

Pain Assessment in Hospital Residents and Fellows

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Major: Psychology, Studio Art

They - Them

Purpose

To quantitatively study the submitted surveys of residents and fellows in hospitals about their education and knowledge in assessing pain in patients.

Challenges

Challenges in this study arose while contacting participants. This may be due to multiple factors that are creating more challenge for the hospitals and those work in them, such as:

1. High turnover rate with hospital workers
2. Hospitals often having work force shortages
3. Hospitals still recovering and continuing to battle COVID-19, on top of Monkey Pox
4. Resident cycles starts July 1st, along with many summer adjustments for all residents and administrators

Assessing the Impact on the Performance of Players with Families in the NBA

Justin Robbins 



Abstract

- Except for a very small number of players that have no-trade clauses in their contracts, professional athletes can be freely traded from one team to another. Players being traded can change the course of a season within an instant. Being traded involves a move to a new city and playing with a new set of teammates, two things that can significantly impact performance. For players who are married and/or have children, being traded can be even more challenging as either the spouse and/or children are being left behind, or they are being forced to relocate with no notice. This project looks to answer the research question “Does being traded have a differential negative impact on the performance of players with families?” To answer this question, I collected data on player’s actual basketball stats, as well as their marital status/if they have children. Regressions are estimated to test for the relationship between being traded and performance after the trade. The sample is split by whether players are married, and whether they have children, to see if player who are married and/or have children perform worse after a trade than those who are/do not. I find that being traded has a negative impact on games played and shooting percentage, and that having children makes the negative impact worse, but being married does not.

Introduction

- The NBA, also known as the National Basketball Association, is the professional men’s basketball league in the United States. There are 30 different teams in the NBA located in major cities across the US.
- While veteran players have some choice in where they decide to sign a contract, teams have the option to trade players signed with their organization. Trading a player to another team allows organizations to swap players for other teams’ future draft picks, or current players.
- Within the process of trading, many things switch for the player. Picking up and moving to a different city is not easy. The transition may be especially difficult for players with families.
- This leads us to my research question, “Does being traded have a differential negative impact on the performance of players with families?”
- My theory is that moving to a new city may add certain stress which will lead to a greater impact on stats within the players with a family, compared to those who do not.

Data and Methods

- The data that I collected involved looking at a player’s points, assists, rebounds, steals, etc. These metrics are attributes that determine how well an athlete is performing throughout the season.
- The seasons within the years 2010 – 2019 are the ones being observed.
- NBA.com was the primary website that allowed me to see specific stats for every player in the NBA. The stats were then split into two files, before and after the trade deadline for that season. The trade deadline is a date that is roughly past halfway of the season, in which after this date, teams are no longer allowed to trade players to another team.
- I then hand collected data on the player’s status on marriage and the number of children they have. Within this section, various websites were used, as well as diving into the player’s social media accounts to determine their status. This data collection is still ongoing, which is why the sample sizes for the Marriage and Children variables in Table 1 are smaller than the sample size for the performance measures.
- Linear regression analysis is used to test for the impact of being traded on performance after the trade deadline. The key independent variable in each regression is a binary variable that takes on a 1 if the player was traded.
- Summary statistics are presented in Table 1 for all variables included in the regression analysis. Marriage and Children are both binary variables, as is traded, so the means represent the shares of players who are married, have children, and were traded. Performance variables are cumulative totals for either the before the trade deadline or after the trade deadline period.

Table 1. Summary Statistics

Variable	Obs	Mean	Std. Dev.	Min	Max
Married	1,691	0.241	0.428	0	1
Children	1,679	0.279	0.449	0	1
Traded	4,845	0.128	0.335	0	1
GP Before Deadline	4,617	36.095	16.323	1	60
GP After Deadline	4,462	23.077	15.653	1	82
PTS Before Deadline	4,617	349.466	314.450	0	1861
PTS After Deadline	4,462	227.666	237.545	0	2376
FG% Before Deadline	4,617	43.649	10.698	0	100
FG% After Deadline	4,462	44.188	11.435	0	100

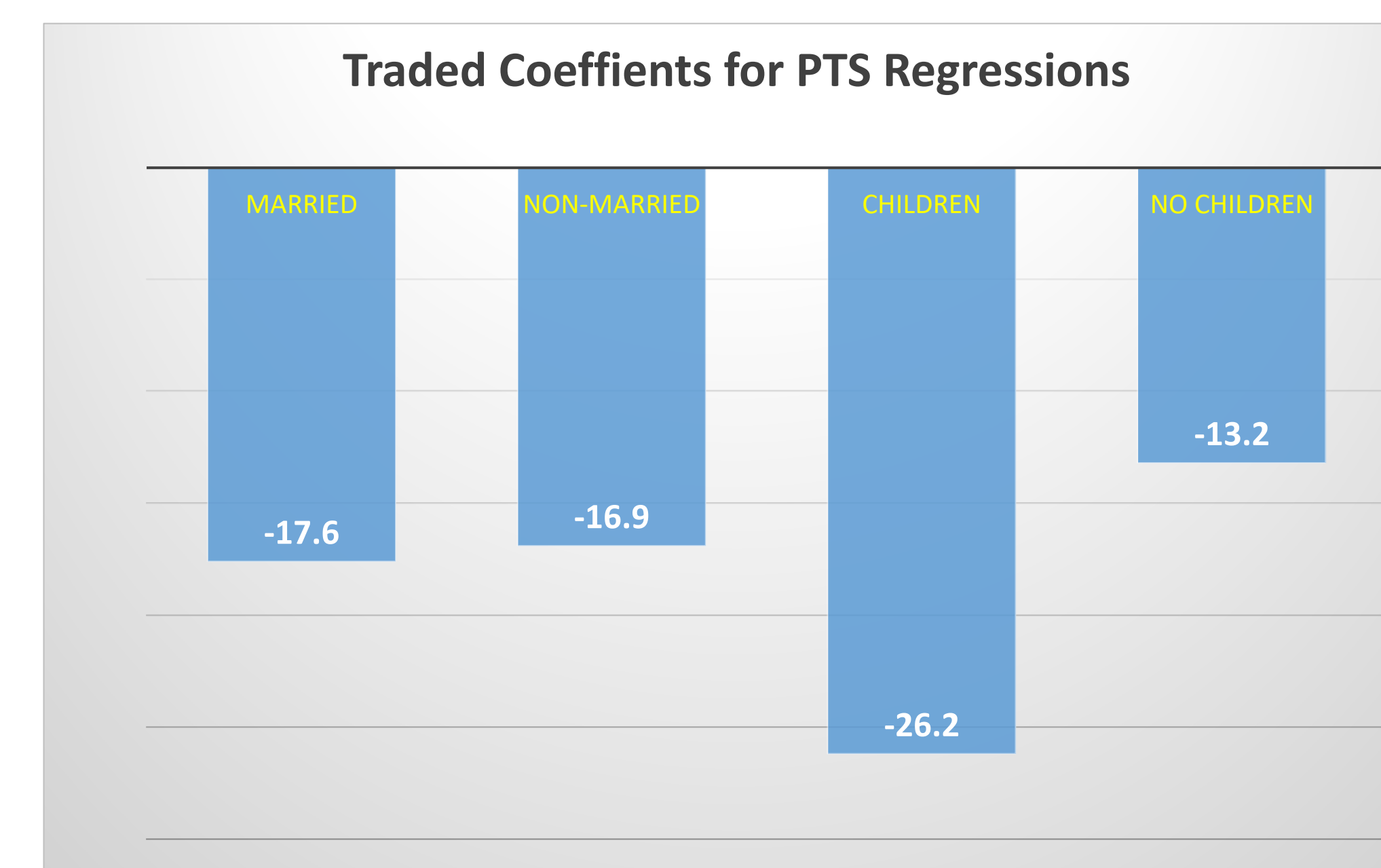
Results

- Table 2 presents regression results. Three regressions were run initially with dependent variables of Games Played after the Trade Deadline, Points Scored after the Deadline, and Field Goal Percentage after the Deadline.
- There was evidence that players perform worse after they are traded. The coefficients on the Traded variable are negative and statistically significant at $p < 0.01$ in both the Games Played and Field Goal % regressions.
- Figures 1 and 2 present the coefficients on the variable Traded from individual regressions where the sample is split into players who are married and unmarried, and those with and without children, for the PTS and FG% dependent variables. As the graphs illustrate, there is some evidence that being traded has a larger negative impact on performance for players with children, but no difference in the impact for those who are married.

Table 2: Regression Results

Variable	Games Played	Points	FG%
Performance Before Deadline	0.391*** (0.013)	0.537*** (0.013)	0.430*** (0.032)
Traded	-1.884*** (0.590)	-4.000 (3.899)	-1.428*** (0.552)
Games Played Before Deadline		-4.701*** (0.212)	0.038*** (0.014)
Games Played After Deadline		10.230*** (0.254)	0.054*** (0.010)
Sample Size		3,845	3,845
R-Squared		0.156	0.8398

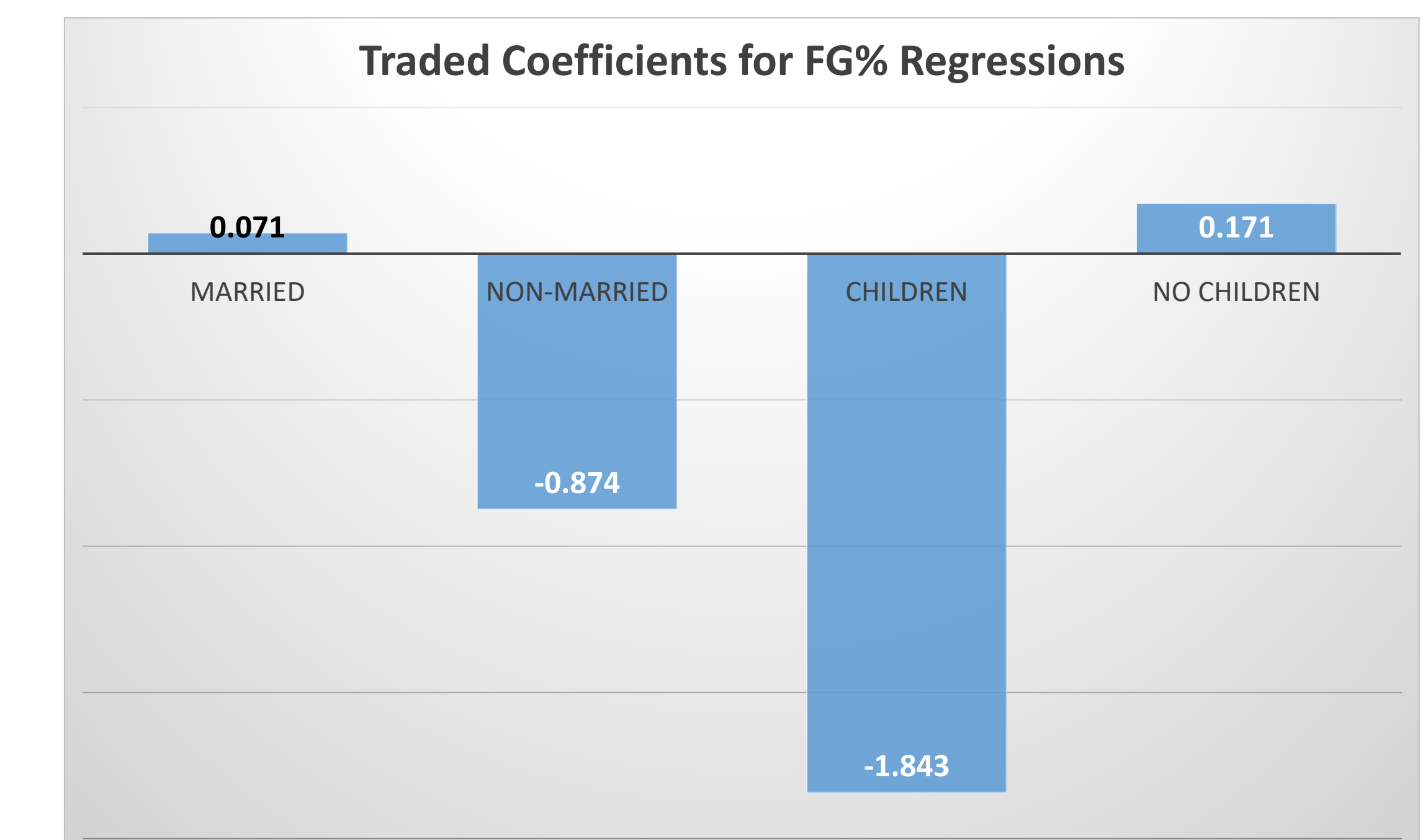
Figure 1: Graph of PTS Regressions Coefficients



Conclusions

- Players shot worse after being traded to a new team. This could be due to many factors. Team chemistry is the biggest one. When in an unfamiliar environment with teammates who are unfamiliar, all cylinders may not be clicking.
- There is some evidence that family impacts performance after trades. From the team’s perspective, this should be taken into consideration when trading for players who may be forced to either leave family behind or uproot their family.
- Currently the data collection is still ongoing, so it will be interesting to see if more results are statistically significant as the sample size increases.
- Currently I am only looking at PTS and FG%, so it will be interesting to see if being traded has an impact on other areas of performance as well.

Figure 2: Graph of FG% Regressions Coefficients



*Thank you to:
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Introduction

Marijuana Use and Perceptions

In 2020, 44% of college students reported using marijuana (National Institutes of Health, 2021). That's nearly half of the college population and we still do not have a clear understanding of this drug's effects. Existing literature has emphasized the necessity for further research into the influence of marijuana use, especially because of the substance's growing popularity and accessibility (Suerken et al., 2016). In addition, there is a gap in the literature regarding the influence of perceptions of marijuana use.

Academic success is very important to the population we are examining, college students. Previous studies focusing on the relationship between marijuana use and academic success have been limited and we are not aware of any studies done in this geographic location measuring the influence of marijuana on academic success (Arria et al., 2015).

Academic Success

While the relationship between marijuana use and other cognitive domains such as long-term memory have been largely explored, the domain of attention has received less research and previous studies have found conflicting results regarding the influence that marijuana use may have on attention abilities in college students/young adults (Petker et al., 2020).

Attention

Hypotheses

- Marijuana users will report lower attention capabilities and self-regulating learning strategies than students who are not marijuana users.
- Marijuana users will report graduating late more than students who are not marijuana users as well as lower GPAs.
- Marijuana users will report that marijuana use negatively influences attention and grades less than students who are not marijuana users.

Method

Participants

Consisted of students enrolled in summer courses at Bloomsburg University. Pilot sample: $n = 38$, $M_{age} = 20.89$, 29 female, 7 male, 2 non-binary/third gender. 89.5 % were White, 7.9 % were Black or African American, and 2.6 % were Asian. Participants included 5 freshman, 11 sophomores, 10 juniors, and 12 seniors. 22 participants had used marijuana (MJ) in their lifetime while 16 had not. Participants were considered MJ users if they had ever used marijuana, but only 9 participants reported currently using marijuana, however, all MJ users reported that they had used marijuana between 2019 and now.

Procedure

An anonymous Qualtrics XM survey was distributed to the instructors of multiple Bloomsburg University summer 2022 courses. Instructors then could distribute the link to the survey and informed consent and decide if they wanted to offer extra credit in their course as compensation. The survey measured basic demographics (age, gender, race, heritage, and academic status) as well as the information detailed under measures. Data were analyzed via Microsoft Excel and IBM SPSS with independent t-tests.

Measures

Marijuana Use

- Modified Drug History Questionnaire (DHQ) (Sobell et al., 1995) - Lifetime use, use duration, last year used, use within last year
- Use in the last 30 days (Wallis et al., 2018)
- Method and motivation for use (Dai & Richter, 2019)
- Age of use onset (Petker et al., 2020)
- Time period use is most frequent

Academic Success

- Motivated Strategies for Learning Questionnaire self-regulation subscale (MSLQ) (Pintrich & de Groot, 1990) – Use of self-regulating strategies that correlate with academic performance
- Self-reported high school, last semester, and current GPA (Suerken et al., 2016)
- Self-reported graduation time and class skipping habits (Arria et al., 2015)

Attention

- The Adult ADHD Self-Report Scale (ASRSv1.1) (Kessler et al., 2005) – Attention abilities within the last 6 months

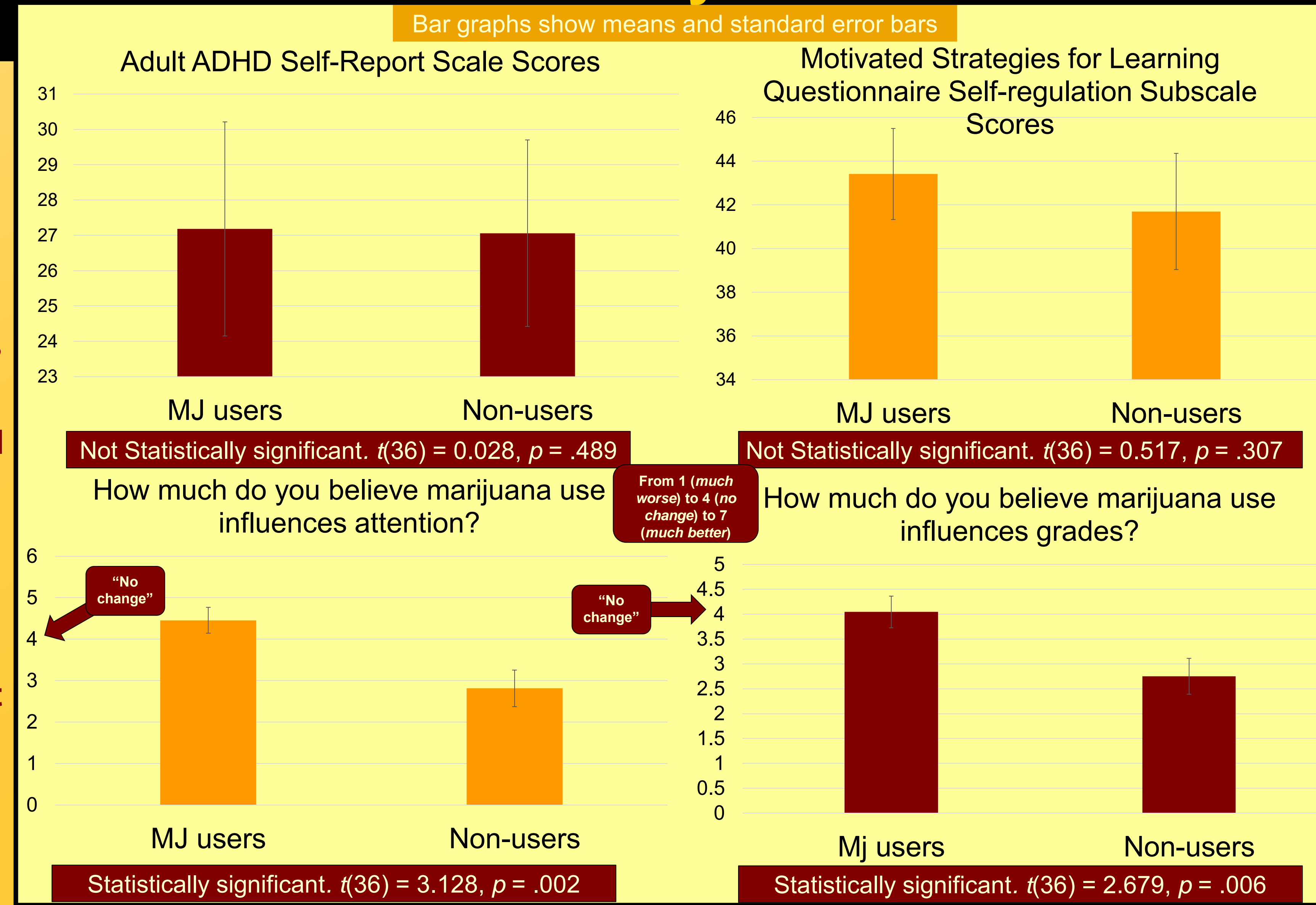
Perceptions

- “How much do you believe marijuana use influences attention?” and “How much do you believe marijuana use influence grades?” possible answers were on a scale from 1 (*much worse*) to 4 (*no change*) to 7 (*much better*)
- “If you have used marijuana, how much do you agree with the following statements: Since beginning to use marijuana, I have had more trouble paying attention and Since beginning to use marijuana, I have had more trouble getting good grades.” possible answers were on a 5-point scale from “totally disagree” to “totally agree” with an additional option of “I have never used marijuana”
- “Is there anything else about marijuana use, attention, and academics that you'd like to add?”

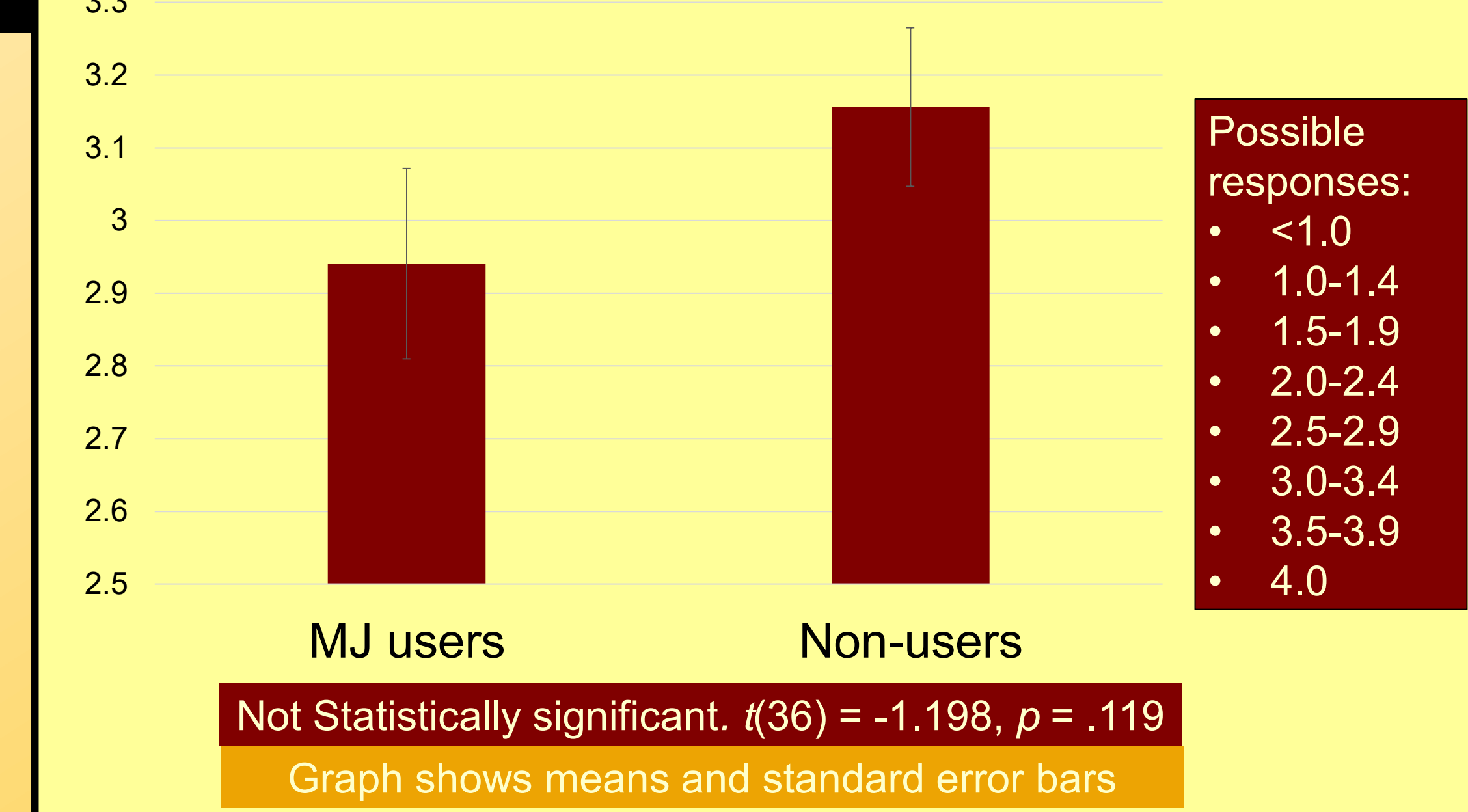
Covariates

- General Health Questionnaire (GHQ-12) (Goldberg & Williams, 1988) - psychological health
- Modified DHQ - assess use of other substances including alcohol, nicotine, cocaine, etc.
- Psychological disorders diagnosis, treatment, medications, symptoms, day-to-day influence
- Involvement with academic accommodations and honors college

Preliminary Results



What is your current cumulative GPA?



“After seeing the effects of people around me after a long-term use, I think that marijuana gives you less motivation, focus, and want to succeed.”

