

The Role of Surface and Interface Science in Muscle Contraction - A Testable Model

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ABSTRACT

Few people have paid much attention to the role of surface and interface science of the liquid myoplasm in the contraction process. But in 1970, Albert Szent-Györgyi, in an opening address to a symposium on Muscle, said

“the greatest experience of my scientific life” was the moment I saw “...motion produced for the first time in vitro by constituents of muscle ...” He had earlier succeeded in extracting actomyosin which “... forms a resilient gel. It is excessively hydrophilic.” He went on to say, “...Under influence of ATP actomyosin loses hydrophillity. The hydrophillic colloid becomes entirely hydrophobic, the most striking change I ever saw.”

Szent-Györgyi recognized in 1940-43 that contraction is triggered by a dramatic change in the surface physics at the fluid filament boundary. Sadly, he abandoned work in muscle when he was unable to reconcile this critical observation with the sliding filament theory.

During contraction the chemical structure of the filaments don't significantly change, but the chemistry of the myoplasmic fluid changes dramatically. Thus, reinterpreting Szent-Györgyi's observations, rather than the filaments changing from hydrophilic to hydrophobic, it is the fluid that changes from being proteophilic to becoming proteophobic.

This paper presents an innovative fluid surface energy contraction model. This accounts for force generation, filament sliding, filament shortening, contraction beyond overlap and heat of shortening. The filaments define the fluid/filament boundary. The cross-bridges participate in the hydrolysis of the ATP changing the chemistry of the fluid thus changing the surface energy. A surface energy gradient is set up between the overlap and non-overlap region due to the thin film effect in the overlap region which produces force and movement. A meaningful theoretical model must be testable. This paper suggests experiments to confirm this theory.

INTRODUCTION

Surface and Interface science deals with the physics of both solid and liquid surfaces. The more surface there is relative to volume, the more it is likely to play a role. The smaller the size of an object the larger its relative surface area becomes. For example, a tennis ball with a 6.3 cm diameter has a surface area of about 0.0125 m², whereas a similar volume of skeletal muscle has a fluid-filament surface area of about 7000 m² which is equivalent to the area of 25 tennis courts. Surface tension and surface energy have the same units (ML²/T²) and thus the potential for fluid-filament surfaces to do work is very great.

Major contributions to biophysics have been made to the understanding of conformational changes in biomolecules by the application of the science of surface physics. These primarily have been at the level of individual molecules, such as that which occurs at the actin-myosin junction during hydrolysis.

It can be argued that filament sliding during contraction is a conformational change on a much larger scale which may be brought about by changes in the cytoplasmic fluid surface energy. These cytoplasmic surface energy changes result from the changes in the cytoplasmic chemistry and electrical charge conditions during the contraction cycle.

Muscle is a very complex machine which has a remarkably precise structural design consistency. There is something about this design which suggests that the structural configuration is strongly linked to the force generation and contraction mechanism. Heretofore, the focus has been almost completely on the solid elements in the sarcomere while ignoring any role of the fluid. The assumption has been that the entire load has to be carried by these solid structures. When an engineer is asked to analyze the loading and stress in a previously unseen structure it is essential that all the load bearing elements are taken into consideration. If one load bearing element is missed the entire analysis is flawed. Fluid surfaces are load bearing structures.

In this paper we will start by primarily focusing on the fluid, while all the solid elements (that is, the filaments, cross-bridges and connecting filaments) define the shape of the fluid surfaces. Together the fluid-filaments surfaces and the filaments act together as an interface energy engine.

ENERGY GRADIENTS, FORCE AND MOVEMENT

Objects in energy gradients always exhibit force and/or movement. Consider Sir Isaac Newton's proverbial apple. The universal gravitational constant, G , causes massive objects in proximity to each other to be in a gravitationally induced energy gradient. The difference in the potential (free) energy of the apple between its position attached to the branch and its height, h , above the ground is $M \cdot g \cdot h$, where g is the acceleration due to gravity and h is the height above the ground (or the top of Newton's head.)

