Ionic electroactive polymer actuators as active microfluidic mixers

Catherine Meis [1], and Reza Montazami [2,3], Nastaran Hashemi [2,3*]

[1] Department of Materials Science and Engineering, Iowa State University, Ames, Iowa 50011, USA

[2] Department of Mechanical Engineering, Iowa State University, Ames, Iowa 50011, USA

[3] Center for Advanced Host Defense Immunobiotics and Translational Comparative Medicine, Iowa State University, Ames, IA 50011, USA

* Author to whom correspondence should be addressed; nastaran@iastate.edu

Abstract:

On-chip sample processing is integral to the continued development of lab-on-a-chip devices for various applications. An active microfluidic mixer prototype is proposed using ionic electroactive polymer actuators (IEAPAs) as artificial cilia. A proof-of-concept experiment was performed in which the actuators were shown to produce localized flow pattern disruptions in the laminar flow regime. Suggestions for further engineering and optimization of a scaled-down, complete device are provided. While the device in its current state of development necessitates further engineering, the use of IEAPAs addresses issues currently associated with the use of electromechanical actuators as active microfluidic mixers and may prove to be a useful alternative to other similar materials.

Keywords: active microfluidic mixer, artificial cilia, electroactive polymers, soft actuator

1. Introduction

On-chip automated sample processing is essential to the progression of biological analysis devices from the laboratory to commercially feasible and practical products. Currently, sample analysis can be accomplished on-chip, but most sample pre-processing requires larger and more expensive laboratory equipment. The results of this work could potentially be used in the development of a small, portable, integrated device capable of analyzing ~~biological~~ samples, without the need for ~~the~~ trained personnel necessary to perform traditional analysis procedures. Specifically, this work focuses on active micro-mixing and its application in biological analyses and assays.

Within microfluidics, the mixing of fluids is generally accomplished by either active or passive mixing. Passive mixing devices consist of microchannels specifically designed to increase diffusive mixing between the fluids; active mixing devices typically utilize a mechanical transducer to achieve the same. While passive mixing of fluids can be achieved quickly, it is often less efficient and requires lengthy microchannels. Active micro-mixers have the advantage of being externally controllable as well as generally allowing for shorter microchannels, more efficient mixing, and faster mixing times. [1]

The development of artificial cilia as active micro-mixers has become a growing field. In nature, cilia are small hairs found on the outside of microorganisms that function as fluid manipulation mechanisms to propel an organism through its environment. [2] Several different materials and approaches have been explored by researchers to mimic the function of cilia using technology. As classified in a recent review by den Toonder and Onck, artificial cilia can be categorized into magnetic artificial cilia, optically-driven cilia, electrostatic cilia, hydrogel-actuated cilia, and resonance-actuated cilia. [3] Magnetic artificial cilia and micromixers have seen the most progress [4-9], although a drawback for these cilia is the need to apply some kind of external magnetic field, which poses challenges for the development of smaller, more portable microfluidics devices.

In particular, we are investigating the use of ionic electroactive polymer actuators (IEAPAs) as active micromixers and artificial cilia. IEAPAs are smart materials categorized as ionic polymer metal composites (IPMCs); the concept of using them as cilia is similar to that of electrostatic cilia, with the main difference being that of their composition and operation mechanism. IEAPAs function as a result of ion migration through the polymer matrix rather than electrostatic

displacement forces, and the specific IEAPAs employed in this work have been well-characterized. [10-16]

Den Toonder *et al*. developed very effective electrostatic artificial cilia composed of a polymer film with a thin chromium layer attached to a dielectric and ITO electrode, which were manufactured with microfabrication processes including lithography. The actuators were arranged in tiny arrays and were able to completely mix two fluids in the channel in 1.5 seconds. [17] However, there are a few noted issues which are common to these type of cilia: 1) the high electric field may disrupt the fluid or any biological specimens, and 2) the mechanism driving the cilia only functions in non-conductive fluids. [3] These issues have served to limit development of these types of active micro-mixers. Another group recently reported the use of segmented ionic polymer metal composite (IPMC) actuators as functional artificial cilia that closely mimic the motion of natural cilia and could have applications for aquatic robotics [18].