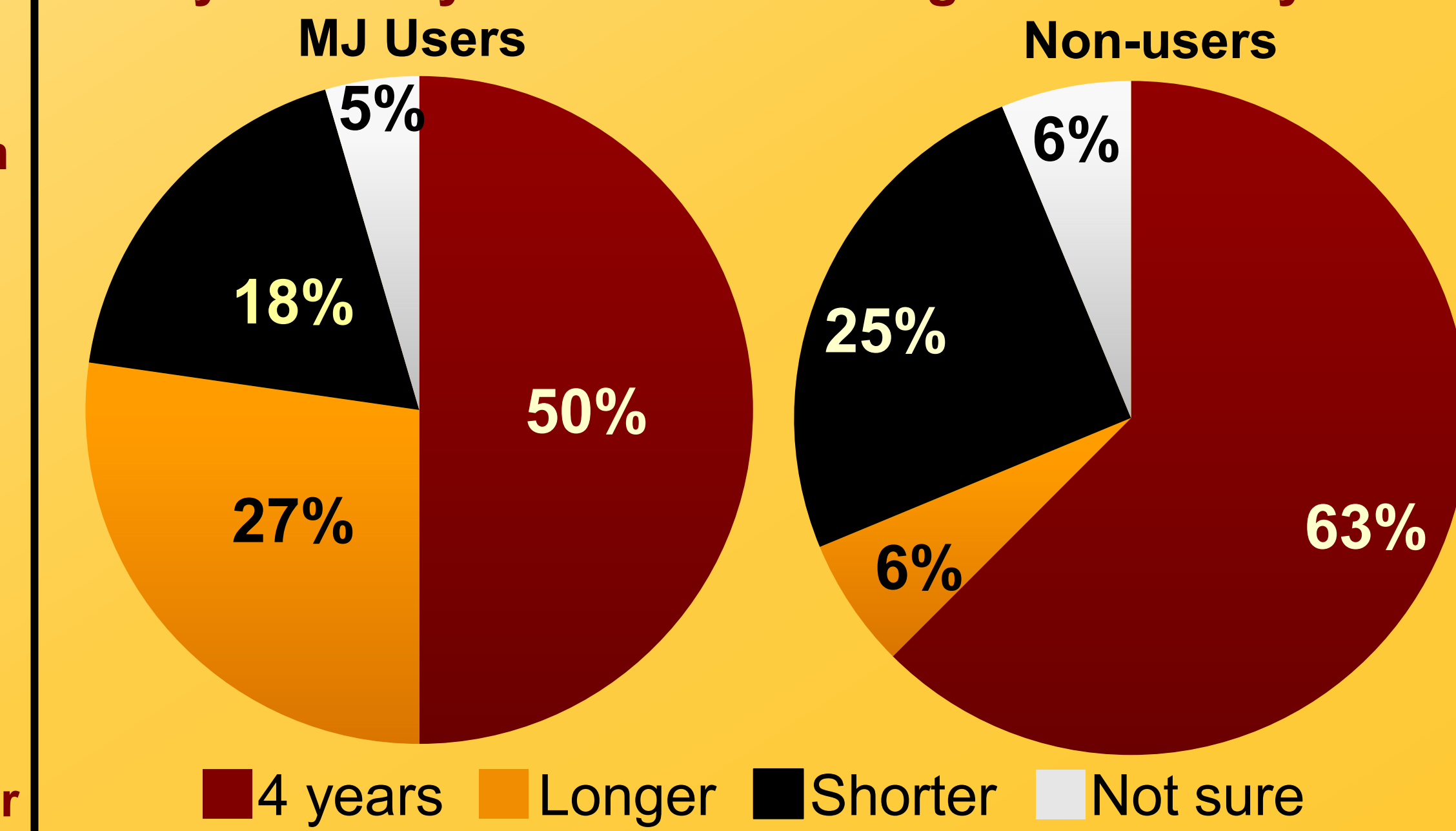
“Marijuana brings my anxiety down to a level that I can actually focus on the task at hand without worrying about future parts of it, the grade, other classes, etc.”

“My academic performance has not changed at all while using marijuana. I still receive good grades and put in all the effort I can in my work.”

“Often people who are using marijuana, are trying to distract from other factors in their life going on.”

“People I know that use marijuana more frequently than I do, seem to not care as much about their academics as before. Almost like it made them lazier all the time.”

“Will you earn your bachelor’s degree within 4 years?”



Discussion

-The measured covariates were not included in the preliminary results for the pilot study.
 -The results of the pilot study showed that there was no significant difference in scores on the ASRSv1.1 between marijuana users and non-users, suggesting that marijuana use may not influence attention abilities in this population. This was not in support of our hypothesis.
 -In addition, there was no significant difference in scores on the MSLQ Self-regulation subscale between marijuana users and non-users, suggesting that marijuana use may not influence learning strategies that can be used to predict academic success. This also did not support our hypothesis.
 -For the questions measuring how much participants believed marijuana use influences attention and grades, the results showed that there was a significant difference between groups as MJ users were more likely to report that marijuana use had less of a negative influence on attention and grades than non-users, which was in support of our hypotheses.
 -The results also showed that there was no significant difference between groups regarding current cumulative GPAs, which was not in support of our hypothesis.
 -The pilot study revealed any necessary changes to be made to the survey before it will be released to a larger recruitment group in the Fall in order to ensure we can accurately test all hypotheses as well as control for confounding variables.

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Effectiveness of Current Mental Wellness Resources for Criminal Justice Professionals

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Introduction

Police Officers in the United States suffer from suicidal ideation at a higher rate than the general population, 25% for females and 23.1% for male officers compared to 13.5% overall (Violanti, 2008). Over 20% of all officers are expected to have suffered from the negative effects of police work in the Northeastern part of England (Burnett et al., 2019). Suicidal ideation and other negative effects result from the build-up of compassion fatigue and burnout experienced by professions that help people for a living; therapist, police officers, and probation officers (Figley, 2002). Officers who use either organizational or peer support resources are less likely to suffer from burnout and compassion fatigue, while those who only go through a formal debriefing resulted in higher levels of burnout, but no change in fatigue, (Miller et al., 2017). This study was the only US based study found on effective resources given to officers.

Goals

- Using the Professional Quality of Life Scale (ProQOL) the study examined the mean score for compassion satisfaction, burnout, and secondary traumatic stress / compassion fatigue experienced by criminal justice professionals.
- Future analysis may also examine if race, gender, marital status, years of service, size of agency where employed, and rank or position plays a role in the level of compassion satisfaction, compassion fatigue, and burnout.
- Previous research found psychotherapy (Martinmäki et al., 2021), organizational support, peer support, debriefing (Miller et al., 2017), yoga programs (Smith et al., 2022), and chaplain services to be the most widespread and effective.
- Future analysis will also examine the availability of mental health resources and their impact on compassion satisfaction, burnout, and secondary traumatic stress / compassion fatigue.

Methods

This study was a mixed methods study with the quantitative section being completed during the summer URSCA session. The qualitative portion and additional quantitative data analysis for this study will be completed during the fall of 2022 during a Sociology Independent Study at Bloomsburg University. This study was approved by the Bloomsburg University IRB.

Survey

- The survey contained demographic questions such as; race, gender, marital status, years in the field, size of agency where employed, education level and rank or position.
- Approval was obtained to use the The Professional Quality of Life Scale 2nd Edition from the Center for Victims of Torture. The ProQOL is designed to measurement compassion satisfaction, burnout, and secondary traumatic stress / compassion fatigue (Stamm, 2010).
- Data related to mental health resources offered to the professionals was also gathered. Examples include; therapy, peer support programs, yoga, and Chaplin Services and their perceived effectiveness. These resources were chosen from existing research related to the ProQOL.

Distribution

- The survey was distributed via Qualtrics to multiple chiefs of police, county sheriffs, wardens, and chief probation officers throughout Pennsylvania via email using an anonymous link since anonymity was crucial to many of the participants. The agency administrators were requested to forward the survey to the criminal justice professionals employed by their agency.

Analysis

- The data was exported from Qualtrics to SPSS for analysis.
- ProQOL's questions were scored as established by Stamm (2010). The three categories that are measured via the ProQOL are compassion satisfaction, burnout, and secondary traumatic stress (STS) / compassion fatigue.
- The intent in the preliminary analysis was to determine the mean scores for compassion satisfaction, burnout, and secondary traumatic stress /compassion fatigue.

Results

Demographic Information

- There were a total of **61** participants that completed the survey.
- Sex**
 - 46 (75.4%) of participants were male and 15 (24.6%) of participants were female
- Race**
 - 60 (98.4%) of participants were white and 1 (1.6%) of participants were Asian
- Marital Status**
 - 49 (80.3%) of participants were married
 - 2 (3.3%) were divorced, 3 (4.9%) were separated
 - 5 (8.2%) were never married
 - 2 (3.3%) of participants did not answer this question.
- Years of service**
 - 4 participants (6.6%) had 0-5 year of service
 - 5 participants (8.2%) had 6-10 years of service
 - 3 participants (4.9%) had 11-15 years of service
 - 5 participants (8.2%) had 16-20 years of service
 - 8 participants (13.1%) had 21-25 years of service
 - 35 participants (57.4%) had greater than 25 years of service
- Agency size**
 - 18 participants (29.5%) were employed by agencies that employed less than 25 people
 - 14 participants (23.0%) were employed by agencies that employed between 26 and 50 people
 - 26 participants (42.6%) were employed by agencies that employed greater than 50 people
 - 3 participants (4.9%) did not answer this question
- Education Level**
 - 5 participants (8.2%) had a high school diploma (or equivalent)
 - 3 participants (4.9%) earned an associates degree
 - 27 participants (44.3%) earned a bachelor's degree**
 - 20 participants (32.8%) completed more than a bachelor's degree**

Cronbach's Alpha

- Cronbach's Alpha for reliability was evaluated for each of the ProQOL scales. Cronbach's alpha is a measure of internal consistency. Cronbach's alpha is generally acceptable if it is higher than 0.70 (Field, 2018). The Cronbach's Alpha scores for this study were all above 0.70. The scale appears to have internal consistency.
- The Compassion Satisfaction alpha for this study was 0.94. The Compassion Satisfaction alpha reported by Stamm (2010) was 0.88.
- The Burnout alpha for this study was 0.84. The Burnout alpha reported by Stamm (2010) was 0.75.
- The Secondary Trauma alpha for this study was 0.87. The Secondary Trauma alpha reported by Stamm (2010) was 0.81.

Compassion Satisfaction

- The mean score for compassion satisfaction for this study was 38.58. A score between 23 and 41 is moderate satisfaction.

Burnout

- The means score for burnout in this study was 22.51. A score below 23 reflects positive feelings about the ability to be effective in your work.

Secondary Traumatic Stress / Compassion Fatigue

- The mean score for secondary traumatic stress / compassion fatigue was 22.03. A score of 22 or less is related to a little secondary traumatic stress / compassion fatigue.

Discussions

- Additional analysis will be conducted on the data during the Fall 2022 semester as the project is continued as a Sociology Independent Study.
- Interviews will also be conducted during the Fall 2022 semester to gather qualitative data related to this study.
- During the Fall 2022 Sociology Independent Study the data will be analyzed to determine if agency size impacts compassion satisfaction, burnout, and secondary traumatic stress/compassion fatigue. Not enough variability exists in the other variables to use them in an analysis.
- It appears that a significant amount of agency heads completed the survey but few of the officers they employed completed the study. Therefore the results cannot be generalized to younger officers. Additional studies or additional data should be collected to examine compassion satisfaction, burnout, and compassion fatigue/secondary trauma experienced by officers that are not administrators.
- It is rare for law enforcement agencies in Pennsylvania to require college, however, other criminal justice agencies do require a bachelor's degree. This makes it challenging to examine these agencies together in one study.

Conclusions

- It is a challenge to get criminal justice professional to talk about and share information about mental health related issues.
- Law enforcement agencies were the most frequent contacted but had the least amount of response.
- It would be beneficial to study law enforcement, corrections, and other criminal justice professional in separate studies instead of in a combined study.
- More data should be gathered from lower ranking employees to determine if there is a difference in scores based on rank / position held in the agency. Administrators may have experience less burnout and secondary traumatic stress and greater compassion satisfaction because they are in an administrative role.

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Attitudes and Opinions of Prison Officials and Students on Prison Reform: A Qualitative Study

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INTRODUCTION

The United States of America has the highest incarceration rate in the world, 664 out of 100,000 people incarcerated. This meant nearly 2.1 million people were incarcerated as of 2021 (Widra and Herring 2021). When comparing this number to Scandinavian countries in particular, it is alarming. Denmark has an incarceration rate of 72, Sweden's is 68, Norway's is 54, and Finland's is 53 (Widra and Herring 2021).

Not only is the U.S. incarcerating people at a higher rate than any other country, once those people get released from prison, 95% of whom are in state prisons, most of them will return to incarceration (James 2015). The U.S. has one of the highest recidivism rates in the world, being 76.6% (Benecchi 2021), which is much higher than Norway (20%) and Denmark (27%) (World Population Review 2022). These numbers highlight a large disparity and show that the U.S. is in need of reform.

Although plenty of research has been conducted to understand the disparities of the U.S. system and the need for prison reform, little to no research has been done to try and understand the attitudes and beliefs of prison officials and employees with regard to prison reform, the people who would be responsible for putting policies into action within the prisons. Silva (2006) studied the attitudes of college students and the general population on prison reform but did not target prison officials specifically.

STUDY AIMS

1. Examine the opinions, attitudes, and beliefs of prison officials and students studying criminal justice regarding prison reform.
2. Provide valuable insight to those seeking to make prison reform policies on how the actors involved will feel and react.

METHOD

In this study I conducted 30–45-minute semi-structured interviews by utilizing video calls and phone calls. Participants were either criminal justice students or people who currently work in or previously worked in prisons in the U.S. These volunteers were found through existing contacts and through snowball sampling. My current findings are based on three interviews, all from students. Up to this point I have interviewed seven people, four students and three professionals. By the end of my project, I hope to have around fifteen participants with close to equal amounts of students and professionals. Interviews were recorded using a digital audio recorder and then transcribed. Transcripts were then coded and analyzed.

RESULTS

Although the results are tentative, as this study is not complete, some compelling discoveries have arisen, nonetheless. The biggest take away I have found thus far after analyzing three interviews is that students tend to have a favorable view of rehabilitation. All participants believed that rehabilitation should be the main purpose of prisons. All participants also believed rehabilitative programming such as education, job training, and treatment were important. One participant, when asked about these types of programs, said she "believed all of it" and said, "you have to educate but as you're educating, giving them treatment to help." With this statement, she emphasized the need for not just one program, but for an all-encompassing approach to rehabilitation, a sentiment put forth by all participants.

During my interviews I presented to the participants a description of a different prison model, the Scandinavian prison model, and I recorded their opinions and views on it. Most of the participants liked the model and believed it should be emulated in the U.S. due to its success abroad and in select scenarios in the U.S. One participant said, "I think we should definitely try and emulate it, if nothing else we can look at the data," referring to the recidivism rates. A common theme when looking at these responses was that some of the participants liked the Scandinavian model and thought the U.S. should emulate it but believed it may take time and that there should be a slow integration of new programs. One participant stated that she thinks "it would take a long time to be able to get to the open cells" but that she "could see the treatment, the more open relationships, that kind of stuff soon."

A second big theme that was discovered after analyzing the data was that compassion for inmates was common. When participants discussed their favoring of rehabilitation, they tended to also convey a level of compassion. One participant stated that "offering those rehabilitation programs in prisons...like the music, the arts, that gives them something to do when they get out of prison because right now in America when people get out of prisons they're just thrown into the streets." Participants also showed feeling a level of compassion in their responses when discussing the conditions of the prisons. One participant talked about the cells and living conditions afforded to inmates and believed inmates should have more humane conditions. She stated when talking about cells that they were "so small there's not even room to live in there. You're not treated like a human."

Compassion was also a theme when discussing staff behavior towards inmates. One participant believed prison staff "think their job is just locking people up and they treat them like animals" which makes it hard for the inmates to rehabilitate, another sentiment that was common in two of the interviews.

The third major theme discovered was the concept of stigma. All participants discussed this in two distinct ways. The first being the stigma that comes from society and the inmates' communities, especially upon release from prison. Participants talked about how upon release from prison, the inmates' communities continue to hold that stigma against them which makes it hard to reintegrate.

RESULTS (continued)

They all discussed the desire to see that stigma go away with one participant saying "I know it follows them out of prison which is why they return a lot. No one wants to hire inmates, no one wants to lease to inmates, it pops up on every background check. So, I think maybe de-stigmatizing that labeling." The other type of response from participants on the topic of stigma came in the form of the stereotype afforded to inmates specifically. All participants discussed how all inmates have a stigma of being aggressive and dangerous, but that that is not true for all, with one participant stating, "sometimes I view them as aggressive, though I recognize a lot of that is just stigma and most of them aren't in there for violent offenses...So I know that's not really accurate, but that is ultimately where my mind originally jumps to." When I asked what came to mind when they thought of inmates, another participant even made the statement "inmates? Misunderstood." All conveyed the sentiment that all inmates have stigma, but that it is not always warranted.

CONCLUSIONS

- All participants favor some form of rehabilitation for inmates.
- Most participants like the Scandinavian prison model and think it should be emulated in the U.S. slowly.
- All participants conveyed compassion for inmates in some form.
- Stigma was identified by all participants as being a problem.

I have learned that all participants have a favorable view of rehabilitation in some form and think rehabilitative programming is important. They all also believe rehabilitation should be the main purpose of prisons. Most of the participants liked the Scandinavian model and believed it should be emulated in the U.S. but agreed there needs to be a slow integration. They all also conveyed some level of compassion for inmates when discussing the need for more rehabilitation, more humane conditions, and better treatment from the prison and society. Lastly, I found that all participants recognized that stigma has been afforded to inmates and all discussed the importance of that stigma being eradicated. I am still in the process of analyzing data, so these results are tentative, and I will have more data from participants who are professionals. Through this research I seek to examine the opinions and attitudes of those who are involved and hope to be involved in the prison system to be able to provide valuable insight to those trying to enact prison reform policies, and so far, I have found that students see rehabilitation and forms of prison reform as important. This group may not be a barrier to reform. In fact, they may push for and facilitate it.

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The Implementation of Augmented Reality and Low Latency Protocols in Musical Instrumental Collaborations

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Emerging Scholars

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Abstract

The project attempts to use augmented reality as a medium of sound production. A synthesizer and two modulators are created in the augmented reality environment. The user can tweak the synthesizer and modulators inside the headset while still being able to adjust the pitch of the synth by playing a physical MIDI instrument. The project was created using the Unity game engine. Various other packages and tools such as the Passthrough API, Oculus Interaction SDK were used. Functions for different kinds of wave forms were used for the synthesizer and the modulators. Further development such as adding multi-user interaction, other kinds of digital instruments, and improving on the existing control buttons and leavers are considered.

Introduction

This is an experimental project with a purpose of implementing sound producing mediums to the VR headset while still being able to play the actual musical instruments in the user's hands. The project is at its early stage with basic controls and augmented reality environment set up, and a built in synthesizer that produces several different sounds. The synthesizer works well with two modulators that are also implemented: frequency modular and amplitude modular.

Augmented Reality Environment and Hand Tracking

The environment was implemented so that the users can see the surroundings and the musical instruments through their VR headsets. Hand tracking is also implemented so that the users can use their hands to interact directly with the virtual objects instead of having to grab physical controllers to interact with the virtual objects.

Transmitting MIDI Signal from Computer to Headset

The keyboard outputs MIDI signals to the connected computer. The computer transmits the signals using a network protocol to the headset. This ensures that no wire is plugged to the headset when playing musical instruments.

Synthesizer

The synthesizer uses wave forms to produce sound. It produces four different kinds of wave forms: sine wave, triangle wave, square wave, and sawtooth wave. Each of them have different sounds.

Frequency Modular

The frequency modular is an object created to modulate the frequency of the oscillator inside the synthesizer. The modulation also has four different kinds of wave forms.

Amplitude Modular

The amplitude modular is an object created to modulate the amplitude of the oscillator inside the synthesizer. The modulation has the same four different kinds of wave forms.

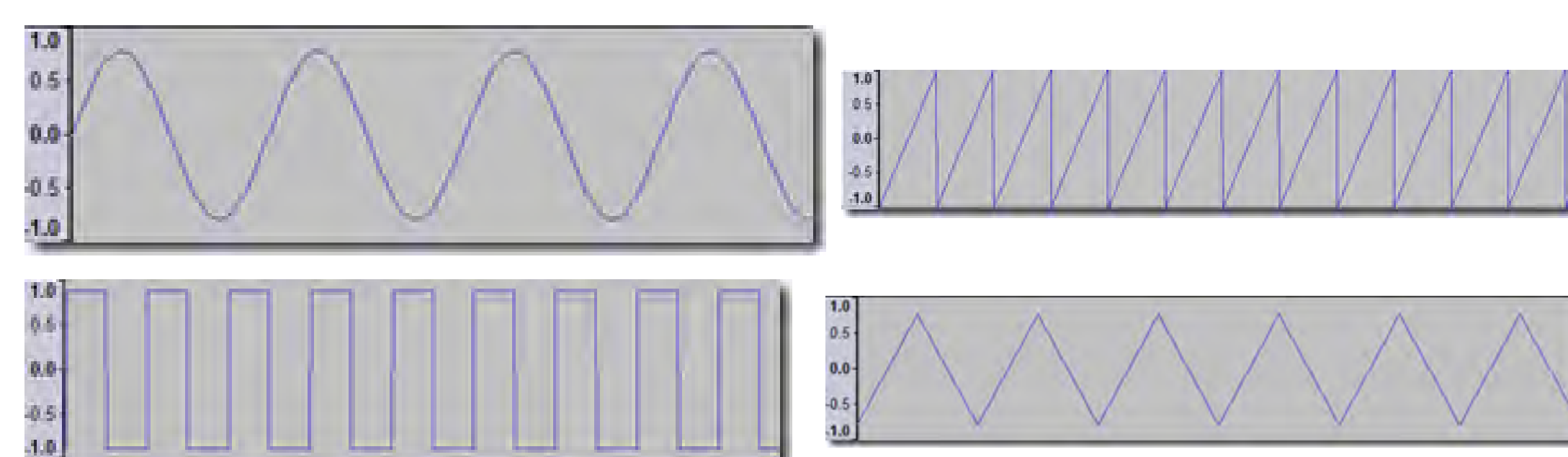
Methods

Tools used throughout the project

- Oculus Quest 2 Headset
 - Allows programs to run on the headset without connecting any wires to other devices
- Unity and C#
 - The scene was set up in the Unity game engine and game objects are coded using Unity C#
- Oculus Passthrough API
 - The only augmented reality API available for Oculus headsets
 - Does not allow passthrough when running the AR program on the computer
- Oculus interaction SDK
 - Hand tracking and hand grab interactions
- UDP protocol using extOSC in Unity C#, PythonOSC in Python
 - Transmitting MIDI signal in the format of an array
- VR Ready Controls
 - An Unity asset with leavers and buttons and the basic code for them
 - The buttons control the state of the synthesizer and the modulators (On/off), other buttons control the wave forms of the three game objects.
 - Leavers control the volume, amplitude, and frequency.

