

Modelling and Simulation of In-Plane Microneedle for Blood Sampling Applications

Reka Bentuk dan Simulasi Jarum Mikro Sesatah untuk Aplikasi Persampelan Darah

Mohd Norzaidi Mat Nawi¹ and Asrulnizam Abd Manaf
Underwater Robotic Research Group, School of Electrical and Electronic
Universiti Sains Malaysia, Engineering Campus
14300 Nibong Tebal, Seberang Perai Selatan, Pulau Pinang, Malaysia.
¹e-mail : norzaidiurg@gmail.com

Abstract

This paper presents the design and simulation of an In-Plane microneedle for blood sampling applications using Microelectromechanical systems (MEMS) CoventorWare software. The characteristics of In-Plane microneedles are far more practical than Out-of-Plane microneedles for blood sampling. Several models of In-Plane microneedle with different dimensions were investigated, and the strength of the In-Plane microneedle has been examined analytically and modeled using finite element modeling tools. Based on human skin thickness, 3 mm long microneedle was used for designing and simulation exercise. Microneedles with 160 μm width and 160 μm height is the optimum size, based on value of mises stress 6.8 GPa. It is the safest model for blood sampling based on the maximum strength value of the silicon material which is equal to 7 GPa. In addition, fluid flow characteristics for microchannel have also been examined analytically and modeled using finite volume method tools. For this purpose, 20 μm width and 20 μm height of the inner microchannel wall was chosen. It gives the velocity of blood flow of 0.003 m s^{-1} inside the microchannel under a 1 kPa inlet pressure.

Keywords microneedle, MEMS, blood sampling

Abstrak

Artikel ini memperihalkan reka bentuk dan simulasi jarum mikro sesatah untuk aplikasi persampelan darah menggunakan perisian *Microelectromechanical systems (MEMS) CoventorWare*. Ciri-ciri yang terdapat pada jarum mikro sesatah lebih praktikal berbanding dengan jarum mikro luar satah bagi digunakan untuk persampelan darah. Beberapa model menggunakan jarum mikro sesatah berbagai dimensi telah diuji dan kekuatannya di analisis menggunakan alat permodelan unsur terhingga. Berdasarkan nilai ketebalan kulit manusia, jarum mikro sepanjang 3 mm telah digunakan dalam reka bentuk dan simulasi. Didapati untuk nilai tegasan mises (*mises stress*) sebesar 6.8 GPa, saiz optimum jarum mikro ialah 160 μm lebar dan 160 μm tinggi. Ini adalah model paling selamat untuk persampelan darah berdasarkan kekuatan maksimum bahan silikon sebesar 7 GPa. Ciri aliran bendalir juga dianalisis dan dimodelkan menggunakan kaedah isipadu terhingga. Untuk tujuan tersebut, dinding dalaman saluran mikro 20 μm lebar dan 20 μm tinggi telah digunakan. Ia memberikan kadar aliran darah 0.003 m s^{-1} di bawah tekanan masuk 1 kPa.

Kata kunci jarum mikro, MEMS, pensampelan darah

Introduction

The number of diabetics is increasing in advanced countries due to the change of life styles and increasing number of aged people. Diabetics have to collect their blood for the glucose level measurement at least twice a day, which is indispensable for health monitoring. During the process of blood collection, their skin is punctured by a solid metal lancet needle having a straight shape to cause small bleeding, which is painful and fearful. Besides this case, a low-invasive needle is desired for different use in medical treatments (Seiji Aoyagi *et al.*, 2008). The general characteristics of microneedles are small volume, small pain during penetration, buried microchannels, and mechanical stability (Seung Joon Paik *et al.*, 2004).

In order to make painless and less-damage on skin for drug injection and blood extraction, research in the transdermal microneedle array is progressively developed. There has been many research studies on the development of microneedles using different material such as silicon, metal and polymer. Hayato Izumi *et al.*, (2008) have come up with bio inspired model such as the mosquito proboscis to evade the pain of the human skin. Today, the smallest conventional needles have 305 μm outer diameter with an inner wall thickness of 76 μm (Jaffrey D. Zahn *et al.*, 2000), and those sizes are not small enough to ease the invasive effects. Therefore, we need to reduce the current needle size. In this research, we focus on the miniaturization of the microneedle for the blood sampling application.