While attached to the branch it exerts a force Mg in the direction of maximum decreasing free energy (i.e. down.) When released from the branch the apple moves in the direction downward doing work of acceleration and eventually converting to heat: thus bopping Newton on the head. This is an expression of the Second Law of Thermodynamics which in practical terms says that all systems will tend to go from a higher energy state to a lower energy state (i.e. increasing entropy.)

This paper proposes that force and movement in muscle does essentially the same thing by going from a higher to a lower surface induced (rather than gravitationally induced) free energy state.

BACKGROUND SURFACE PHYSICS

- 1. Surfaces have a finite thickness.** Atoms and molecules tend to attract one another through both short range and long range (van der Waals) forces. Surface tension and surface free energy arise when the molecules in the fluid at or in the surface

experience out-of-balance force conditions due to the asymmetry of the forces around them as shown in Fig. 1. To increase the surface area it is required that more molecules be pulled into the surface. Work has to be done against the out-of-balance force to move a molecule from the body of the fluid where the forces are all balanced, to the surface where they are most out of balance. Thus, energy is distributed from the surface down to the point where the forces are symmetrically equal. This is several molecular distances in the 5 nm range.

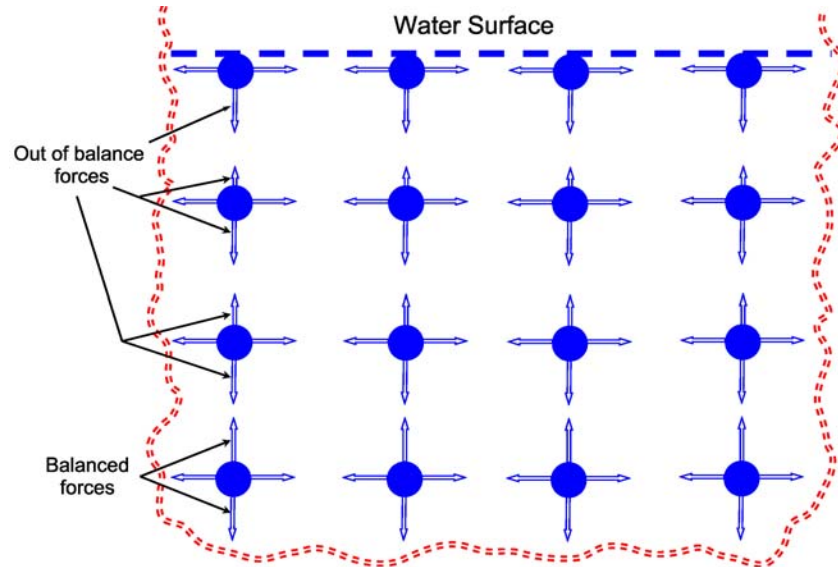


Fig. 1 Schematic showing uneven intermolecular van der Waal forces

- 2. Surfaces are capable of bearing structural load.** Because of surface tension, surfaces are, in effect, load bearing structures and must be taken into consideration when attempting to understand forces, stresses and strains in a complex structure such as muscle. Fig. 2 shows a Water Strider standing on the surface of a pond where it spends most of its life. Obviously the Strider depends upon the structural strength of the surface tension to support the entire weight of its body. Surely, the far higher surface area to weight ratio of the fluid-filament boundaries in the millions of sarcomeres inside the Strider's body also must be taken into account.



Fig. 2 Water Strider fully supported by water surface energy

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- 3. The thin film effect.** What is the initiating event that causes soap bubbles to burst? Obviously, when a bubble develops a hole, the surface tension rapidly widens the hole and the air inside the bubble, which was at a higher pressure than that outside the bubble, gets expelled. But the hole is not the initiating event. The initiating event

occurs when the film gets so thin that the surface outside and the surface inside become so close that the surface zones from each surface merge together. This results in less work being necessary for a molecule to move up into either surface (Fig. 3) and therefore the surface tension is reduced where the two surfaces are closest. This begins to occur when the film thickness drops to roughly 10 nm. The result is that the surface tension along the surface varies. The surface tension is higher where there is a thick film and it is less where it is a thin film. The out-of-balance gradient in surface tension causes molecules to be pulled away from where the film is thin towards the area where the film is thick. This eventually opens up a hole in the bubble and the bubble bursts.



