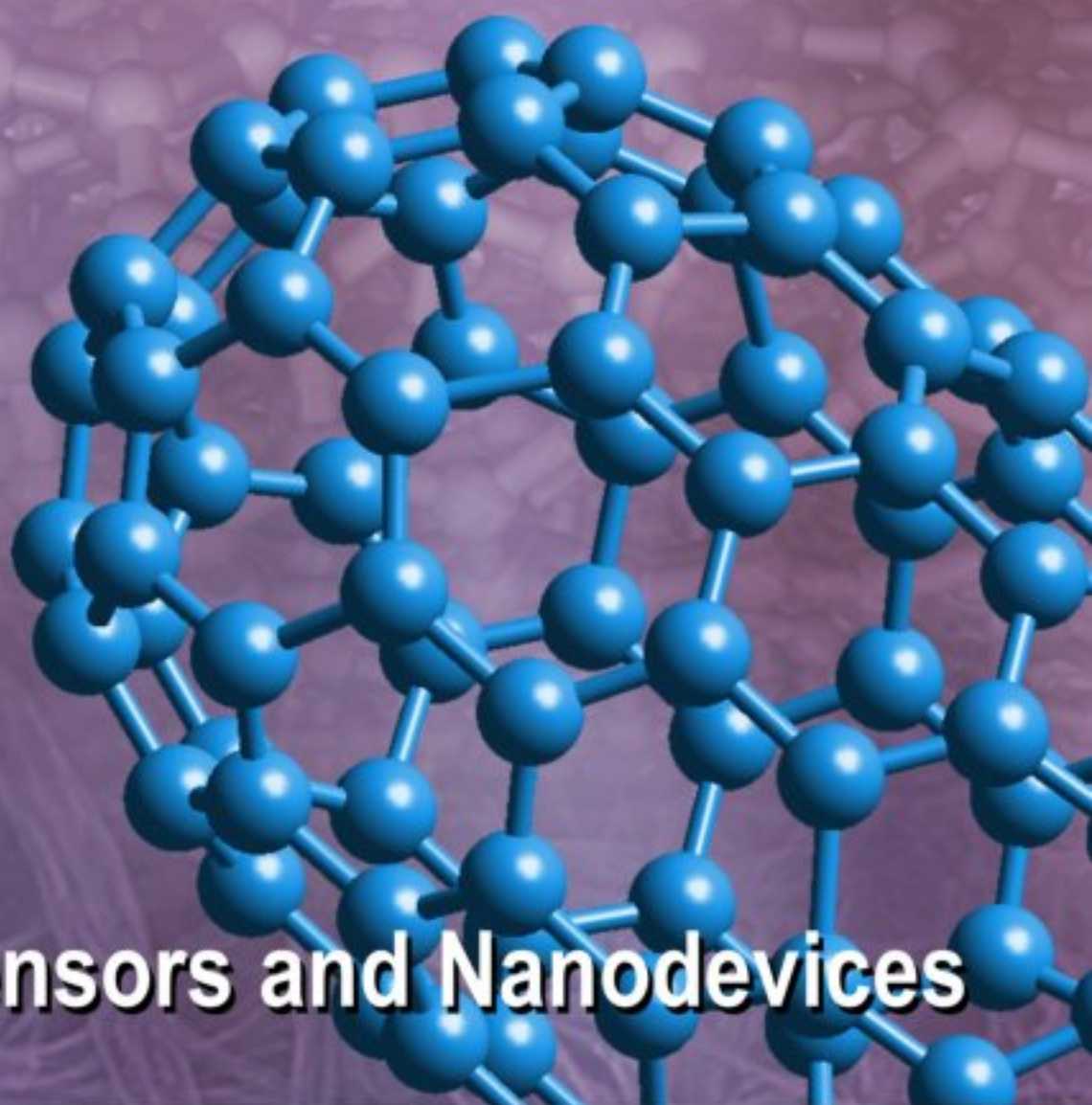


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## Emerging MEMS 2010

*Technologies & Markets 2010 Report*

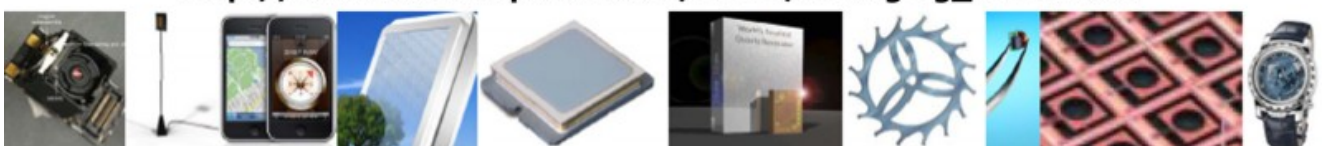
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May 22-27, 2011 - Venice, Italy



**Important deadlines:**

Submission (full paper)	January 10, 2011
Notification	February 20, 2011
Registration	March 5, 2011
Camera ready	March 20, 2011

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- Safety in industrial systems
- Complex Systems

## Fabrication and Analysis of Tapered Tip Silicon Microneedles for MEMS based Drug Delivery System

\*Muhammad Waseem Ashraf, Shahzadi Tayyaba, Nitin Afzulpurkar, Asim Nisar  
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**Abstract:** In this paper, a novel design of transdermal drug delivery (TDD) system is presented. The proposed system consists of controlled electronic circuit and microelectromechanical system (MEMS) based devices like microneedles, micropump, flow sensor, and blood pressure sensor. The aim of this project is to develop a system that can eliminate the limitations associated with oral therapy. In this phase tapered tip silicon microneedles have been fabricated using inductively coupled plasma (ICP) etching technology. Using ANSYS, simulation of microneedles has been conducted before the fabrication process to test the design suitability for TDD. More over multifield analysis of reservoir integrated with microneedle array using piezoelectric actuator has also been performed. The effects of frequency and voltage on actuator and fluid flow rate through  $6 \times 6$  microneedle array have been investigated. This work provides envisage data to design suitable devices for TDD.  
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**Keywords:** Tapered tip silicon microneedles, Coupled multifield, Finite element method, Transdermal drug delivery system.

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### 1. Introduction

Transdermal drug delivery (TDD) has been considered as a patient-friendly method to deliver the pharmaceutical compound by eradicating pain, gastrointestinal absorption, liver metabolism and degradation that are associated with conventional drug delivery approaches like hypodermic injections and oral administration of drugs. The use of microelectromechanical systems (MEMS) technology has been increasing rapidly in biomedical devices. Due to MEMS technology, the fabrication of miniature size and soaring performance medical devices has become practicable to congregate the critical medical requirements like controlled delivery with negligible side effects, improved bioavailability and therapeutic effectiveness. The first study for the improvement of TDD was conducted by inserting the

microneedle in cadaver skin [1]. The microneedles have different design according to their lengths, structure, shape, array density and materials [2]. The detail of microneedle categories is shown in Table 1.