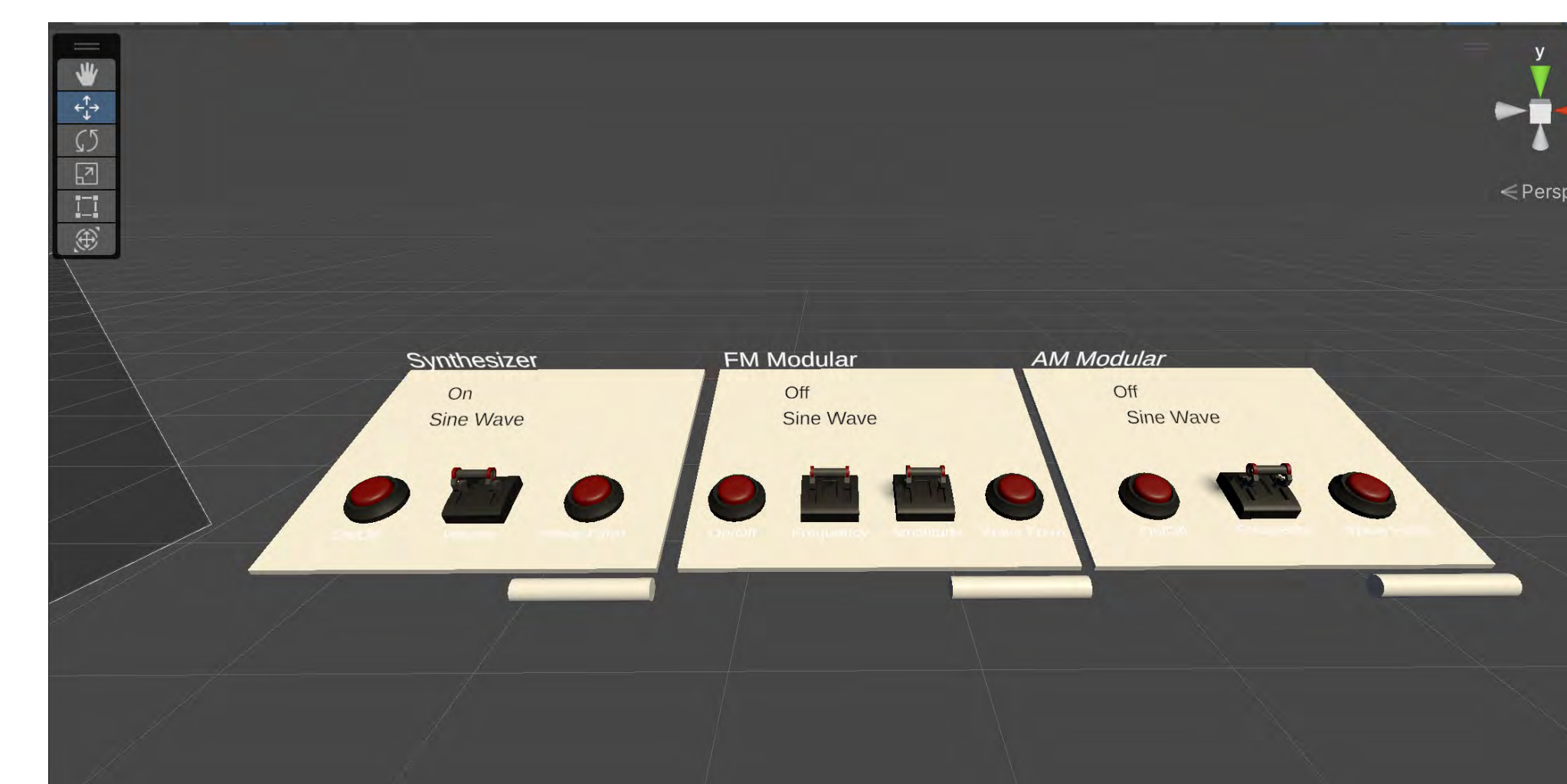
Formulas of wave forms are used to make oscillators inside synthesizer

- Sine wave: $\text{Sample} = \text{Amplitude} * \sin(t * i)$
- Square wave: $\text{Sample} = \text{Amplitude} * \text{sgn}(\sin(t * i))$



Images from: Intro to Audio Programming Part 4, Microsoft Docs/Blog Archive/Game Theory [1]

Results



The synthesizer works fine and produces sound through the headset. Tweaking the synthesizer with the modulators produces a variety of different kinds of sounds.

Discussion

Result and Drawbacks

- The result is a synthesizer implemented inside the headset.
- The synthesizer's interface is not movable by the user because of the physics of the buttons and leavers (they get stuck by wobbling when moved).
- The sawtooth wave forms inside the two modulators still has some problems functioning. I am trying to find simpler sawtooth functions that I can use.
- Due to the nature of the wave functions, heavy computation capability is required. The Quest 2 headset still lacks a bit in this field. There is noticeable latency when the synthesizer produces sound after user physically pressing the keys.

Possible Ways of Improvement and Future Plans

- The button and leavers should be re-implemented without physics so that the interface of the synthesizer can be moved without buttons and leavers wobbling.
- Change the wave functions to pre-generated arrays of numbers that follow the wave forms.
- Will implement an arpeggiator for the synthesizer
- Will add in avatars for the user and connect two headsets so they can see and hear each other

Conclusion

The project in its state right now might not be a product that can be provided to people and function as a more effective way of producing music, but it can be something that is more effective in the future (with lighter and more powerful headsets and MIDI instruments with built in networking).

References

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Acknowledgements

Thanks to my mentor Dr. Paul J. Botelho for helping and giving directions to the project. Thanks to Emerging Scholars and the Schotz Family Fund for this opportunity and funding.

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Abstract

Histones are proteins which bind to DNA forming the nucleosome core particle. Nucleosomes typically have two copies each of histones H2A, H2B, H3, and H4. Histones regulate DNA-templated processes. The most abundant variant of histone H2A is H2A.Z. H2A.Z is placed in discreet regions of chromatin and misplacement can lead to cellular defects such as issues with transcriptional regulation. The same chaperones deposit H2A and H2A.Z, however the cell can differentiate between the two; we are interested in finding residues that distinguish H2A from H2A.Z. We hypothesized that threonine 87 is one of these residues. Mutation of threonine 87 leads to cellular defects like those in the Δ htz1 strain. To address this; WT, Δ htz1 and htz1 T87A were grown, the chromatin was isolated, and Western blot analysis was done. It was found that the T87A mutation led to diminished chromatin levels. This contrasts previous findings that the T87A mutation does not appear to affect placement of H2A.Z at gene promoters.

Figure 1. H2A.Z sequence alignment

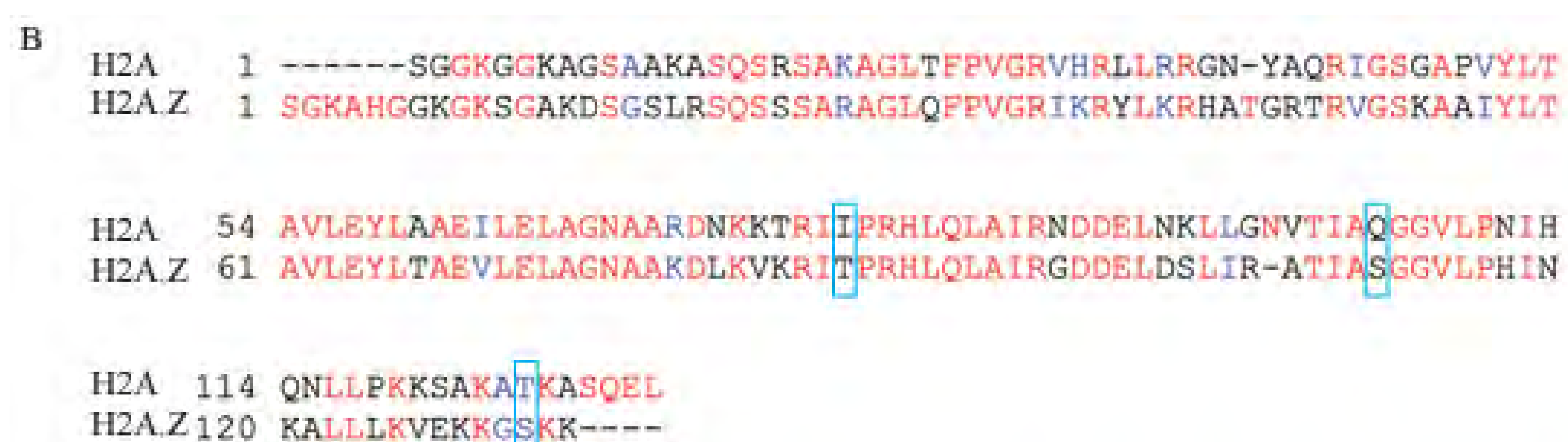


Figure 1. A. H2A.Z is located at the boundary of the telomere and at the promoters of several genes. Most nucleosomes contain histone H2A whereas approximately 10% contain histone variant H2A.Z. The sequence alignment of both histone H2A and H2A.Z is not conserved in threonine 87. Threonine 87 could potentially be a residue which allows the cell to differentiate between H2A and H2A.Z. The residue is variant between H2A and H2A.Z, the threonine of H2A.Z aligning with the isoleucine of H2A.

Figure 2. The position of threonine 87

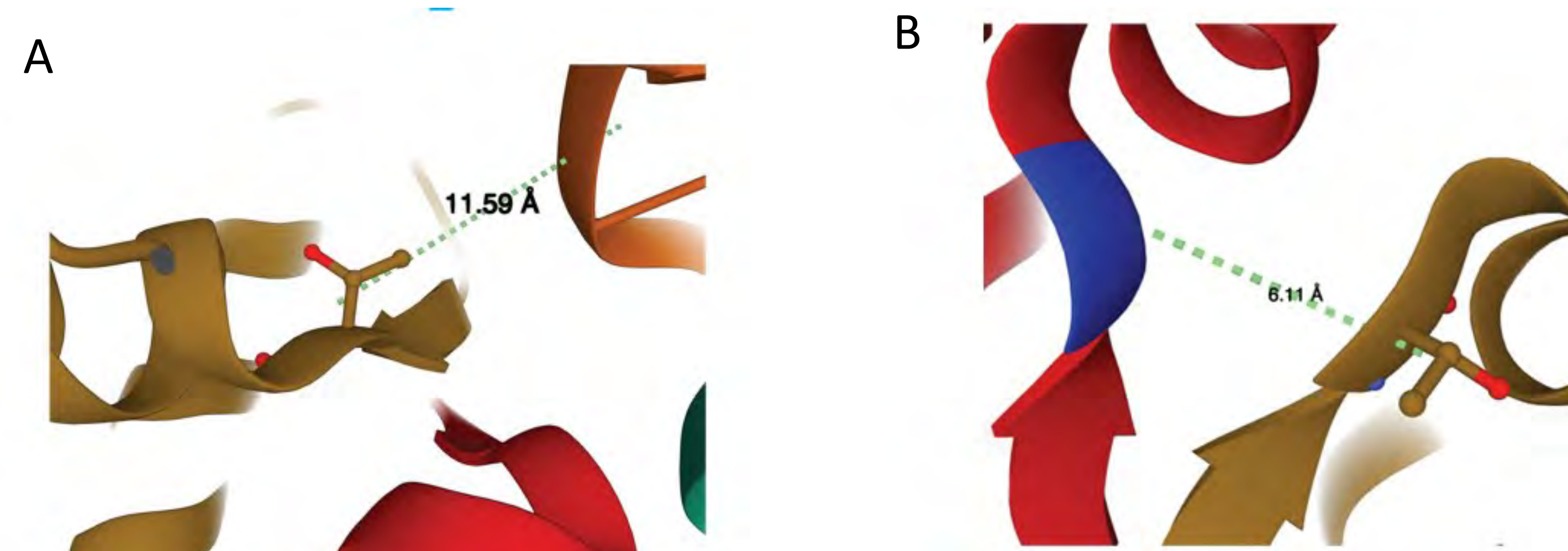


Figure 2. A. Threonine 87 is 11.59 angstroms away from the DNA backbone and leaves adequate space for phosphorylation. **B.** Threonine 87 is 6.11 angstroms away from H2B.

Figure 3. mRNA levels and protein concentrations of chromatin samples.

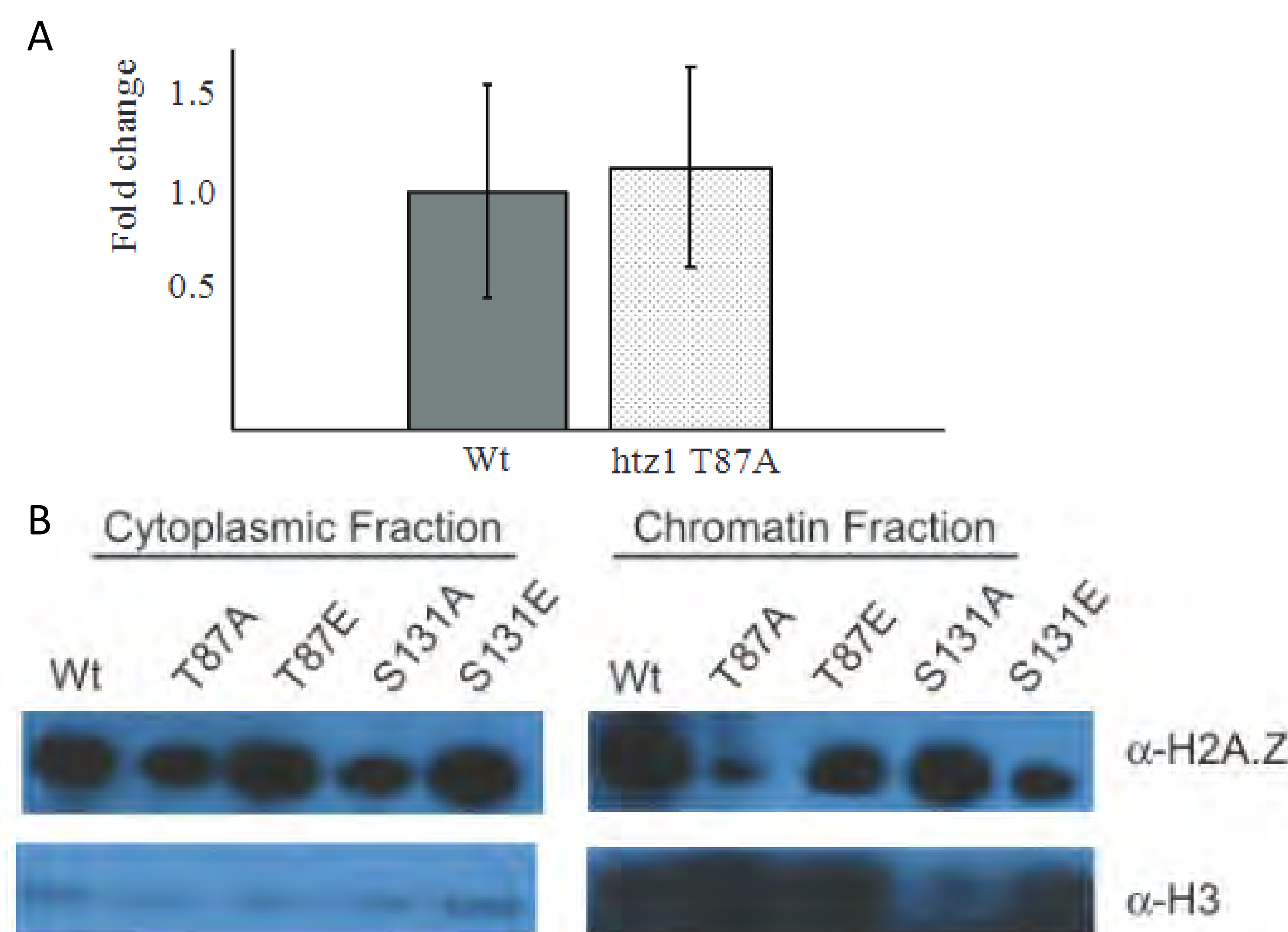


Figure 3. A. The graph shows that the mRNA levels in both WT and T87A were found to be similar after monitoring protein levels in H2A.Z. **B.** The cytoplasmic fractionation shows that mutation of T87 to alanine leads to decreased protein levels in whole cell extract in comparison to WT. The chromatin fractionation shows that protein levels in cells expressing the htz1 T87A mutant are down in comparison to those in wild-type when studied in histone variant H2A.Z.

Figure 4. Graph of standard curve from Bradford assay.

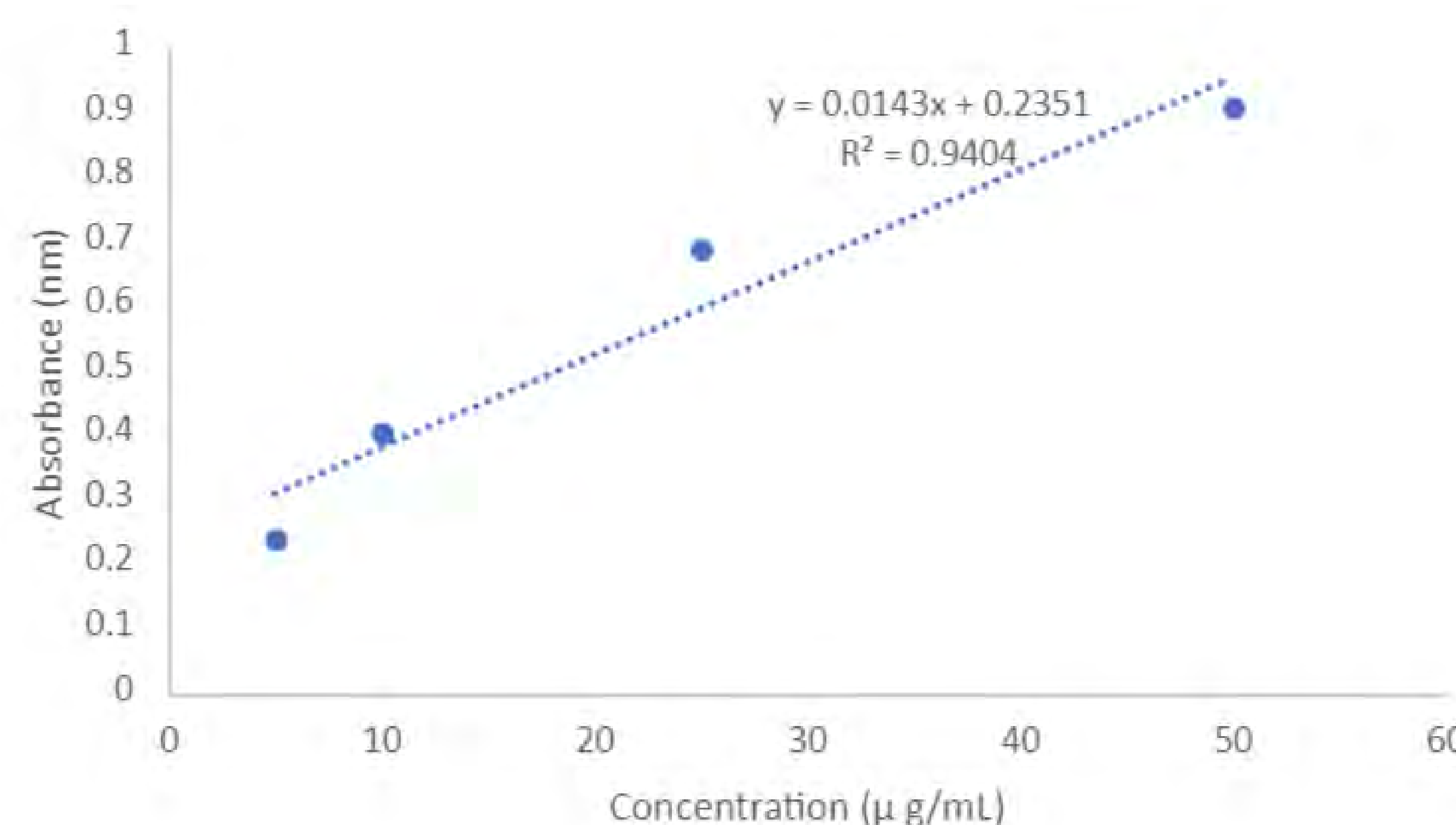


Figure 4. The standardization of protein samples was done via Bradford assay. The Bradford assay generated an equation which was used to calculate the concentration of protein in chromatin samples. All chromatin samples were diluted to the lowest calculated concentration before a Western blot analysis was done.

Table 1. Protein concentrations of the chromatin samples.

Sample	Concentration (µg/mL)
WT ¹	3.55
WT ²	10.95
WT ³	37.75
htz1 Δ ¹	7.52
htz1 Δ ²	41.79
htz1 Δ ³	16.07
htz1 T87A ¹	30.57
htz1 T87A ²	43.85
htz1 T87A ³	39.73

Conclusion

The threonine 87 mutation leads to diminished protein levels in histone variant H2A.Z. The low protein levels in the threonine 87 mutation are not caused by a difference in mRNA between WT and the mutant as mRNA levels had relatively the same concentration between H2A.Z and H3.

Future Work

We plan to determine if the mutation has other chromatin impacts, specifically histone H3 lysine 56 acetylation. We would like to study protein stability to determine if the loss of the protein is due to instability.

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Acknowledgments

We would like to thank Susquehanna University and the McGrath Scholars program for financial support for this project. We would also like to thank Dr. Brian Strahl for providing the yeast strains used in these studies. I would like to thank fellow lab members for their contributions to this study.

Emily Larkins, Emily Harling, Elizabeth Misner, Taylor Nattress and Dr. Michael Parra
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Abstract

In eukaryotic genomes, DNA is wrapped around histones to create nucleosomes that form chromatin. The association between DNA and histone proteins leads to histones having an important role in cell cycle progression, DNA repair and transcription. H2A.Z is a histone variant of H2A. H2A is replaced by H2A.Z in about 10% of the nucleosomes in the yeast *Saccharomyces cerevisiae*. It has been observed that when H2A.Z is mutated to replace threonine 87 with alanine the cell becomes more sensitive to stressors than if H2A.Z is deleted. This mutation also resulted in decreased protein levels of H2A.Z which may lead to incorrect deposition of H2A.Z in chromatin. Incorrect deposition may, in turn, result in protein degradation. The decreased protein levels of H2A.Z show that the mutation also affects the deposition of H2A.Z in chromatin. These results suggest that the threonine 87 residue is important for the function of H2A.Z.

Figure 1: H2A vs. H2A.Z

A. H2A 1 -----SGKGGKAGSAAKASQSRSAKAGLTFPVGRVHLLRRGN-YAQRIGSGAPVYLT
H2A.Z 1 SGKAHGGKSGAKDSSGLRSQSSARAGLQFPVGRVHLLRRGN-YAQRIGSGAPVYLT

H2A 54 AVLEYLAAEIIELEAGNAARDNKKRTRIPRHLQLAIRNDELNKLGNVTIAQGGVLENIH
H2A.Z 61 AVLEYLAEVLELAGNAARDLKVKRITIPRHLQLAIRNDELNKLIR-ATIASGGVLEPHIN

H2A 114 QNLLPKKSAKATKASQEL
H2A.Z 120 KALLLKVEKKGSKK----

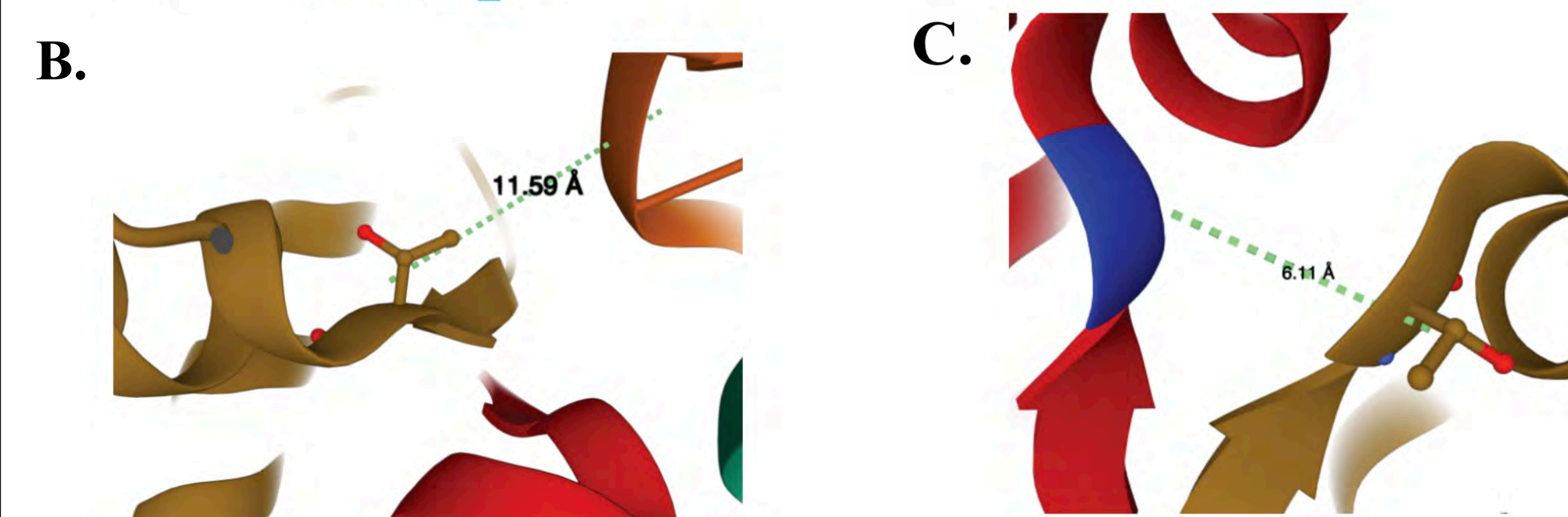


Figure 1: H2A.Z is a histone variant of H2A and they share 65% identity. We are investigating the threonine 87 residue as it differs to the corresponding residue in H2A (as shown in Figure 1A). This difference in the amino acid sequence suggests the threonine residue may play an important role in the cell differentiating between H2A and H2A.Z. Figure 1B shows the short 11.59 Å distance between the threonine 87 residue and the DNA. Figure 1C shows the 6.11 Å distance from threonine 87 to the H2B interface.

