BIOLOGIA (PAKISTAN)
June, 2018, 64 (1), 75-83

PKISSN 0006 – 3096 (Print)
ISSN 2313 – 206X (On-Line)

Simulation of a Nanoneedle for Drug Delivery by Using MATLAB Fuzzy Logic

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ABSTRACT

The emerging technology of nanoneedle employ the nanoneedle for the penetration in cell membrane to investigate and manipulate biomedical procedures in the living cells. This study presents a simulated methodology on the basis of fuzzy logic for flow rate of drug delivery through a nanoneedle for drug delivery. The outflow rate is measured as 1.32 mL/min through MATLAB simulation. The measurements are verified by the Mamdani's model and the previous research. The simulated results given in this study specifies that the fuzzy logic deliver an effective modeling presentation by showing good agreement with the parametric measurements. Therefore, Fuzzy Logic is an alternate method to obtain outflow rate and other parameters for nanoneedles. This nanoneedle technology is revealed as a dominant and multipurpose technology. It can deal with many new customs to discover biomedical procedures with new bio-physical characteristics of the living cells.

Keywords: MATLAB, Nanoneedle, Cell membrane, Drug delivery

INTRODUCTION

Recently, the boundary of biology and nano-technology fetched and created exciting growth in biomedical field. This nano-technology delivers novel methods for learning biomedical science. Biomedical science presents the vital examples for practical nano-machines. The study of living cells and their diseases in biomedical science is the most inspiring task. The supreme critical element is the nanoneedle.

Almost five decades ago, microneedles were first hypothesized for vaccine delivery. The practical research has been started from 1990's with the evolution of microfabrication technology for microneedles. There are four types of micro-needles: solid microneedles for pretreatment of skin, drug coated microneedles, polymer microneedles which can fully melt in the skin due to temperature and hollow microneedles for the drug delivery. Different researchers worked on this emerging field for transporting low weight vaccines and biotherapeutics at molecular level. For example, influenza vaccine is to be inserted with the help of hollow microneedle and also solid microneedles are used for the face makeup purpose. Furthermore in applications, microneedles have been used for delivery of microscopic organisms (bioactives) into the eye and cells. Researchers worked on hollow microneedle made from silicon for drug delivery (Ashraf et al., 2010 ; Kim et al.. 2012). Some researchers worked on MEMS based drug delivery system for through microneedles (Ashraf et al., 2010). The fabrication of microneedles was done by etching technology (Ashraf et al., 2012). Bio-microneedles were also developed for drug delivery (Ma & Wu 2017).

The shape of nanoneedle is cylindrical, conical straight with the diameter of 1 to 100 nanometer. Its length is usually taken as 1 to 20 micrometer (Prinz et al., 2003, Bai et al., 2006). The developments in nano-technology have presented novel methods to fabricate structures for nanoneedles. A simple technique is the one-

Author's Contribution: M.W.A.,&S.T. Conceived idea**; M.J.A. & F.J.** Designed simulated work**; M.A.& A.A.** Performed simulated work**; M.J.A** Wrote basic draft, executed simulated work and data analysis**; M.A.&F.J.** Did language and grammatical edits
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dimensional nanostructures which are manufactured chemically like nanowires and the nanotubes. The material used for their fabrication are silicon and boron nitride. They are of small size but huge in applications. The fabrication of ZnO nanoneedles was proved to be important (Zhang et al., 2003). Au nanoneedles were also fabricated (Sugimoto et al., 2017). Nanoneedles were also used for sensing the biological systems (Chiappini 2017). Nanoneedles were being used on cancer therapy (Wu et al., 2017). The volumetric flow rate1.0 mL/min was obtained in case of nanoneedles (Wu et al., 2017). 1.0 mL/min flow rate was obtained through nanoneedles (Hu et al., 2017). Nanoneedles (Nds) were also studied electrochemically with the thinnest with hydro-oxidation (Park et al., 2018). Researchers worked on graphene-oxide nanoneedles at normal temperatures (Zito et al., 2018). Some more work was also done on zinc oxide nanoneedles for inside nitric oxide recognition (Gonzalez-Chavarri et al., 2018). The magnesium oxide nanoneedles were used to create multi-enzyme structure (Sun, Fu et al. 2018). MATLAB Fuzzy Logic simulation is a very good technique to obtain outflow rate and other parameters in micro/nanochannel and micro/nanoneedles (Afzal et al., 2017, Pires; Nogueira et al. 2017; Afzal et al., 2018).

