Mimicking Blood Rheology for More Accurate Modeling in Benchtop Research

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MIMICKING BLOOD RHEOLOGY FOR MORE ACCURATE MODELING IN BENCHTOP RESEARCH

by

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ABSTRACT

To confirm computer simulations and Computational Fluid Dynamics (CFD) analysis, benchtop experiments are needed with a fluid that mimics blood and its viscoelastic properties. Blood is challenging to use as a working fluid in a laboratory setting because of health and safety concerns. Therefore, a blood analogue is necessary to perform benchtop experiments. Viscosity is an important property of fluids for modeling and experiments. Blood is a shear thinning fluid, so it has a decreasing viscosity with higher shear rates. This project seeks to create a blood mimicking fluid for benchtop laboratory use. Numerous fluids with different combinations of water, glycerin, and xanthan gum were created to mimic the shear thinning property of blood at different hematocrit levels. Since the amount of xanthan gum is very small, an analytical balance was used. To mix the solution, an immersion blender and a heat circulator were used. The data were obtained from 10-90 torque percent, which is the range over which the rheometer is accurate, so the exact ranges of shear rate tested depended on the test fluid. The created solutions were compared to blood at the equivalent hematocrit and previously performed tests. The three different equivalent hematocrits all produced results similar to viscosities of blood. The results were similarly representative of blood at different equivalent hematocrit for the 0.0075% xanthan gum and the 0.075% xanthan gum by weight. The solutions were able to mimic the shear thinning behavior of blood at different equivalent hematocrits. The fluids with 0.075% xanthan gum, 50% water, and 50% glycerin is a better representative than the fluids with 0.075% xanthan gum, 60% water and 40% glycerin.

DEDICATION

For my family, especially my mom, dad, sister, and grandma, and Jenny Le for their support.

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CHAPTER ONE: INTRODUCTION

Background

To confirm computer simulations and Computational Fluid Dynamics (CFD) analysis, benchtop experiments are needed with a fluid that mimics blood and its viscoelastic properties. Ultimately, the goal is to use this blood surrogate fluid in Left Ventricular Assist Devices (LVAD) benchtop flow loop experiments aimed at tailoring the outflow graft conduit implantation to reduce stroke. It is challenging to use blood as a working fluid in a laboratory setting because of health and safety concerns. Blood clots and becomes unusable, it is opaque, it is not easily stored, it is expensive, and it is not re-useable. Therefore, a blood analogue is necessary to perform benchtop experiments. Viscosity is an important property of fluids for modeling and experiments. Blood is a non-Newtonian fluid, which means the viscosity changes with imposed shear stress. Shear stress causes slippage of fluid layers which deforms the fluid element. Blood is a shear thinning fluid, so it has a decreasing viscosity with higher shear rates.

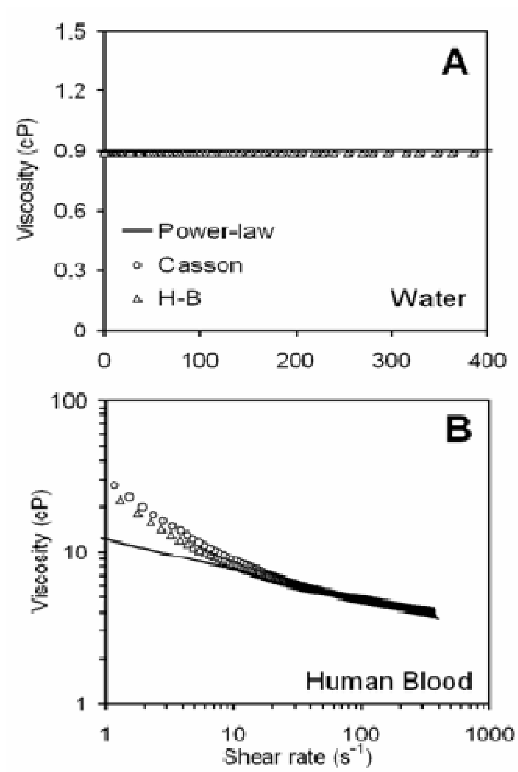

Figure 1- Shear Rate vs Viscosity for Water and Human Blood

Figure 1 shows shear rate vs viscosity for water and for human blood. Note that the human blood shear rate has a logarithmic scale [1]. Figure 1 shows how the viscosity of blood decreases as shear rate increases while the viscosity of water does not change with changing shear rates. At room temperature, water has a viscosity of 1 cP, and at higher temperatures, viscosity decreases. At 37^{o}C blood viscocity is around 3 cP to 4 cP.