While the approaches mentioned previously are all viable ways to accomplish active micro-mixing, the use of ionic electroactive polymer actuators (IEAPAs) as active micromixers has some advantages that make it a promising addition to the field of active microfluidic mixing. The proof-of-concept device described in this work utilizes an IEAPA inserted in a transverse direction across the microchannel as an artificial ciliuma for active mixing. We designed a thin polyethylene cover to protect the actuators inside the microchannel because the electrodes on the actuator rapidly degrade when exposed to aqueouswater and water-based solutions. The polyethylene cover itself has excellent chemical resistance, which would allow for the use of almost any solvent inside the microchannel, with aqueouswater-based biological samples as the intended fluids to be used in the device. The IEAPAs are relatively easy to fabricate compared with some of the more complex microfabrication techniques necessary to produce the artificial cilia found in other devices. They are also characterized as having a relatively fast response time, high strain, and high efficiency [11, 14]. However, the most important advantage is the low operating voltage; these actuators are typically operated at less than 5 V. In comparison, the cilia utilized in the work by den Toonder *et al*. were operated at 70 V, although they are arguably some of the most efficient micro-mixers using polymer actuators developed to date. [17] Since the ultimate goal of much of microfluidic development is to produce a portable lab-on-a-chip device, low power solutions are critical to each function that will be integrated on the chip. Our device is intended to be integrated as a sample pre-processing step for

a microflow cytometer previously developed for quantifying algae for environmental monitoring [19-21]. On-chip active mixing is necessary to the development of integrated microfluidic systems, and the design proposed here has potential to be used in a variety of biosensing and environmental monitoring systems. With further optimization and engineering, this prototype active micromixer demonstrates thate IEAPAs could become a viable alternative to many of the active mixing methods mentioned above and offer increased flexibility of design for specific microfluidic system applications. In this work, the design and fabrication of the proof-of-concept device are described in detail. An image-based analysis of fluid dynamics and mixing is presented, followed by suggestions for future device iterations for improved performance.

2. Experimental

2.1 Microchannel and actuator fabrication

The microchannels were fabricated in polydimethylsiloxane (PDMS) (Sylgard 184 – Dow Corning) using a novel microchannel fabrication method for easy and rapid prototyping termed the "ProtoFlo" channel method. To create ProtoFlo channels, a mold was assembled from several basic metal shapes that are manually configured and semi-permanently attached to a substrate to create a reusable, modifiable mold. The flat, thin metal pieces (laser cut from Stainless Steel 17-7 or 17-4 magnetic 0.004" inch thickness, Gateway Laser Services) comprising the mold were adhered to a glass substrate with liquid cyanoacrylate adhesive. PDMS was poured and cured directly on the mold to form the microchannel. For this application, a straight microchannel with a T-junction was utilized (channel cross-section in mixing region: 5000 μm width x 400 μm height). This channel size was chosen for ease of manufacture; the "ProtoFlo" method becomes more difficult with smaller channel sizes as it is intended for rapid prototyping and not high-precision, smaller microchannels. TwoTwo identical PDMS samples form one complete channel. The IEAPAs were fabricated using materials and methods published previously and described briefly here. [11, 12, 14] The IPMC portion of the actuator consists of 25 μm thick Nafion (NR-211) ionomer on which alternating layers of polycations and polyanions, poly(allylamine hydrochloride) (PAH) and gold nanoparticles respectively, were deposited using the layer-by-layer (LbL) method. The layered ionomer was soaked in 1-ethyl-3-methylimidazolium trifluoromethanesulfonate (EMI-Tf) ionic

liquid and then gold leaf (50 nm thickness) was hot-pressed on either side for electrodes. Actuators were cut to approximately 1 x 10mm size for testing.

2.2 Device assembly

In order to integrate the actuators inside the microchannel, it was necessary to develop a protective barrier to prevent the actuator from sustaining damage due to the fluids. Based on observations and the known properties of Nafion ~~(NR-211)~~, specifically its high absorption of water [22], it was deduced that the expansion of the Nafion when it absorbs water causes the degradation of the external gold leaf electrodes; this is most likely because the gold leaf cannot physically stretch with the Nafion and so it detaches or tears. The degradation of the electrodes when the actuators are exposed to fluid has been experimentally observed on numerous occasions. The gold electrodes are essential to the proper function of the actuator as they deliver the uniform electric stimulus to induce actuation; without complete intact surface electrodes, uniform actuation will not occur. A protective cover was developed using a thin HDPE/LDPE blend sheet (Product #618574, Berry Plastics Corporation, Evansville IN). The polyethylene was first stretched approximately 2x its original dimensions (resulting thickness ~50 μm), folded in half, heat sealed on 2 sides and excess polyethylene removed using a razor. The actuators were then carefully inserted into the cover. The covers were fabricated to fit the actuators as closely as possible so as to minimize excess weight and bulk.

