Tarbiat Modares University

FATIGUE

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INTRODCTION

- Physical exercise affects the equilibrium of the internal environment.
- During exercise the contracting muscles generate force or power and heat.
- Depending on the form of exercise, sooner or later sensations of fatigue and exhaustion will occur.
- The physiological role of these sensations is protection of the exercising subject from the deleterious effects of exercise.

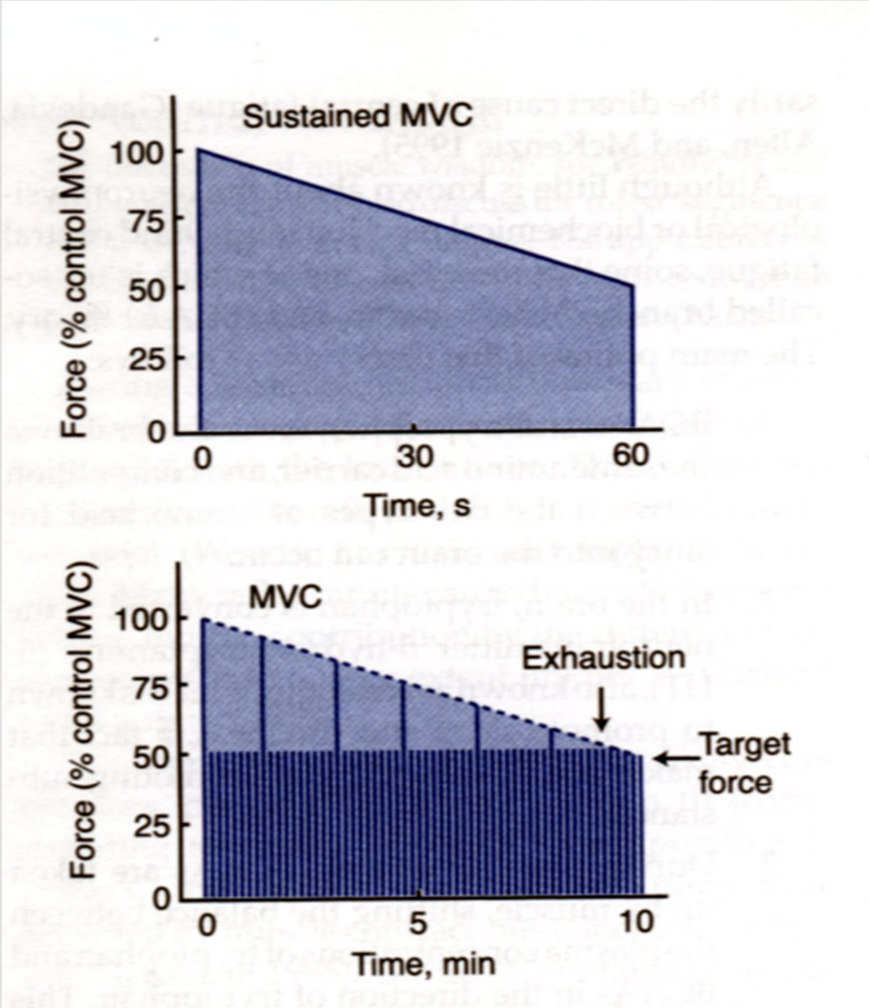
FATIGUE DEFINITION

- According to the dictionary *Trésor de la langue française informatisée*, **fatigue is a reduction of organisme forces following excessive work, too long a duration of work, or a defective functional state.**

- In 1983, **Edwards** defined muscle fatigue as **the inability to maintain the required power output**, and thus the degree of fatigue is dependent on the extent of decline in both force and velocity.

- The 1990, **a National Heart, Lung, and Blood Institute workshop on respiratory muscle** defined fatigue as “**a condition in which there is a loss in the capacity for developing force and/or velocity of a muscle, resulting from muscle activity under load which is reversible by rest**.”

WHEN FATIGUE PROCESS START?

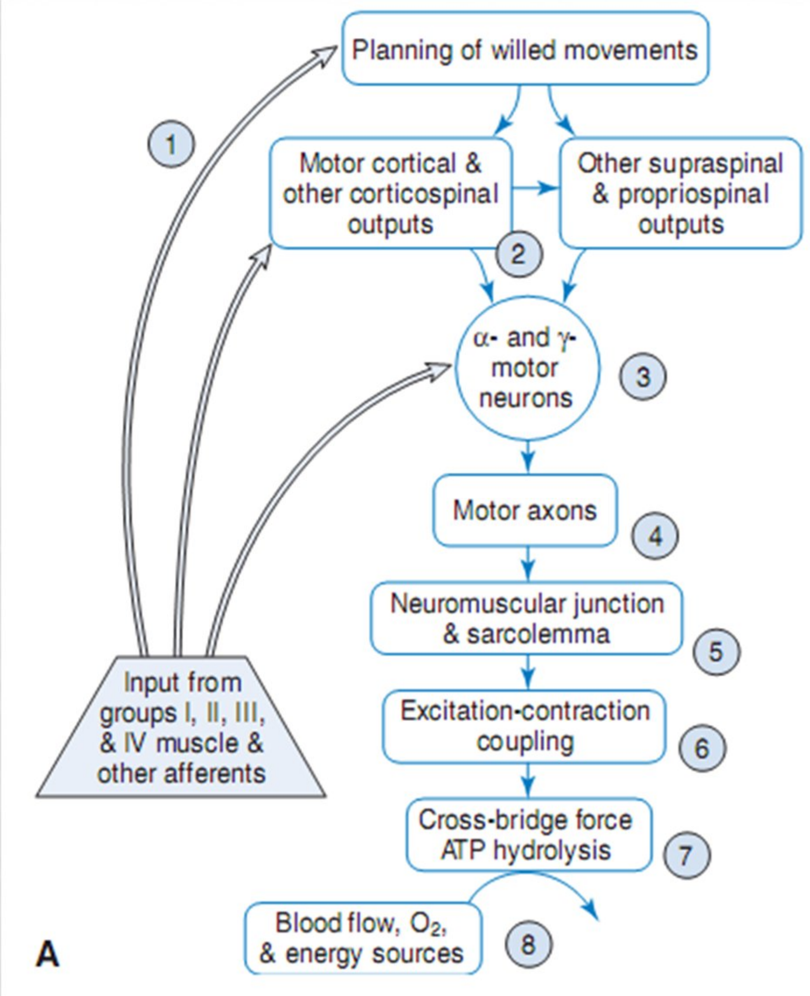


POTENTIAL SITES OF FATIGUE

Bigland-Ritchie(1984):

1. Excitatory input to higher motor centers
2. Excitatory drive to lower motor neurons
3. Motor neuron excitability
4. Neuromuscular transmission
5. Sarcolemma excitability
6. Excitation-contraction (E-C) coupling
7. Contractile mechanisms
8. Metabolic energy supply and metabolite accumulation

POTENTIAL SITES OF FATIGUE



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THE ETIOLOGY OF MUSCLE FATIGUE

- The etiology of muscle fatigue is complex as it results from multiple factors acting at various sites within the muscle (**peripheral fatigue**) and/or the central nervous system (CNS; **central fatigue**).

- The extent and time course of muscle fatigue is influenced by

- **The individual's age**
- **State of fitness**, and
- **The type of exercise performed**.

PHYSIOLOGICAL ASPECTS OF EXERCISE

Effects of Exercise on the Motor Unit

1- **Accumulation of Metabolites within Muscle Fibers**

- Increase in adenosine diphosphate (ADP)
- Accumulation of P_i
- Increased production of hydrogen ions (H_+)

They all have direct effects on

the efficiency of the cross-bridge interactions.