Xanthan gum is a readily available food additive that can be acquired over the counter. It is used as a thickening agent, especially in salad dressings. Xanthan gum has been previously used with a mixture of water and glycerin to produce a shear thinning fluid that behaves as a blood analogue [2]. Another advantage to using water, glycerin, and xanthan gum is that the equivalent hematocrit, a volume percentage of red blood cells in blood, can be changed by manipulating the relative amounts of xanthan gum to glycerin and water. Many patients who have cardiac issues, especially those with LVADs, take blood thinners and have lower levels of hematocrit and therefore have lower blood viscosities [3]. This is important because different blood viscosities affect blood flow and other properties. Also, there is a natural range for levels of hematocrit within humans: 40-54% for men and 36-48% for women [4]. Changes in levels of hematocrit change the viscosity of blood and therefore can change the outcome of benchtop experiments. When blood is under high shear conditions, the red blood cells are well mixed and blood viscosity decreases to a typical value of 3 cP for a normal 40-50 Hematocrit range [5]. When blood is under low shear rates (below 100/s) conditions, the red blood cells align into structures called Rouleaux and blood viscosity increases [5]. Blood is also opaque, so if it is important to examine the flow in the benchtop flow-loop, the fluid needs to be transparent. The solution of water, glycerin, and xanthan gum fulfill this requirement.

The ultimate goal is to have benchtop studies of LVADs to help determine placement, function, and risk for maximum efficacy and safety due to blood's limiting factors: it is difficult to obtain, dangerous, spoils, opaque, and it has unique shearing qualities make blood a very difficult fluid to work with. The main goal of the study is to improve the effectiveness of the non-Newtonian fluid for use in the lab to involve further studies without complications.

Because water is polar and glycerin is slightly polar, adding salt to a mixture with both of those ingredients could increase the intermolecular bonds between the molecules. When salts dissolve, they form dissociated ions. Those ions can form strong ion-dipole intermolecular bonds with the solvent. Strong intermolecular bonds make it hard for the fluid molecules to flow over each other, thereby increasing the fluid viscosity.

Selected Literature Review

[2] K. A. Brookshier and J. M. Tarbell, 1993, "Evaluation of a Transparent Blood Analog Fluid: Aqueous Xanthan Gum/Glycerin," Biorheology, **30** (2), pp. 107-116

This article tests 3 different xanthan gum, glycerin, and water solution combinations to compare them to porcine blood with different levels of hematocrit. The authors concluded that their solutions were sufficiently similar to use as blood analogues in in-vitro testing.

[6] Valérie Deplano, Yannick Knapp, Lucie Bailly, Eric Bertrand, 2014, "Flow of a blood analogue fluid in a compliant abdominal aortic aneurysm model: Experimental modelling," Journal of Biomechanics, **47,** pp. 1262-1269

This article attempts to model an aortic aneurism with Newtonian and shear thinning fluid. They concluded that the xanthan gum blood analogue solution models were different than the high blood viscosity at lower shear rates. A Newtonian fluid model cannot provide a reliable prediction of the flow dynamics in an abdominal aortic aneurysm. The higher viscosity values make the shear thinning even more important so the study of this article would not be inconsequential.

[7]Hyung Kyu Huh, Hojin Ha, Sang Joon Lee, 2015, “Effect of non-Newtonian viscosity on the fluid-dynamic characteristics in stenotic vessels,” Experiments in Fluids, **56**(167)

“Xanthan gum based solutions are similar to blood with hematocrits of a wide range of 20-80%” with shear rates of 1-1000 1/sec. The viscosity of a non-Newtonian fluid sharply increases as shear rate decreases. This increase in viscosity reduces blood flow in the vessels causing more work for the heart and possible overload. The flow rate effect of non-Newtonian fluids is negligible under high flow conditions.

[8]P. C. Sousa, F. T. Pinho, M. S. N. Oliveira, and M. A. Alves, 2011, “Extensional flow of blood analog solutions in microfluidic devices,” Biomicrofluidics, **5** (014108), pp. 1-19

This article compared polyacrylamide and xanthan gum by using a rotational rheometer. These are two non-newtonian fluids employed as blood analogue. They exhibit different behavior under strong, extensional flow. Rheological analysis shows that both have a shear thinning behavior very similar to that of whole human blood. The consideration of only shear viscosity to manufacture a blood analogue solution with a viscoelastic character is not adequately demonstrated by the different responses obtained in strong extensional flow studies using the two common blood analogue solutions.