**Table 1.** Categories of microneedles.

Material	Overall shape	Tip shape	Structure	Application
Silicon	Cylindrical	Volcano	Hollow	Drug delivery
Silicon dioxide	Pyramid	Snake fang	Solid	Blood extraction
Silicon nitride	Candle	Micro- hypodermis	In-plane	Fluid sampling
Glass	Spike	Tapered	Out-of-plane	Cancer therapy
Semiconductor	Spear			Micro-dialysis
Metals	Square			Ink-jet-printing
Alloys				Sensing
Polymers				

The earliest out-of-plane microneedle array consisted of 100 microneedles with a length of 1.5 mm was reported in 1991 [3]. The tetrahedron sharp tip in-plane microneedles reported for TDD [4]. Different techniques have been described in literature to fabricate microneedles like photolithography [5], deep x-ray lithography [6], deep reactive ion etching (DRIE) [7], micro-molding [8], bi-mask technique [9], surface micromachining [10], LIGA [11], hot embossing [12], UV excimer laser [13], laser micromachining [14], coherent porous silicon etching (CPS) [15], Injection molding [16] and micropipette pulling technique [17]. In these processes, silicon and polymer can be used as substrate materials for microfabrication. However, application of silicon as the substrate material is still dominant because of some excellent mechanical properties, electrical properties and possibility to directly integrate circuit on the transducer's substrate.

In past, various studies have been done on the design, analysis and fabrication of MEMS based microneedles, micropumps and miniature mixer for TDD applications. However, only few have been converted as commercial products. The main reasons are the complications of bio-MEMS devices, difficulties in integration with other devices and finally packaging is the great challenge. MEMS based integrated TDD system consists of microneedles, micropump, blood pressure sensor, flow sensors, and electronic circuits. A simplified block diagram of proposed integrated TDD system is shown in Fig. 1.

Electronic module provides the required circuitry. Blood pressure sensor monitors the patient's blood pressure. Based on the results and requirements, TDD automatically injects the desired dose of drug into patient's body. To insure the safety of patient, the flow sensor accomplishes the real time sensing of release volume of drug. The flow of drug is scrutinized by the flow sensor to avoid the large vacillation of flow rate. Drug delivery device consists of piezoelectric actuator and a reservoir integrated with microneedle array. Actuator provides actuation mechanism to vibrate the membrane. Reservoir provides drug storage and microneedles provide the interface between TDD system and patient's body to liberate the drug.

In this study, the authors present the fabrication of tapered tip hollow out-of-plane silicon microneedles and multifold analysis of reservoir integrated with 6×6 microneedle array for TDD system. In integrated device the reservoir and piezoelectric actuator behave like micropump. The in-depth numerical analysis of piezoelectric valveless micropump [18] and fabrication of piezoelectric micropump were been done [19] in the first stage of project. The analysis shows that the fabricated microneedles can be integrated with our fabricated micropump. In coupledfield analysis, the effect of frequency and voltage on the deflection of piezoelectric actuator and fluid flow rate through microneedles is studied.



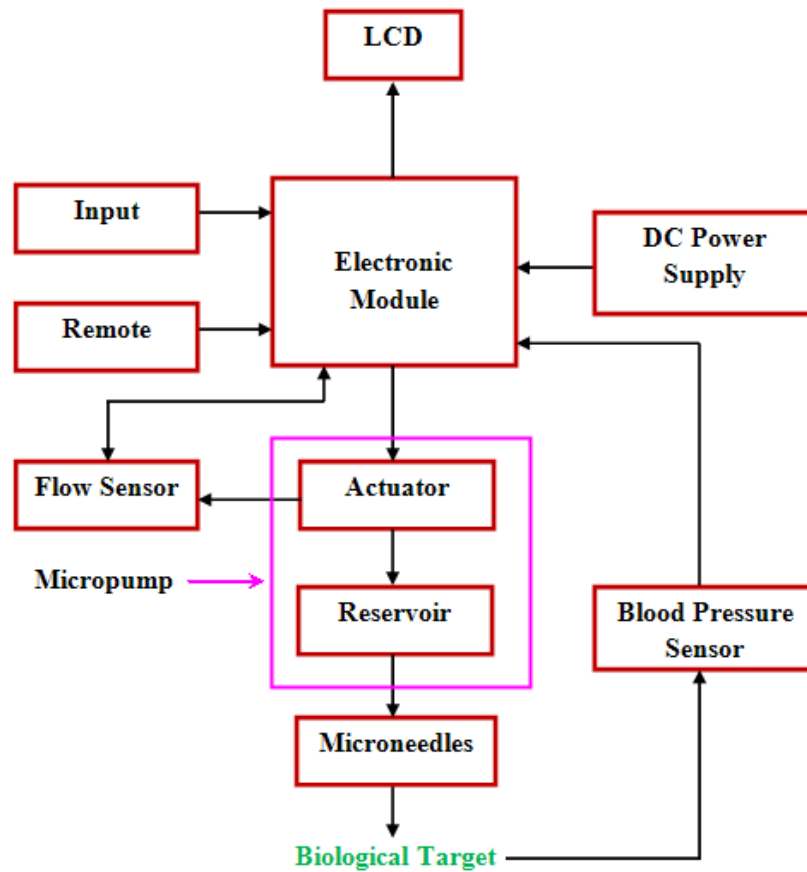


Fig. 1. Block diagram of drug delivery system.

## 2. Fabrication

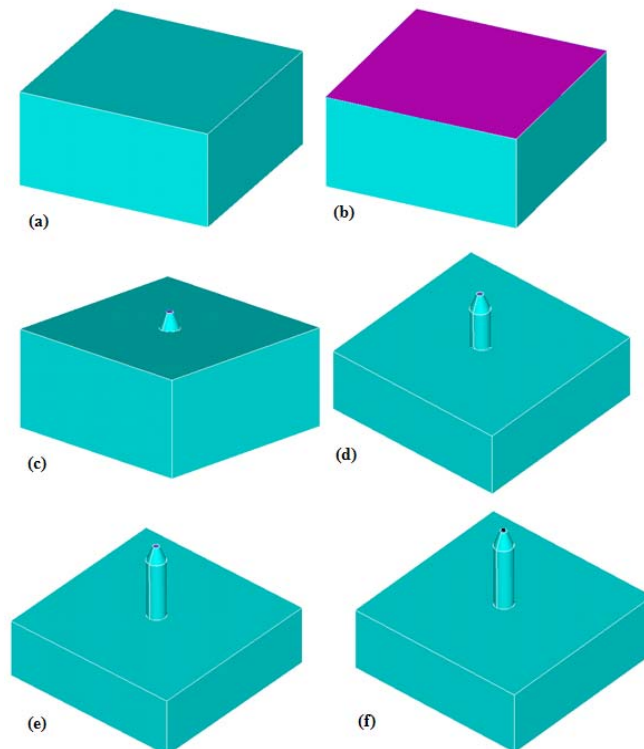
The microneedle design is cylindrical with tapered tip section, which provides enough strength and ease of skin insertion. Combination of isotropic and anisotropic etching has been used to fabricate tapered tip hollow out-of-plane silicon microneedles in inductively coupled plasma (ICP) etcher. Required shape of microneedles has been accomplished by controlling the etch time at different processing steps. The DRIE process parameters are shown in Table 2.

Table 2. DRIE process parameters.

