Anatomy and Electro-Magnetic-Static Physiology of Muscles

(a) Photomicrograph of portions of two isolated muscle fibers (700x). Notice the obvious striations (alternating dark and light bands).

(b) Diagram of part of a muscle fiber showing the myofibrils. One myofibril extends from the cut end of the fiber.

(c) Small part of one myofibril enlarged to show the myofilaments responsible for the banding pattern. Each sarcomere extends from one Z disc to the next.

(d) Enlargement of one sarcomere (sectioned lengthwise). Notice the myosin heads on the thick filaments.

(e) Cross-sectional view of a sarcomere cut through in different locations.

Author - Editor: Professor of Medicine Desire’ Dubounet, D. Sc. L.P.C.C April 30, 2015 for Medical Expose’
WE ARE BEINGS OF ENERGY + OUR MUSCLES WORK MAGNETICALLY

We will start to teach the lesson from fifth grade where we were all taught our bodies are made of atoms. The atoms have electrons in their outer shell and electrons do not touch, they repel each other. So no two atoms can touch. You cannot touch the chair you sit in. the atoms in your body are held in place by many different energy fields. It is the balance of these fields that makes health possible. So we are beings of energy.

Muscles contract by using Electro-magnetic-static attraction forces to grab and slide over each other and provide energy from ATP etc to make muscles work. It is obvious that if the body electric is balanced and the voltage and amperage maximized, muscles will work better.

![Figure 17-30](molecular-cell-biology-sixth-edition.png)

*Figure 17-30
Molecular Cell Biology, Sixth Edition
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![Diagram of muscle filaments](image)
The action area of this magnetic static grabbing in the muscles is so small (molecular) it is not affected by macro magnetic action but:

Here is proof that muscles make magnetic action


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PMCID: PMC1280763

Magnetic field of a single muscle fiber. First measurements and a core conductor model.

J M van Egeraat, R N Friedman, and J P Wikswo, Jr

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Abstract

We present the first measurements of the magnetic field from a single muscle fiber of the frog gastrocnemius, obtained by using a toroidal pickup coil coupled to a room-temperature, low-noise amplifier. The axial currents associated with the magnetic fields of single fibers were biphasic and had peak-to-peak amplitudes ranging between 50 and 100 nA, depending primarily on the fiber radius. With an intracellular microelectrode, we measured the action potential of the same fiber, which allowed us to determine that the intracellular conductivity of the muscle fiber in the core conductor approximation was 0.20 +/- 0.09 S/m. Similarly, we found that the effective membrane capacitance was 0.030 +/- 0.011 F/m2. These results were not significantly affected by the anisotropic conductivity of the muscle bundle. We demonstrate how our magnetic technique can be used to determine the transmembrane action potential without penetrating the membrane with a microelectrode, thereby offering a reliable, stable, and atraumatic method for studying contracting muscle fibers.

Full text
Here is proof that muscles are affected by magnetic action


A strong constant magnetic field affects muscle tension development in bullfrog neuromuscular preparations.

Satow Y¹, Matsunami K, Kawashima T, Satake H, Huda K.

Author information
Abstract
Effects of a constant magnetic field (CMF) of 0.65 T on muscle tension over 9 h were studied in the neuromuscular preparation of the bullfrog sartorius muscle. Tension was developed every 30 min by stimulation of the sciatic nerve (nerve stimulation) or of the sartorius muscle itself (muscle stimulation). In sciatic nerve stimulation, tension decreased rapidly for the first 3-4 h at a similar rate in both test (exposed to CMF) and control muscles. However, the rate of decrease became smaller and almost leveled off after 3-4 h in the test muscles, whereas tension continued to decrease monotonically in control muscles. The slope of the decrease for these later periods was significantly different between the test and the control conditions. Accordingly, tension was larger in test than in control muscles. In muscle stimulation, tension decreased monotonically from the start of experiments in control muscles, while tension in test muscles maintained their initial values for almost 3 h. Thereafter they started to decrease with a similar rate to the control. Hence, tension was always larger in test than in control muscles. A similar pattern of temporal change was observed for the rate of rise of the maximum tension for nerve or muscle stimulation. However, a significant difference was detected only in the case of muscle stimulation. The present results showed that a strong CMF of 0.65 T had biological effects on tension development of the bullfrog sartorius muscle by stimulation of the sciatic nerve as well as by stimulation of muscle itself. The presence of a small AC magnetic field component leaves open the possibility of an AC, rather than a CMF effect.

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Effects of a magnetic field on pelvic floor muscle function in women with stress urinary incontinence.

Bergman J¹, Robertson JR, Elia G.

Author information
Abstract
CONTEXT:
Magnetic fields have been found to affect neuromuscular function.
OBJECTIVE:
To study the effect of a magnetic field on measurements of urethral function in women with stress urinary incontinence.

PATIENTS OR OTHER PARTICIPANTS:
Twenty-six consecutive women with diagnosis of stress urinary incontinence (SUI).

EVALUATION:
History and physical examination, neurologic exam, urethrocystoscopy, urodynamic testing with water-filling cystometry, urethral profilometry at rest, during coughing, and during coughing while performing a levator ani contraction (knack maneuver).

INTERVENTION:
The same urodynamic procedures were performed again after the subjects were asked to step on specifically designed magnets (magnetic cushion device).

STATISTICAL ANALYSIS:
Two-tailed student t test.

MAIN OUTCOME MEASURES:
Urethral pressure at rest, during coughing, and during coughing while performing a levator ani contraction.

RESULTS:
Mean age was 58.3 years (range: 36-81), mean parity 2.8 (range: 0-8). The urodynamic parameters measured without and with the use of the magnetic cushion device were not found to be different except for the knack maneuver. The pressure in the urethra during the knack maneuver while the subjects were stepping on the magnetic device was significantly higher than the 1 obtained without the magnetic field.

CONCLUSION:
In our patient population, a magnetic field increases the efficacy of voluntary levator ani contractions.
Anatomy of Skeletal Muscle

A single skeletal muscle, such as the triceps muscle, is attached at its

- origin to a large area of bone; in this case, the humerus.
- At its other end, the insertion, it tapers into a glistening white tendon which, in this case, is attached to the ulna, one of the bones of the lower arm.

As the triceps contracts, the insertion is pulled toward the origin and the arm is straightened or extended at the elbow. Thus the triceps is an extensor. Because skeletal muscle exerts force only when it contracts, a second muscle — a flexor — is needed to flex or bend the joint. The biceps muscle is the flexor of the lower arm. Together, the biceps and triceps make up an antagonistic pair of muscles. Similar pairs, working antagonistically across other joints, provide for almost all the movement of the skeleton.

The Muscle Fiber

Skeletal muscle is made up of thousands of cylindrical muscle fibers often running all the way from origin to insertion. The fibers are bound together by connective tissue through which run blood vessels and nerves. Each muscle fiber contains:

- an array of myofibrils that are stacked lengthwise and run the entire length of the fiber;
- mitochondria;
- an extensive smooth endoplasmic reticulum (SER);
- many nuclei (thus each skeletal muscle fiber is a syncytium).

The multiple nuclei arise from the fact that each muscle fiber develops from the fusion of many cells (called myoblasts). The number of fibers is probably fixed early in life. This is regulated by myostatin, a cytokine that is synthesized in muscle cells (and circulates as a hormone later in life). Myostatin suppresses skeletal muscle development. (Cytokines secreted by a cell type that inhibit proliferation of that same type of cell are called chalones.) Cattle and mice with inactivating mutations in their myostatin genes develop much larger muscles. Some athletes and other remarkably strong people have been found to carry one mutant myostatin gene. These discoveries have already led to the growth of an illicit market in drugs supposedly able to suppress myostatin.

