THE IMPORTANCE OF BIOMECHANICS

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ABSTRACT

When neuroscientists gather to discuss "Movement and Sensation", they tend to discuss neurons rather than muscles and bones. Neurons may be more interesting, but their roles in motor control depend on the mechanical properties of the system to be controlled. Understanding of those properties has been surprisingly elusive, despite the well-developed disciplines of biomechanics and muscle physiology. Each experimental field has its favorite, often unique preparation. Mathematical models range in scale from individual cross-bridges to articulated limbs, usually written in different computer languages. The shortcomings of such fragmented knowledge become particularly apparent when biomedical engineers must design safe and effective control systems for real limbs, such as for functional electrical stimulation (FES) of reach and grasp in quadriplegic patients. We are addressing the question of how to model neuromusculoskeletal systems so that they are sufficiently complete, valid and accessible to be useful in both basic and applied sensorimotor research.

INTRODUCTION

This essay focuses on three elements that are required to appreciate fully the role of biomechanics in sensorimotor control:

1. **Prioritization** according to the importance of various attributes of the component parts. Models inevitably simplify reality because they are based on limited experimental data and because they must be computationally tractable. This makes it necessary to determine which attributes can be simplified or omitted from the model and which attributes require additional experimental data to define their models.

2. **A computational platform** in which to bring the component parts together. This is required because models of complete neuromusculoskeletal systems are inherently complex and subject to changes and upgrades that are likely to be derived from many different sources. It is not practical for one researcher to build and maintain a complete model and it would be difficult for other researchers to benefit from such a personal model system.

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3. **A real-world application** to serve as a test of the adequacy of our understanding. This is required because artificial scenarios may obscure the shortcomings of model controllers (not always coincidentally). If we truly understand what the nervous system must compute to control a limb, then we should be able to build a prosthetic controller that works successfully when interfaced with the real biomechanical system.

PRIORITIZATION OF ATTRIBUTES

Most models incorporate various terms that represent well-known aspects of biomechanical systems that seem to be important, such as the active force-length relationship and the sluggish response of skeletal muscle in response to dynamically changing neural activation. Other attributes tend to be omitted because they are less well-known or less well-described experimentally or because their mathematical descriptions appear to be too complex; the relative importance of the omitted attributes often is neither obvious nor tested. The space available here does not permit an exhaustive presentation of model components, so we will focus on two that are often omitted or over-simplified but seem to be particularly important.

Cross-Bridge Cooperativity

In most muscle models, the cycle of cross-bridge attachment/detachment is described in terms of Ca^{++} regulation alone. There is, however, a substantial body of evidence that attached, force-producing cross-bridges can themselves facilitate the formation of nearby cross-bridges (see Gordon et al., 2000 for review). This is in addition to the cooperativity that arises from the second order kinetics of calcium binding to troponin and from the distributed reconfiguration of tropomyosin along the thin filament. For muscle models that use a black-box approach to describe activation dynamics (e.g. Brown and Loeb, 2000), understanding cooperativity is not necessary. Such models tend to become arbitrarily complex, however, as they are extended to account for important properties such as the frequency dependence of relaxation time and the energy consumption of muscle under varying conditions of work. By incorporating both types of cooperativity explicitly in our newer model, we have found that the overall structure of the model actually becomes simpler even as the fit to experimental data improves.

The various forms of cooperative binding for both Ca^{++} and cross-bridges all contribute importantly to the steepness of the force-frequency relationship. In Figure 1 we plot two force-frequency relationships, one for a 'realistic' fiber and one for a 'hypothetical' fiber that is lacking only the cross-bridge cooperativity term. The steeper curves are for the realistic fiber, with model coefficients adjusted to fit the measured force-frequency relationships. The equation used for this plot is the biochemical Hill equation, with a Hill co-efficient (n_H) of 5. Typical values of n_H for single fibers range from 4-6 (Gordon et al., 2000). The shallower force-frequency relationship is an estimate for our 'hypothetical' fiber in which there is no cross-bridge cooperativity. We used $n_H=2$ for this fiber based upon the range of measured Hill co-efficients for Ca^{++} binding to troponin (these range from 1.2-2.0; Gordon et al., 2000). In order to compare the force-frequency relationships of these two fibers we had to assume relative values for cross-bridge attachment/detachment and Ca^{++} sensitivity. We have matched the two simulations to produce identical rise and fall times for force and to consume similarly low

