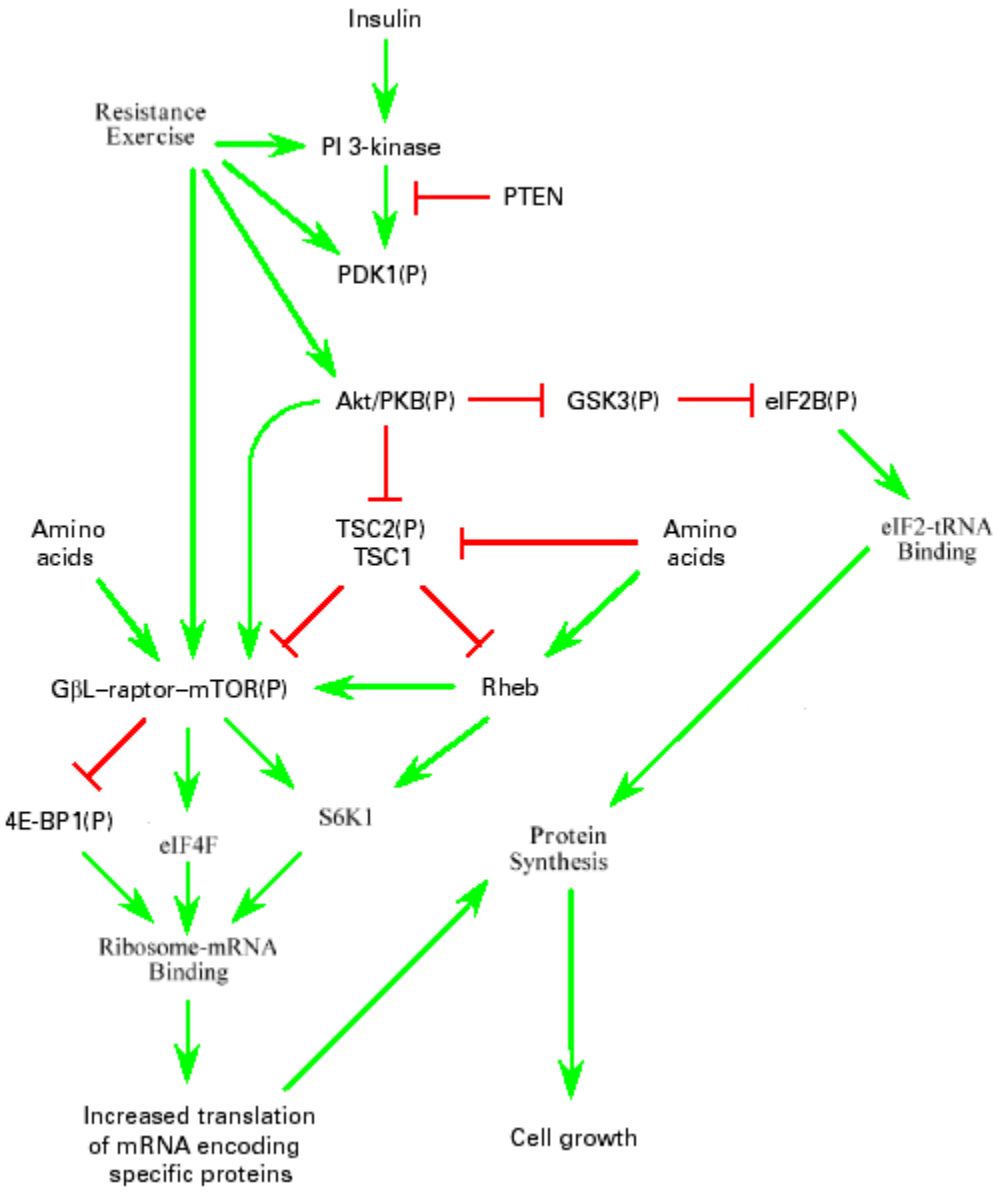
Max-Stimulation™



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Acknowledgements

There are many that I should thank and acknowledge but none are more important to me than my wife, Kimberly. Her trust and faith in me have always been an inspiration and the lord knows I have tried her patience over the 19 years of our marriage.

In the realm of researching hypertrophy there have been two very influential people at my side. One is my mentor, Bryan Haycock, without his work I am sure I would still be quite lost in this maze of molecules and proteins. The second is my comrade in arms in this battle of research, Ron Sowers who has proved time and again what a valuable ally he is.

Forward

Much has been written about the art of Bodybuilding and the quest for a better physique. The one thing that can be said about the mountain of written material is in some respect or another they are all right. There is no wrong way to build to muscle, just about everything has been tried and just about everything works, there is a reason for this and it's something that has been explored and we will touch upon it in this book.

What I am presenting in this book isn't going to move mountains or magically add 20 pounds of muscle tissue on you over night. That just isn't real and I would be lying if I told you it would. That's not me. I am not going to over hype this as so many others have and promote it as "30 days to 30 Lbs." or what ever catchy phraseology is used to get you to buy the book.

What I will show is ….

How science is making some decent headway into the abyss known as skeletal muscle hypertrophy and this book is a result of the research I have invested the last number of years going over. It explores the events that lead up to increases in muscle cell size. The events themselves are, in my opinion, very important, as it's these events that make or break your gains no matter which routine you use. If you are not into the science behind building muscle then the first chapter is not going to thrill you. If you are then the first chapter will give you a great reference for furthering your own studies and research.

How you can incorporate some useful techniques that can be used either selectively, or completely, to enhance your training and gains.

Chapter 1-A Brief on the Science

Translation, Protein Synthesis and Hypertrophy

Increases in skeletal muscle mass are mediated via protein turnover, the balance between protein synthesis and protein breakdown also known as net protein balance (1).

There are many controls that govern changes in protein synthesis and eventual gain in muscle mass. Incorporation of both transcriptional and translational inputs can influence the protein synthetic rate (2). Generally, alterations in protein synthesis associated with altered gene transcription generally occur over a period of days to weeks (3), whereas increased mRNA translation (i.e. the process of synthesizing a protein based on the information encoded by the mRNA) can be manifested within minutes to hours (4).

Transcription and translation each contain three distinct steps (initiation, elongation, termination) with the predominant influence owing to the initiation phase (5,6). However, translation is different and unique because mRNA is summoned and recruited rather than produced and this process is responsive to acute mechanical, metabolic, nutritional alterations (7).

