AutoSyringe Injection:

Mass transfer driven by a plunger to force medication through a needle

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Executive Summary

The AutoSyringe is an automatic device that allows patients with limited dexterity to administer medication to themselves as painlessly as possible. The device allows patients to inject themselves subcutaneously, where the needle goes into the fat layer between the outer skin and the muscle. In this study, given a constant pressure applied at the plunger, the flow of medication through the barrel and needle of a syringe was modeled in terms of velocity and pressure. Furthermore, through this model it was found that the flow rate at the tip of the needle decreases with increased viscosity of the medication. It was also determined that the flow rate increases with increased applied pressure at the plunger. These analyses were performed using the software package FIDAP, PreSTO, with imported geometry from GAMBIT.

Introduction and Design Objectives

AutoSyringe is an automatic needle/injection device used to treat patients who suffer from diseases that require chronic injection therapy, such as multiple sclerosis. The syringe is designed to deliver the medication to the patient at a steady rate allowing for a quick, painless injection. The injections are often subcutaneous (Figure 1) where the needle goes into the fat layer between the outer skin and the muscle to deliver a certain amount of medication. These injections are administered on a part of the body that contains enough of fat layer to easily deliver the medicine into the correct area, such as the outer surface of the upper arm, top of the thighs, and the buttocks.

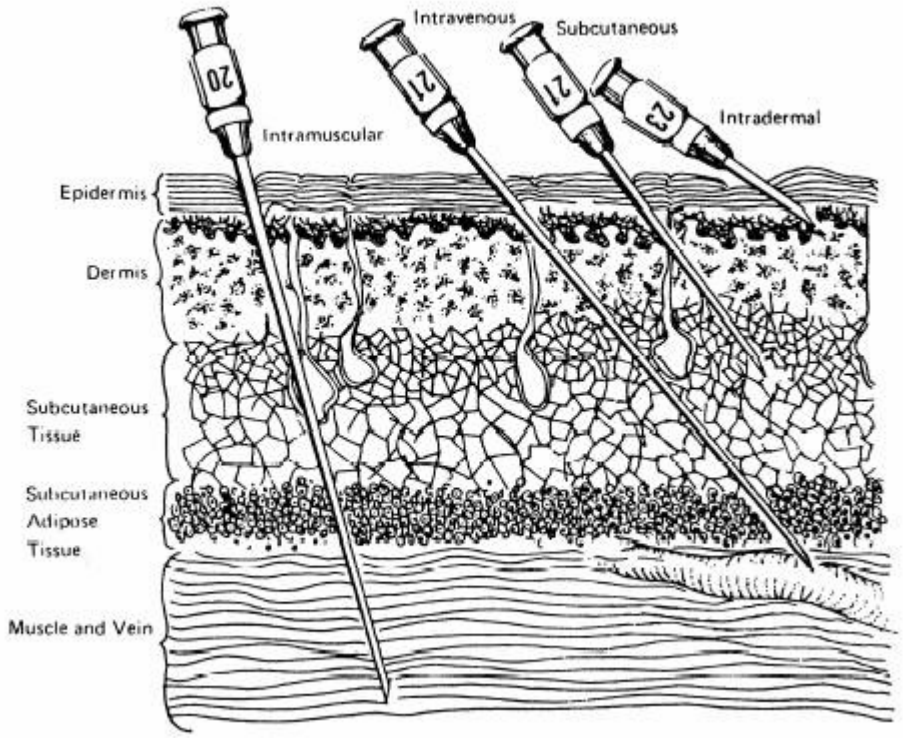


Figure 1. Various types of needle injection

Design Objectives

The goal of this study is to model the flow of medication through the barrel and needle (Figure 2) of a syringe. In order to accurately model this we will be specifically interested in how this fluid behaves during injection into a porous tissue. This interaction between fluid and tissue will allow for us to set appropriate boundary conditions at the ejection tip of the needle. After preliminary research we have found scientific support for treating tissue as a porous media.

> "*As is well known, biological systems are comprised of porous capillary beds and cells that are heterogeneous, multi-phasic, and surface-dominated. Therefore, treating the tissues as a porous media, which consists of solid particles and water is reasonable* (Gui, 74)."

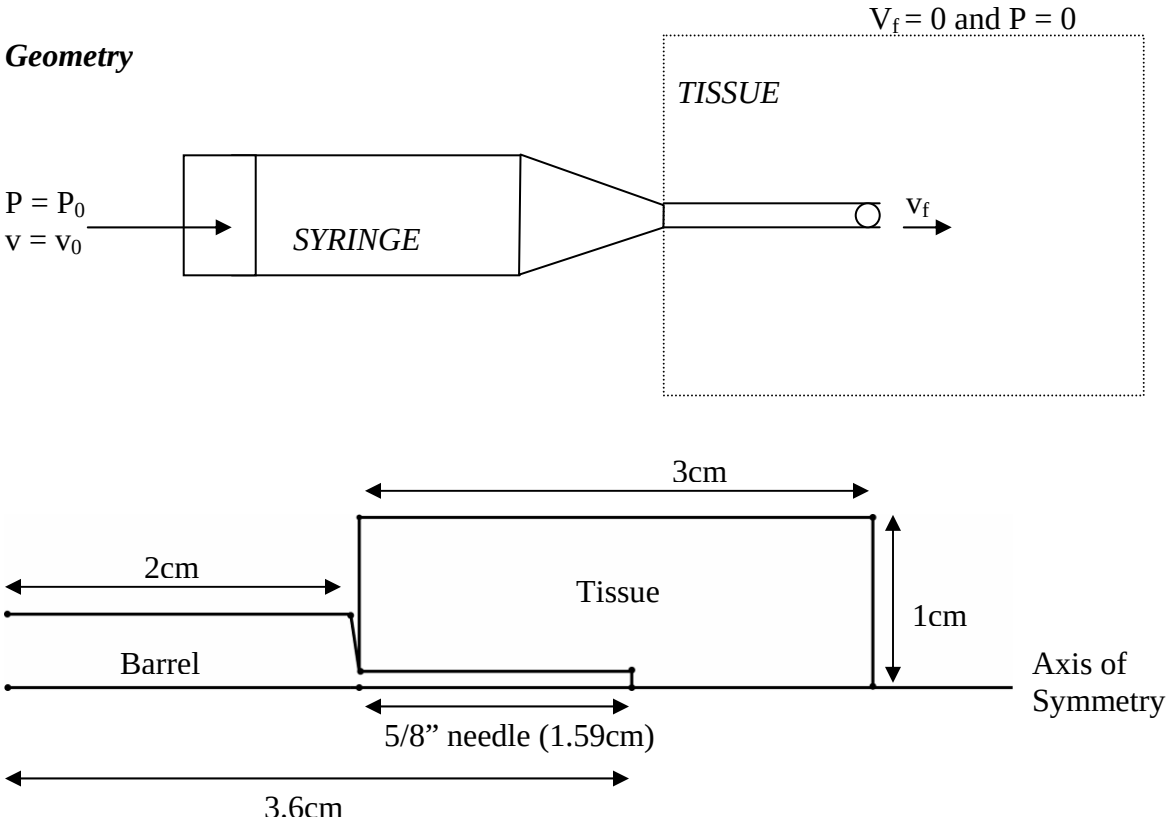
The software will be able to model the tissue as porous media. Further investigation into the abilities of the software and the nature of tissue/fluid interaction will allow for an accurate model to be depicted.