energy in the relaxed state. The timing constraint leads us to conclude that cross-bridge attachment/detachment rates should be identical as should Ca^{++} release/uptake. Minimizing basal energy consumption requires us to equate Ca^{++} sensitivities at some small value of [Ca]. We chose arbitrarily to equate these at the level necessary to produce a force of $0.05\ F_0$. This approximation probably overestimates the hypothetical Ca^{++} sensitivity, thus underestimating the differences between realistic and hypothetical fibers. Note that our choice of n_H for the hypothetical fiber at the high end of the range for Ca^{++} binding alone will also tend to underestimate the differences between the fibers.
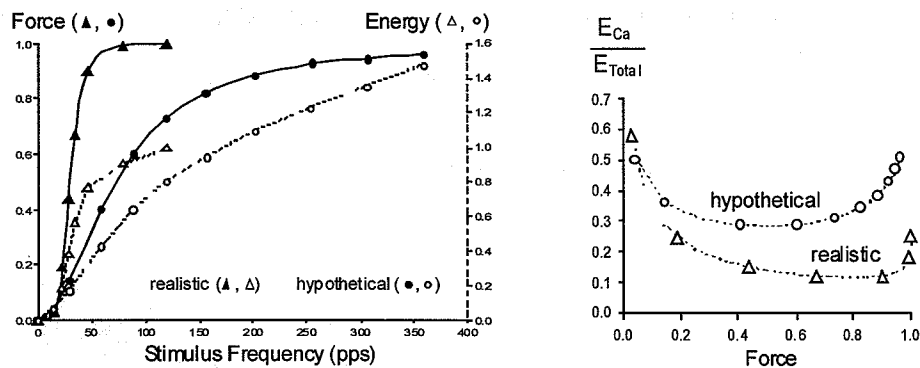

Figure 1. Isometric active force and energy consumption for models of mammalian skeletal muscle with realistic cross-bridge cooperativity (triangles) and no cooperativity (circles). Force and energy are each normalized to their peak realistic values. See text for model details. On the right we show the fraction of energy consumption related to calcium kinetics at equivalent force levels for the two models.

As would be expected, the hypothetical fiber has a much shallower force-frequency relationship. We have also plotted the total energy consumption vs. frequency relationships for the two fibers on the same plot (open symbols, dashed lines). To calculate energy consumption from the Ca^{++} pump, we assumed that under tetanic conditions (120 pps for the realistic fiber) ~25% of the total energy consumption is due to Ca^{++} uptake (Homsher, 1987). For a given stimulus frequency the plots show that the hypothetical fiber consumes less energy. This result is expected given that the hypothetical fiber is producing less force (i.e. fewer cross-bridges are cycling). A more relevant comparison is shown in Figure 1 (right) in which we plot the fraction of Ca^{++} pump energy consumption vs. total energy. At optimal force levels, the realistic fiber uses only ~15% of its energy consumption on Ca^{++} uptake. In order to achieve the same force levels, the hypothetical fiber must operate at a higher frequency, forcing it to use at least ~30% of its energy on Ca^{++} uptake. This result suggests that one of the reasons that cross-bridge cooperativity evolved may have been to minimize energy wasted by the Ca^{++} pump so as to maximize the force and work production per unit energy consumption. Omission of effects due to cross-bridge cooperativity has large effects on both force and energy predictions in skeletal muscle models.