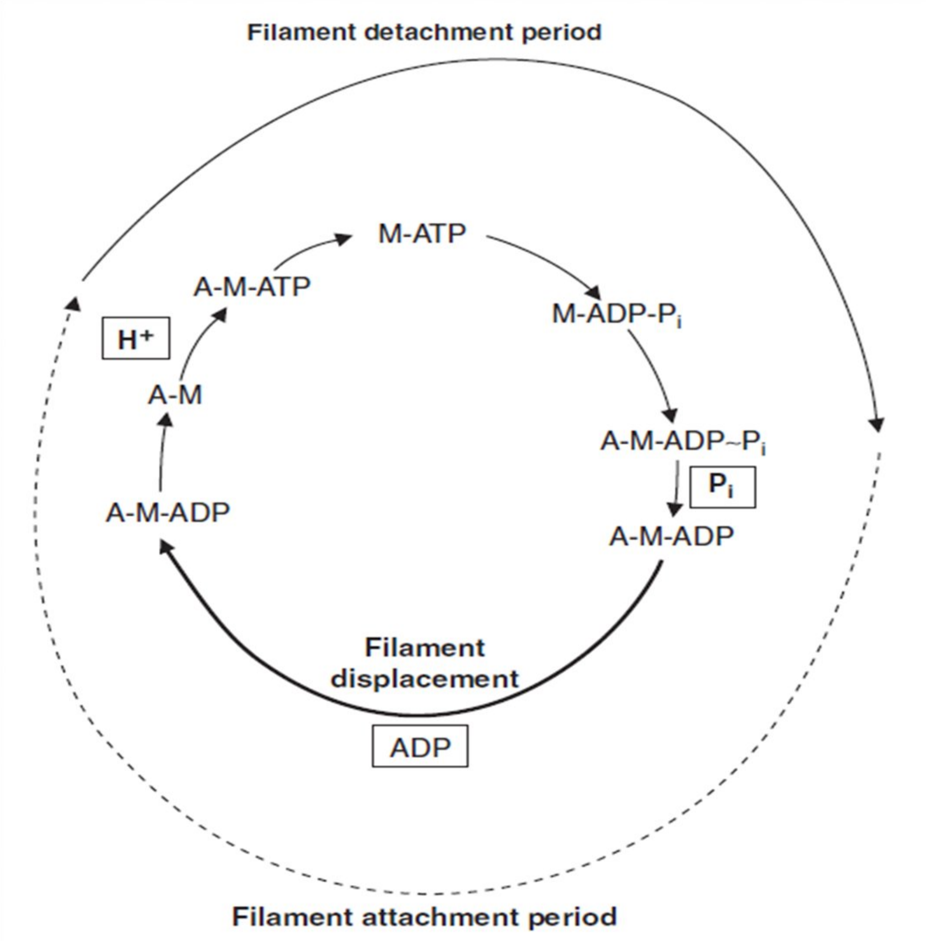
THE EFFICIENCY OF THE CROSS-BRIDGE

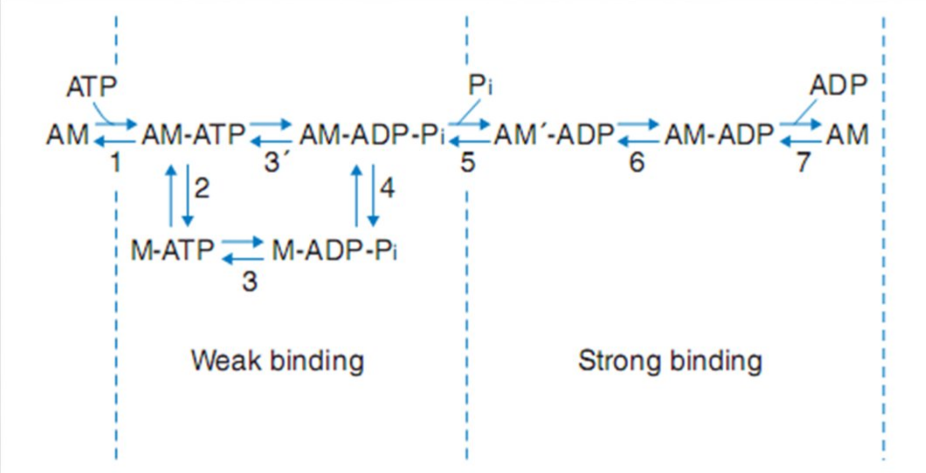
The efficiency of the cross-bridge interaction is estimated by two factors:

(i) **The duration of attachment and detachment of the actin and myosin filaments during the cross-bridge cycle**

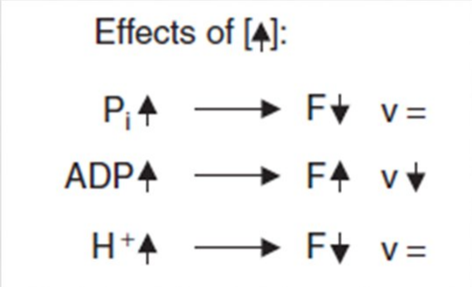
(ii) **The speed of the cross-bridge cycle**

MODEL OF THE CROSS-BRIDGE CYCLE



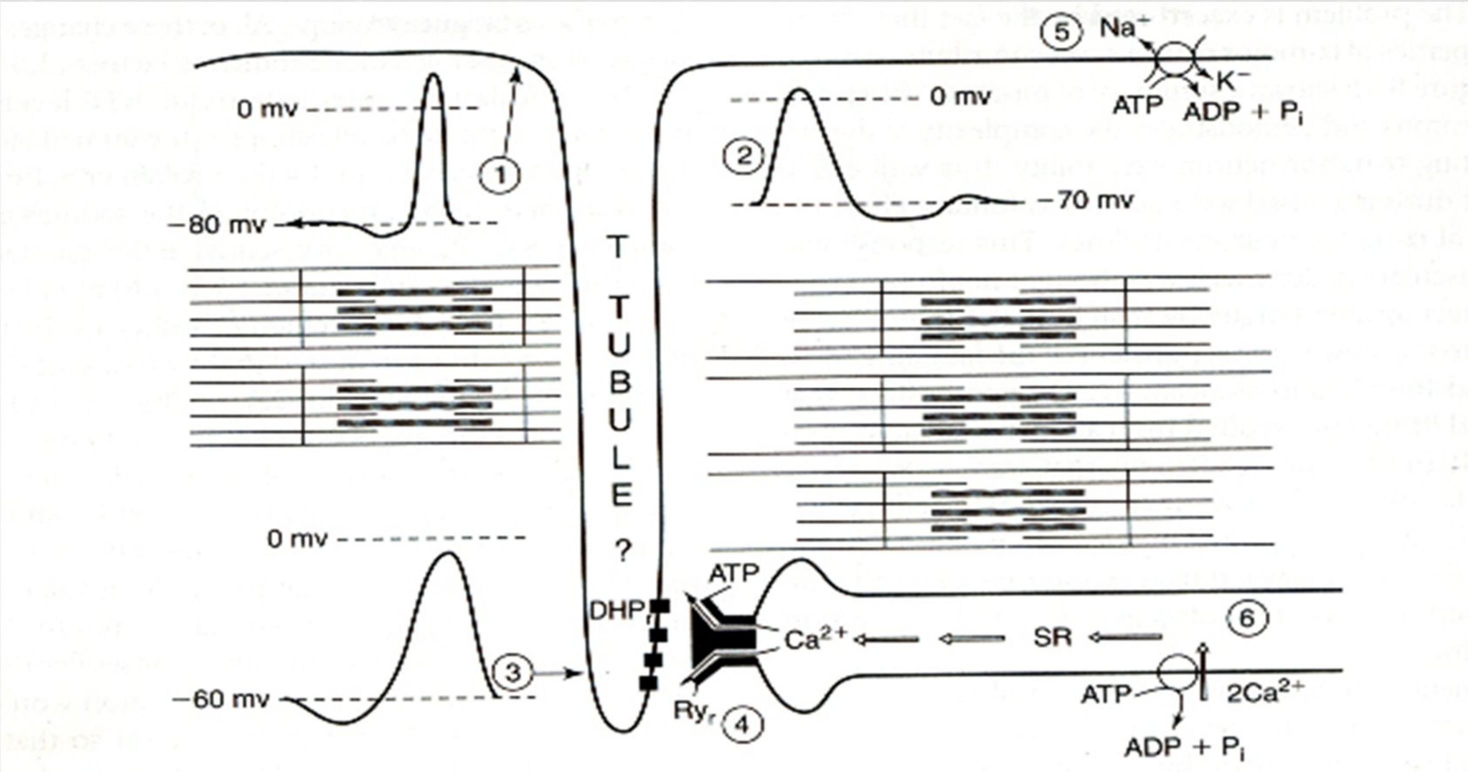


This kinetic scheme has proven useful in assessing the cellular mechanisms of muscle fatigue for those factors acting at the cross-bridge



