supernatant and pellet fractions. Co-sedimentation of NMR-unP with isolated molluscan thin filaments revealed that in this case the interaction was $Ca^{2+}$-dependent. NMR-unP slightly inhibited the $Mg^{2+}$-ATPase activity of actomyosin reconstructed from molluscan myosin and rabbit F-actin. In contrast, NMR-P as well as intact phosphorylated myorod increased actomyosin $Mg^{2+}$-ATPase activity of about 1.5-3 fold depending on the experimental conditions. This finding was supported by a 3-fold higher binding affinity of NMR-P for myosin filaments with comparison of that of NMR-unP. Taken together these results implicate that myorod, a thick filament protein of molluscan catch muscle, can modulate actin-myosin interaction in a phosphorylation-dependent manner.

**2798-Pos**

**Smooth Muscle Tropomyosin Forms Semi-Rigid End to End Polymers**

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Variation in the structural mechanics of tropomyosin isoforms may govern differences in their affinity and positioning on F-actin. Such differences may influence the access of actin-binding proteins along the sides of actin filaments and also the cooperativity of actin-myosin interactions. Here, smooth and striated muscle tropomyosin were rotary shadowed and compared by electron microscopy. EM shows that cardiac and skeletal tropomyosin primarily consist of 40 nm long single molecules, whereas smooth muscle tropomyosin is a mixture of varying length chains of end-to-end linked molecules found together with single molecules. The tendency of smooth muscle tropomyosin to polymerize reflects greater end-to-end interaction, possibly required on smooth muscle thin filaments, which lack troponin to stabilize this interaction. Measurement of the apparent persistence length (PL) of single smooth muscle tropomyosin molecules and the chain-like polymers yield indistinguishable values, which are comparable to those that we find for cardiac tropomyosin. The semi-rigidity of smooth muscle tropomyosin polymers may ensure a high degree of positional fidelity of tropomyosin on smooth muscle thin filaments, despite the lack of troponin (*cf*. Lehman *et al*., 2009). It is unlikely, however, that stiff, polymerized superhelical chains of tropomyosin can bind directly to F-actin. However, *in vitro* an equilibrium may yield sufficient single smooth muscle tropomyosin molecules or short chains to bind. *In vivo,* actin and smooth muscle (or cytoskeletal) tropomyosin may copolymerize or, alternatively, G-actin may polymerize on a scaffold of tropomyosin chains. Thus differing mechanisms of thin filaments assembly may be related to tropomyosin end-to-end binding strength.

**2799-Pos**

**Airway Smooth Muscle Dynamics are Governed by the Imposed Rate of Strain**

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It is commonly believed that the time scale governing the rheology of airway smooth muscle (ASM) is set by the internal viscosity and elasticity of the muscle. We show here, to the contrary, that this time scale is set by the externally imposed rate of strain.

For any fixed strain rate amplitude (SRA), the elastic modulus of the ASM showed a sigmoidal dependence upon frequency. Remarkably, as the SRA was increased over a range spanning almost four decades, sigmoidal response curves demonstrated little change of shape but shifted dramatically to higher frequencies. As such, the time scale of underlying molecular processes is set not by any internal viscosity, elasticity, or any spontaneous internal rate process, but instead is set by the imposed rate of strain. When the muscle is loaded at a small strain-rate, the molecular dynamics are slow; when loaded at a large strain-rate, the dynamics are fast.

Using numerical computations, we then assessed the contribution of myosin bridge kinetics to this behavior. In the regime where frequency was the highest, a good agreement between data and computations was obtained; ASM dynamics could, therefore, be attributed to forced acto-myosin crossbridge dynamics. But at the lowest frequencies, the slopes differed dramatically and stiffness values differed by an order of magnitude, exposing a new domain of slow dynamics that cannot be accounted for by acto-myosin interactions.

Interestingly, these results unify scale-free dynamics, fluidization, and length adaptation. While this unification is not explained by any traditional physical picture of cell rheology or polymer dynamics, it deepens substantially the analogy between living and inert soft matter, and in doing so, reveals a central role for microstructural fragility.

