Application Form

Profile Information

Registration ID
[redacted]

Full Name
[redacted]

Date of Birth
[redacted]

Email Address
[redacted]

Pho
[redacted]

Address
[redacted]

Gender
[redacted]

Ethnicity
[redacted]

Language Preference
[redacted]

Legal Residence Information

Citizenship
[redacted]

Legal Residence Address
[redacted]

City
[redacted]

State
[redacted]

Zip Code
[redacted]

Your U.S. Congressional House District

[redacted]

Career Goals/Professional Aspirations

What is the highest degree you plan to obtain?

Ph.D.

In one or two sentences, describe your career goals and professional aspirations (see example below). This statement will be used in publications if you are selected as a scholar.

I aspire to make an impact in the medical field, specifically in cardiology, through a career in research. I plan to earn a Ph.D. in Biomedical Engineering and focus on cardiac research.

What are your career goals and professional aspirations? Indicate which area(s) of mathematics, science, or engineering you are considering pursuing in your research career and specify how your current academic program and your overall educational plans will assist you in achieving your career goals and professional aspirations.

Living a healthy life is important to me, and I have always appreciated and been intrigued by the medical advances which help people lead healthy lives. I know the difference which good health can make and know that helping an individual through a health crisis can change the world for that person. I hope to contribute to the medical field through a career in cardiac and circulatory research. By continuing my educational plans and actively involving myself in research, I am confident that I can positively influence medicine through a research career.

To prepare myself for a career in medical research, I have chosen to study biomedical engineering. After completing my B.S. in biomedical engineering at the University of Utah, I plan to earn a Ph.D. in the same discipline. Thus far, the biomedical engineering program has been a great fit for me; it has given me an integrated exposure to the sciences and engineering in a medical context. To improve my educational background, I plan to focus the remainder of my undergraduate coursework on medical device design. I am confident that the knowledge and study skills acquired from my courses will help me think critically and effectively as a student and researcher.

I have made it a priority to be actively involved in research during my undergraduate career. Over the past 20 months, I have studied the mechanics of angiogenesis, the growth of new vessels from existing vessels, in soft-tissue engineering. This work has helped me think like a researcher as I have asked questions, worked through problems, and collaborated with others to solve complex research questions. By following the scientific process and building off of previous experiments, I have been able to confidently defend my results to colleagues, peers, and the scientific community through various presentations. The progress I have made as a researcher has encouraged my decision to pursue a doctorate degree and research career by giving me the confidence that I can succeed.

Describe an activity or experience that has been important in helping shape or reinforce your desire to pursue a research career in science, mathematics or engineering.

I have always enjoyed asking questions and seeking answers. My favorite books answered questions of “why?” or “what if?” and I looked forward to science fairs with anticipation. I sought ways to answer my questions and had great early research experiences. I worked on one project at a local university, and I presented my research at the Intel International Science and Engineering Fair. This experience fostered my desire to pursue research through college.

Two weeks before my first semester at the University of Utah I found myself in an operating room with a cardiologist. A cardiac angiogram found that circulation to my heart was restricted by a swollen pericardium. The reason for the swelling was “unknown.” I wanted to know why and found “unknown” to be an unsatisfactory answer. In that moment, I knew that I wanted to focus my life on finding solutions to medical problems, particularly those regarding the cardiac system. To help me succeed in this endeavor, I chose to study biomedical engineering.

Within a couple weeks of starting the biomedical engineering program at the University of Utah, one professor shared how he had researched a variety of medical problems during his career. Inspired by him, I was sure I had found the right academic path. His experiences reinforced in me the desire to conduct medical research and reminded me what biomedical engineering is all about: researching and engineering to solve complex medical problems and improve patients’ lives.

In what way did COVID-19 or other hardships affect your research career plans and did those events alter your ability to pursue those plans? If COVID-19 did not influence your plans, simply state that there was no effect.

Prior to COVID-19, we had designed and validated our protocols to use time-series imaging to study growing neovessels. We completed our first experiment during which we tracked a small number of neovessels for 10 hours. With this dataset, I was able to find and demonstrate that neovessels respond to and deform the extracellular matrix. I decided to use this data to submit an abstract to an approaching conference. My abstract was accepted, and I was excited to present at the 2020 “Summer Biomechanics, Bioengineering, and Biotransport Conference” in Vail, Colorado. Due to COVID-19, the conference was held virtually. I am glad to say that I was still able to present, but I was disappointed that the interactive and network-building aspects of the experience were dampened.