DRIE (Bosch process parameters)	Etching from front side	Etching from back side
Temperature (°C)	15	20
Etching time (min)	15	25
Stop time (min)	3	3
Power RF (W)	1400	1600
<b>Etching/Passivation</b>		
Flux SF <sub>6</sub> /C <sub>4</sub> F <sub>8</sub> (sccm)	250/150	250/100
Pressure SF <sub>6</sub> (Pa)	3.5	4

Various steps were involved during microneedles fabrication process. In first step, 6 inch silicon wafer was cleaned (Fig. 2a). Then silicon wafer was blown dry with air gun. The second step was to cap photoresist mask (Fig. 2b). This step involved various substeps such as spin coating photoresist AZ4620 @3000 rpm, soft bake (100-150 sec @ 100 °C), expose wafer, develop in developer solution

AZ 400K and hard bake. Then isotropic dry etching was done in ICP etcher using  $\text{SF}_6/\text{O}_2$  gases for tip and outside shape of microneedle in standard photolithography process (Fig. 2 c, d, e). The first etch depth was  $15\ \mu\text{m}$ . Then photoresist is stripped off and wafer is cleaned. The next step is to thermally grown silicon oxide layer on the wafer in oxidation furnace by wet oxidation at  $1000\ ^\circ\text{C}$ . Then wafer is protected by capping with another wafer for mask oxide etching. Then photoresist was striped. To fabricate the inner hole the ICP etching was performed. The photoresist was first coated with  $5\ \mu\text{m}$  thickness. The etching depth for first ICP etch is  $150\ \mu\text{m}$ . This is followed by second ICP etch up to  $200\ \mu\text{m}$  (Fig. 2f). The final step involved release, oxide etch and dicing. The fabricated microneedles are shown in results and discussion section of the paper. The fabrication process flow of microneedles is shown in Fig. 2.



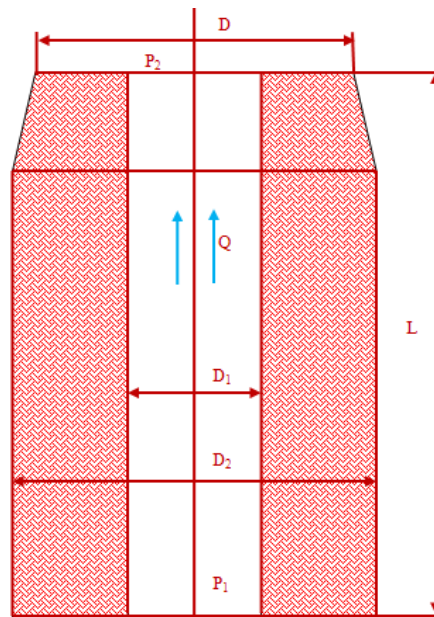
**Fig. 2.** Fabrication process flow.

### 3. Theoretical Analysis

Microneedle design is cylindrical with tapered tip as shown in Fig. 3.  $P_1$  and  $P_2$  are the inlet and outlet pressure of the microneedle.  $D$  represents the tip diameter of microneedle.  $D_1$  and  $D_2$  represent internal and outer diameter of microneedle.  $L$  is the length of the microneedle and  $Q$  is the flow rate in the lumen section.

#### 3.1. Mechanics of Microneedle

Microneedle can be broken during insertion because various forces are acting on the needles like bending, buckling, axial, and resistive forces. An axial force is experienced on the tip of microneedle. This force may cause buckling of the microneedle.  $F_{axial}$  is the force which the microneedles can withstand without fracture as shown:



**Fig. 3.** Cross section of microneedle.

$$F_{axial} = \sigma_y A , \quad (1)$$

where  $\sigma_y$  is the yield strength,  $A$  is the cross-sectional area of needle tip.

Human skin offers the resistive forces against the microneedle penetration. The pressure on the microneedle should be greater than the resistive forces.  $F_{resistance}$  before the skin punctured is expressed by the following equation:

$$F_{resistance} = P_{pierce} A , \quad (2)$$

where  $P_{pierce}$  is the required pressure to puncture the skin.

Fractional forces are experienced by the microneedles after the penetration into human skin. These forces arise because tissues and microneedle contact.  $F_{Bending}$  is the force which microneedle can withstand without breaking shown as:

$$F_{Bending} = \frac{\sigma_y I}{cL} , \quad (3)$$

where  $L$  is the length of microneedle.

### 3.2. Fluidic Analysis

Fluid flow characteristics are extremely important because array of microneedle is used to inject the drug into human skin. Fluid pressure drop through the microneedle array is based on various reasons like microneedle array geometry, roughness of surface fluid viscosity, and microneedle array density. The dimensions of microneedles are in micron, so the behavior of fluid flow is different from macro level. There is significant resistance to fluid flow through the microneedles. Poiseuille's law is

considered to measure the fluid flow through microneedle array as shown below:

$$Q = \frac{\pi D_1^4 (\nabla p)}{64 \mu (L)} \quad (4)$$

where  $Q$  is the flow rate,  $D_1$  is the diameter of microneedle and  $\mu$  is the viscosity.

Modified Bernoulli equation is considered to model the microneedles geometry. The pressure loss is calculated by considering the friction losses given by [20]:

$$\frac{P_1}{\rho g} + \frac{V_1}{2g} + Z_1 = \frac{P_2}{\rho g} + \frac{V_2}{2g} + Z_2 + \frac{fl}{d} + \frac{V^2}{2g} + \sum \frac{kV^2}{2g} \quad (5)$$

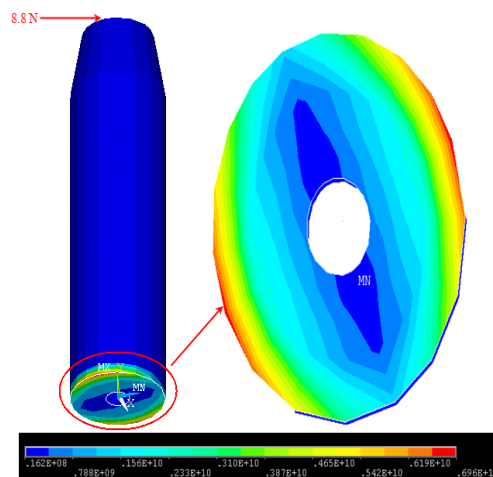
where  $P_1$  is the inlet pressure,  $P_2$  is the outlet pressure,  $V_1$  is the inlet velocity and  $V_2$  is the outlet velocity.

## 4. Numerical Simulation

In this study, structural and fluidic analysis has been conducted using ANSYS. Single microneedle was considered for structural analysis. For transient multifield analysis 6×6 microneedle array was considered.

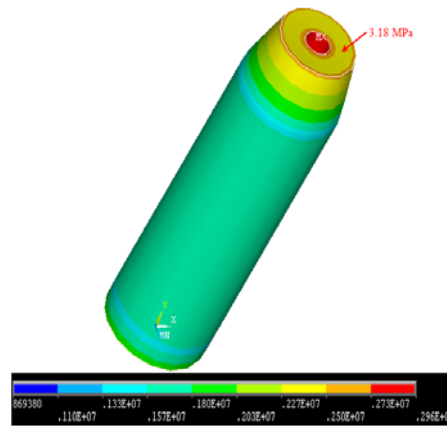
### 4.1. Structural Analysis

Finite element method (FEM) was used to perform the structural analysis. Single out-of-plane needle was modeled using element SOLID 186. The base of needle is fixed in all direction. Tip of microneedle is allowed free to move during analysis. The young modulus of 169 GPa and Poisson ratio of 0.22 were used for FEM analysis [21, 22]. In the simulation study, bending and axial stress analyses were performed by applying transverse and axial loads respectively. The range of transverse load is assumed according to the fracture strength of the material. For stress analysis the bottom of the microneedle was taken into consideration with applied tip force 8.8 N as shown in Fig. 4.



