Factors Controlling Movement of Skeletal Muscles

Miranda D. Grounds, School of Anatomy, Physiology and Human Biology, The University of Western Australia, Australia 6009. E-mail: <miranda.grounds@uwa.edu.au>. Web: <school.anhb.uwa.edu.au/personalpages/grounds/>.

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Abstract
The contraction of specialized skeletal muscle cells results in classic movements of bones and other parts of the body that are vital for life. There is exquisite control over the movement of diverse types of muscles. This paper indicates the way in which skeletal muscles (myofibres) are formed; then factors that contribute to generating the movement are outlined: these include the nerve, sarcomeres, cytoskeleton, cell membrane and the extracellular matrix. The factors controlling the movement of mature myofibres in 3-dimensional tissues in vivo are vastly more complex than for tissue cultured immature muscle cells in an artificial in vitro environment.

Skeletal muscles represent about 40% of the human body mass; the functional components are myofibres, long multinucleated cells filled with specialized contractile proteins organised to form sarcomeres. Activation of these complex structures results in muscles contracting and relaxing to move the bones of the body. There are over 600 different muscles that control a dazzling array of movements for posture, running, breathing, hearing, talking, playing musical instruments, blinking and twitching your ears. Plus the metabolism of muscles is of major importance for general health. The length of myofibres is very variable with an average length of about 30mm in humans: the stapedius muscle in the ear is the smallest (2mm) and the sartorius muscle in the thigh can be extremely long, up to about 600mm [1]. The dimensions and architecture of the various muscles are dictated by the anatomical location and overall function. A few examples illustrate the variables of movement. The small precise movements of the eyeball are achieved by very fine control of 6 extracocular muscles; the maintenance of posture where the whole body may be held vertical for long periods of time requires the coordinated action of many slow contracting muscles in the torso and also the legs; other muscles specialized for generating power include limb muscles like the large quadriceps in the legs that are important for running and raising the weight of the body from the sitting position; and muscles containing fast myofibres are essential for very rapid movement such as reflexes. Exquisite control of the contractile properties of each muscle is required to manifest the various movements.

Formation and Growth of Skeletal Muscle
Skeletal muscles are formed from mononucleated cells (myoblasts) that proliferate, differentiate and then fuse together to form long cells (myotubes) that contain many nuclei (Fig. 1). These enlarge to become myofibres filled with a complexity of contractile proteins (including actins, myosins and tropomyosins) that are highly organized to form sarcomeres; these give the muscle a striped (striated) appearance (see Fig. 1). The myofibre must be connected to a nerve to become functional. Another critical component of muscle tissue is the extracellular matrix (ECM) between the myofibres.

A few myoblasts remain on the surface of the myofibres, (where they are called satellite cells) beneath a layer of specialized ECM called the basement membrane (see Fig. 1). The satellite cells are normally quiescent in mature muscle. However, they are essential for regeneration. If part of a muscle is damaged and dies, the satellite cells become activated, and myogenesis forms segments of new muscle to replace the damaged portions of the myofibres.

Mechanism of Muscle Contraction and Movement
The nerve provides the electrical signal that is essential to start the contraction process: it tells the muscle when and how to contract in either a fast or a slow way. Ultimately it is the brain that controls the complex network of nerves throughout the body; thus the skeletal muscles are under voluntary control. The end of the nerve connects onto the surface of the myofibre through a special neuromuscular junction [2] (Fig. 2). Here, the electrical signal that comes down the nerve generates little packages of chemicals that rapidly cross the junction and talk to the waiting muscle surface, to generate another fast electrical signal that travels down the muscle cell membrane. This electrical signal releases calcium into the myofibre and initiates contraction of the sarcomeres to generate force. If the nerve is cut or damaged, the muscles cannot work. In very old muscles the nerves can detach; this leads to the age-related loss of muscle function [3].

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The force generated by the sarcomeres is transferred via the cytoskeleton (involving various proteins including desmin and actin) to the surface of the muscle cell. Actin is a particularly important component of the cytoskeleton, that is literally an internal skeleton of the cell. It is the assembly and disassembly of this cytoskeleton that allows other cells to move across surfaces in tissue culture and within living organisms; actin is also involved in movement of organelles such as mitochondria within cells [4]. This same basic mechanism has become far more sophisticated in the organization of sarcomeres in specialized contractile cells such as skeletal, and also heart, muscles.

The contractile force (that is generated by the sarcomeres and passed via the cytoskeleton to the surface of the muscle cell) then engages with proteins outside the cell (Fig. 3). This is achieved through protein complexes (integrins and dystroglycan) that span the cell membrane and connect with the ECM [5]. The initial connections are to molecules in specialised ECM called the basement membrane that is in intimate contact with the surface of the myofibre: here a key protein component is laminin [5]. Finally, the force is transferred to strong collagen fibres that do most of the work to move the bones and other parts of the body: collagen is stronger per unit weight than steel! Defects in a huge range of proteins that contribute to the generation of muscle force – from the cytoskeleton to the ECM – result in a diversity of human diseases where muscle function and hence movement is impaired [6].

**Important Differences between In Vivo and In Vitro**

These events of skeletal muscle contraction are fundamentally similar across many species, e.g. flies and humans. The study of muscles in vivo using animal models or humans can be difficult and there are important ethical issues to consider. A popular alternative is to grow cells outside the body under tissue culture (in vitro) conditions, since this is flexible, relatively inexpensive, and ethically simplified. Tissue culture is widely used to study many aspects of myogenesis and myotube function, but the many limitations of these artificial conditions must be considered. Myotubes do not fully represent the complex situation of mature innervated myofibres in vivo. Specifically, myotubes are immature growing cells where the response to many factors can be far greater than for mature myofibres of a fixed length in vivo [1]; plus cultured myotubes lack the influence of the nerve/NMJ, and also the full ECM.

**Summary**

The macroscopic movement of muscles and all parts of a living organism is the result of beautifully integrated microscopic cell biology. The co-ordinated nervous system is connected to the muscles to provide the electrical signal to alter the contractile proteins within myofibres; this generates force that is transferred across the muscle cell membrane to the ECM to move different parts of the body. Such movement is vital for life.

**Author’s Note**

As a scientific researcher for over 40 years, I consider that creativity and tangential thinking are fundamental to innovative good science and thus welcome closer interactions between Science and Art. My vision as a co-founder of SymbioticA was to facilitate opportunities for artists to engage more closely with biological scientists and the extraordinary developments and beauty of sciences. The creation of new opportunities for dynamic cross-disciplinary interactions, to push the boundaries of provocative possibilities, results in many diverse presentations, such as the symposium on Agency in Movement.

**References and Notes**

“This article is based on a paper presented at the ‘Agency in Movement’ symposium held by SymbioticA on 21 June 2013 at the University of Western Australia, Perth.