Designing Artificial Muscles : A Biomimetic Approach

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"I was always led in research by my conviction that the primitive, basic functions of living matter, like contraction, are brought about by ions, ions being the only powerful tools which life found in the sea-water, originated."

Albert Szent-Gyorgi, Nobel Laureate 1941

Abstract

This paper presents preliminary results of our ongoing work on the biomimetic muscle-like behaviour of poly(sodium acrylate) (PSA) hydrogels. Using Hill's model as a basic framework, interpenetrating network (IPN) hydrogels consisting of a contractile PSA network and an elastic poly(vinyl alcohol) PVA network were designed. The hydrogels so formed reversibly contract in the presence of a critical Ca^{2+} concentration via a monovalent-divalent ion exchange mechanism. Ca^{2+} is shown to provoke a shortening of the gel through cross-bridge formation akin to biological muscles. The contractile behaviour of these hydrogels in Krebs physiological media is presented. Force-length measurements display a non-linear rubber-like profile of the hydrogel in the relaxed state as well as a stiffening in the contracted state, both of which are characteristic of biological muscles. In addition, there is evidence of both isometric and isotonic contraction.

Keywords: polyelectrolyte gels, ion exchange, Hill's model, implantable muscle, physiological solution, Ca^{2+} -induced contraction

Introduction

Electroactive Polymers (EAP) are being considered for a range of artificial muscle applications, notably in robotics [1-5]. To date, a wide variety of EAPs are being considered including conducting polymers [2], ionic-polymer-metal composites (IPMC) [3], liquid crystalline elastomers [4], ionic hydrogels [5] amongst others.

It is also believed that EAPs have immense potential as actuators in a wide variety of biomedical actuators. Amongst the devices being considered are a heart compression device and a smart eye band [6]. It is also hoped that it could one day replace damaged muscles [7]. Successful application of EAPs for various biomedical applications would

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call for the design of structures that are biocompatible and are able to function in a physiological environment.

Polyelectrolyte hydrogels are three-dimensional charged polymer networks swollen in water. Owing to their similarities with biological tissues, they are used as synthetic physicochemical models for cornea [8], cartilage [9] and nerves [10] amongst others. It has been mentioned that it may also serve as a model to understand muscle contraction.

In accordance with Hill's model (Figure 1), a muscle is considered an elasto-contractile material with an elastic element connected in parallel with a contractile element. Muscle contraction is a complex series of events leading to Ca^{2+} release into contractile proteins to cause contraction through cross-bridges [11]. In our endeavor to design EAPs that can function as a muscle in a physiological environment, we have synthesized polyelectrolyte hydrogels with elastic and contractile components that contract in response to a Ca^{2+} stimulus.

Figure 1: Hill's rheological muscle model

Materials and Methods

Synthesis of Interpenetrating Network of Poly(Sodium Acrylate) and Poly(vinyl alcohol): Sodium acrylate (SA), ammonium persulphate (APS), methylene bisacrylamide (MBA), Tetramethyl ethylene diamine (TEMED) and polyvinyl alcohol (PVA) of molecular weight were all purchased from Aldrich and used as received. APS was recrystallized in methanol before use. A stock solution of PVA was prepared by adding 1 gm of PVA to 30 ml of water and gently heating the mixture till complete dissolution. A stock solution of TEMED was prepared by adding 1 ml of TEMED to 30 ml of deionized water. 0.4 g of SA and 0.05 g of MBA were dissolved in 1 ml of deionized water, 1 ml of PVA stock solution and 1 ml of the TEMED stock solution. 0.02 g of APS were dissolved in 30 μl of water and quickly added to the reaction mixture. The mixture was transferred to a cylindrical mould of diameter 1 cm, the mixture sealed and degassed with N_2 to remove dissolved oxygen. The reaction was left overnight to gel. Thereafter, the gel was frozen overnight at -60°C and thawed at room temperature for four hours. This cycle was repeated 8 times to obtain firm elastic hydrogels. The gel was carefully removed from the mould and left to soak in deionized water for four days to remove residual monomers and solvents.

Ca²⁺-Induced Contractile Behaviour : Once washed, the gel was allowed to swell to equilibrium in deionized water. Thereafter, the gel was immersed in a deionized water bath and the concentration of CaCl₂ was systematically increased. The change in length at each successive increase in [Ca²⁺] was measured using a Varnier Callipers. Ca²⁺- free Krebs Ringer's solution was prepared as follows: NaCl 118 mM, KCl 4.7 mM, MgSO₄, 1.2 mM, KH₂PO₄ 1 mM NaHCO₃. The solution was adjusted to a pH of 7.4 and kept in a water bath at 37.5 C. The change in length as a function of [Ca²⁺] was monitored using a Varnier Callipers.

Force-Displacement Measurements: The set-up used to measure the force produced as a function of displacement is represented in Figure 2. Surgical thread was used to attach the hydrogel to a stationary point at one end and to the piezoelectric force transducer on the other end. The hydrogel was kept swollen in a water bath over a scale. In the relaxed state, the hydrogel was stretched, the displacement was noted on the scale and the force was recorded on the cathode ray oscilloscope via the force transducer. 3mM of CaCl₂ was added to the bath and the gel allowed to equilibrate for two minutes. The change in length was noted. The force and displacement produced as a result of elongation was noted as described above. Standard weights were used to calibrate the oscilloscope.

