BIOGRAPHICAL SKETCH

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NAME: Aaron L. Fogelson

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POSITION TITLE: Professor of Mathematics, Adjunct Professor of Biomedical Engineering, University of Utah

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Wesleyan University, Middletown CT	B.A.	05/1977	Mathematics
Courant Institute, New York University	M.Sc.	06/1979	Mathematics
Courant Institute, New York University	Ph.D.	10/1982	Mathematics
University of California, Berkeley	Postdoc	06/1985	Mathematics

A. Personal Statement

I am an applied mathematician who has been developing mathematical models of complex physiological processes for over 40 years (starting with my PhD research with Charles Peskin at NYU). Much of this work has focused on hemostasis and thrombosis with a particular emphasis on understanding the effects of flow (through transport and forces) on platelet deposition and coagulation. Mine were the first models of platelet deposition that actually allowed the thrombus to grow and perturb the fluid motion, thus affecting the forces the fluid exerts on the thrombus and the future transport of cells and proteins to and from the thrombus. I have developed models of platelet activation, adhesion, and aggregation that track the motion and behavior of a number of discrete platelets as they interact with one another, the vessel wall, the blood plasma, and chemicals. I have developed similar models that treat platelets via population densities. I have developed models of the same processes, but on a larger scale, suitable for looking at thrombosis following plaque rupture in vessels the size of the coronary arteries. My group has also developed the most comprehensive models to date that describe the integrated processes of platelet deposition and coagulation biochemistry, and the effects of flow on these processes. We have recently adapted our models to the setting of venous thrombosis where activation of endothelial cells initiates thrombus growth. We continue to develop these models, as well as our models of fibrin polymerization and fibrinolysis. Our models require state-of-the-art computational methods that we develop or adapt as needed.

I have had extensive experience in mentoring graduate students and postdocs. So far, 14 PhD students have completed thesis research under my supervision; nine of them did research directly connected with modeling hemostatic and thrombotic events and/or in developing sophisticated computational methods for studying such models. I have also supervised 15 postdocs on a variety of projects in modeling biological fluid dynamics or physiology more generally. I am currently supervising 5 PhD students, one working on novel models of platelet adhesion and its regulation, one working on models of fibrin gelation under flow, a third looking at the flow dynamics in chains of lymphatic pumps, another looking at models of the regulation of platelet integrin activation, and one developing computational models for whole blood flow, including platelet interactions with red blood cells and the vascular wall.

For years, I have been immersed in the hemostasis and thrombosis literature and have interacted with numerous engineers and life scientists who do laboratory research in these fields. I have presented my models and findings in conferences and seminars organized and attended by researchers in these fields (e.g., the Biomedical Engineering Society Meetings, the Fibrinogen Society Workshop, the Gordon Conference on Hemostasis, the Department of Medicine at the University of North Carolina, International Society of Thrombosis and Hemostasis

congress). I have developed a facility in explaining our modeling results in terms appropriate for these audiences and in translating questions from these laboratory scientists into tractable mathematical questions.

I have been PI or co-PI of several multi-investigator projects and know how to work with other scientists, their students and mine, to push forward in research projects in an efficient and effective manner.

1. Walton, B.L., Lehmann, M., Skorczewski, T. Beckman, J.D., Lori A. Holle, L.A., Cribb, J.A., Mooberry, M.J., Wufsus, A.R., Cooley, B.C., Homeister, J.W., Falvo, M.R., **Fogelson, A.L**., Neeves, K.B., Wolberg, A.S. (2017) Elevated hematocrit promotes arterial thrombosis, Blood, 129, 2537-2546.
2. Bannish, B.E., Chernysh, I.N., Keener, J.P., **Fogelson, A.L.,** Weisel, J.W. (2017) Molecular and Physical Mechanisms of Fibrinolysis and Thrombolysis from Mathematical Modeling and Experiments, Sci Rep, 7, 6914.
3. **Fogelson, A.L.**, Neeves, K.B. (2015) Fluid Mechanics of Blood Clot Formation, Annual Review of Fluid Mechanics, 47, 377-403.
4. Leiderman, K., Chang W., Ovanesov, M., **Fogelson A.L.** (2016) Synergy Between Tissue Factor and Factor XIa in Initiating Coagulation, Arterioscler Thromb Vasc Biol, 36, 2334-2345.