Dynamic Moment Arms

Muscles generate forces along their effective lines of pull. These must be multiplied by moment arms to compute the joint torques that actually move a limb. Moment arms in biological systems are more complex than they might seem because muscles often cross joints obliquely to one or more axes of rotation and because the paths that their tendons follow across those joints are often constrained by boney protuberances, ligamentous retinacula and the bulging of adjacent muscles. Thus, the actual moment arm in any one axis tends to depend on the angular position of the joints in all axes. These changes in moment arm, and hence muscle torque, may be quite large. Furthermore, the contractile force of the muscle cannot be computed accurately without knowing the length and velocity of the muscle itself. This is usually computed from the same features of the musculotendon path on the skeleton that are used to define the moment arms.
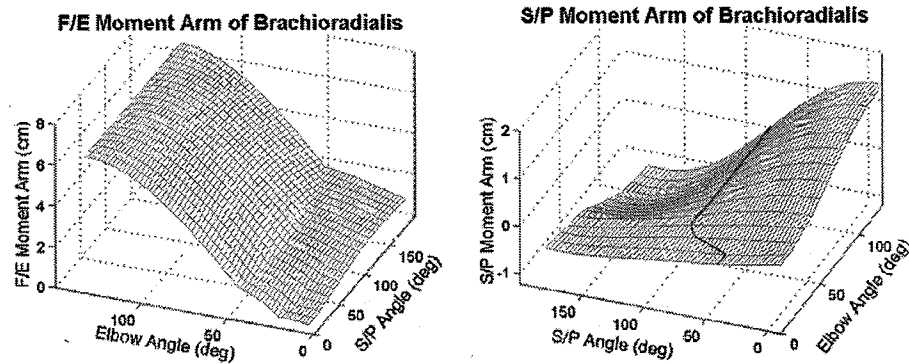

Figure 2. Moment arms of brachioradialis muscle as functions of elbow flexion/extension angle (left: F/E, 0° = full extension) and forearm supination/pronation (right: S/P; 0° = max. pronation) posture. The S/P angle for which the S/P moment arm reverses sign (heavy line) changes with elbow angle.

Moment arms may actually change sign as joint angles change. In at least two systems, these zero-crossings effectively define "equilibrium joint angles"; any contractile force in the muscle will tend to resist motion away from the neutral angle at which moment arms (and torques) go through zero. Young et al. (1993) described the tendency of several feline muscles to stabilize the ankle in neutral inversion/eversion and abduction/adduction postures regardless of flexion/extension angle or torque. The figure above shows one example from an even more complex system in which the human elbow flexors tend to pull the forearm toward equilibrium angles in pronation/supination. The surface plots were generated by operating an anatomically accurate model of the musculotendon path. This was created in the graphical environment of the SIMM™ commercial software package (see Figure 3 below) and adjusted to match the available data on flexion/extension moment arms (Murray, 2000). The slopes and zero-crossings of the pronation/supination moment arms change as flexion/extension angle changes; biceps has a similar pattern with different zero-crossings. It seems likely, but remains unproven, that the central nervous system selects kinematic trajectories and muscle activation patterns that take advantage of these biomechanical features.

COMPUTATIONAL PLATFORM

The two attributes described above belong to different levels of the musculoskeletal system. Cross-bridge cooperativity is a feature of muscle physiology that is probably universal to all mammalian skeletal muscles, while dynamically changing moment arms are a consequence of the anatomical details of a given musculotendon unit and its attachments to the skeleton. A set of sensors and a control system constitute still other levels of the system, all of which must exchange data about state variables with the other levels. The neural control system itself is organized into hierarchical levels such as spinal cord and cerebral cortex (Loeb et al., 1999).

We have selected the commercially supported Simulink™ software application in which to develop and link the components into complete systems. We are developing a set of modeling tools to facilitate the construction and manipulation of the component models. The first two tools are largely complete:

- MMS™ (Musculoskeletal Modeling in Simulink) is a C program that operates on SIMM musculoskeletal models (see Fig. 3), converting them to Simulink blocks.
- Virtual Muscle™ (Cheng et al., 2000) is a Matlab program that creates Simulink blocks representing the tension-generating properties of mixed fiber-type muscles under the full dynamic range of length, velocity and recruitment history.