References

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2. Luger, K., Mäder, A.W., Richmond, R.K, Sargent, D.F., and Richmond, T.J. Crystal structure of the nucleosome core particle at 2.8 Å resolution. (1997) Nature, 389: 251-260.

Acknowledgements

I would like to acknowledge Susquehanna University, Summer Research Fellows and my fellow lab members Kaitlyn Galliher, Emma Oley, Bri Watts and Isiah Blatt.

Figure 2: Use of Plasmids in One Step Transformation

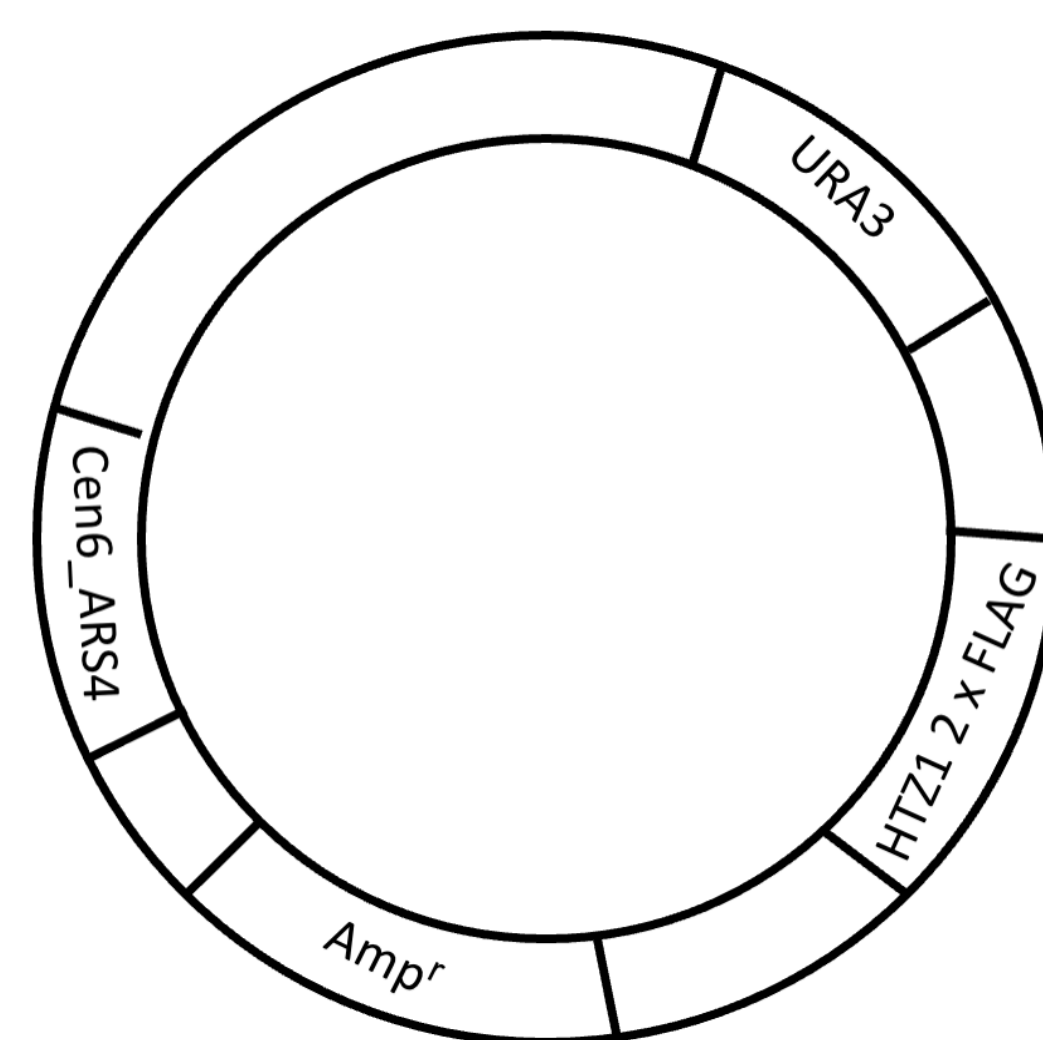


Figure 2: To investigate how the threonine 87 mutation (to replace threonine with alanine) affects how H2A.Z interacts with its chaperone proteins; a one step transformation was carried out on yeast strains YMP213, YMP216, and YMP218. YMP213 has the chaperone protein CHZ1 tagged, YMP216 has the chaperone protein NAP1 tagged, and YMP218 has the chaperone protein SWR1 tagged. A one step transformation was carried out with two different plasmids PMP008 and PMP035. The plasmid PMP008 contains wildtype H2A.Z. Whereas the plasmid PMP035 contains the gene for H2A.Z with the T87A mutation. The gene that codes for H2A.Z is HTZ1 and is labelled on this figure. The Amp^r gene is a marker for bacteria and the URA3 gene is a marker for yeast. These markers allow you to know if the plasmid has been taken up by bacteria or yeast. The Cen₆_ARS4 gene on the plasmids we insert codes for an artificial centromere. The artificial centromere allows for the plasmid to be replicated and passed onto the daughter cells.

Figure 3: Successful Transformants

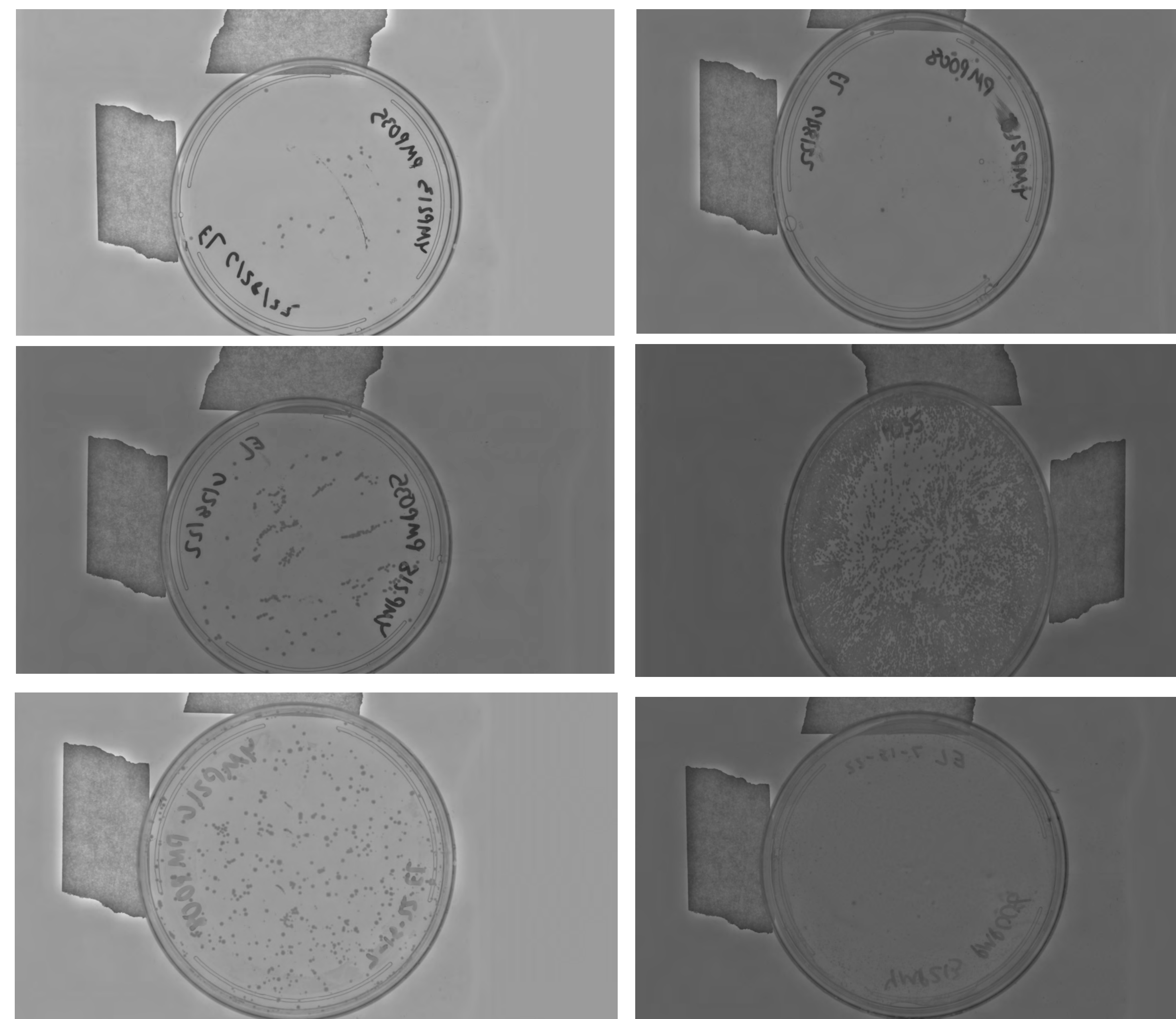


Figure 3: A. After the one step transformation has been carried out the yeast cells are grown up on SC-Ura plates and if colonies are observed it shows us the cells have successfully taken up the plasmid. The cells would not be able to survive on the plate without the plasmid. The plasmid contains the gene that allows the cell to produce Uracil a nitrogenous base required for the cell to make RNA.

Figure 4: A. The HAR Domain, B. The Cell Cycle, C. HAR Domain Mutants Affect Cell Cycle Progression

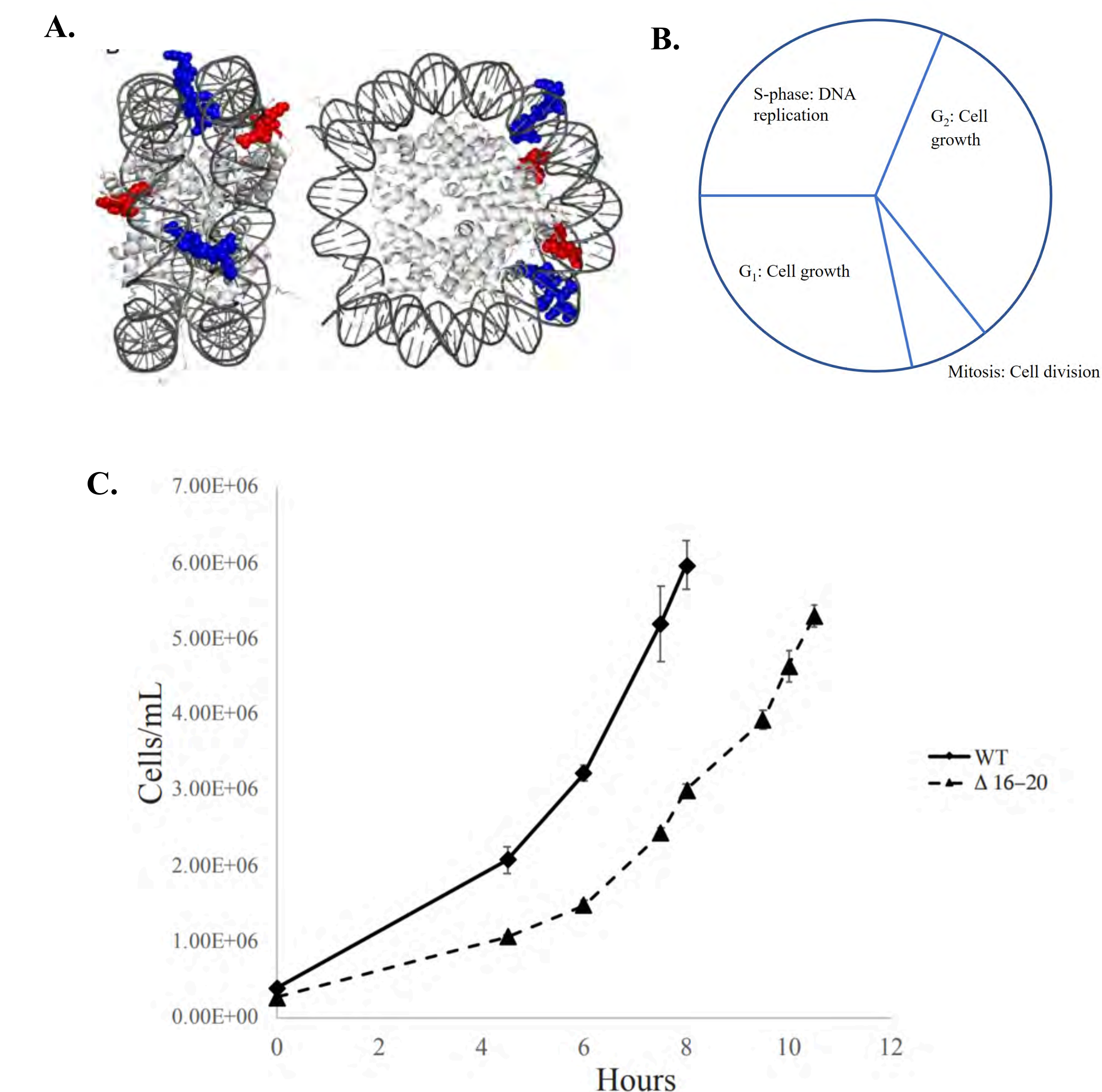


Figure 4: This graphic depicts a nucleosome core particle that includes the histone H2A, represented in red (5A)¹. Deletion of the histone H2A Repression domain (HAR), which consists of amino acids 16-20, leads to impaired cell growth. The data collected in figure 5C shows that the H2A mutant is a slow grower which is likely due to the HAR domain having an effect on cell cycle progression. We hypothesized this was due to misregulation of the cell cycle (5B), particularly the G₂/M transition. We monitored the expression of several genes known to promote cell cycle progression in strains bearing HAR mutants. The expression of genes was investigated using RT-PCR.

Conclusions

- We successfully transformed the TAP-Tagged strains
- HAR mutants are slow growers likely due to defects in cell cycle progression

Future Directions

We plan to carry out a TAP-tag purification on the successful transformants resulting from the one step transformation of YMP213, 216, 218 using plasmids PMP008 and PMP035. This will allow us to see the interaction between the H2A.Z mutant and its chaperone proteins.

We also plan to carry out an RT-PCR on a wildtype yeast strain, HTA1Δ 16-20 strain, and HTA1Δ 16-20 Ala strain using a specific set of primers which target genes required for the progression from the G₂ to M phase of the cell cycle.

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Abstract: Most eukaryotic cells contain a complex network of cytoskeletal proteins that play vital roles in a range of cellular processes such as cell motility and cell division. Cells achieve these functions by altering their cytoskeletal components--actin, microtubule, and intermediate filaments by tuning the binding proteins and ionic conditions. We use optical tweezers and confocal microscopy to characterize how varying the relative concentrations of actin-vimentin impact the mechanics and structural dynamics of the actin-vimentin composites. We show that filamentous actin (F-actin) and vimentin intermediate filaments (VIFs) form interpenetrating networks. Upon increasing the relative concentration of the proteins, we observe that the force response of the composite increases monotonically. An important insight emerging from this work is that F-actin and VIFs interact within the cell cortex, enabling a cell's mechanics and structural dynamics.

Procedure: Actin monomers suspended in G-buffer [2 mM Tris, pH 8.0, 0.2 mM ATP, 0.5 mM DTT, and 0.1 mM CaCl₂] are polymerized in F-buffer [10 mM Imidazole, pH 7.0, 50 mM KCl, 1 mM MgCl₂, 1 mM EGTA, 0.2 mM ATP]. Purified vimentin is dialyzed against urea-containing buffer by reducing urea concentration in a stepwise fashion from 8 to 0 M urea concentration. Assembly of the network took place in a custom-built flow cell. Composite networks of actin-vimentin were formed at the molar ratios of 0, 0.25, 0.5, 0.75, and 1, with a fixed total protein concentration of 11.6 μM. A trace amount of 4.19 μm (diameter) fluorescently labeled polystyrene beads are mixed and allowed to polymerize for 30 min before measurement. Force data is collected by optically driving the microspheres through the composite at a constant speed of 10 μm/s over a 10 μm distance. Further, we collect z-stack (0.5 μm step size) of the labeled composite using confocal microscopy to shed light on the structural changes that give rise to the observed viscoelastic response of the composite.

Laser scanning confocal micrograph of 11.6 μM of actin-vimentin composite network with variable relative actin-vimentin concentrations

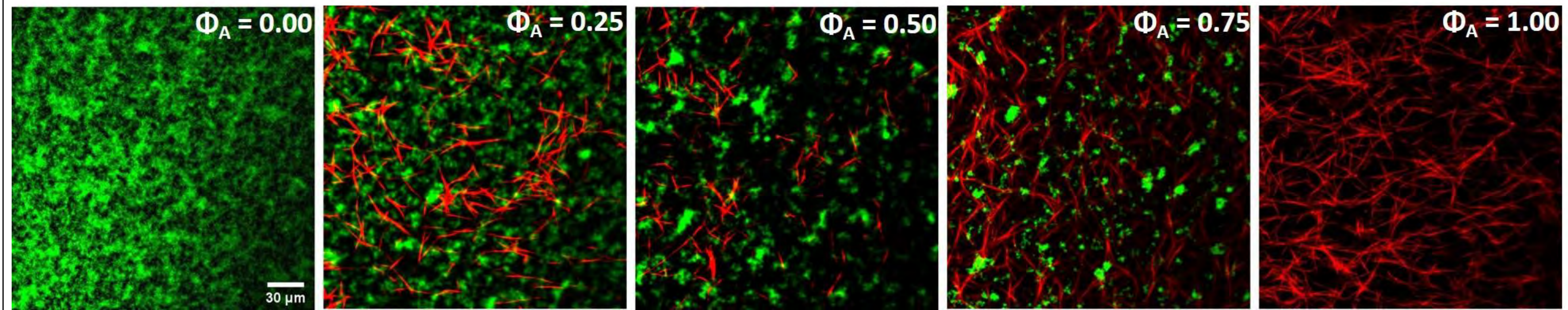


Figure 3: Collapsed z-stack of laser scanning confocal images of actin-vimentin composite networks. The total protein concentration was held fixed at 11.6 μM with variable relative actin (Red) and vimentin (Green) concentrations as $\Phi_A = CA/(CA+CV)$ shown at the right-top hand side of each image. An important insight emerging from this work is that cytoskeletal composite interacts within the cell cortex in playing the vital roles in the mechanics, structure, and dynamics of a cell.

F-actin/VIFs reorganizations are key requirements for the function of a cell

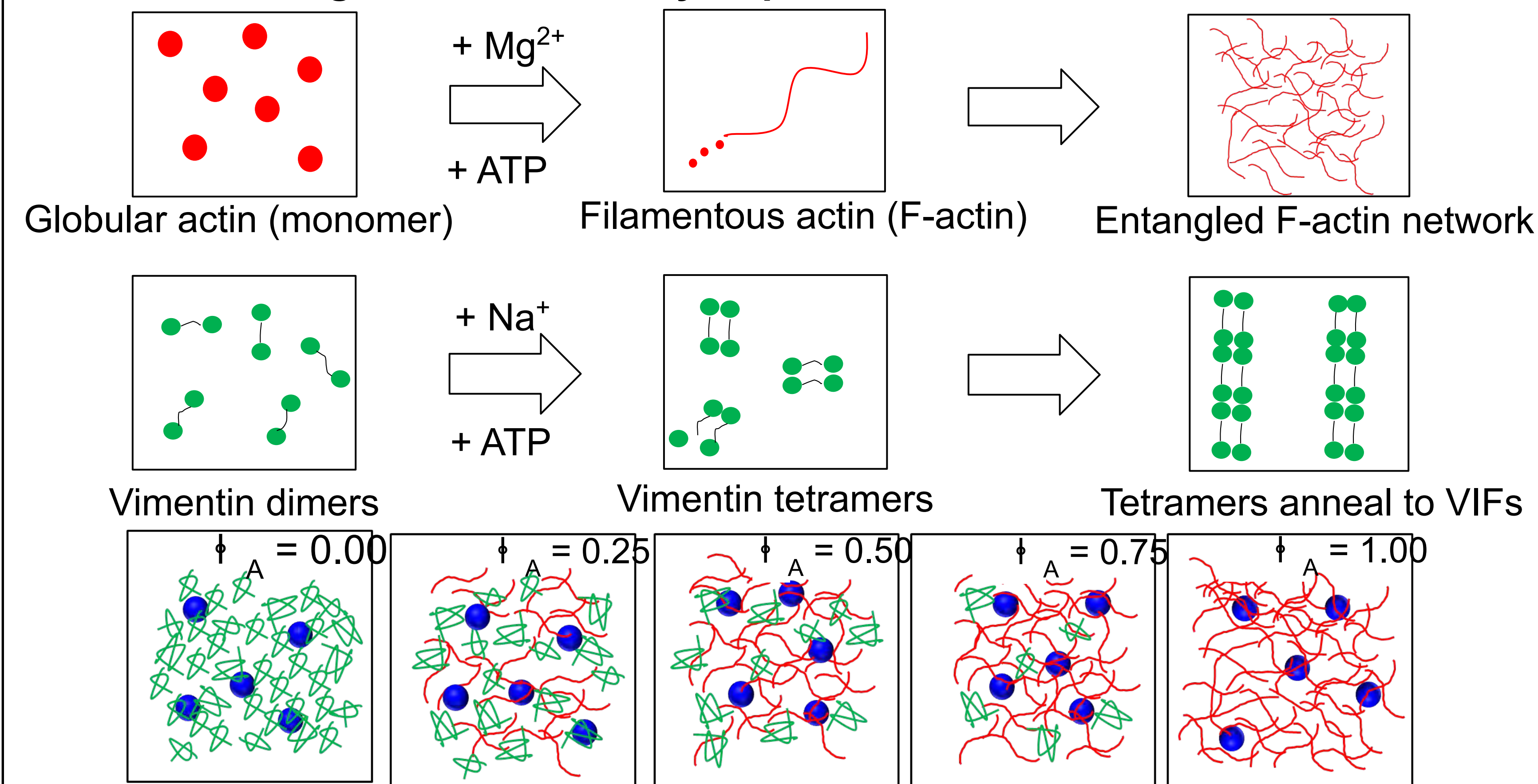


Figure 1: Sketches of actin/vimentin polymerizations and composite formation.