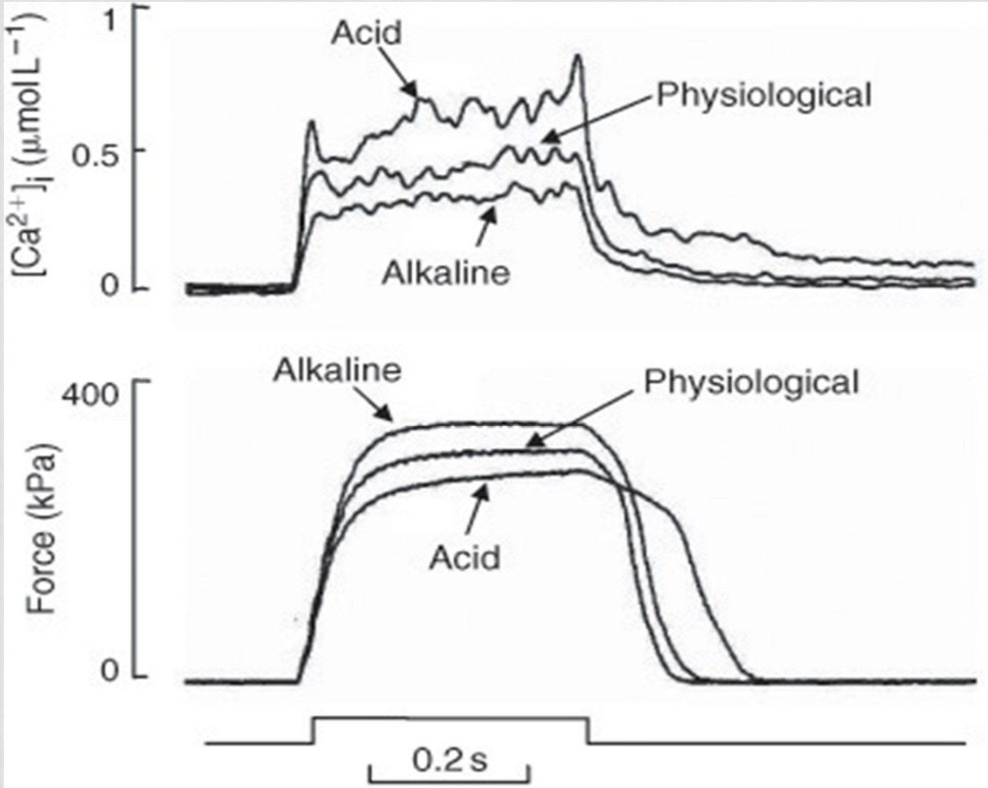
MUSCLE FIBER ATP CONTENT

Reduction in muscle fiber ATP content can affect the muscle contraction



HYDROGEN IONS

Increased production of hydrogen ions affect force production not in calcium release



2- Depletion of Glycogen Stores in Muscles

- limiting factor for endurance exercises is the availability of glucose.

- Nitric oxide (NO) plays a role in the uptake of glucose by exercising muscles.

- Exercise → the calcium increase in the sarcoplasm → activation of NO-synthetase → NO release from the contracting muscle → NO increases the activity of the glucose transporter

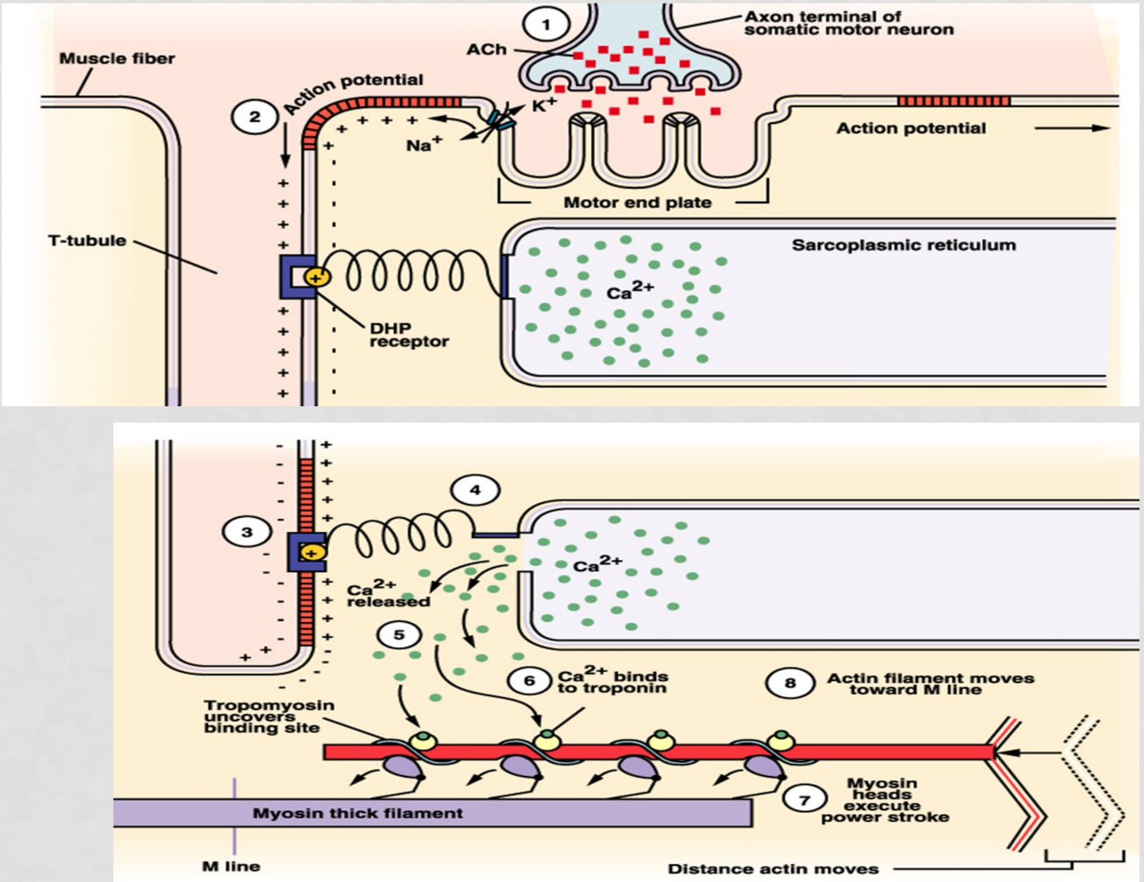
- During endurance exercise, the intracellular glycogen stores decrease little by little

- The concentration of blood glucose may even decrease

- The athlete experiences this as ‘**the hitting of a wall**’

- The trigger for these sensations may be a direct reaction of the brain to the decreased concentration of blood glucose

3-**The Effect of Exercise on Muscle Membrane Structures: Excitation-Contraction Coupling**



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A decreased efficiency or block of EC-coupling will lead to a decrease or disappearance of contractile force:

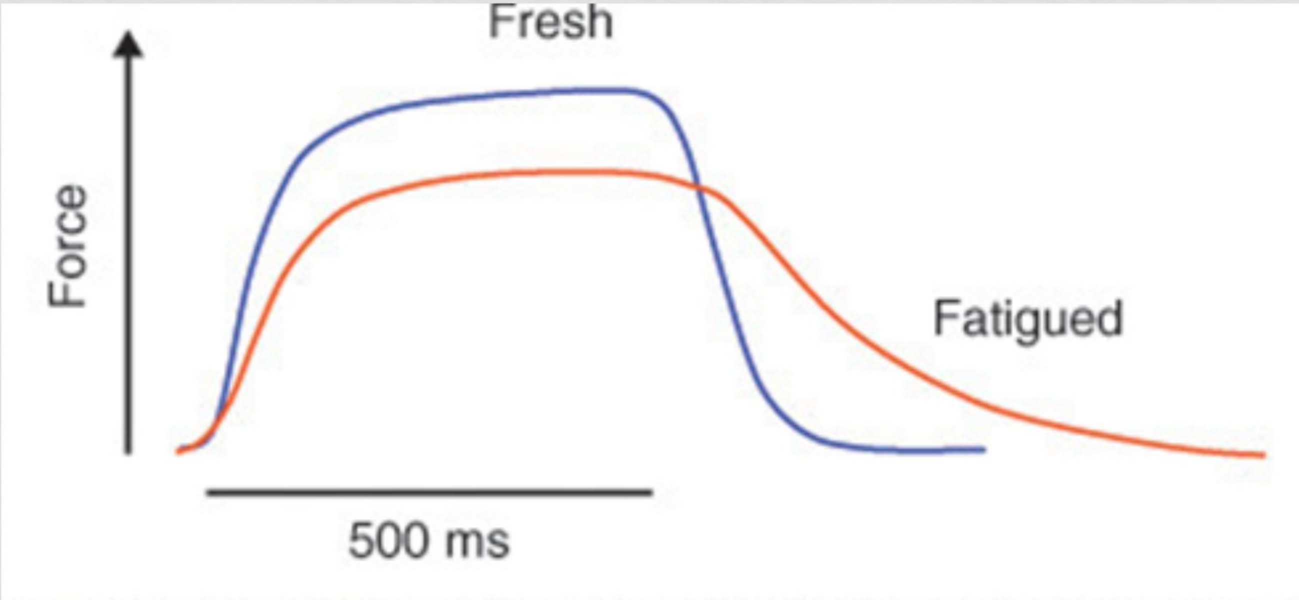
1-The amplitude of sarcolemmal action potentials (and of the EMG) may decrease during prolonged activation

2-Decrease in the propagation velocity of the action potentials along the sarcolemma

3-Action potential propagation along t-tubules seems to become gradually blocked during intense activity, leading to an inhibition of muscle fiber activation

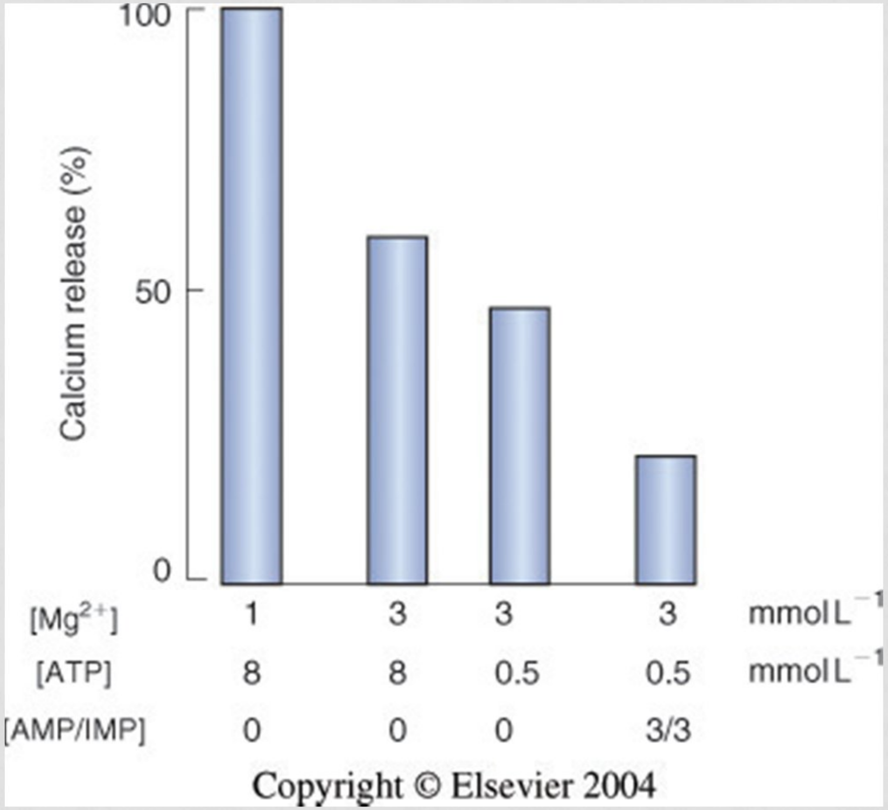
a sign of muscle fatigue

In fatigued muscles, the speed of force relaxation at the end of a contraction is slowed down (Increased relaxation time)



- As a result of a decreased rate of Ca transport back into the SR caused by the increased concentration of H ions

During muscle activation, an increased Mg concentration in the sarcoplasm reduces the Ca fluxes across the membrane of the SR



During repeated tetanic stimulation, sarcoplasmatic Ca concentration in the active skeletal muscle fibers increases in the first and decreases in the last period of stimulation

The drop of muscle fiber contraction force at the end stage of the stimulation period is caused by an impaired Ca release by the SR because:

1-the decline of the amplitude of the action potential across the sarcolemma

2-the effect of the relatively high sarcoplasmatic P_i concentration

High sarcoplasmatic P_i concentration, which has two effects at the SR Ca release:

- Precipitation of calcium phosphate in the lumen of the SR
- Phosphorylation of the Ca release channels of the SR
- Drop in Ca efflux by the SR

4 -The Neuromuscular Junction and the Peripheral Nerve

- A decrease in the amount of released acetylcholine from the presynaptic nerve terminal

- Propagation failure of the axonal action potential

5-Differentiation of Muscle Fiber and Motor Unit Properties

- Within a single muscle, they typically vary greatly in their contractile speed, maximum force and resistance to fatigue

Type of motor units:

1- The slowest, fatigue resistant & weak; type I fibers

2- The strongest, fast & relatively sensitive to fatigue; type II fibres

- Type I fibers tend to be relatively more frequent in muscles with a crucial role in posture (e.g. in antigravity muscles needed for standing).

The differences between type I & II muscle fiber:

- Differences in the ‘vulnerability’ of the EC-coupling
- Differences in the myofilament ATPase activity that affect the cross-bridge cycle rate
- Isometric force generation of type II fibers decreases more than type I fibers during P_i accumulation at 30 mmol/L
- Contraction speed of type I fibers is more susceptible to P_i accumulation than type II fibers

The latest 2 effects are more evident at low temperatures

Effects of Exercise on the Internal Environment

Factors that influence the impact of the active muscles on the internal environment:

- **The intensity of the workload**
- **The amount of muscle tissue involved**
- **The type of exercise**
- **The duration of exercise**

Anaerobic exercise

- Under anaerobic conditions, the breakdown of glucose (glycogen) generates **lactate**

- The increase of lactate concentration in blood and extracellular fluids shows a marked acceleration above a certain workload, i.e. the ‘**lactate threshold(LA)**’ or **OBLA**

Lactate threshold(LA)

- The lactate threshold can be defined as **the workload at which tissue lactate production is exactly in equilibrium with the tissue lactate consumption**.