Translation initiation essentially revolves around two main components mediated by eukaryotic initiation factors (eIFs) that control rate-limiting events. The first of the two components allows the ribosome to bind to the mRNA (eIF4F complex), the second brings the ribosome to the site on the mRNA where translation begins (eIF2/eIF2B). An essential mechanism for regulating growth within translation initiation involves the mammalian 'target of rapamycin' (mTOR) protein. Two common downstream targets of mTOR are the 70-kDa ribosomal proteins S6 kinase (S6K1) and the eIF4E-binding protein-1 (4E-BP1)(8).

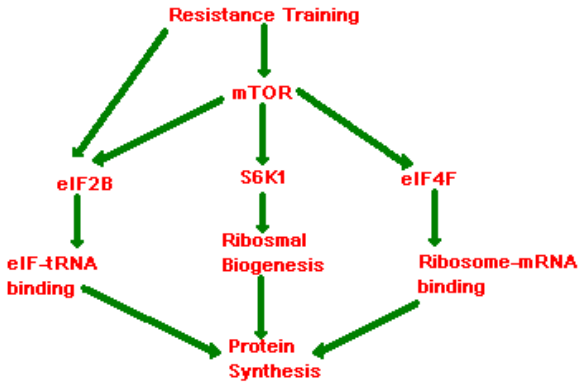

Figure 1. Translational control map of currently known paths.

A common misconception regarding changes in translation initiation is that activation of any protein in this pathway corresponds with increases in protein synthesis. For our purposes, after resistance exercise, elevations in protein synthesis have shown to be delayed for several hours yet mTOR controlled events can be rapidly upregulated during this period same (9). Later increases in protein synthesis appear to coincide with eIF2B changes (10). It's becoming indisputable that chronic mTOR signalling is very valuable for increasing cell size and therefore increased muscle mass as blocking this pathway almost completely blocks the response (11). The downstream mTOR target, S6K1, strongly linked with muscle hypertrophy (12), is also crucial.

Currently it is safe to propose that both components of translation initiation are essential to increased muscle mass. Events associated with eIF2B regulation may orchestrate the acute changes

in protein synthesis following resistance exercise, whereas activation of mTOR/4E-BP1/S6K1 appears to result in synthesis of proteins necessary to enhance the translational process, optimizing the capacity for protein synthesis with long-term training.

Chronic vs. Acute-Once is not enough

Recent studies designed to better understand the regulation of translation initiation show us that following an acute bout of resistance exercise distinct eIF proteins are rapidly phosphorylated (13). Intermittent and transient activation of these proteins may provide more precise control for modulating a growth response. Specifically, the responses appear to be temporal and the acute impact of resistance exercise on mRNA translation likely becomes cumulative with each successive bout performed; this suggests that this pathway is intermittently turned 'on' with repetitive resistance exercise and distinct mRNAs (ribosomal proteins, etc.) may accumulate to a point where an increase in the amount of specific proteins occurs (14). These responses highlight the longer-term and more rapid control mechanisms associated with transcription and translation, that contribute to achieving muscle hypertrophy (Fig. 2).

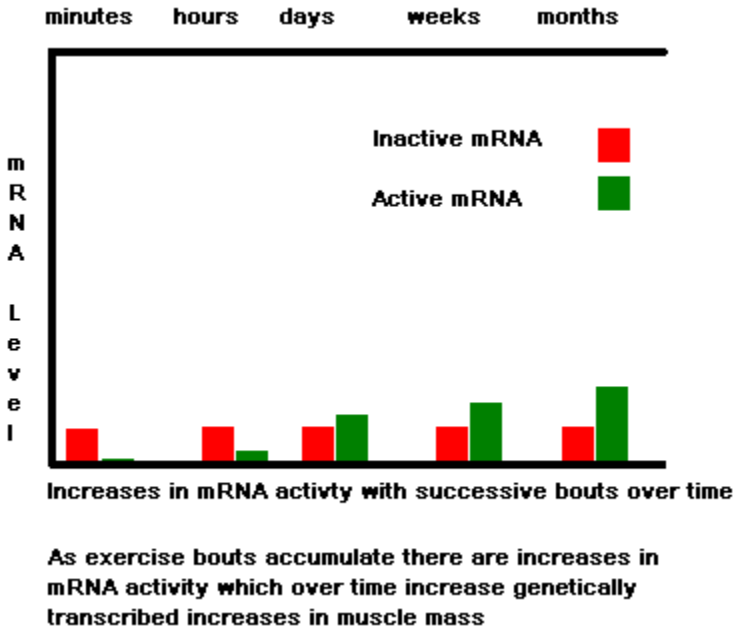

Figure 2

Contractions, Stretch and Strain-Negatives vs. Positives, how about both

Over time the world of body building has seen many routines come and go and all had their own dogma on how to perform the reps. Many have touted slow or fast reps, full or diminished range of motion, static or isotonic. But again there was some commonality in them all, strain. It has been shown that strain is a potent stimulator of hypertrophy (15).

What hasn't been so pronounced is which mode of contraction produces the most hypertrophic response (16-20). The debate still rages as to whether eccentrics (negatives) are better, worse or the same as concentric (positives).

What can be seen is that the issue of contraction mode isn't much of an issue at all. Most human *in vivo* movement uses both and resistance training is the same. We raise the weight, we lower the weight, we do it again. Lending the tissue to the extremes of both contraction modes. The extent of muscle fiber strain is dependant on the compliance of the series elastic elements that not only tie the muscle fibers to our bones but also hold the fibers in their respective place. These elastic series elements take a large amount of force before stretching to a point where the force is then transmitted to the fibers themselves. What this means to a person moving an object is; even when stretching the entire muscle tendon complex the degree of stretch needed before actual strain is felt

on the fiber depends on many things but there is hope. Looking into the mechanics of muscle tendon units (21) it's been seen that two things predominantly affect the level of fiber strain, the length of the muscle when the stretch shortening begins and the number of stretch shortening cycles themselves.

If a muscle is pre-stretched *in vivo* the series elastic elements are already stretched and become stiffened, allowing a greater amount of force to be directly applied to the fiber. Using the other means it's apparent that repetitive stretch shortening cycles stiffen the series elastic elements as well, again allowing more force to be directly applied to the muscle fibers (22).

How this ties into translation is two fold.