In adults, increased muscle mass comes about through an increase in the thickness of the individual fibers and increase in the amount of connective tissue. In the mouse, at least, fibers increase in size by attracting more myoblasts to fuse with them. The fibers attract more myoblasts by releasing the cytokine interleukin 4 (IL-4). Anything that lowers the level of myostatin also leads to an increase in fiber size. Because a muscle fiber is not a single cell, its parts are often given special names such as

- sarcolemma for plasma membrane
- sarcoplasmic reticulum for endoplasmic reticulum
- sarcosomes for mitochondria
- sarcoplasm for cytoplasm

although this tends to obscure the essential similarity in structure and function of these structures and those found in other cells. The nuclei and mitochondria are located just beneath the plasma membrane. The endoplasmic reticulum extends between the myofibrils.

Seen from the side under the microscope, skeletal muscle fibers show a pattern of cross banding, which gives rise to the other name: striated muscle.

The striated appearance of the muscle fiber is created by a pattern of alternating

- dark A bands and
- light I bands.
The A bands are bisected by the **H zone** running through the center of which is the **M line**.

The I bands are bisected by the **Z disk**.

Each myofibril is made up of arrays of parallel **filaments**.

- The **thick filaments** have a diameter of about 15 nm. They are composed of the protein **myosin**.
- The **thin filaments** have a diameter of about 5 nm. They are composed chiefly of the protein **actin** along with smaller amounts of two other proteins:
  - **troponin** and
  - **tropomyosin**.

**The anatomy of a sarcomere**

The entire array of thick and thin filaments between the Z disks is called a **sarcomere**.

- The **thick filaments** produce the dark **A band**.
- The **thin filaments** extend in each direction from the Z disk. Where they do not overlap the thick filaments, they create the light **I band**.
- The **H zone** is that portion of the A band where the thick and thin filaments do not overlap.
- The **M line** runs through the exact center of the sarcomere. Molecules of the giant protein, **titin**, extend from the M line to the Z disk. One of its functions is to provide a scaffold for the assembly of a precise number of myosin molecules in the thick filament (294 in one case). It may also dictate the number of actin molecules in the thin filaments.

Shortening of the sarcomeres in a myofibril produces the shortening of the myofibril and, in turn, of the muscle fiber of which it is a part. [This electron micrograph of a single sarcomere was kindly provided by Dr. H. E. Huxley.]

**Activation of Skeletal Muscle**

The contraction of skeletal muscle is controlled by the nervous system. The Dying Lioness (an Assyrian relief dating from about 650 B.C. and supplied through the courtesy of The Trustees of the British Museum) shows this vividly. Injury to the spinal cord has paralyzed the otherwise undamaged hind legs. In this respect, skeletal muscle differs from smooth and cardiac muscle. Both cardiac and smooth muscle can contract without being stimulated by the nervous system. Nerves of the **autonomic branch of the**
The Neuromuscular Junction

Nerve impulses (action potentials) traveling down the motor neurons of the sensory-somatic branch of the nervous system cause the skeletal muscle fibers at which they terminate to contract. The junction between the terminal of a motor neuron and a muscle fiber is called the neuromuscular junction. It is simply one kind of synapse. (The neuromuscular junction is also called the myoneural junction.)

The terminals of motor axons contain thousands of vesicles filled with acetylcholine (ACh).

When an action potential reaches the axon terminal, hundreds of these vesicles discharge their ACh onto a specialized area of postsynaptic membrane on the muscle fiber (the folded membrane running diagonally upward from the lower left). This area contains a cluster of transmembrane channels that are opened by ACh and let sodium ions (Na⁺) diffuse in.

The interior of a resting muscle fiber has a resting potential of about −95 mV. The influx of sodium ions reduces the charge, creating an end plate potential. If the end plate potential reaches the threshold voltage (approximately −50 mV), sodium ions flow in with a rush and an action potential is created in the fiber. The action potential sweeps down the length of the fiber just as it does in an axon.

No visible change occurs in the muscle fiber during (and immediately following) the action potential. This period, called the latent period, lasts from 3–10 msec.

Before the latent period is over,

- the enzyme acetylcholinesterase breaks down the ACh in the neuromuscular junction (at a speed of 25,000 molecules per second)
- the sodium channels close, and
- the field is cleared for the arrival of another nerve impulse.

- the resting potential of the fiber is restored by an outflow of potassium ions.

The brief (1–2 msec) period needed to restore the resting potential is called the refractory period.
Tetanus
The process of contracting takes some 50 msec; relaxation of the fiber takes another 50–100 msec. Because the refractory period is so much shorter than the time needed for contraction and relaxation, the fiber can be maintained in the contracted state so long as it is stimulated frequently enough (e.g., 50 stimuli per second). Such sustained contraction is called tetanus.
In the figure,
• When shocks are given at 1/sec, the muscle responds with a single twitch.
• At 5/sec and 10/sec, the individual twitches begin to fuse together, a phenomenon called clonus.
• At 50 shocks per second, the muscle goes into the smooth, sustained contraction of tetanus.
Clonus and tetanus are possible because the refractory period is much briefer than the time needed to complete a cycle of contraction and relaxation. Note that the amount of contraction is greater in clonus and tetanus than in a single twitch.
As we normally use our muscles, the individual fibers go into tetanus for brief periods rather than simply undergoing single twitches.

The Sliding-Filament Model
Each molecule of myosin in the thick filaments contains a globular subunit called the myosin head. The myosin heads have binding sites for
• the actin molecules in the thin filaments and
• ATP
Activation of the muscle fiber causes the myosin heads to bind to actin. An allosteric change occurs which draws the thin filament a short distance (~10 nm) past the thick filament. Then the linkages break (for which ATP is needed) and reform farther along the thin filament to repeat the process. As a result, the filaments are pulled past each other in a ratchetlike action. There is no shortening, thickening, or folding of the individual filaments.
Electron microscopy supports this model.
As a muscle contracts,
• the Z disks come closer together;
• the width of the I bands decreases;
• the width of the H zones decreases, but
• there is no change in the width of the A band.
Conversely, as a muscle is stretched,
• the width of the I bands and H zones increases,
• but there is still no change in the width of the A band.
This is seen in these electron micrographs (courtesy of Dr. H. E. Huxley).
Other evidence supporting the sliding-filament model is presented on another page. Link to it.
**Coupling Excitation to Contraction**

 Calcium ions (Ca\(^{2+}\)) link action potentials in a muscle fiber to contraction.  
- In resting muscle fibers, Ca\(^{2+}\) is stored in the endoplasmic (sarcoplasmic) reticulum.  
- Spaced along the plasma membrane (sarcolemma) of the muscle fiber are inpocketings of the membrane that form **tubules** of the "T system". These tubules plunge repeatedly into the interior of the fiber.  
- The tubules of the T system terminate near the calcium-filled sacs of the **sarcoplasmic reticulum**.
Each action potential created at the neuromuscular junction sweeps quickly along the sarcolemma and is carried into the T system. The arrival of the action potential at the ends of the T system triggers the release of Ca$^{2+}$. The Ca$^{2+}$ diffuses among the thick and thin filaments where it binds to troponin on the thin filaments. This turns on the interaction between actin and myosin and the sarcomere contracts. Because of the speed of the action potential (milliseconds), the action potential arrives virtually simultaneously at the ends of all the tubules of the T system, ensuring that all sarcomeres contract in unison. When the process is over, the calcium is pumped back into the sarcoplasmic reticulum using a Ca$^{2+}$ ATPase.

**Isotonic versus Isometric Contractions**

If a stimulated muscle is held so that it cannot shorten, it simply exerts tension. This is called an isometric ("same length") contraction. If the muscle is allowed to shorten, the contraction is called isotonic ("same tension").

**Motor Units**

All motor neurons leading to skeletal muscles have branching axons, each of which terminates in a neuromuscular junction with a single muscle fiber. Nerve impulses passing down a single motor neuron will thus trigger contraction in all the muscle fibers at which the branches of that neuron terminate. This minimum unit of contraction is called the motor unit.