- Others define the lactate threshold as **the workload at which blood lactate concentration exceeds 1 mmol/L above baseline.**

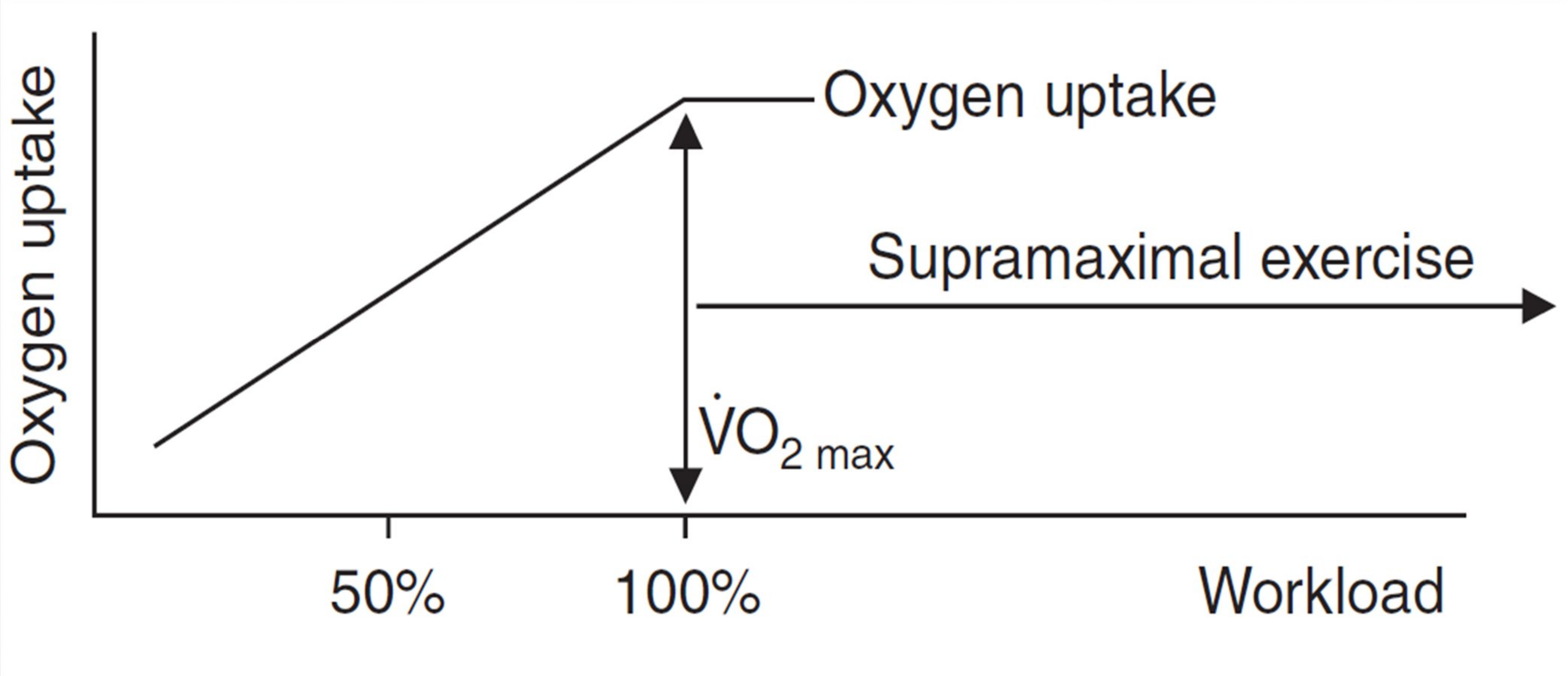
Onset of blood lactate accumulation(OBLA)

- OBLA is defined as **the workload at which the blood lactate concentration exceeds 4 mmol/L.**

- For **untrained** subjects OBLA occurs at about **50–60% VO2max**, and for **trained** subjects at about **70–80% VO2max**.

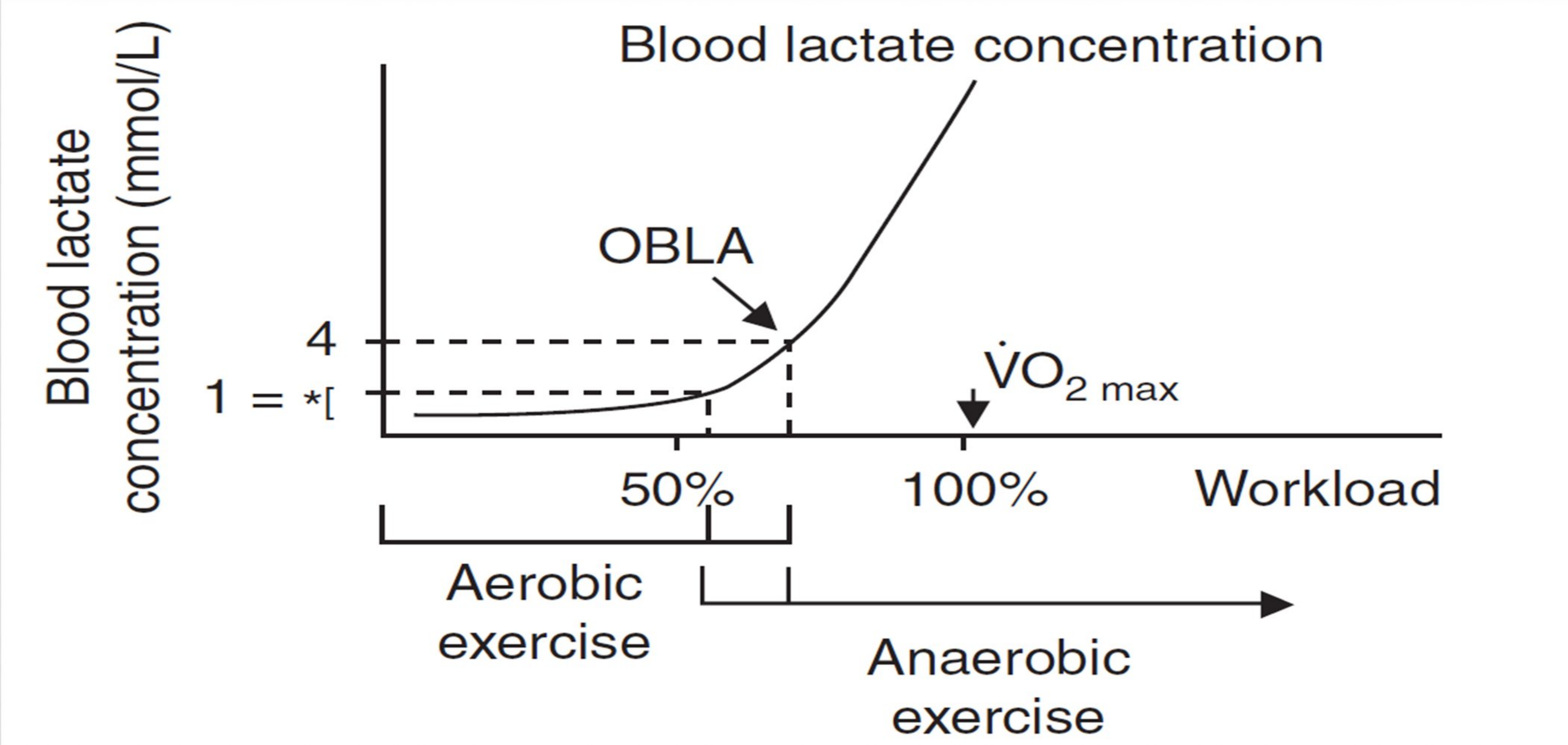
- An increased concentration of acid means an increased concentration of hydrogen ions, i.e. a lowering of pH. This increased proton load is partly buffered according to the reaction:

$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow H_2O + CO_2$$



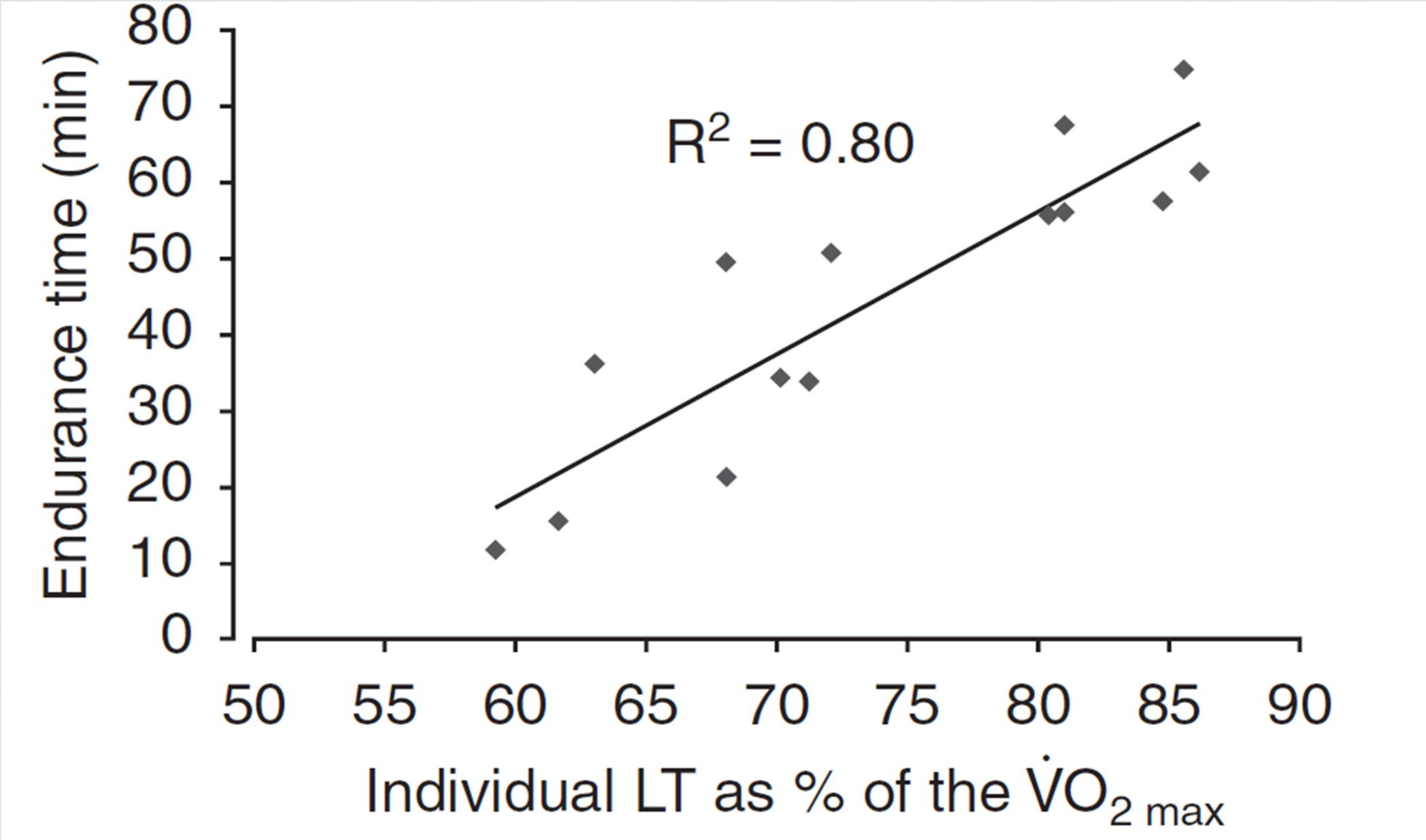
Relationship between workload and oxygen uptake

Workloads above maximal oxygen uptake (VO2max) are ‘supramaximal workloads’. At these supramaximal workloads, most of the power is produced by type II muscle fibers, which generate their intracellular ATP; necessary for the cross-bridge interaction), by the glycolytic pathway and breakdown of CP.



Relationship between workload and blood lactate concentration

Aerobic exercise is defined as the workload until the LA or OBLA has been reached. During aerobic exercise, muscle power is produced predominantly by type I muscle fibers, which generate most of their ATP via the aerobic pathway



Relationship between LT and endurance time

- In muscle tissue, the metabolism of the **anaerobic glycolysis** and **purine nucleotide breakdown** are linked to each other.
- **Ammonia** emerges as adenosine 5'-monophosphate and is broken down to inosine monophosphate.

The blood concentrations of both **ammonia** and **lactate** will increase during graded exercise.

Heat loading

- During graded exercise, only about 20–25% of all the consumed metabolic energy is converted into mechanical work, while the rest emerges as heat.
- Thus, exercise causes a ‘**heat loading**’ in the internal environment

Summarizing, the large number of effects of muscle exercise on the internal environment include:

1. **An increased consumption and potential lack of oxygen and nutrients (glycogen, glucose, fatty acids);**

2. **An increased production and potential accumulation of CO_2, hydrogen ions ('proton loading'), lactate and ammonia;**

3. **An increased production and accumulation of heat ('heat loading').**

Effects of Exercise on the CNS

1- Afferents and Motor Control

The CNS controls motor behavior using sensory signals via feedback mechanism:

- **Gamma loop: gamma motor neurons / muscle spindles / a motor neurons**

- **Muscle afferents (thin myelinated [III] or unmyelinated [IV or C] fibers**

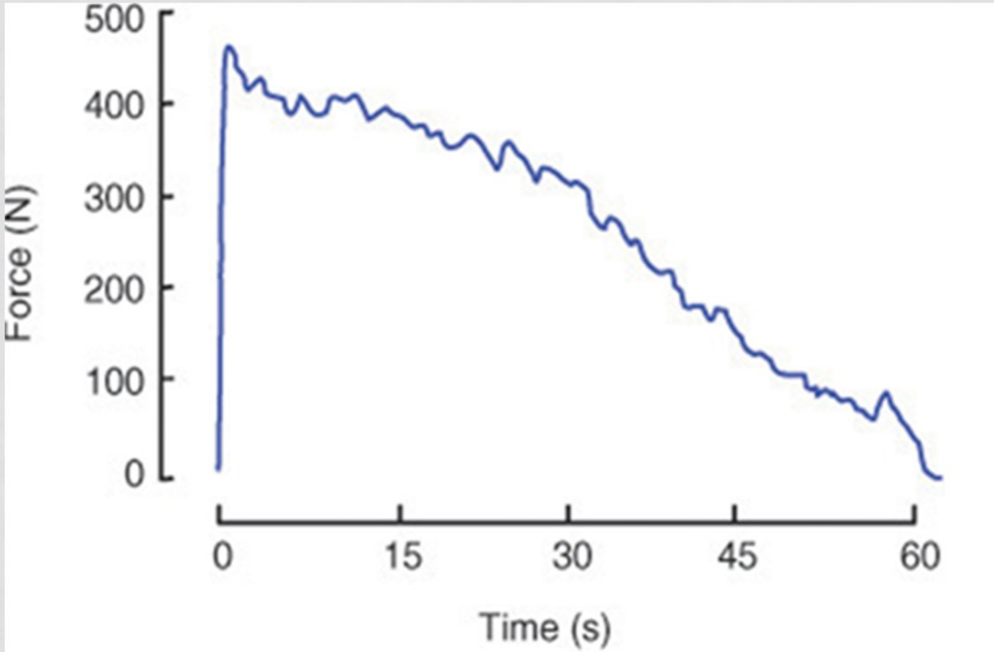
In summary, muscle afferents of type III and IV nerves have three effects:

- **A decrease of the firing frequency of the motor neuron**
- **An inhibition or facilitation of the motor neuron**
- **An inhibition of the motor cortex neuron**

