MUSCLE

Key Concepts

- there is an ordered sequence of events involved in skeletal muscle contraction during exercise from motor cortical activation to excitation-contraction coupling and the generation of force and power
- there are several energy dependent processes involved in muscle contraction and this energy is provided directly by ATP
- ATP levels within skeletal muscle are relatively low and their rate of utilization is directly related to exercise intensity
- ATP is generated within metabolic pathways ("energy systems") that involve both substrate level and oxidative phosphorylation
- these energy systems are creatine phosphate degradation, "anaerobic" glycolysis (glucose ➔ lactate) and the oxidative metabolism of carbohydrate (CHO) and lipid/fat, with a small contribution from protein

- the motor unit comprises the α-motoneuron and all the muscle fibres that it innervates – the nerve has a major influence on the characteristics of the muscle fibres via its firing frequency and released trophic factors
- human skeletal muscles are composed of two main types of motor units/muscle fibres – type I (slow) and type II (fast), that differ in their contractile, biochemical and morphological characteristics
- motor units are recruited in proportion to the force/intensity of contraction and from smallest (slow) to largest (fast) – Henneman's "size principle"
- muscle fibre type distribution differs between athletes specialized for strength/power and endurance sports – this reflects the interaction between genetic and environmental (mainly training) factors

- muscles undergo specific adaptations to acute and chronic, depending on the mode, intensity and duration of exercise – traditionally, endurance, sprint and resistance exercise training programs have been considered to result in quite different adaptations, although in recent years it has been recognized that there is greater overlap between these modes
- various stimuli during muscle contraction are detected by specific proteins/kinases resulting in recruitment and activation of various processes that affect gene transcription, translation and protein synthesis – ultimately, changes in the expression and/or activity of key proteins affects the size and functional properties of skeletal muscle

Muscle Contraction & Energetics

The sequence of events in muscle contraction:

- motor cortical activation
- descending motor activation and α-motoneuron excitation
- neuromuscular transmission
- sarcolemma and t-tubule excitation
- excitation-contraction coupling – SR Ca^{2+} release
- contractile activation – actin-myosin cross-bridge cycling
- ATP utilization at various steps

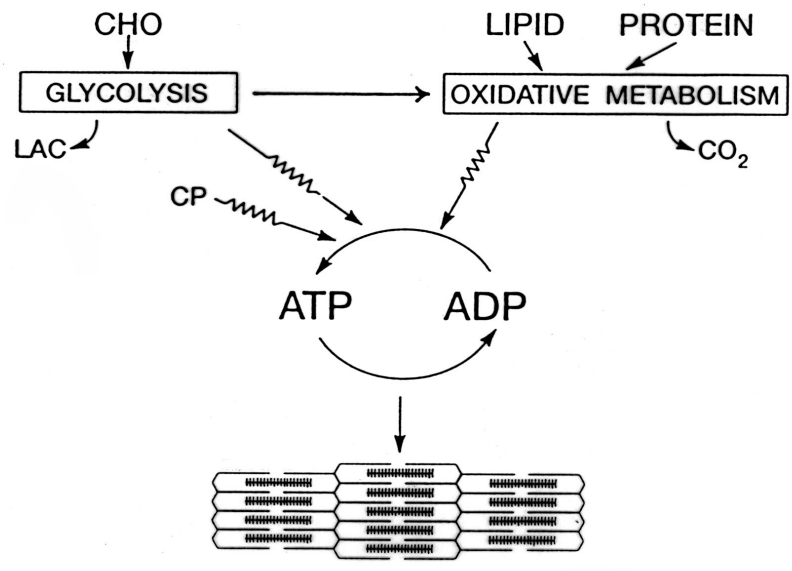
ATP-dependent process in skeletal muscle:
cross-bridge cycling (myosin ATPase)
sarcolemmal excitability (Na^+/K^+ ATPase)
calcium pumping into sarcoplasmic reticulum (SERCA – Ca^{2+} ATPase)