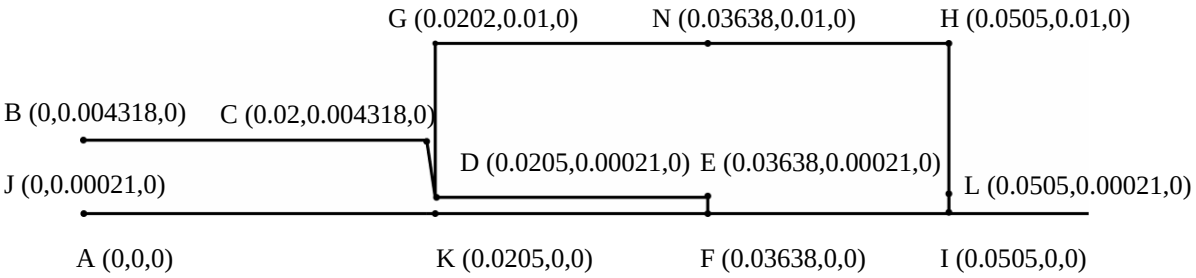
Figure 2. Basic structure and parts of a syringe

Objective Outline:

1. Model diffusivity of medication though a 27 gauge needle.
2. Determine pressures necessary to drive medication based on various tissue conditions, assuming tissue as a porous media.
3. Use axis symmetry to model the barrel and needle

Geometry





- Needle = 27 gauge (0.42mm diameter) and 5/8" long (1.59cm)
- Barrel diameter = 0.340" (0.86cm)

Table 1: List of Edges of within our model and their boundary type

	Names	**Boundary Type**
A→F	**SyringeAxis**	**Plot**
E→F	**NeedleTip**	**Plot**
D→E	**NeedleSide**	**Plot**
A→B	**SyringeTop**	**Plot**
B→C	**SyringeSide**	**Plot**
C→D	**SyringeCone**	**Plot**
D→G	**SkinSurface**	**Plot**
G→H	**SkinSide**	**Plot**
H→I	**SkinDeep**	**Plot**
F→I	**SkinAxis**	**Plot**

Note: The boundary type 'Wall' is specific for a fluid continuum where a no-slip condition is desired, that is the velocity of the fluid is 0 at the wall of the barrel.

We must separate our problem into two regions. The first part deals with fluid flow through the syringe as a result of the movement of the plunger down the barrel. The second part of our problem describes the movement of the drug once it enters the tissue.

Results and Discussion

Overall, we were able to effectively model the injection of drug through a 1 ml syringe into the tissue. The following velocity vector plot (Figure 3) shows the fluid entering the needle. As it entered the needle, the velocity increased dramatically, while in the syringe the velocity of the fluid was minimal. In addition, as the fluid approached the axis of symmetry of the needle, the velocity of the fluid was the greatest, while the fluid velocity approached zero at the wall of the needle due to the no slip condition that was set as one of our boundary conditions on the needle wall. The no slip condition was illustrated more dramatically in Figure 4 of the velocity contour plot as the shaded blue area.