The equation used for finding the flow rate is Hagen–Poiseuille which can relate flow rate (Q) of the drug through the nanoneedle of radius (R), the pressure (P) with viscosity (η) and the length (L) (Gooch 2011; Tayyaba et al., 2016).

$$Q = \frac{\pi R^4 \Delta P}{8 \eta L} \quad (1)$$

FUZZY SIMULATION

Consider a Fuzzy Logic Inference system with two limiting inputs (inner pressure and inner diameter) and one limiting output (rate of outflow). There are three membership functions for each limiting variable. The Fuzzy Logic Inference system (FLI) for nanoneedle and the nanoneedle is shown below in Figure 1(a, b)

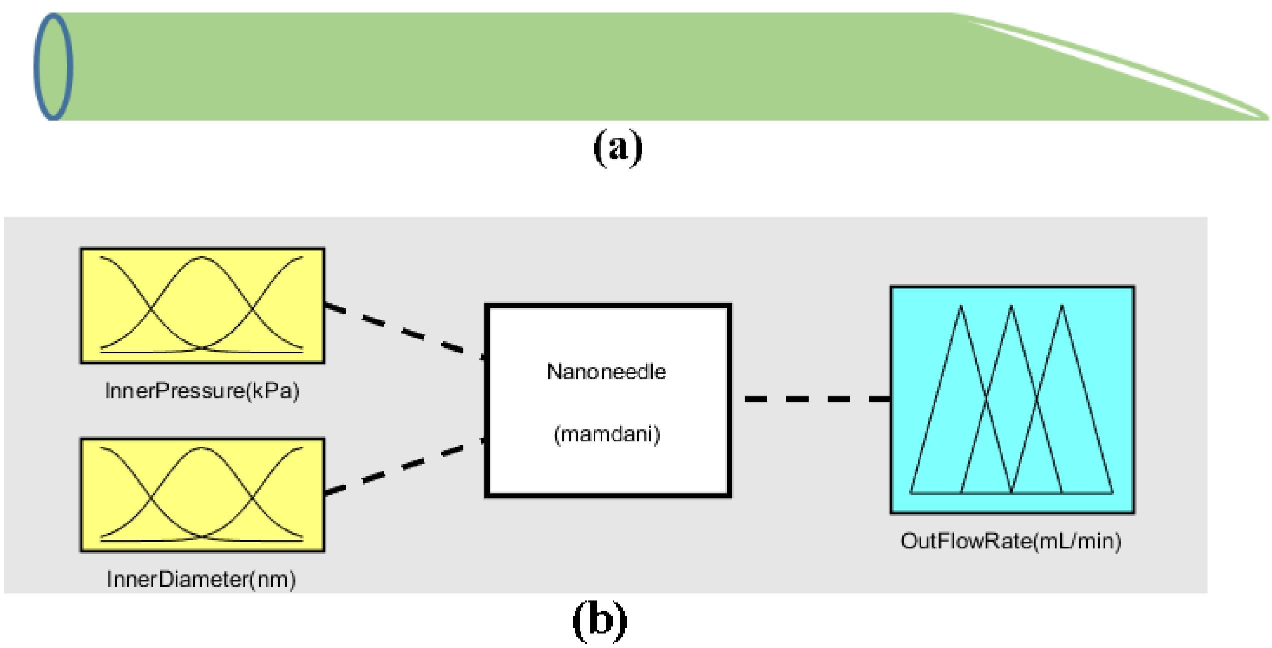

Fig. 1: (a) Nanoneedle (b) FLI system

The actual values of inner pressure and diameter are used in this study (Prinz, Prinz et al. 2003, Martanto, Moore et al. 2006, Wu, Bai et al. 2006). The MFs (membership function) for each parameter is given below in table I.

Table I: MFs

Membership Functions	Inner Pressure (kPa)		Inner diameter(nm)		Outflow rate(mL/min)	
	Ranges	mf_1	Ranges	mf_2	Ranges	mf_3
mf_1	100 ~ 125	Reduced	10 ~ 55	Diminished	0.5 ~ 1	Minimal
mf_2	100 ~ 150	Moderate	10 ~ 100	Medium	0.5 ~ 1.5	Good
mf_3	125 ~ 150	Supreme	55 ~ 100	Large	1 ~ 1.5	Top

The membership functions for each variable are given below in Figure 2 (a. b. c).