Microneedle Design

In designing the microneedle, the In-Plane microneedle model was considered because it is more suitable and more reliable than Out-of-Plane microneedles for transdermal drug delivery and blood sampling compare with Out-of-Plane microneedles that have limitations in terms of penetrations of depth, microchannel shapes, and connection with other microfluid systems (Seung-Joon Paik *et al.*, 2004). In order to withdraw blood samples from the subcutaneous fat layer, which occurs at a distance of 2000 to 4000 μm below the skin surface, the length of the In-Plane microneedle has been set to 3000 μm . This length is impractical for Out-of-Plane microneedles. Drug delivery and blood samplings place the requirement in terms of minimal needle dimensions and force withstanding capabilities, which are inversely related to each other. The strength of the microneedles has been examined analytically and modeled using finite element modeling tools. The optimal dimensions of the MEMS based needles were calculated through mechanical analysis.

This research will also focus on blood velocity inside microchannel in order to ensure that the blood can flows through the hollow of microneedle. For human being, the blood pressure is about 80 to 120 mmHg. Based on the fluid characteristics, the pressure at the base of microneedle must be smaller than the pressure in the skin to allow blood flow from the inside to the outside. The better way to control the base pressure is by using the Micro microsyringe.

Methodology

For the methodology, we study on the mechanical and fluidic analysis. The mechanical analysis will be discussed on the structural parameter such as buckling force, bending force

and stress acting on the microneedle. The fluid movement inside the microchannel for different dimension will be discussed in the fluidic analysis.

Mechanical Analysis

The various forces acting on the microneedle such as compressive, bending and buckling forces are shown in Figure 1. Assuming the microneedle is solid and width equal

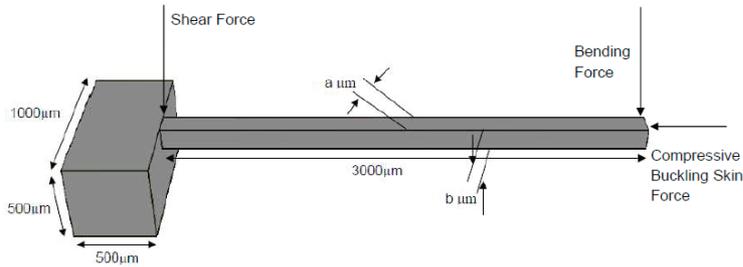


Figure 1 The various force acting on the microneedle

to height, the maximum compressive force that the microneedle can withstand without breakage is given by equation 1 (Rashad Sharaf *et al.*, 2003).

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

where σ_y and A are the yield strength of the microneedle (silicon = 7 Gpa) and the cross sectional area of microneedle respectively. The maximum buckling force that a microneedle can withstand without breaking is given by the following equation

$$F_{MaxBuckling} = \frac{C\pi^2 E}{L^2} \quad (2)$$

where E , I , and L represent the Young's modulus of silicon (169 GPa), moment of inertia (m^4) and length of the microneedle (m), respectively. In the computation, the base of the microneedle is modeled as a fixed joint while the tip is modeled as a pivoted slider, giving the constant value $C = 0.25$; calculated from equation 3

$$C = \frac{1}{k^2} \quad (3)$$

where k is the column effective length factor, whose value depends on the conditions of end support of the column. The value for k is 2 for one end fixed and other is free to move. Then, the moment of inertia for microneedle is given by

$$I = \frac{bh^3}{12} \quad (4)$$

where b and h are the width and height of microneedle respectively. In an ideal situation, a microneedle would be inserted with a completely axial force with negligible bending moment. However, in real applications there is a large chance that the needle would experience a bending moment generated by a transverse tip force, due to misalignment as the needle is inserted. The needle was modeled as a cantilevered beam to approximate the transverse force and bending moment a needle could support. The maximum bending stress is