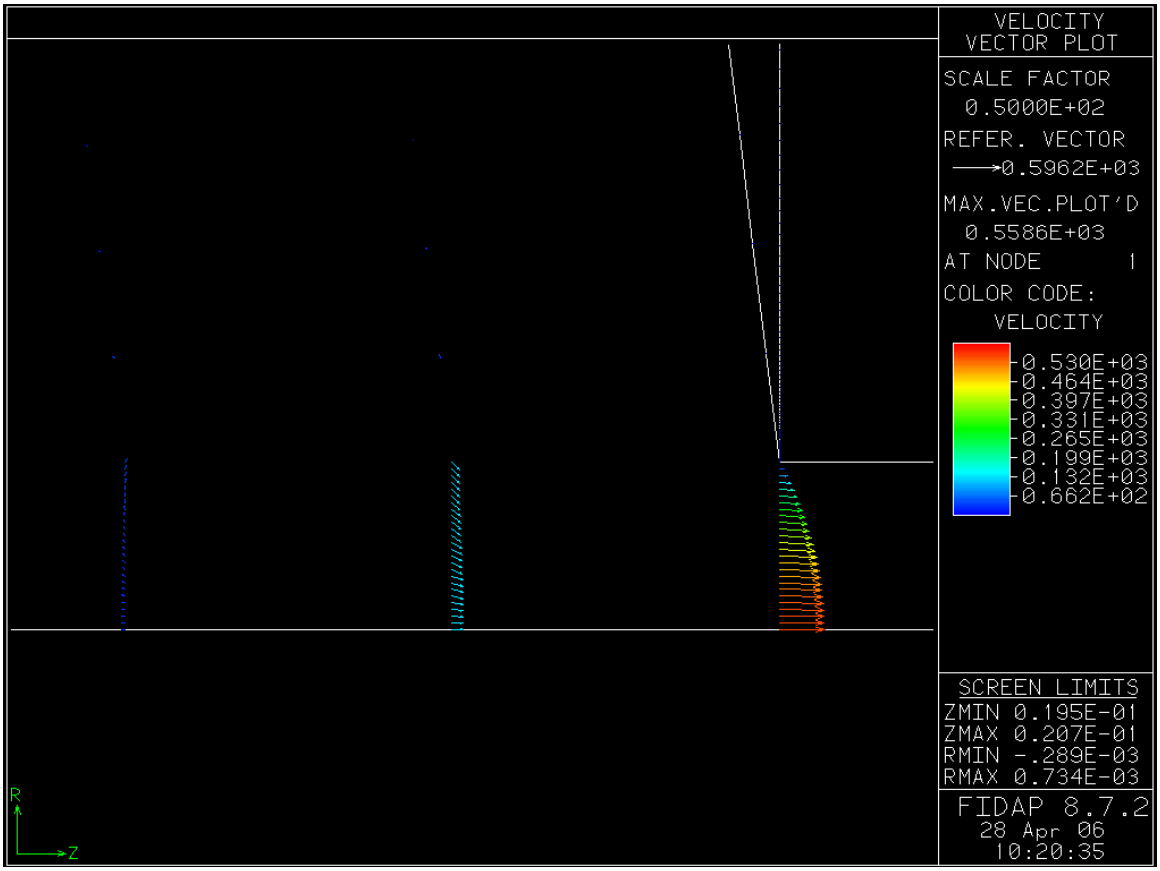


Figure 3: Velocity Vector Plot of fluid entering the needle from the syringe

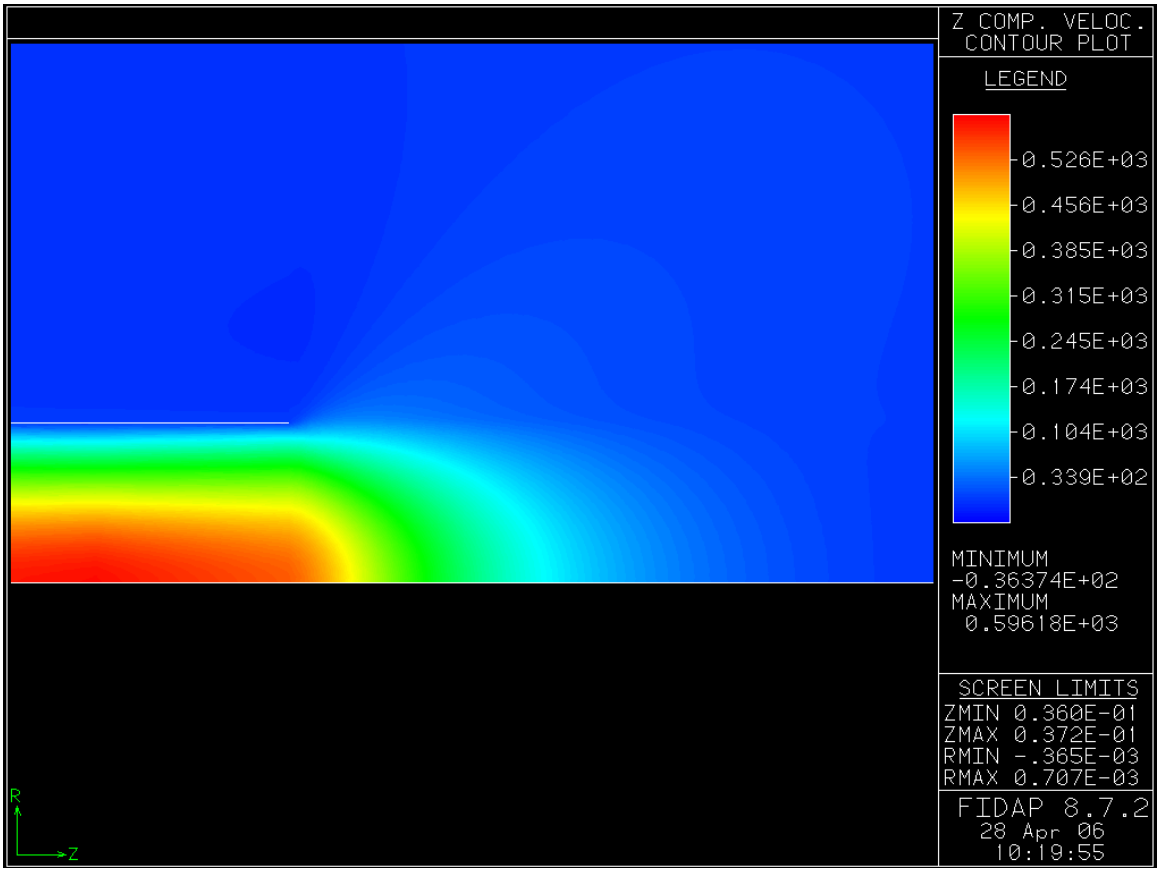


Figure 4: Velocity Contour Plot of fluid entering the tissue from the needle

The following velocity vector plot (Figure 5) showed the fluid exiting the needle and entering the tissue. Again, the largest velocity occurred at the axis of symmetry. However, once it entered the tissue, the velocity slowed down as shown in the plot. Eventually, the velocity of the fluid slowed down dramatically as it diffused further away from the end of the needle. Once the velocity due to pressure from the needle slowed in the tissue, diffusion and blood flow (not accounted for in our model) would carry the drug (in this case water) away from the needle tip.