The size of the motor unit is small in muscles over which we have precise control. Examples:
- a single motor neuron triggers fewer than 10 fibers in the muscles controlling eye movements;
- the motor units of the muscles controlling the larynx are as small as 2–3 fibers per motor neuron;
- In contrast, a single motor unit for a muscle like the gastrocnemius (calf) muscle may include 1000–2000 fibers (scattered uniformly through the muscle).

Although the response of a motor unit is all-or-none, the strength of the response of the entire muscle is determined by the number of motor units activated. Even at rest, most of our skeletal muscles are in a
state of partial contraction called **tonus**. Tonus is maintained by the activation of a few motor units at all times even in resting muscle. As one set of motor units relaxes, another set takes over.

**Fueling Muscle Contraction**

ATP is the immediate source of energy for muscle contraction. Although a muscle fiber contains only enough ATP to power a few twitches, its ATP "pool" is replenished as needed. There are three sources of high-energy phosphate to keep the ATP pool filled.

- **creatine phosphate**
- **glycogen**
- **cellular respiration** in the mitochondria of the fibers.

**Creatine phosphate**
The phosphate group in creatine phosphate is attached by a "high-energy" bond like that in ATP. Creatine phosphate derives its high-energy phosphate from ATP and can donate it back to ADP to form ATP.

\[
\text{Creatine phosphate + ADP} \leftrightarrow \text{creatine + ATP}
\]

The pool of creatine phosphate in the fiber is about 10 times larger than that of ATP and thus serves as a modest reservoir of ATP.

**Glycogen**
Skeletal muscle fibers contain about 1% **glycogen**. The muscle fiber can degrade this glycogen by **glycogenolysis** producing glucose-1-phosphate. This enters the **glycolytic pathway** to yield two molecules of ATP for each pair of lactic acid molecules produced. Not much, but enough to keep the muscle functioning if it fails to receive sufficient oxygen to meet its ATP needs by respiration. However, this source is limited and eventually the muscle must depend on cellular respiration.

**Cellular respiration**
Cellular respiration not only is required to meet the ATP needs of a muscle engaged in prolonged activity (thus causing more rapid and deeper breathing), but is also required afterwards to enable the body to resynthesize glycogen from the lactic acid produced earlier (deep breathing continues for a time after exercise is stopped). The body must repay its **oxygen debt**.

**Type I vs. Type II Fibers**
Several different types of muscle fiber can be found in most skeletal muscles: Type I and two (in humans) and three (in mice) subtypes of Type II fibers. Each type differs in the myosin it uses and also in its structure and biochemistry.

**Type I Fibers**
- loaded with mitochondria and
- depend on cellular respiration for ATP production
- fatty acids: the major energy source
- resistant to fatigue
- rich in myoglobin and hence red in color (the "dark" meat of the turkey)
- activated by small-diameter, thus slow-conducting, motor neurons
- also known as "slow-twitch" fibers
- dominant in muscles used in activities requiring endurance (leg muscles) and those that depend on tonus, e.g., those responsible for posture

**Type IIb Fibers**
- few mitochondria
- rich in glycogen and
- depend on creatine phosphate and glycolysis for ATP production
- fatigue easily with the production of lactic acid
- low in myoglobin hence whitish in color (the white meat of the turkey)
- activated by large-diameter, thus fast-conducting, motor neurons
- also known as "fast-twitch" fibers
- dominant in muscles used for rapid movement, e.g., those moving the eyeballs.

The other subtypes of Type II fibers have properties intermediate between those of Type IIb and Type I. Most skeletal muscles contain some mixture of Type I and Type II fibers, but a single motor unit always contains one type or the other, never both. In mice, the number of Type I vs Type II fibers can be changed with exercise and drug treatment. Whether the same holds true for humans remains to be seen. Perhaps training in humans does not alter the number of fibers of a particular type but may increase the diameter of one type (e.g., Type I in marathoners, Type IIb in weight lifters) at the expense of the other types.

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**RESULTS**

Autonomic neurotransmitters alter membrane resting potential and thereby determine the rate that smooth muscle cells fire action potentials.

Conclusion: Smooth muscle contraction is stimulated by stretch and by the parasympathetic neurotransmitter acetylcholine.

### 47.2 Mechanisms of Smooth Muscle Activation

Stretching depolarizes the membrane of smooth muscle cells, and this depolarization causes action potentials that activate the contractile mechanism. The neurotransmitters acetylcholine and norepinephrine also alter the membrane potential of smooth muscle, making it more or less likely to contract.
Sliding filaments cause skeletal muscle to contract

Skeletal muscle carries out, or effects, all voluntary movements, such as running or playing a piano, and generates the movements of breathing. Skeletal muscle is also called striated muscle because of its striped appearance (Figure 47.1, bottom). Skeletal muscle cells, called muscle fibers, are large. Unlike smooth muscle and cardiac muscle cells, each of which has a single nucleus, skeletal muscle fibers have many nuclei because they develop through the fusion of many individual cells. A muscle such as your biceps (which bends your arm) is composed of many muscle fibers bundled together by connective tissue.

What is the relation between a skeletal muscle fiber and the actin and myosin filaments responsible for its contraction? Each muscle fiber is packed with myofibrils—bundles of contractile filaments made up of actin and myosin (Figure 47.3). Within each myofibril are thin actin filaments and thick myosin filaments. If we cut across the myofibril at certain locations, we see only thick filaments; if we cut at other locations, we see only thin filaments. But, in most regions of the myofibril, each thick myosin filament is surrounded by six thin actin filaments, and conversely, each thin actin filament sits within a triangle of three thick myosin filaments.

A longitudinal view of a myofibril reveals the reason for the striated appearance of skeletal muscle (and cardiac muscle). The myofibril consists of repeating units, called sarcomeres, which are the units of contraction. Each sarcomere is made of overlapping filaments of actin and myosin, which create a distinct band pattern. As the muscle contracts, the sarcomeres shorten, and the appearance of the band pattern changes.

The observation that the widths of the bands in the sarcomeres change when a muscle contracts led two British biologists, Hugh Huxley and Andrew Huxley, to propose a model of muscle contraction.
A skeletal muscle is made up of bundles of muscle fibers. Each muscle fiber is a multinucleate cell containing numerous myofibrils, which are highly ordered assemblages of thick myosin and thin actin filaments.
skeletal muscle is made up of bundles of muscle fibers. Each muscle fiber is a multinucleate cell containing numerous myofibrils, which are highly ordered assemblages of thick myosin and thin actin filaments. The structure of the myofibrils gives muscle fibers their characteristic striated appearance.

Single myofibril

Z line

Where there are only actin filaments the myofibril appears light; where there are both actin and myosin filaments the myofibril appears dark.

Z line

Where there are only actin filaments the myofibril appears light; where there are both actin and myosin filaments the myofibril appears dark.

molecular mechanism of muscle contraction. Let's look at the band pattern of a sarcomere in detail (see the micrograph in Figure 47.3). Each sarcomere is bounded by Z lines, which are structures that anchor the thin actin filaments. Centered in the sarcomere is the A band, which contains all the myosin filaments. The H zone and the I band, which appear light, are regions where actin and myosin filaments do not overlap in the relaxed muscle. The dark stripe within the H zone is called the M band; it contains proteins that help hold the myosin filaments in their regular arrangement.

The bundles of myosin filaments are held in a centered position within the sarcomere by a protein called titin. Titin is probably the longest polypeptide in the body; it runs the full length of the sarcomere from Z line to Z line, and each titin molecule runs right through a myosin bundle. Between the ends of the myosin bundles and the Z lines, titin molecules have the properties of a bungee cord—they are very stretch-able. In a relaxed skeletal muscle, resistance to stretch is mostly due to the elasticity of the titin molecules.