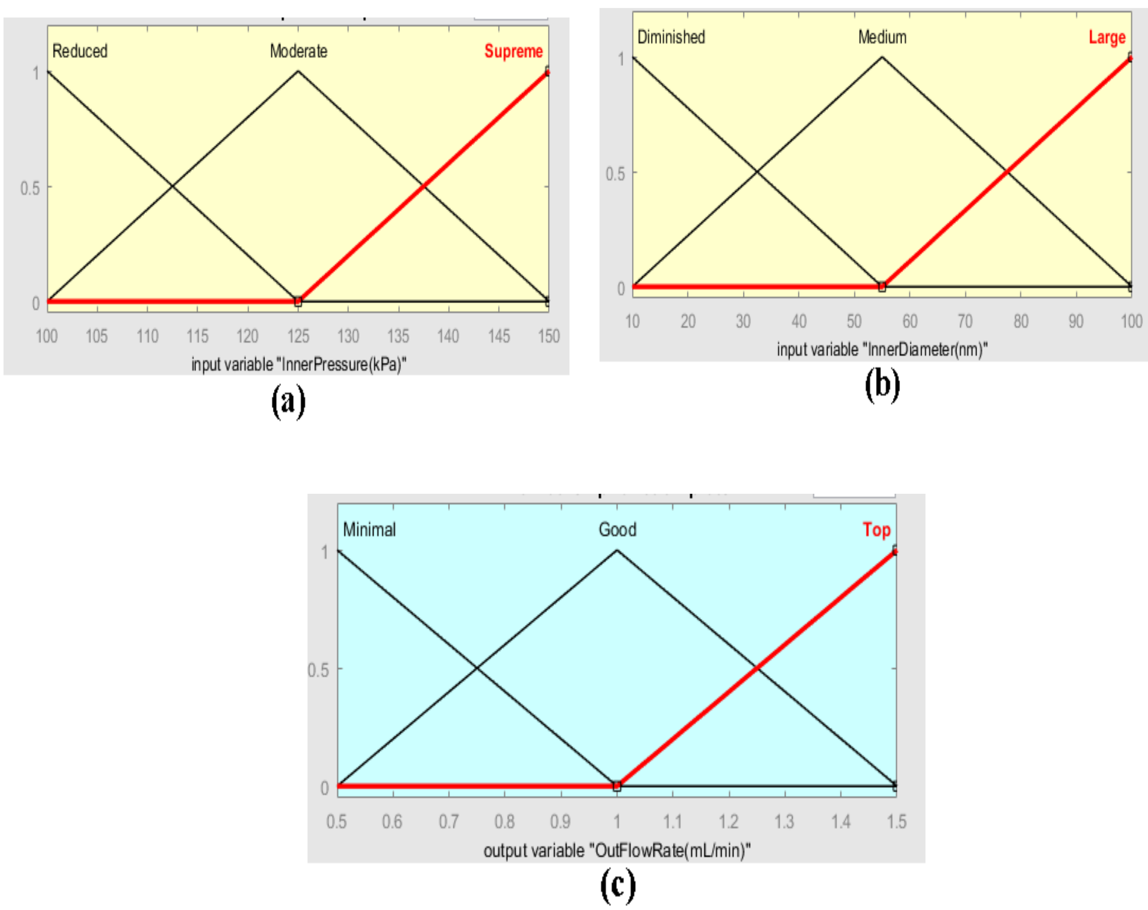

Fig. 2: Membership functions for (a) inner pressure, (b) inner diameter and (c) outflow. The nine (32) rules are made from "IF and Then" statement in table II and Figure 3.

Table II: Rules Editor

S. No.	Inner Pressure (kPa)	Inner diameter (nm)	Outflow rate (mL/min)
1.	Reduced	Diminished	Minimal
2.	Reduced	Medium	Good
3.	Reduced	Large	Top
4.	Moderate	Diminished	Good
5.	Moderate	Medium	Top
6.	Moderate	Large	Top
7.	Supreme	Diminished	Good
8.	Supreme	Medium	Top
9.	Supreme	Large	Top