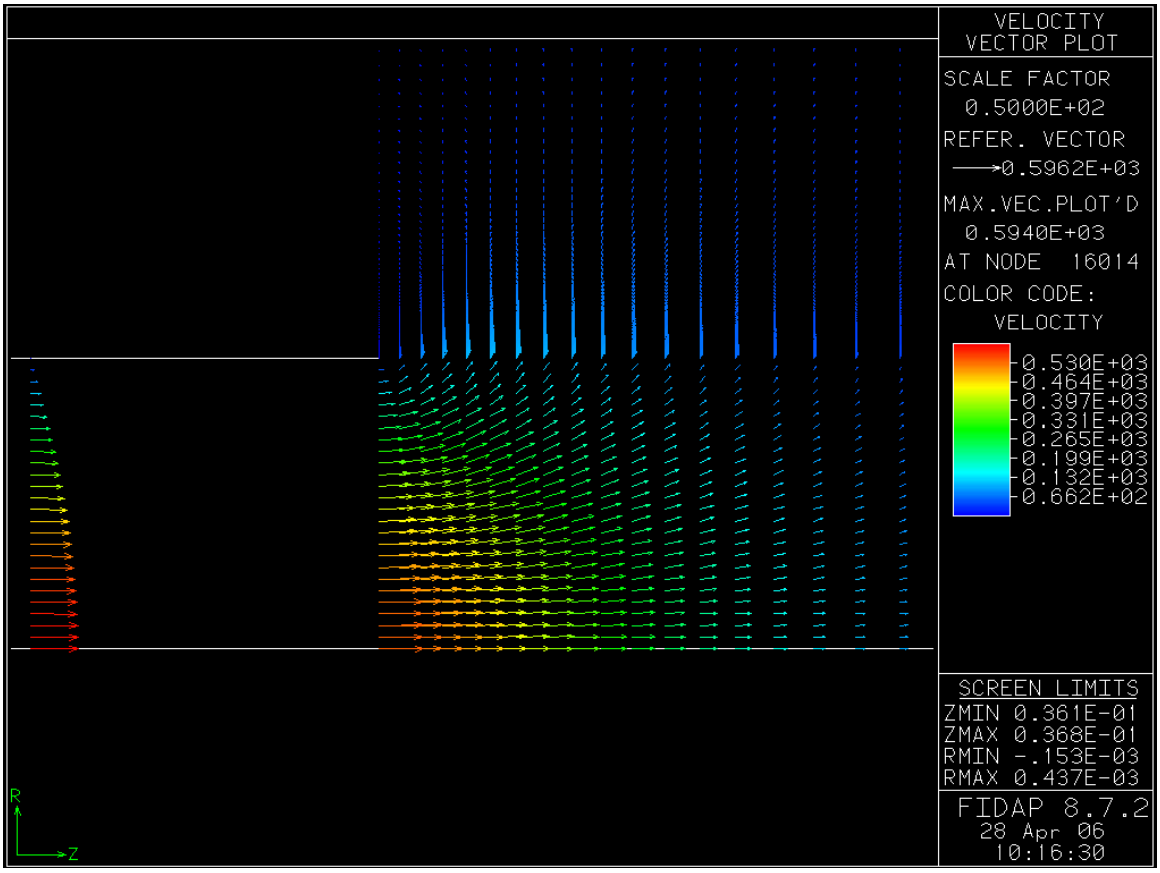


Figure 5: Velocity Vector Plot of fluid entering the tissue from the needle

The contour plot (Figure 6) shown below depicts the pressures throughout the entire model. The greatest pressure occurred in the syringe, which was most likely due to the constant pressure that was applied to the barrel of the syringe within our boundary conditions. Within the needle, the pressure gradually decreased to equilibrate with that of the low pressure found within the tissue. This makes sense because we set the pressure equal to zero (gauge pressure) far away from the injection site in the surrounding tissue.

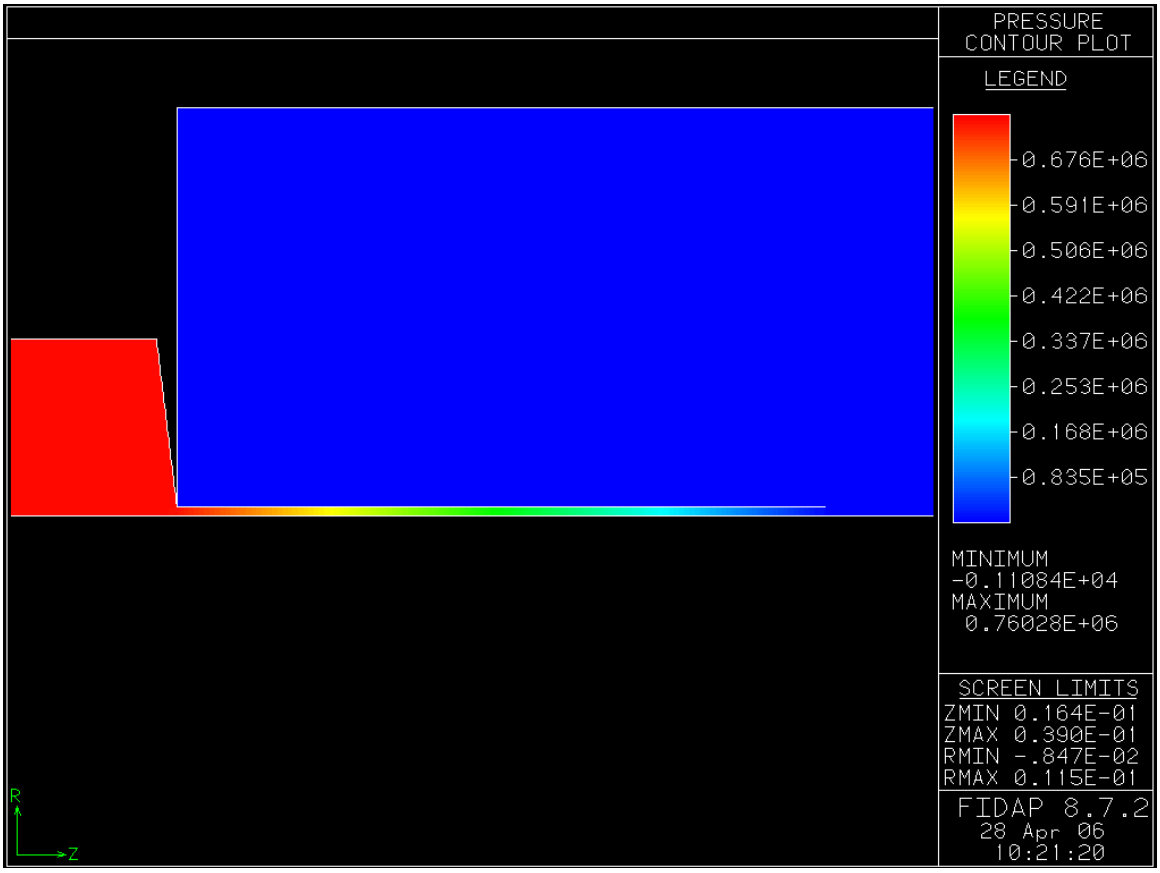


Figure 6: Pressure Contour Plot of the syringe, needle, and tissue

Sensitivity Analysis

Our sensitivity analysis involved the changing of certain variables important to our model. The variables tested included constant pressure at the top of the barrel, viscosity of the drug, permeability, porosity, and density. The variable chosen to reflect changes in our model due to variation in parameters was the average flow rate through the end on the needle tip. All parameters were tested, however three of our 5 parameters did not affect the flow rate through the needle; these will be explained later.

The first major parameter tested was that of the pressure applied to the plunger. This parameter was determined and set by the company as one of the specifications to be met by the auto syringe design. It was determined the plunger would have a constant force of 10 pounds applied to the plunger to force a drug out of the syringe. The pressure was determined by using the cross sectional area and the specified force. We then varied this parameter by 10% in each direction to see its affect on flow rate out of the needle. As expected and seen in Figure 7, an increase in pressure (i.e. force) would increase the flow rate in the needle.