Strain phase: Composite network leads to increased network elasticity

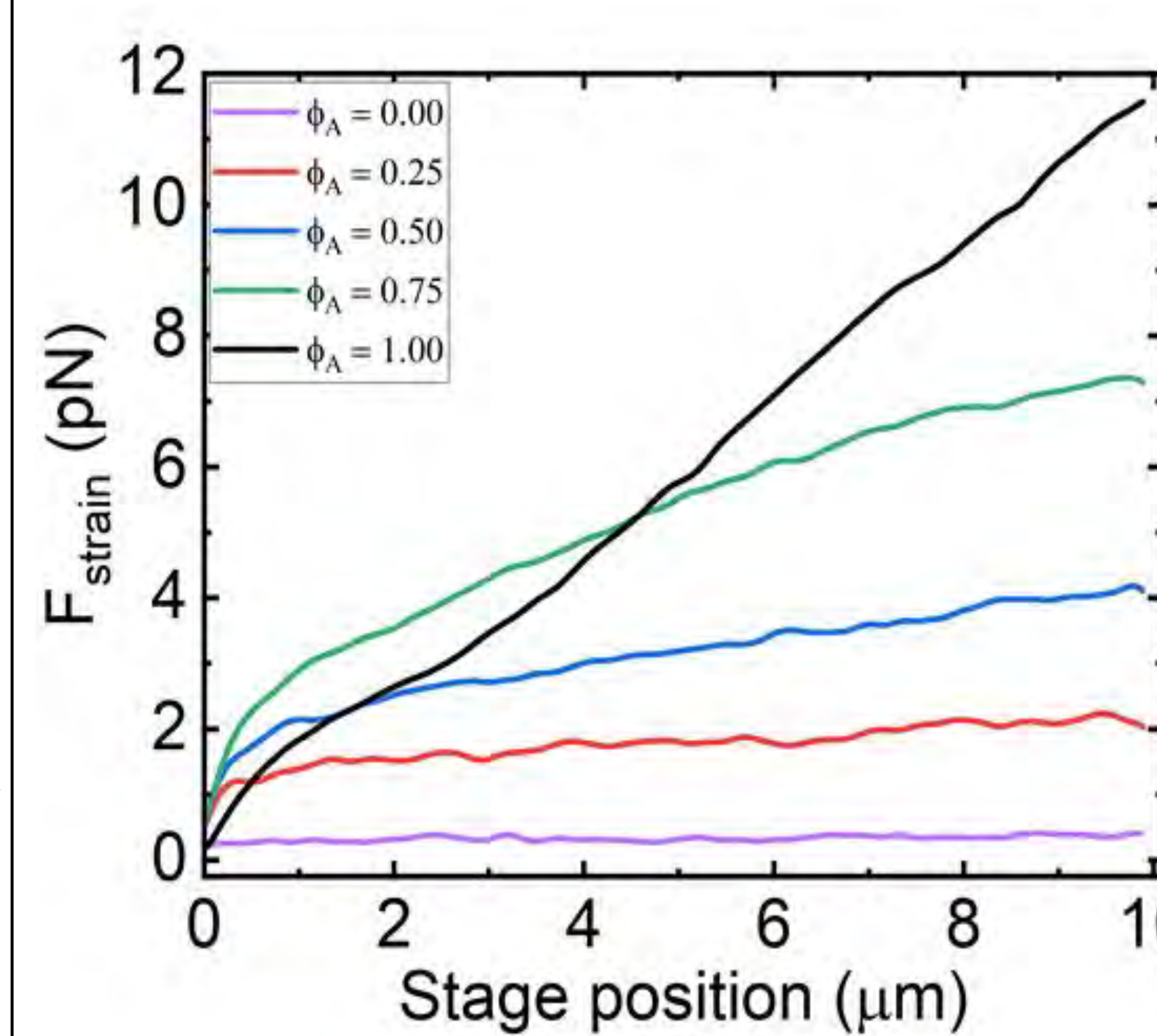


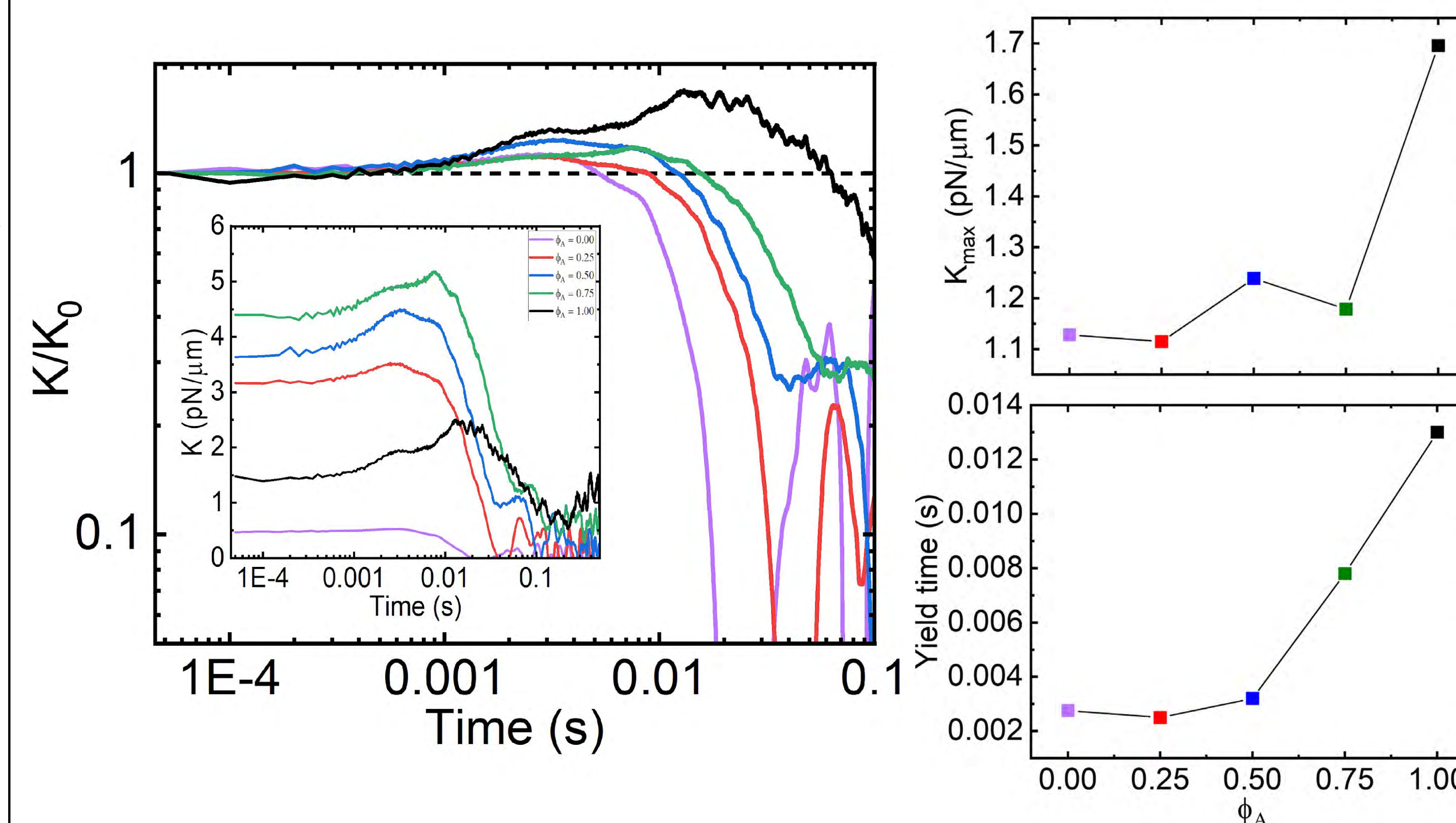
Figure 4: Strain force response.

Left (top): Force response of the composite networks during the strain phase at 10 μm/s.

Left (bottom): Normalized (main) and unnormalized (inset) differential moduli (dF/dx) of the strain forces shown above it.

Right (top): Maximum stiffening rate of the composite networks as a function of Φ_A (taken from the normalized K).

Right (bottom): Yield times as a function of Φ_A . The yield time is when the K_{max} occurs.



Relaxation phase: Induced force relaxation

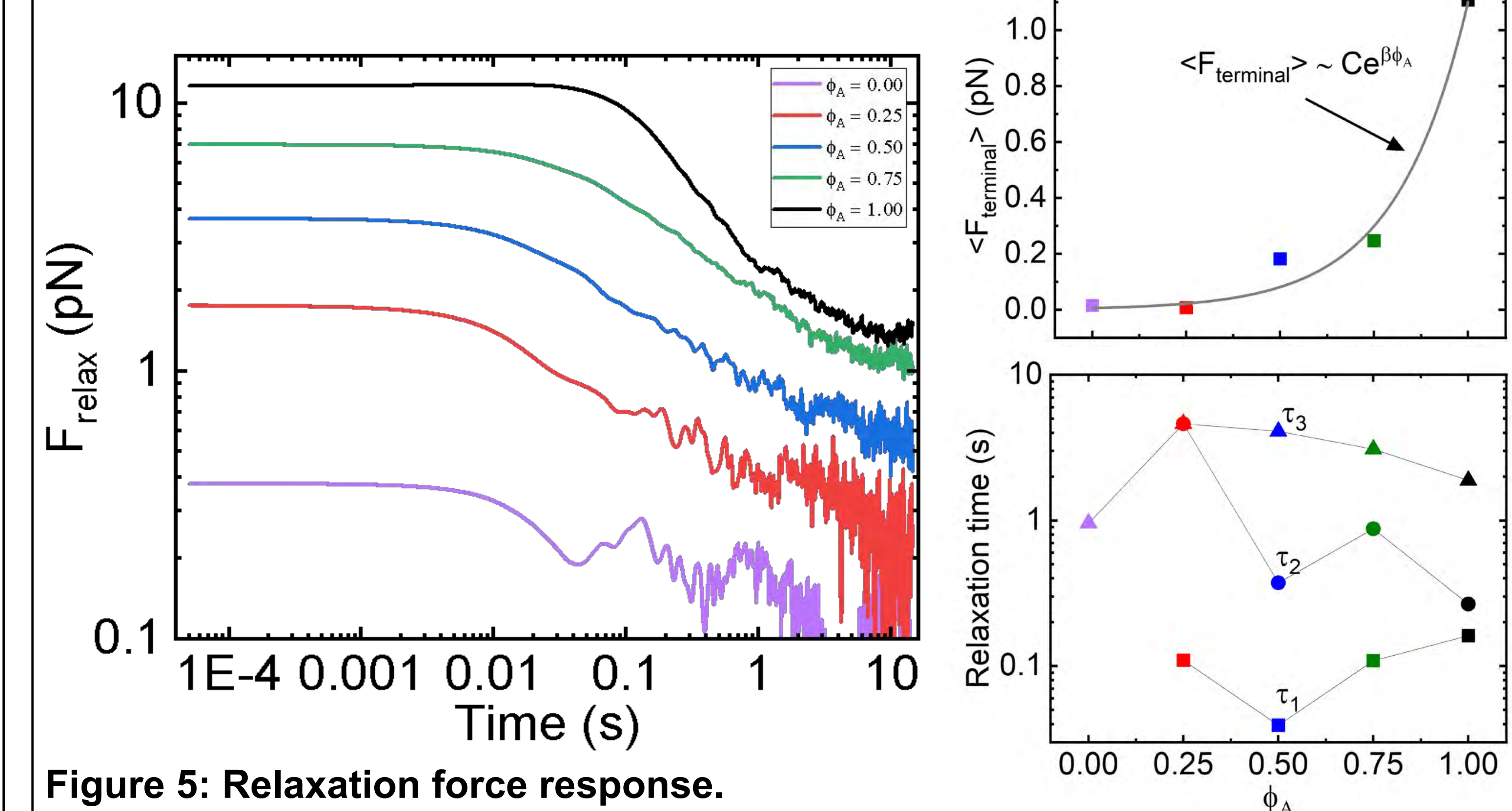


Figure 5: Relaxation force response.

Left: Force response of the composite networks during the relaxation phase.

Right (bottom): Terminal relaxation force averaged over the last 5000 data points.

Right (top): Relaxation times obtained from curve fitting the force to a single exponential for $\Phi_A = 0.00$ and triple exponential for the rest.

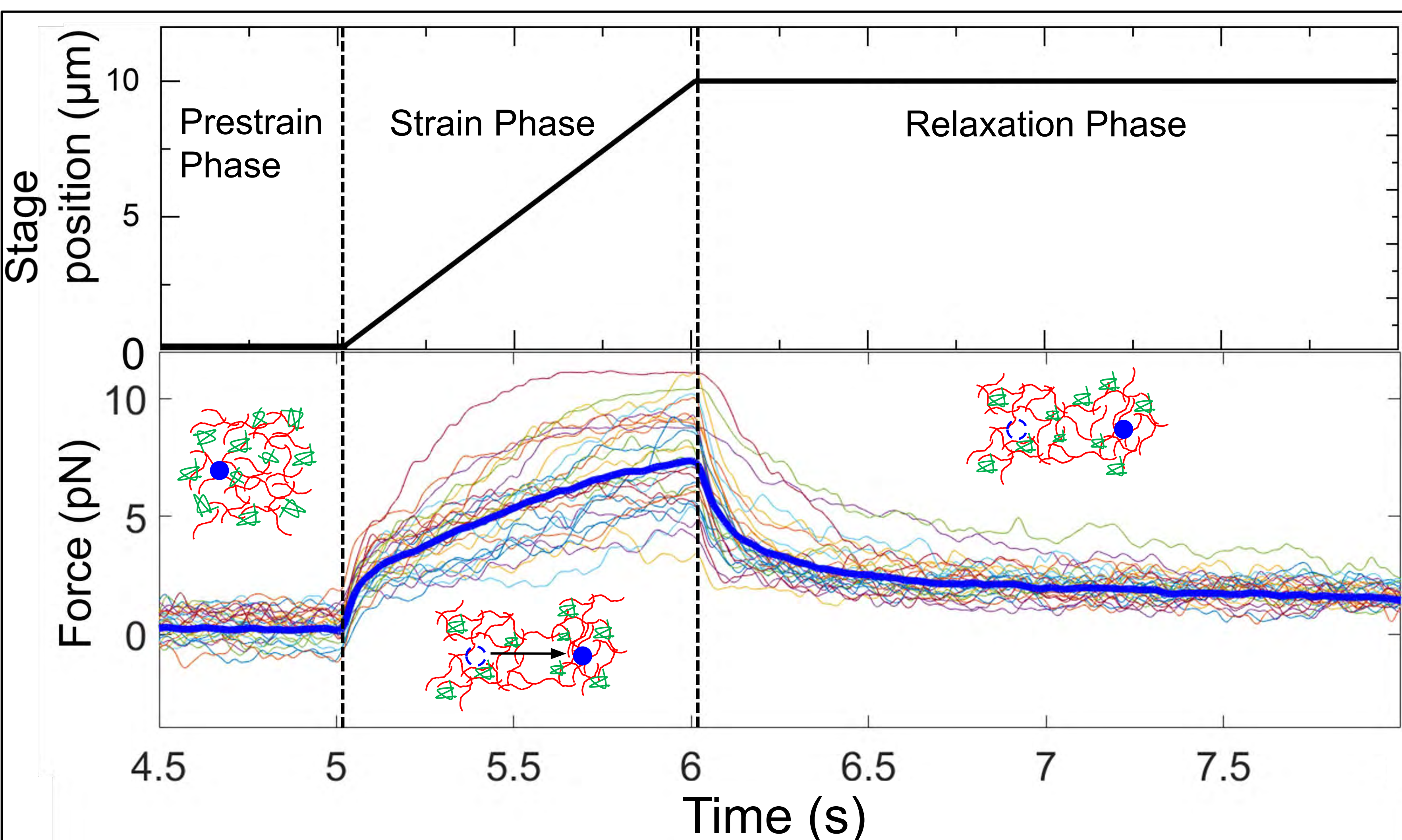


Figure 2: Schematics of a typical experimental setup. We use optical tweezers to trap a microsphere in the network and study the mechanical properties of the networks at different actin-vimentin ratios. By pulling the microsphere through the network, we measure the forces the network exerts on the probe during and after this stress.

Conclusion:

- VIFs and F-actin proteins are thought to form separate coexisting networks independent of each other but we show that they form interpenetrating networks that enhance their mechanical responses.
- Networks with higher actin concentrations exhibit stronger and more sustained elastic force responses to induced stress than networks with high vimentin concentrations.
- Higher concentrations of vimentin exhibit complete relaxation/dissipation of induced force.

Acknowledgements:

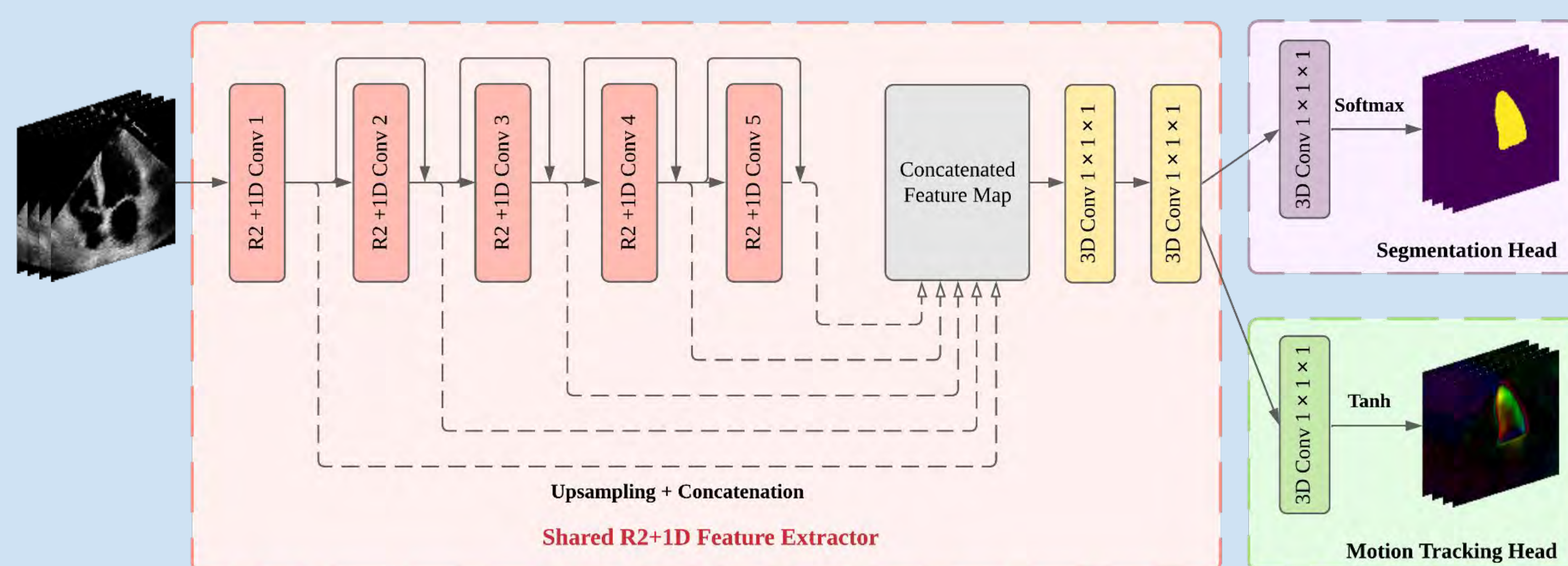
Bucknell University Department of Physics and Astronomy

Applications of Motion Tracking in Temporally Coherent Echocardiography Video Segmentation

Motivation

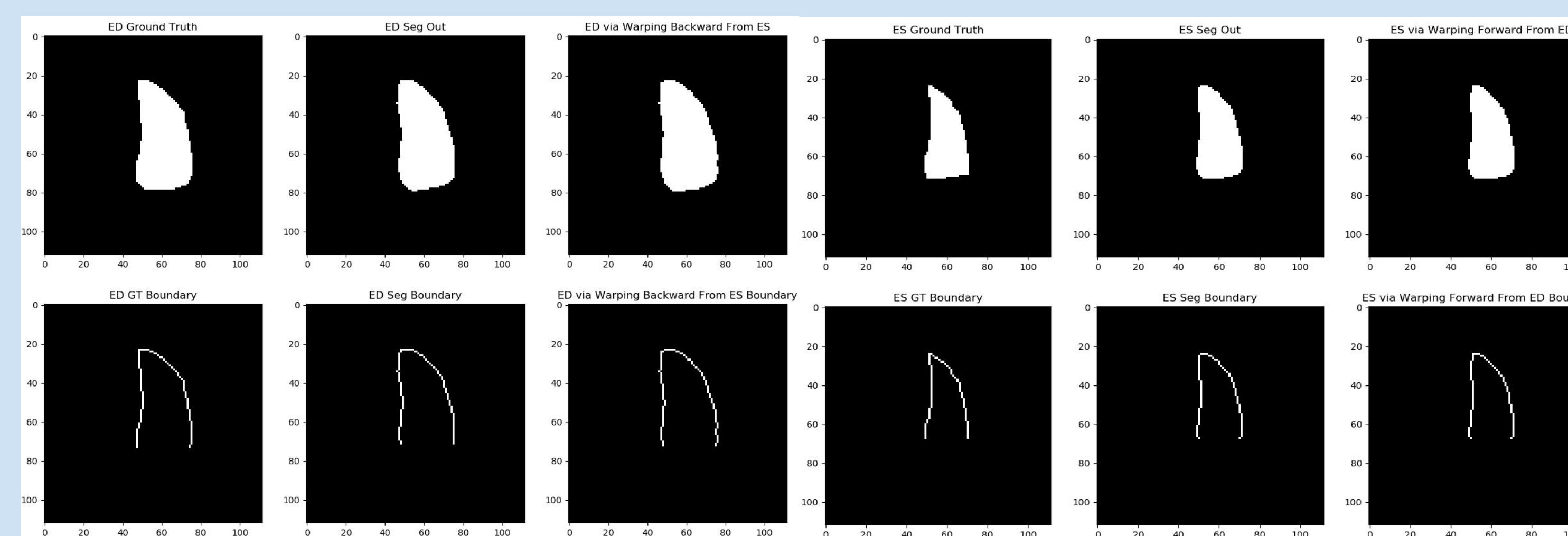
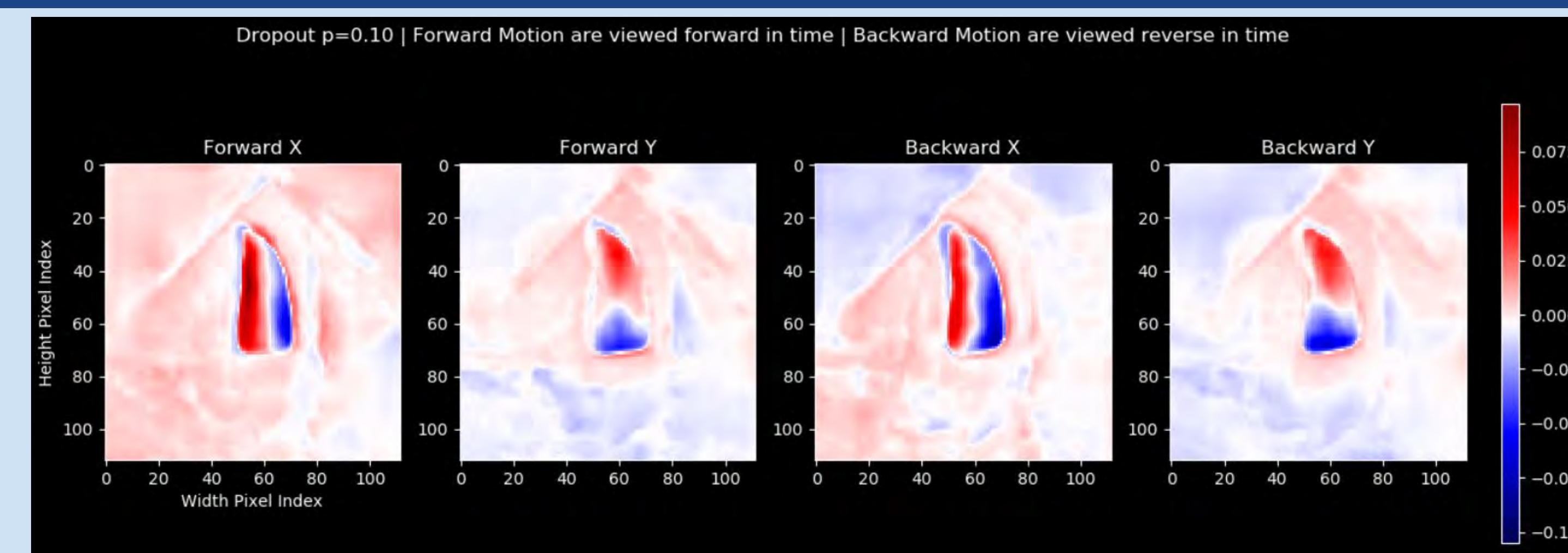
- Global Longitudinal Strain (GLS) and Regional Strain Analysis can deliver more insights about the heart condition
- A prior fully automated method of producing left ventricular segmentations and motion tracking can be used to calculate Ejection Fraction (EF) and potentially cardiac strain [1]

Starting Point

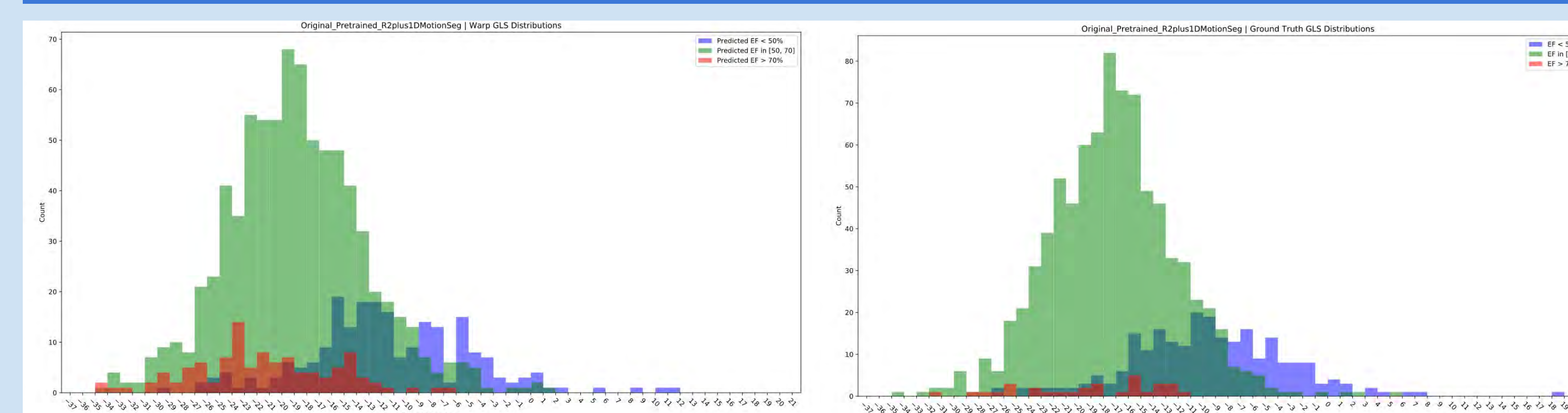


- Chen et al. [1] proposed their CLAS-FV model which they build off of Wei et al. [2]'s proposal of the CLAS architecture with the goal of automating LV segmentation for calculation of EF on the EchoNet-Dynamic Dataset provided by Ouyang et al. [3]
- Motion Tracking output is used during training in loss functions, but not post training or post inference; we try to use in complement with the segmentation output post inference to calculate GLS and regional strain