Fiber strain acts on the Mechanotransduction (23) mechanisms within the cell itself. This is a term used which denotes the bodies ability to turn a mechanical signal into a chemical signal. When cells are stretched the stretch is picked up by a couple notable elements. One of these is the Focal Adhesion Complex (24). The FAC, as it's known, are sites where the extracellular matrix is physically coupled to the cytoskeleton within the cell. In skeletal muscle FAC can be found at the myotendinous junctions, neuromuscular junctions and in structures that lie above the z-bands named costameres. The FAC are protein dense regions and most of the molecules in the FA contain multiple domains that can interact with a variety of molecular partners. One of the major constituents of the FA is the family of cell surface receptors termed integrins (24). As the cell wall is stretched these integrins then transmit the stretch to the cell nucleus, which in turn up-regulates or down-regulates translational mechanisms. Another stretch sensor is the Stretch Activated Channel (25) or SAC. As a cell is stretched these channels are opened allowing ion flow in or out of the cell, the increased flux of ions can then increase translation items relevant to protein synthesis, metabolism or other cellular functions.

Much of the work on translational events revolved around the autocrine and or paracrine release of growth factors. It is proposed that the PI3K/Akt-1 pathway and subsequent mTOR pathway was dependant on the growth factor input. However it's been shown (26) that mechanical stimuli are indeed similar to growth factors in that they require signalling through both PI3K and mTOR to promote an increase in protein synthesis but, unlike growth factors, mechanical stimuli activate mTOR-dependent signalling events through a PI3K/Akt1-independent mechanism and the release of locally acting factors is not needed for the induction of this pathway. Since PI3K is indispensable for growth factor-based signalling through mTOR, it appears that mechanical stimuli and growth factors provide their own distinct inputs through which mTOR co-ordinates an increase in the translational upregulation and efficiency.

<u>Amino Acids-The building blocks</u>

Over the last 25 years numerous studies on protein metabolism involving oxidation, synthesis and breakdown have been performed (27). It's is this body of evidence that makes it abundantly clear that amino acids are a critical component to building muscle mass. It's also become convincingly clear that the exogenous amounts of available AA are critical to signalling chains (28). Of the EAA's made available through the infusion or oral dosing studies, the importance of the Branch Chain Amino Acid Leucine is coming to the forefront (29-31). Not so much in its role during energy expenditure but because of it's prominence in signalling anabolic translational events leading to increased protein synthesis (32).

Leucine's effect on protein synthesis is controlled through upregulation of the initiation of mRNA translation. As in the case of mechanical stimulation a number of differing mechanisms, including phosphorylation of ribosomal protein S6K, eIF4E BP1, and eIF4G, contribute to the effect of leucine on translation initiation. These mechanisms not only promote global translation of mRNA but also contribute to processes that mediate the selection of mRNA for translation. MTOR again is a key component in a signaling pathway controlling these phosphorylation-induced mechanisms. The activity of mTOR toward downstream targets is controlled in part through its interaction with the regulatory-associated protein of mTOR (known as raptor) and the G protein b-subunit-like protein.

Upstream members of the pathway such as Rheb, a GTPase that activates mTOR, and TSC1 and 2, also known as hamartin and tuberin respectively, also control signaling through mTOR.

Inhibitory Signalling

With the advent of newer research putting light on the known mTOR/S6 chain it is becoming more and more clear that the AKT/mTOR/EIF4 chain is a very important regulatory mechanism in muscle growth (33). As with all signal chains in the human body there are signals that also combat the actions. Hypertrophy and increased protein synthesis via increased translation is no different.

The Switch

It has been noted by many researchers that protein synthesis does not occur for several hours after the exercise is completed (34-36). Recent work (37) has identified one possible mechanism that can be the cause. Called the "AMPK-AKT" switch (37), this switching of translational events leading to protein synthesis can be seen during the difference in exercise mode. Long duration endurance type activity causes increased activity in AMPK (5'AMP-activated protein kinase) this kinase then turns on events that switches off events that use ATP for anything other than fuel replenishment inside the cell, including the mTOR activated protein synthesis chain.

AMPK is another member of the heterotrimeric serine/threonine protein kinase. AMPK is composed of a catalytic alpha subunit and non-catalytic beta and gamma subunits (38, 39). The mammalian genome contains seven AMPK genes encoding two alpha, two beta, and three gamma isoforms. AMPK signaling is elicited by cellular stresses that deplete ATP (and consequently elevate AMP), the AMP/ATP ratio, by either inhibiting ATP or accelerating ATP consumption. Although AMP is produced in several cellular reactions, it most importantly appears to be the adenylate kinase reaction: 2ADP <> ATP + AMP. In healthy, resting muscle the ATP:ADP ratio is maintained at a high level, and therefore AMP is very low. However, if the cell experiences a stress that depletes ATP, the ATP:ADP ratio will fall (analogous to the battery becoming discharged), and a large increase in AMP will ensue. These are exactly the conditions in which AMPK is activated. Treatments that activate AMPK can either be stresses that interfere with ATP production, such as heat shock, metabolic poisons, glucose deprivation, hypoxia, or ischaemia (40,41) or stresses that increase ATP consumption, such as exercise in skeletal muscle (42). These findings led to the concept that the AMPK system acted as a "fuel gauge" or "cellular energy sensor" (41). This concept was reinforced by findings that AMPK was allosterically inhibited by physiologically relevant concentrations of phosphocreatine (43).

It has been shown that AMPK is a central mediator of insulin-independent glucose transport, which enables fuel-depleted muscle cells to take up glucose for ATP regeneration under conditions of metabolic stress (40). When rat epitrochlearis muscles were isolated and incubated in vitro under conditions that evoke metabolic stress accompanied by intracellular fuel depletion, rates of glucose transport in the isolated muscles were increased by all of these conditions, contraction (5-fold above basal), hypoxia (8-fold), and hyperosmolarity (8-fold) Fig. 3. All of these simultaneously increased both isoforms of AMPK, alpha1 and 2. There was close correlation between alpha1 and alpha2 AMPK activities and the rate of glucose transport, irrespective of the metabolic stress used, all of which compromised muscle fuel status as judged by ATP, phosphocreatine, and glycogen content.

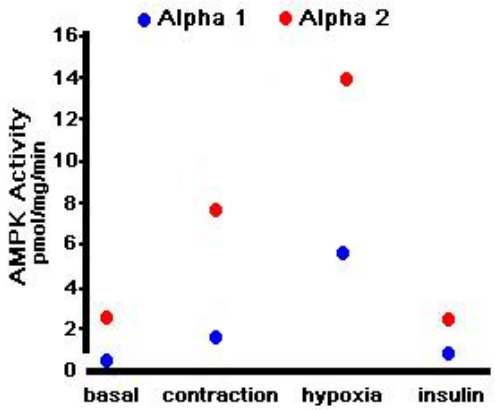

Fig. 3 The fold increase in AMPK during differing metabolic stress

Fatigue-The TUT party crasher

During contractions, whether sustained static or repeated dynamic a big influence over the duration or number of contractions performed is fatigue. The overall cause of fatigue is still being debated as its effects on contraction are so pronounced in varying systems and no single consensus has been defined.