$$\sigma = \frac{Mc}{I} \quad (5)$$

where c , M , and I are the distance from the neutral axis to the outermost edge, the bending moment and the moment of inertia of microneedle, respectively. By replacing the bending moment with the tip force F multiplied by the length, L , we can solve for the maximum transverse tip force (Bending force) that the needle can support, given as

$$F_{MaxBuckling} = \frac{\sigma_y I}{cL} \quad (6)$$

where σ_y is the yield strength of silicon. When the microneedle is fully inserted into the skin, the pressures of skin give the bending moment and resultant force. To calculate bending force, we need to consider the reaction force at the z-axis only. Assuming the resultant force, F is concentrated at the center of microneedle ($L/2$). The bending moment, M given by

$$M = \frac{F_z L}{2} \quad (7)$$

And

$$F_{Bending} = \frac{M}{L} \quad (8)$$

Solving the equation above, we get

$$F_{Bending} = \frac{F_z}{2} \quad (9)$$

Reaction force at z-axis is given

$$F_z = F \cos \theta \quad (10)$$

where F is resultant force, and A is the surface area, for this case the area is at the top ($3000 \mu\text{m} \times b \mu\text{m}$). Given that,

$$F = P_{piercing} A \quad (11)$$

where $P_{piercing}$ is the skin pressure ($P_{piercing} = 3.18$ MPa) and given the angle

$$\theta = \frac{FL^2}{6EI} \quad (12)$$

where L is the length of microneedle (μm) ; $E=169$ GPa represent the Young's modulus of silicon, and I is the moment of inertia (m^4). When the microneedle is fully inserted into the skin, it may also experience a transverse force (shear force) at the base of microneedle. The maximum shear force the microneedle can withstand is given by

$$F_{MaxShear} = \frac{\sigma_y A}{2} \quad (13)$$

Examination of the previous equation for silicon shows that the forces with the most impact on the determination of the dimensions of the structure are the buckling and bending forces. The resistance offered by skin is given by the following equation

$$F_{Skin} = P_{piercing} A \quad (14)$$

where A is the cross sectional area of the microneedle.

The simulation for the mechanical analysis was conducted using mechanical solver MemMECH from CoventorWare. In this simulation, we study on the resistance offered by skin and bending force for different height of microneedle. The microneedle with $160 \mu\text{m}$ width and $160 \mu\text{m}$ height was design and simulated for the first model. The mesh was generated as shown in Figure 2 before the pressure of human skin is applied to the microneedle. For the bending force, we only considered the reaction force on z-axis where the equation of the bending force was given

$$F_{Bending(Simulation)} = \frac{F_z}{2} \quad (15)$$

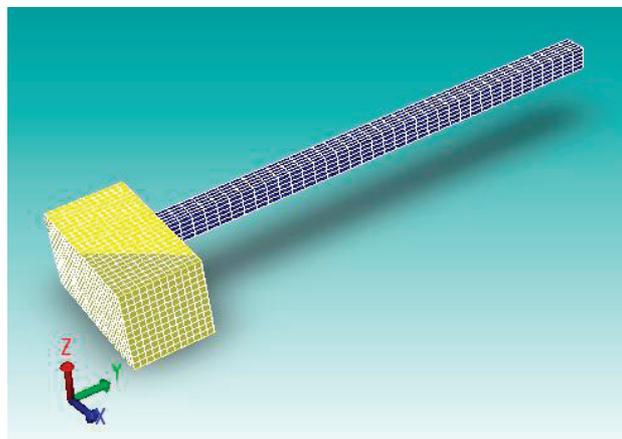


Figure 2 3D meshing of the microneedle model in CoventorWare

Fluidic Analysis

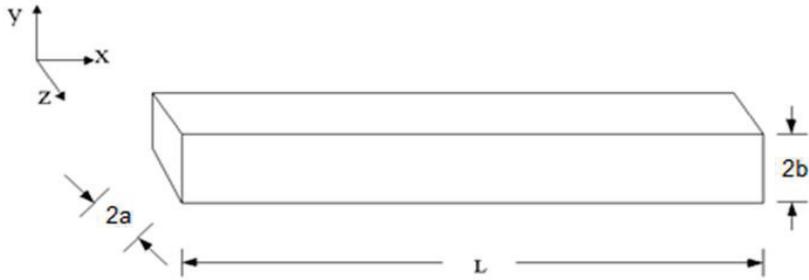


Figure 3 Model of rectangular duct for microchannel

It is important to model fluid flow characteristics in microneedle especially in rectangular duct condition (see Figure 3). The average flow rate, Q in a rectangular duct with y and z cross section and the average velocity of blood flow, U are given by