When the muscle contracts, the sarcomere shortens. The H zone and the I band become much narrower, and the Z lines move toward the A band as if the actin filaments were sliding into the region occupied by the myosin filaments. This observation led Huxley and Huxley to propose the sliding filament theory of muscle contraction: Actin and myosin filaments slide past each other as the muscle contracts.

**Actin-myosin interactions cause filaments to slide**

To understand what makes the filaments slide, we must examine the structures of actin and myosin (Figure 47.4). Each myosin molecule consists of two long polypeptide chains coiled together, each ending in a large globular head. A myosin filament is made up of many myosin molecules arranged in parallel, with their heads projecting laterally from one or the other end of the filament. An actin filament consists of a helical arrangement of two chains of actin monomers twisted together like two strands of pearls. Twisting around the actin chains is another protein, tropomyosin, and attached to it
at intervals are molecules of troponin. We'll discuss the roles of these last two proteins in the following section.

The myosin heads have sites that can bind to actin and thereby form cross-bridges between the myosin and the actin filaments. The myosin heads also have ATPase activity; that is, they bind and hydrolyze ATP. The energy released when this happens changes the conformation, and therefore the orientation, of the myosin head.

**Myosin filament**

47.4 Actin and Myosin Filaments Overlap to Form Myofibrils Myosin filaments are bundles of molecules with globular heads and polypeptide tails. Actin filaments consist of two chains of actin monomers twisted together. They are wrapped by chains of the polypeptide tropomyosin and studded at intervals with another protein, troponin.

Together, these details explain the cycle of events that cause the actin and myosin filaments to slide past each other and shorten the sarcomere. A myosin head binds to an actin filament (see Figure 47.6). Upon binding, the head changes its orientation with respect to the myosin filament, thus exerting a force that causes the actin filament to slide about 5 to 10 nm relative to the myosin filament. Next, the myosin head binds a molecule of ATP, which causes it to release the actin. When the ATP is hydrolyzed, the energy released causes the myosin head to return to its original conformation, in which it can bind again to actin. It is as if the energy from ATP hydrolysis is being used to cock the hammer of a pistol, and contact of the myosin head with an actin binding site pulls the trigger.

We have been discussing the cycle of contraction in terms of a single myosin head. Don't forget that each myosin filament has many myosin heads at both ends and is surrounded by six actin filaments; thus the contraction of the sarcomere involves a great many cycles of interaction between actin and myosin molecules. That is why when a single myosin head breaks its contact with actin, the actin filaments do not slip backward.

An interesting aspect of this contractile mechanism is that ATP is needed to break the actin-myosin bonds, but not to form them. Thus muscles require ATP to stop contracting. This fact explains why muscles stiffen soon after animals die, a condition known as rigor mortis. Death stops the replenishment of the ATP stores of muscle cells, so the actin-myosin bonds cannot be broken, and the muscles stiffen. Eventually the proteins begin to lose their integrity, and the muscles soften. These events have regular time courses that differ somewhat for different regions of the body; therefore, an examination of the stiffness of the muscles of a corpse can help a coroner estimate the time of death.

**Actin-myosin interactions are controlled by calcium ions**

Muscle contractions are initiated by action potentials from motor neurons arriving at the neuromuscular junction (see
Troponin has three subunits: one binds actin, one binds tropomyosin, and one binds Ca2+.

Actin filament

Actin monomer

Tropomyosin Troponin

Troponin has three subunits: one binds actin, one binds tropomyosin, and one binds Ca2+.

Actin filament

Actin monomer

Tropomyosin Troponin

Linear polypeptide chain

**Linear polypeptide chain**

Figure 44.13). The axons of motor neurons are generally highly branched and can synapse with up to a hundred muscle fibers each. All the fibers activated by a single motor neuron constitute a motor unit and contract simultaneously in response to action potentials fired by that motor neuron.

Like neurons, muscle cells are excitable; that is, their plasma membranes can generate and conduct action potentials. In the case of skeletal muscle fibers (but not smooth or cardiac muscle fibers), all action potentials are initiated by motor neurons. When an action potential arrives at the neuromuscular junction, the neurotransmitter acetylcholine is released from the motor neuron, diffuses across the synaptic cleft, binds to receptors in the postsynaptic membrane, and causes ion channels in the motor end plate to open. Most of the ions that flow through these channels are Na+, and therefore the motor end plate is depolarized. The depolarization spreads to the surrounding plasma membrane of the muscle fiber, which contains voltage-gated sodium channels. When threshold is reached, the plasma membrane fires an action potential that is conducted rapidly to all points on the surface of the muscle fiber.

An action potential in a muscle fiber also travels deep within the cell. The plasma membrane is continuous with a system of tubules that descends into and branches throughout the cytoplasm of the muscle fiber (also called the sarcoplasm) (Figure 47.5). The action potential that spreads over the plasma membrane also spreads through this system of transverse tubules, or T tubules.
The T tubules come very close to a network of intracellular membranes called the sarcoplasmic reticulum. The sarcoplasmic reticulum forms a membrane-enclosed compartment that surrounds every myofibril. Calcium pumps in the sarcoplasmic reticulum cause it to take up Ca\(^{2+}\) ions from the sarcoplasm. Therefore, when the muscle fiber is at rest, there is a high concentration of Ca\(^{2+}\) in the sarcoplasmic reticulum and a low concentration of Ca\(^{2+}\) in the sarcoplasm.

Spanning the space between the membranes of the T tubules and the membranes of the sarcoplasmic reticulum are two proteins. One protein, which is located in the T tubule membrane, is voltage-sensitive and changes its conformation when an action potential reaches it. The other protein is located in the sarcoplasmic reticulum membrane and is a Ca\(^{2+}\) channel. When it is activated by an action potential, the voltage-sensitive protein opens the Ca\(^{2+}\) channel, and Ca\(^{2+}\) ions diffuse out of the sarcoplasmic reticulum and into the sarcoplasm surrounding the actin and myosin filaments. It is these Ca\(^{2+}\) ions that trigger the interaction of actin and myosin and the sliding of the filaments. How do the Ca\(^{2+}\) ions do this?

An actin filament, as we have seen, is a helical arrangement of two strands of actin monomers. Lying in the grooves between the two actin strands is the two-stranded protein tropomyosin (see Figure 47.4). At regular intervals, the filament also includes a globular protein, troponin. The troponin molecule has three subunits: One binds actin, one binds tropomyosin, and one binds Ca\(^{2+}\).

When Ca\(^{2+}\) is sequestered in the sarcoplasmic reticulum, the tropomyosin strands block the sites on the actin filament where myosin heads can bind. When the T tubule system depolarizes, Ca\(^{2+}\) is released into the sarcoplasm, where it binds to troponin, changing its conformation. Because the troponin is bound to the tropomyosin, this conformational change of the troponin twists the tropomyosin enough to expose the actin-myosin binding sites. Thus the cycle of making and breaking actin-myosin bonds is initiated, the filaments are pulled past each other, and the muscle fiber contracts. When the T tubule system repolarizes, the calcium pumps remove the Ca\(^{2+}\) ions from the sarcoplasm, causing the tropomyosin to return to the position in which it blocks the binding of myosin heads to actin, and the muscle fiber returns to its resting condition. Figure 47.6 summarizes this cycle.

Motor neuron An action potential (black arrows) arrives at the motor neuron terminal.

47.5 T Tubules in Action An action potential at the neuromuscular junction spreads throughout the muscle fiber via a network of T tubules, triggering the release of Ca\(^{2+}\) from the sarcoplasmic reticulum.

Motor neuron An action potential (black arrows) arrives at the motor neuron terminal.
The muscle fiber plasma membrane generates an action potential that spreads down T tubules, which causes the release of Ca²⁺ stored in the sarcoplasmic reticulum.

Myofibril

Released Ca²⁺ stimulates muscle contraction.