Muscle contraction increases muscle metabolism by an order of magnitude (44), this magnitude is influenced by type, intensity, duration and frequency of contraction and the fatigue rate in muscle falls in line with this magnitude. It has long been realized that the metabolic cost of muscle activation is a primary factor in fatigue (45), not necessarily the only factor but the buildup of metabolic byproducts (46-48) and depletion of substrate (49) have a large part to play. The results of many metabolic studies do not demonstrate, with any consistency, that it's a matter of only one metabolite being the cause of fatigue, but they do show that several substances can alter force generation under varying conditions (50-52). In further support of a metabolic basis for fatigue, several studies have demonstrated that during short-duration, high-intensity exercise (both voluntary contraction and electrically evoked contraction), protocols that produce the greatest metabolic change also produce the greatest fatigue (53-57), although other factors, such as activation failure, are likely to be involved in the decline in force (58), but this factor goes far beyond the scope and intent of this brief.

The metabolic demand of muscle contraction is associated with the ATP hydrolysis occurring at three ATPases: *1*) the sodium/potassium (Na+/K+) ATPase associated with maintaining the resting membrane potential of the sarcolemma, *2*) the actin myosin (AM) ATPase associated with cross-bridge cycling and force production, and *3*) the sarcoplasmic reticulum (SR) Ca2+ ATPase associated with Ca2+ reuptake at the SR. The demand of the AM-ATPase is related to the force produced by a muscle (59), as ATP consumption increases proportionately with force during voluntary contractions. ATPase activity, however, is lower in fibers that have been chemically skinned to remove the SR, this eliminates the metabolic demand associated with the SR Ca2+ ATPase. This coincides with findings suggesting that between 20 and 40% of the ATP hydrolysis that occurs with muscle contraction is thought to result from noncontractile (i.e., non AM ATPase) ATPase activity (60). This indicates that with repeated contractions the ATP used for all three ATPases would be higher than what is seen during isometric exercises.

The increased ATPase activity indicates that during repetitive contractions AMPK activity would also be higher especially if the AMP/ATP ratio is severely affected.

Now that we've reviewed how the metabolic fatigue induced during repetitive contractions can cause a diminished response through the AMPK-AKT switching event, lets look into how the lactic acid burn and the pump can also affect it through increased acidosis, hypoxia and hyperosmolarity.

Blood Flow and it's Effects

Adequate perfusion, blood flow across the tissue bed, is vital to the health and proper functioning of skeletal muscle. In healthy tissue, the metabolic demands of the muscle will largely determine the degree of its perfusion. While blood flow through the arteries is important in determining how much blood can reach the muscle, the amount of blood that enters the muscle bed via the micro-vasculature will determine the degree of gas and nutrient exchange, profoundly impacting the contractile state of the tissue.

Blood flow during resistance exercise highly oscillates due to the high intra-muscular pressures that are generated during contractions. High intra-muscular pressures impede (occlude) muscle blood flow, with the result that blood flow approaches zero during contractions but is greatly elevated after contractions (62,63).

The extent of temporary occlusion is directly proportional to the intensity of contraction and this continues to about 60% MVC (64). At this point the muscle blood flow becomes completely occluded and remains occluded for the duration of the contraction phase regardless of any further increases of force (65,66).

The ischaemia that occurs during the occluded state causes an increase in non-oxidative metabolism via hypoxia a.k.a. ischeamic hypoxia (67). Hypoxia is a condition of lessened oxygenation. The reduced blood flow during ischaemia does not allow the blood to circulate and therefore it does not re-oxygenate.

Interestingly this is true also when contraction frequency is increased, or the contractions retain sufficient tension for a prolonged period. The expansion of the muscle blood volume, as contraction frequency increases, is a result of the muscle vascular bed being expanded by vasodilator processes that occur with an increased metabolic rate, and occurs even though the time between contractions ("filling" time) is decreased (68). One of the more interesting observations seen is that the volume of blood contained in the muscle is greater during these states. A greater volume of blood contained in the muscle allows for a greater ejection of blood for a given contraction during the relaxation phase. In the case of prolonged tension or insufficient relaxation times the pooling that occurs interferes with nutrient and gas exchange.

All of these blood flow responses to contraction have an impact on the internal environment and metabolic state of the muscle. Every time ATP is broken down to form ADP and Pi, a proton is released. When the ATP demand of muscle contraction is met by mitochondrial respiration, IE oxidative metabolism, there is no proton accumulation in the cell, as protons are used by the mitochondria for oxidative phosphorylation. When the exercise intensity increases beyond steady state or there is a reduction in oxygen availability that there is a need for greater reliance on ATP regeneration from glycolysis and the phosphagen system (69). The ATP that is supplied from these non-mitochondrial sources is eventually used to fuel muscle contraction, which increases proton release and causes the acidosis that accompanies intense exercise. Lactate production increases under these cellular conditions to prevent Pyruvate accumulation and supply the NAD + needed for the second phase of glycolysis. Thus increased lactate production coincides with cellular acidosis.

Secondarily to the energetic effects are the cross sectional area changes that occur within the cell itself. The shifting of water and pooling of blood is what is commonly referred too as the "*pumped*" look. Increased perfusion directly increases muscle CSA. Edema, water shifting caused by hyperosmolarity and fluid pressures can also cause this temporary increase (70-72).

The human body is composed of 50-60% water, which corresponds to ~70% of lean body mass being water. Skeletal muscle amounts to ~40% of body weight, of which in the resting state 75% is water, accounting for around one-half the body water. The distribution of total muscle water in muscle at rest is ~90% cellular, ~9% in interstitial spaces, and ~1% in plasma.

The fluid distribution volumes are substantially changed during muscular activity. During exercise, there is an acute uptake of fluid by the active muscle cells; hyperosmolarity is one mechanism that explains this shift.

Some of the osmolytes that may be responsible for this are lactate, potassium, sodium and chloride (73). Another osmolytes that appears to have a profound effect on cellular volume is CrP (Creatinephosphate) (74). During exercise CrP is broken down to 1 mol of Creatine and 1 mol of inorganic Phosphate, the new steady state level effect on osmolality of this breakdown may be considerable causing increased water shifting to occur (75).