**Fig. 4.** Bending stress analysis.

Results show maximum stress of 6.96 GPa occurs at inner part of tip that is less than the yield strength of materials. Human skin resistance is 3.18 MPa during needle penetration [23, 24]. So microneedle is strong enough to bear load more than 3.18 MPa. The effect of applied pressure on tip of microneedle is shown in Fig. 5.

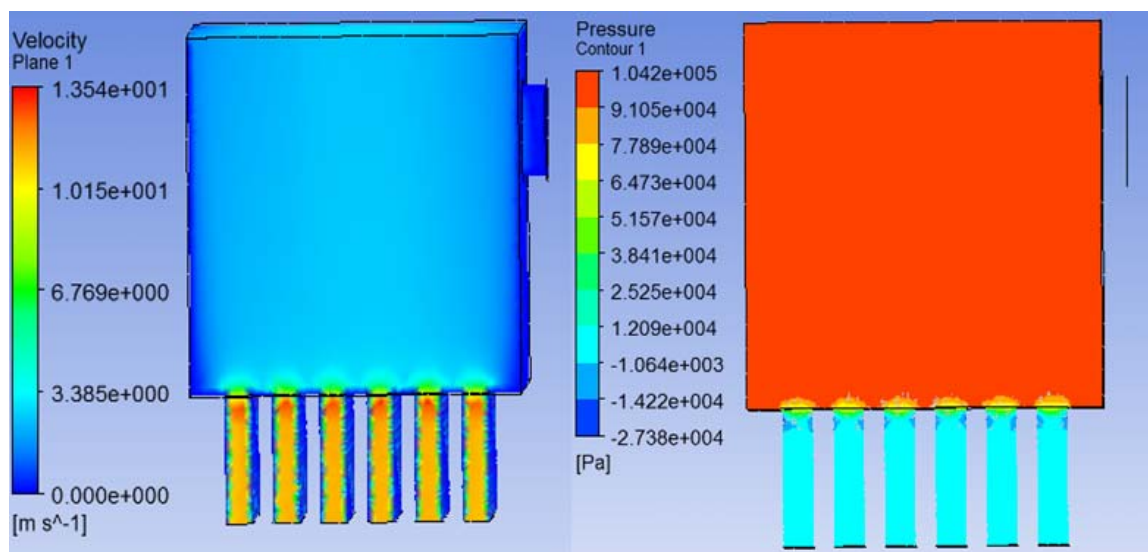


**Fig. 5.** Axial stress analysis.

Simulation results of axial stress analysis shows that the maximum stress 2.96 MPa occurs inside the lumen section of the microneedle at applied pressure of 3.18 MPa with negligible deflection.

#### **4.2. CFD Analysis at Different Inlet Pressures**

Simulation shows the effect of different applied inlet pressures on the flow rate. Single row of microneedle array (6 microneedles) was considered for analysis. The static pressure 20 kPa to 140 kPa was applied at the microneedle inlet. Isothermal fluid domain was chosen for analysis during the simulation. Ethanol was considered for flow analysis in isothermal domain. The simulation results for the applied inlet static pressure are shown in Fig. 6.

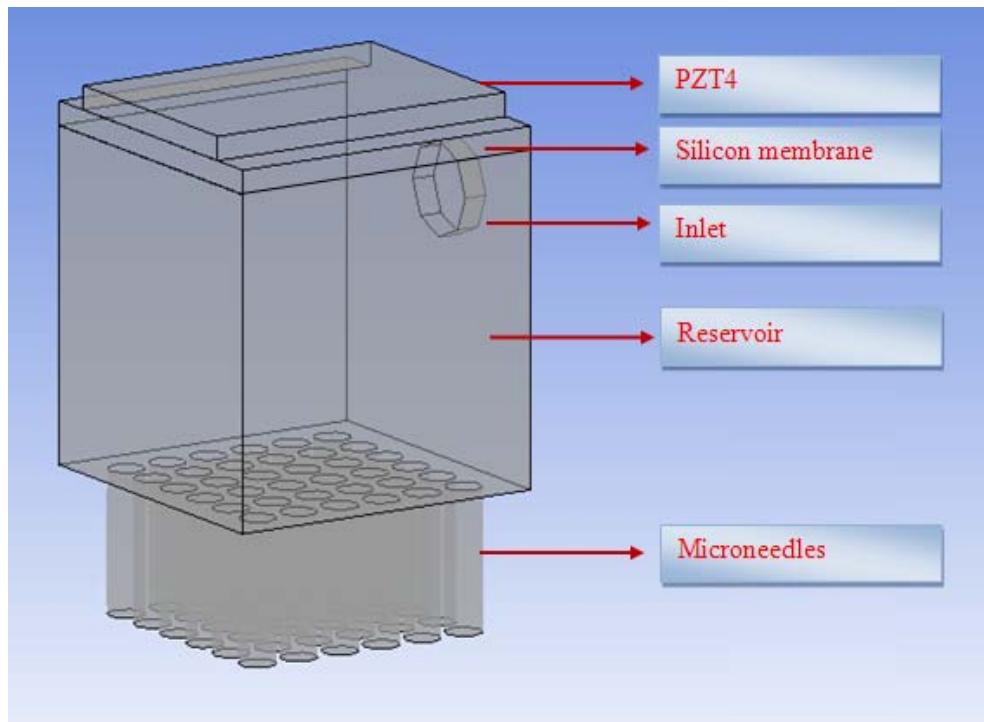


**Fig. 6.** Velocity and pressure distribution in CFD static analysis.

The result shows that the fluid velocity is negligible in the reservoir due to large area. Velocity of fluid increases in the microneedle lumen section and along the length due to small area [25]. Due to frictional losses between fluid and wall, the fluid velocity is less near wall as compared to the central region of lumen section. Pressure is high and remains constant in the reservoir. It decreases in the lumen because the fluid is flowing towards the outlet (Pressure at outlet = 0 kPa).