With the success of our first experiment, we were excited and ready to continue with more experiments. However, COVID-19 suspended our ability to experiment in the lab which prevented us from attaining data needed to move publications forward. In response to these limitations, I moved forward with my research where possible, focusing on the computational aspects of the project. I have worked to develop new computational programs which will allow us to study neovessels’ responses to their surroundings and the forces which neovessels exert during growth.

Research Projects and Skills

Research Project #1

A Study of the Genotoxicity of Caffeine using the Comet Assay

Starting Month

09

Starting Year

2014

Ongoing

No

Ending Month
05

Ending Year
2015

Average Hours/Week (Academic Year)
20

Average Hours/Week (Summer)
n/a

Name of Project Mentor
Justin Livingston

Position of Project Mentor
Graduate Student

Affiliation of Project Mentor
Brigham Young University

Institution where this research was performed
Brigham Young University

Description of research, including your involvement in AND contribution to the project. A separate narrative box has been provided for you to describe the research skills you acquired while working on this project.
To learn more about DNA damage and the harmful effects of certain substances on cellular DNA, I began researching the topic and decided that I wanted to conduct a study for myself. I developed an experimental design whereby I could perform experiments using the comet assay, or “single cell gel-electrophoresis” to quantify DNA damage on individual cells. I contacted a professor at a local university who used the comet assay in his lab, and he put me in contact with one of his students to mentor me through this project. After further research and training with my mentor, I was ready to conduct the experiments. Through image analysis, I determined the proportion of DNA which was damaged for each sampled cell and reported my results.

Research Skills (Briefly describe any research skill(s) you developed while working on this project that will be important going forward in your research career.)
I learned the importance of collaborating and presenting in research. Without the help of a mentor, I never would have conducted the experiments. Additionally, I gained my first experience presenting at a large conference, the Intel International Fair, which inspired me to continue researching.

Do you have Papers/Publications associated with this research project?
No

Do you have Presentations associated with this research project?
Yes

If yes, how many presentations are associated with this work?
1

Citation
Manning J, Livingston J. A Study of the Geno-toxicity of Caffeine using the Comet Assay. Poster session presented at: Intel International Science and Engineering Fair; 2015 May 14; Pittsburgh, USA.

Campus, Regional, National or International
International

Presentation type
Poster

How are you listed on the presentation?
Presenter

Additional Research Projects and Skills

Research Project #2
Microvascular Growth Increases with Matrix Anisotropy in 3D Collagen Hydrogels

Starting Month
04

Starting Year
2019

Ongoing
Yes

Average Hours/Week (Academic Year)
12

Average Hours/Week (Summer)
30

Name of Project Mentor
Jeffrey A. Weiss, PhD

Position of Project Mentor
Professor of Biomedical Engineering

Affiliation of Project Mentor
University of Utah

Name of Project Mentor
Steven LaBelle

Position of Project Mentor
Graduate Student

Affiliation of Project Mentor
University of Utah

Name of Project Mentor
Adam Rauff

Position of Project Mentor
Graduate Student

Affiliation of Project Mentor
University of Utah

Institution where this research was performed
University of Utah

Description of research, including your involvement in AND contribution to the project. A separate narrative box has been provided for you to describe the research skills you acquired while working on this project.
The interface between two tissues inhibits neovessels from growing between them, leading to poor vascularization in soft-tissue implants. We studied how the alignment of the surrounding tissue influences neovessel growth during angiogenesis. Microvessel fragments were suspended in collagen hydrogels with varying degrees of alignment. We analyzed the neovessel growth relative to the fibril alignment of each hydrogel. Neovessels preferentially grew along the direction of the collagen fibrils. We hope to apply this knowledge to create a tissue implant model which promotes vascularization across the interface boundary. My contributions include determining how to best align the collagen fibrils and writing the program to analyze fibril alignments. I determined the fibril directions and quantified the overall alignment, or anisotropy, of each gel. I also developed the protocols used to quantify neovessel growth, including neovessel length and direction.