Methods

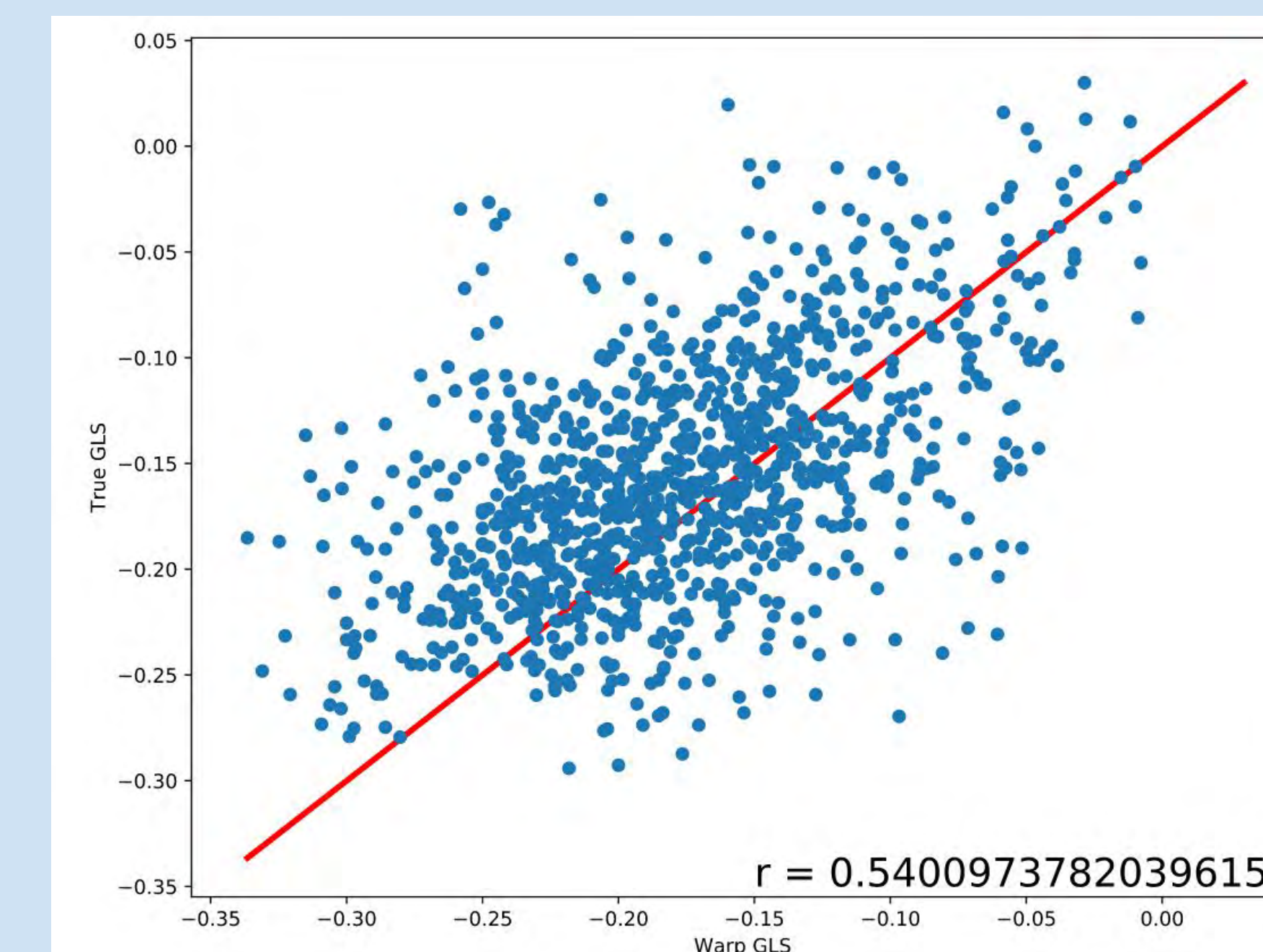


- We can apply boundary and corner detection techniques in the OpenCV python library to find pixels constituting the outermost region of the LV segmentation from the model
- Strain Rate is calculated as the percentage change in the length of the myocardium at ED and at ES; we count the number of white pixels as our lengths



- We can view the GLS calculated via warping grouped into three EF distributions of low, normal, and high and compare it to the GLS calculated from the ground truth labels and EF
- Automated method labels more patients as high EF compared to GT

Results



After excluding the top and bottom 1% of data for outlier removal, we achieve a correlation of $r=0.54$ for 1065 patients from the test dataset using the model's ED frame and then warping to ES frame.

Conclusions

- Motion tracking produces anatomically correct results in movement of cardiac tissue during diastolic and systolic phases
- GLS and Regional Strain has potential to be determined from our model's segmentation and motion tracking outputs

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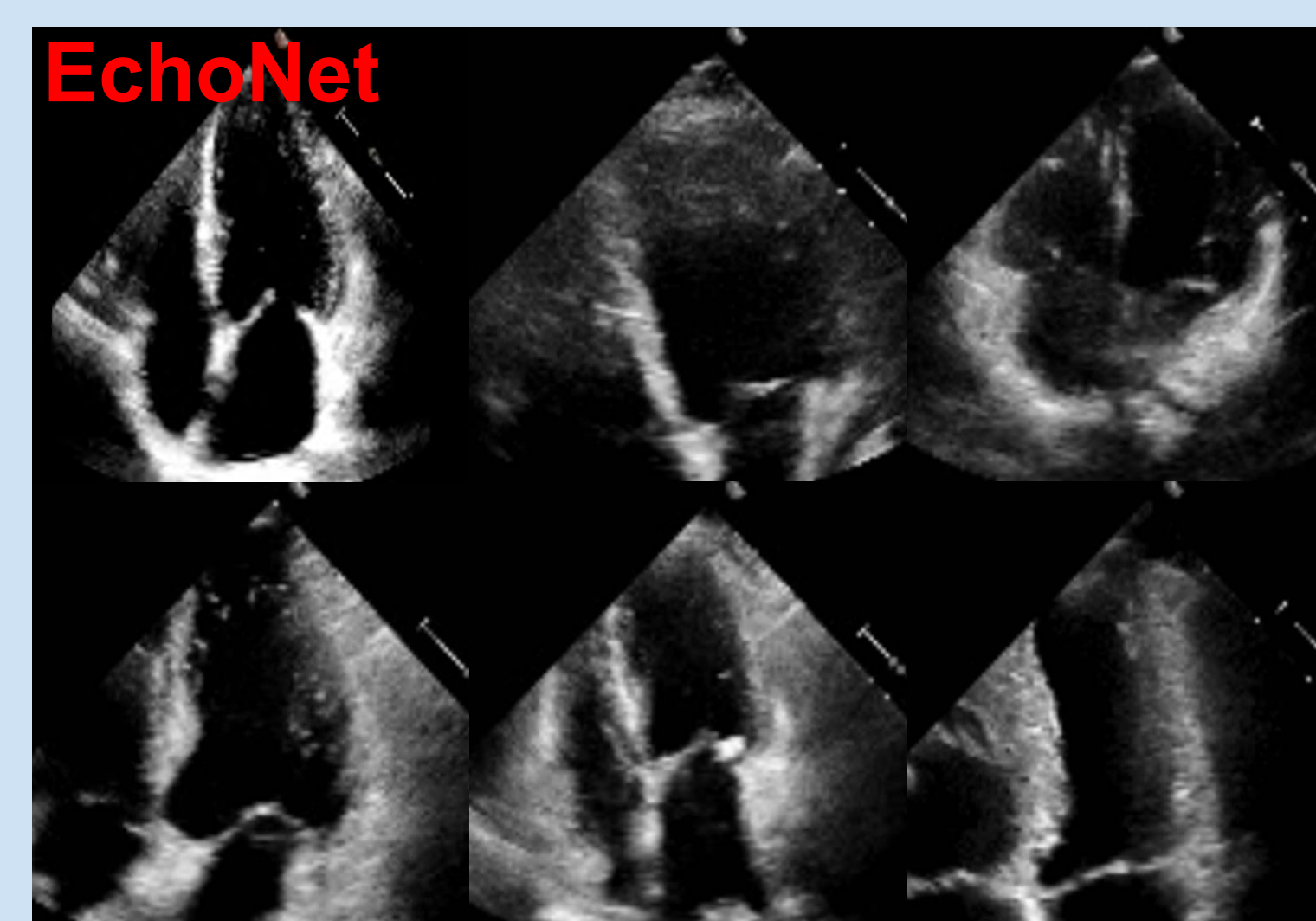
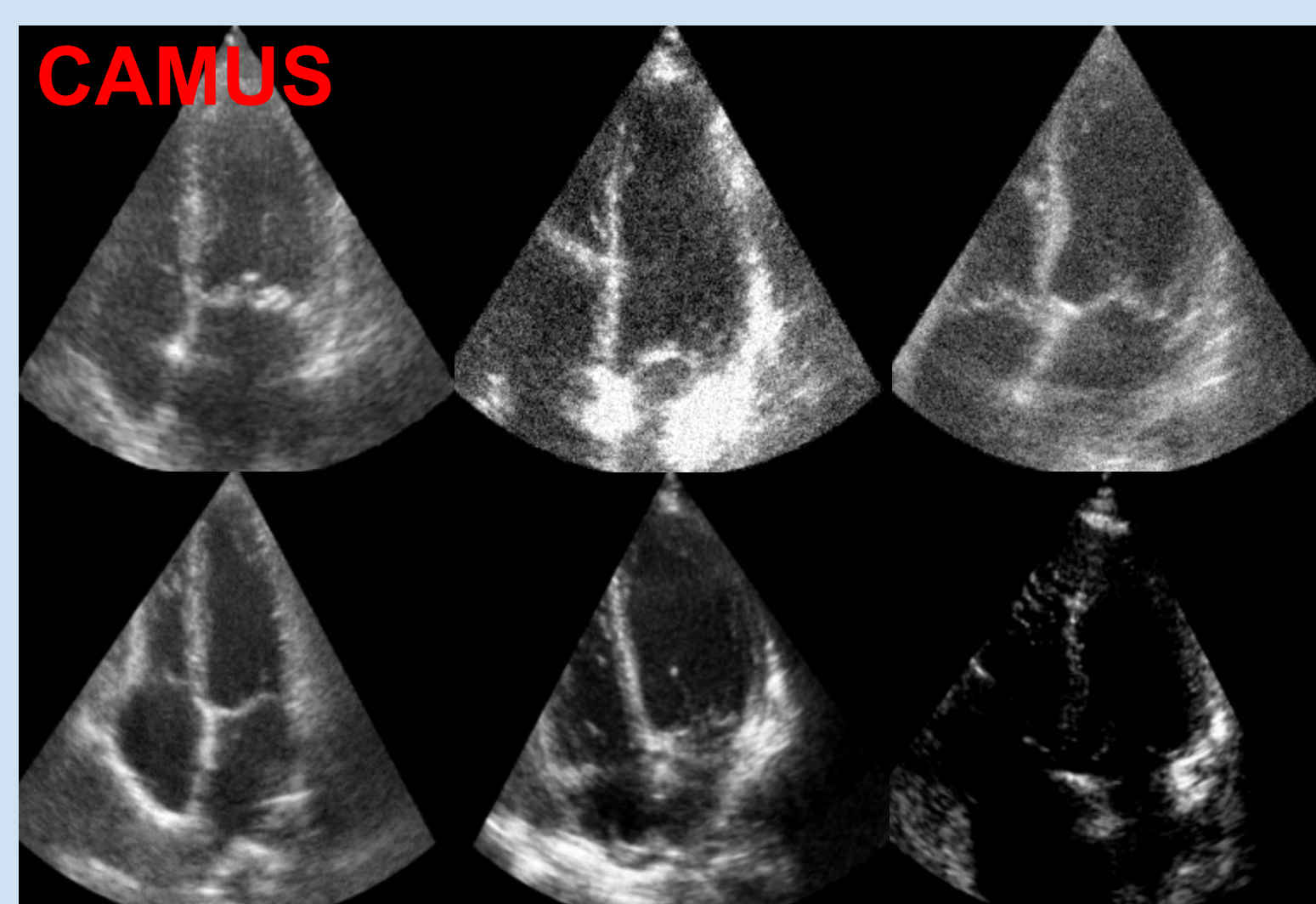
Acknowledgement

- Bucknell University Department of Computer Science
- Bucknell Geisinger Research Initiative
- Ciffolillo Healthcare Technology Inventor Program

Motivation

- Echocardiography segmentation using convolutional neural network (CNN) is a promising solution for diagnosis of cardiovascular disease.
- The performance of such machine learning models trained from a particular source domain, when transferred to a different target domain can drop unhelpfully[1].
- We want to integrate and analyze domain adaptation techniques to build a CNN for echocardiography segmentation that generalizes well across datasets and outperforms other models that do not use domain adaptation.

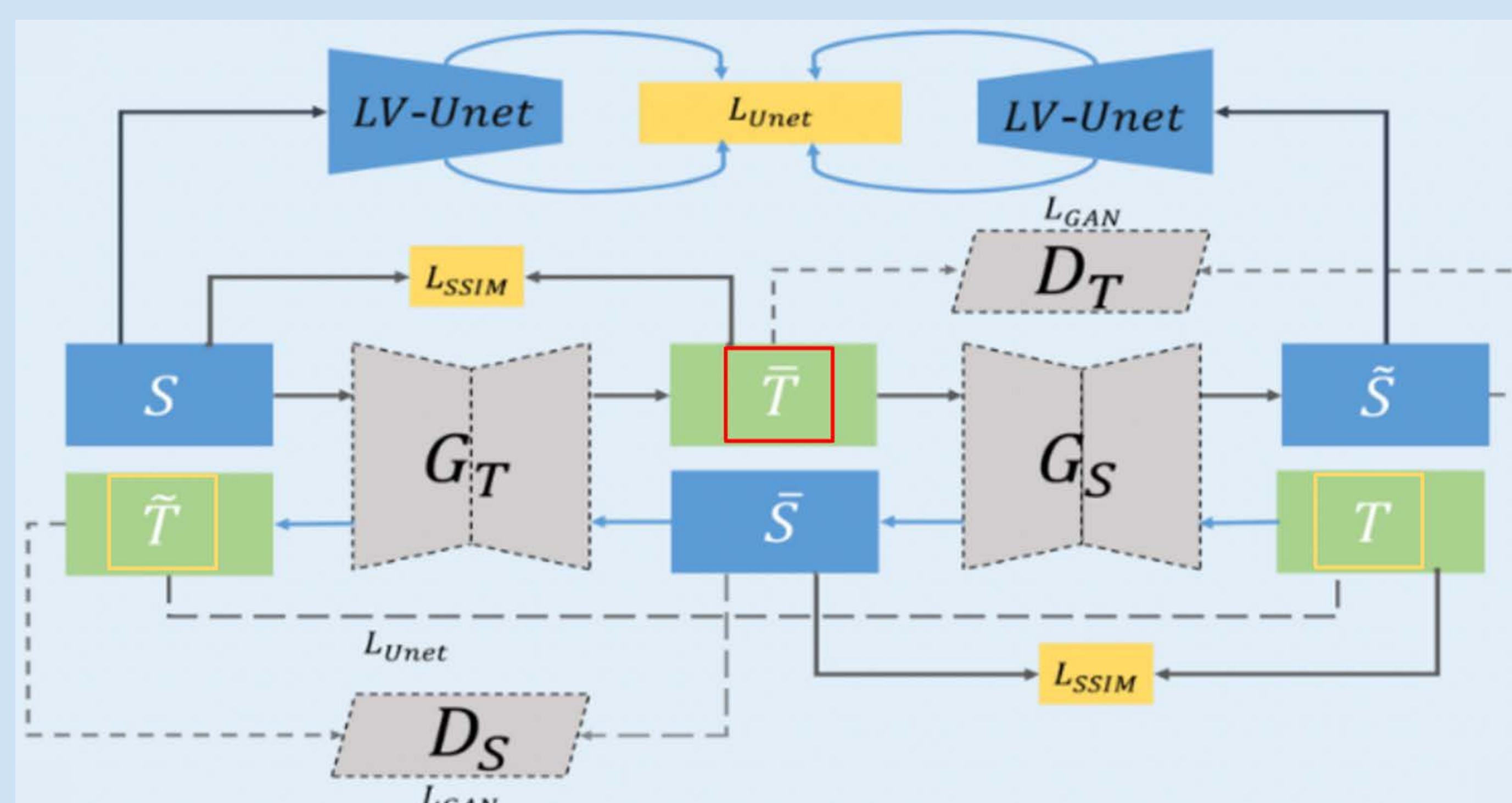
Datasets and Experiment Setup



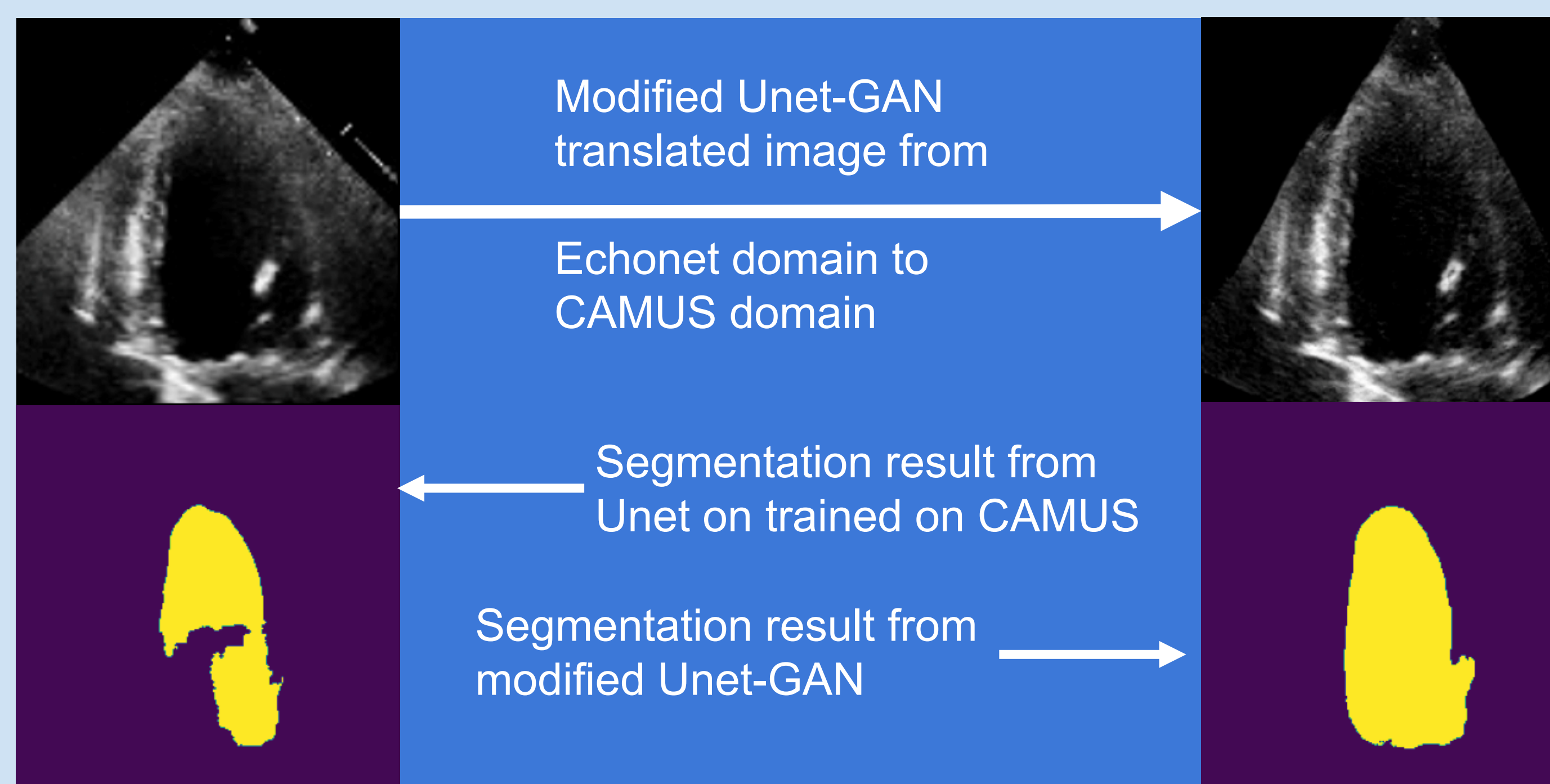
- We have two datasets of echocardiogram images: CAMUS[2] and EchoNet[3]. The experimental setup for this research is:
 1. Train on CAMUS dataset, Test on EchoNet dataset (current standard, baseline)
 2. Train on EchoNet dataset, Test on EchoNet dataset (best possible performance, only possible when you have enough annotated data in target domain)
 3. Domain adaptation train on CAMUS and EchoNet dataset, Test on EchoNet dataset (expect to perform better than 1 and hopefully close to 2)

Modified Unet-GAN

- Yan et al. [1] proposed a generic framework called Unet-GAN which can translate an image from a source domain to a target domain in the absence of paired examples while keeping the anatomical structure the same.
- We modified the Unet-GAN by including training the Unet model through the training process of the GAN to ensure our Unet model become more generalized on both domains.

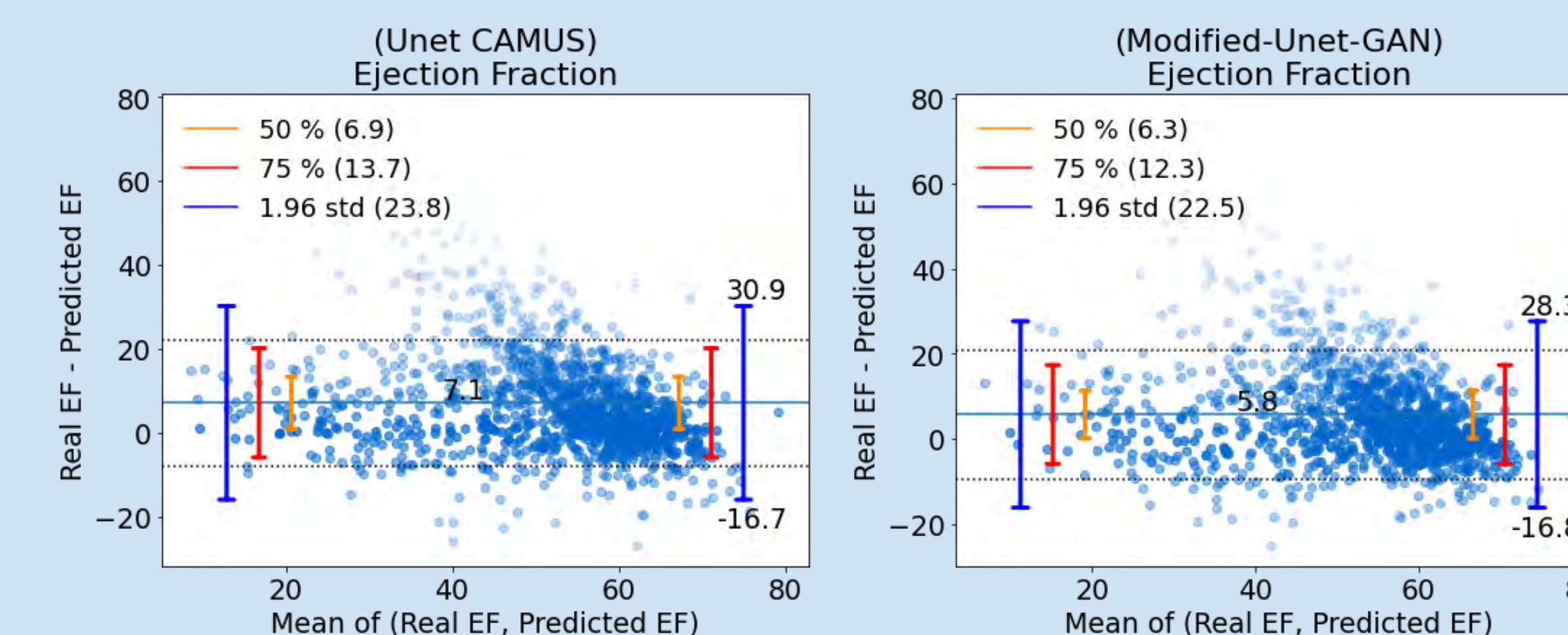


Example of one case



Results

- Mean absolute error of EF from 1264 patients:
 - 11.47% on Unet CAMUS (experiment 1)
 - 11.29% on original Unet-GAN
 - 9.84% on Modified Unet-GAN (experiment 3)
 - 6.91% on Unet EchoNet (experiment 2)



Conclusions

- Domain adaptation can help overcome domain shift problems.
- Our modified Unet-GAN with colearning image translation and segmentation is better than original Unet-GAN.