The PDMS microfluidic chip was bonded through surface activation using oxygen plasma treatment at 500 MTorr for 20 s (Harrick Plasma). To assemble the device, a covered actuator was sandwiched between two activated PDMS layers and alignment was monitored using an optical microscope. The actuators were inserted across approximately 3/4 of the microchannel width. Standard silicone laboratory tubing was attached using epoxy.

2.3 Mixing test parameters and analysis

The IEAPAs were operated using a function generator (Tektronix AFG3022 Dual Channel Aribitrary function generator, 250 MS/s, 25MHz)~~;~~ producing a square wave function of 4.5 V (9

Vpp) amplitude and 1 Hz frequency. ~~with~~ Potential~~voltage~~ and capacitance, indicating proper actuator function, were monitored with~~by~~ an oscilloscope (Tektronix DPO 3014 Digital Phosphor Oscilloscope, 100 MHz, 2.5 GS/s)~~, using a square wave function of 4.5 V (9 Vpp) amplitude and 1 Hz frequency.~~ A syringe pump (GenieTouch Infusion/Withdrawal Dual Syringe Pump, Kent Scientific Corp, Torrington CT) introduced water colored with concentrated food dye into the microchannel. All tests were conducted at a flow rate of 10 µl/min; a combination of 2 inlets with input flow of 10 µl/min each yields a net flow of 20 µl/min. The microfluidic chip was mounted in a vertical orientation (exposed actuator upwards) in an~~the~~ in-house made micro probe station in order to supply the actuator with proper electrical stimulation. Laminar flow was established by introducing a different color of dye into each side of the T-junction, as illustrated in Figure 1. Visible mixing of laminar flow by the actuator was recorded with a charge-coupled device (CCD) camera at a rate of 30 fps. Adobe Photoshop CC software was used to extract individual frames from the high-definition video files with minimal loss. ImageJ (Image Processing and Analysis in Java) free software was used to analyze selected frames.

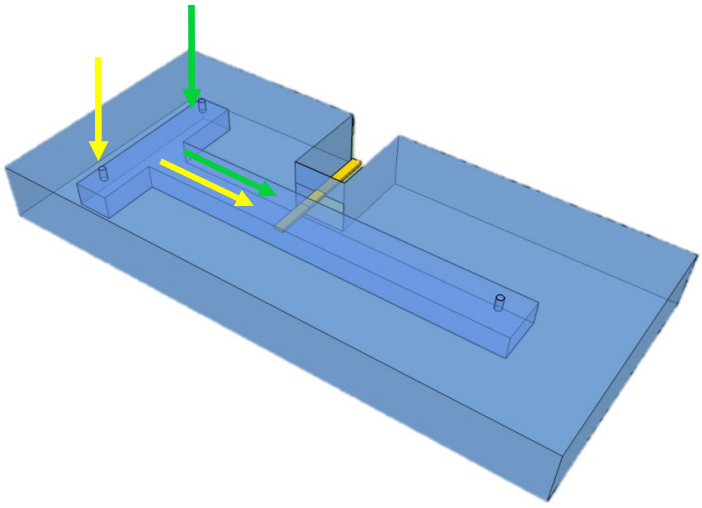

Figure 1. (a) Schematic of assembled microfluidic mixing device (not to scale). Flow directions as shown. The actuator acts in a transverse direction to the fluid flow (in the z-direction as shown in this schematic).

3. Results and Discussion

3.1. Analysis of mixing pattern

Individual frames were selected from t=0 when the actuator was activated (denoted as T0) until 10 s (T10), at which time the fluid flow pattern downstream from the actuator no longer appeared to evolve. (The complete video file can be found in Figure S1). ImageJ software was used to generate surface plots of pixel intensity and to determine mean histogram values for selected frames in order to analyze the visual mixing of fluids from a top-down perspective in the microchannel region immediately surrounding the actuator.