$$Q = \frac{4ba^3}{3\mu} \left(-\frac{dP}{dx} \right) \left[1 - \frac{192a}{\pi^5 b} \sum_{i=1,3,5,\dots}^{\infty} \frac{\tanh\left(\frac{i\pi b}{2a}\right)}{i^5} \right] \quad (16)$$

$$U = \frac{Q}{4ab} \quad (17)$$

where $4ab$ is the cross sectional area. Meanwhile, $2a$ and $2b$ is the width and height of the microchannel wall respectively. In micro size, the fraction factor is the major losses in fluid flow, the fraction factor of the microneedle is

$$f = \frac{64}{Re} \quad (18)$$

where Re is Reynolds Numbers, given by

$$Re = \frac{\rho U D_h}{\mu} \quad (19)$$

where ρ , U , μ , and D_h are the density of fluid, the average velocity, hydraulic diameter and the dynamic viscosity, respectively. The pressure drop for fraction factor is given

$$\Delta P = f \frac{L}{D_h} \frac{1}{2} \rho U^2 \quad (20)$$

where L is the length of microneedle, by substituting equation 17 into equation 16 and after simplification, we obtained equation 21

$$U = \frac{4a^2}{12\mu} \left(\frac{\Delta P}{L} \right) (0.42175) \quad (21)$$

From the value of velocity, the flow rate can be determined using the equation below

$$Q = vA \quad (22)$$

where v and A are velocity and cross sectional area, respectively. The simulation was done by using MemCFD with different pressure is applied to outlet pressure to study the blood velocity. The microchannel with 20 μm width and 20 μm height was design and mesh as shown in Figure 4. In this simulation, the inlet pressure is fixed to 1 kPa where the pressure difference is obtained from the difference between outlet pressure and inlet pressure. Given the density and viscosity of blood are 1060 kg m^{-3} and 0.004 kg s m^{-1} respectively.

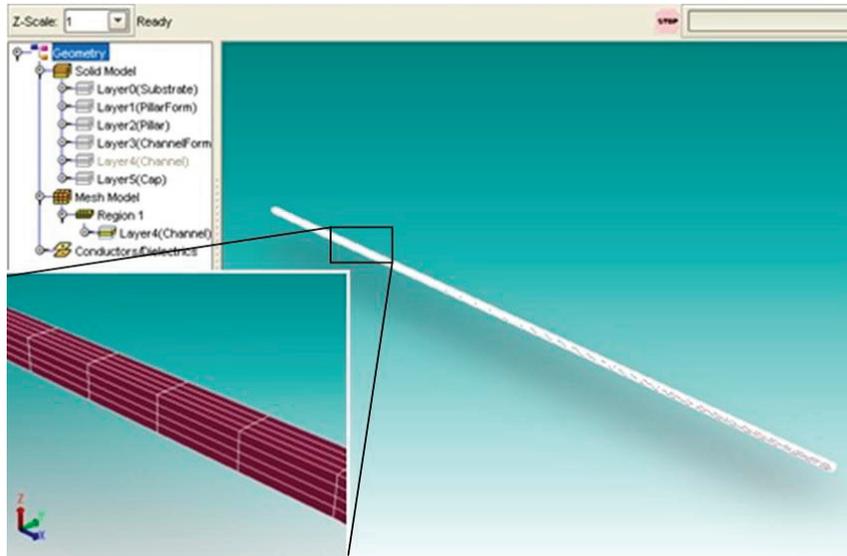


Figure 4 Meshing model of microchannel in MemCFD

Result and Discussion

The microchannel with 160 μm height, 160 μm width and 3000 μm length successfully simulated for the mechanical analysis using memMECH in CoventorWare software. Figure 5 shows the distribution stress on the microneedle which is the red in color indicating the maximum stress. The applied pressure is equal to the skin pressure for the human skin. Table 1 shows the simulation result for the maximum mises stress value for different height of microneedle. Rationally, the mises stress is used to select the optimal dimension to make sure the microneedle does not break during insertion. From the table, we can see that the safest microneedle is of height 160 μm , because the value of stress does not exceeds the yield strength of silicon material which is equal to 7 GPa.