Now that we have gone through several mechanisms that can contribute to the inhibitory signalling during resistance training let's begin to peace it together and knit a plan of action to counter or at least diminish the effect.

Applying the science

M-Time-Making fatigue look retarded

When I first began reviewing the translational mechanisms involved in hypertrophy my beliefs were pretty well in line with the norm. Do a set, rest, do another, rest, this has been established as the way to not only provide enough work but also provide enough metabolic influence to increase the metabolic signalling chain as well.

During all my research it's rare to see human studies that tried to actually manipulate fatigue and strain in any way except for the conventional set/rest scheme. Although some bodybuilders have used anecdotal variations of a rep/rest scheme most of these revolved around either increasing the inroad to fatigue via continuation of a set after substantial fatigue or in the case of competitive lifters, the use of singles for neural conditioning and surpassing plateaus in strength.

Not that there is anything wrong with either of these situations but in essence they are not aimed at reducing the inhibitory effects of fatigue on force and subsequently strain or the inhibitory effects of increased AMPK elevations (76).

It wasn't until I was reading a study I referred too in the contraction section dealing with strain by Butterfield and Herzog that I began to piece it together.

Delving into many studies that manipulated the time between reps to see how this influenced many signalling events and the force fatigue relationship. Several studies on rats by Booth and Wong, the group of Farrell, Kubica, Jefferson and Kimball gave me the information I was looking for (77-81).

Looking further on force reduction and fatigue I also began to see a pattern where AMPK and energetics where strictly tied (82). A drastic reduction in metabolites, mostly revolving around the phosphagen system, caused a dramatic elevation in AMPK and tying that to the earlier work I saw on hypertrophy and protein synthesis I began to see more than just a casual relationship emerge.

Taking into account that any type of repetitive contractions have a larger influence on energy metabolism and that increasing the intensity only compounds this, I tried a very simple experiment.

In my weak arm I used my known 8-10RM during dumb bell curls and used a 5 second rest between each rep (what I have termed M-Time), one where I tried to remove all tension by setting the weight down after each dumb bell curl, just to make sure there was no occlusionary effect by holding onto the weight. In my strong arm I used a conventional set of my 8-10 RM to failure. I was astonished when I finally stopped doing reps in my weak arm after the 20^{th} rep, yes 20 reps with my 8-10 RM. I was amazed and suffice it to say my strong arm failed on cue, right on the 10^{th} rep and I mean failed, no way could I have gotten another rep. Others who have participated in this experiment experienced similar or even more extraordinary results. One participant actually achieved 42 reps before hitting failure when using M-Time reps with his know 8RM.

For any readers who are reading this for the first time and would like to try a simple experiment then follow what I have mentioned above, try it and see for yourself how this can dramatically change your training.

Progressive Work Overload-Getting it done

Secondly much of my research has shown or actually proven what several well-known trainers, have said now for some time. In order to grow one must progressively increase the work that the muscle has been subjected too. Now since work is a product of load and distance moved, in our case reps, how we increase work is important. Increasing work via increasing the load has shown dramatic results in not only protein synthesis but also hypertrophy (77-81), yet increasing the number of reps has a much larger influence on the metabolic efficiency of the muscle cell. When trying to accommodate this into this training method this simplest solution is to keep a consistent number of reps throughout the entire cycle while periodically increasing the load.

Contraction Mode

Much has been said about which contraction mode (eccentric or concentric) contributes more to hypertrophy and even though I am mentioning this in this book I am not going to go into great detail. Suffice it to say that even though eccentrics appear to cause more micro trauma than concentrics the most important aspect of training is progressing the work via mechanisms I alluded to above. In the case of this book eccentrics may not be necessary as we will be able to increase the work with heavy enough loads that continually increase the translation efficiency, which is truly the most critical event in hypertrophy of skeletal muscle.

Chapter 2- The Routine

M-Time – The Max Factor

M-Time is the time between each rep, after each rep the weight should be racked or set down and gotten completely out of your hands for the duration of the M-Time. This time can be manipulated as advancing fatigue ensues, IE first few reps use 3-5 seconds, next 5 to 10 - use 7 seconds, during the last 5 use 10 seconds. The starting time is usually going to be dictated by your own recovery from repetitive contractions and the intensity you are using. As the cycle progresses the M-Time may need to be increased to combat the effects of fatigue from heavier loading. The ideal starting time will vary and some experimentation will probably be needed to find the adequate time to use. In any case the M-Time should be used from the very first rep.

Frequency

As we've mentioned in the previous chapter once per week isn't going to cut it when you are trying to build as much muscle tissue in the shortest amount of time possible. With that said the workout is set up in an alternating workout fashion, A&B routines, they are both full body workouts but may be split to upper/lower, push/pull or whatever you deem necessary to fit into your training schedule.

Each Body part should be hit at least 2 times per week with at least 1 set of the primary movement and if needed 1 set of the secondary.

A typical implementation would be-

Monday and Thursday A routine,
Tuesday and Friday B routine, this can be arranged in any fashion depending on your training level or schedule.

Other examples;
3X week
Week 1

Monday-A
Wends-B
Fri-A
Week 2
Monday-B
Wends-A
Fri-B

2X week
Monday-A
Thursday-B

Rep Cadence and Tempo

Each Compound movement IE the first movement for each exercise should have a cadence of as fast as possible concentric, a controlled eccentric. After each complete rep is performed the weight should be racked for the M-Time being used. (see M-Time above)

Each isolation or subsequent movement (if chosen to do so) should be performed with as fast as possible concentric and a controlled eccentric. Again after each rep the weight should be racked for the M-time being used.

Rest Between Sets

If choosing to do multiple sets, I only recommend one, the rest between sets should allow for enough strength recovery to successfully complete at least 80% of the same number of reps as the previous set.

Working in a circuit fashion may be advantageous as this may allow enough time between sets but if working in a gym where equipment availability is an issue then simply use a rest period as described in the previous paragraph.

Bicep and Tricep Work

Although direct bicep and tricep work may not be necessary since many of the pulling and pushing movements already activate these muscles many trainees simply can not have a successful workout without the addition of direct upper arm work. With this in mind you may add in any of your favorite bi and or tri work but I do not recommend doing this more than 1 or 2X week and I recommend the volume be kept low for each workout these are used. If you do I also recommend you use the same set up, a compound followed by an isolation exercise that concentrates on stretch, racking the weight between reps.