B. Positions and Honors

Positions and Employment

2014 – 2017	Associate Dean for Research, College of Science, University of Utah
2000 – Present	Adjunct Professor, Biomedical Engineering, University of Utah
1994 – Present	Professor, Mathematics, University of Utah
1992 – 1993	Visiting Associate Professor, Applied Mathematics, University of Washington
1989 – 1994	Associate Professor, Department of Mathematics, University of Utah
1989	Visiting Member, Courant Institute, New York University
1985 – 1989	Assistant Professor, Mathematics, University of Utah
1985 – 1986	Associate Research Scientist, Courant Institute, New York University
1982 – 1985	NSF Postdoctoral Fellow, Department of Mathematics, University of California, Berkeley

Honors and Awards

2008	Chair, Gordon Research Conference on Theoretical Biology and Biomathematics
1999 – 2000	John Simon Guggenheim Fellowship
1987 – 1991	Alfred P. Sloan Research Fellowship
1982 – 1984	NSF Postdoctoral Fellowship
1979 – 1982	SIAM Institute for Mathematics for Society Fellowship
1977	B.A. Summa Cum Laude, Wesleyan University
1976	Phi Beta Kappa

Other Experience and Professional Memberships

Society for Industrial and Applied Mathematics (SIAM), International Society on Thrombosis and Hemostasis, Biophysical Society, American Association for the Advancement of Science. Vice-chair of SIAM Activity Group on the Life Sciences (2011 – 2013). Associate Editor, SIAM Journal on Applied Mathematics (2017 – Present) Co-Editor Special Issue of *Current Opinion in Biomedical Engineering* on Mathematical Models of Blood Clotting (2021). Co-Editor Special Issue of *Computer Methods in Applied Mechanics and Engineering* on Immersed Boundary Methods (2008).

C. Contributions to Science

1. We introduced the first mathematical models of blood coagulation that account for platelet involvement, platelet deposition, and flow. The models made important predictions, especially about the system having a threshold response, since confirmed experimentally. We postulated an important physical inhibitory role for platelets. A paradigm in which platelets play dual pro- and anti-coagulant roles helps us understand a variety of observed phenomena including the appearance of the threshold, a reason for bleeding risk in hemophilia, and the consequences of reduced (or excessive) platelet count.

a. Kuharsky, A.L., **Fogelson, A.L**. (2001) Surface-mediated Control of Blood Coagulation: The Role of Binding Site Densities and Platelet Deposition. Biophysical Journal, 80, 1050-1074.
b. **Fogelson, A.L**. Hussain, Y.H, Leiderman, K. (2011) Blood Clot Formation Under Flow: The Importance of Factor XI on Thrombin Production Depends Strongly on Platelet Count, Biophysical J, 102, 10-18.

c. Link K.G., Stobb, M.T., Di Paola, J.A., Neeves, K.B., **Fogelson, A.L**., Sindi, S.S., Leiderman, K. (2018) A local and global sensitivity analysis of a mathematical model of coagulation and platelet deposition under flow, PLoS ONE, 13, e0200917.
d. Link K.G., Stobb M.T., Sorrells MG, Bortot M., Ruegg K., Manco-Johnson M.J., Di Paola, J.A., Sindi, S.S, **Fogelson, A.L.**, Leiderman, K., Neeves, K.B. (2020) A mathematical model of coagulation under flow identifies factor V as a modifier of thrombin generation in hemophilia A. J Thromb Haemost, 18, 306-317.

2. Recent experimental observations of intravascular thrombi reveal that the structure of the thrombus (e.g., density of bound platelets) is spatially and temporally heterogeneous, as is the pattern of activation of platelets that make up the thrombi. Using a novel spatial-temporal model of coagulation and platelet deposition under flow, which fully accounts for disturbance of the flow field by the growing thrombi, we have elucidated the importance of intra-clot fluid, protein, and platelet transport in contributing to this heterogeneity.

a. Leiderman K., **Fogelson A.L.** (2011) Grow with the Flow: A Spatial-temporal Model of Platelet Deposition and Coagulation Under Flow, Mathematical Medicine and Biology, 28, 47-84.
b. Leiderman K, **Fogelson, A.L.,** (2013) The Influence of Hindered Transport on the Development of Platelet Thrombi Under Flow, Bulletin of Mathematical Biology, 75, 1255-1283.
c. Onasoga A., Leiderman K. **Fogelson, A.L**. Wang M., Manco-Johnson M.U., DiPaola J.A., Neeves, K.B. (2014) The Effect of Factor VIII Deficiencies and Replacement Bypass Therapies on Thrombus Formation Under Venous Flow Conditions in Microfluidic and Computational Models, PLOS ONE, 8, e72732.
d. Schoeman, R.M, Rana, K., Danes, N., Lehmann, M., Di Paola J.A., **Fogelson, A.L**., Leiderman, K., Neeves, K.B. (2017) A microfluidic model of hemostasis sensitive to platelet function and coagulation, Cellular and Molecular Bioengineering, 10, 3-15.