### 4.3. Transient Multifield Analysis

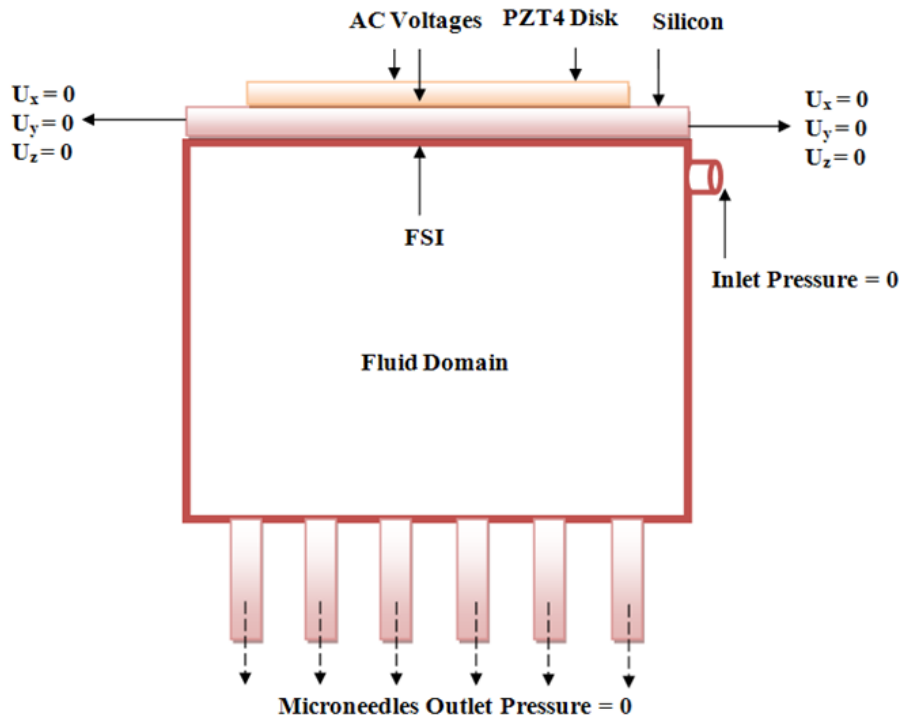
In this analysis, fluid model and structural piezoelectric actuator model were created in ANSYS separately. Then these mechanical inputs were solved in ANSYS mechanical APDL product launcher using MFX-ANSYS/CFX environment. Multiple code coupling method was used in this analysis [26]. The element Brick-20node-226 and SLOID-20node-186 were considered for PZT4 disk and silicon membrane. Circuit-124 element was considered for sinusoidal voltage degree of freedom. The elements Facet 200 and FLOTRAN CFD 142 were considered to create 3D fluid model. Ethanol was assumed as working fluid in isothermal domain. The thickness of the piezoelectric disk and silicon membrane was  $200\ \mu\text{m}$  each. The complete model of device is shown in Fig. 7.



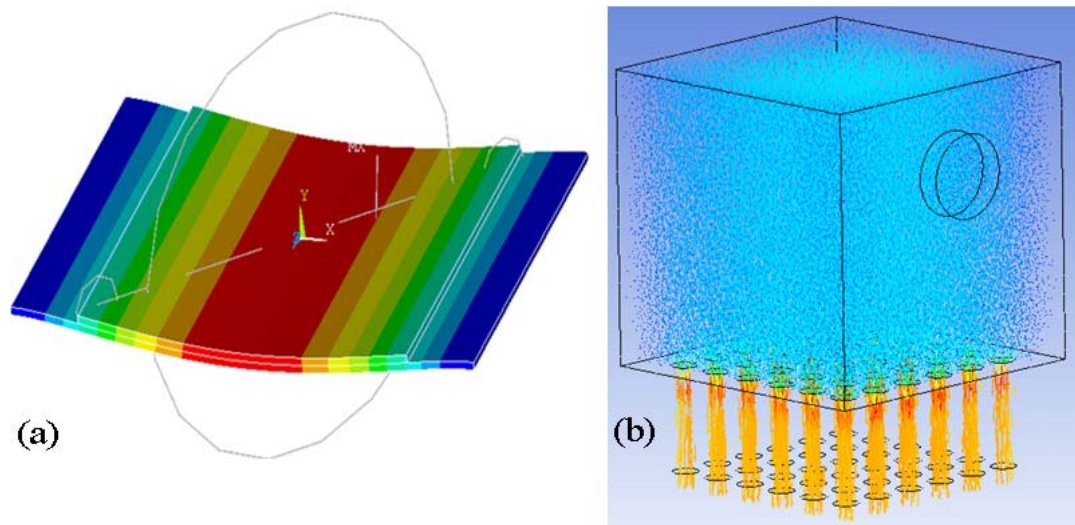
**Fig. 7.** CFD model of integrated device.

Boundary conditions applied on the device are shown in Fig. 8 [26].

The simulation results of multifield analysis (piezoelectric actuator and fluid model) are shown in Fig. 9. Simulation results show that the actuator has maximum deflection at the center. In fluid model fluid flows in the central region, while near the walls flow is negligible because of frictional forces.



**Fig. 8.** Boundary condition on integrated device.



**Fig. 9.** Multifield simulation results.

## 5. Results and Discussion

Tapered tip hollow out-of-plane silicon microneedles were fabricated successfully. The length of microneedle is  $200\ \mu\text{m}$  to avoid contact of microneedle with sensory organs. The internal diameter of microneedle is  $40\ \mu\text{m}$ . The centre-to-centre distance in microneedle array is  $750\ \mu\text{m}$ . The scanning electron microscope (SEM) images of fabricated microneedle are shown in Fig. 10.

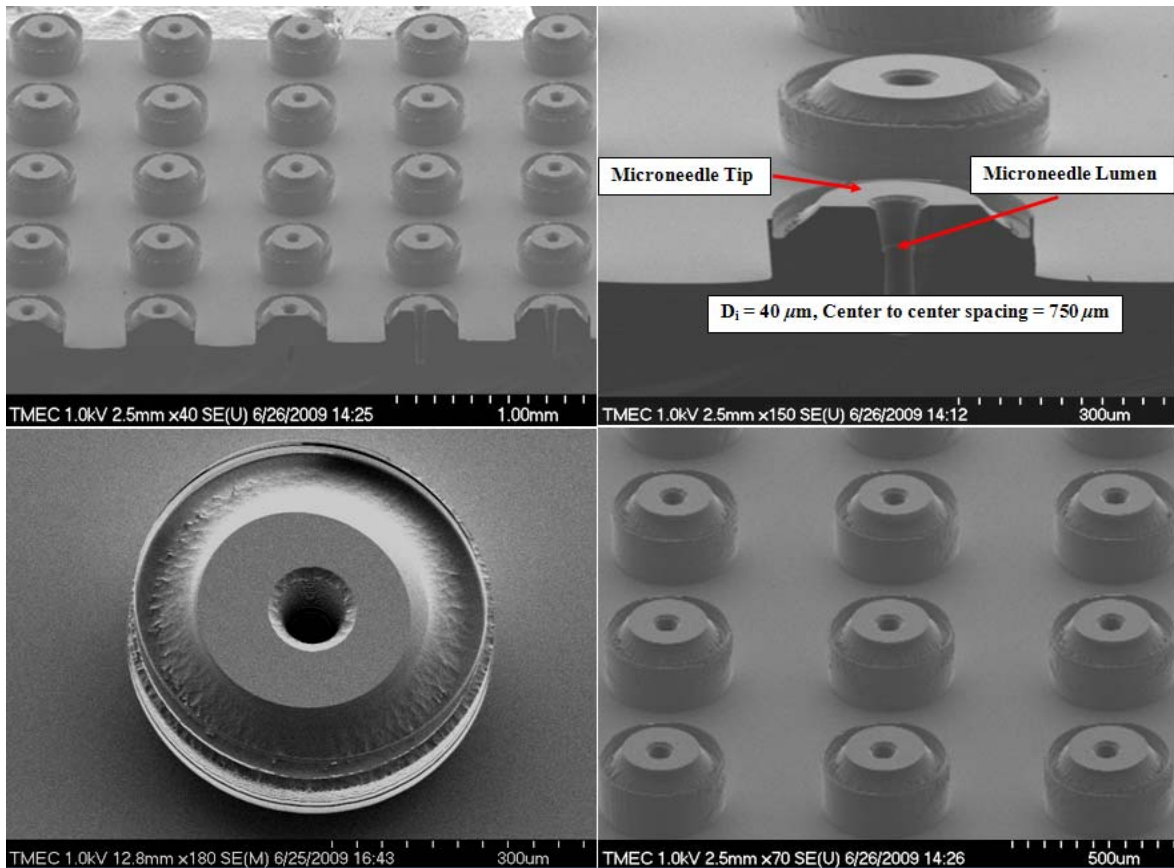


Fig. 10. SEM images of microneedles.

