

DEVELOPMENT OF AN ARTIFICIAL EXCITABLE MEMBRANE FOR USE AS A TUBE PUMP

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Abstract

A polymer based artificial cell that mimics the excitability and refractoriness of cardiac myocytes is in the first stages of development. The ultimate goal of this project is to connect many of these excitable cells together to produce a medium exhibiting contraction similar to that of a real heart. This contracting medium will be used for the development of a tube pump capable of propelling fluids along its entire length. The conceptual design of the individual cell has been completed, and a series of experiments needed to test the components has been developed. Experimental results to date include the incorporation of tracer potassium ions into the foundation of the cell, which is a PVDF-HFP based ionic fluid polymer gel. A method for the measurement of the conductivity of these gels using electron impedance spectroscopy (EIS) has been established. Furthermore, carbon nanotubes have been successfully incorporated into the PVDF-HFP material, creating the basis for an electrode in the cell. Finally, the production of PPy membranes, an electroactive polymer, has begun and their electrochemical properties established using cyclic voltammetry.

Introduction

There is a pressing need for smaller, lighter and more intelligent designs aboard air and spacecraft as we push the limits of speed, energy reduction, and flight duration. Transporting fluids such as fuel and water across these vehicles requires careful reevaluation as conventional pumps today still require precious space, energy and weight.

There are two major types of pumps; positive displacement and dynamic pumps. Of the two, positive displacement pumps are generally lighter and arguably more efficient. They still however haven't reached full potential in weight and energy consumption reduction and still have room to grow. In fact, an easy conceptual improvement on these pumps is to permit the tube itself to propel fluids, eliminating the need for complex, heavy components. This is in fact a subcategory of positive displacement pumps referred to as standing wave pumps (Fig. 1). The few pumps in existence today which boast this attractive technology still fail to produce purely peristaltic movement which in and of itself can push along fluid. It is to the best knowledge of the author that no such technology truly exists today.

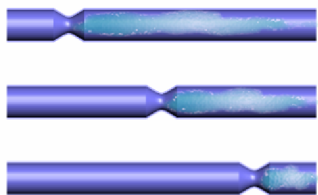


Figure 1: Fluid propulsion mechanism in a standing wave pump.

It is the objective of this research to produce a standing wave pump out of smart polymer materials. The advantage of these materials is that they are light, pliable and can be made to mimic the energy efficiency of biology. In fact, we will be using electroactive materials to mimic an incredibly efficient pump; the heart. This research has for objective to reproduce, using electroactive polymers, the excitable and contractile nature of the cells which make up the heart (i.e. cardiac myocytes). Ultimately connecting large numbers of these individual cells together, we will obtain an artificial membrane capable of propagating a contracting wave down its length and thus pumping fluids along very efficiently.

Methods and Results

Cell concept

The first step towards this goal was to develop a conceptual design for a cell which reproduces the cardiac myocyte. As an excitable cell, the cardiac myocyte analog must include qualities such as activation threshold, refractoriness and signal propagation. These are basic properties for any excitable medium. An activation threshold is needed to keep cells from responding indiscriminately to any incoming signal. For example, in the more familiar terms of the heart, if threshold limits did not exist, a signal to begin contractions at the top of the heart would propagate throughout the entire heart much too rapidly and would result in overexertion, among other problems. Refractory periods are necessary for the establishment of unidirectionality in wave propagation. For example in the tube pump, it would not be desirable for a standing wave pump to suddenly reverse pumping direction. This is also true in the heart and is a particularly important concept for excitable media. The refractory period simply refers

to the duration of time over which the cell cannot be recruited again, even if a threshold for activation has been reached. Incorporating the capacity to pass along the signal to fire will also be important in our cardiac myocyte polymer analog, however we will not be concerned with its implementation at this point. Here we have simply developed the conceptual design for a cell which bases its mechanisms closely on the way biology approaches each of these steps. We plan to achieve this analogy in electroactive polymers by controlling the flux of ions with electrical gradients and gating membranes.