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- [3] Ouyang, D., et al.: Video-based ai for beat-to-beat assessment of cardiac function. Nature 580(7802), 252–256 (2020)

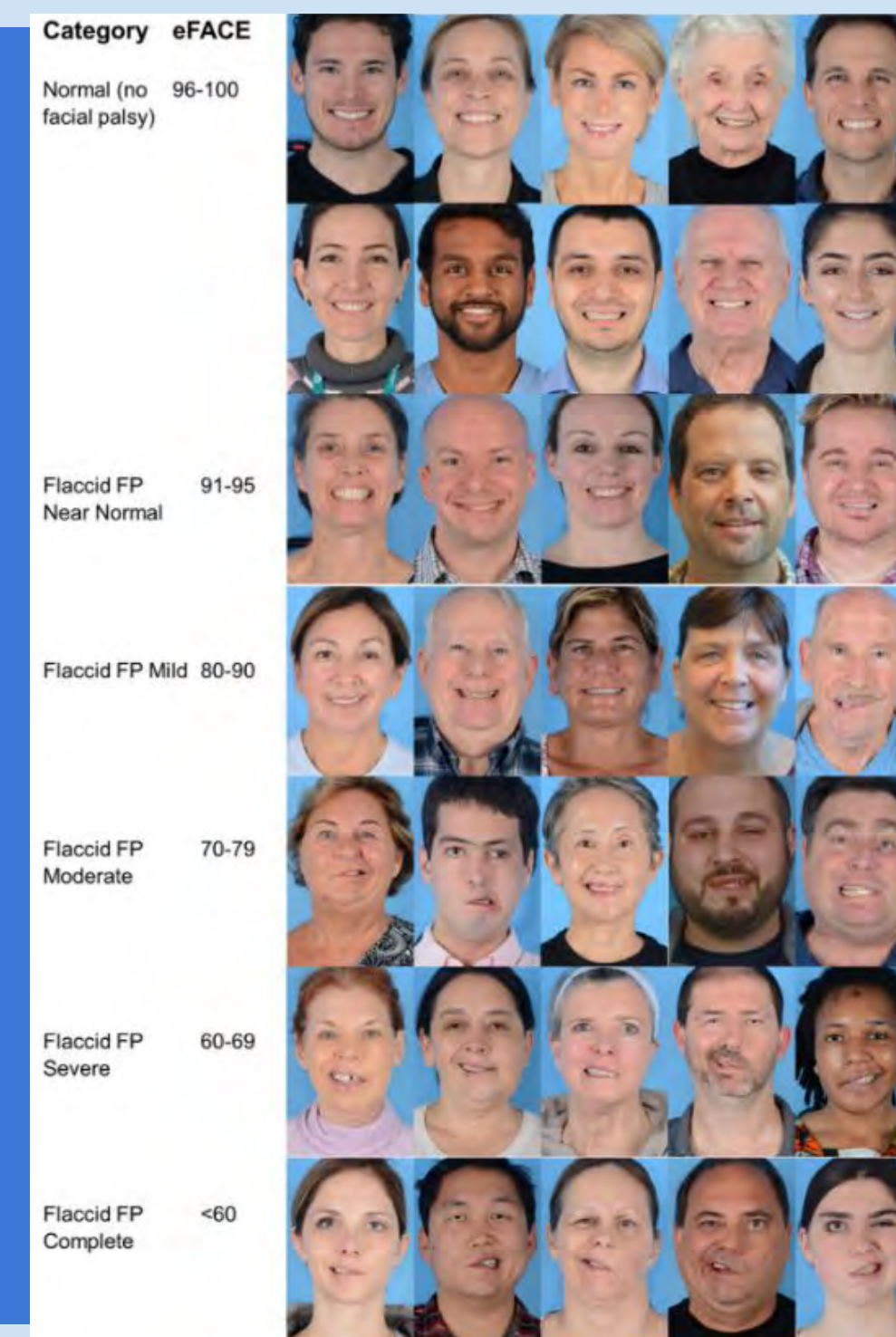
Acknowledgement

- Bucknell University Department of Computer Science
- Bucknell Geisinger Research Initiative.
- Ciffolillo Healthcare Technology Inventors Program

Facial Nerve Paralysis Severity Grading by Computer Vision and Machine Learning

Background & Motivation

- **Goal:** Develop computer vision and machine learning software to **grade Facial Nerve Paralysis (FNP)** and to assist diagnosis and recovery tracking.
- **Observer bias** commonly arises when FNP patients are seen and diagnosed by clinicians, as reported in [1] which showed that a machine learning (ML) based approach found less facial asymmetry in severe FNP patients and more asymmetry in healthy faces than clinicians.
- We hope to train an ML model that grades patient facial palsy severity on the House-Brackmann scale.



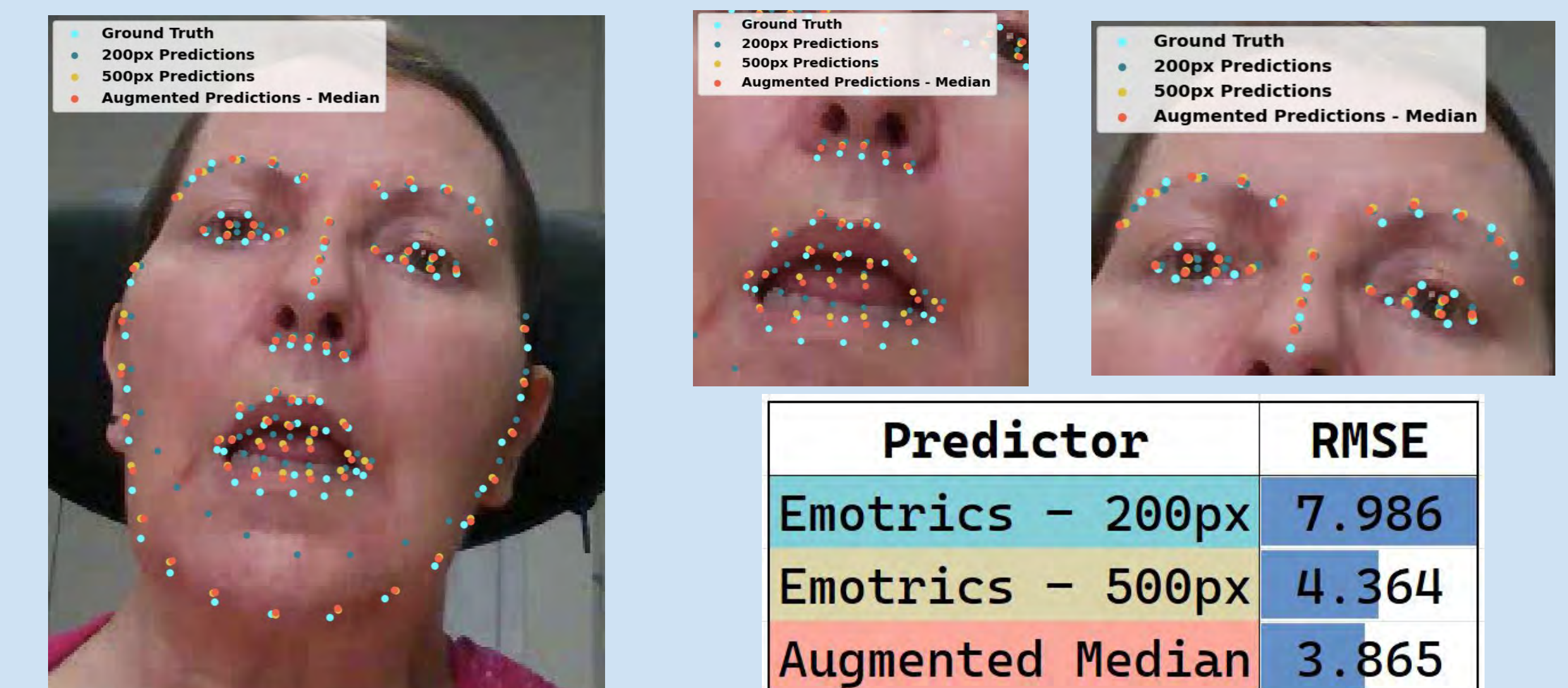
Validating Landmark Detection

- Emotrics [2] claims to have accurate results under various conditions; however small image changes, i.e., rotations or adding noise, leads to less accurate results.
- Applying test-time augmentation leads to better results by intentionally introducing random small rotations and/or noise and using the resulting median of the predicted landmarks.

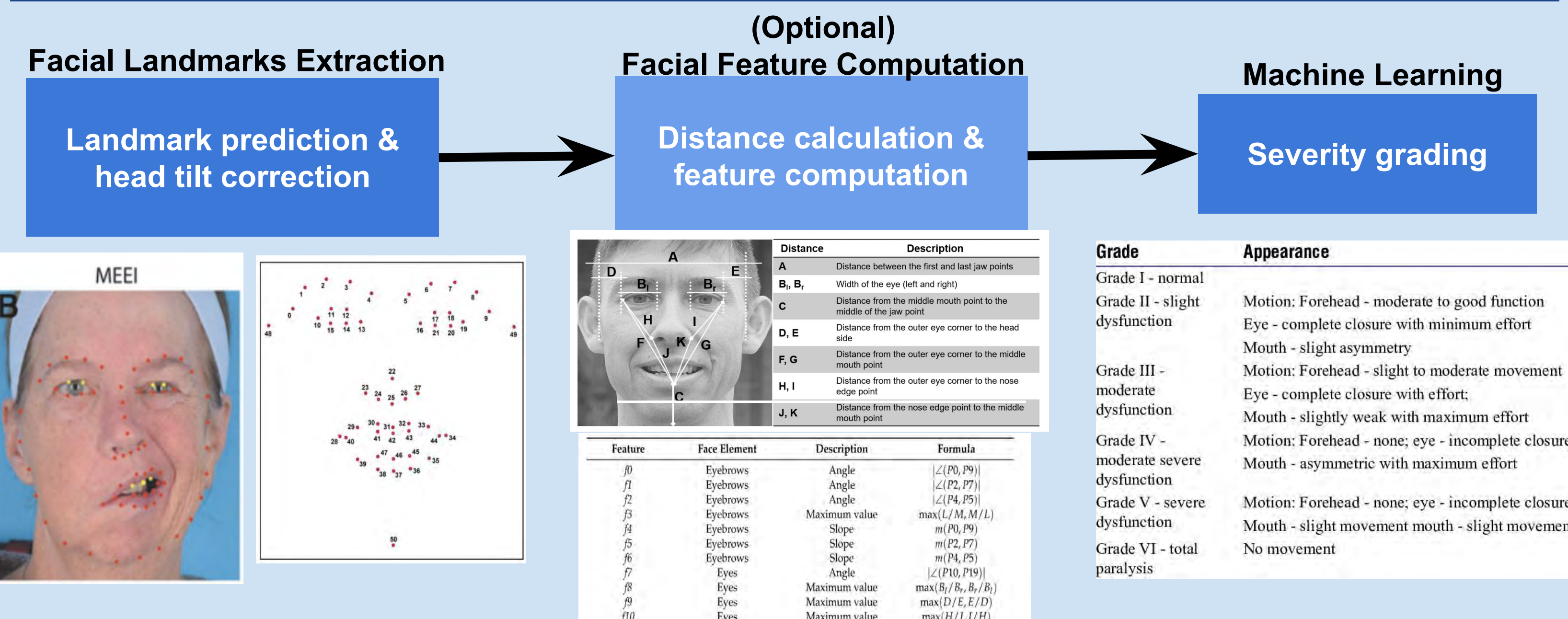


Preliminary Results

- Difference between predicted landmarks and Ground Truth landmarks using the Toronto NeuroFace (TNF) Dataset [5].
- Calculation of RMSE to quantitatively compare landmark detection accuracy using various algorithm on one image.



Approach



Feature Computation

- While feature computation can be used to train the ML algorithm to grade the severity of FNP, landmarks alone can be used in the training and may reduce structural bias.
- Features also serve informative purposes by highlighting certain characteristics (i.e., asymmetry in certain regions of the face) that are abnormal relative to healthy patients.

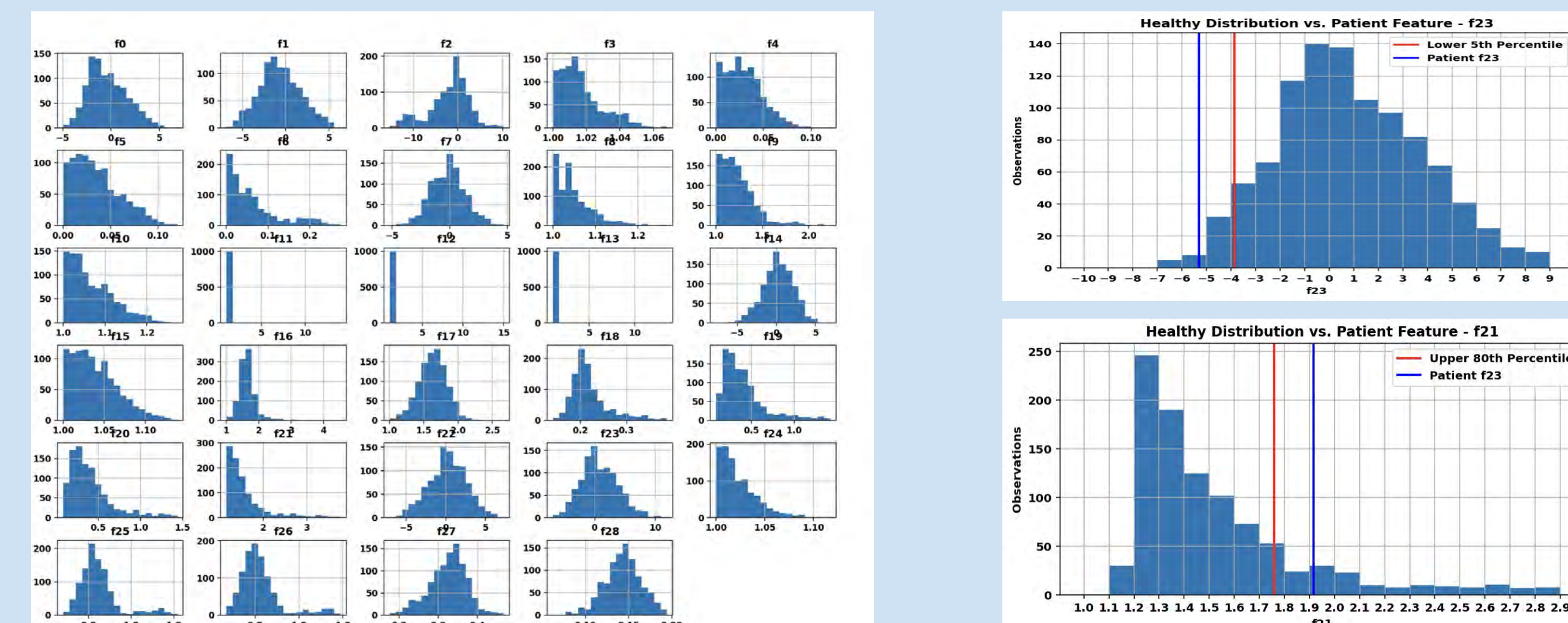
Conclusions

- Assessed the performance of a landmark predictor and applied test-time augmentation to improve accuracy.
- Using the NeuroFace dataset, we preliminarily showed that the median of augmented points is more accurate.
- After acquiring more patient data, we plan to begin training the model to provide FNP grading with the landmark points as input.

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- Work in [2] demonstrated successful application of ML in determining whether a face is healthy or ill with FNP by using the ML-based software Emotrics [3] to automatically predict key facial landmarks from facial images and then computing facial features to determine health or illness.
- Emotrics [3] is also used as a landmark detector after training on a dataset [4] consisting of 60 patients with a spectrum of types and severities of FNP.
- A landmark detector trained on the patient population minimizes potential model bias [5].



1. Background

- Aneurysms are a condition where the artery walls weaken allowing for a bubble to form either pushing out or widening the artery.
- Blood clots are a collection of blood cells and other molecules that clump together to prevent blood loss when there is damage to the vessel wall or to our skin. However, the blood clotting in the vessels can be dangerous as the blood clot does not dissolve, or it breaks down and travels through the vessels possibly affecting other parts of the body as the vessels decrease in size.
- A stroke occurs when there is a blockage of blood flow to the brain preventing it from receiving oxygen and other essential nutrients. There are two types ischemic strokes, where the loss of oxygen and nutrients will result in the death of brain cells within a few minutes, and hemorrhagic stroke, where sudden bleeding can cause damage to the brain cells.
- Genetic sequences are made up of exons, part of the sequence that codes for the protein, and introns, part of the sequence that is non-coding. Introns are cut out at splice donor and splice acceptor sites; however, when there is a mutation at these sites it can lead to the inclusion of introns that can alter the shape or length of the gene.

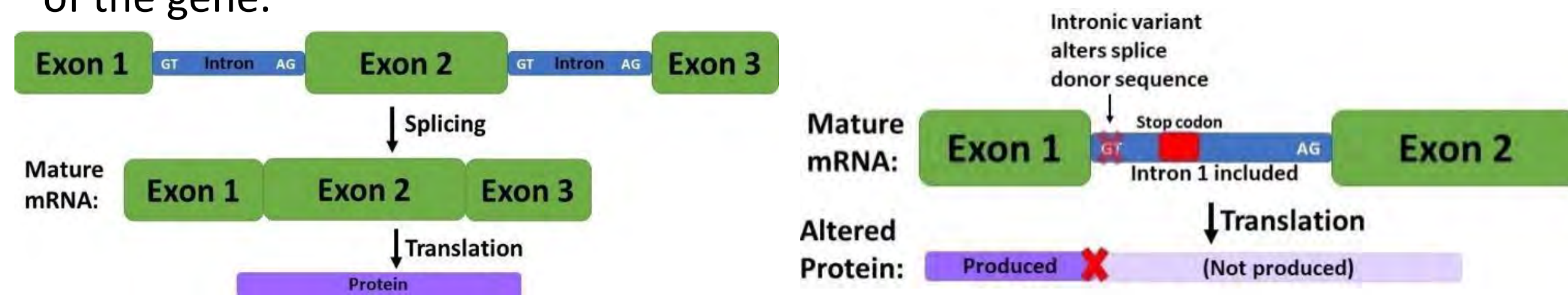


Figure 1. Normal Splicing. The GT splice donor and AG splice acceptor sites lead to the removal of the introns to make mRNA and then protein.

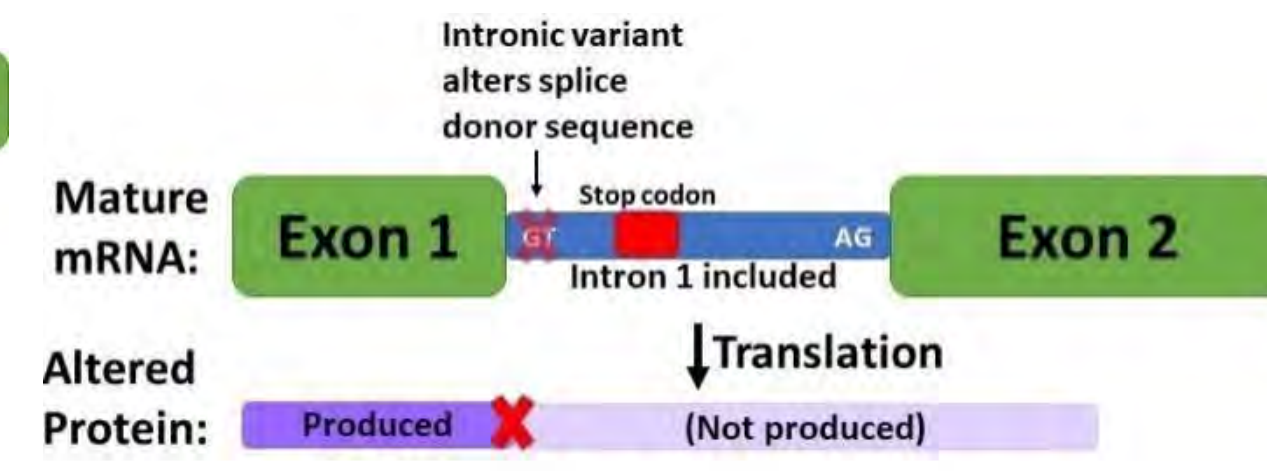


Figure 2. Poison Exon. The loss of the GT splice donor site leads to the inclusion of the intron which causes a premature stop, and shortened protein.

2. Purpose

The goal of this project is to identify poison exons in genes thought to be linked with blood clots, strokes, and aneurysms

- Aim 1: Identify and summarize clinical information of splice variants in cases with the stated conditions in ClinVar and gnomAD.
- Aim 2: Assessment of poison exons with splice variants in the genes
- Aim 3: Compare the total number of poison exons in ClinVar and gnomAD

3. Methods

1) Identifying Genes Associated with Blood Clots, Aneurysms, and Strokes

- Genes that were associated with blood clots, aneurysms, and strokes were identified through articles and publications found in PubMed
- Once a list of 37 genes was collected, and splice donor variants were recognized.

2) PEX-DETEX

- Collected CSV files from gnomAD and FASTA files from ClinVar for the 37 genes.
- These files were run through the PEX-DETEX algorithm which provided the location and total number of poison exons in the splice variants.

3) Verification of the Results

- The total number of poison exons was compared to the totals found in ClinVar and gnomAD.
- The 309 poison exons were evaluated using screenshots of the UCSC Genome Browser using the Human Genome 38.

4) Fisher's Exact Test

- Used to determine if the 37 genes are associated with blood clots, strokes, and aneurysms by poison exon enrichment based on ClinVar and gnomAD.
- Significant p-values were recorded.

4. Results

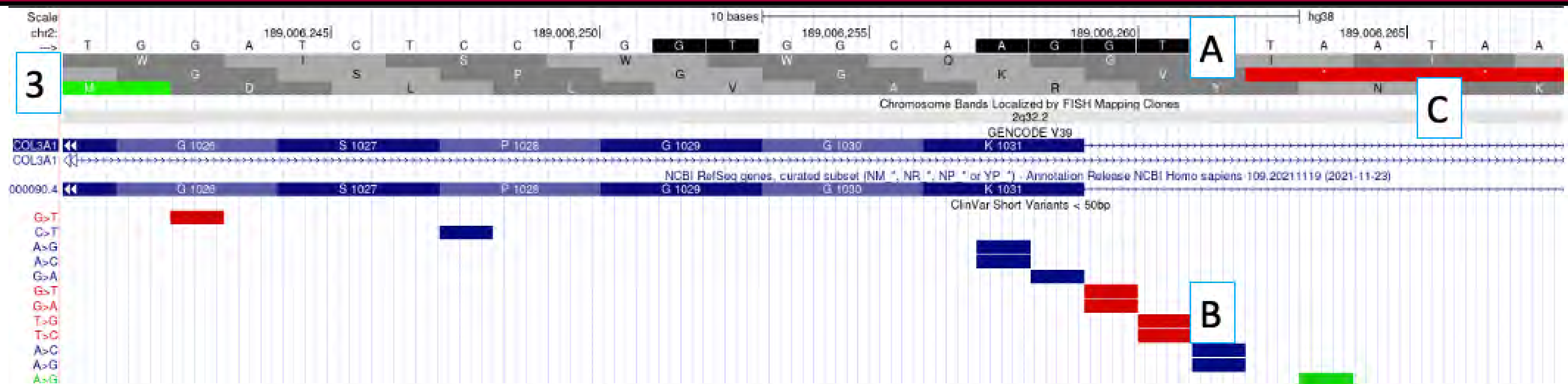


Figure 3. UCSC Genome Browser. This figure is a screen shot from the UCSC Genome Browser, which demonstrates a poison exon in ClinVar that was predicted by PEX-DETEX.

- The UCSC Genome Browser was used to verify the poison exons that was a result of PEX-DETEX. The GT splice donor site, marked as A, is located on the top near the location and the mutations are on the side, we are specifically looking at is T>C, marked as B. The stop codon that is included because of the mutations is marked with C.

	Poison Exon	Non-Poison Exon
ClinVar	309	240
gnomAD	39	42

Table 1. This table is the total amount of poison exons and non-poison exons in the splice variants for each cohort.



Figure 4. PyMol. These are the predicted structures for the genes MYLK and TGFBR1. One normal gene and one mutated gene is shown.

- The structures were modeled using PyMol. A and C are the normal structures of the MYLK gene and TGFBR1 gene. The mutated MYLK gene is marked by B, and it demonstrates an alteration in shape that may lead to a loss of function. The mutated TGFBR1 gene, D, demonstrates a truncation of the gene and may be indicative to nonsense mediated decay.