During structural analysis it was found that 6.69 GPa stress occurs at the microneedle bottom with 20 μm deflection at the tip for applied force of 8.8 N. The relation between stress and deflection at applied force is shown in Fig. 11.

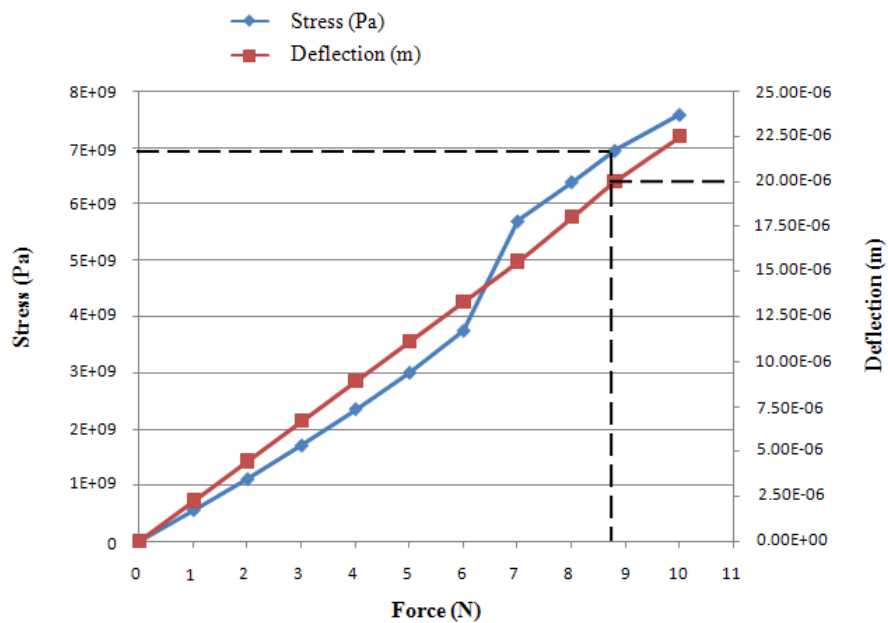
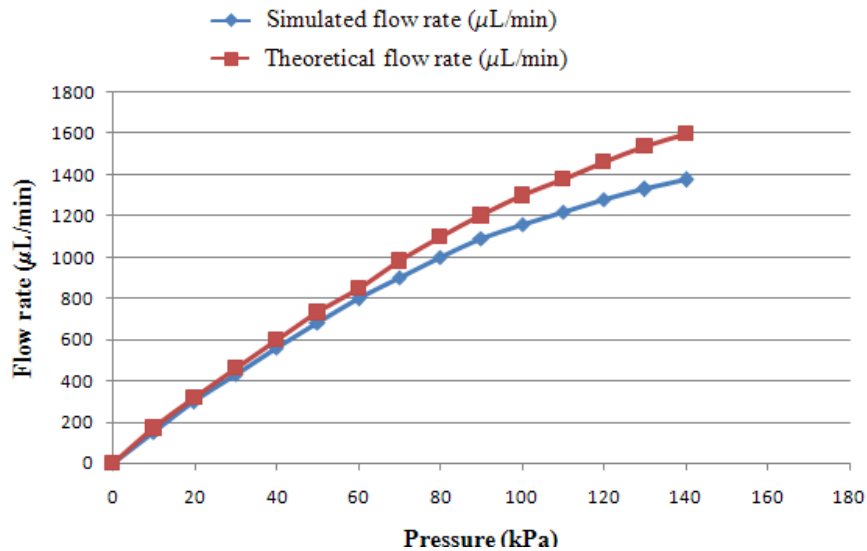


Fig. 11. Stress vs. deflection at applied bending force.



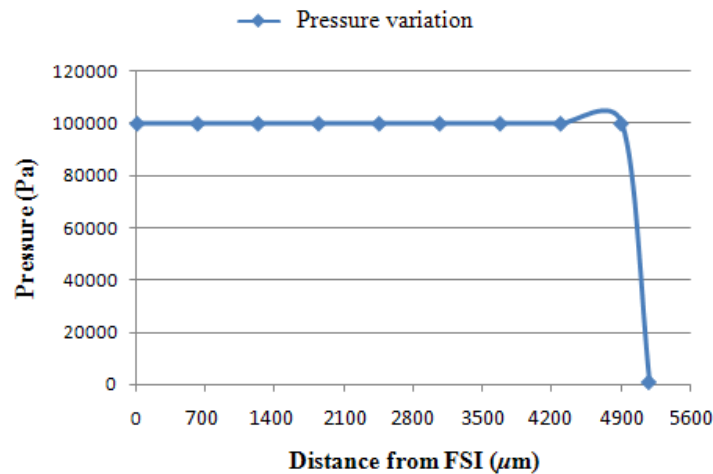
The microneedle fails if the stress value exceeds the yield stress of the material. Results show that maximum stress is less than the yield stress. So, microneedle is strong enough to bear the force up to 8.8 N.

In static CFD analysis, flow rate at various applied pressures is shown in Fig. 12. Fluid flow increases with the increase in inlet pressure. The maximum flow rate 1375  $\mu\text{L}/\text{min}$  is observed at 140 kPa.



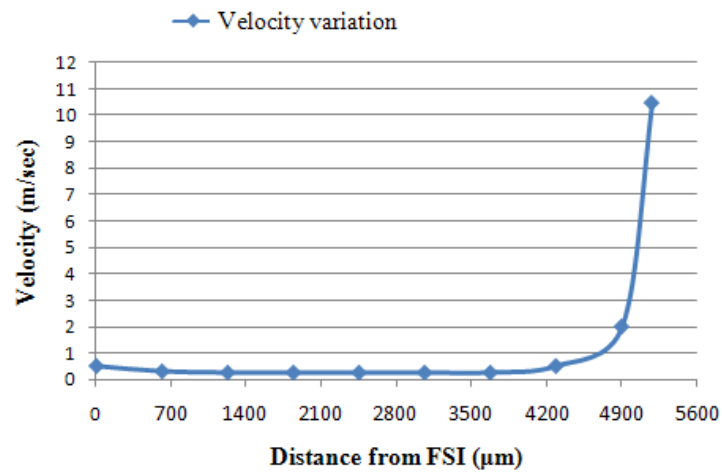
**Fig. 12.** Fluid flow at applied pressures.

The pressure variation in CFD analysis through the microfluidic device is shown by the Fig. 13. Pressure is high and remains constant through the reservoir because of large area and decreases in the lumen region because of small area and considered zero at the outer end.



