MEMS Biofluidic Device Concept Based on a Supramolecular Motor

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ABSTRACT

The supramolecular machine, called the nuclear pore complex (NPC), controls the transport of all cellular material between the cytoplasm and the nucleus that occurs naturally in all biological cells. In the presence of appropriate chemical or geometrical stimuli, the NPC opens or closes, like a gate, and permits the flow of material into, and out of, the nucleus. Given the natural design of the nuclear pore complexes, their motor like function, and their direct engineering relevance to bio-molecular motors technology, our approach is to understand its design and mimic the supramolecular motor in an example of a biofluidic device through MEMS. A proof-of-concept based on a MEMS fluid pump will be designed and fabricated to demonstrate the applicability of the bio-inspired motor. The inspiration comes from the bio-inspired motor (Nuclear Pore Complex) which acts like a bi-directional pump for specific substances. While the NPC is about 200 nanometers in size, our proof-of-concept will be about 100,000 times larger in size. After fabrication of each MEMS component, process characterization, prototype evaluation and design evaluation will occur to iterate the modeling and simulation aspects of the project. The evaluations of the MEMS component will be done within a test fluid pumping environment.

Keywords: MEMS, motor, biofluidic, supramolecular

1 INTRODUCTION

The human body is a complex array of organs, each composed of a variety of tissues, composed of many cell types. It is the study of the individual cells which has led us and other researchers to be so marveled by the nature of cellular activity that we try to imitate what cells do. It is this impressive and efficient order of sub-cellular activities that has led to our study of the Nuclear Pore Complex (NPC) as a model of functionality that we wish to imitate.

This supra-molecular pump is located at the junction of the cytoplasm and the nucleoplasm [1]. It appears to represent a point of transition from the cytoplasmic cisterns, the smooth and rough endoplasmic reticulum, and the perinuclear cistern. It is the junction where nuclear material such as mRNA (messenger material produced by the nuclear code (DNA)) is sent as instructions to the rough endoplasmic reticulum to encode the production of specific molecules for use by the cell or distribution out of the cell for use elsewhere by the organ or organism. In the opposite direction material can be sent into the nucleus for messengering or wrapping and/or unwrapping DNA to allow for varied areas of DNA to be exposed for code production.

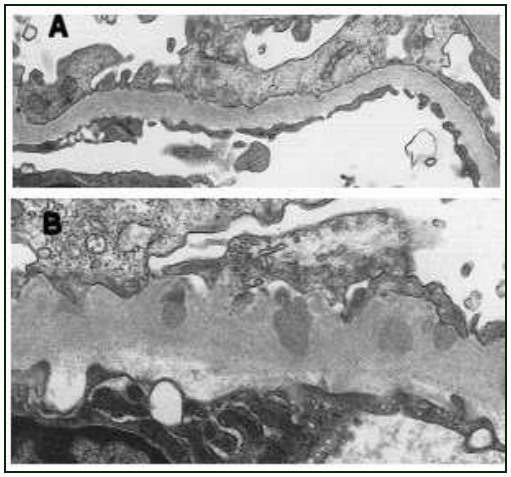

Figure 1: A: Normal peripheral capillary loop in kidney. B: Abnormal peripheral capillary loop with electron dense deposits in the basement membrane, representing chemical complexes trapped passing through the membrane.

Electron microscopic studies of the NPC has revealed an arrangement of filaments and ultrastructural forms which have been interpreted to be the backbone of the complex [2]. Our graphic representation of this suggests that the outer elements at both ends represent filaments and lipoprotein complexes used to anchor the core elements. It is these core elements, which appear to give specificity to the functionality of the NPC. Studies have shown that at different times the staining of the core at electron microscopy varies [1]. From studies of routine electron microscopy of normal and diseased kidney biopsies, we have demonstrated that at times of varied filtration by the lamina densa in electron micrographs it is possible to see materials in transition through the renal basement membrane [3][4]. (Figure 1) These materials in transition give darker and varied staining at electron microscopy.

Just as in the kidney biopsies shown, these pictures represent a dynamic liquid to semisolid material functioning as molecular elements and as supra-molecular structures. The kidney biopsies show immune complex disease frozen in a moment of time. The electron micrographs reveal the NPC when the complex is at a moment in time where molecular material may or may not be in the core area. How the material enters and transitions the core has been demonstrated using encapsulated viral material presented to the NPC [2]. Urs. F. Greber and Suomalainen demonstrated that the NPC has specific geometry, which must be met for the complex to allow transition through to the nucleus. It is unreasonable to assume that only geometry is in use to accomplish transition through the core area. It is reasonable from these studies to assume that when the geometry of the viral coat meets the requirements of the NPC, other chemistry takes place, allowing transition to the nuclear side. This process has been demonstrated to use APT as an on site energy source, consistent with most other supra-molecular reactions requiring energy input [2]. Reverse transitioning is most likely also based on some combination of geometry, chemical reactions and/or electro-mechanical activity, requiring energy.