Plasma membrane

Sarcoplasmic reticulum

The muscle fiber plasma membrane generates an action potential that spreads down T tubules, which causes the release of Ca²⁺ stored in the sarcoplasmic reticulum.

Myofibril

Released Ca²⁺ stimulates muscle contraction.

Sarcoplasmic reticulum

Plasma membrane

6 ATP is hydrolyzed and the myosin head returns to its resting conformation.

6 ATP is hydrolyzed and the myosin head returns to its resting conformation.
47.6 The Release of Ca$^{2+}$ from the Sarcoplasmic Reticulum Triggers Muscle Contraction
When Ca$^{2+}$ binds to troponin, it exposes actin-myosin binding sites. As long as binding sites and ATP are available, the cycle of actin and myosin interactions continues, and the filaments slide past each other.

Calmodulin mediates Ca$^{2+}$ control of contraction in smooth muscle

Smooth muscle cells do not have the troponin-tropomyosin mechanism for controlling contraction, but Ca$^{2+}$ still plays a critical role. A Ca$^{2+}$ influx into the sarcoplasm of a smooth muscle cell can be stimulated by action potentials, by hormones, or by stretching. The Ca$^{2+}$ that enters the sarcoplasm combines with a protein called calmodulin. The calmodulin-Ca$^{2+}$ complex activates an enzyme called myosin kinase, which can phosphorylate myosin heads. When the myosin heads in smooth muscle are phosphorylated, they can undergo cycles of binding and releasing actin, causing muscle contraction. As Ca$^{2+}$ is removed from the sarcoplasm, it dissociates from calmodulin, and the activity of myosin
kinase falls. In addition, another enzyme, myosin phosphatase, de-phosphorylates the myosin and helps stop the actin-myosin interactions.

Single skeletal muscle twitches are summed into graded contractions

In skeletal muscle, the arrival of an action potential at a neuromuscular junction causes an action potential in a muscle fiber. The spread of that action potential through the T tubule system of the muscle fiber causes a minimum unit of contraction, called a twitch. A twitch can be measured in terms of the tension, or force, it generates (Figure 47.7a). A single action potential stimulates a single twitch, but the ultimate force generated by a muscle can vary enormously depending on how many muscle fibers are in its motor units. In muscles responsible for fine movements, such as those of the fingers, a motor neuron may innervate only one or a few muscle fibers, but in a muscle that produces large forces, such as the biceps, a motor neuron innervates a large number of muscle fibers. Still, however, at the level of the single muscle fiber, a single action potential stimulates a single twitch.

If action potentials reaching the muscle fiber are adequately separated in time, each twitch is a discrete, all-or-

\[
\text{Force} \quad \text{Stimulus} \\
\text{Force} \quad \text{Stimulus}
\]

A stimulus elicits a twitch, the minimum unit of contraction of a muscle fiber.

Two twitches in quick succession have a summed effect.

A stimulus elicits a twitch, the minimum unit of contraction of a muscle fiber.

Two twitches in quick succession have a summed effect.

**47.7 Twitches and Tetanus**

(a) Action potentials from a motor neuron cause a muscle fiber to twitch. Twitches in quick succession can be summed. (b) Summation of many twitches can bring the muscle fiber to the maximum level of contraction, known as tetanus.

i Muscles relax when stimulation stops.

i Muscles relax when stimulation stops.
Cardiac Muscle

Cardiac or heart muscle resembles skeletal muscle in some ways: it is striated and each cell contains sarcomeres with sliding filaments of actin and myosin. However, cardiac muscle has a number of unique features that reflect its function of pumping blood.

- The myofibrils of each cell (and cardiac muscle is made of single cells — each with a single nucleus) are branched.
- The branches interlock with those of adjacent fibers by adherens junctions. These strong junctions enable the heart to contract forcefully without ripping the fibers apart.
- The action potential that triggers the heartbeat is generated within the heart itself. Motor nerves (of the autonomic nervous system) do run to the heart, but their effect is simply to modulate — increase or decrease — the intrinsic rate and the strength of the heartbeat. Even if the nerves are destroyed (as they are in a transplanted heart), the heart continues to beat.
- The action potential that drives contraction of the heart passes from fiber to fiber through gap junctions.
  - Significance: all the fibers contract in a synchronous wave that sweeps from the atria down through the ventricles and pumps blood out of the heart. Anything that interferes with this synchronous wave (such as damage to part of the heart muscle from a heart attack) may cause the fibers of the heart to beat at random — called fibrillation. Fibrillation is the ultimate cause of most deaths, and its reversal is the function of defibrillators that are part of the equipment in ambulances, hospital emergency rooms, and even on U.S. air lines.
- The refractory period in heart muscle is longer than the period it takes for the muscle to contract (systole) and relax (diastole). Thus tetanus is not possible (a good thing, too!).
- Cardiac muscle has a much richer supply of mitochondria than skeletal muscle. This reflects its greater dependence on cellular respiration for ATP.
- Cardiac muscle has little glycogen and gets little benefit from glycolysis when the supply of oxygen is limited.
  - Thus anything that interrupts the flow of oxygenated blood to the heart leads quickly to damage — even death — of the affected part. This is what happens in heart attacks.
Smooth Muscle

Smooth muscle is made of single, spindle-shaped cells. It gets its name because no striations are visible in them. Nonetheless, each smooth muscle cell contains thick (myosin) and thin (actin) filaments that slide against each other to produce contraction of the cell. The thick and thin filaments are anchored near the plasma membrane (with the help of intermediate filaments).

Smooth muscle (like cardiac muscle) does not depend on motor neurons to be stimulated. However, motor neurons (of the autonomic system) reach smooth muscle and can stimulate it — or relax it — depending on the neurotransmitter they release (e.g. noradrenaline or nitric oxide, NO)). Smooth muscle can also be made to contract

- by other substances released in the vicinity (paracrine stimulation)
  - Example: release of histamine causes contraction of the smooth muscle lining our air passages (triggering an attack of asthma)
- by hormones circulating in the blood
  - Example: oxytocin reaching the uterus stimulates it to contract to begin childbirth.

The contraction of smooth muscle tends to be slower than that of striated muscle. It also is often sustained for long periods. This, too, is called tonus but the mechanism is not like that in skeletal muscle.

Muscle Diseases

The Muscular Dystrophies (MD)

Together myosin, actin, tropomyosin, and troponin make up over three-quarters of the protein in muscle fibers. Some two dozen other proteins make up the rest. These serve such functions as attaching and organizing the filaments in the sarcomere and connecting the sarcomeres to the plasma membrane and the extracellular matrix. Mutations in the genes encoding these proteins may produce defective proteins and resulting defects in the muscles.

Among the most common of the muscular dystrophies are those caused by mutations in the gene for dystrophin.

The gene for dystrophin is huge, containing 79 exons spread out over 2.4 million base pairs of DNA. Thus this single gene represents about 0.1% of the entire human genome (3 x 10^9 bp) and is almost half the size of the entire genome of E. coli!

- Duchenne muscular dystrophy (DMD)Deletions or nonsense mutations that cause a frameshift usually introduce premature termination codons (PTCs) in the resulting mRNA. Thus at best only a fragment of dystrophin is synthesized and DMD, a very severe form of the disease, results.
- Becker muscular dystrophy (BMD). If the deletion simply removes certain exons but preserves the correct reading frame, a slightly-shortened protein results that produces BMD, a milder form of the disease.