3. Fibrin gel formation and fibrinolysis are critical aspects of blood clot formation. Experimental evidence suggests an important role for the flow characteristics in influencing the ability of fibrin to gel. Fibrin gels form branching structures without the use of a specific branching molecule and the branching structures vary substantially depending on the concentrations of enzyme and substrate involved. The rate at which the fibrinolytic system degrades a fibrin clot depends on its branching structure. We have developed novel mathematical models to look at fibrin polymerization and fibrinolysis, that give an explanation for the flow-dependence of fibrin formation, provide a mechanism for fibrin branching that is sensitive to concentrations, and give insight into the role a clot's structure plays in determining its rate of lysis.

a. **Fogelson, A.L.**, Keener J.P. (2010) Toward an understanding of fibrin branching structure. Physical Review E, 21, 051922.
b. Bannish, B.E., Keener J.P., **Fogelson, A.L.** (2014) Modeling fibrinolysis: a 3D stochastic multiscale model. Mathematical Medicine and Biology, 31, 17-44.
c. **Fogelson, A. L**., Nelson A. C., Zapata-Allegro, C., Keener J.P., Development of Fibrin Branch Structure Before and After Gelation', (2022), SIAM Journal on Applied Mathematics, 82, 267-293.
d. Nelson. A. C., **Fogelson, A. L.**, Understanding the effect of fibrinogen interactions on fibrin gel structure, (2023), Physical Review E, 107, 024413.

4. The development of platelet thrombi involves substantial biomechanical and biophysical interactions at multiple spatial and temporal scales. We have developed two classes of models of these interactions; one at a scale appropriate for arterioles and venules in which it is feasible to track platelets as discrete entities, and another for larger vessels, such as the coronary arteries, where only a number-density-based description of platelet populations is tractable. The dynamic behavior of these models (e.g., thrombus growth to occlusion or embolization) in different physiologically-relevant fluid dynamic situations is very revealing of the importance of mechanical forces in the formation and stability of thrombi. A related issue is the physical effects that red blood cells have on platelet distribution in flowing blood has received much attention because of its potential impact on thrombus development. We have developed computational models of flowing whole blood and have used them to characterize the mechanism underlying the developed of enhanced near-wall concentration of platelets, and to show that platelet contact with a growing thrombus is enhanced because of the presence of moving red blood cells in a hematocrit and thrombus-porosity dependent way.

a. Skorczewski, T, Crowl-Erickson L., **Fogelson, A.L**. (2013) Platelet Motion Near a Vessel Wall or Thrombus Surface in Two-Dimensional Whole Blood Simulations, Biophysical Journal, 104, 1764-1772.
b. Crowl, L., **Fogelson, A.L.** (2011) Analysis of Mechanisms for Platelet Near-Wall Excess Under Arterial Flow Conditions, Journal of Fluid Mechanics, 676, 348-375.

c. Du, J., **Fogelson, A.L.** (2018) A two-phase mixture model of platelet aggregation, Mathematical Medicine and Biology, 35, 225-256.
d. Du, J., Kim D., Alhawael G., Ku D.N, **Fogelson, A.L.** (2020) Clot Permeability, Agonist Transport, and Platelet Binding Kinetics in Arterial Thrombosis', Biophysical Journal,119:2102-2115.

5. Many biological materials are comprised of a polymer network embedded in a viscous fluid, e.g., mucin, actin, or fibrin gels, and the complex mechanics of the composite material are influenced by both physical factors and chemically-modulated ones. Systematic derivation of mathematical models of these mechanics is difficult, and, often, heuristic models are studied instead. We have systematically developed models for gel mechanics including fluid and elastic mechanics, transport of macromolecules, fluid, and small molecules, appropriate biophysical forces, and regulatory chemistry. We have applied these models to understand mucin exocytosis and are applying them to study the dynamics of the mucin layer that lines the gastric system. We have also developed sophisticated new numerical methods (and implemented them in efficient codes) to meet the challenges of studying the multi-material models computationally.

a. Sircar, S, Keener J.P. **Fogelson, A.L.** (2013) The Effect of Divalent vs. Monovalent Ions on the Swelling of Mucin-like Polyelectrolyte Gels: Governing Equations and Equilibrium Analysis, J Chem Phys, 138, 014901.
b. Lewis, O., Keener, J.P., **Fogelson, A.L**. (2017) A Physics-based Model for Maintenance of the pH Gradient in the Gastric Mucus Layer, Am J Physiol Gastrointest Liver Physiol, 313, G599-G612.
c. Lewis, O., Keener, J.P., **Fogelson, A.L**. (2018) Electro-diffusion-mediated swelling of a two-phase gel model of gastric mucus, Gels, 2018, 4, 76.
d. Du J., Lewis O., Keener, J.P., **Fogelson, A. L**. (2021), Modeling and Simulation of the Ion-Binding-Mediated Swelling Dynamics of Mucin-like Polyelectrolyte Gels, Gels, 7(4) 244.