Inspired by this complex and sophisticated supra-molecular activity, we have devised a MEMS pump, which will accomplish material transfer based on geometry (size) and electro-mechanical activity.

2 MEMS BIO-FLUIDIC DESIGN CONCEPT

The objective of developing a MEMS bio-fluidic proof-of-concept is to explore the design features of the NPC. For each of the components of the design its advantages, manufacturability and design features will be analyzed. Together, the proof-of-concept data and information obtained from the scaled prototype models will be used to refine the computational models for assessing the mechanical characteristics (assembly, weight, cost, stress concentrations, etc.) and scaling properties.

While the NPC is about 200 nanometers in size, our proof-of-concept will initially be about 10,000 times larger in size with the possibility 2 to 3 times larger in thickness and 1,000 times larger in width. The bio-inspired fluid pump initial concept is shown in Figure 2. The proof-of-concept NPC will be manufactured using MEMS related technologies. Specifically, the proof-of-concept will utilize electrostatic actuation, piezoelectric actuation and Silicon-On-Insulator (SOI) wafer processing.

Examining the NPC reveals the following characteristics. First, the NPC acts like a bi-directional pump. Second, the NPC has two types of sensors on each opening for the identification of specific substances: a geometric sensor and a chemical sensor. Third, the NPC has two controlling inputs from the nucleus: a controlling input that directs the NPC to pump a specific substance out of the cell and a controlling input that directs the NPC to pump a specific substance in to the cell. Fourth, the NPC contains all of the controlling logic to make the NPC pump function. These characteristics are summarized in a system schematic illustrated in Figure 3.

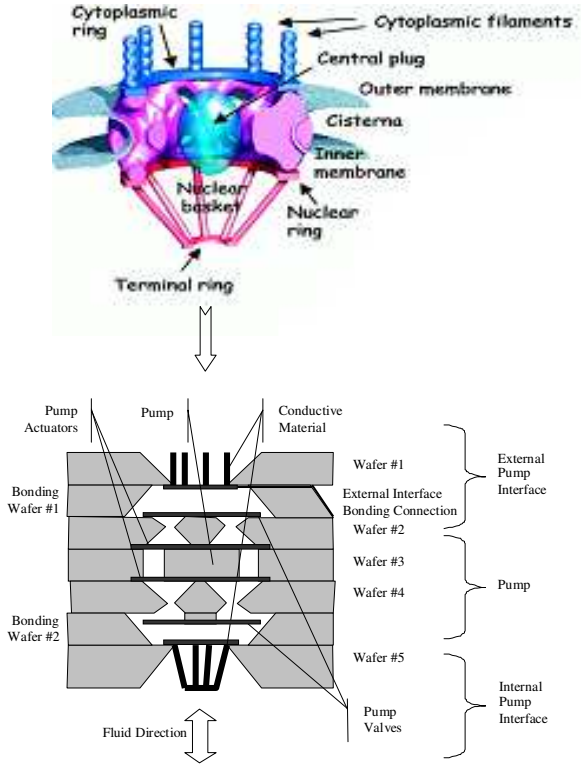

Figure 2: Bio-inspired MEMS fluid pump concept. [5]

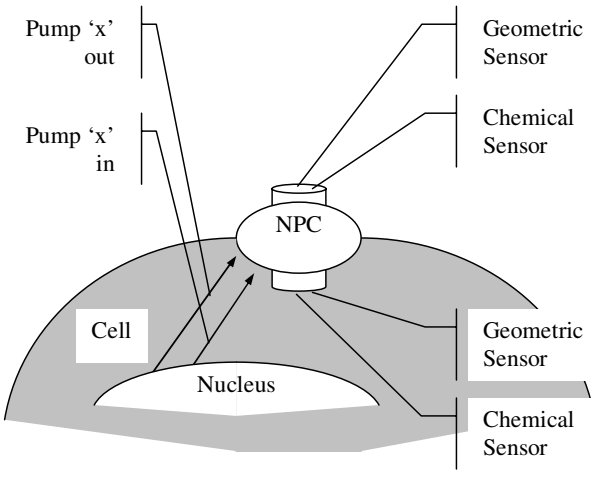

Figure 3: NPC system schematic.