Each Virtual Muscle block is driven by a neural command signal that produces recruitment and frequency modulation of its various motor units. Muscle path length (L_p) information from the SIMM block is apportioned among muscle fascicles and tendon-aponeurosis to provide the fascicle length (L_f) and velocity information needed to compute contractile force and to drive a model of a spindle primary afferent. The forces of all the muscles produce torques on the limb segments according to the SIMM musculoskeletal model; the limb moves according to Newtonian mechanics incorporated in a kinetic model generated by SD-FAST™ (another commercial software package linked to SIMM). Figure 3 shows the SIMM anatomical model and corresponding Simulink blocks required to represent and simulate its operation and control by a simple, hierarchical sensorimotor nervous system.
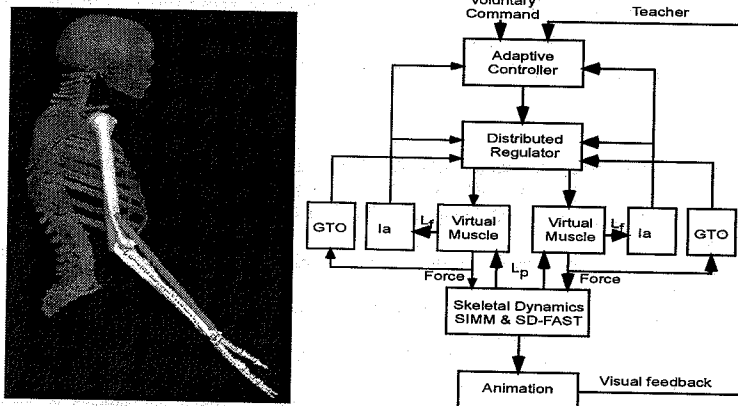

Figure 3. Left: anatomical model of the human arm in SIMM with two muscles, brachioradialis (elbow flexor) and triceps lateralis (elbow extensor). Right: Simulink blocks corresponding to this system with sensors (Ia = spindle primary; GTO = Golgi tendon organ) and a simple hierarchical controller based on a spinal-cord like distributed regulator and a brain-like adaptive controller. L_p = musculotendon path length, L_f = fascicle length
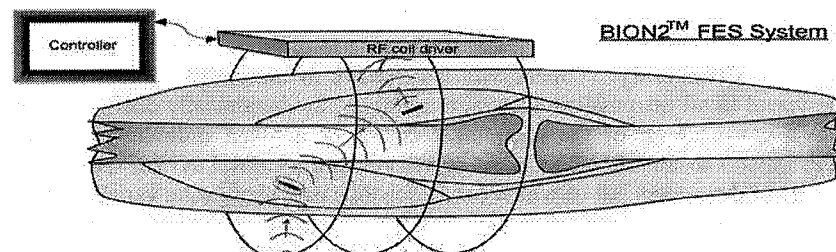
TEST APPLICATION

Figure 4. BION™ (BIOnic Neuron) modules for stimulation and sensing of muscle activity. Each injectable module receives power and digital command signals from a common external RF inductive coil. Each module can stimulate a muscle (now in clinical trials to treat disuse atrophy in patients with stroke and osteoarthritis); future modules will also transmit data from internal sensors, such as the range-finding function depicted here between two such implants to create a BIONic muscle spindle for joint angle sensing.

We have chosen the neural prosthetic control of functional reach and grasp movements in quadriplegic patients in order to apply and test biomechanically realistic strategies for sensorimotor control:

- Quadriplegia as a result of spinal cord injury is a fairly common and particularly devastating disability because it leaves the patient entirely dependent on an attendant for even simple self-care activities like eating.

- Reach and grasp tasks require the simultaneous coordination of distal hand muscles (normally controlled mostly directly by sensorimotor cortex) as well as proximal arm muscles (normally controlled mostly indirectly through propriospinal and other interneuronal circuits of the spinal cord).

- A new neural prosthetic interface technology is available that facilitates implantation of large numbers of independent stimulation and sensing channels in many arm muscles without requiring extensive surgery (Loeb et al., 2001; Figure 4 above).

- Many quadriplegic patients retain voluntary control of shoulder motion, which can be used to infer the location, orientation and grasp state desired for the hand.

- Biomimetic design principles will be used in an intermediate "regulator" that integrates the output of an adaptive controller with sensory feedback from the periphery, much as the spinal cord does normally (Loeb et al., 1999).

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