Table 1 Maximum Stress value for microneedles

Height (μm)	σ_{stress} (GPa)
120	10
140	8.9
160	6.8
180	5.7
200	4.6

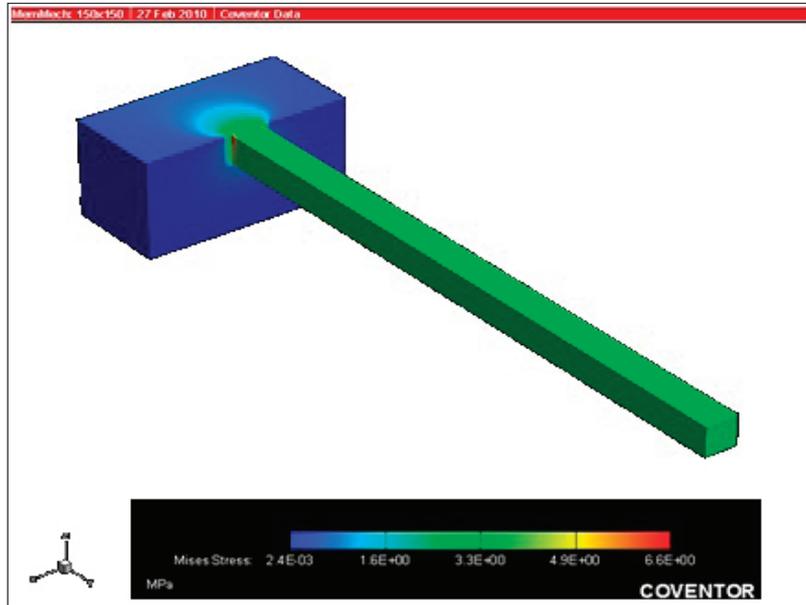


Figure 5 The distribution stress on the microneedle

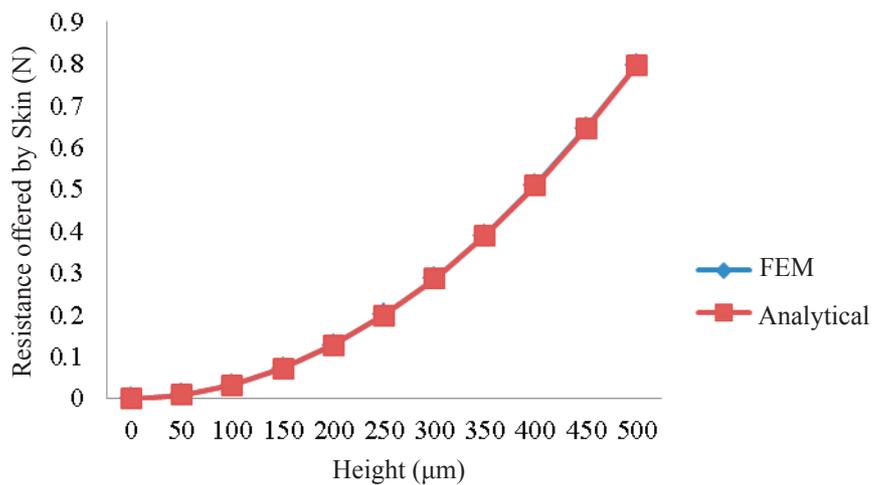


Figure 6 Resistance offered by skin with difference height

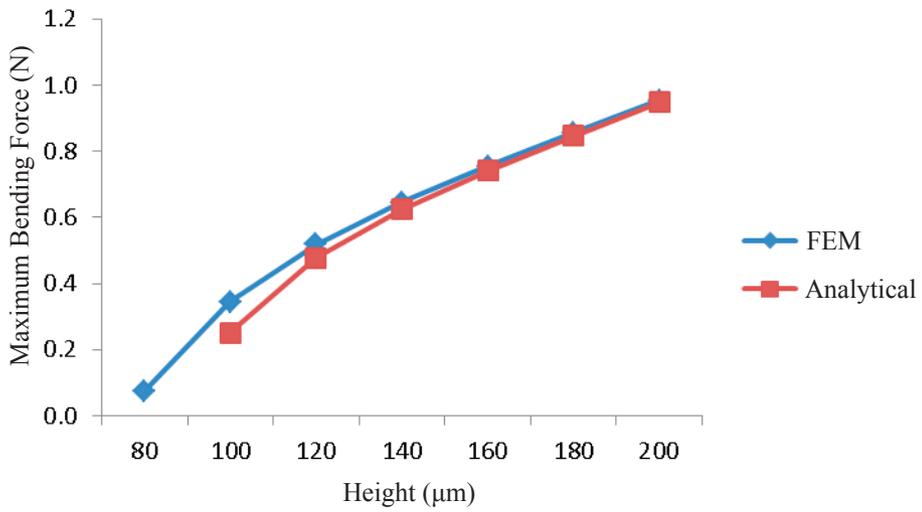


Figure 7 Bending force with difference height

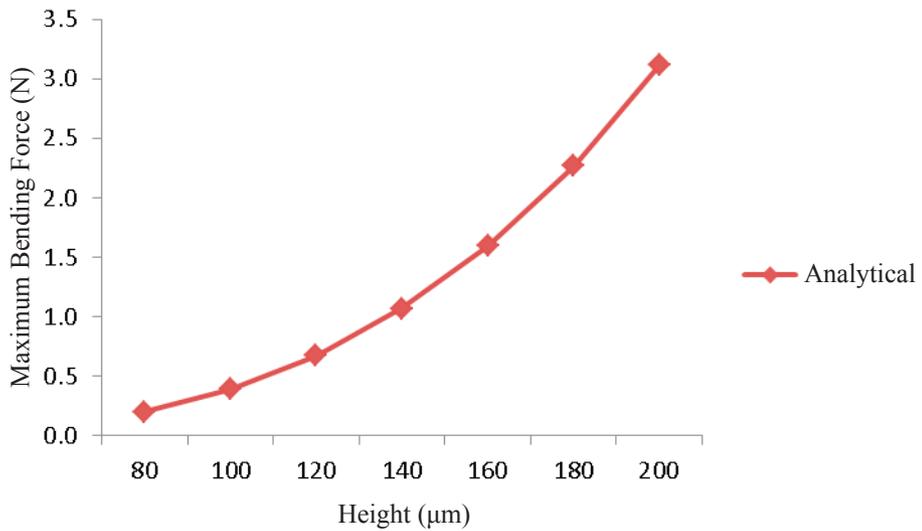


Figure 8 Maximum bending force with difference height

The variation of the forces offered by skin relative with different height of the microneedle (assuming that the microneedle is solid and width is equal to the height) is shown in Figure 6. The FEM result is obtained from the simulation and analytical result where the analytical result was calculated using equation 14. As expected, the resistance of the skin increases as the height of the microneedle increases.

Figure 7 shows the variation of bending force with different height when microneedle is fully inserted into the human skin. At height $80\ \mu\text{m}$, the resultant angle in a z-direction is greater than 90° and analytically cannot be calculated using standard equation for bending force ($F_z = F \cos \theta$). The maximum bending force was calculated using equation 6 and the plotted graph shown in Figure 8. The comparative study between Figure 7 and Figure 8 shows that the bending forces for fully inserted does not exceed the maximum bending force value. Therefore, the microneedle can withstand without fracturing when microneedle fully inserted into the human skin.