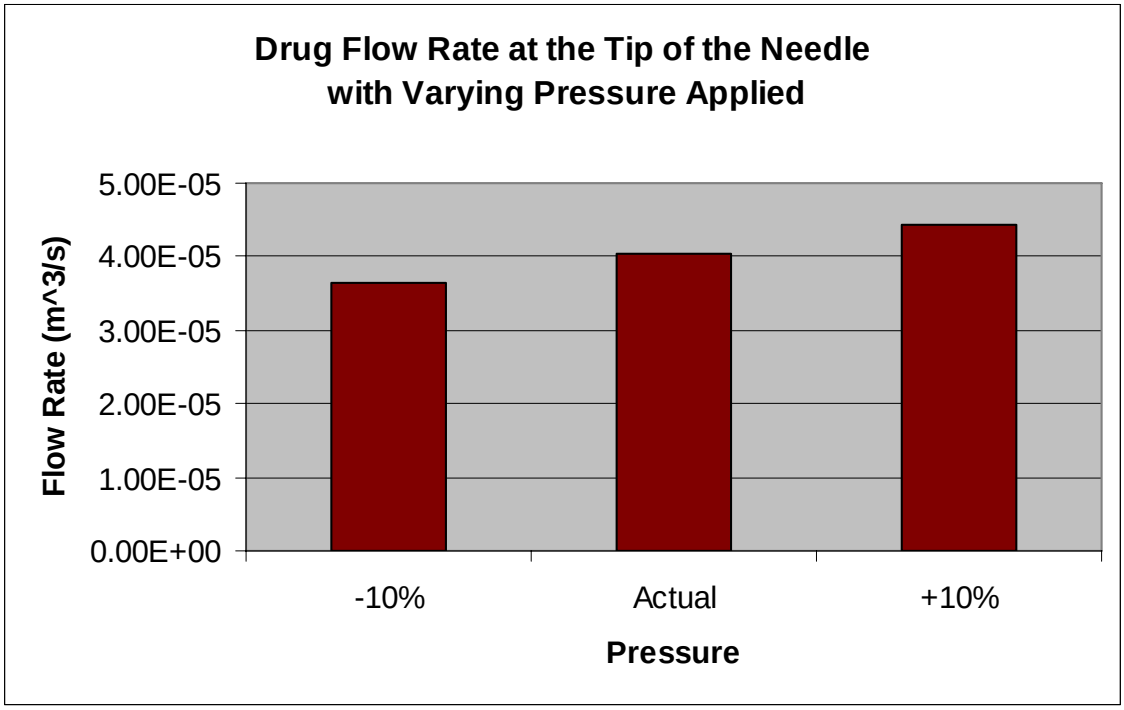


Figure 7: The flow rate of the fluid at the tip of the needle with ±10% variation of the applied pressure of 10 pounds of force at the plunger.

Our second major variable analyzed was the used of different drug viscosity; assuming use of different drugs in the auto syringe in the market place. The range of viscosities tested was extremely large due an inability to find viscosity values of drugs found in today's market. The viscosity was varied 20% and 50% in each direction to account for the unknown actual values (Figure 8). Intuitively, increasing the viscosity of the drug decreased the flow rate through the needle tip; this is seen in Figure 8 below. This made sense as a thicker fluid is more difficult to pass through a tube or flow. As a note, FIDAP asked the user to provide a viscosity not only for the drug but for the entity of the tissue. This tissue viscosity was assumed to be the viscosity of the drug flowing through its pores; making it necessary to change both the viscosity of the entity drug and the entity tissue by the same percentage for the sensitivity analysis.

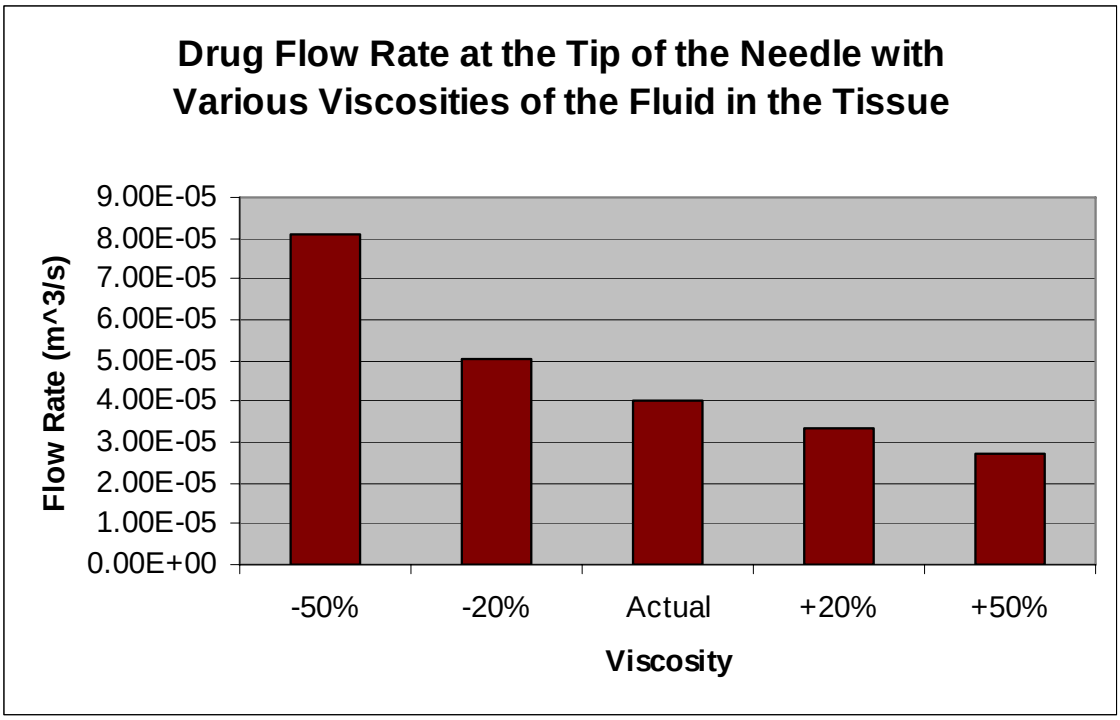


Figure 8: The effect on the flow rate of the fluid at the tip of the needle with ± 20% and ± 50% variation from the viscosity of water for the drug viscosity.

The other three variables tested, drug density, tissue permeability, and porosity, all showed no affect on the flow rate through the needle. No affect due to drug density is easy to explain, as in the flow rate equation there is no term to take density into account. Any change made to the density would therefore have no affect on flow rate through the needle tip. The permeability and porosity both had no affect on the flow rate through the needle tip. This will be explained below.

For the most part, our results were expected. The affect of changing pressure at the plunger and viscosity of the drug were very intuitive for anticipating a change in flow rate. However, the change in permeability and porosity were not expected. Originally, the team thought that an increase in permeability or porosity would increase the flow rate out of the needle as less resistance was encountered at the needle tip. In contrast, a decrease in permeability or porosity would create a backpressure that would in essence slow down the flow rate through the needle tip. However, neither of these situations was the case. When varying the permeability and porosity, no change was elicited in the flow rate of our fluid. After analyzing all possible graphs, an important clue was found in the pressure contour graph (Figure 6). The pressure drop from the constant set at the barrel to the gauge pressure in the skin is observed completely in the needle. This would suggest that all resistance to the fluid is encountered in the needle and makes this portion of the model a limiting factor. Since we are limited by the needle, any changes made in the permeability or porosity of the tissue had no affect on the flow rate. One possible way to examine this sensitivity would be to change the size of the needle to make the tissue the limiting factor.