Research Skills (Briefly describe any research skill(s) you developed while working on this project that will be important going forward in your research career.)
During this project, I learned to apply engineering concepts to the image analysis of our research. I have gained experience in maintaining and imaging cell cultures and developing programs to process and analyze images.

Do you have Papers/Publications associated with this research project?
No

Do you have Presentations associated with this research project?
Yes

If yes, how many presentations are associated with this work?
1

Citation
LaBelle S, Dinkins D, Rauff A, Manning J, Strobel H, Hoying J, Weiss J. Microvascular Growth

Increases with Matrix Anisotropy in 3D Aligned Collagen Hydrogels. Poster session presented at: Summer Biomechanics, Bioengineering, Biotransport Conference; 2020 June 19; Virtual (Vail, USA).

Campus, Regional, National or International
National

Presentation type
Oral

How are you listed on the presentation?
Author(not as presenter)

Additional Research Projects and Skills

Research Project #3
Time-Series Imaging of Angiogenesis Reveals Extracellular Matrix Remodeling

Starting Month
04

Starting Year
2019

Ongoing
Yes

Average Hours/Week (Academic Year)
15

Average Hours/Week (Summer)
30

Name of Project Mentor
Jeffrey A. Weiss, PhD

Position of Project Mentor
Professor of Biomedical Engineering

Affiliation of Project Mentor
University of Utah

Name of Project Mentor
Adam Rauff

Position of Project Mentor
Graduate Student

Affiliation of Project Mentor

University of Utah

Institution where this research was performed
University of Utah

Description of research, including your involvement in AND contribution to the project. A separate narrative box has been provided for you to describe the research skills you acquired while working on this project.
A limiting factor in soft-tissue engineering is poor implant vascularization due to a lack of vascular growth across host-implant interfaces. The interface is a region of abruptly changing tissue structure which prevents growing neovessels from crossing between the tissues. Our goal was to create an implant model which guides neovessels across interfaces to promote implant vascularization. To elucidate the mechanical interactions responsible for limited crossing events, we tracked neovessels as they navigated various 3D, in vitro constructs. I have been involved in designing our experiments, including validating our time-series imaging methods and developing protocol to extract relevant statistics from our images. My contributions include programs which quantified the fibrillar structure of the ECM and tracked growing neovessels as functions of time. My programs enabled us to determine how neovessels responded to and remodeled the fibrillar structure of the extracellular matrix.

Research Skills (Briefly describe any research skill(s) you developed while working on this project that will be important going forward in your research career.)
Designing experiments has helped me become a better researcher. To test hypotheses and find solutions to complicated problems, I have had to think critically and follow the scientific process. Additionally, I have presented and defended my results to my peers and the scientific community.

Do you have Papers/Publications associated with this research project?
No

Do you have Presentations associated with this research project?
Yes

If yes, how many presentations are associated with this work?
1

Citation
Manning J, Rauff A, LaBelle S, Strobel H, Hoying J, Weiss J. Time-Series Imaging of Angiogenesis on a Multiphoton Microscope Reveals Extracellular Matrix Remodeling. Poster session presented at: Summer Biomechanics, Bioengineering, Biotransport Conference; 2020 June 19; Virtual.

Campus, Regional, National or International
National

Presentation type
Oral

How are you listed on the presentation?
Presenter

Mentor Recognition Information

Mentor Name
Jeffrey Weiss

Title
Dr.

Mentor Name
Adam Rauff

Title
Mr.

Other Activities and Accomplishments

Activity/Accomplishment
Connect2Health Volunteer

Organization (if applicable)
Connect2Health

Scope of Activity/Accomplishment
Community

Role/Involvement
Volunteered at a health clinic which served local homeless and less-fortunate individuals access healthcare and enroll in assistance programs. Served in an outreach program to follow up with patients' well-being.

Leadership Position
Member

Length of Involvement
Academic Year

Additional Other Activities and Accomplishments

Activity/Accomplishment
State Level Soccer Referee

Organization (if applicable)
Utah Youth Soccer Association

Scope of Activity/Accomplishment
Community

Role/Involvement
My involvement with my local soccer community spans 10 years. In addition to officiating

matches, including regional tournaments and state championships. I work with the my local league president to train new referees.