Bicep Recommendation-following your last set of Back exercises add 1 or 2 sets of incline DB curl, concentration curl, BB curl or whatever isolation exercise you choose to use.

Tricep Recommendation-following your last pressing/pushing movement for chest or shoulders add 1 or 2 sets of Tricep Extensions, pushdowns or whatever isolation exercise you choose to use.

Muscle Specific

This setup may also be used in conjunction with any individual muscle group in order to specifically induce growth to lagging muscle groups or address symmetry issues.

Progression and starting intensity.

The progression is set up in an undulating linear fashion. There are 3 phases to this program.

Phase 1- Using your 10 RM load 4 workouts per week
Phase 2- Using your 8 RM load 4 workouts per week
Phase 3- Using your 6 RM load 4 workouts per week

Each phase starts out at 75% of the RM for that phase and increases over the duration to a maximum of 110% of the RM.

Example.
10RM load = 100 lbs
Week 1
Workout 1, A routine- 20 Reps –75 lbs.
M-Time- 1 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.
Workout 2, B routine- 20 reps –75 lbs.
M-Time- 1 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.

Workout 3, A routine-20 reps – 80 Lbs
M-Time- 2 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.
Workout 4, B routine- 20 reps –80 lbs.
M-Time- 2 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.

Week 2
Workout 5, A routine-20 reps – 85 Lbs
M-Time- 3 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.
Workout 6, B routine- 20 reps –85 lbs.
M-Time- 3 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.

Workout 7, A routine-20 reps – 90 Lbs
M-Time- 4 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.
Workout 8, B routine- 20 reps –90 lbs.
M-Time- 4 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.

Week 3
Workout 9, A routine-20 reps – 95 Lbs
M-Time- 3 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.
Workout 10, B routine- 20 reps –95 lbs.
M-Time- 3 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.

Workout 11, A routine-20 reps – 100 Lbs
M-Time- 4 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.
Workout 12, B routine- 20 reps –100 lbs.
M-Time- 4 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.

Week 4
Workout 13, A routine-20 reps – 105 Lbs
M-Time- 5 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.
Workout 14, B routine- 20 reps –105 lbs.
M-Time- 5 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.

Workout 15, A routine-20 reps – 110 Lbs
M-Time- 6 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.
Workout 16, B routine- 20 reps –110 lbs.
M-Time- 6 sec. Or whatever is needed to complete 20 reps without achieving any significant burn.

For planning your routine please download the Excel Spreadsheet @ http://www.hypertrophy-research.com/maxstim/maxstim.xls

Increasing the reps-The system is based on 20 reps throughout the cycle. This can be changed if desired. However I do recommend trying to stick to at least 15- 20 reps as it allows sufficient TUT and it is much easier than trying to identify varying reps when fatigue is manipulated in this way.

Decreasing the duration- to decrease the duration from 12 weeks to fewer simply remove the duplicate intensity workouts IE each or every other workout would increase in intensity.

Work Out A
Follow the Exercise order, thigh and calf work may be put last if you prefer
Thighs-
Squat or Leg Press
Super set with Leg Ext or Sissy Squat (if desired)
Leg Curl
Super Set with SLDL or Good Morning (if desired)
Calves-
Standing Calve Raise
Superset with Donkey Calve Raise on Blocks (if desired)
Back-
Wide Grip Pronated Pull Up/Down
Bent BB Row to Bottom of Rib Cage or similar
Chest-
Flat Bench BB/Dips or DB Bench Press
Superset with Fly (if desired)
Shoulder-
Military Press or Shoulder DB Press
Superset with DB Incline Lateral Raise (if desired)
Traps, Rear Deltoid-
BB Laying Chin Row or Seated High Row
Superset with Prone or Bent Shoulder Lateral (if desired)

Workout B
Thigh-
Squat or Leg Press
Super set with Leg Ext or Sissy Squat (if desired)
Leg Curl
Super Set with SLDL or Good Morning (if desired)
Calves-
Standing Calve Raise
Superset with Donkey Calve Raise on Blocks (if desired)
Back-
Narrow Grip Supinated Pull Up/Down
Bent BB Row narrow grip to beltline
Chest-
20 Degree BB or DB Bench Press
Superset with Incline Fly (if desired)
Shoulder-
Primary-Upright Row
Secondary-Superset with Upright Lateral Raise (if desired)
Traps, Rear Deltoid-
DB or BB Shrugs Seated or Standing
Superset with Laying or Bent Shoulder Lateral (if desired)

If knees, shoulders or back is of concern then substitution of exercises can be done as long as plane of movement and degree of stretch is relatively equal for the substitutions. Whether done on free weight or machine should not make a difference. Machines will make this program inherently easier as the racking movement is already accommodated for in most machines. **When substituting exercises always keep safety as your top priority.**

Tracking

I have included a preformatted spreadsheet for your convenience.

Q&A Forum Link

If you have any questions about this program please feel free to contact me, or those who have experience with this training, via the Max-Stimulation discussion forum located at http://www.max-stimulation.hypertrophy-research.com.