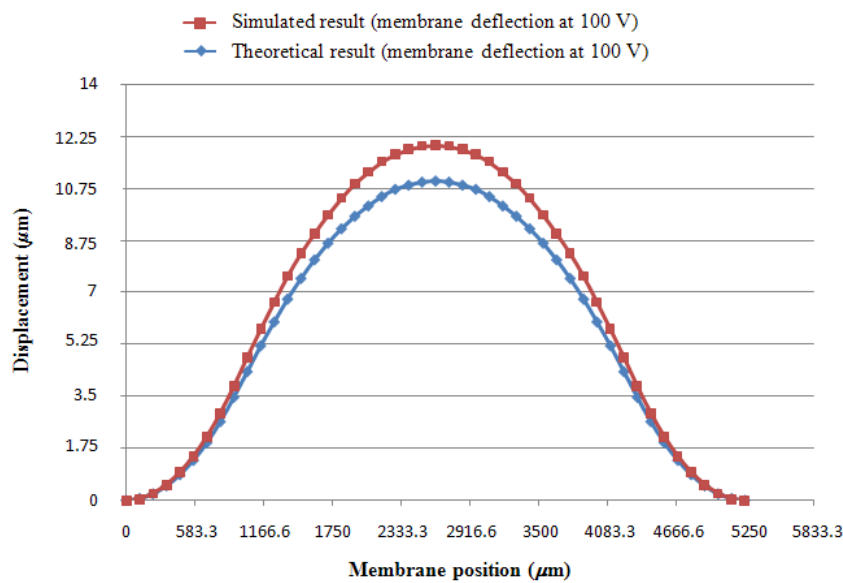
**Fig. 13.** Pressures variation.

The velocity variation in CFD analysis through the device is shown by the Fig. 14. Initially velocity is little high at first stroke volume and then remains constant through the reservoir because of large area and increases in the lumen region because of small area.



**Fig. 14.** Velocity variation.

In FEM analysis the bending of actuator at sinusoidal applied 100 V is shown in Fig. 15. The frequency of 250 Hz was considered constant. The deformation is calculated along the length of the actuator. The maximum displacement of 12.24 µm occurs at the centre of the membrane.



**Fig. 15.** Membrane deflection.

In FEM analysis the membrane deflection and frequencies relationship is shown by Fig. 16 at various applied voltages.

The flow rate for excitation frequencies at various applied voltages is shown by Fig. 17.

When the excitation frequency is increased, fluid flow rate also increases. The highest flow rate is achieved at applied 100 V.

In transient multifield analysis the fluid flow rate at applied 100 V with deflection of actuator 12.24 µm is shown by the Fig. 18.

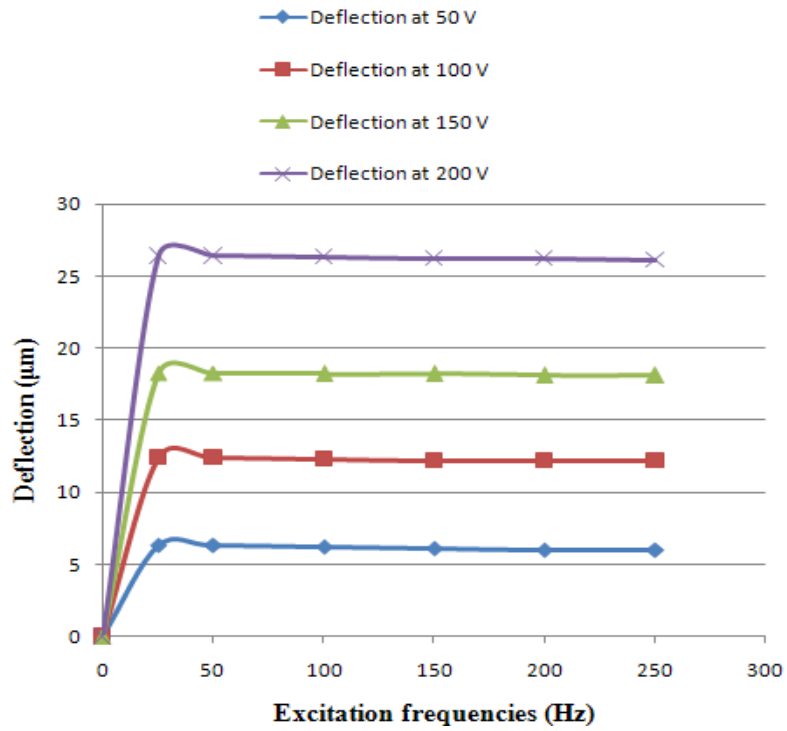


Fig. 16. Deflection of membrane at different applied voltages.

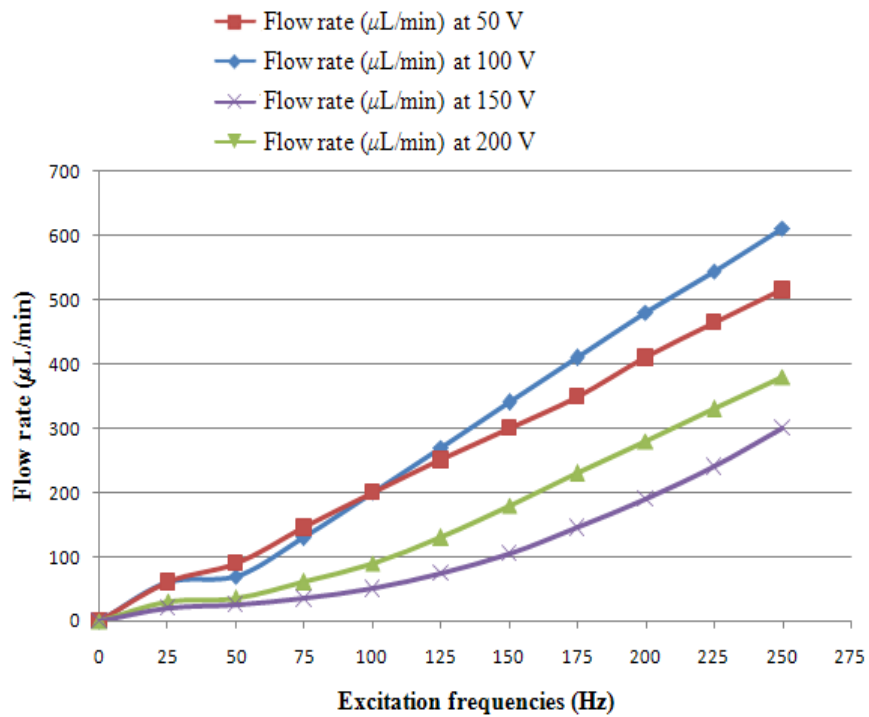
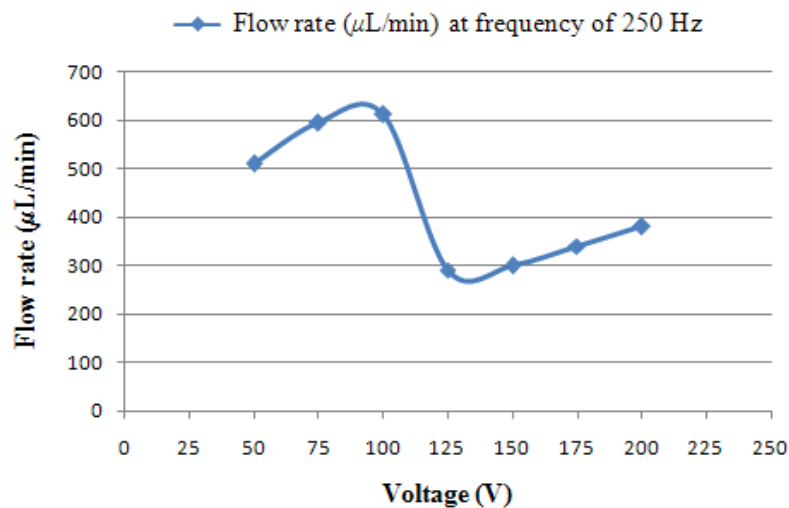


Fig. 17. Effect of frequencies on fluid flow at different applied voltages.



