Fluid Flow Velocity Using Navier-Stokes Project Report

**Problem**

The paper-based lateral-flow immunoassay (LFA) is a potential affordable, portable, equipment-free, and user-friendly point-of-care (POC) diagnostic device for infectious diseases. The LFA utilizes specific antigen-antibody binding for detection. It relies on capillary action to first move the sample solution from the sample pad and through the detection zone with immobilized primary and secondary antibodies for the test line and control line respectively. The test line checks for the presence of the target biomarker while the control line validates flow through the test. Lastly, the solution moves into the flow-facilitating absorbent pad.

In the case where the biomarkers present in the sample solution, the biomarkers will bind to the primary antibodies on the typically colorimetric or fluorescent probes. Focusing only on the test line, the immobilized primary antibodies that constitute the test line will catch some of the biomarkers bound to the probes as the solution continues to flow. If enough is caught, a visible line will appear, indicating to the user a positive result. While the antigen-antibody interaction itself can be specific, the flow through the strip affects binding and the sensitivity of the assay. For example, if the sample solution flows too quickly, meaning little too little time is spent in the test line region, little to no binding can occur, resulting in a negative result even in the presence of the biomarker. However, if too much time is spent in the test line region, non-specific binding can occur, resulting in a positive result even in the absence of the biomarker. Therefore, it is important to understand the flow of a sample solution over the test line region in an LFA in order to optimize physical setup and running methods for maximum sensitivity as well as accuracy. This includes varying parameters such as LFA orientation, pore size of the paper, and sample solution composition. Furthermore, this information can be used to fine-tune novel techniques, such as phase separation on paper and reagent delivery with an aqueous two-phase system.

**Schematic**

**Diagram, schematic

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**Assumptions**

* Fluid flows only in z-direction
  + since fluid does not flow into the walls of the LFA.
  + since axisymmetric in the theta direction.
  + Therefore, only have
* Once dipped, do not feel entrance or exit effects, so does not vary in z-direction. However, have time dependence, so do not have steady flow.
* Fluid flow does not change with respect to theta as axisymmetric
  + .
* Therefore, is a function of time and radius only
  + .
* Pores are one, uniform size for each type of paper
  + R is a constant
* All LFAs have the same dimensions and all overlaps are exactly the same
  + Test line is 1 mm wide and the end of the test line is 18 mm away from the beginning of the strip
* Use same volume for sample solution
  + Height of sample solution is a constant
* All tests are performed at room temperature and with the same humidity conditions so that the EOPO-citrate ATPS tie line does not shift and a 3:1 volume ratio is achieved.
  + Viscosities of each phase are set to constant values
* Conventional paper setup
  + Not considering a treated sample pad that would affect contact angle when applying the sample solution
  + Not considering a conjugate pad that would contain dehydrated probes and optionally, surfactants, proteins, etc. that would affect flow
  + Not considering the sample solution flowing through any 3D paper structure
  + Not considering the use of a casing that would apply additional pressure
  + Neglecting any nicks or scratches on LFA or along edges that would affect flow/catch probes