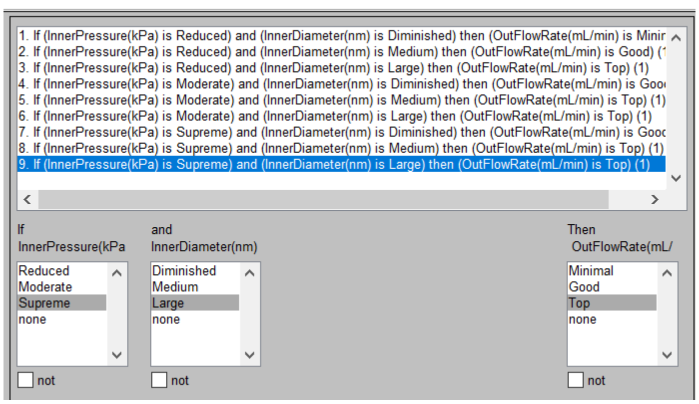

Fig. 3: Rules Editor MATLAB

DISCUSSION

According to MATLAB simulation the inner pressure was kept at 140 kPa with inner diameter 100 nm. Then the outflow rate was obtained as 1.32 mL/min as shown in Figure 4 MATLAB rule viewer. The inner pressure can be varied from 100 to 150 (KPa). The inner diameter can be varied from 10 to 100 (nm). Hence, the out flow rate can be obtained between 0.5 to1.5 (mL/min) for any value of inner pressure and inner diameter.

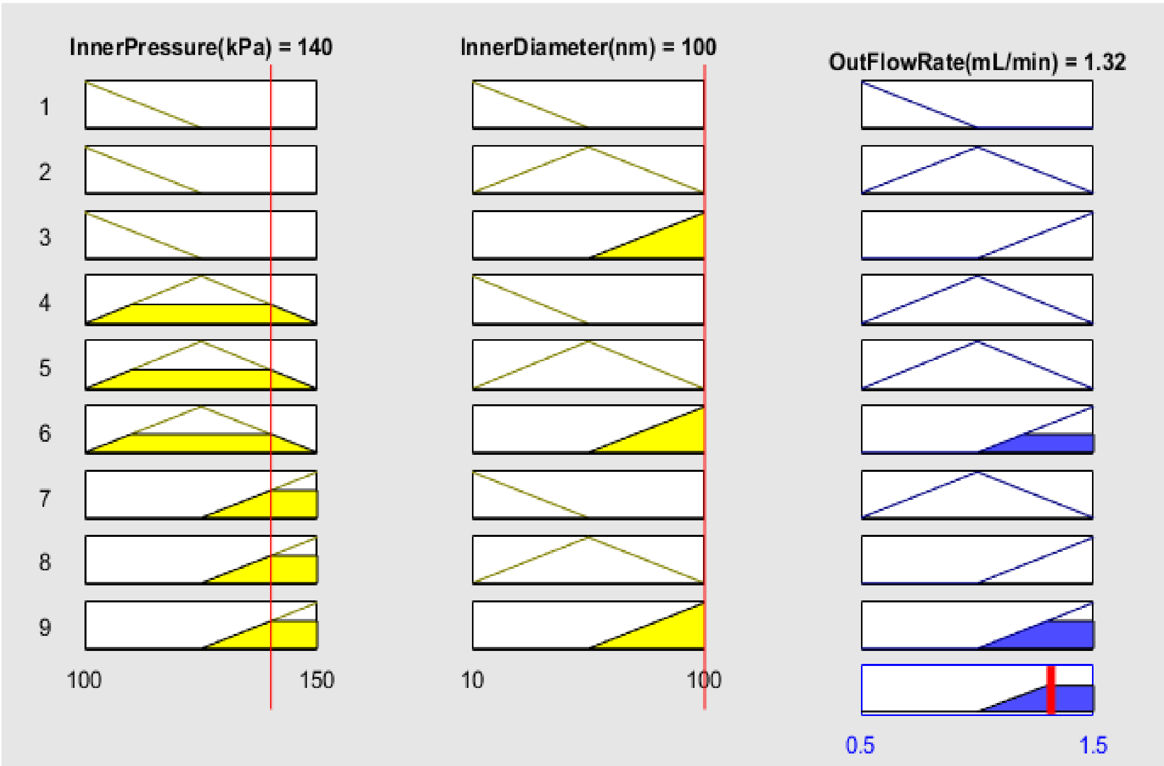

Fig. 4: MATLAB Rule viewer

The rule viewer is exhibited to assess the whole procedure from start to end. The red track indicates that the output was corresponding to the inputs. Therefore, by rearranging this track new output can be calculated. The three and two dimensional graphs between outflow rate (mL/mim) and inner pressure (kPa) and inner diameter (nm) is shown below in Figure 5 (a, b, c).