**Fig. 18.** Fluid flow rate at applied 100 V.

Fluid flow rate is effected by various factors like material properties, applied voltage, thickness of membrane and piezoelectric disk. The maximum flow rate of 612  $\mu\text{L}/\text{min}$  is achieved through the 6 $\times$ 6 microneedle array at applied 100 V with membrane deflection of 12.24  $\mu\text{m}$ .

## 6. Conclusions

In this study, fabrication of tapered tip hollow out-of-plane silicon microneedles is presented for TDD system. ICP technology is used to facilitate the fabrication of microneedles. Using ANSYS, structural and multiphysics analysis were performed to envisage the mechanical properties of microneedles and fluid flow rate through the microneedles. Numerical results show that the fabricated microneedles design is suitable for TDD. Microneedles can bear the bending and axial load during skin puncturing. Coupled multifield analysis of piezoelectrically actuated device shows that piezoelectric-membrane assembly deflection increases with increase in excitation voltage but slowly decreases with increase in excitation frequency at the same voltage. Maximum fluid flow rate 612  $\mu\text{L}/\text{min}$  is obtained at applied voltage of 100 V through 6 $\times$ 6 microneedle array with actuator deflection 12.24  $\mu\text{m}$ . These fabricated microneedles can be integrated with our previously fabricated piezoelectric valveless micropump. The results of integrated microfluidic device will be shown in subsequent paper.

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- APASN: Architectures, protocols and algorithms of sensor networks
- MECSN: Energy, management and control of sensor networks
- RASQOFT: Resource allocation, services, QoS and fault tolerance in sensor networks
- PESMOSN: Performance, simulation and modelling of sensor networks
- SEMOSN: Security and monitoring of sensor networks
- SECSN: Sensor circuits and sensor devices
- RIWISN: Radio issues in wireless sensor networks
- SAPSN: Software, applications and programming of sensor networks
- DAIPSN: Data allocation and information in sensor networks
- DISN: Deployments and implementations of sensor networks
- UNWAT: Under water sensors and systems
- ENOPT: Energy optimization in wireless sensor networks

<http://www.iaria.org/conferences2011/SENSORCOMM11.html>



The Fourth International Conference on Advances  
in Circuits, Electronics and Micro-electronics

## CENICS 2011

August 21-27, 2011 - French Riviera, France



### Important deadlines:

Submission deadline	March 23, 2011
Notification	April 30, 2011
Registration	May 15, 2011
Camera ready	May 22, 2011

### Tracks:

- Semiconductors and applications
- Design, models and languages
- Signal processing circuits
- Arithmetic computational circuits
- Microelectronics
- Electronics technologies
- Special circuits
- Consumer electronics
- Application-oriented electronics

<http://www.iaria.org/conferences2011/CENICS11.html>

## Guide for Contributors

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### Aims and Scope

*Sensors & Transducers Journal* (ISSN 1726-5479) provides an advanced forum for the science and technology of physical, chemical sensors and biosensors. It publishes state-of-the-art reviews, regular research and application specific papers, short notes, letters to Editor and sensors related books reviews as well as academic, practical and commercial information of interest to its readership. Because it is an open access, peer review international journal, papers rapidly published in *Sensors & Transducers Journal* will receive a very high publicity. The journal is published monthly as twelve issues per annual by International Frequency Association (IFSA). In addition, some special sponsored and conference issues published annually. *Sensors & Transducers Journal* is indexed and abstracted very quickly by Chemical Abstracts, IndexCopernicus Journals Master List, Open J-Gate, Google Scholar, etc.

### Topics Covered

Contributions are invited on all aspects of research, development and application of the science and technology of sensors, transducers and sensor instrumentations. Topics include, but are not restricted to:

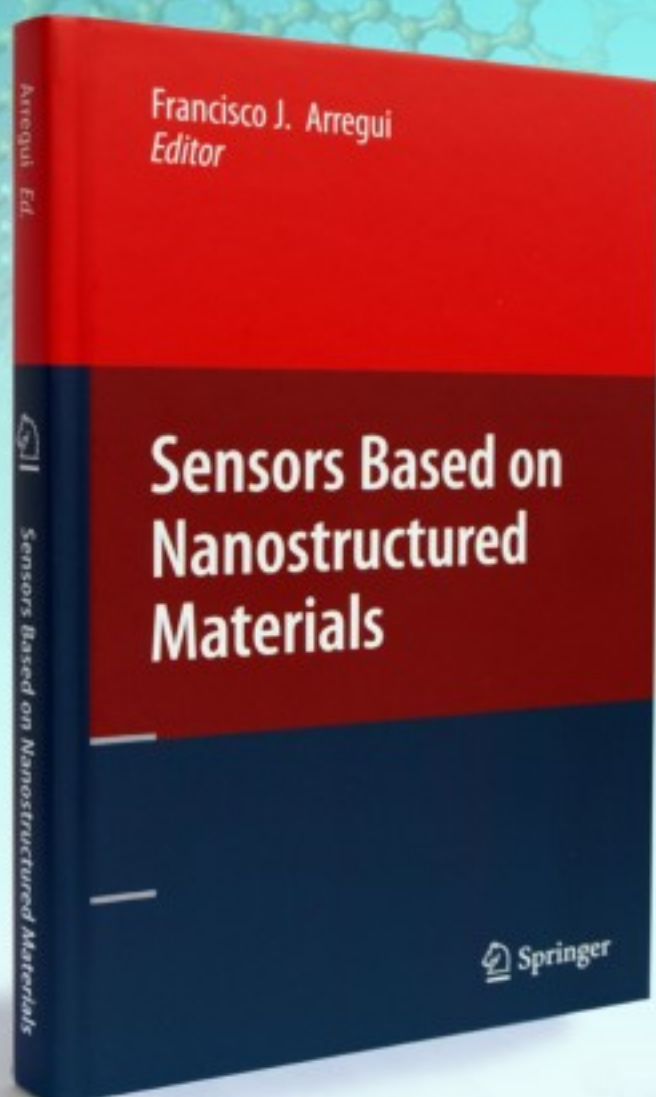
- Physical, chemical and biosensors;
- Digital, frequency, period, duty-cycle, time interval, PWM, pulse number output sensors and transducers;
- Theory, principles, effects, design, standardization and modeling;
- Smart sensors and systems;
- Sensor instrumentation;
- Virtual instruments;
- Sensors interfaces, buses and networks;
- Signal processing;
- Frequency (period, duty-cycle)-to-digital converters, ADC;
- Technologies and materials;
- Nanosensors;
- Microsystems;
- Applications.

### Submission of papers

Articles should be written in English. Authors are invited to submit by e-mail [editor@sensorsportal.com](mailto:editor@sensorsportal.com) 8-14 pages article (including abstract, illustrations (color or grayscale), photos and references) in both: MS Word (doc) and Acrobat (pdf) formats. Detailed preparation instructions, paper example and template of manuscript are available from the journal's webpage: <http://www.sensorsportal.com/HTML/DIGEST/Submission.htm> Authors must follow the instructions strictly when submitting their manuscripts.

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