Fig. 3 In a liquid film the surface energy (surface tension) decreases where the surface phases overlap

- 4. Gradients in surface tension (surface free energy) must be balanced by force and/or movement.** There are numerous examples that demonstrate this. In addition to the reason that bubbles burst, given above, here are a few more:-

A favorite children's toy is the **camphor boat** which is a small piece of balsa wood with a fragment of camphor wedged at back end. When this is floated on the surface of water the camphor lowers the surface tension of the water and the higher surface tension on the bow of the boat pulls the boat forward.

Another simple experiment involves a small **loop of cotton thread** floated on the surface of water in a dish. When a bar of soap touches the water inside the loop, the surface tension in the center of the loop is lowered and the higher surface tension outside of the loop instantly pulls the loop into a circle.

A more interesting experiment is done with a simple glass of wine. Alcohol lowers the surface tension of water. When the wine is swirled around to coat the glass with a film of wine, the alcohol in the film evaporates leaving a higher surface tension on the coating nearest to the top. The higher tension near the top pulls wine up from the bottom causing wine to accumulate at the top forming **wine tears**. See Fig. 4 below. As these wine tears get heavier, gravity pulls them down the side of the glass. When they touch the wine in the bottom there is a mismatch of surface tension and the surface of the tear pulls the lower surface tension in the bottom wine up. This wine tear "sucks" up more wine in a pumping action until it eventually falls into the wine in the bottom. This is a dramatic demonstration of the ability of surfaces to do work.



Fig. 4 Alcohol in wine evaporates more at top causing surface tension to be greater at the top of film on the side of the glass. This pulls wine up accumulating at the top forming "wine tears"

The above three examples show how chemical changes within the fluid effect the surface energy. Temperature also affects the surface energy by causing greater mobility of the molecules which reduces the surface energy. Electrical charges also have an effect.

APPLICATION TO MUSCLE STRUCTURE

The preceding discussion will serve as a foundation for the following proposal for how surface physics will explain most of what we know about muscle motility as well as some of what we don't know.

PROPOSITION 1. When muscle is relaxed the myoplasmic fluid is proteophilic (hydrophilic)

This means that the fluid surface energy at the fluid-filament boundary is at or near zero.

PROPOSITION 2. When muscle is activated the chemical and electric charges within the myoplasmic fluid cause the fluid to become proteophobic (hydrophobic)

PROPOSITION 3. Where there is filament overlap there is a "thin film" effect causing the surface energy to be less than that in the non-overlap region.

The space between the myosin filament and actin filament in the overlap region is much less than the space between the actin-actin and myosin-myosin in the non-overlap regions. In the overlap area, where the myosin heads make contact with the actin the fluid thickness falls to zero. Fluid surface energy is expected to be significantly lower in the overlap region compared to the non-overlap region.

PROPOSITION 4. Movement towards more overlap is movement towards a lower total surface energy state, therefore force and/or contraction (filament sliding) must result.

Taking the diameters of the thick and thin filaments and their number it can be calculated that it takes only a surface tension difference of about 6 dynes/cm between the overlap and non-overlap regions to produce the maximum isometric tension load of skeletal muscle. Considering that the surface tension at a water-air interface is 72 dynes/cm at 25o C, a 6 dyne/cm difference seems reasonably attainable. However, at this time the actual surface tension of the fluid interface during activation in the non-overlap and overlap regions have yet to be determined.

PROPOSITION 5. In the overlap region the thin film effect is brought about by a merging of the fluid interface zones at the actin and myosin fluid interfaces. There is, therefore, a continuity of the fluid-actin interface with the end of the myosin filament and with the myosin interface with the end of the actin filament.

The fluid surface tension of the actin may, therefore, pull directly on the end of the myosin filament while the myosin fluid interface may pull on the end of the actin filament further promoting sliding.

PROPOSITION 6. The surface tension of the fluid boundary surrounding the filaments will place the filaments in compression which will be offset by the tensile force developed at the ends and overlapping region during isometric contraction.