The gene for dystrophin is on the X chromosome, so these two diseases strike males in a typical X-linked pattern of inheritance.
A treatment for DMD? Deletions of one or more exons in the huge dystrophin gene are the cause of most of the cases of DMD. Exon 50 is a particularly notorious offender. When it is deleted, splicing of the pre-mRNA introduces a frameshift which then introduces a premature termination codon resulting in no functional dystrophin synthesized ("B"). However, an antisense oligonucleotide targeted to exon 51 causes the splicing mechanism to skip over it resulting in the stitching together of exons 49 and 52. This restores the correct reading frame so that only a slightly-altered version of dystrophin is produced, i.e., a BMD-type dystrophin ("C"). Seventeen weeks of weekly injections of 12 young DMD patients in the Netherlands with the oligonucleotide caused their muscles to synthesize sufficient amounts of dystrophin to enable 8 of them to walk better than before. (See Goemans, N., et al., in the 21 April 2011 issue of The New England Journal of Medicine.)
**Myasthenia Gravis**

Myasthenia gravis is an **autoimmune disorder** affecting the neuromuscular junction. Patients have smaller **end plate potentials** (EPPs) than normal. With repeated stimulation, the EPPs become too small to trigger further action potentials and the fiber ceases to contract. Administration of an inhibitor of acetylcholinesterase temporarily can restore contractility by allowing more ACh to remain at the site. Patients with myasthenia gravis have only 20% or so of the number of ACh receptors found in normal neuromuscular junctions. This loss appears to be caused by **antibodies** directed against the receptors. Some evidence:

- A disease resembling myasthenia gravis can be induced in experimental animals by immunizing them with purified ACh receptors.
- Anti-ACh receptor antibodies are found in the **serum** of human patients.
- Experimental animals injected with serum from human patients develop the signs of myasthenia gravis.
- Newborns of mothers with myasthenia gravis often show mild signs of the disease for a short time after their birth. This is the result of the transfer of the mother's antibodies across the placenta during gestation.

The reason some people develop autoimmune antibodies against the ACh receptor is unknown.

**The Cardiac Myopathies**

Cardiac muscle, like skeletal muscle, contains many proteins in addition to actin and myosin. Mutations in the genes for these may cause the wall of the heart to become weakened and, in due course, enlarged. Among the genes that have been implicated in these diseases are those encoding:

- actin
- two types of myosin
- troponin
- tropomyosin
- myosin-binding protein C (which links myosin to **titin**)

The severity of the disease varies with the particular mutation causing it (over 100 have been identified so far). Some mutations are sufficiently dangerous that they can lead to sudden catastrophic heart failure in seemingly healthy and active young adults.
Magnetic field effects on activity and ageing in honeybees*

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Summary. Artificial magnetic fields (MF) influence physiological processes in bees.
1. An inhomogeneous, static magnetic field (IMF) reduces the flying activity of bees and increases their life span by more than 60%.
2. The content of the ageing pigment lipofuscin in brain and, to a lesser extent, in thorax muscles increases with the physiological age. The content of lipofuscin of the thorax muscle is only 1/5 that of the brain.
3. Despite their increased chronological age (60–74%) brain lipofuscin of bees under conditions of an inhomogeneous, static magnetic field is slightly reduced compared with bees in natural earth’s magnetic field (EMF) conditions. No effects could be registered in the muscle lipofuscin of the thorax.
4. There was no correlation between the content of lipofuscin and the chronological age.
5. Flying activity is also reduced by horizontal magnetic fields (0.40–1.45 Oe). Drone tempo is drastically reduced if compensation of the EMF is followed by application of a 5 Hz magnetic field with 1.04 Oe, directed E–W.

Introduction
In bees magnetic field effects are known to influence spatial and temporal orientation (Lindauer and Martin 1968; Lindauer 1976; Martin and Lindauer 1977; Martin et al. 1983; Korall 1987; Korall and Martin 1987; Korall et al. 1988). In these papers emphasis is laid on the MF-induced misdirection of the waggle-dance and the temporal flying activity of bees under LL-conditions (flight box) which have either been time-trained or submitted to conditions of continuous feeding. However, the influences of MF effects are not restricted to the orientation behaviour. In vertebrates, Cremer-Bartels et al. (1984) and Reuss and Okese (1986) report MF influences on metabolic activity in the retina resp. the pineal gland. The feeding activity of termites is dependent on geomagnetic activity (Becker and Gerisch 1977). The motility of bees is influenced by periodically interrupted static MFs (Heppworth et al. 1980) whereas flying activity is related to inhomogeneous static MFs (Martin et al. 1983). It seems likely that there is an interrelation between orientational behaviour and metabolic changes under different MF conditions.
The life span of honeybees is correlated to their total flight performance and, therefore, to activity and energy turnover of the animals (Neukirch 1978, 1981). This asks for a metabolic correlate. Cellular lipofuscin deposits offer an excellent means of determining the physiological age of the bees. It is particularly in the poikilothermic insects that the depositing of lipofuscin is proportional to the animals’ activity: a certain level of accumulation is obtained earlier in animals showing a greater activity (Sohal and Donato 1979; Sohal 1981; Sohal et al. 1981). The accumulation of lipofuscin is discussed as the result of damage of cellular compartments, mainly the membranes (Hochschild 1971). Especially for ageing muscle cells and neurons (Brizze and Ordy 1981; Basset al. 1982) the depositing of the chemically inert lipofuscin granula reflect the former metabolic activity of these cells. In flying insects, the cells of the brain and the flight muscles are appropriate for the study.
Low Strength Static Magnetic Field Inhibits the Proliferation, Migration, and Adhesion of Human Vascular Smooth Muscle Cells in a Restenosis Model Through Mediating Integrins β1-FAK, Ca2+ Signaling Pathway

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Abstract—The proliferation, migration, and adhesion of vascular smooth muscle cells (VSMCs) and their interactions with extracellular matrix are key features of atherosclerosis and restenosis. Recently, there has been evidence that magnetic fields exert multiple effects on the biological performance of cells and may aid in the treatment of vascular disease. However, the effect of a static magnetic field (SMF) on human VSMCs still remains unknown. In this study, we aimed to determine the effects of low strength SMF on human VSMCs in an in vitro restenosis model. A SMF was established using neodymium–yttrium–iron permanent magnet. Human umbilical artery smooth muscle cells (hUASMCs) were isolated and seeded to a sterile standard plate to form an in vitro restenosis model and then exposed to a vertically oriented field of 5 mT. MTT, tranwell, and adhesion assays were used to demonstrate that the proliferation, migration, and adhesion potential of hUASMCs were significantly decreased after exposure to 5 mT SMF for 48 h compared with a non-treated group. Meanwhile, confocal microscopy analysis was used to demonstrate that integrin β1 clustering was inhibited by exposure to 5 mT SMF. Furthermore, the phosphorylation of focal adhesion kinase (FAK) was markedly inhibited, and the up-regulated cytosolic free calcium had been reversed (p < 0.05). However, the biological effects of low strength SMF on hUASMCs could be blocked by the administration of GRGDSP—γ-ile blockade of integrins. In conclusion, a low strength SMF can influence the proliferation, migration, and adhesion of VSMCs by inhibiting the clustering of integrin β1, decreasing cytosolic free calcium concentration, and inactivating FAK. With further validation, SMF’s may aid in attenuating abnormal VSMC biological performance and has potential to block atherogenesis and prevent restenosis.

Keywords—Static magnetic field, Atherosclerosis and restenosis, Human vascular smooth muscle cells, Integrins, FAK, Intracellular calcium ion.

INTRODUCTION

Atherosclerosis and restenosis are common cardiovascular diseases and a major threat to global human health.15,16 Vascular remodeling, proliferation, migration, and adhesion of vascular smooth muscle cells (VSMCs) are key features of these pathologies.21 While there has been enormous progress in drug development and clinical management of these disorders, current treatment modalities are not always efficacious.24

Emerging biophysical medicine brings new hope for treating some common diseases, such as cardiovascular disease,25 cancer,10 and neuron disease.31 Biophysical medicine is the application of biophysical technology for treatment, diagnosis, monitoring, and control of biological systems. These applications9,13 range from targeted therapy, in vivo imaging and in vitro diagnostics to biomaterials and active implants.