Conclusions and Design Recommendations

Our design objective was to model the flow of medication through the barrel and needle of a syringe. It is clear through our results that we were successful in this objective. We also set out to determine the effect of several variables on this flow model. Our results show that at lower viscosities with constant applied pressure, the velocity increases. We also see that a result of higher pressure results in a similar increase in velocity. Therefore, we can conclude that drugs with lower viscosity would require less applied pressure on the plunger. Drug viscosity, therefore, is a very important factor to consider when determining the necessary pressure application. It is important to consider this conclusion in terms of design requirements. The team should research the different drugs for which this device could be used for (i.e. medications for MS, Diabetes, Rheumatoid Arthritis, etc). The medication with the high drug viscosity should then be used to set the threshold of pressure necessary. However, if there is a wide range of viscosities it is important to make sure that the threshold set would still represent a safe pressure for use with lower end viscosities.

The results also show that porosity and permeability of the tissue had no observable effect on the flow model. The model only accounted for flow within the needle, however, and did not consider flow into the tissue as the readings were taken as an average at the tip. Therefore, since porosity and permeability are not in the momentum equation, these variables would not be factors in the results. One way to resolve the issue of the effect of permeability and porosity would be to examine flow rate values just within the tissue. A difficulty with this solution could be that when the fluid leaves the needle tip it spreads out in all directions. Therefore, the multiple pathways that the fluid could take might limit the effect of these variables on fluid flow in the tissue. The needle proved to be a limiting factor rather than the fluid build-up in the tissue because the small diameter of the needle is what slows down fluid flow, not resistance due to back pressure from the tissue. More assumptions were made in modeling the tissue than were made in modeling the needle. In addition, the properties of the tissue will vary from patient to patient whereas the properties of the needle will remain constant. Therefore, it is advantageous for us to have the limiting factor be in the needle.

The conclusions above are essential to continuing this project to its completion and creating a physical auto-injection device. However, there are still several realistic constraints which we must face. This model relies on a constant pressure applied to the top of the plunger. In order to apply this pressure the team must develop a feasible power source which can provide the necessary force output. Our ultimate objective is to design a power source that can drive the fluid flow needed to deliver medication to a patient. In this project we were required to use a 27 gauge needle. Since we've determined that needle gauge and length are the limiting factors in fluid flow, we should further analyze different needle sizes to develop an overall picture of the required pressures. Further, the power source must be economically feasible. If the device is to be disposable then there can't be an additional cost greater than 3 to 5 cents. However if the device is reusable the cost can vary depending on many injections it will last for. Additionally, a high upfront

cost may prove to be a barrier to market uptake. The power source must also fall well within all health and safety requirements. There must be adequate control over the source as well as significant testing to prove it's efficacy of delivery.

Appendix A

***Governing Equations**: The Syringe*

Since we are engaged in a problem that deals with mass transfer, we are interested in the Conservation of Momentum that occurs in the syringe. For this we use the 2-D Navier-Stokes equation.

x-coordinate:

$$\rho\left(v_x\frac{\partial v_x}{\partial x}+v_y\frac{\partial v_x}{\partial y}\right)=-\frac{\partial p}{\partial x}+\mu\left(\frac{\partial^2 v_x}{\partial x^2}+\frac{\partial^2 v_x}{\partial y^2}\right)$$

Our problem assumes that there is no heating or cooling of the drug while traveling through the syringe. As a result, we are not interested in the Energy Conservation Equation. The velocity along the glass boundary will also be zero according to laws of fluid flow.

We also must consider the continuity equation of the fluid.

$$\frac{\partial v_x}{\partial x}+\frac{\partial v_y}{\partial y}=0$$

***Boundary Conditions:** The Syringe*

- Left side (the plunger) has constant pressure; $P = P_0$
- The side of the barrel will have a no slip condition where v = 0 [m/s]
- The syringe is completely insulated (no heat loss)

***Governing Equation:** The Tissue*

In this portion, we are concerned with how the drug will disperse and diffuse into the tissue from the penetration site. For this, we will have to evaluate the velocity of the drug in this region, and the following equation:

$$\rho\left(u'\nabla u'\right)=-\nabla\left(\Phi p'\right)-\frac{\mu}{k}\Phi-\frac{c}{k^{\frac{1}{2}}}\Phi^2\left|u'\right|u'+\mu_e\nabla^2 u'$$

***Boundary Conditions:** The Tissue*

- Far away from the injection site, the pressure is equal to the atmosphere

- Drug velocity is 0 far away from the injection site
- We specify for initial solution, the initial velocity profile for the fluid in the syringe as a parabolic velocity profile with the equation $v = 4.76x10^{-4}(1 - (r^2/(.021)^2))$
- There is no drug initially in the tissue

Constant Parameters

- Drug viscosity = 0.00089 kg/(m*s)
- Tissue drug density= 1.05 X 10^3 kg/m^3
- Tissue Porosity = 0.3
- Skin permeability = 5.61 *10^{-9} h*m^2/g
- Effective viscosity = viscosity/2

Note: We assumed the drug has the same properties of water for the preliminary solution.

Appendix B

Problem Statement

The search to discover the next "big drug" is never ending. While much work has been done to develop these life altering medicines, we rarely consider the methods by which we deliver these drugs. As a result, more recent research is being conducted to develop novel drug delivery systems, such as implantables and transdermal patches. However, the problem remains that we rely on syringes, or more specifically needles, to deliver much of our medicine. Perhaps the reason is we have come to expect manually operated syringes as the industry standard for drug delivery. Perhaps something better has yet to come along.

On the other hand, we must understand that not all patients are able to inject themselves with the current syringe technology. Most likely the lack of dexterity required to operate the syringe is the problem. Whether they suffer from diseases like Multiple Sclerosis or Parkinson's, which directly affect the control of body movements, or the patient is limited by the effects of aging, ultimately self injection is just not possible.

Whatever the case, an opportunity has developed to help these disabled people and individuals requiring self-injections. Transitioning the traditional syringe from manual operation to automatic has distinct advantages to those self-injecting individuals. Besides ease of use, an automatic syringe requires less energy from the user, while still administering the correct dosage. As stated previously, automatic syringe technology already exists. However, none can incorporate traditional glass or plastic syringes used today. These technologies require a completely new device to achieve automatic delivery.