During isometric contraction, or contraction under no load, filament shortening is thus explained.

In contrast, the cross-bridge model is impotent in explaining filament shortening. If the cross-bridges ratchet the filament along, the filament – being elastic – must always stretch, under all conditions of contraction. This doesn't happen. Furthermore, the tensile load is all taken by tension in the filament. Yanagida has shown that the breaking strength of actin (albeit absent the nebulin) is less than the maximum load it is known to carry. Isometric contraction will always produce filament lengthening in the cross-bridge ratchet model.

PROPOSITION 7. Contraction beyond overlap is fully accounted for by the fluid surface tension running along the surface of the connecting filaments and myosin filaments from Z-line to Z-line.

Carlsen, et. al. (1965); Gordon, Huxley and Julian (1966); Walcott and Dewey (1980) and de Beer et.al. (1988) have all documented contraction beyond overlap. For cross-bridge ratches to work there must be overlap, and thus, beyond overlap there cannot be any contraction. The cross-bridge theory fails to explain this.

The surface energy (tension) theory, on the other hand accounts for it. When considering the connecting filaments that connect the ends of the myosin filaments to the Z-lines one can see that there is a continuity of the fluid interface from Z-line to Z-line. The tension (shortening) force transmitted to the ends of the sarcomere is given by the total surface tension in the periphery of the connecting filament plus/minus the elastic tension/compression of the connecting filament. This will equal the surface tension load in the periphery of the myosin plus/minus the tension/compression of the myosin filament.

The proteophobicity of the myoplasmic fluid during activation beyond overlap may be caused by the influx of calcium ions during the activation proces plus any residual ATP hydrolysis which is likely to be small due to the absence of cross-bridge contact with the actin.

PROPOSITION 8. A. V. Hill's heat of shortening.

Heat of shortening is characterized by being proportional to force of contraction and distance shortened and is independent of velocity of contraction. The independence on velocity indicates that it is not viscous in nature. Most experiments confirm the viscous components are negligible. The characteristics are most consistent with structural damping due to Coulomb friction.

The cross-bridges are most often shown in animations to detach from the actin and pull away while moving forward during a contraction stroke. This would result in little sliding occurring and more viscous drag.

It is more likely that the cross-bridge head, while not bound to the actin, will slide passively along the actin surface causing Coulomb friction during active contraction. While the muscle is not activated and the fluid is proteophilic, the cross-bridge may move away from the actin. Upon active contraction, the chemical and charge changes in the myoplasmic fluid make the fluid proteophobic. The cross-bridge head which is in contact with the actin will have to generate more fluid-filament and more fluid-myosin head surface area as it pulls away from the actin. It takes work to generate this extra fluid surface energy under conditions of proteophobicity and thus the myosin head will tend to be forced against the actin as it is dragged along the actin filament. The force pushing the myosin head against the actin will be proportional to the proteophobicity which is proportional to the contractile force generated. Therefore the heat of shortening will be proportional to (contractile force) x (distance shortened) x (coefficient of sliding Coulomb friction) which is consistent with Hill's findings.

CONCLUSIONS

Consideration of the science of Surface and Interface Physics of the myoplasmic fluid at the fluid-filament boundaries has led to a surface energy theory which explains force generation and contraction as well as experimentally observed anomalies that are not explained by the widely accepted cross-bridge ratchet theory.

Briefly this theory hypothesizes that when at rest, muscle proteins are essentially hydrophilic. Put another way – the myoplasmic fluid is proteophilic. Upon activation, all of the changes that take place in the fluid due to the activation process change the chemical and electrical conditions in the fluid such that it becomes – in the words of Albert Szent-Györgyi – extremely hydrophobic (proteophobic.) The energy released by the ATP hydrolysis and other chemical changes manifests itself as free surface energy at the fluid-filament boundaries. This surface energy is then converted into mechanical work in the manner described above.

This theory should be highly testable experimentally. The challenge to the motility community is to study and measure the surface physics properties discussed above. In particular, the eight propositions described above can be tested in the laboratory.