2- Central and Peripheral Fatigue

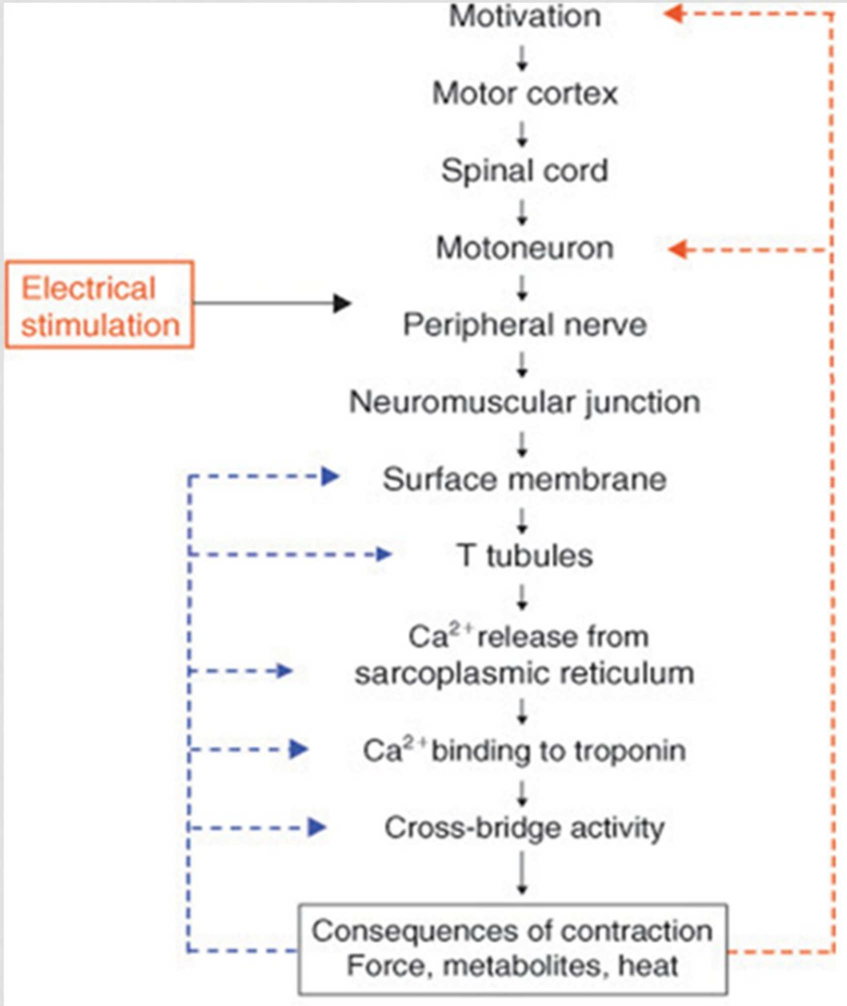
- **Peripheral fatigue**

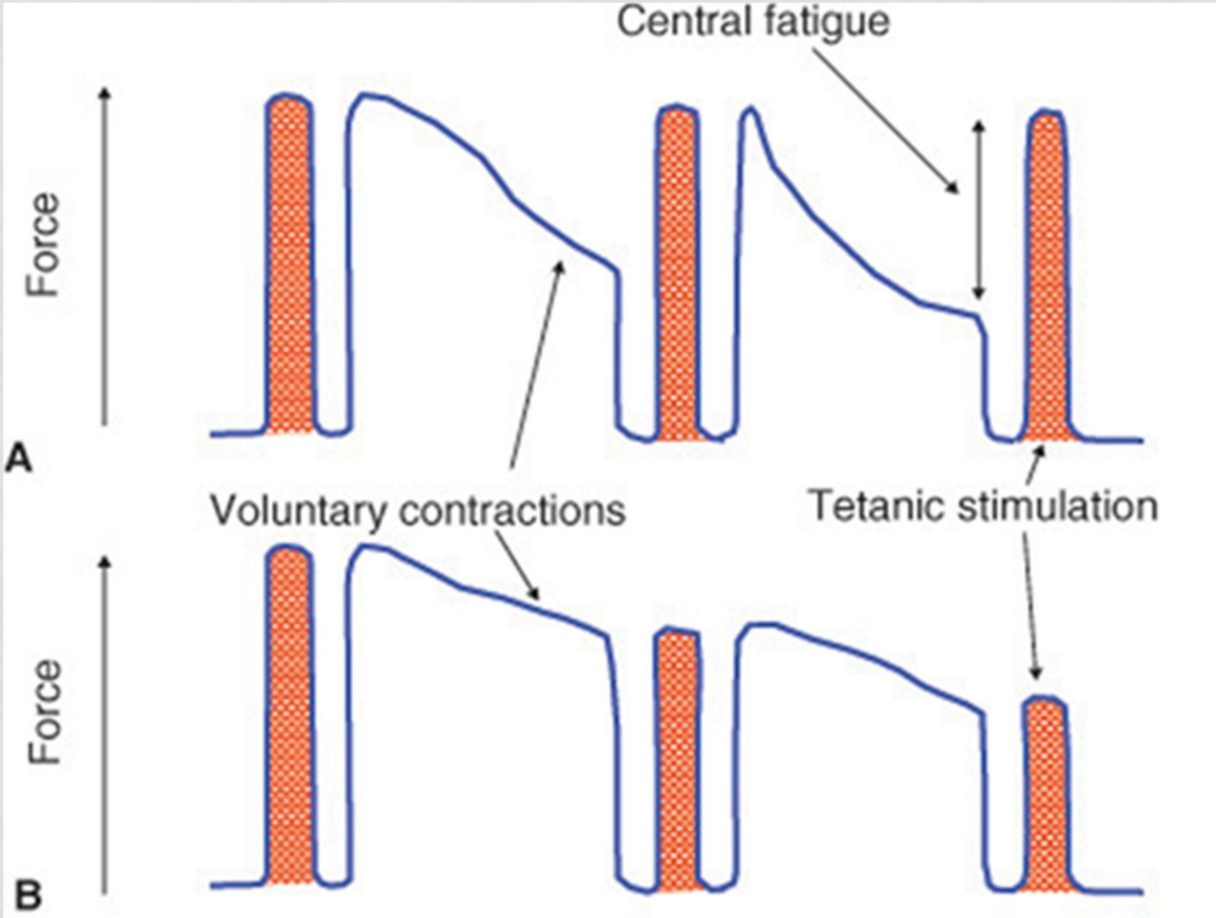
The loss of contraction force or power; the origin of fatigue is outside the CNS.



- **Central fatigue**

The loss of contraction force or power caused by processes distal to the neuromuscular junction





Distinguish between peripheral fatigue and central fatigue

3- The Motor Cortex

The excitability of the motor cortex changes during a fatiguing muscle contraction that are considered to be a sign of central fatigue.