For the fluidic analysis, it is observed that the velocity of fluid depends on the pressure difference between outlet and inlet of microchannel. In this simulation using memCFD software, the pressure has been set at 80 to 120 mmHg which is the normal range of human body blood pressure. As mention before, in order to allow the blood to flow inside microchannel, the pressure at the base of the microneedle must be smaller than the blood pressure. The Figure 9 shows the blood velocity for 1kPa pressure difference where the velocity equal to $0.0023\ \text{m s}^{-1}$. The blood velocity inside the microchannel increase as the pressure difference is increased (as shown in Figure 10) where the analytical for the blood velocity was calculated using equation 21. The flow rate of blood was obtained using equation 22 and plotted in Figure 11. However, the designing of the microcneedle for different material is needed to improve the puncture force and skin resistance during insertion into the human skin. Also, by applying vibration during insertion will makes the insertion much easier.

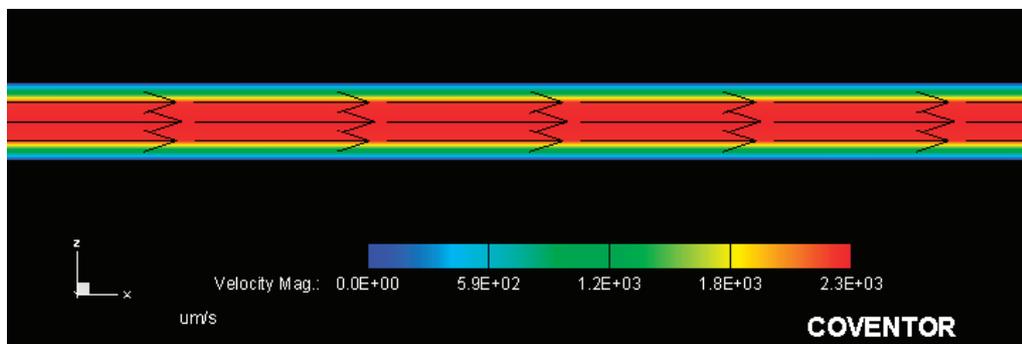


Figure 9 The blood velocity for pressure difference 1 kPa

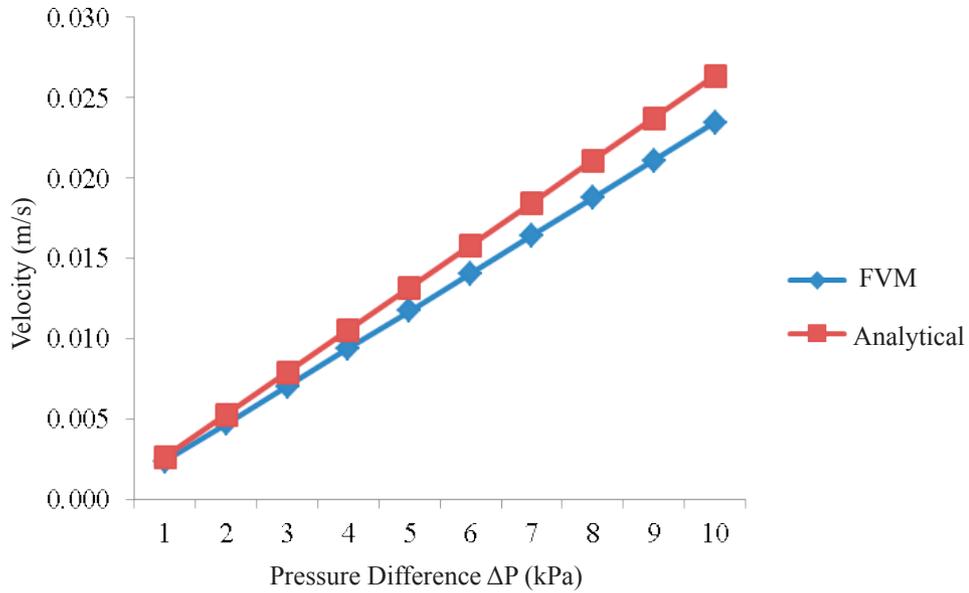


Figure 10 Velocity of blood with pressure difference

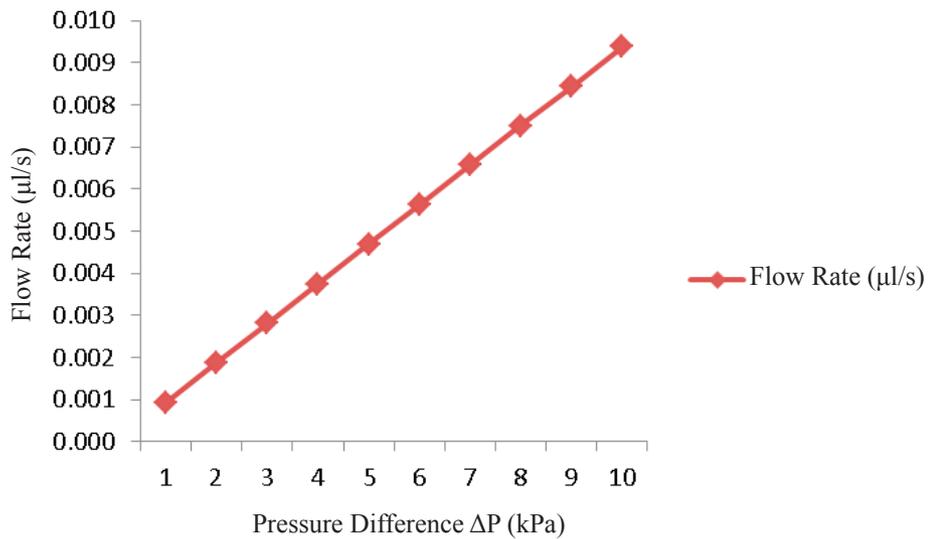


Figure 11 Flow rate of blood inside microchannel for difference pressure difference

Conclusion

A microneedle has been successfully designed and simulated by using CoventorWare software. The In-Plane microneedle was designed based on the influence of the skin resistance on the dimension (length and cross sectional area) of the microneedle. Analytical and simulation analysis of human skin resistance proved that the human skin resistance increases when the height of microneedle increased. When the microneedle is inserted into the human skin, the value of the bending force must not exceeds the maximum bending force of microneedle. So, the safest dimension for blood sampling application for a 3 mm