Skeletal muscle ATP generation during exercise:
Substrate level phosphorylation

- ATP/CP
- "anaerobic" glycolysis

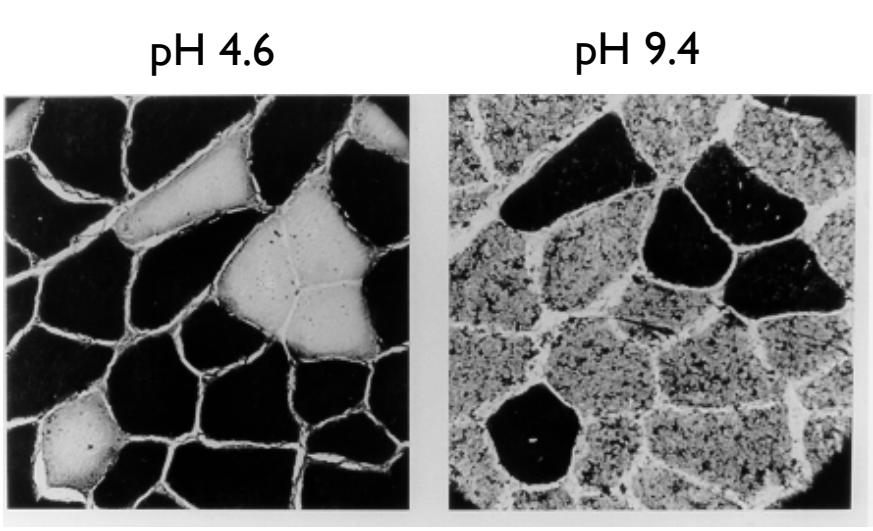
Oxidative phosphorylation

- CHO and lipid/fat (small contribution from protein)



Muscle Fibre Types

Human skeletal muscles are composed of two main types of motor units/muscle fibres – type I (slow) and type II (fast), that differ in their contractile, biochemical and morphological characteristics. Traditionally, muscle fibre type distribution was determined histochemically by staining cut, frozen sections of muscle biopsy samples for myosin ATPase after either acidic or alkaline preincubation. More recently, muscle samples can be analysed by immunoblotting with specific antibodies for different isoforms of the myosin heavy chain proteins.

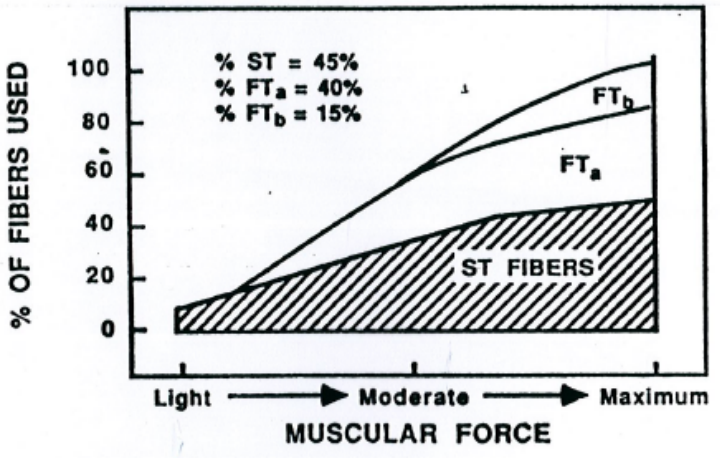


Myosin ATPase staining in serial sections after either acidic or alkaline pre-incubation. Type I fibres stain dark after acidic, and type II dark after alkaline, pre-incubation.

Properties*	**I**	**IIa**	**IIx**
Alternative names	SO, ST	FOG, FTa	FG, FTb
Myosin heavy chain isoform	MHC1	MHC2A	MHC2X
Time to peak tension (msec)	80	30	
Force/power output	+	++	+++
Endurance capacity	+++	++	+
Distribution in whole muscle (%)	50-55	30-35	10-20
Mitochondrial density	+++	++	+
Capillary density (cap/fibre)	4.2	4.0	3.2
Fibre area (μm^2)	5310	6000	5600

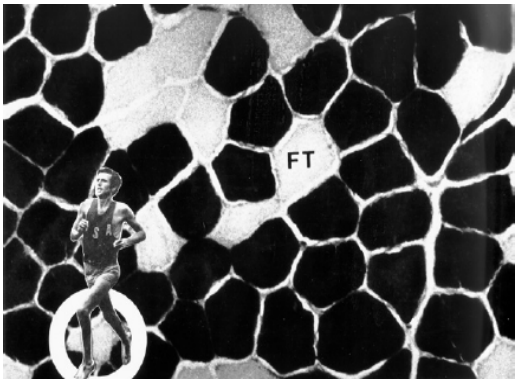
* Data are from vastus lateralis in untrained men

Muscle fibre recruitment during exercise is determined by the force/intensity and duration of exercise and occurs from small (type I) to larger (type II) motor units, according to Henneman's "size principle".

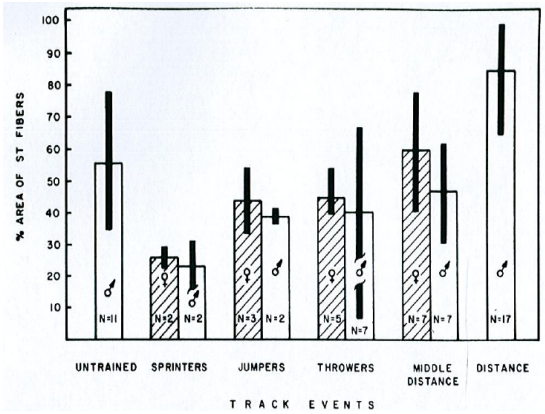


(Image courtesy of Prof. David Costill)

The muscle fibre type distribution differs between athletes specialized for strength/power and endurance sports – this reflects the interaction between genetic and environmental (mainly training) factors



(Image courtesy of Prof. David Costill)



(Image courtesy of Prof. David Costill; data from D.L. Costill et al. J. Appl. Physiol. 40: 149-154, 1976)

Muscle Adaptations to Exercise

The concept of "skeletal muscle plasticity" is well established in exercise physiology, based on observations that muscle function and size can be enhanced in response to increased loading, and reduced in response to unloading associated with inactivity. Traditional views are that endurance training increases the ability of muscle to undertake oxidative metabolism and resistance training increases the size of muscle. These probably represent the extremes of a continuum in which there are multiple adaptations depending on the nature, intensity and duration of the exercise stimulus.

