the idea? And the goal here is to put your chin over the bar. Hence the name chin-up, okay. Now the muscles that are used for that are primarily the flexors of the forearm, and that would be notably the biceps and its [inaudible]. So most of the MT is coming from what? The biceps to do that, right? And that of course is a function of a number of myofibrils, a number of motor units, a number of actin and myosin molecules and all that. But could we derive some benefit from ET, and if so, how would

we have to change this effort? There are two ways. There are a couple ways to do this. You can grab onto the bar with your feet on the ground, okay? Or you can jump up to the bar and let your whole body what? Hang there. Which of those would elongate the biceps more? Feet on the ground? Or feet off the ground? And therefore, when your biceps are elongated, even a little bit, you're stretching some of these connective tissues, therefore giving a little bit of what? Which would be added to the? MT. So with that said, would it be easier to do a chin-up with your feet off the ground or on the ground? Off the ground. Try it sometime. You think, oh it would be better if I'm on the ground. At least I'm not, you know, at least I'm – it's easier. No, it's actually harder because here you don't have the benefit of the what? The stretch. The stretch imposes more elongation of the connective tissues. And another: you can do these chin-ups one way. You can do them underhand like this, yes? Or you can pronate like this. This would be the supinated position. This would be the pronated position. Which is easier? It's actually this position because when you pronate, you're actually making it harder for this biceps to be stretched, therefore not getting as much what? So in short, the underhanded method is easier than the overhanded method because you get more stretch, therefore more what? ET. And remember, MT is pretty much the same. So the advantage doesn't come from more MT, it comes from more ET. So certainly this is important in athletics or cases where bursts of action could benefit from the ET. Most of the time we don't notice or really appreciate much difference because of the two, which is the most important contributor to TT? TT, total tension? Mostly contributed by the MT. This is a bonus which may or may not occur, but only can occur if, only a factor if the muscle is what? Stretched by the load. So if I lift a weight off the table, is that load stretching the muscle prior to the effort? No. If I move it the same distance here, that load is now stretching the muscle and benefits, slight benefits are obtained. Well then, questions? Alright. Tomorrow we're going to do single twitches and – what was the T word? Titanic? No, tetanic. We're going to go right next door for those that can stay for the Q&A.