The problem, in concept, is basic. We must transform a conventional syringe into an automatic device, while preserving the standardized design. In essence, we want to keep the barrel and needle, but replace the plunger with a controllable power device that can be operated simply and safely by the user. In doing so, we would like to develop a computer model that will allow us to analyze the variables intrinsic to the syringe and skin tissue that can affect the required pressure necessary for a complete injection. These variables include drug density, drug viscosity, skin density, skin permeability, and skin porosity. Upon completion of the model, we will have a complete understanding of the injection process and can base power designs off of our conclusions.

Solution statement

Our solution integrates a multitude of biological and physical variables that can affect the operation of an automatic syringe. With the use of GAMBIT, PreSTO, and FIDAP software, we were able to develop models to analyze pressure and fluid velocities in the syringe and tissue surrounding the injection site. We found that the majority of the pressure loss was in the needle, which would correspond with the high fluid velocities we

encountered in the region. In addition, our solution indicated that the effect of skin parameters, such as porosity and permeability, did not contribute any additional resistance to the fluid flow. As a result of our model, we have determined that altering needle gauge and length will be the largest factor in determining the pressure required for a complete injection. Further research, both computational and experimental, should be conducted to confirm our findings.

Time Integration Statement

Company requirements for the time allotted for an injection is three seconds. However, our computer model required us to incorporate two regions, one of fluid, and the other of a porous media. Due to the difficult nature of the problem, we elected to run a steady state time integration instead of a transient model. As a result, we do not see the fluid flow develop in the syringe, only the steady state result. Nevertheless, we would expect a similar solution to the steady state when three seconds into the transient model. Therefore, we still find our steady state model to be an accurate representation of the injection process.

Mesh Convergence

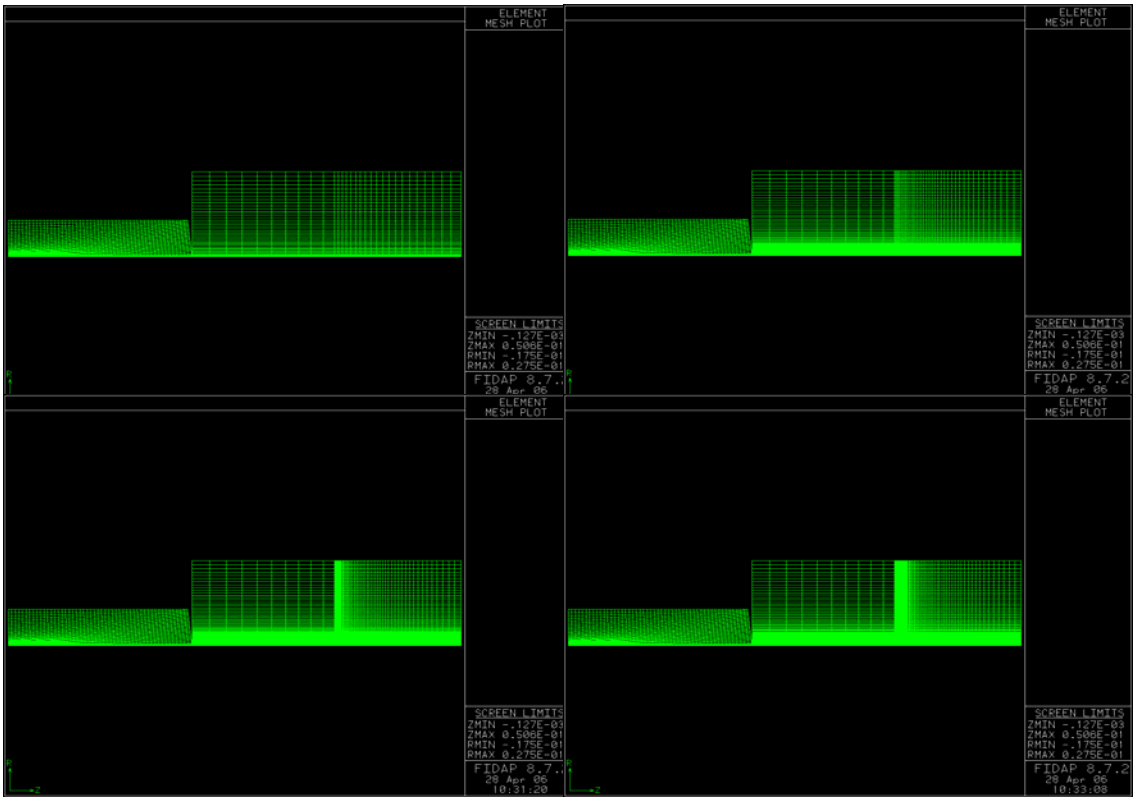


Figure 9: Increasing mesh densities used to evaluate solution convergence. The top left is the least dense, while the bottom right was most dense and used as the geometry for analysis.

Figure 9 above depicts the various densities of mesh we used in arriving at a final geometry suitable for further analysis. We approached nearly 40,000 total nodes before reaching mesh convergence (Figure 10). Fine mesh was most critical in the needle portion of the syringe and at the needle tip as the fluid was ejected. Initially, we did not concentrate as much on the tip of the needle. However, we noticed that our solution was not generating the fluid velocity in the tissue close to the needle tip as expected. As we refined the mesh, we discovered that fluid flow was occurring, but the mesh was not fine enough to show an accurate picture. Therefore, we used the bottom right picture of the mesh (Figure 9) because it offered the best depiction of the fluid flow out of the syringe.

