3170-Pos Board B217
Modeling Muscle With A Continuum Approach, New Insights Into An Old Problem
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Muscle contraction has long been modeled using partial differential equations (PDEs) to describe the chemical states of myosin as a function of time and strain. These models typically assume constant shortening rate and sparse myosin binding sites on actin. However, oscillatory shortening occurs in Monte-Carlo simulations of small ensembles of myosin (N=150) with fixed near-stall load and continuous binding sites (e.g. Duke 2000). Are these oscillatory solutions physiologically important? Should we re-examine the convenient assumptions of constant shortening rate and sparse binding? If so, then we should find oscillations in realistic PDE muscle models without these assumptions. Here, we develop a realistic muscle model. Using a soft-spring approximation, where we assume that external force on myosin induces a deformation primarily along a single degree of freedom, we develop relationships between rate constants and strain. These rate functions may be defined with a few parameters. The parameters not known from biochemical and biophysical studies may be determined by an optimization-of-fit to data. This approach generalizes previous expressions (e.g. Duke 1999, Smith and Geeves 1995). We then develop two models: 1) a PDE model with discrete binding sites and fixed load. This model shows near-stall oscillations only with finite N. 2) an integro-PDE model with continuous binding sites (after Hoppensteadt and Peskin 1992) and fixed load. This model exhibits oscillations that decay to a uniform steady-state. We introduce a reduced model to explain the N-dependence of these large load-oscillations and show that they are a result of small (N~O(102)) ensemble size. Thus, we argue that the continuum modeling approach should not be rejected based on large-load oscillations or continuous binding sites.

3171-Pos Board B218
Short-range Mechanical Properties Simulated With A Mathematical Model Incorporating Multiple Half-sarcomeres
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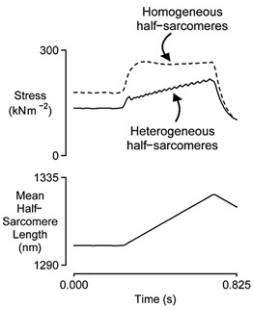
When an activated skeletal muscle fiber is stretched, force rises rapidly until the muscle reaches its 'elastic limit'. This 'short-range' response probably reflects the effects of interfilamentary movement on the dynamic behavior of cycling cross-bridges. Most mathematical models of the response predict that the cross-bridge force will plateau during the latter stages of the stretch. There are however some experimental preparations (including rabbit psoas fibers) in which force continues to rise at a gradual rate beyond the elastic limit. One explanation for this behavior is that titin filaments have calcium dependent mechanical properties. Another possibility is that the slow increase in tension beyond the elastic limit reflects dynamic interactions between inhomogeneous half-sarcomeres. A mathematical model of 40 half-sarcomeres arranged in series was developed to test this hypothesis. The solid line in the figure shows the simulated response when half-sarcomeres at the ends of the model had fewer cross-bridges than half-sarcomeres in the middle. The dashed line shows the simulated response when all the half-sarcomeres were identical. These simulations suggest that the gradual rise in tension beyond the elastic limit observed in some preparations may reflect interactions between inhomogeneous half-sarcomeres.



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A Simple Two-state Model For Auto-oscillation Of Sarcomeres (SPOC)
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The contractile system of striated muscle usually takes either contraction or relaxation state, which is regulated by the concentration of free Ca2+. On the other hand, we found that under the conditions intermediate between contraction and relaxation, the auto-oscillation of sarcomeres (named SPOC) occurs (Okamura, N. and Ishiwata, S., 1988. J. Muscle Res. Cell Motil. 9, 111-119). During SPOC, each sarcomere repeats the cycle of slow shortening and rapid lengthening periodically under constant micromolar [Ca2+] (Ca-SPOC) or in the presence of high concentration of MgADP and the absence of Ca2+ (ADP-SPOC). Many experimental results on the characteristics (e.g., period and amplitude of oscillation of sarcomere length) of SPOC have been obtained under various conditions (various concentrations of free Ca2+, MgADP and inorganic phosphate, pH and temperature). However, the molecular mechanism of SPOC is not yet clearly understood.
Recently, we observed that the width of sarcomeres, which corresponds to the lattice spacing between the thick and thin filaments, also oscillates during SPOC. It was found that the subtle change (less than nm) in the lattice spacing is responsible for the SPOC to occur. Based on these experimental findings, we constructed a simple two-state model to explain the SPOC phenomena, where the lateral force balance in addition to conventional longitudinal force balance was newly taken into account.

3173-Pos Board B220
On the physics of muscle contraction Force - velocity
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Whichever energy source is chosen as an engine, its force will decrease with increasing velocity. This is connected with a limited power of any engine. Thus, Hill's formula is a mere sequence of the law of energy conservation.
To derive a mathematical dependence ''force-velocity'', all the means of consumption of fuel energy should be determined - in our case, the energy of the ATP hydrolyze. Moreover, the conformation energy of the crossbridges attached serves as the force source as well.
We state that part of the energy release transforms into the energy of oscillations of myosin proteins; the other part goes into thermal energy of the sarcoplasmic solution. Interaction of the oscillating myosin system with the sarcoplasmic solution controls the process of force generation by a muscle. It is just this interaction that leads to the temperature dependence of force.
The presentation is devoted to constructing a theory based on these simple considerations.
A constructive critic is especially wanted.

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The Fluorescence Lifetime of a Single Actin-bound Fluorophore During Contraction of Skeletal Muscle
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During interaction of actin with myosin, cross-bridges impart cyclical impulses to thin filaments. A cross-bridge spends part of cycle time strongly attached to actin (t_s) during which it generates force, and remaining time (t_d) detached from thin filaments. The environment of a binding site on actin is different when a cross-bridge is attached and detached from thin filaments. Here we report, for the first time, measurements of the environment of a single actin binding site in rigor, relaxed and during isometric contraction of skeletal muscle. The environment was monitored by tracking the fluorescent lifetime (τ) of single Alexa488-phalloidin molecule bound to actin. The fluorescent lifetime is the averaged rate of decay of fluorescent species from the excited state. It depends on a variety of environmental factors. Lifetime of a single phalloidin molecule located at the center of the Overlap-band was measured every 50 msec during 60 sec of rigor, relaxation and contraction of muscle. The lifetime of rigor muscle was large when a cross-bridge was bound to actin, low when it was dissociated from it and intermediate during contraction. The ''duty cycle'' of a cross-bridge (Ψ) - defined as the fraction of the total cross-bridge cycle that myosin spends attached to actin in a force generating state [$\Psi = t_s/(t_s+t_d)$] was calculated from lifetime as 60%.

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Modelling X-ray Diffraction From The Myosin Superlattice Of Vertebrate Muscle
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Muscular force is generated by molecular interactions between the contractile proteins actin and myosin. The myosin filaments in the sarcomere of vertebrate muscle pack on a triangular array into which the actin filaments are interdigitated. High resolution studies of the actin-myosin interactions are performed by x-ray fiber diffraction analysis of whole muscle fibers. In most vertebrate muscles however, the myosin filaments pack in a so-called ''superlattice'' arrangement that involves a semi-random distribution of two filament