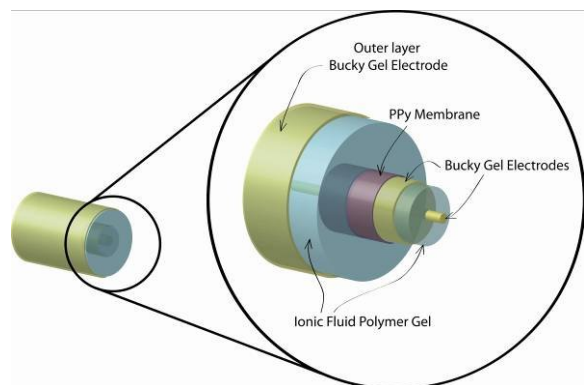


Figure 2: Electroactive polymer cell conceptual design, broken down by layer. Bucky gel electrodes are made with an electrically conductive carbon nanotube mix and used as electrode material. PPy membranes gate the flux of cations depending on their ox/redox state. Ionic fluid polymer gel is the foundation polymer for our cell design.

More specifically, our polymer cell contains three major polymeric materials (Fig. 2); ionic fluid polymer gel, bucky gel electrodes, and a polypyrrole (PPy) membrane. The ionic fluid polymer gel is the base material for our cell, through which potassium ions are free to flow. An electrode which can be used to direct the flow of ions is made from a mixture of carbon nanotube and ionic fluid polymer gel, the result of which is permeable to ions. This carbon nanotube mixture is commonly referred to as a bucky gel electrode. These electrodes, in addition to controlling the flux of ions, will serve as the building blocks for the electropolymerization of an ion-gating membrane, namely polypyrrole (PPy). The oxidation/reduction state of PPy dictates ion permeability and is easily controlled by voltage potential application. Controlling the flow of ions in such a way is an essential key to giving the cell its ability to ‘fire’ or contract when ready.

Combining these materials carefully we produced a theoretical cell concept with activation threshold and refractoriness. This is the conceptual foundation for what will later become a series of cells

capable of propagating activation. We focus now however simply on the feasibility of creating such an excitable cell.

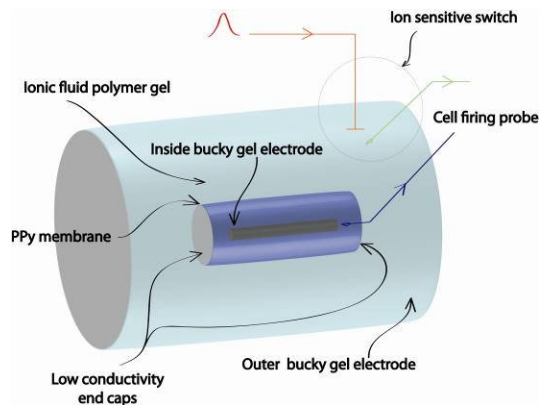


Figure 3: Overview of cell components and placement.

Cell Cycle

The cell layout is shown again from a different perspective in figure 3 for clarity. Here we see clearly the presence of an inner capsule surrounded by a PPy membrane. The control of ion flux through the cell is best described by figure 4, which highlights the major stages which contribute to the excitability of these cells. The cycle begins with a cell at rest (Stage 1, Fig. 4) where ions are dispersed throughout the ionic fluid polymer gel. In response to an activation signal, the cell’s outer electrode energizes and becomes attractive to the ions. As the ions migrate towards the outer electrode, an ion-sensitive probe located near the electrode responds once a threshold concentration of ions has been reached by sending a signal to the inner capsule (Stage 2). The electrical signal sent has a three-fold function; it reverses the polarity of the outer electrode now making it repulsive to ions, energizes the inner electrode so it now attracts ions, and reverses the polarity of the PPy membrane making it now permeable to ions. In stage 3, a short amount of time has elapsed and now ions have accumulated around the inner capsule due to the attractive and repulsive electrodes. The electrochemical changes taking place in PPy are not instantaneous. In fact, it has been shown that PPy membrane conductivity may take as long as 50 seconds after activation to reverse its conductivity for ions.¹ In stage 4, ions have now entered the inner capsule and have sent a signal for neighboring cells to fire in turn (propagation signal). Essentially, this step represents the cell firing. As enough time has elapsed, the initial signal which reversed the charge on both the inner and outer electrodes and PPy membrane subsides and ions now start to flow out of the inner capsule as the PPy