Figure 2: Force-Length measurements

Results and Discussion

Synthesis of Elasto-contractile Hydrogel: Hill's model describes a muscle as an active contractile element connected in parallel with a passive elastic element [12]. The contractile element corresponds to the contractile proteins present in the muscle, while the parallel element corresponds to connective tissue. Using Hill's muscle model as a basic framework, an elastocontractile hydrogel was designed in the form of an interpenetrating network (IPN). An IPN is a polymer blend consisting of one polymer network embedded in another polymer network through physical entanglement and, occasionally, chemical interactions. To this end, poly(sodium acrylate) was chosen as the contractile network and poly(vinyl alcohol), the elastic hydrogel. PSA hydrogels are formed using MBA as a chemical crosslinker. PVA hydrogels are prepared by subjecting a concentrated solution of PVA through a series of freeze-thaw cycles. Each freeze-thaw cycle creates crystallites through hydrogen bonding. These crystallites act as physical crosslinks which produce a three-dimensional network. A PVA concentration of 0.1 g/ml

and 8 freeze-thaw cycles were found to be sufficient to produce firm, elastic gels. A composite hydrogel possessing both elastic and contractile properties was thus formed.

Ca²⁺- induced Contractility: Monovalent-Divalent Ion Exchange: Ca²⁺ is the ion directly responsible for provoking contraction in biological muscles. Extracellular Ca²⁺ plays a key role in regulating muscle contraction especially in cardiac and smooth muscles. Furthermore, the contraction of muscles is believed to be a phase transition and is caused by a critical change in Ca²⁺ concentration [13]. Poly(sodium acrylate) is a polyelectrolyte known to undergo a discontinuous phase transition in the presence of Ca²⁺. This phase transition in poly(sodium acrylate) occurs both as linear polymers in solution [14] and as hydrogels [15]. The divalent Ca²⁺ ions create ionic crossbridges along the polymer chain, causing the hydrogel to contract and expel Na⁺ and water. Figure 3 reveals the contractile behaviour of the poly(sodium acrylate) elastocontractile hydrogel in the presence of Ca²⁺. An abrupt decrease in length is observed at a critical [Ca²⁺] in a physiologically significant range. This corresponds to a phase transition, akin to the "all or nothing" contraction observed in biological muscles. The relaxation profile (Figure 3b) of the hydrogel shows that Na⁺ facilitates the recovery of the hydrogel.

Ca²⁺-induced contraction (Figure 3) and Na⁺-induced relaxation (Figure 4) of artificial muscle gel

Contractile Behaviour in Krebs Physiological Media: Krebs physiological media, commonly used as a bathing medium in muscle physiology studies, contains Na⁺, Mg²⁺, K⁺ and Ca²⁺ and has the same osmolarity as serum. used as the. As we can see in Figure 3, a slight change in length is observed even in the absence of Ca²⁺. One also observes a slight shift in the phase transition of the gel. This could be attributed to the interference from monovalent ions present in the solution. Based on these results, we can see that the PSA/PVA hydrogels maintain their contractile behaviour in physiological media. However, these graphs also point to the need to develop a system based on electrodes and ion-selective membranes to control and regulate the flow of ions into and out of the gel.

Force-Length measurements: Force-length measurements are one of the essential tools used to describe the characteristics of biological muscles. In Figure 5, the curve on the right shows the force-length profile of the gel in its relaxed state. Here, the hydrogel

shows the same non-linear rubber-like deformation characteristic of biological muscles. This could be attributed to the presence of PVA as the elastic component. On addition of Ca^{2+} , the hydrogel shortens. The curve on the left corresponds to the force-length profile of the gel in its contracted state. Here, one can observe a drastic change in slope of the curve which corresponds to the stiffening of the gel on contraction, yet another characteristic of biological muscles. One also observes two different force values recorded for the same length (isometric contraction) as well as two different lengths corresponding to the same force value (isotonic contraction).

Figure 5: Force-length profile of artificial muscle at rest and on activation

Conclusions and Perspectives

This paper represents, to our knowledge, the first published results of the contractile behaviour of polyelectrolyte hydrogels in physiological media. In our endeavor to explore the potential of electroactive polymers for various clinical applications, we have adopted a biomimetic approach by preparing a composite hydrogel system that consists of a contractile hydrogel (PSA) interpenetrated with an elastic hydrogel network (PVA). Furthermore, the contractile hydrogel so formed contracts in response to Ca^{2+} , the ion directly responsible for contraction through cross-bridge formation in biological muscles. that the muscle shortening and force generated is a function of Ca^{2+} concentration. The contraction/relaxation mechanism is brought about through $\text{Na}^+/\text{Ca}^{2+}$ ion exchange, one of the key mechanisms that regulates the Ca^{2+} content in biological muscle fibers. The synthesis of porous scaffolds based on contractile polymers paves the way for various tissue engineering applications as mechano-active scaffold to support the growth and organization of muscle cells into tissue. Finally, both PSA and PVA are biocompatible and non-cytotoxic and are already widely used in pharmaceutical and clinical applications.

Evidently, the results presented above are preliminary and part of a work in progress. We are currently working on a system using a combination of electrodes and ion-selective membranes to control and regulate the flow of ions into the gel. We are also exploring the possibility of incorporating liquid crystalline moieties into the hydrogel to impart order and uniaxial contraction.

Thus, the work presented above could form the basis for implantable artificial muscles in the distant future. Above all, artificial structures whose contractility is regulated by ions

already present in physiological fluids opens up the possibility of eventually developing muscles “powered” by the human body itself.

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