Factors to consider in understanding muscle adaptations to exercise:
Stimuli

- Ca^{2+}, energy status, redox state, tension, temperature, metabolites, hormones?

Signalling

- CaMK, AMPK, MAPK, mTOR

Gene/mRNA/protein regulation by transcription factors/coactivators

- MEF2, GEF, MyoD, NFAT, PGC-1α, NRF-1, PPARδ?
- microRNAs

Muscle adaptations to endurance training:

- increased mitochondrial density and oxidative enzymes
- increased capillary density
- increased GLUT4 and enhanced muscle glycogen storage
- increased Na^+/K^+ ATPase activity
- fibre type changes??
- reduced CHO oxidation and lactate production and increased fat oxidation during exercise
- improved insulin action

Recently, there has been renewed interest in the potential of high intensity training ("sprint training") to elicit many of these adaptations with a considerably smaller time investment.

Muscle adaptations to resistance training:

- increased muscle force and power generating capacity
- increased neuromuscular recruitment
- muscle fibre hypertrophy and increased muscle cross-sectional area
- some studies have demonstrated metabolic adaptations with potential health benefits

Reading

Zierath, J. and J.A. Hawley. Skeletal muscle fiber type: influence on contractile and metabolic properties. PLoS Biol. 2(10): e348, 2004

http://www.plosbiology.org/article/info%3Adoi%2F10.1371%2Fjournal.pbio.0020348

Discussion Topic

"Sprinters are born, but marathoners are made". Consider this statement in the context of potential genetic and exercise training influences on skeletal muscle fibre type distribution.

Abbreviations

AdipoR1	adiponectin receptor 1
ADP	adenosine diphosphate
Akt	serine/threonine-specific protein kinase also known as protein kinase B
AMP	adenosine monophosphate
AMPK	AMP-activated protein kinase
AS160	Akt substrate of 160 kDa
ATP	adenosine triphosphate
BDNF	brain-derived neurotrophic factor
CaMKII	calcium/calmodulin-dependent kinase II
CAT	carnitine acyltranferase
CoA	co-enzyme A
CP (PCr)	creatine phosphate (phosphocreatine)
CPT	carnitine palmitoyltransferase
Cr	creatine
CSA	cross-sectional area
CXCL-1	chemokine (C-X-C motif) ligand 1
EMG	electromyogram
ETC	electron transport chain.
FABPc	fatty acid binding protein (cytosolic)
FAT/CD36	fatty acid transporter
FFA	free fatty acid
FGF	fibroblast growth factor
FoxO	forkhead box protein O
FSR	fractional synthetic rate (used in relation to protein synthesis)
FT	fast twitch fibre
G-1-P	glucose-1-phosphate
G-6-P	glucose-6-phosphate

GEF	GLUT4 enhancer factor
GLP-1	glucagon-like peptide-1
GLUT4	glucose transporter 4
Gly	glycogen
HAT	histone acetyltranferase.
HDAC5	histone deacetylase class II isoform 5
IGF-1	insulin-like growth factor 1
IL	interleukin
IM	inner mitochondrial membrane
IMTG	intramyocellular triglyceride
IRS	insulin receptor substrate
LAT1	L-type amino acid transporter
LIF	leukemia inhibitory factor
MAPK	mitogen activated protein kinase
MEF2A	myocyte enhancer factor isoform 2A
MHCI	myosin heavy chain isoform I
MHCII	myosin heavy chain isoform II
mTOR	mammalian target of rapamycin
MVC	maximal voluntary contraction
MyoD	a myogenic regulatory factor
NAD	oxidised nicotinamide adenine dinucleotide
NADH	reduced nicotinamide adenine dinucleotide
NFAT	nuclear factor of activated T-cells
OM	outer mitochondrial membrane
p38MAPK	p38 mitogen-activated protein kinase
PAS	periodic acid-Schiff
PGC-1α	peroxisome proliferator-activated receptor-α coactivator-1
PI3K	phosphatydilinositide-3 kinase
PM	plasma membrane
PPAR	peroxisome proliferator-activated receptor
ROS	reactive oxygen species
SIRT	sirtuin
SR	sarcoplasmic reticulum
ST	slow twitch fibre
TCA	tricarboxylic acid
TG	triglyceride/triacylglycerol
TnC	troponin C.
UCP-1	uncoupling protein 1