Leadership Position
Member

Length of Involvement
More than one academic year

Recognitions

Recognition
SB3C Student Paper Competition

Type
National

Award Description
I placed 3rd in the undergraduate student paper competition at the 2020 Summer Biomechanics, Bioengineering, and Biotransport Conference. I had the opportunity to network with professors and other members of the research community.

Award Year
2020

Additional Recognitions

Recognition
Undergraduate Research Opportunites Program Grant

Type
College/University

Award Description
I wrote proposals and received two separate grants from the University of Utah Office of Undergraduate Research to pursue my research project. One of my written proposals is now displayed on the university website as an example to other students.

Award Year
2020

Additional Recognitions

Recognition
Dean's List

Type
College/University

Award Description
Through my academic career at the University of Utah, I have been able to balance my school, work, and personal lives while maintaining a high GPA.

Award Year
2020

Current College/University

Institution type:
4-year institution

Are you a transfer student (i.e., Did you transfer from another academic institution to the institution that is nominating you for a Goldwater scholarship?)
No

Field of study
Engineering

Engineering areas of specialization
Biomedical

Period through the end of which you will be reporting your GPA
Fall 2020

Official cumulative unweighted GPA through the period reported above
3.95

How many credit hours does your school require for graduation?
122

How many credit hours will you achieve as of January 1, 2021?
78

How many credit hours do you plan to achieve for graduation?
132

Expected baccalaureate graduation month
04

Expected baccalaureate graduation year
2022

According to the definition provided above, indicate whether you are a sophomore or junior.
Junior

Matriculation status at the institution you will be attending during the 2021-2022 academic year
Currently Enrolled

Have you been involved in or do you plan to Study Abroad?
No

Coursework

Current Course 1
Thesis II

Course Level
Undergraduate

Current Course 2
BioDesign I

Course Level
Undergraduate

Current Course 3
Biomolecular Engineering

Course Level
Graduate

Current Course 4
BioTransport

Course Level
Undergraduate

Future Course 1
BioDesignII

Course Level
Undergraduate

Future Course 2
Regulatory Affairs I

Course Level
Graduate

Future Course 3
Systems Physiology I: Cardiac System

Course Level
Graduate

Future Course 4
Cell and Tissue Engineering

Course Level
Graduate

Course outside of Major 1
Immunology

Course Level
Graduate

Course outside of Major 2
Design of Experiments

Course Level
Graduate

Previous Schools attended

Future Academic plans

Is the institution you will be attending for the 2021-2022 academic year the same as your current academic institution?
Yes

Certification and Release

App ture
[redacted]

[redacted]
University of Utah

4D Imaging of Sprouting Neovessels Reveals Traction Force Induced Collagen Matrix Remodeling

Insufficient perfusion across the host-implant interface of soft-tissue implants is a limiting factor in tissue engineering [1]. Without sufficient perfusion, implanted tissues become necrotic. Typically, tissues are vascularized to provide perfusion through a process called angiogenesis [2]. During angiogenesis, neovessels sprout from existing "parent" vessels, navigate their surroundings, and inosculate with other neovessels to complete perfusion circuits [1,2]. However, *in vivo* and *in vitro* studies have shown that the interface between the host and implant creates a barrier across which neovessel growth is significantly limited [1,3]. It is hypothesized that interfaces prevent neovessel crossings through mechanical means [1,3]. We use an *in vitro* model of angiogenesis to study the mechanical modulation of neovessel growth [4]. The use of a multiphoton microscope enables us to track growing neovessels over time as well as analyze images of neovessels and the ECM independently [5]. Our aim is to better understand the mechanics of neovessel growth at interfaces in order to design *in vitro* constructs which guide neovessels across an interface. Such a design, applied to soft-tissue implants, could promote implant vascularization and lead to better implant acceptance.

During angiogenesis, neovessel tip cells interact with their surroundings by exerting traction forces [3,5]. The traction forces deform local fibrils, inducing regions of alignment. Additionally, the traction forces provide feedback to tip cells, allowing them to respond to changing mechanical factors in the ECM [5]. *In vitro* studies have shown increased neovessel branching with increased ECM stiffness and decreased growth with increased ECM density [3]. In aligned constructs, neovessels preferentially grew along the principal axis of alignment [3]. Furthermore, it is hypothesized that neovessels detect and respond to the forces exerted by other neovessels, a process which provides feedback to guide neovessels towards inosculation [5]. The mechanical factors which modulate neovessel growth vary in space within 3D tissues and in time as neovessels advance. In order to collect data regarding neovessel interactions with, and modulation by, the ECM, neovessels need to be tracked over time and through space [5]. This 4D data (3D space + time) is important to elucidate the mechanical interactions between neovessels and the ECM [5].