Focusing on the proof-of-concept NPC pump, the bio-inspired design employs two actuation methods to achieve the pumping action. The bio-inspired pump consists of a moving central plug that is controlled by bimorph piezoelectric supports and two electrostatic actuated check

values. The initial condition of the check values is that each are normally open. The basic pump sequence starts by the central plug actuated to the most outlet position and the outlet check value closed. With the outlet check valve closed, the central plug is actuated to the most inlet position pulling fluid into the void created between the outlet check valve and the central plug. Afterwards, the inlet check valve is closed and then the outlet check valve is opened. Then the central plug is actuated back to the most outlet position which would push the fluid through the outlet.

The MEMS manufacturing process for the proof-of-concept devices will encompass using SIO semiconductor wafers. These wafers provide many useful characteristics like etched cavities that follow crystal structures, doped silicon layers that can be used to create electrical conductors or possible active electronic components and proof-of-concept devices based on the deposited silicon layer thickness that can range from 50nm to 100um instead of wafer thickness of about 375um.

3 DESIGN ANALYSIS

The geometry considered for the bio-fluid pump proof-of-concept is shown Figure 4. Three computational models are considered using plane stress and beam type finite elements. Model-1 as shown Figure 4 is considered as a baseline with all the ports are closed so that no fluid flows through the pump. Model-2 and Model-3 consist of the same geometry as Model-1 but all the ports are completely open except the one at the bottom so that the fluid flows from top to bottom of the pump.

Two different material properties were used for the plane elements and beam elements. All beams have the following elastic properties in the finite element analysis: Young's modulus, E=70 GPa Poisson's ratio, ν=0.31 and density ρ=7600 kg/m^3. The materials properties for solid-planes are Silicon (E=180 GPa; ν=0.17, ρ=2330 kg/m^3).

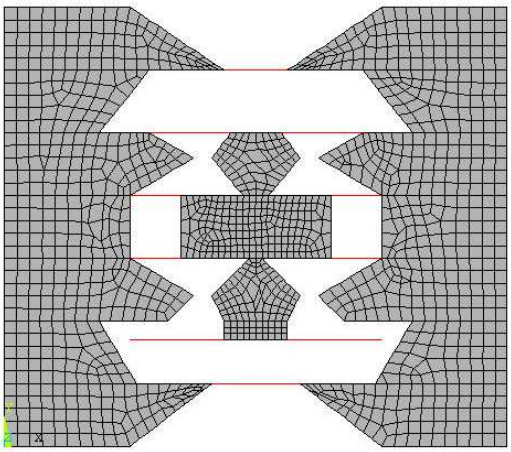

Figure 4: Bio-fluid pump, Model #1.

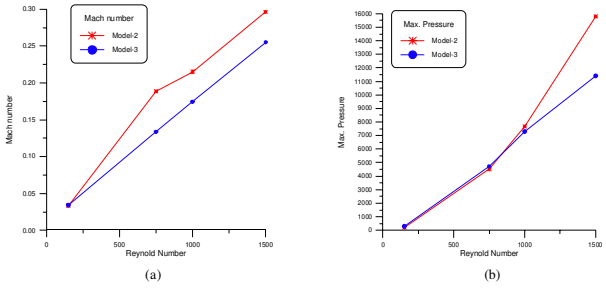

Figure 5: (a) Mach number and (b) pressure using different Reynolds numbers.

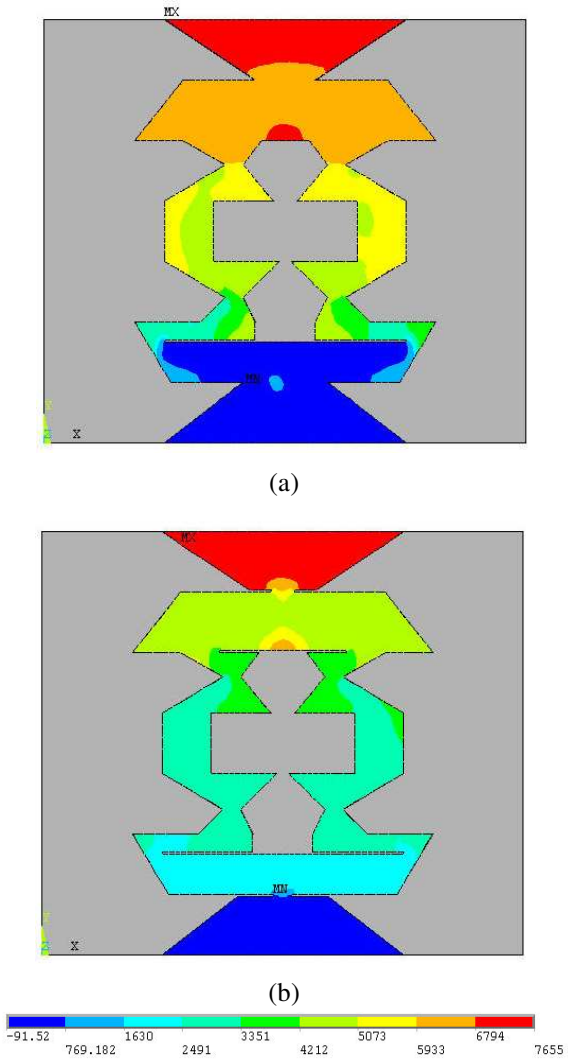

Figure 6: (a) Model-2 and (b) Model-3.