membrane slowly becomes impermeable to ions again. However this time since the ions can no longer pass through the gating PPy membrane, they find an alternative path through the slow-conducting end-caps. These are also made of ionic fluid polymer gels, but this time with a much lower ionic conductivity. Forcing ions to exit slowly through these end-caps (Stage 5) delays the replenishment of ions in the outer region of the cell, effectively creating a refractory period as the critical concentration of ions for activation cannot be reached during this time. Ions then finally return to a neutral distribution throughout the cell which is now ready to fire again (Stage 1).

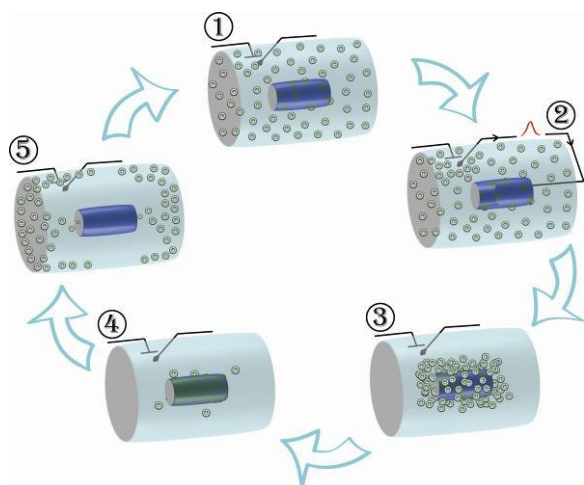


Figure 4: Cell activation cycle. 1) Resting state with potassium ions dispersed throughout cell. 2) Signal received for cell activation. Critical ionic concentration reached at probe, response sent to the center electrode. 3) Center electrode switched on and now attractive to ions, ions accumulate outside of PPy membrane. 4) Ions have entered the center capsule. Cell in this state is refractory. 5) PPy membrane closed again, center electrode now repulsive to ions and they exit through decreased conductivity end caps.

Cell Components

The development of this cell concept was based on the literature about the electroactive polymers used. Each component however now needs to be tested, optimized and ultimately combined into a stand-alone cell. Several of the cell components are currently in the early stages of investigation.

Ionic Fluid Polymer Gel

The ionic fluid polymer gel was made from a mixture of 4-methyl-2-pentanone (MP) solvent, polyvinylidene fluoride-co-hexafluoropropylene (PVDF(HFP)) and ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate (BMIBF₄). The

mixtures were heated to 80 degrees Celsius with constant stirring for 20 minutes, and then poured into a Delrin® cylindrical mold, 10 mm in diameter. 12 hours later, the gel was removed from the mold and left to dry under a chemical fume hood for another 24 hours to remove the volatile MP fraction. At this point, the gel is placed in a Delrin® holder for further characterization of its ionic conductivity by electrochemical impedance spectroscopy (EIS). The holder was designed using a rapid prototyping machine here at the University of Virginia. It holds the gel into place securely between two copper disk electrodes, each 1 mm thick. The mount was designed to allow for reproducible measurements of conductivity.

It has been shown that varying the ratio of polymer to ionic liquid modifies the ionic conductance and mechanical properties of these gels.² A series of gels were thus produced for comparative validation with varying ratios of polymer to ionic liquid from 50/50 to 90/10, giving a range of gels possessing different material properties and conductivities (Fig. 5). Quantification of the ionic conductivity of these gels is in the preliminary stages and is performed using electrochemical impedance spectroscopy (EIS). A ratio of 67/33 polymer to ionic liquid was found thus far to be of ideal consistency.