We set out to develop an experimental framework whereby we could track neovessels over extended periods of time (10+ hours) and quantify neovessel-ECM interactions. Such a framework would allow us to efficiently study angiogenesis and better understand the interactions which inhibit neovessel crossing events. We used a 3D *in vitro* model of angiogenesis and a multiphoton microscope. Rat epididymal microvessel fragments (endothelial cells, arterioles, capillaries, and venules) were suspended in a type I collagen gel (3mg/ml) [4]. Under standard incubation, all aspects of the sprouting phase of angiogenesis are observed as neovessels spontaneously sprout and grow over millimeters in length between days 4-7 [4,5]. After 4 days, the gel was moved to an incubator on a multiphoton microscope for 4D imaging. The multiphoton microscope ensured the viability of the vessels throughout the acquisition period and allowed us to capture data in multiple channels: auto-fluorescence and second harmonic generation (SHG) channels for the vasculature and ECM, respectively [5].

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University of Utah

Our 4D imaging technique effectively maintained neovessel viability during the image acquisition and elucidated the interactions between neovessels and the ECM. Our time series experiment was conducted for a period of 10 hours. During this time, I found that the vascular network interconnectivity increased from 9% to 17%. This indicates that growing neovessel sprouts, originating from different "parent" vessels, fused together. The inosculation between neovessels connected otherwise independent fragments, resulting in a higher interconnectivity (Figure 1). Additionally, I was able to show time-dependent deformations to the ECM as a growing neovessel exerted traction forces (Figure 2).

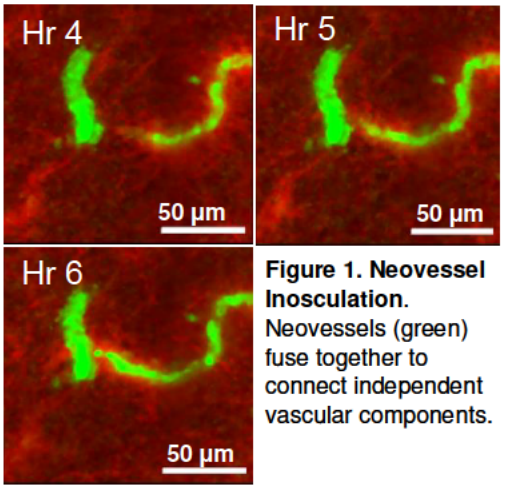

Figure 1. Neovessel Inosculation. Neovessels (green) fuse together to connect independent vascular components.

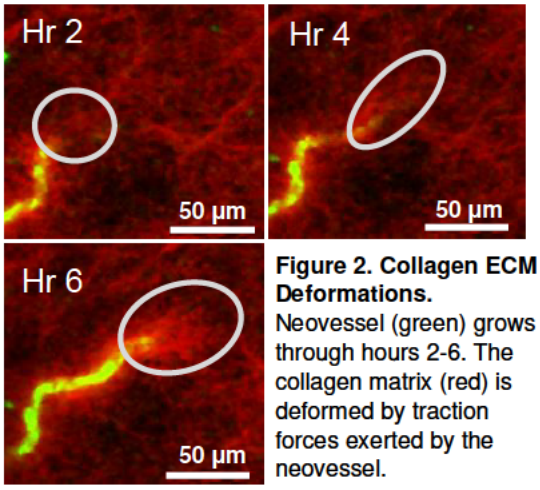

Figure 2. Collagen ECM Deformations. Neovessel (green) grows through hours 2-6. The collagen matrix (red) is deformed by traction forces exerted by the neovessel.

Analyzing the collagen matrix around growing neovessels yielded new insights into neovessel-ECM interactions. I determined that the traction forces exerted by the neovessel tip cells deformed the collagen matrix from an average distance of 45 microns (n=6, std = 15). This indicates that neovessels can detect and respond to changes in the ECM from approximately 45 microns away. With additional data, we will be able to determine the traction forces exerted by neovessels, allowing us to incorporate the forces and ECM deformations into our computational model of angiogenesis.