3.1 Fluid Flow Analysis

The material properties of water were used for the fluid. The material properties for the fluid used in the finite

element analysis are viscosity, $\mu=1.14\times10^{-12}$ kg/nm-s and density $\rho=1000\times10^{-27}$ kg/m^3. The fluids are modeled using two-dimensional finite elements in ANSYS software. The PLANE141 element type is defined by four nodes and has two degrees of freedom in x and y directions at each node. Free mesh is used for creating the finite element model. The boundary conditions for the finite element models are assumed to be at inlet top line v_0 initial velocity, at the other zero and at the outlet bottom line zero pressure.

The results are obtained using the finite element meshes of 2045 for Model-2 and 1305 for Model-3 for the fluid flow with FLOTRAN/CFD, respectively. In addition, Model-2 and Model-3 were solved with using different Reynolds number during this analysis.

The maximum Mach number and maximum pressure for the Model-2 and Model-3 are shown in Figure 5 using FLOTRAN/CFD module in ANSYS software. For Model-2 and Model-3, the locations for maximum pressure are at the inlet, and locations for maximum velocity at the Model-2 are nearly at the bottom beam. The locations for maximum velocity at the Model-3 are nearly bottom beam for Re=150 and 750, and top beam for Re=1000 and 1500.

The pressure results using Reynolds number 1000 are presented in Figure 6 for Model-2 and Model-3.

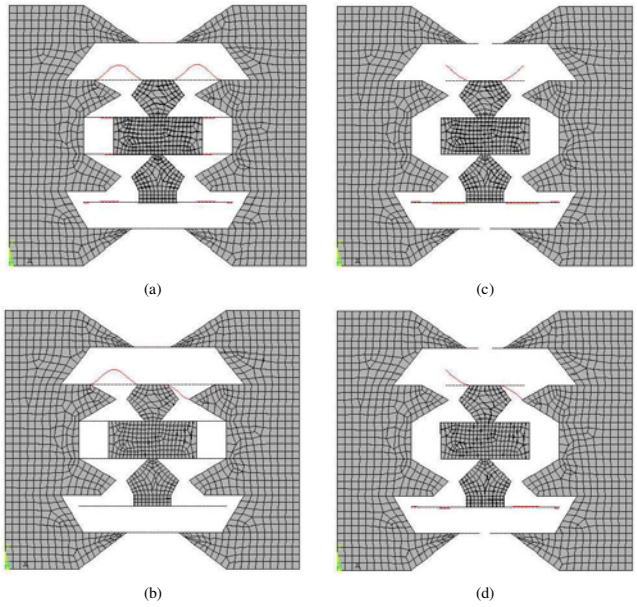

Figure 7: Model-1 and Model-3 Mode shapes.

3.2 Dynamic Analysis

Model-1 and Model-3 were solved for dynamic analysis to investigate the resonance characteristics of the electrostatic actuated check valve beams. The material properties of plane are Silicon. Polyimide and gold materials were used for all beams. The planes and beams are modeled using two-dimensional finite elements in ANSYS software. For planes, the PLANE42 element type is defined by four nodes and has two degrees of freedom (translations in x and y directions) at each node. Free mesh is used for creating the finite element model. The boundary conditions for the finite element models are assumed to be at left and right ends fixed. The results are obtained using the total finite element meshes of 1519, 1406, for Model-2 and Model-3 for the dynamic analysis, respectively. Model-1 has 209 beam elements and Model-3 has 96 beam elements (BEAM3 in ANSYS Software).

Cases	First Mode	Second Mode
Model-1	42727 Hz	43149 Hz
Model-3	26882 Hz	27278 Hz

Table 1: Comparison of frequencies.

The fundamental mode shapes for the Model-1 are shown in Figure 7 using dynamic analysis. Table 1 shows the comparison of frequency values for the Model-1 and Model-3 model cases. It can be seen from Table 1, that first and second frequency values decrease about 37% for model-3 as compared to model-1. The third and fourth stiffnesses increase about 42% for Model-3.

4 SUMMARY

A process has been created and mechanical models explored that enable the creation of a proof-of-concept MEMS-based biofluidic device based on the supra molecular structure of the Nuclear Pore Complex. The device process has the capabilities of creating a 400 nano-meter thick device for testing in a fluid pumping environment.

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