[9]Mohammad Reza Najjari, Jessica A. Hinke, Kartik V. Bulusu, and Michael W. Plesniak, 2016, “On the rheology of refractive-index-matched, non-Newtonian blood-analog fluids for PIV experiments,” Experimental Fluidics, **57** (96), pp. 1-6

By adding NaI and NaSCN to xanthan gum, the viscosity of non-newtonian fluid changes. This is not widely reported and sometimes even misstated. The refractive index of a non-Newtonian blood-analog fluid is difficult to adjust even with NaI or NaSCN at varying concentrations.

CHAPTER TWO: METHODS

Procedure

The research was conducted at the Applied and Computational Biofluids Laboratory at the University of Central Florida. The two research objectives were:

(1) design a fluid with water, glycerin, and xanthan gum, one with salt and one without salt, to mimic the shear thinning property of blood at different hematocrit levels. Since the amount of xanthan gum is very small, an analytical balance was used. To mix the water, glycerin, xanthan gum, and salt together, an immersion blender was used. Because xanthan gum clumps rapidly, many cooking websites recommend using an immersion blender. To measure the viscosity at various shear rates, a cone/plate rheometer was used. To use the rheometer, 0.5mL of the fluid to be tested was placed in the cup and attached to the rheometer. To do the testing, the fluid was heated to 25°C with a device which heats water which circulates around the rheometer to heat the fluid that is being tested. The fluid being tested is allowed to reach 25°C, then the rheometer is turned on and the tests begin. The data are obtained from 10-90 torque percent, which is the range over which the rheometer is accurate, so the exact ranges of shear rate to be tested could not be reliably determined beforehand because it is dependent on the test fluid. The data were obtained starting from the top of the range, at 90 torque percent, and moving down to 10 torque percent.

(2) Test to establish the difference that adding salt makes to the viscosity of the fluids. There were 9 fluids with differing amounts of xanthan gum, water, glycerin and salt with 3 different amounts of xanthan gum. The researcher changed the percent by weight of each of these for each of the different solutions. This models different levels of hematocrit because the benchtop study with the LVADs should model between 20% and 50% hematocrit.

Rheometer

Figure 2- Cone/Plate Rheometer Used

The rheometer used was the Wells-Brookfield Cone/Plate Rheometer. In this rheometer, the cone is rotated, and the rotation is resisted with a beryllium copper spring. From the twist of the spring, the shear stress is calculated, and from the angular speed and dimensions of the cone, the shear rate is calculated.

CHAPTER THREE: RESULTS

Xanthan .075%

The results presented in Figure 2 are symbolic of someone who has a high (79%) hematocrit. This hematocrit could be from someone who is blood doping, adding their blood, which they had previously taken out, through an IV back into their bloodstream so they have a higher amount of red blood cells to increase their oxygen carrying capacity for longer, more arduous exercise. There is not a significant difference between the obtained results and literature values for blood. The salt made no difference in viscosity.