There has been increasing evidence to show that the magnetic fields (MF) are an important biophysical medical method, and has the potential to exert multiple biological effects on cells,19,20 such as influence antioxidant response and DNA integrity.1 In 2003, Iwasaka et al.16 reported that a high-intensity MF (14 T) induced significant effects on the morphology of smooth muscle cells, and the rate of cell proliferation. In 2008, Kobbett et al.18 reported that low-energy electromagnetic fields (EMFs) promoted the proliferation of VSMCs. However, the reported negative effects of MFs is still inconsistent and there is no

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Neurophysiological and behavioral effects of a 60 Hz, 1,800 µT magnetic field in humans

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Abstract The effects of time-varying magnetic fields (MF) on humans have been actively investigated for the past three decades. One important unanswered question is the potential for MF exposure to have acute effects on human biology. Different strategies have been used to tackle this question using various physiological, neurophysiological and behavioral indicators. For example, researchers investigating electroencephalography (EEG) have reported that extremely low frequency (ELF, <300 Hz) MF can increase resting occipital alpha rhythm (8–12 Hz). Interestingly, other studies have demonstrated that human mortality can be modulated by ELF MF: a reduction of anteroposterior standing balance or a decrease of physiological tremor intensity have been reported as consequences of exposure. However, the main limitation in this domain lies in the lack of results replication, possibly originating from the large variety of experimental approaches employed. Therefore, the present study aimed to investigate the effects of a 60 Hz, 1,800 µT MF exposure on neurophysiological (EEG) and neuromotor (standing balance, voluntary motor function, and physiological tremor) aspects in humans using a single experimental procedure. Though results from this study suggest a reduction of human standing balance with MF exposure, as well as an increase of physiological tremor amplitude within the frequency range associated with central nervous system contribution, no exposure effect appeared on other investigated parameters (e.g., EEG or voluntary motor control). These results suggest that 1 h of 60 Hz, 1,800 µT MF exposure may modulate human involuntary motor control without being detected in the cortical electrical activity.

Keywords Time-varying magnetic field · 60 Hz · Human · Electroencephalography · Tremor · Standing balance

Introduction

Recent studies have been trying to characterize the effects of extremely low frequency (ELF, below 100 Hz) magnetic fields (MF) on human biology and performance. Despite the amount of work conducted in this area, there is still no consensus regarding the effects of ELF MF exposure on humans. The main sources of ELF MF in our daily environment are domestic electrical appliances, distribution and transport power-lines, and residential wiring which are producing power-line frequency MF: 50 Hz in Europe and 60 Hz in North America. General public exposure to power-line frequency MF is on average <0.01 µT (Kaufe et al. 2002). Although a few controversial epidemiological
MAGNETIC FIELD EFFECTS ON ASSEMBLY PATTERN OF SMOOTH MUSCLE CELLS

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SUMMARY

Under a strong magnetic field, the diamagnetic properties of biological cells modulate the behavior of the cells themselves, under conditions of both floating and adherence. The morphological effects of strong static magnetic fields on adherent cells are less well understood than the effects of magnetic fields on red blood cells. In the present study, a high-intensity magnetic field of 14 T affected the morphology of smooth muscle cell assemblies, and the shape of the cell colonies extended along the direction of the magnetic flux. The phenomenon was most notable under magnetic fields of more than 10 T, where an ellipsoidal pattern of smooth muscle cell colonies was clearly observed. The ellipticity of the cell colony pattern with a 14 T magnetic field was 1.3, whereas that with a field of 0–8 T was close to a circle at about 1.0. The evidence that smooth muscle cells detect high-density magnetic flux and thus change their cell orientation was shown as a visible pattern of cellular colonies. The speculated mechanism is a diamagnetic torque force acting on cytoskeleton fibers, which are dynamically polymerizing-depolymerizing during cell division and cell migration.

Key words: smooth muscle cell; cell orientation; colony; magnetic field; diamagnetism.

Biological systems and materials are composed of materials with weak magnetic properties, and some effects of diamagnetic properties have been shown to be the tangible results of magnetic fields. An example of this phenomenon is magnetic orientation (Barret et al., 1991; Murthy, 1984; Terbe and Komorese, 1984; Higashita et al., 1993; Tranquillo et al., 1996), where protein polymers are oriented along the direction of magnetic flux. Studies with fibrin and collagen proved that peptide bonds, which are involved in the helix structure of the proteins, are anisotropic in diamagnetic susceptibility under magnetic fields, contributing to the rotation of macromolecules under Tesla-order static magnetic fields. Also, the cell membrane, which has a lipid bilayer, has a distinct diamagnetic anisotropy in the entire cell if the cell shape is not a perfect sphere. Among the cells floating in blood, platelet-shaped cells, such as red blood cells and blood platelets, rotated and oriented along the direction of the magnetic flux (Higashita et al., 1993).

In contrast, few confirmed observations have been made concerning adhering cells. Friction between the cells and the substrate surface disturbs the orientation of the cells adhering to the surface, delaying the discovery of the alignment of the adhering cells under strong Tesla-order static magnetic fields. In our previous study, smooth muscle cells of rat (A7r5) aligned along the magnetic field after several d of exposure to a magnetic field of 3 T (Umemoto et al., 2001), and we analyzed the orientational order parameters in the local areas of cells in a flask. The analyses showed that the orientational order parameters increased in a group of cells sampled manually from a cell culture flask exposed to a magnetic field. However, the flask with a magnetic field of 8 T had a local area where cell orientation was random as well as an area with magnetically aligned cells. We concluded that the majority of cells aligned along the applied magnetic fields. A preliminary experiment provided evidence that the smooth muscle cells did not align with the magnetic field if the cells were not in contact with each other, whereas they did align along the magnetic field when they became confluent. A problem related to the observed phenomenon is the possible effect of a boundary condition, specifically, the side of the flask. It is expected that cell orientation is easily influenced by flask wall when the cell density is high and the cells form a domain on a scale of hundreds of micrometers.

The present study was designed to observe cell alignment under magnetic fields, excluding the effects of boundary conditions, which are determined by the walls of the cell culture flask. We prepared a situation in which the cells form a circular colony pattern; the contour of the colony is observed for evaluating the principal mechanisms for cell alignment induced by external magnetic fields. The experiments are conducted with a 14 T superconducting magnet, and the dependence of the cellular colony pattern on the density of the magnetic flux is shown.

We prepared a cell culture system at room temperature inside a superconducting magnet with a base, where static magnetic fields of up to 14 T were generated. Both the temperature and the magnetic fields were maintained at constant levels for several d of cell culture. Colonies of smooth muscle cells (A7r5) were formed on a polylysine substrate, and the effects of magnetic fields on their morphology were observed after 3 d of incubation. Smooth muscle cells (A7r5, thoracic aorta, endothelium) were purchased from Dainippon Pharmaceutical Co., Ltd, Osaka, Japan. The cells were cul-

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PULSING MAGNETIC FIELD EFFECTS ON BRAIN ELECTRICAL ACTIVITY IN MULTIPLE SCLEROSIS

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Introduction

Multiple sclerosis (MS) is a disease of the central nervous system. Clinical symptoms include central fatigue, impaired bladder control, muscle weakness, sensory deficits, impaired cognition, and others. The cause of MS is unknown, but from histologic, immunologic, and radiologic studies, we know that there are demyelinated brain lesions (visible on magnetic resonance images) that contain immune cells such as macrophages and T-cells (visible on microscopic analysis of brain sections). Recently, a histologic study has also shown that widespread axonal damage occurs in MS along with demyelination. What is the possible connection between MS and bioelectromagnetic fields? We recently published a review entitled "Bioelectromagnetic applications for multiple sclerosis," which examined several scientific studies that demonstrated the effects of electromagnetic fields on nerve regeneration, brain electrical activity (electroencephalography), neurochemistry, and immune system components. All of these effects are important for disease pathology and clinical symptoms in multiple sclerosis (MS).