Thank You,

Daniel Moore

References

1. Wolfe RR Effects of amino acid intake on anabolic processes Can J Appl Physiol. 2001;26 Suppl:S220-7
2. Nader, GA. Translational control: implications for skeletal muscle hypertrophy. Clin Orthop Relat Res. 2002 Oct;(403 Suppl):S178-87. Review.
3. Bolster, DR. Translational control mechanisms modulate skeletal muscle gene expression during hypertrophy. Exerc Sport Sci Rev. 2003 Jul;31(3):111-6. Review.
4. Chen, Y.-W Response of rat muscle to acute resistance exercise defined bytranscriptional and translational profiling. *J. Physiol.* 545:27–41, 2002.
5. Hershey, J. W. B. The pathway and mechanism of initiation of protein synthesis. In: *Translational Control of Gene Expression*,edited by M. B. Mathews. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 2000, p. 33–88.
6. Frank, J. Toward an understanding of the structural basis of translation *Genome Biology* 2003, 4:237
7. Bolster, DR. Regulation of protein synthesis associated with skeletal muscle hypertrophy by insulin-, amino acid- and exercise-induced signalling Proceedings of the Nutrition Society (2004), 63, 351–356
8. Nissim, H. Upstream and downstream of mTOR *Genes & Dev.* 2004, 18: 1926-1945
9. Nader GA . Intracellular signaling specificity in skeletal muscle in response to different modes of exercise. *J Appl Physiol 2001:*90, 1936-1942.
10. Farrell PARegulation of protein synthesis after acute resistance exercise in diabetic rats. *Am J Physiol 1999:*276, E721-E727.
11. Bodine SC, Akt/mTOR pathway is a crucial regulator of skeletal muscle hypertrophy and can prevent muscle atrophy *in vivo*. *Nature Cell Biol 2001:* 3, 1014-1019.
12. Baar K. Phosphorylation of p70S6k correlates with increased skeletal muscle mass following resistance exercise. *Am J Physiol 1999:* 276, C120-C127.
13. Bolster, DR.Immediate response of mammalian target of rapamycin (mTOR)-mediated signalling following acute resistance exercise in rat skeletal muscle. *J Physiol 2003:*553.1, 213-220.
14. Neufer PD. Exercise induces a transient increase in transcription of the GLUT-4 gene in skeletal muscle. *Am J Physiol Cell Physiol 1993:* 265, C1597-1603.
15. Vandenburgh HH. Mechanical forces and their second messengers in stimulating cell growth in vitro. *Am J Physiol Regul Integr Comp Physiol* 262: R350–R355, 1992.
16. Moore D. Myofibrillar and collagen protein synthesis in human skeletal muscle in young men after maximal shortening and lengthening contractions. *Am J Physiol Endocrinol Metabol* 288: E1153-E1159, 2005.
17. Phillips S. Mixed muscle protein synthesis and breakdown after resistance exercise in humans. *Am J Physiol Endocrinol Metab* 273: E99-107,1997.
18. Hortobagyi T. Adaptive responses to muscle lengthening and shortening in humans. *J Appl Physiol* 80: 765–772, 1996.
19. Jones DA. Human muscle strength training: the effects of three different regimens and the nature of the resultant changes. *J Physiol* 391: 1–11, 1987.
20. Cuthbertson, D.J. Anabolic signaling and protein synthesis in human skeletal muscle after dynamic shortening or lengthening exercise. Am J Physiol Endocrinol Metab. 2006 Apr;290(4):E731-8.
21. Huijing, P.A. Adaptation of muscle size and myofascial force transmission: a review and some new experimental results Scand J Med Sci Sports 2005: 15: 349–380
22. Butterfield, T.A. Repetitive stretch-shortening cycles: Quantification of muscle fiber strain during in vivo 99:593-602, 2005. *Journal of Applied Physiology*
23. Hornberger, T.A. Proceedings of the Nutrition Society (2004), 63, 331–335
24. Plopper, G.E. (1995) Convergence of integrin and growth factor receptor signaling pathways within the focal adhesion complex. Molecular Biology of the Cell 6, 1349–1365.
25. Sackin, H. Mechanosensitive channels. *Annu Rev Physiol* 57: 333-353, 1995)
26. Hornberger,T.A. Mechanical stimuli regulate rapamycin-sensitive signalling by a phosphoinositide 3-kinase-, protein kinase B- and growth factor-independent mechanism Biochem. J. (2004) 380, 795–804)
27. Rennie, M.J. Branched-Chain Amino Acids as Fuels and Anabolic Signals in Human Muscle J. Nutr. 136: 264S–268S, 2006.
28. Bohe´ J, Human muscle protein synthesis is modulated by extracellular, not intramuscular amino acid availability: a dose response study. J Physiol. 2003;552:315–24.
29. Buse, M.G. Leucine: a possible regulator of protein turnover in muscle. J Clin Invest. 1975;56:1250–61.
30. Buse, M.G. Studies concerning the speci.city of the effect of leucine on the turnover of proteins in muscles of control and diabetic rats. Biochim Biophys Acta. 1977;475:81–9.
31. Alvestrand, A.. Infuence of leucine infusion on intracellular amino acids in humans. Eur J Clin Invest. 1990;20:293–8.
32. Kimball, S.R. Signaling Pathways and Molecular Mechanisms through which Branched-Chain Amino Acids Mediate Translational Control of Protein Synthesis J. Nutr. 136: 227S–231S, 2006.
33. Bodine, S.C. (2001) Akt/mTOR pathway is a crucial regulator of skeletal muscle hypertrophy and can prevent muscle atrophy in vivo. Nat. Cell Biol. 3, 1014–1019)
34. Biolo, G.Increased rates of muscle protein turnover and amino acid transport after resistance exercise in humans. *Am. J. Physiol.* 268 (*Endocrinol. Metab.* 31): E514–E520, 1995.