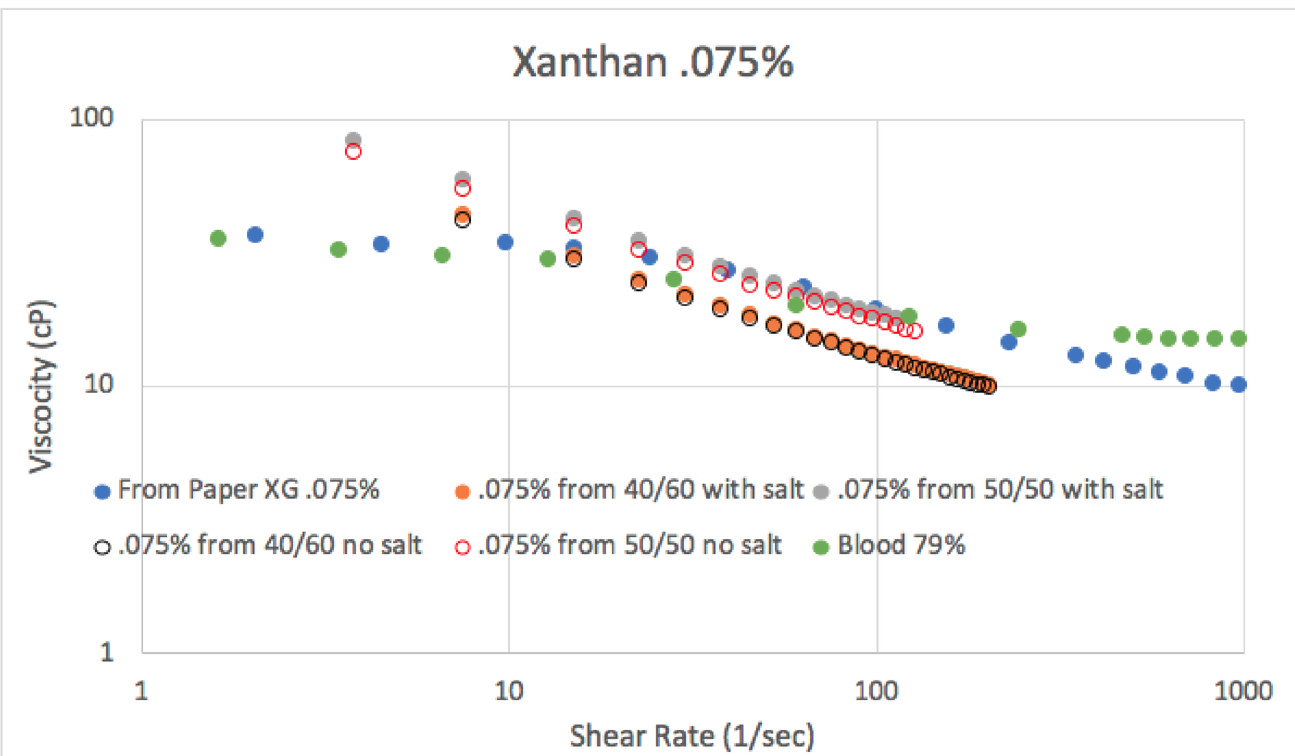

Figure 3 - 0.075% Xanthan Gum

Xanthan .0075%

The results shown in Figure 3 are symbolic of someone who is has low (20%) hematocrit. The low hematocrit could be caused by taking blood thinners, which is a common part of the treatment for LVAD patients. There is not a significant difference between the obtained results and literature values for blood. The researcher's results were closer to the literature values for blood than another similar xanthan mixture found in the literature. Again, the salt made no difference in viscosity.