**Parameters**

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Value** | **How parameter was estimated** |
| LFA orientation () | 0°, 90° | Measure angle of incline starting from a flat, horizontal surface  0° if the LFA is ran horizontally  90° if the LFA is ran vertically (Note: against gravity) |
| Pore size (R) | 0.45-11 µm   * 1. µm   \*Code took too long when on order of µm, so changed to be higher values | Radius of pore depends on what paper is used. Found from specification sheets/literature  - 0.45-11 µm: sample pad (from literature, a double pore size sample pad containing the smaller and larger pore size bounds) (1)  - 8-15 µm: nitrocellulose membrane (CN95, CN110, CN140, CN150, CN180) (2)  -Absorbent pad (could not find for specific papers used in lab, pore size is not specified for this type of paper) |
| Viscosity of fluid () | EOPO-rich:  25-56 cP  Water:  1 cP | Google for water and EOPO-rich from literature. Experimentally found with by extracting each phase in three 3:1 EOPO-citrate ATPS with different initial EOPO and salt concentration measuring viscosities of with a digital viscometer. (3) |
| Density () | EOPO: 1000.56 kg/m3  Water: 1000 kg/m3 | Google for water and MSDS sheet for EOPO (4) |
| Length | 0.018 m | 0.018 m: length from beginning of sample pad to end of test line obtained by measuring an LFA with a ruler. Other measurements:  Sample pad: 10 mm  Nitrocellulose membrane: 29 mm  Absorbent pad: 22 mm  Test/control line: 1 mm |
| Height of sample solution (h) | 1 cm | Estimated in this project but can be found experimentally by adding sample solution to container used to dip LFA into and measuring. |
| Surface tension () | 0.07 N/m | From literature. Given as a constant in surface tension force equation.  (5) |
| Contact angle () | 26° | From literature. Experimentally found with a drop test method of water onto alpha-cellulose (more porous than nitrocellulose) (5) |
| Change in pressure in z-direction  () |  | From lecture 11. Calculated from Hagen-Poiseuille equation by applying Young-Laplace and using analogy to capillary rise. |

**Equations**

* Z-component of Navier-Stokes equations in cylindrical coordinates

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* Summary of assumptions
* Applying assumptions and simplifying,

]

Where ) and

* For ,

**Plots of velocity over time with varying parameters**

* LFA orientation
  + When =0 (horizontal),

Chart, diagram

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* + When =90 (vertical),

Chart, diagram

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* + We would expect the velocity for the horizontal test is faster than the vertical test. In the vertical case, the flow of fluid is working against gravity. However, because of how we defined our equation for , the terms with sin() cancel out.
* Pore size (R)
  + When R= 0.0005 m,

Chart, diagram

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* + When R = 0.001 m,

Chart

Description automatically generated

* + As pore size gets smaller, the velocity curves initially jump higher before plateauing off. From the name, we would expect fluid to flow faster in larger pores. However, from the trend, we can see this is the opposite.
  + Real life example: flow in CN95 (smaller pores) is faster than flow in CN140 (larger pores)
* Viscosity of fluid ()
  + When = 1cP (water),

Chart

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* + When = 25 cP (lower end of EOPO-rich phase),

Chart

Description automatically generated

* + When = 50 cP (higher end of EOPO-rich phase),

Chart

Description automatically generated

* + As viscosity increases, the velocity curves jump higher to their maximum value and begin plateauing earlier., This means that after applying the sample to the LFA, the viscous fluid travel at the same speed throughout. However, they still reach the maximum velocity values, but we expected the maximums to decrease.
* Density ()
  + When = 1000 kg/m3 (water),

Chart

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* + When = 100 kg/m3 (10-fold lower than water)

Chart

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* + = 10000 kg/m3 (10-fold higher than water),

Chart

Description automatically generated

* + For the last graph, I am comparing only it’s absolute value to the others because I believe the negative slope came from the coded calculations and not the real-life meaning. As density increases, the initial jump for the velocity decreases, and it takes longer to reach the final velocity values. This makes sense as having more mass in the same volume is heavier and affects its velocity, so it takes longer to move.

**Moving forward**

In the future, we would like to modify the code to account for the different paper sections in the LFA. We would also like to see if dP/dz can be derived to match the effects of the different papers together more closely. After, we would like to obtain the average velocity of the different sections. Dividing the test line region (m) by the average velocity (m/s) will give us the amount of time spent in that region (s).

Some ideas

* Can have 3 different Navier-Stokes equation files for each piece of paper (sample pad, nitrocellulose membrane, and absorbent pad in the LFA. Inside each, change parameters to match respective paper. In main function, find the three different velocity values and take their weighted average based on their respective lengths (LFA’s total length is 52 mm)
  + If above method is repetitive, maybe can have parameters in main function. Make helper function that takes in parameters for Navier-Stokes? Then take that output and use ode45.
* Found paper with more complicated Navier-Stokes equation for fluid flow (6)

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References

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