**2800-Pos**

**Role of Nonlinear Serial Elasticity on Airway Smooth Muscle Contraction**

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Both the elevated shortening velocity and maximal shortening capacity of airway smooth muscle (ASM) in asthmatic airways have been associated with airway hyperresponsiveness, even though the isometric force-generating capacity of the muscle is the same as in normal airways. This paradox may be partly explained by the relaxing role of tidal breathing, which is associated with perturbed equilibria of myosin binding. We have developed a theoretical model of airway narrowing to quantitatively assess how and in what degree the observed alterations in ASM contractility and nonlinear ASM serial elasticity (SE) can account for hyperresponsiveness in asthma. The model includes the elasticity and geometry of the lungs, ASM contractility, and the dynamics of breathing. The airway caliber, proportional to ASM length, is dynamically determined by the balance between the airway wall reaction force (AWRF) and ASM contractile force. AWRF depends on the instantaneous difference between pleural pressure and airway pressure at each generation of Weibel's symmetrical bronchial tree, elasticity and geometry of the airway wall, tethering of the airway to the lung parenchyma, and the state of lung inflation. ASM contractile force depends on myosin binding kinetics and the level of ASM activation. From equliriated ASM length the airway resistance is calculated. The model enables simulation of breathing in normal and asthmatic airways exposed to an increasing dose of spasmogen. Increasing the dose causes a contraction of the ASM, narrowing of the airways, and an exponential increase airway resistance. We show that an airway with asthmatic or sensitized muscle (increased level of myosin $LC_{20}$ phosphorylation, by 30-50%) narrows faster and significantly more than a normal airway. These results lead to a plausible mechanism by which the rate of bridge cycling and its regulation may account for airway excessive narrowing in asthma.

**2801-Pos**

**Structural Dynamics of the Dystrophin-Actin and Utrophin-Actin Complexes**

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Dystrophin and utrophin bind actin *in vitro* with similar affinities, but with different molecular contacts. It is proposed that these differences alter the elasticity of dystrophin-actin and utrophin-actin linkages to the sarcolemma, affecting the cell's response to muscle stretches. To test this hypothesis, we have determined the effects of dystrophin and utrophin on the microsecond dynamics of phosphoresescent-labeled actin, using transient phosphorescence anisotropy (TPA). At higher levels of saturation, utrophin was more effective than dystrophin in causing changes to the final anisotropy, correlation time, and initial anisotropy of actin dynamics. The simplest interpretation of these changes is that utrophin restricted the amplitude and increased the rates of actin to a substantially larger extent than dystrophin. Further analysis indicated that the actin-utrophin complex is much more torsionally flexible than the actin-dystrophin complex. We propose that these differences between dystrophin and utrophin in their effects on actin dynamics affect elastic properties of actin-mediated linkages with the sarcolemma. Preliminary data on fragments containing all the proposed actin binding domains (DN-R17/UN-R10) show less of an effect on regulating rotational amplitude and nearly no effect on rotational rate. Future experiments looking at other fragments of dystrophin and utrophin, and constructs with engineered disease-causing point mutations will determine which structural elements of these proteins are critical in determining the flexibility of actin filaments and what level of actin flexibility is physiologically optimal. Finally, to test the hypothesis that different orientation or conformation of the actin binding domain in dystrophin and utrophin contributes to changes in actin dynamics, we are using spectroscopic probes to do direct distance measurements between the 2 Calponin homology actin-binding domain heads to differentiate between the 4 currently proposed models of CH domain conformations.

**2802-Pos**

**Congenital Contracture Syndrome Caused by Mutation in Embryonic Myosin Heavy Chain Characterized by Significant Changes in Adult Muscle Contractility**

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Congenital contracture syndromes affect 1 out of every 1000 live births, and of those syndromes, distal arthrogryposis (DA), characterized by contractures of