It should be noted that the actuator is inserted directly across the channel, at equal vertical distance from the top and bottom of the microchannel. This orientation was chosen in order to take advantage of the full range of motion of the IEAPA and to simplify the device assembly. When activated, IEAPAs bend along their length and the direction of displacement is reversed in synchronization with reversal of polarity of the applied voltage. Because the actuator is positioned across the vertical center of the microchannel perpendicular to the direction of the laminar flow, the tip will displace into the regions of the microchannel above and below center. Essentially, the actuator displaces transverse to the direction of fluid flow. In addition, inserting the actuator between the layers of PDMS composing the microchannel allows for fast assembly and minimal leakage; both inserting the actuator and sealing the channel itself in a single bonding step is a simple and elegant assembly method that eliminates the need for adhesives.

As shown in Figure 2, the actuator produces a clear local disruption to the laminar flow over the 10 second time frame. IOver time, it is evident that the yellow and green flows interpenetrate downstream from the actuator and the color intensity changes for corresponding regions on each image. Figure 3 shows the mean intensity for specific regions compared between T0, T5, and T10. The intensity values for boxes 1 and 2 decrease from T0 to T10 as the green flow penetrates around the tip of the actuator. Intensities for boxes 3 and 6 remain relatively constant at the lower and upper limits of the plotted range. The mean intensity of box 4 decreases as the green flow penetrates into the yellow flow, and the intensity of box 5 increases as the yellow flow penetrates into the green flow. At T0 the difference in mean intensities between boxes 4 and 5 is 15.13 units but at T10 the difference is -2.28 units, indicating that the intensity of box 5 actually has surpassed box 4.

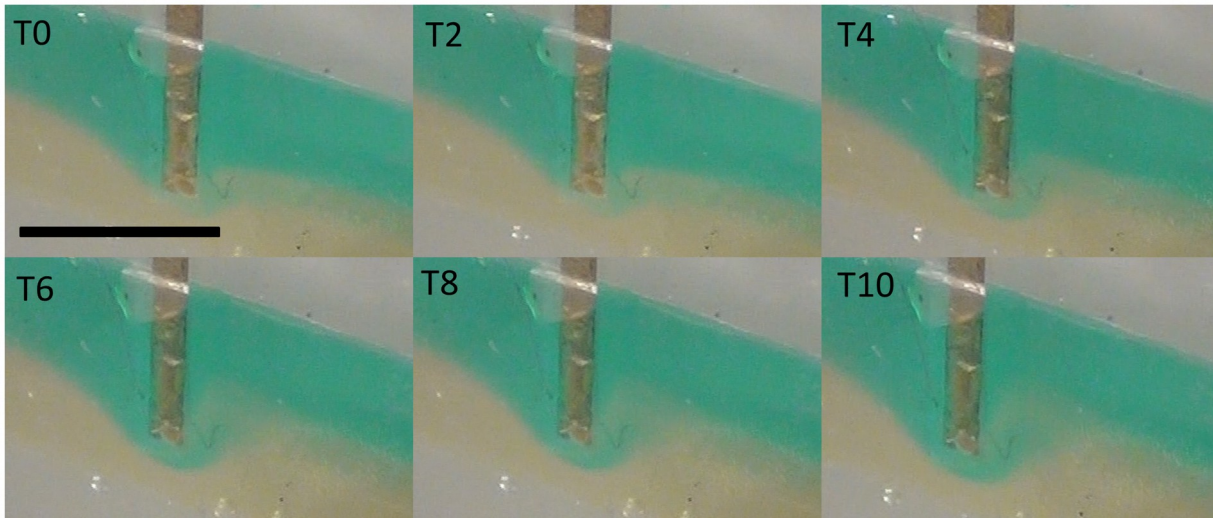

Figure 2. Time lapse from T0 (where T0 represents ~~the~~ time 0 s when the actuator was activated) to T10 of the channel area immediately surrounding the actuator. Flow direction is from left to right across the images. Scale bar is 5 mm.

The 3D surface plots in Figure 4 of intensity over the entire region downstream from the actuator offer a descriptive summary of the variation of intensity and mixing patterns of the fluid flows over time. At T0 the boundary between green and yellow flows is straight and sharp; from T5 to T10 the separate flows seem to swirl and interpenetrate in the region immediately surrounding the actuator tip, which corresponds to the rectangular region near the front and center of each surface plot that remains static across the time lapse. Around the actuator tip, a circular region of intermediate gradient develops, indicating mixing of the two flows.