Complete List of Published Work: http://www.ncbi.nlm.nih.gov/sites/myncbi/collections/bibliography/42362636

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

PROJECT TITLE: Modeling gastric mucus layer physiology
PRINCIPAL INVESTIGATOR: Aaron L. Fogelson
AGENGY: NIGMS
GRANT NUMBER: 1R01GM131408
PERIOD: 08/01/18-05/31/22
GOALS: With a team of mathematical and experimental scientists at Utah, Montana State University, Boston University, and the Florida Institute of Technology, to develop and validate models of the mucus layer that lines the stomach mucosa, and to use the models to study maintenance and regulation of the gastric layer, the mechanisms by which the layer protects the mucosa from stomach acids and enzymes, and the interactions of H. pylori with this layer.
RESPONSIBILITIES: MPI

PROJECT TITLE: Multiscale Modeling of Clotting Risk in Atrial Fibrillation
PRINCIPAL INVESTIGATOR: Boyce E. Griffith (UNC)
AGENGY: NHLBI
GRANT NUMBER: 1U01HL143336
PERIOD: 08/01/18-07/31/23
GOALS: With Boyce Griffith (UNC) and Craig Henriquez (Duke) to develop models of clot formation and to embed them in a computational model of a beating heart to study thrombosis a fibrillating left atrium to improve assessment of patient's risk of thrombosis.
RESPONSIBILITIES: MPI

PROJECT TITLE: An integrated computational and experimental approach to understanding the hemostatic response during treatment of bleeding
PRINCIPAL INVESTIGATOR: Karin Leiderman (Colorado School of Mines)
AGENCY: NHLBI
GRANT NUMBER: 1 R01 HL151984-01

PERIOD: 04/10/20-03/31/24
GOALS: With Karin Leiderman (Colorado School of Mines) and Keith Neeves (University of Colorado) to develop mathematical and microfluidic models of intravascular and extravascular clotting and using them to probe the effects of different anti-coagulants, different pro-hemostatics, and different vascular beds on bleeding.
RESPONSIBILIES: MPI

PROJECT TITLE: Computational and experimental modeling of subclinical leaflet thrombosis in bioprosthetic aortic valves
PRINCIPAL INVESTIGATOR: Boyce E. Griffith (UNC)
AGENCY: NHLBI
GRANT NUMBER: 1 R01 HL157631
PERIOD: 12/24/21-12/23/25
GOALS: With Boyce Griffith (University of North Carolina) and Arash Kheradvar (University of California, Irvine) to develop models of clot formation and to embed them in a computational model of the cardiac aortic outflow passage to study thrombosis on bioprosthetic aortic valve replacements and to conduct validating in vitro experiments to improve assessment of patient's risk of thrombosis.
RESPONSIBILITIES: MPI

Completed Research Support

PROJECT TITLE: Collaborative Research: Blood Clotting at the Extreme -- Mathematical and Experimental Investigation of Platelet Deposition in Stenotic Arteries
PRINCIPAL INVESTIGATOR: Aaron L. Fogelson
AGENGY: NSF
GRANT NUMBER: DMS-1716898
PERIOD: 08/01/17-07/31/21
GOALS: With J. Du (Florida Institute of Technology) and D. Ku (Georgia Institute of Technology) to develop models of vWF-mediated thrombus formation in stenotic arteries at extreme shear rates and to refine and validate the models by comparison with in vitro experiments.
RESPONSIBILITIES: PI

PROJECT TITLE: A Systems Biology Approach to Predicting Bleeding in Hemophilia
PRINCIPAL INVESTIGATOR: Aaron L. Fogelson
AGENCY: NHLBI
GRANT NUMBER: R01HL120728
PERIOD: 09/01/14-05/31/20
GOALS: With MPIs K. Neeves (Colorado School of Mines), J. DiPaola (University of Colorado), K. Leiderman (Colorado School of Mines) to develop mathematical models of bleeding and in vitro microfluidic physical models of bleeding and to identify factors, in addition to the basic protein deficiencies, that influence bleeding phenotype in hemophiliacs.
RESPONSIBILITIES: MPI

PROJECT TITLE: Upstream Priming of Platelets for Adhesion to Biomaterials
PRINCIPAL INVESTIGATOR: Aaron L. Fogelson
AGENCY: NHLBI
GRANT NUMBER: R01HL126864
PERIOD: 04/01/15-09/30/19
GOALS: With MPI V. Hlady (Utah) to develop experimental data showing the effect of various upstream priming stimuli on downstream platelet deposition and to develop mathematical models that capture these observations and can predict the outcome of priming by various stimuli for different biomaterials and flow regimes.
RESPONSIBILITIES: MPI