Richards 1997 Pulsing Electromagnetic Study on Multiple Sclerosis

In 1996 and 1997, we performed a double-blind study to measure the clinical and sub-clinical effects of an alternative-medicine magnetic device on disease activity in MS. The MS patients were exposed to a magnetic pulsing device (Enermed) where the frequency of the magnetic pulse was in the 4 to 13 Hz range (50-100 milliGauss). A total of 30 MS patients wore the device on preselected sites between 10 to 24 hours a day for 2 months. Half of the patients (15) randomly received a device which was magnetically inactive and the other half received an active device. Each MS patient received a set of tests to evaluate MS disease status before and after they had worn the Enermed device. The tests included: 1) a clinical rating (Kurtzke, EDSS); 2) patient-reported performance scales 3) quantitative electroencephalography (QEEG) during a language task. Although there was no significant change between pre- and post-treatment in the EDSS scale; there was a significant improvement in the performance scale combined rating for bladder.
Transmembrane potential induced on the internal organelle by a time-varying magnetic field: a model study

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Abstract

Background: When a cell is exposed to a time-varying magnetic field, this leads to an induced voltage on the cytoplasmic membrane, as well as on the membranes of the internal organelles, such as mitochondria. These potential changes in the organelles could have a significant impact on their functionality. However, a quantitative analysis on the magnetically-induced membrane potential on the internal organelles has not been performed.

Methods: Using a two-shell model, we provided the first analytical solution for the transmembrane potential in the organelle membrane induced by a time-varying magnetic field. We then analyzed factors that impact on the polarization of the organelle, including the frequency of the magnetic field, the presence of the outer cytoplasmic membrane, and electrical and geometrical parameters of the cytoplasmic membrane and the organelle membrane.

Results: The amount of polarization in the organelle was less than its counterpart in the cytoplasmic membrane. This was largely due to the presence of the cell membrane, which "shielded" the internal organelle from excessive polarization by the field. Organelle polarization was largely dependent on the frequency of the magnetic field, and its polarization was not significant under the low frequency band used for transthalamic magnetic stimulation (TMS).

Both the properties of the cytoplasmic and the organelle membranes affect the polarization of the internal organelle in a frequency-dependent manner.

Conclusions: The work provided a theoretical framework and insights into factors affecting mitochondrial function under time-varying magnetic stimulation, and provided evidence that TMS does not affect normal mitochondrial function by altering its membrane potential.

Background

Time-varying magnetic fields have been used to stimulate neural tissues since the start of 20th century [1]. Today, pulsed magnetic fields are used in stimulating the central nervous system, via a technique named transcranial magnetic stimulation (TMS). TMS is being explored in the treatment of depression [2], seizures [3,4], Parkinson’s disease [5], and Alzheimer’s disease [6,7]. It also facilitates long-lasting plastic changes induced by motor practice, leading to more remarkable and lasting clinical gains during recovery from stroke or traumatic brain injury [8].

When exposed to a time-varying magnetic field, the neural tissue is stimulated by an electric current via electromagnetic induction [9], which induces an electrical potential that is superimposed on the resting membrane potential of the cell. The polarization could be controlled by appropriate geometrical positioning of the magnetic coil [10-12]. To investigate the effects of stimulation, theoretical studies have been performed to compute the magnetically induced electric field and potentials in the neuronal tissue, using models that represent nerve fibers [13-18] or cell bodies [19].

Mitochondria are involved in a large range of physiological processes such as supplying cellular energy, signaling, cellular differentiation, cell death, as well as the control of cell cycle and growth [20]. Their large negative membrane potential (~180 mV) in the mitochondrial inner membrane, which is generated by the electron-transport chain,
Static magnetic field effect on the arterial baroreflex-mediated control of microcirculation: implications for cardiovascular effects due to environmental magnetic fields

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Abstract Increasing evidence suggests that time-varying and static magnetic fields in the environment might affect the cardiovascular system. To explore the underlying physiology, the effect of static magnetic fields (SMFs) on the carotid baroreflex control of microcirculation was studied. Twenty-four hemodynamic measurements were performed in rabbits sedated by pentobarbital infusion (5 mg/kg/h) during experiments that lasted 120 min. Mean femoral artery blood pressure, heart rate, and earlobe skin microcirculatory blood flow, measured by microphotoelecetric plethysmogram (MPPG), were simultaneously recorded before and after a 40 min exposure of the sinoaortic baroreceptors to Nd$_2$Fe$_{14}$B alloy magnets (n = 14) or sham magnets (n = 10, control series). The local SMF field was 250 mT, at the baroreceptors’ site. Arterial baroreflex sensitivity (BRS) was estimated from heart rate/blood pressure response to intravenous bolus injections of nitroprusside and phenylephrine. A significant positive correlation was found between the SMF-induced increase in BRS (ΔBRS = BRS$_{afterSMF} -$ BRS$_{beforeSMF}$) and the increment in microvascular blood flow (ΔMPPG = MPPG$_{afterSMF} -$ MPPG$_{beforeSMF}$) (r = 0.66, p < 0.009). The SMF probably modulated the arterial baroreflex-mediated microcirculatory control. This could represent one possible mechanism how environmental magnetic fields act on the cardiovascular system, and a method to complexly adjust macro- and microcirculation with potential clinical implementation.

Introduction

Increasing evidence suggests that environmental and occupational magnetic fields have an effect on the cardiovascular system [1–9]. To investigate the underlying physiology, the effects of static magnetic fields (SMFs) on separate parts of the richly branched regulatory chain of the cardiovascular system were studied. This approach allows identification of most sensitive biological structures, and determination of mechanisms or sequences of changes in physiological functions that give rise to the observed biological effects. It has already been reported earlier that SMFs of different intensity significantly affect hemodynamics including blood pressure, heart rate (HR) [10–17] microcirculation [18, 19] and arterial baroreflex [20–22].

It is widely recognized that arterial baroreceptors play a key role in the operation of cardiovascular functions and in the reflex regulation of blood pressure, under normal and pathological conditions. Arterial baroreceptors, located in the aortic arch and carotid sinuses, normally respond to stretch by initiating reflexes that promote parasympathetic and restrain sympathetic activities, significantly modifying HR, peripheral vasoconstriction and cardiac output. These reflex responses result in negative feedback regulations of the arterial blood pressure, by which its liability is minimized [23]. The arterial baroreflex regulatory effect on microcirculation is less explored. The microcirculatory network of the skin, like other body tissues, continuously exhibits rhythmic changes in diameter and flow [24–26].
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Magnetic measures of reaction into the head (not red).

Cybermagnetic autofocusing of the body magnetic and electric.

Sound and Magnetic vibration into the body (in Black).

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\[ B \Rightarrow \text{magnetic moment of proton, spin dependent} \]
\[ \hspace{1cm} = \text{H bond} \]

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Oriented Spin control

Water molecule

Dialectical Interface

Paramagnetic domain

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Cybermagnetics Unlocks Epigenes
Cybermagnetic

Using the computers headphone and microphone jacks we can first analyze the patient’s voice patterns for energetic disturbance and then chose sound files for relaxation, healing or energy. The music is sent into the body thru the headphones and a magnetic field generator. A magnetic field detector then receives the signals from the body establishing a cybermagnetic loop. The computer can then change the music to help the patient’s body electric.

Sound and Magnetic Vibration into the body (in Black)

Magnetic measures of reaction into the Computer (in Red)

Cybermagnetic autofocusing of the Body Magnetic and the Body Electric

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Magnetic Energy and is Sent into
the Heart Chakra

The Energy
Penetrates into
the Whole Body
Thru the Magnetic
Waters of the Body

Then We Measure the
Magnetic Energy at the
Stomach Chakra and use
a CyberMagNetic Loop to
AutoFocus the Therapy
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