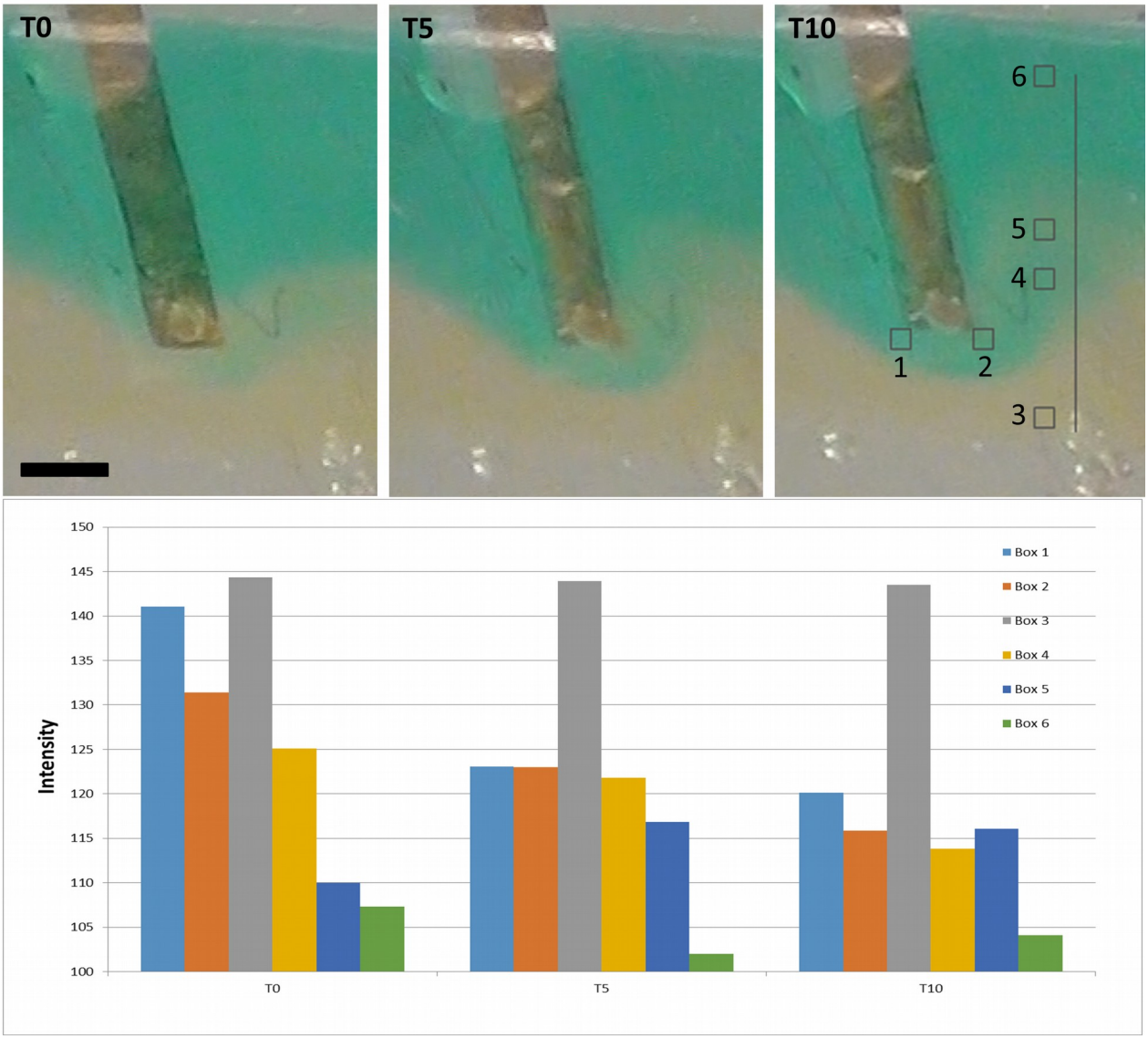

Figure 3. Top right: Reference image at T10 of selected pixel regions used for analysis. Plot of mean intensity values generated from histograms of the labeled boxes 1-6 (10x10 pixel areas) shown in T10. Lower intensity values correspond to darker colors (green) in the images and higher intensity values correspond to brighter colors (yellow). Reference images for T0 and T5 are also shown; identical box scheme was used for analysis. Scale bar is 1 mm.