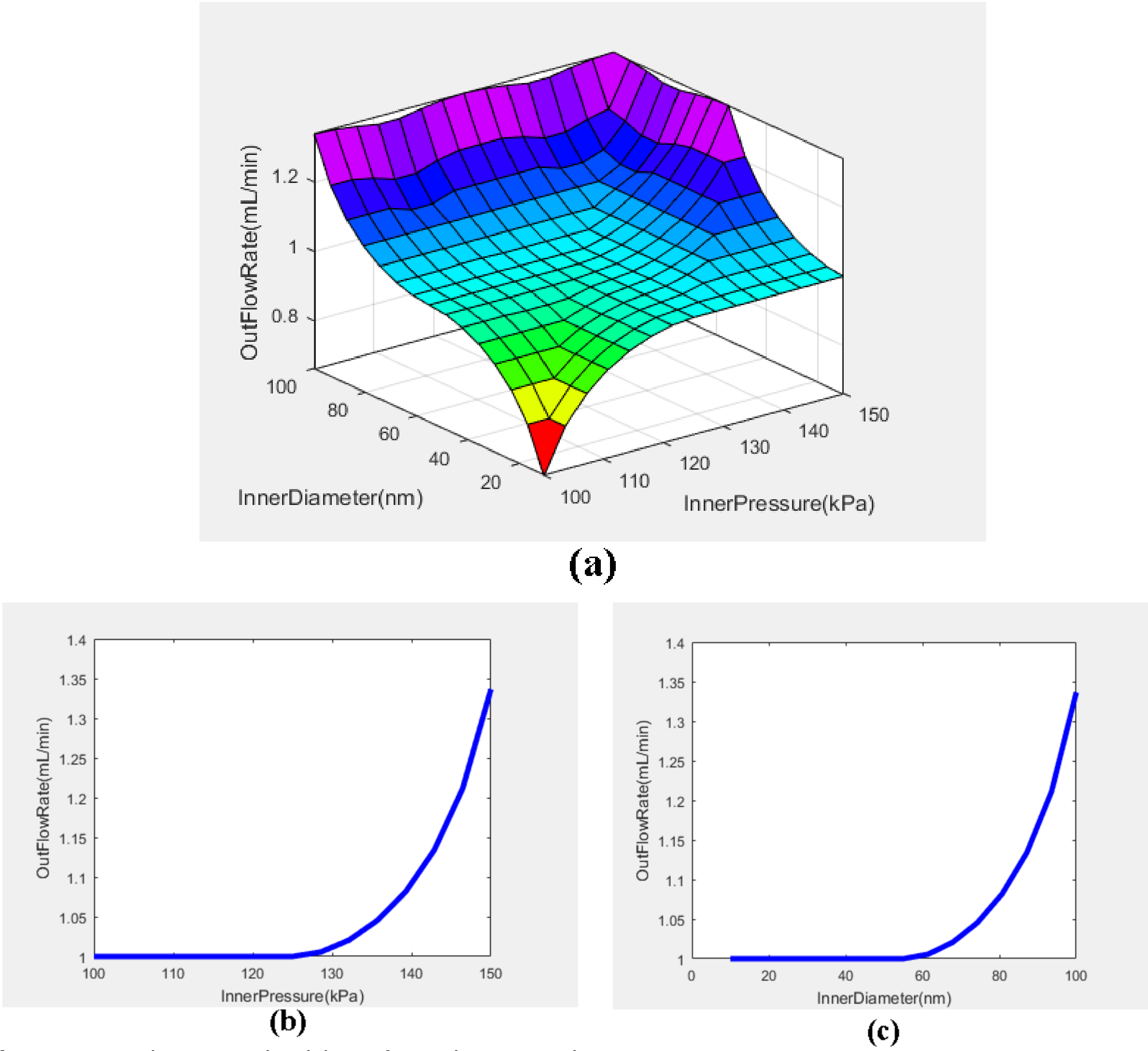

Fig. 5: 3D and 2D Graphs (a) Surface viewer raph for inner pressure and inner diameter with outflow rate, (b) graph between outflow rate and inner pressure and (c) graph between inner diameter and outflow rate.