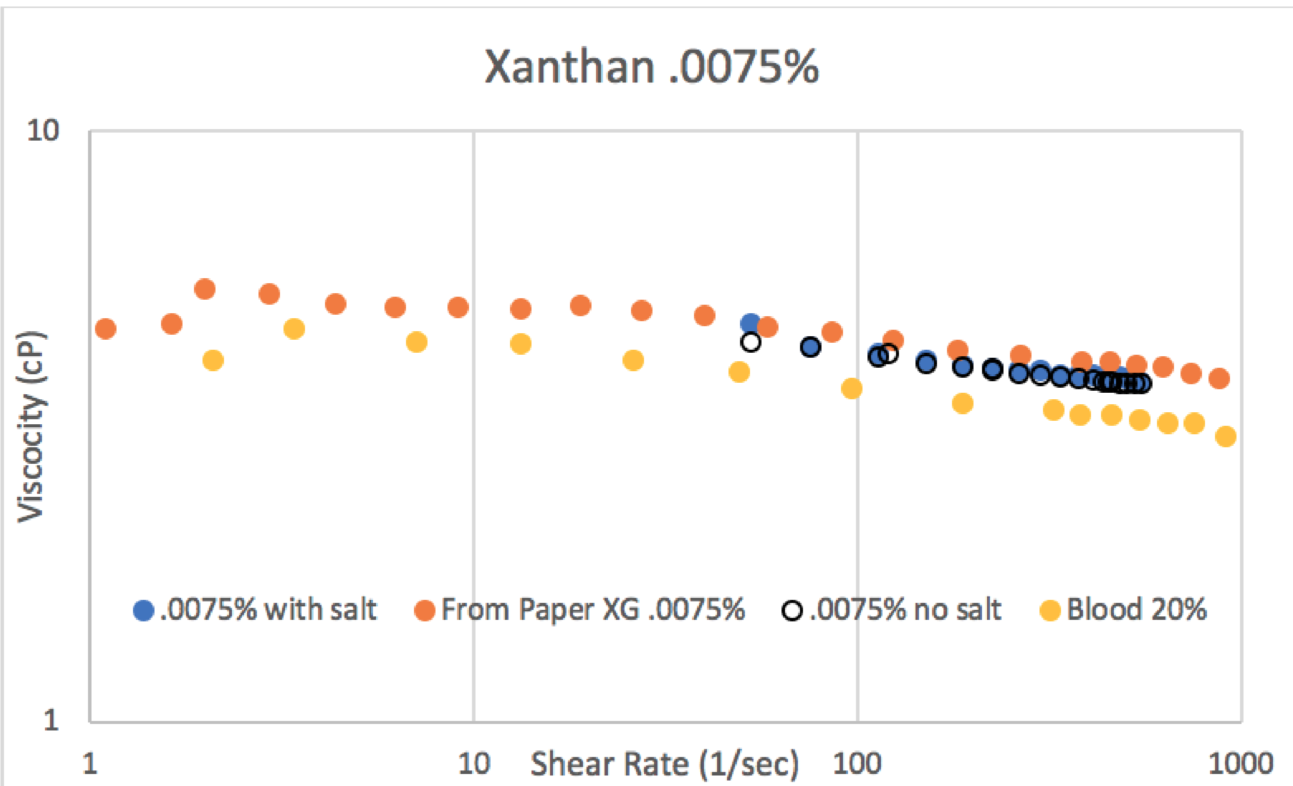

Figure 4 - 0.0075% Xanthan Gum

Xanthan .04%

The results shown in Figure 4 are symbolic of someone with normal (46%) hematocrit levels. There is not a significant difference between the obtained results and literature values for blood. As with the previous results, the salt made no difference in viscosity.