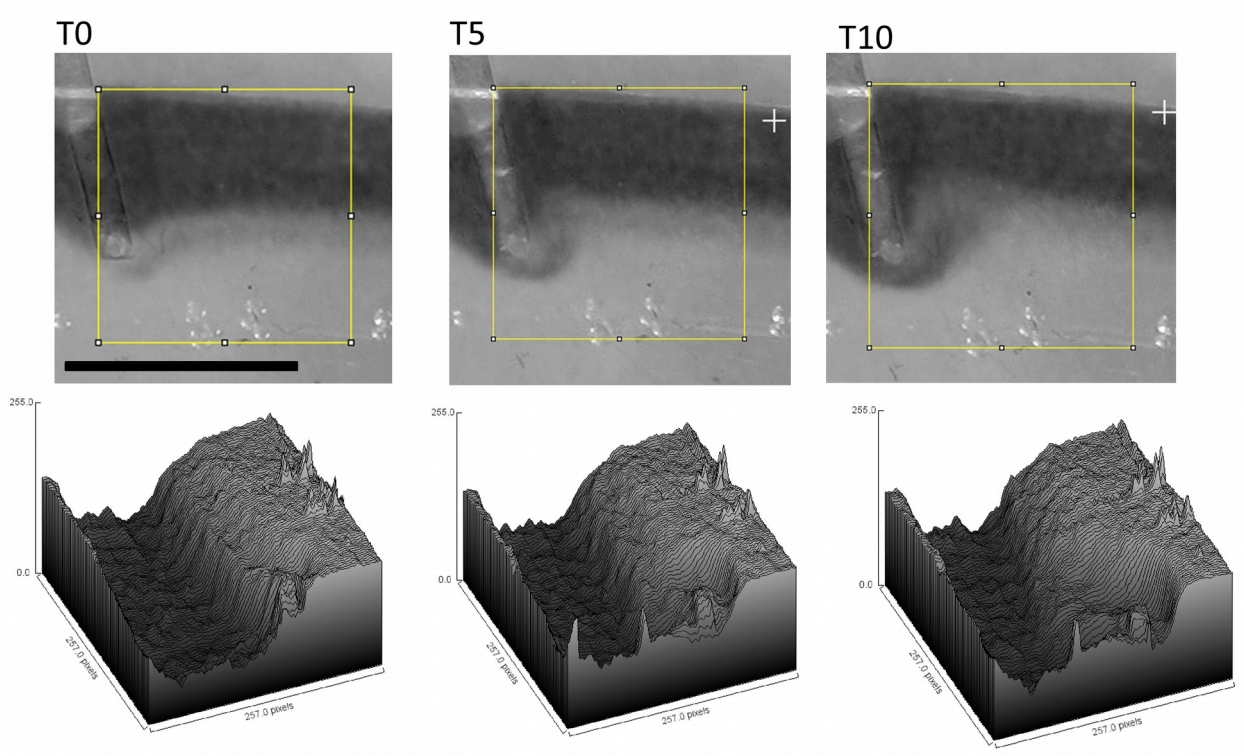

Figure 4. Time-lapse surface plots of the region immediately downstream from the actuator for time T0, T5, and T10. Note that the left-hand edge of the 257 x 257 pixel (corresponding to approximate 5.5 mm x 5.5 mm area) selected area in each image corresponds to the front-most axis (x-axis) of the surface plot below; intensity is plotted on the z-axis. Lower intensity values correspond to darker regions on the associated image and higher intensity values correspond to brighter regions. To generate each surface plot, individual frames as RGB images were split into three 8-bit grayscale images, one for each color channel (red, green, and blue). The red channel was selected for analysis because it demonstrated the greatest intensity contrast. Scale bar is 5 mm.

The Reynolds number for the mixing portion of the microchannel was found to be 0.123, which is very low. This indicates that viscous forces dominate the bulk fluid flow and that laminar flow conditions should occur; this can be seen in Figure 2. The Péclet number is 1230, which is considered high and indicates that advection is expected to be the dominant means of mass transport. Methods for calculating both Reynolds and Péclet number can be found in the supporting material. It is hypothesized that the actuator induces advection through bulk fluid flow when electrically stimulated, resulting in mixing flow patterns. However, as shown by den Toonder *et. al.*

and Baltussen *et. al.,* it is possible that the local Reynolds number around the tip of the actuator is greater than 1, indicating that inertial effects are responsible for the mixing process. [2, 23]