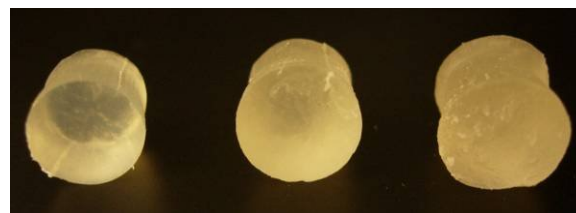


Figure 5: Ionic fluid polymer gels. A variety of polymer /ionic liquid ratios are shown. From left to right: 50/50; 25/75; 90/10.

Incorporation of a tracer ion into the ionic fluid polymer gel matrix has also been initiated. Potassium (K⁺) was specifically chosen as our cation since it has the highest flux rate through the PPy membrane. This is in part due to its small electron orbital which enables it to pass easily through the porous PPy membrane. Potassium incorporation into the gel has encountered some setbacks as the solubility of this ion in some of the reagents is very low. Further experiments will be needed to combine these chemicals fully.

PPy Electropolymerization

Electroactive polymer membranes are voltage-controlled ion gates which are often used to separate ions. Three major ion gates exist: polypyrrole, polyaniline, and polythiophene.³

Polypyrrole was carefully chosen for incorporation into our system since it has the following advantages over the other two: it is pH-insensitive, has previously been used in combination with PVDF⁴ and is permeable to a range of cations, including potassium (K^+). The oxidation/reduction state of PPy controls the permeability of the membrane to ions. When the membrane is oxidized it is permeable to cations, and in the reduced state its permeability is reduced about a thousand-fold.⁵

The vacuum distillation of pyrrole is a necessary first step in the preparation of PPy membranes. Following distillation, the pyrrole solution, potassium chloride (KCl) solutions, acetonitrile and water must be deaerated for 30 minutes under nitrogen (N_2) gas prior to each experiment. A solution of 0.1M pyrrole + 0.1M KCl + 1 wt % water is then prepared.⁶ This mixture is placed under nitrogen atmosphere in a 3-electrode electrochemical bath for the electropolymerization of PPy using a Pot/Gal 273A (Princeton Applied Research).⁷ Membranes were electropolymerized onto a gold electrode using constant current (galvanostatic). Cyclic voltammograms were produced in the analysis of the PPy membranes; however we have insufficient data at this time to draw any conclusions about the integrity of the membranes or membrane thickness, which we however approximated to be on the order of 200 nm.

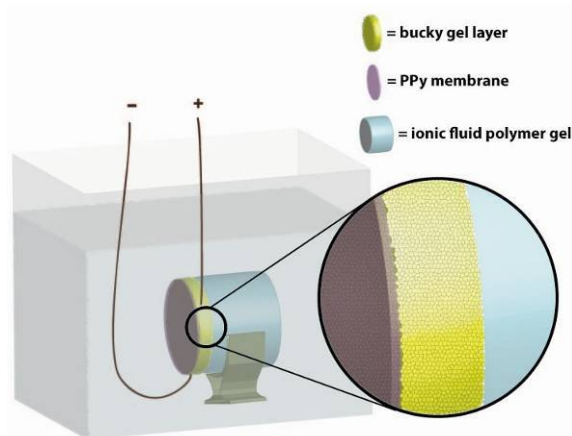


Figure 6: PPy layer formation using an electrochemical bath.

Bucky Gel Electrodes

Single walled carbon nanotubes (SWNT) were incorporated into a mixture of ionic fluid polymer gel to produce bucky gel electrodes. SWNT concentration is currently being varied for the optimal concentration and conductivity. These bucky gel electrodes will be used eventually to replace the gold electrode in the electropolymerization of PPy,

thus growing the membrane directly onto the gel (Fig. 6). Careful optimization will be needed to produce a maximally electrically conductive bucky gel, while also retaining maximum permeability to potassium ions.