microneedle length, is of width 160 μm and height 160 μm . The blood velocity inside the microneedle was also simulated and as expected the increase of the pressure difference between inlet and outlet will increase the blood velocity. Also, the flow rate of blood increases linearly with the pressure difference.

References

- Seiji Aoyagi, Hayato Izumi., Mitsuo Fukuda 2008, Biodegradable polymer needle with various tip angles and consideration on insertion mechanism of mosquito's proboscis, *Sensors and Actuators A*, 143 : 20–28.
- Hayato Izumi, Tsubasa Yajima, Seiji Aoyagi, Nario Tagawa, Yasuhiko Arai, Masayuki Hirata, Shiro Yorifuji 2008, 'Combined Harpoonlike Jagged Microneedles Imitating Mosquito's Proboscis and Its Insertion Experiment with Vibration', *Institute of Electrical Engineers of Japan*, 3 : 425-431.
- Jaffrey D. Zahn, Neil H. Talbot, Dorian Liepmann, Albert P. Pisano 2000, 'Microfabricated Polysilicon Microneedles for Minimally Invasive Biomedical Devices', *Biomedical Microdevices*, 2(4): 295-303.
- Seung-Joon Paik, Sangwon Byun, Jung-Min Lim, Yonghwa Park, Ahra Lee, Seok Chung, Junkeun Chang, Kukjin Chun, Dongil "Dan" Cho 2004, 'In-plane single-crystal-silicon microneedles for minimally invasive microfluid systems', *Sensors and Actuators A*, 114 : 276–284
- Rashad Sharaf, Priyanka Aggarwal, Karan V.I.S. kaler, Wael Badawy 2003, 'On The Design of an Electronic Mosquito: Design and Analysis of the Micro-needle', *Proc. of the International Conference on MEMS, NANO and Smart Systems (ICMENS'03)*.