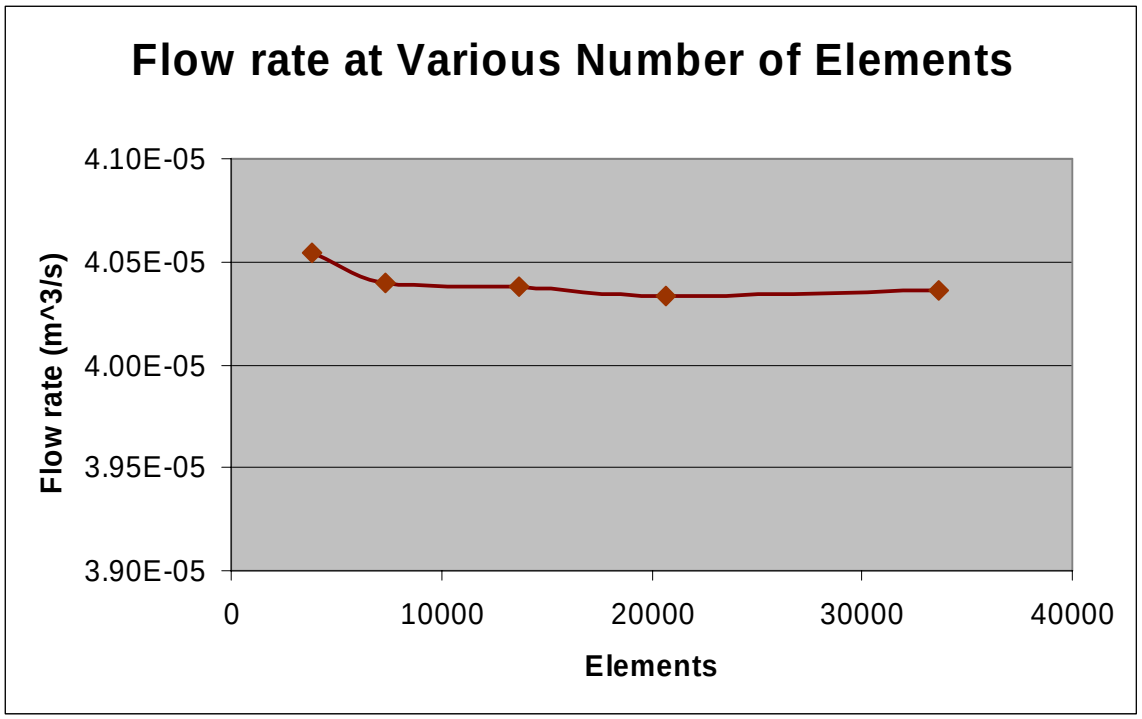


Figure 10: The flow rate at the tip of the needle as a function of the amount of total nodes in the geometry.

Appendix C

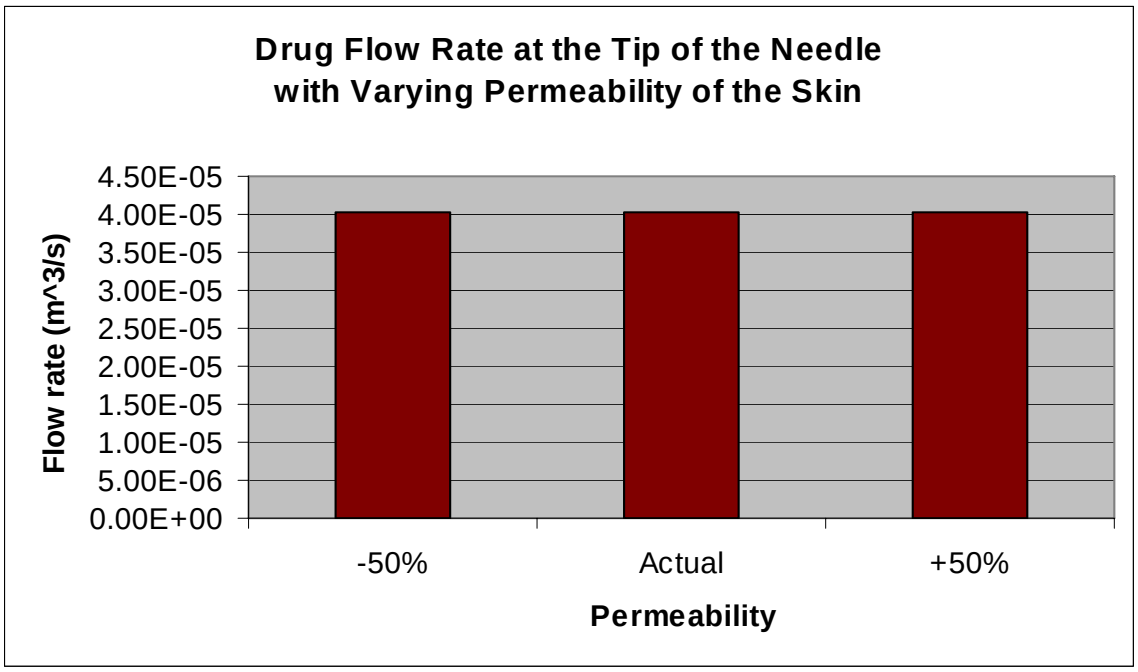


Figure 11: The effect on the flow rate of the fluid at the tip of the needle with ± 50% variation in permeability value. No change in the flow rate was elicited.

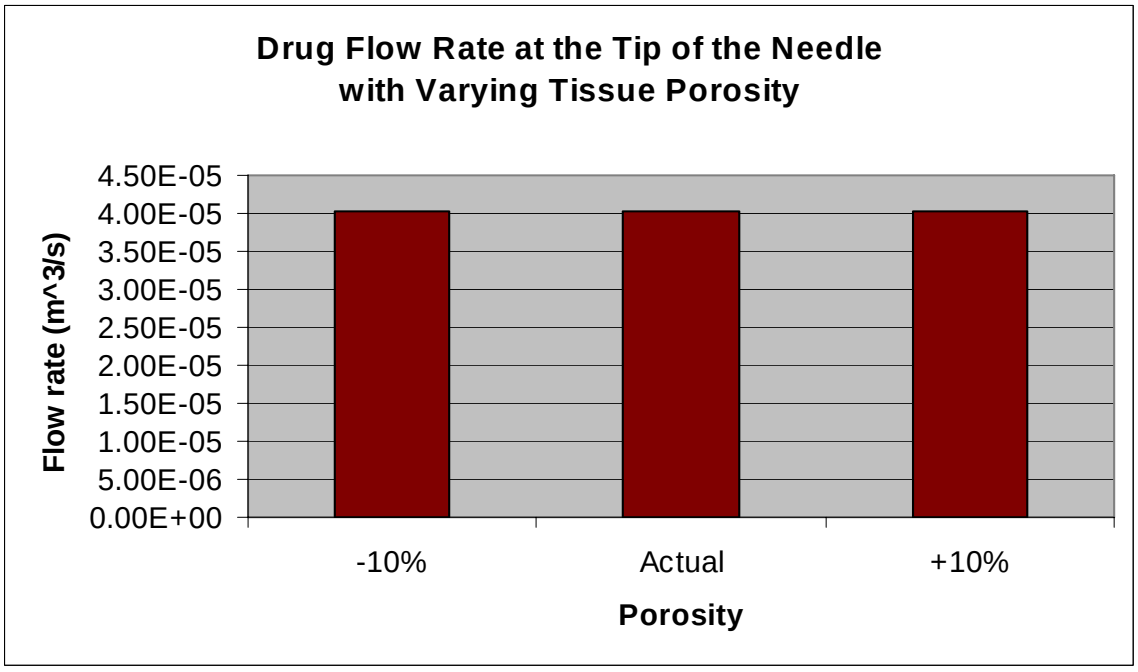


Figure 12: The effect on the flow rate of the fluid at the tip of the needle with ± 10% variation in porosity. No change in the flow rate was elicited.

Appendix D: References

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