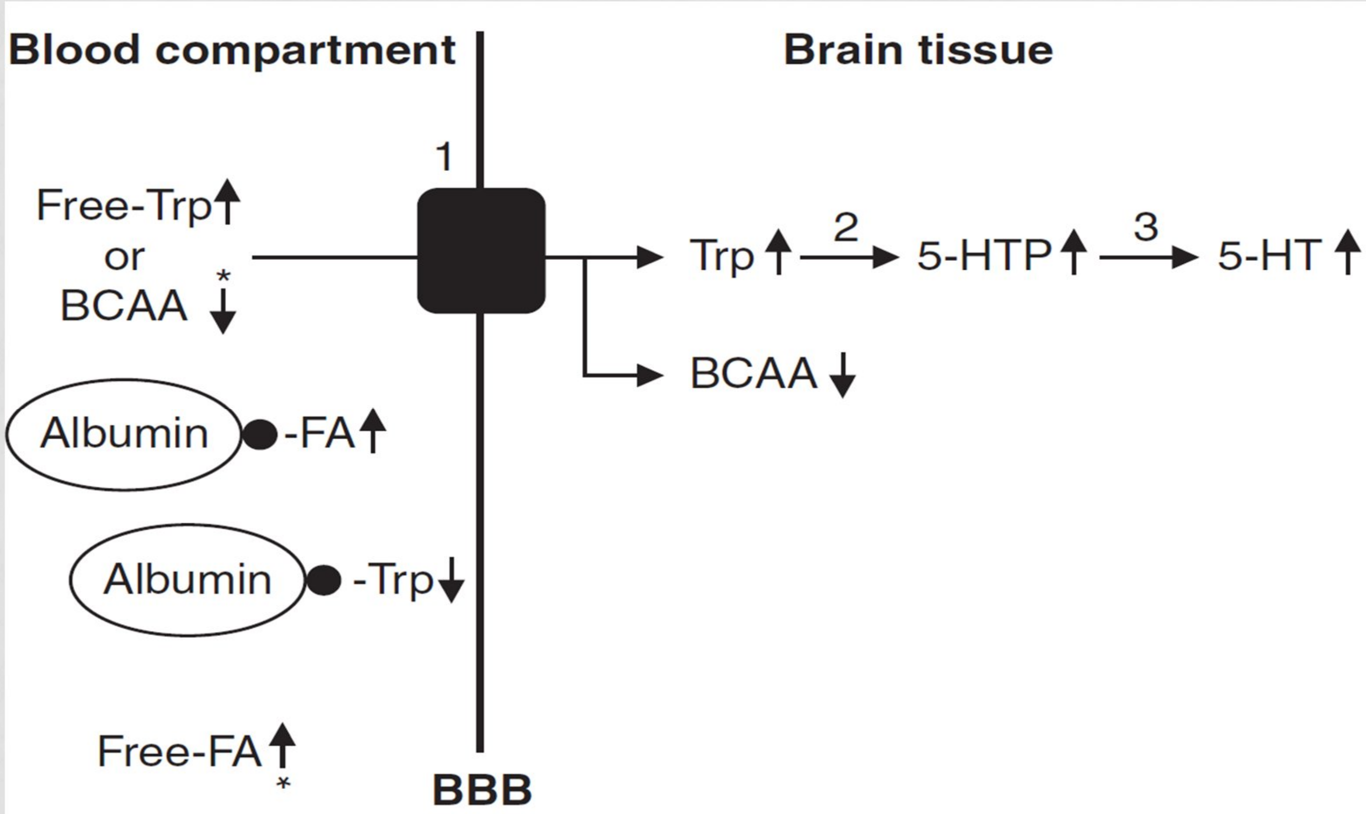
4- The Core Temperature

- The CNS is vulnerable to hyperthermia.
- If it exceeded 40C, the central drive of the subjects faded away and they were unable to maintain the workload.

Mechanisms:

- **During exercise the progressive heat loading is stressing the cardiovascular system, which in turn could limit the blood flow to the brain**
- **The increased brain temperature may introduce the sensations of fatigue and the sense of effort during exercise directly**.

5-Branched Chain Amino Acids and the Serotoninergic System



Tryptophan brain uptake and synthesis of serotonin (5-hydroxytryptamine; 5HT) during prolonged exercise

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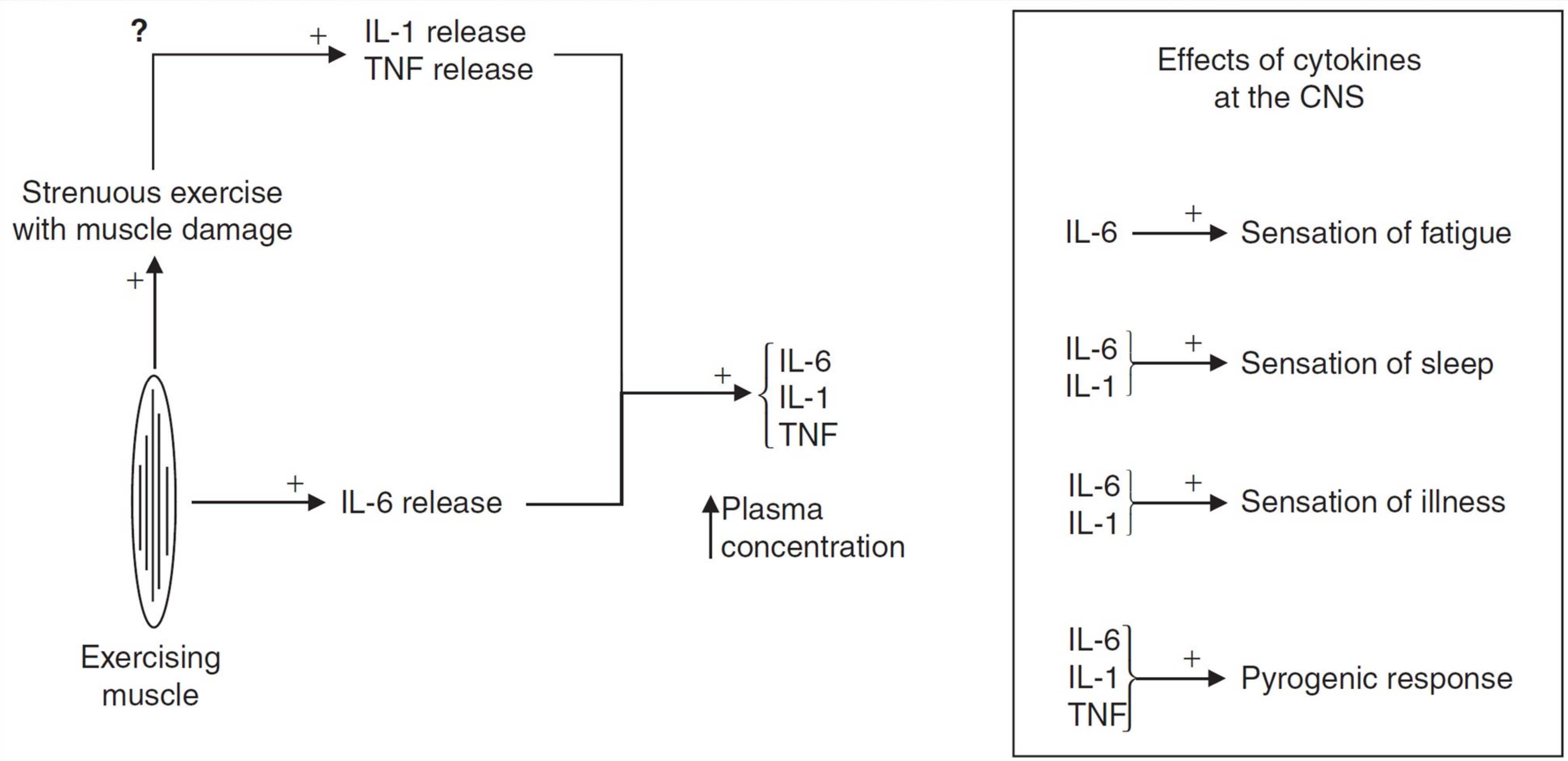
6- The Role of Cytokines



Overview of the interaction between exercise and cytokines

7- Brain Metabolism during Exercise

- Cerebral **blood flow** is impaired during exercise

- **Oxygen uptake** by brain tissue is increased, especially during intensive workloads

- The ratio of brain tissue oxygen uptake to brain glucose uptake is **6 : 1**.

- During starvation, the oxidation of **ketone bodies** contributes to a considerable proportion (up to 25–50%) of brain metabolism.

- The ratio of the cerebral **oxygen/glucose uptake** decreases during an exercise workload of 60% of the maximum oxygen uptake.

- **During exercise**, brain tissue shows a disproportionately **higher uptake from glucose and lactate** than from oxygen.

- These observations suggest that exercise might have an **anabolic effect** on brain tissue.

- It was hypothesized that **the brain glucose uptake was reduced due to an increased brain lactate uptake with increasing exercise loads** and that brain tissue used lactate in favor of glucose for its oxidative energy production.