35. Chesley, A. Changes in human muscle protein synthesis after resistance exercise. *J. Appl. Physiol.* 73: 1383–1388, 1992.
36. Phillips, SM. Mixed muscle protein synthesis and breakdown after resistance exercise in humans. *Am. J. Physiol.* 273 (*Endocrinol. Metab.* 36): E99–E107, 1997.
37. Atherton, PJ. Selective activation of AMPK-PGC-1alpha or PKB-TSC2-mTOR signaling can explain specific adaptive responses to endurance or resistance training-like electrical muscle stimulation. FASEB J. 2005 May;19(7):786-8.
38. Hardie, DG. (1998) *Annu. Rev. Biochem.* 67, 821–855
39. Kemp, BE. (1999) *Trends Biochem. Sci.* 24, 22–25
40. Hayashi, T. Metabolic stress and altered glucose transport: activation of AMP-activated protein kinase as a unifying coupling mechanism. Diabetes. 2000 Apr;49(4):527-31.
41. Hardie, D. AMP-activated protein kinase: the energy charge hypothesis revisited. *BioEssays* 23:1112–1119,2001.
42. Winder, W. Inactivation of acetyl-CoA carboxylase and activation of AMP-activated protein kinase in muscle during exercise. *Am. J. Physiol.* 270:E299–E304, 1996.
43. Ponticos, M. Dual regulation of the AMP-activated protein kinase provides a novel mechanism for the control of creatine kinase in skeletal muscle. *EMBO J.* 17:1688–1699, 1998.
44. Sweeney HL. The importance of the creatine kinase reaction: the concept of metabolic capacitance. *Med Sci Sports Exerc* 26:30–36, 1994.
45. Meyer R. Cellular processes integrating the metabolic response to exercise. In: *Handbook of Physiology.Exercise: Regulation and Integration of Multiple Systems*. Bethesda, MD: Am. Physiol. Soc., 1996, sect. 12, part III, chapt. 18, p. 841–869.
46. Cooke R. The inhibition of rabbit skeletal muscle contraction by hydrogen ions and phosphate. *J Physiol (Lond)* 395: 77–97, 1988.
47. Nosek T.M . It is diprotonated inorganic phosphate that depresses force in skinned skeletal muscle fibers. *Science* 236: 191–193, 1987.
48. Stephenson D.G. Events of the excitation-contraction-relaxation (E-C-R) cycle in fast- and slow-twitch mammalian muscle fibres relevant to muscle fatigue.*Acta Physiol Scand* 162: 229–245, 1998.
49. Sahlin K. Energy supply and muscle fatigue in humans. *Acta Physiol Scand* 162: 261–266, 1998.
50. Favero T.G. Lactate inhibits Ca2_-activated Ca2_-channel activity from skeletal muscle sarcoplasmic reticulum. *J Appl Physiol* 82: 447–452, 1997. p. 841–869.
51. Fryer M.W. Effects of creatine phosphate and Pi on Ca2_ movements and tension development in rat skinned skeletal muscle fibres. *J Physiol (Lond)* 482: 123–140, 1995.
52. Williams JH. Contractile apparatus and sarcoplasmic reticulum function effects of fatigue, recovery, and elevated Ca2_. *J Appl Physiol* 83: 444–450, 1997.
53. Baker A>J. Slow force recovery after long-duration exercise: metabolic and activation factors in muscle fatigue. *J Appl Physiol* 74: 2294–2300, 1993
54. Chasiotis D. ATP utilization and force during intermittent and continuous muscle contractions. *J Appl Physiol* 63: 167–174, 1987.
55. Hogan M.C. Contraction duration affects metabolic energy cost and fatigue in skeletal muscle. *Am J Physiol Endocrinol Metab* 274: E397–E402, 1998. 783–789, 1993.
56. Russ D.W. Metabolic cost of different stimulation trains during fatigue of skeletal muscle (Abstract). *FASEB J* 13: A690, 1999.
57. Spriet L.L. ATP utilization and provision in fast-twitch skeletal muscle during tetanic contractions. *Am J Physiol Endocrinol Metab* 257: E595–E605, 1989.
58. Enoka R.M. Neurobiology of muscle fatigue. *J Appl Physiol* 72: 1631–1648, 1992.
59. Boska M. ATP production rates as a function of force level in the human gastrocnemius/soleus using 31P MRS. *Magn Reson Med* 32: 1–10, 1994.
60. Baker A.J. Energy use by contractile and noncontractile processes in skeletal muscle estimated by 31P-NMR. *Am J Physiol Cell Physiol* 266: C825–C831, 1994.
61. Russ D. Effects of muscle activation on fatigue and metabolismin human skeletal muscle *J Appl Physiol* 92: 1978–1986, 2002
62. Bangsbo J. Muscle blood flow and oxygen uptake in recovery from exercise. *Acta Physiol Scand* 162: 305–312, 1998.
63. Barcroft H. The blood flow through muscle during sustained contraction. *J Physiol* 97: 17–31, 1939.
64. Wigmore, D.M. MRI measures of perfusion-related changes in human skeletal muscle during progressive contractions. J Appl Physiol. 2004 Dec;97(6):2385-94.
65. Sadamoto T. Skeletal muscle tension, flow, pressure, and EMG during sustained isometric contractions in humans. Eur J Appl Physiol Occup Physiol. 1983;51(3):395-408.
66. Sjogaard, G. Muscle blood flow during isometric activity and its relation to muscle fatigue. Eur J Appl Physiol Occup Physiol. 1988;57(3):327-35.
67. Hogan, M.C. Effect of contraction frequency on the contractile and noncontractile phases of muscle venous blood flow. J Appl Physiol. 2003 Sep;95(3):1139-44.
68. Mason, S.D. Loss of skeletal muscle HIF-1alpha results in altered exercise endurance. PLoS Biol. 2004 Oct;2(10):e288.
69. Vaghy PL. Role of mitochondrial oxidative phosphorylation in the maintenance of intracellular pH. *J Mol Cell Cardiol* 11: 933–940, 1979.
70. Nygren, A.T. Changes in cross-sectional area in human exercising and non-exercising skeletal muscles. Eur J Appl Physiol. 2000 Feb;81(3):210-3.
71. Nygren, A.T. Water exchange induced by unilateral exercise in active and inactive skeletal muscles. J Appl Physiol. 2002 Nov;93(5):1716-22.
72. Sjoogard, G. Water and ion shifts in skeletal muscle of humans with intense dynamic knee extension. Am J Physiol. 1985 Feb;248(2 Pt 2):R190-6.
73. Sejersted, O.M. (2000). Dynamics and consequences of potassium shifts in skeletal muscle and heart during exercise. *Physiol Rev* 80, 1411–1481.

74. Lindinger, M.I. Plasma volume and ion regulation during exercise after low-carbohydrate and high-carbohydrate diets. *Am J Physiol Regulatory Integrative Comp Physiol* 266: R1896-R1906, 1994
75. Trombitas, K. Contraction-induced movements of water in single fibres of frog skeletal muscle. *J Muscle Res Cell Motil* 14: 573-584, 1993
76. Thomson D. Diminished overload-induced hypertrophy in aged fast-twitch skeletal muscle is associated with AMPK hyperphosphorylation J. Appl. Physiol. 98:557-564, 2005.
77. Farrell, P.A. Hypertrophy of skeletal muscle in diabetic rats in response to chronic resistance exercise. J. Appl. Physiol. 87(3): 1075-1082, 1999.
78. Kubica, N. Resistance Exercise Increases Muscle Protein Synthesis and Translation of Eukaryotic Initiation Factor 2B mRNA in a Mammalian Target of Rapamycin-dependent Manner J. BIOLOG. CHEM. 280(9): 7570-7580, 2005
79. Farrell, S.R. Immediate response of mammalian target of rapamycin (mTOR)-mediated signalling following acute resistance exercise in rat skeletal muscle J. Physiol. 2003;553;213-220;
80. Farrell, P.A. Effects of intensity of acute-resistance exercise on rates of protein synthesis in moderately diabetic rats. J. Appl. Physiol. 85(6):2291-2297, 1998.
81. WONG, T.S. Skeletal muscle enlargement with weight-lifting exercise by rats. J. Appl. Physiol. 65(2): 950-954, 1988.
82. Ponticos, M. Dual regulation of the AMP-activated protein kinase provides a novel mechanism for the control of creatine kinase in skeletal muscle The EMBO Journal Vol.17 No.6 pp.1688–1699, 1998