3.2. Further Engineering and Scalability

For applications that require small mixers, the device can be scaled down with more sophisticated microfabrication techniques. The actuators can be fabricated as small as physically possible and still retain their electromechanical properties. In addition, variation in mixing flow dynamics could be achieved by varying the length-to-width aspect ratio of the actuator protruding into the microchannel. **One limiting factor to scaled-down applications in the current design is the polyethylene cover.** Tests were conducted to quantify the effects of the polyethylene cover on performance (described in Figure S2). The polyethylene cover has been shown to reduce the tip displacement of the actuator, thus limiting its ability to affect the fluid flow. **If the polyethylene cover can be replaced with something lighter and more flexible but with similar chemical and electrical properties, then the mixing efficiency can be improved** and smaller microchannel sizes are possible. One solution could be parylene, which can be fabricated as a very thin, uniform waterproof film that is also an electrical insulator. It ~~and~~ could potentially be deposited directly onto the IEAPAs, depending on the deposition method, without adding significant thickness or weight. Parylene has recently been studied for the encapsulation of flexible electronics intended for biomedical applications. [24, 25]

A future iteration of the device could involve multiple actuators embedded in sequence down the channel length to increase mixing efficiency. [26] It has been demonstrated that multiple cilia or active mixers arranged in a sequence or array and activated simultaneously can improve mixing efficiency; configurations can be optimized by examining both the 2D and 3D induced flow patterns. [2, 27, 28] A horizontal actuator orientation is described in this work, although exploring other orientations with respect to the microchannel and fluid flow is one possibility to improve mixing performance. Future work should include improving conditions for mixing efficiency by varying the frequency and voltage at which the actuator(s) are operated. With IEAPAs, increasing frequency results in decreased tip displacement because the bending mechanism is the result of ion migration through the polymer matrix; at higher frequencies the ions have less time to migrate, resulting in a more vibration-like motion. Similarly, if the frequency is decreased the tip displacement will increase. A compromise must be made between switching speed and magnitude

of tip displacement, and there must be some optimum value where maximum mixing efficiency is achieved for a certain device configuration. Although the mixing time for the single actuator device presented is a rather slow 10 s, a combination of actuators in a sequence or array and operating under optimal conditions cshould significantly reduce the mixing time.

4. Conclusions

IEAPAs have been shown to cause local disruption of laminar fluid flow in the low Reynolds number regime. The use of IEAPAs rather than other similar materials addresses some of the issues associated with the use of electromechanical actuators as active microfluidic mixers or artificial cilia while offering benefits such as low voltage and relative ease of manufacture. Although further optimization and engineering is necessary to reduce mixing time, characterize external control, and further investigate the nature of the flow patterns, IEAPAs could be a viable alternative to other active microfluidic mixing methods and contribute to the progression of lab-on-a-chip devices.

Acknowledgements

This work was funded in part by the Iowa State University Foundation, and in part by the U.S. Department of Energy Office of Science, Office of Workforce Development for Teachers and Scientists (WDTS) under the Science Undergraduate Laboratory Internship (SULI) Program at Ames Laboratory. We also acknowledge the William March Scholar program and the Iowa State University Presidential Initiative for Interdisciplinary Research and Health Research Initiative (ISU-HRI) for support of this work.