Discussion and Conclusions

Many steps remain for the development of our polymer excitable cell. We have shown here the progress thus far on this project, which consists of the detailed conceptual design for an excitable cell and the groundwork for the development, testing and optimization of each individual cell component. Upcoming experiments are planned to further analyze PPy electropolymerization using cyclic voltammetry, and determine a method for membrane thickness quantification. We also plan to pursue more EIS experiments and detail the relationship between polymer concentration and ionic conductivity for our ionic fluid polymer gels. There is a great need for the optimization of cell component properties, which will be accomplished in the next year by systematically varying parameter values to affect refractory period and excitability.

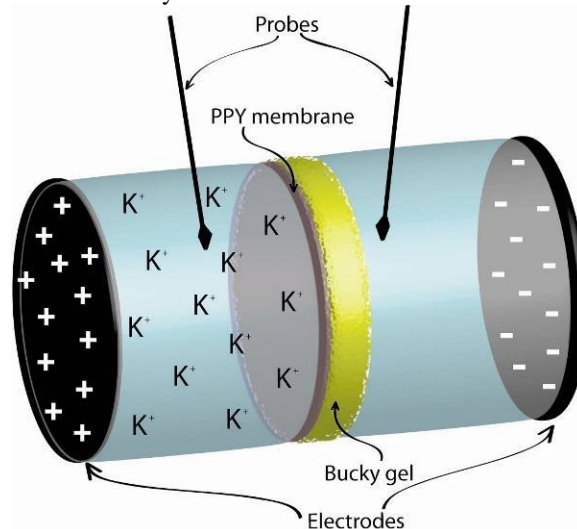


Figure 7: Experimental setup for potassium ion transport measurements across the PPy membrane using electrical probes.

Furthermore, we plan to study the short time flux of K^+ through PPy membranes grown onto bucky gel electrodes. This will be done by assembling a split cell as seen in figure 7 and measuring the appearance of K^+ ions across the membrane on a short time-scale. This will be of particular importance as there has been no previous literature characterizing short-term behavior of these membranes. Typically, interest in cation transport across electroactive membranes has been on the order of hours.⁸ There is a legitimate concern that the PPy

membrane may simply not respond fast enough to electrical stimulus for our intended purposes. However, if this becomes a problem, we may be able to increase the speed of oxidation and reduction by incorporating carbon nanotubes as the dopant for PPy instead of potassium.⁹ Such proximity to the carbon nanotubes should increase the PPy access to much needed electrical charge energy for its oxidation/reduction state changes and it is hypothesized that this may solve a time-dependence problem if one occurs.

Another important upcoming step for this research will be the integration of a contractile element into the cell design. It has been shown that the flux of ions controlled by electrical gradients can cause dimensional changes in ionic fluid polymer gels gated by membranes, i.e. exhibiting contraction upon stimulation. We therefore believe the incorporation of contraction into this design will be relatively straightforward and a logical flow to the setup.

Once the foundation of our cell has been well characterized, we plan to fully assemble the cell, in a layer by layer casting method as seen in figure 8.

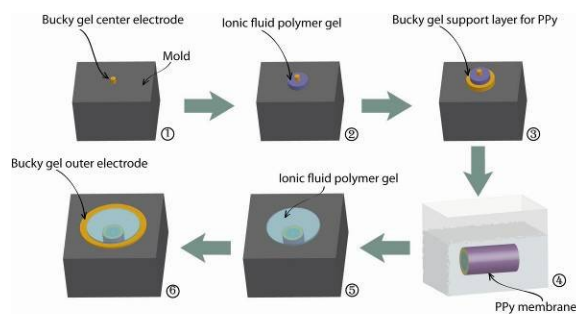


Figure 8: Mold production sequence for polymer cells. Casting of bucky gel and ionic fluid gels is followed by the electrochemical deposition of PPy membrane, and then by more casting of ionic fluid gels.

Finally, beyond the assembly of a single cell, we anticipate that our research will eventually focus on downsizing the cell to the dimensions of a myocyte, which is on the order of microns. This process will necessitate the development of microfabrication techniques and more sophisticated probing methods. Application of the layer-by-layer casting method for ionic fluid polymer gel assembly allows for seamless connection between components and will hopefully be compatible to the miniaturization of these gels.¹⁰

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