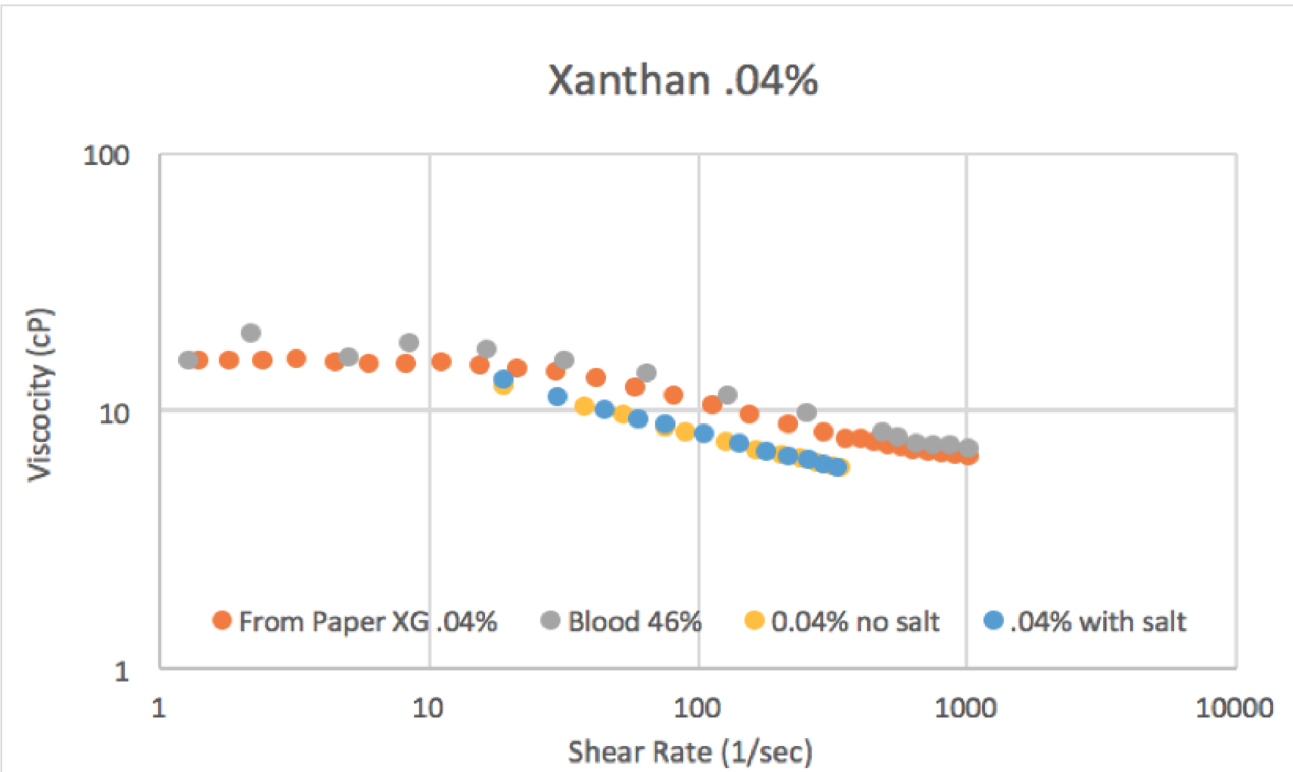

Figure 5 - 0.04% Xanthan Gum

Discussion

Adding salt did not make a difference for the viscosity of the fluids. This was an unexpected result because salt should increase the intermolecular bonds in the fluids. Since salt is ionic and water is polar, adding the salt in the fluid would cause the ion-dipole intermolecular bonds to form. Ion-dipole intermolecular bonds are strong intermolecular bonds. This intermolecular interaction would make it more difficult for the molecules to flow over one another and make the fluid more viscous.

This study used tap water in its mixture. This was because tap water will be used for the future benchtop experiments. It is unknown at this time if the ions in the tap water affected the results and DI or distilled water would have had lower viscocities. In the future, distilled water may be a better choice to see if salt affects the outcome.

CHAPTER FOUR: CONCLUSION AND FUTURE WORK

It was shown that adding salt does not affect viscosity. It was also demonstrated that the solutions were able to mimic the shear thinning behavior of blood at different equivalent hematocrits. The fluids with 0.075% xanthan gum, 50% water and 50% glycerin is a better representative than the fluids with 0.075% xanthan gum, 60% water and 40% glycerin because the former is closer to the literature values of blood. More work needs to be done to be able to know the xanthan gum, water, and glycerin amounts needed for more hematocrit values. More specifics are needed for around the normal range of hematocrit (40-54% for men and 36-48% for women).

REFERENCES

1. S. Kim, B. Namgung, P. Ong, Y. Cho, K. Jin Chun, D. Lim, 2009, "Determination of rheological properties of whole blood with a scanning capillary-tube rheometer using constitutive models," Journal of Mechanical Science and Technology, **23** pp. 1718-1726

2. K. A. Brookshier and J. M. Tarbell, 1993, "Evaluation of a Transparent Blood Analog Fluid: Aqueous Xanthan Gum/Glycerin," Biorheology, **30** (2), pp. 107-116

3. Ayan Sen, Joel S. Larson, Kianoush B. Kashani, Stacy L. Libricz, Bhavesh M. Patel, Pramod K. Guru, Cory M. Alwardt, Octavio Pajaro, and J. Christopher Farmer, 2016, "Mechanical circulatory assist devices: a primer for critical care and emergency physicians" **20** (153), pp. 1-20

4. Henny H. Billett, 1990, *Clinical Methods: The History, Physical, and Laboratory Examinations*, Butterworths, Boston, Chap.151 "Hemoglobin and Hematocrit"

5. M Anand and KR Rajagopal, 2004, "A Shear-Thinning Viscoelastic Fluid Model for Describing the Flow of Blood," International Journal of Cardiovascular Medicine and Science, **4** (2), pp 59-68

6. Valérie Deplano, Yannick Knapp, Lucie Bailly, Eric Bertrand, 2014, "Flow of a blood analogue fluid in a compliant abdominal aortic aneurysm model: Experimental modelling," Journal of Biomechanics, **47,** pp. 1262-1269

7. Hyung Kyu Huh, Hojin Ha, Sang Joon Lee, 2015, "Effect of non-Newtonian viscosity on the fluid-dynamic characteristics in stenotic vessels," Experiments in Fluids, **56**(167)

8. P. C. Sousa, F. T. Pinho, M. S. N. Oliveira, and M. A. Alves, 2011, “Extensional flow of blood analog solutions in microfluidic devices,” Biomicrofluidics, **5** (014108), pp. 1-19

9. Mohammad Reza Najjari, Jessica A. Hinke, Kartik V. Bulusu, and Michael W. Plesniak, 2016, “On the rheology of refractive-index-matched, non-Newtonian blood-analog fluids for PIV experiments,” Experimental Fluidics, **57** (96), pp. 1-6

PRESENTATIONS

1. Webb L, Figueroa R, Rodriguez G, DeCampli W, Kassab A. "Mimicking Blood Rheology for More Accurate Modeling in Benchtop Research." *Biomedical Engineering Society Annual Meeting*, Georgia World Congress Center, Atlanta, GA, October 2018