References

1. Lee, C.-Y., et al., *Microfluidic mixing: a review.* International journal of molecular sciences, 2011. **12(5): p. 3263-3287.**
2. **Den Toonder, J.M., et al., *Artificial Cilia.* Vol. 30.** 2013: Royal Society of Chemistry.
3. Toonder, J.M.d. and P.R. Onck, *Microfluidic manipulation with artificial/bioinspired cilia.* Trends in biotechnology, 2012.
4. Gao, Y., et al., *Strong vortical flows generated by the collective motion of magnetic particle chains rotating in a fluid cell.* Lab on a Chip, 2015.
5. Wang, Y., et al., *Out of cleanroom, self-assembled magnetic artificial cilia.* Lab Chip, 2013.
6. Van Reenen, A., et al., *Integrated lab-on-chip biosensing systems based on magnetic particle actuation–a comprehensive review.* Lab on a Chip, 2014. **14**(12): p. 1966-1986.
7. Chen, C.-Y., et al., *Magnetically actuated artificial cilia for optimum mixing performance in microfluidics.* Lab on a Chip, 2013. **13**(14): p. 2834-2839.
8. Lin, C.-Y., et al. *Fluid dynamics analysis of magnetically actuated ciliated nano/micro structures for flow mixing and propulsion applications*. in *Nano/Micro Engineered and Molecular Systems (NEMS), 2013 8th IEEE International Conference on*. 2013. IEEE.
9. Rahbar, M., L. Shannon, and B.L. Gray, *Microfluidic active mixers employing ultra-high aspect-ratio rare-earth magnetic nano-composite polymer artificial cilia.* Journal of Micromechanics and Microengineering, 2014. **24**(2): p. 025003.
10. Hong, W., et al., *Evidence of counterion migration in ionic polymer actuators via investigation of electromechanical performance.* Sensors and Actuators B: Chemical, 2014. **205**: p. 371-376.
11. Montazami, R., D. Wang, and J.R. Heflin, *Influence of conductive network composite structure on the electromechanical performance of ionic electroactive polymer actuators.* International Journal of Smart and Nano Materials, 2012. **3**(3): p. 204-213.
12. Meis, C., N. Hashemi, and R. Montazami, *Investigation of spray-coated silver-microparticle electrodes for ionic electroactive polymer actuators.* Journal of Applied Physics, 2014. **115**(13): p. 134302.
13. Liu, S., et al., *Layer-by-layer self-assembled conductor network composites in ionic polymer metal composite actuators with high strain response.* Applied Physics Letters, 2009. **95**(2): p. 023505-023505-3.
14. Montazami, R., et al., *Thickness dependence of curvature, strain, and response time in ionic electroactive polymer actuators fabricated via layer-by-layer assembly.* Journal of Applied Physics, 2011. **109**: p. 104301.
15. Hong, W., A. Almomani, and R. Montazami, *Influence of ionic liquid concentration on the electromechanical performance of ionic electroactive polymer actuators.* Organic Electronics, 2014. **15**(11): p. 2982-2987.
16. Moghadam, A.A.A., et al., *Nonlinear dynamic modeling of ionic polymer conductive network composite actuators using rigid finite element method.* Sensors and Actuators A: Physical, 2014. **217**: p. 168-182.
17. den Toonder, J., et al., *Artificial cilia for active micro-fluidic mixing.* Lab on a Chip, 2008. **8**(4): p. 533-541.
18. Sareh, S., et al., *Swimming like algae: biomimetic soft artificial cilia.* Journal of The Royal Society Interface, 2013. **10**(78).
19. Hashemi, N., et al., *Optofluidic characterization of marine algae using a microflow cytometer.* Biomicrofluidics, 2011. **5**: p. 032009.
20. Hashemi, N., et al., *Microflow Cytometer for optical analysis of phytoplankton.* Biosensors and Bioelectronics, 2011. **26**(11): p. 4263-4269.
21. Hashemi, N., et al., *Dynamic reversibility of hydrodynamic focusing for recycling sheath fluid.* Lab on a Chip, 2010. **10**(15): p. 1952-1959.

22. Peron, J., et al., *Properties of Nafion< sup>®</sup> NR-211 membranes for PEMFCs.* Journal of Membrane Science, 2010. **356**(1): p. 44-51.
23. Baltussen, M., et al., *Inertial flow effects in a micro-mixer based on artificial cilia.* Lab on a Chip, 2009. **9**(16): p. 2326-2331.
24. Jarboui, A., et al. *Parylene C for hermetic and flexible encapsulation of interconnects and electronic components*. in *4th Flexible and Stretchable Electronics conference 2013*. 2013.
25. Trantidou, T., et al., *Parylene C-Based Flexible Electronics for pH Monitoring Applications.* Sensors, 2014. **14**(7): p. 11629-11639.
26. Meis, C., R. Montazami, and N. Hashemi. *Ionic Electroactive Polymer Actuators for On-Chip Sample Processing Integrated With Microflow Cytometer*. in *ASME 2013 Summer Bioengineering Conference*. 2013. American Society of Mechanical Engineers.
27. Khaderi, S., J. den Toonder, and P. Onck, *Fluid flow due to collective non-reciprocal motion of symmetrically-beating artificial cilia.* Biomicrofluidics, 2012. **6**(1): p. 014106.
28. Chen, C.-Y., C.-Y. Lin, and Y.-T. Hu, *Inducing 3D vortical flow patterns with 2D asymmetric actuation of artificial cilia for high-performance active micromixing.* Experiments in Fluids, 2014. **55**(7): p. 1-9.