Verification from Mamdani's Model

The following Figure 6 (a, b) shows portions 1 and 2 for the values of inner pressure and diameter for the calculation of k_1, k_2, k_3 and k_4

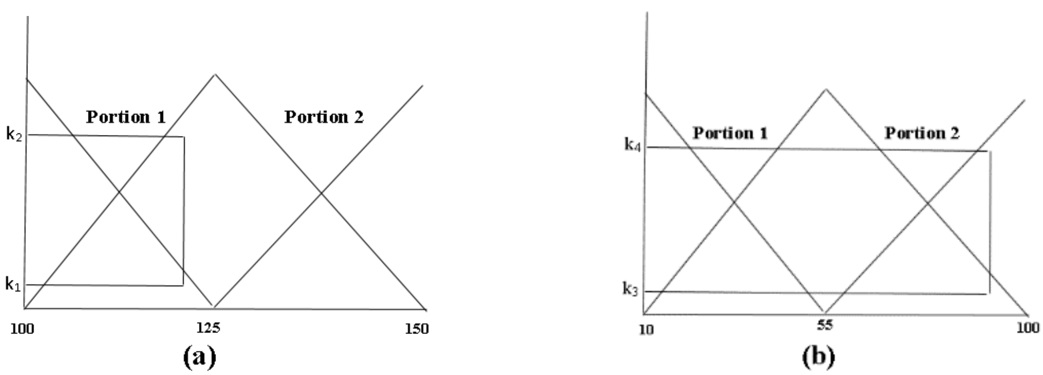

Fig. 6 (a) graph for k_1 and k_2 (b) graph for k_3 and k_4

The calculation of Mamdani's model for inner pressure (k_1, k_2) and inner diameter (k_3, k_4) are given below:

$$k_1 = (150 - 120) / 150 = 0.2\, kPa$$

$$k_2 = 1 - k_1 = 1 - 0.2 = 0.8\, kPa$$

and

$$k_3 = (100 - 80) / 100 = 0.2\, mn$$

$$k_4 = 1 - k_3 = 1 - 0.2 = 0.8\, mn$$

The complete description of orders with membership functions for the particular orders are given in the following table III.

Table III: Complete description of orders with membership functions

Order No	Inner pressure (kPa)	Inner diameter (nm)	Outflow rate (mL/min)	MFs	Minimal value Oi	Outflow rate singleton value Si	Outflow rate Oi x Si
O_1	Reduced	Medium	Good	$k_1 \wedge k_3$ = 0.2 x 0.2	0.2	0.01	0.002
O_2	Reduced	Large	Top	$k_1 \wedge k_4$ = 0.2 x 0.8	0.2	0.015	0.003
O_3	Moderate	Medium	Minimal	$K_2 \wedge k_3$ = 0.8 x 0.2	0.2	0.01	0.002
O_4	Moderate	Large	Top	$K_2 \wedge k_4$ = 0.8 x 0.8	0.8	0.015	0.012

These are the actual crisp parameteric values for FLI system by using Mamdani's model. The exact mathematical expressions are

$$\Sigma(\mathrm{Oi} \times \mathrm{Si}) = 0.019, \Sigma\mathrm{Oi} = 1.4$$

$$\text{Mamdani's Model} = [\, \Sigma(\mathrm{Ri} \times \mathrm{Si}) / \Sigma\mathrm{Ri}\,] * 100 = 1.35$$

The simulated value is 1.32 while the value from Mamdani's model is 1.35. The difference is very small as 0.02 with 2.2% error.

Evaluation of all values with previous results

The evaluation of results are given below in table IV.

Table IV: Results Evaluation

Category	Outflow rate (mL/min)
MATLAB value	1.32
Mamdani's value	1.35
Difference	0.02
%age error	2.2

In this study the settlement of results are very close and also with the previous results (Su, Hu et al. 2017, Wu, Yang et al. 2017).

CONCLUSION

The developmental research is ongoing with MATLAB fuzzy logic simulation. The FLI system can be applied to regulate multipart systems, nonlinear lively plant life and human body. MATLAB Fuzzy Logic is another way to obtain the good results because there are infinite values between Boolean Logic values. In this study the authors tried their best to find another alternate method to find the outflow rate for nanoneedles in drug delivery with actual values of pressure and diameter. The difference in results is just 0.02 with 2.2 % error. Therefore the outflow rate can be calculated successfully for any nanoneedle with the help of simulation through MATLAB Fuzzy Logic. In order to shape the solid base for the nano-technology with manifold benefits of productive drug delivery then the nanoneedles should be dignified to progress further in biomedical field. These nanoneedles empower superior medicinal treatments, immunization and several other biomedical applications.

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