Over the course of this research, I have actively contributed to each stage of the research process. I helped design and perform experiments and played an integral role in developing and validating our image analysis programs. During the experimentation, I prepared collagen gels and took a lead role in acquiring and processing our 4D images. During image acquisitions, I discovered multiple problems with the microscope and worked with the appropriate faculty members to communicate these issues to industry personnel. Additionally, I contributed the protocols to extract vascular network data and developed the programs used to quantify mechanical features of the ECM (alignment and density). To validate our protocols, I performed validation studies on our vascular network and ECM data. To further contribute to the lab, I am working to quantify traction forces exerted by neovessels and have created a program which measures the range of the resulting ECM deformations (Figure 3).

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University of Utah

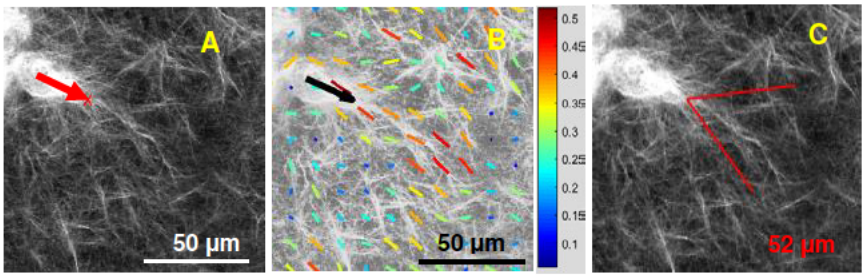

Figure 3: Collagen ECM Deformations. Second harmonic generation image of the collagen matrix around a growing neovessel, marked by a red arrow (A). Principle fibril directions (indicated by lines) and anisotropy, or degree of alignment (indicated by the color-bar) for the region around the neovessel tip (B). The distance from which this neovessel deformed the matrix was calculated as 52 microns and is indicated by red lines (C).

When we are able to resume experiments, we will use the experimental design and programs developed herein to track neovessels near *in vitro* interfaces. Specifically, we will investigate the mechanisms which prevent neovessel crossing events. In the meantime, I will further investigate the forces exerted by neovessel tip cells. By using known material properties of collagen, I can convert a collagen ECM deformation caused by a neovessel to the traction force exerted. We hypothesize that the force exerted will provide a robust metric which we can incorporate into our computational model of angiogenesis. This will provide us with insights into how tip cells navigate through varying matrix architectures and "find" other neovessels. Of particular interest are how neovessels "feel" the interface and whether traction forces span the interface. Improving our computational model of angiogenesis by including the traction forces and resulting deformations will further our research by allowing us to efficiently experiment on varying interface constructs. I look forward to understanding the mechanics of neovessel growth around interfaces and hope we develop a tissue model which guides neovessels across interfaces to promote implant vascularization.

References

[1] Shepherd B.R., Chen H.Y., Smith C.M., Gruionu G., Williams S.K., Hoying J.B., (2004). *Rapid perfusion and network remodeling in a microvascular construct after implantation.* Arterioscler Thromb Vasc Biol, 24:898–904.

[2] Gurevich D.B., Severn C.E., Twomey C., Greenhough A., Cash J., Toye A.M., Mellor H., Martin P., et al., (2018). *Live imaging of wound angiogenesis reveals macrophage orchestrated vessel sprouting and regression.* The EMBO journal, 37(13).

[3] Edgar L.T., Underwood C.J., Guilkey J.E., Hoying J.B., Weiss J.A., (2014). *Extracellular Matrix Density Regulates the Rate of Neovessel Growth and Branching in Sprouting Angiogenesis.* PLoS One, 9(1).

[4] Hoying J.B., Boswell C.A., Williams S.K., (1996). *Angiogenic potential of microvessel fragments established in three-dimensional collagen gels.* In Vitro Cellular and Developmental Biology Animal, 32(7):409–419.

[5] Utzinger U., Baggett B., Weiss J. A., Hoying J. B., Edgar L. T., (2015). *Large-scale time series microscopy of neovessel growth during angiogenesis.* Angiogenesis 18, 219–232.