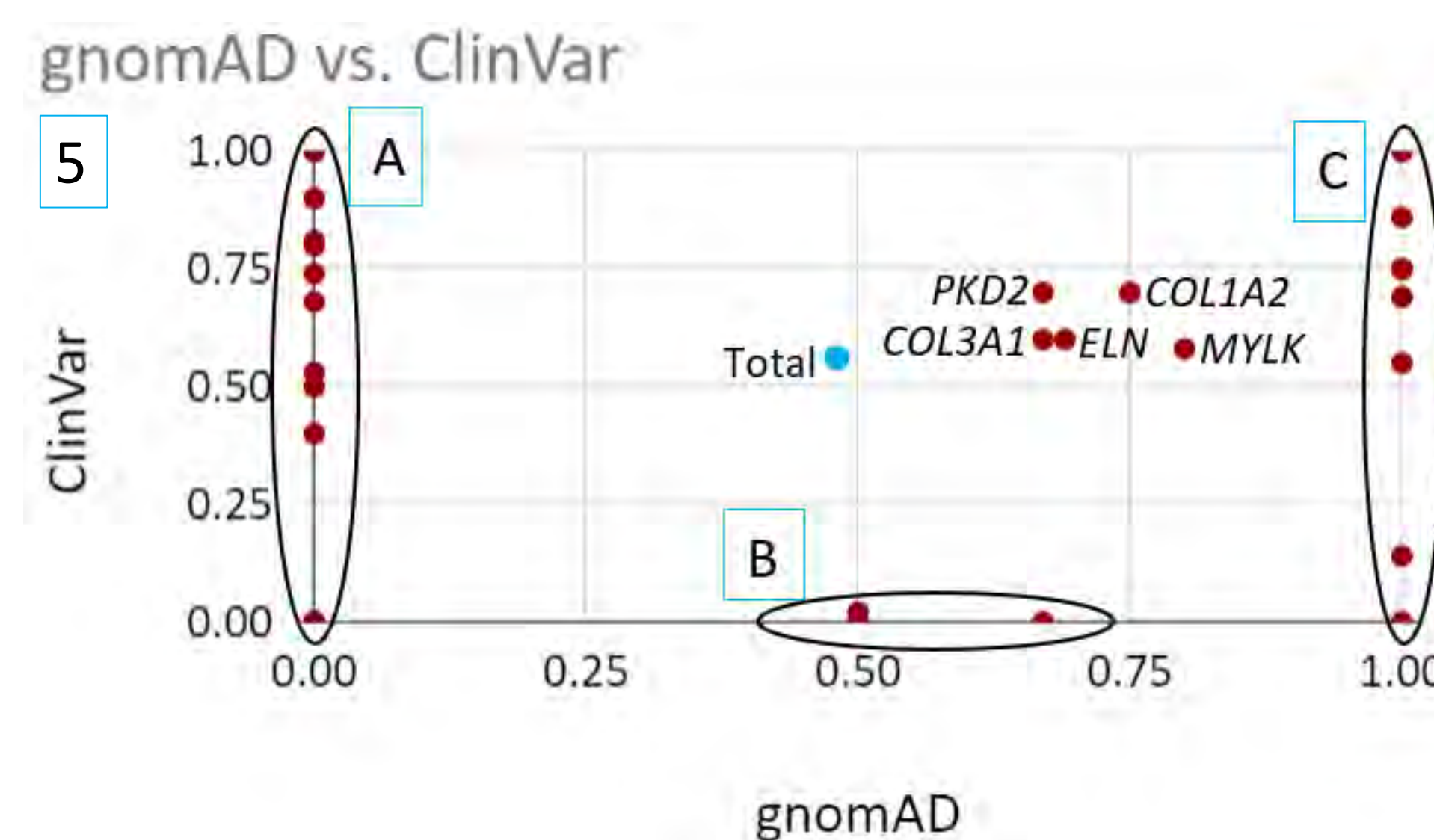


Figure 6. The graph compares the number of poison exons in ClinVar and gnomAD.

- Graph of Fisher Exact values for each gene.

- Group A are genes that are pathogenic or likely pathogenic. It is composed of ACTA2, ADAMTS13, BGN, COL5A1, FBN1, FLNA, FOXE3, MAT2A, MFAP3, MYH11, NOTCH1, PKD1, PRKG1, SMAD2, SMAD3*, SMAD4, SMARCA5, SNRPB, and TGFBR2.
- Group B are genes that are benign. It is composed of EFEMP2, and EMILIN1.
- Group C are genes that are likely benign. It is composed of COL5A2, FBN2, SKI*, SLC2A10, SMAD6, TGFBR2, TGFBR1, and TGFBR2.
- The genes in the middle are uncertain, but they are suspected to lean towards being pathogenic or likely pathogenic.
- The total leans more towards the ClinVar, but it is mostly centered, which can explain why there is little significance when performing the Fisher's Exact Test.

Note genes that are significant enriched in poison exons are marked with *

5. Discussion

Classifications:	Total:
Pathogenic	146
Likely Pathogenic	115
Pathogenic/Likely Pathogenic	29
Uncertain	19
Total Mutations:	309

Table 2. This table highlights the amount of poison exons in each of the classifications.

- 146 poison exons are considered pathogenic in ClinVar.
- 115 poison exons are considered likely pathogenic in ClinVar.
- 29 poison exons are considered pathogenic/likely pathogenic in ClinVar.
- 19 poison exons are considered uncertain in ClinVar.
- The uncertain classifications are important to the research as it may provide stronger evidence that these variants might be pathogenic

6. Future Directions

- Analyze phenotypic data in other cohorts such as UK BioBank and All of Us by looking at individuals that have blood clots, aneurysms, and strokes.
- Analyze the genotypic data in other cohorts such as UK BioBank and All of Us by looking at splice variants in the 37 genes.

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8. Acknowledgements

Principal Investigator: Abby E. Hare-Harris Ph. D.
Graduate Student Researcher: Katelyn E. Kelchner

The drift fence hypothesis: Testing an adaptive function for projectile directional defecation in the purseweb spider *Atypus karschi*



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ABSTRACT

The purseweb spider, *Atypus karschi*, is an atypical tarantula that lives inside vertical silk tubes (webs) that extend above and below ground. Prey that contact the tube are bitten then pulled inside without the spider ever exiting the web. Since the spider rarely leaves and may live for up to a decade, we investigated how these spiders may increase prey contact with the web and how they adapted their latrine habits to accommodate a sessile foraging mode. Under laboratory conditions, we documented spider excretion frequency, distance, and pattern around their tubes. Although spiders occasionally exited their tubes, almost all of them excreted by projectile defecating via the top of the web about every 36 hours. Maximum ejection distances reached approximately forty body lengths (over half a meter from the tube). Spiders also ballistically produced linear or V-shaped excreta patterns along vectors extending an average of 14 cm from the web but sometimes reaching over 70 centimeters long. Excretions showed strong directional bias both on the individual and population level. Spiders with their webs against a vertical wall, defecated significantly more in a single direction opposite the wall. When placed in the center of a large circular arena without walls, they showed strong and significant bidirectional defecation patterns, creating a line through the diameter of the arena. We hypothesized that such linear excreta patterns function as a drift fence trap for prey. If this is the case, small ground arthropods should avoid or walk along these excreta lines rather than through them, increasing the probability of excreta-adverse prey contacting the web. We tested the drift fence hypothesis with female *Pardosa milvina* wolf spiders. Individual *Pardosa* were placed in a circular arena superimposed over a purseweb excreta line and measured prey avoidance of excreta and the propensity of prey to walk along rather than through spider excreta deposits. We found *Pardosa milvina* spent significantly more time on the side with the excreta, traveled greater distances on the side without excreta, and avoided areas with excreta. This indicates higher freeze responses and possible redirected movement when detecting excreta. *Pardosa* showed excreta-mediated behavioral changes suggesting some support for projectile defecation functioning as a capture drift fence. We are currently testing other prey types (woodlice) and contact frequency with the center of an arena with and without the presence of purseweb excreta.

INTRODUCTION

Defecation is a necessary biological process for animals¹ For most, the main purpose of defecating is waste elimination.¹ Others use specific defecation sites (latrines) to limit possible parasitic interactions² or to eliminate odor cues that may attract predators or induce antipredator responses in prey.³ For central place terrestrial foragers that may live years, buildup of excretory products around living spaces can be especially problematic since it may allow easy detection of the spider in the area.

The purseweb spider, *Atypus karschi*, is an atypical tarantula that lives permanently within a vertically-oriented tube that projects underground for approximately 16 cm. The spiders wait until prey contact the web. After contact, the spider bites through the web and pulls the prey inside without ever leaving the web. These spiders projectile defecate from the top of their burrows to eliminate waste. We quantified the frequency, pattern, and distance of excretory ejection and tested if they excrete in a non-random direction. Since prey may use predator excretions to detect the presence of a predation threat, we hypothesized that these purseweb spiders may use their excreta adaptively to channel or redirect prey nearby toward the web and therefore increase contact frequency and predation efficiency on a web with a relatively small surface area.

QUESTIONS

- What is the frequency, distance and dispersal pattern of excretion (defecation) in the purseweb spider *Atypus karschi*?
- Is their projectile defecation directionally non-random?
- Do purseweb prey modify their behavior when encountering purseweb excreta?
- Could purseweb spider excretion patterns function as a drift fence trap for prey?

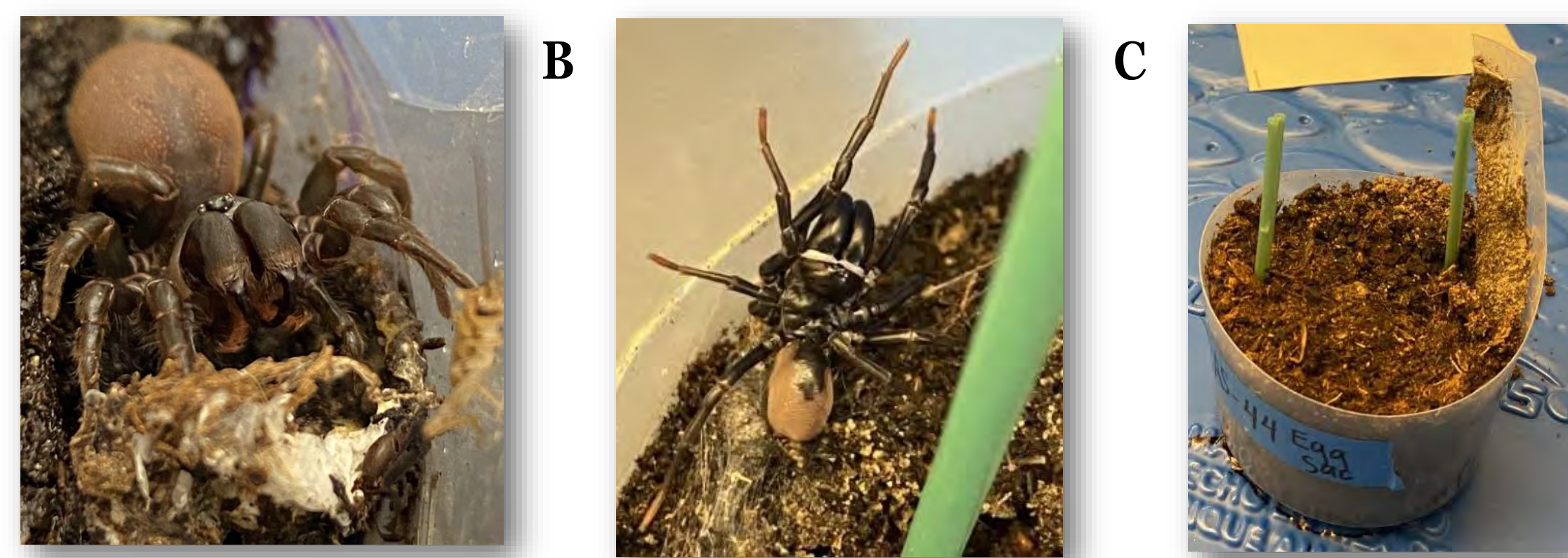


Figure 1. A. Female *Atypus karschi* located out of web with fangs drawn B. Male *Atypus karschi* located out of web. C. Container placed in testing arena with vertical web at right.

METHODS

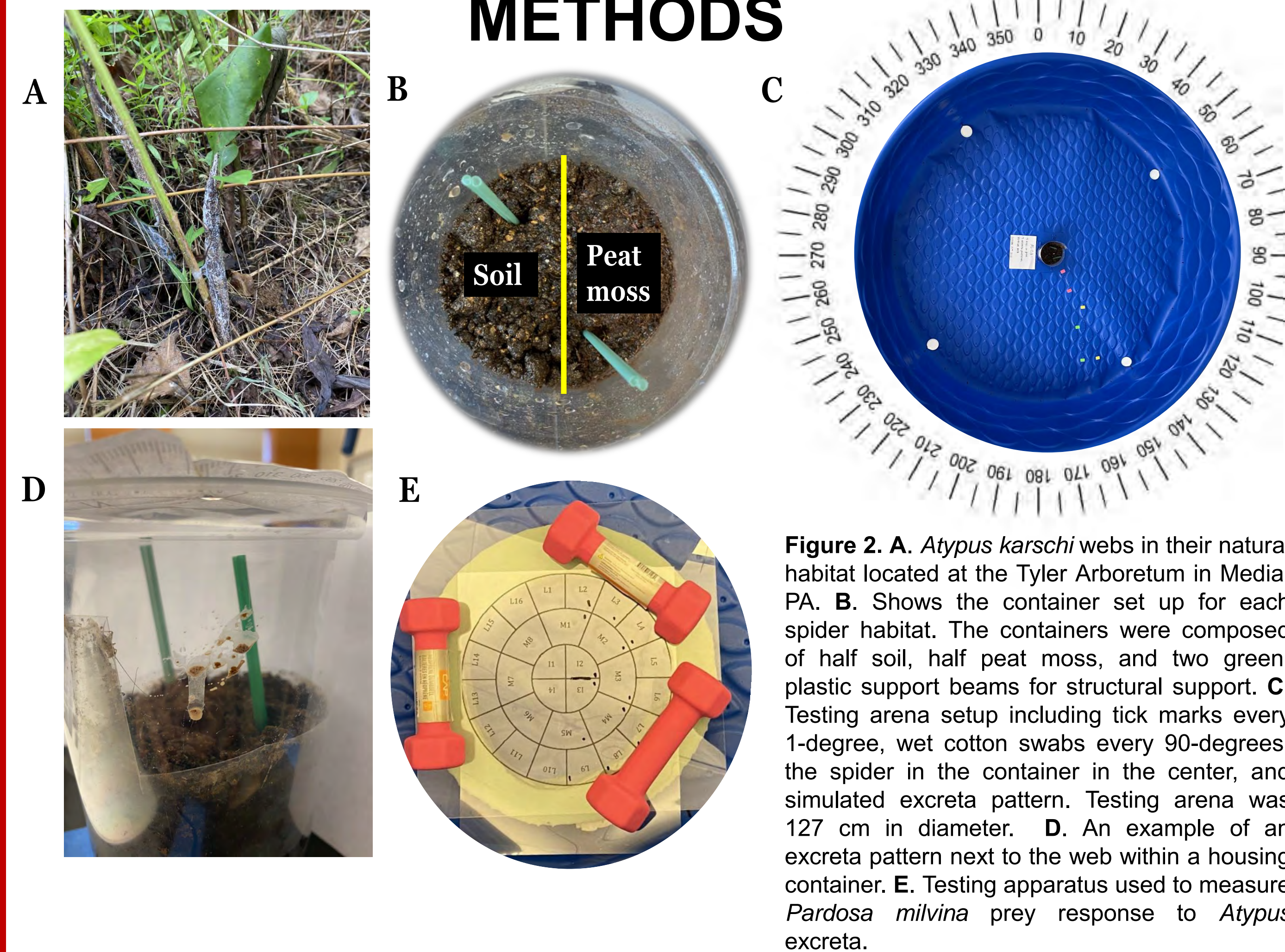


Figure 2. A. *Atypus karschi* webs in their natural habitat located at the Tyler Arboretum in Media, PA. B. Shows the container set up for each spider habitat. The containers were composed of half soil, half peat moss, and two green, plastic support beams for structural support. C. Testing arena setup including tick marks every 1-degree, wet cotton swabs every 90-degrees, the spider in the container in the center, and simulated excreta pattern. Testing arena was 127 cm in diameter. D. An example of an excreta pattern next to the web within a housing container. E. Testing apparatus used to measure *Pardosa milvina* prey response to *Atypus* excreta.

RESULTS

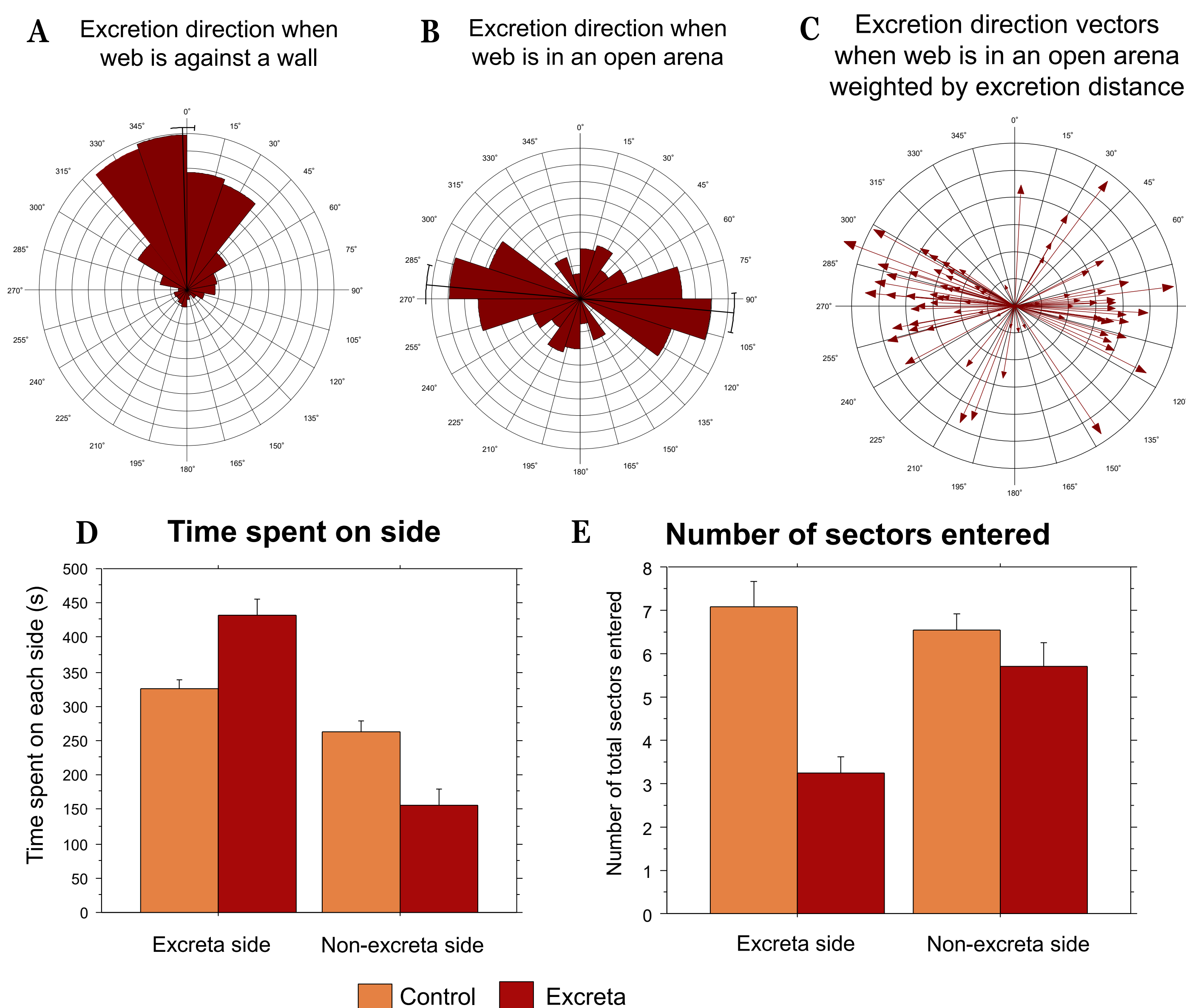


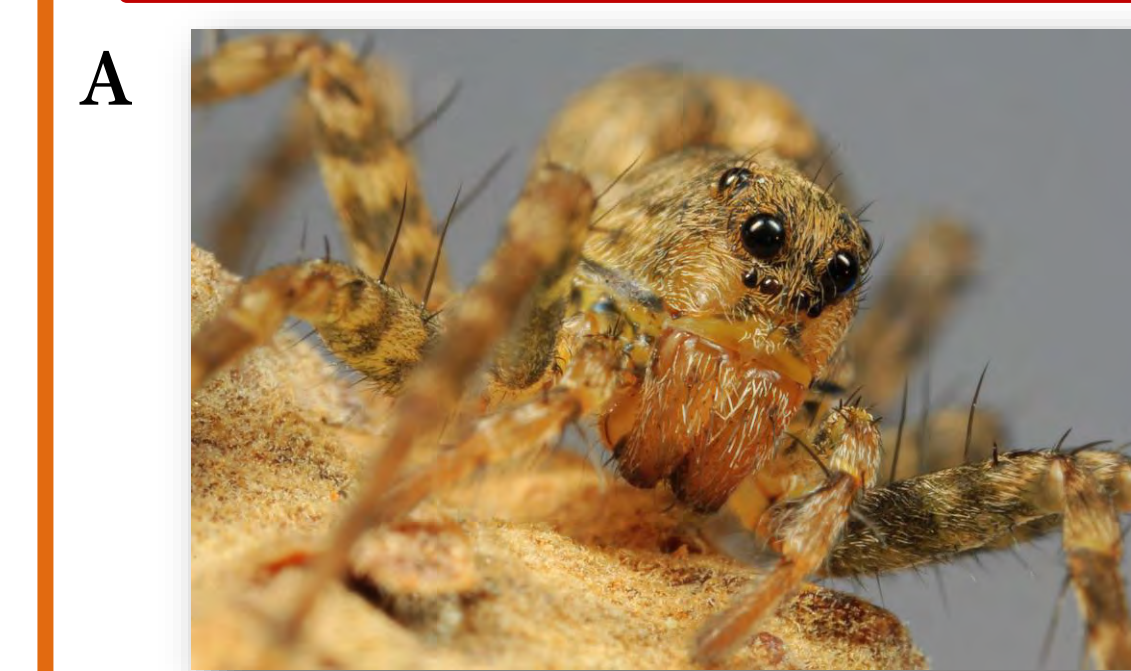
Figure 3. A. The mean angle of defecation within their housing containers (Fig. 2A) (0-360°) for all spiders combined over a two-month period (Rao's Spacing Test, $U=345.2$, $p<0.01$; 46 test subjects, $n=680$ defecation events) B. Mean angle of defecation from the center of wading pools (0-360°) ($N=46$ spiders, $n=82$). Rao's Spacing Test, $U=192.58$; $p<0.01$) C. Testing arena mean angle (0-360°) weighted and including mean distance of excreta (cm) ($N=46$, $n=82$). D. Time *Pardosa milvina* prey spiders spent on the excreta side versus the time spent on the non-excreta side ($N=23$). Two-way within-between subjects ANOVA test (Excreta presence: $F=0.50$, $p=0.8243$; Time on side: $F=35.139$, $p<0.0001$; Excreta presence * Time on side: $F=14.246$, $p=0.0005$). *Pardosa* tended to freeze when encountering excreta from *Atypus*. E. The mean number of total sectors entered on the excreta side with the presence or absence of excreta. Two-way within-between subjects ANOVA test (Excreta presence: $F=26.312$, $p<0.001$; Number of total sectors entered on excreta side $F= 3.807$, $p=0.574$), and presence of excreta*number of total sectors entered, $F=9.388$ ($p=0.0037$). Spiders showed significant avoidance of sectors with excreta.

SUMMARY

- Some spiders were able to shoot excreta over 70cm (ca. 40 body lengths). To our knowledge, this may constitute the greatest projectile defecation distance of any animal relative to body length.
- Spiders defecated approximately every three days and produced long linear or V-shaped patterns extending outward from the web. They also showed a highly significant bias in their excretion direction at both the individual and population level.
- When the vertical web was against the side of a container (Fig.2D) or other continuous wall, spiders excreted along a single vector equidistant and maximally distant from the side of the container (Fig. 3A).
- When the vertical web was centered away from any continuous wall (Fig. 2C), spiders showed a strong axial or bidirectional excretion pattern with two excretion lines 180 degrees apart (Fig. 3B,C) This pattern was also highly significant at the individual and population level.
- A potential prey, *Pardosa milvina*, spent longer periods of time on the excreta side but crossing fewer sectors than areas without excreta. This indicates higher freeze responses of prey and less general activity when encountering *Atypus* excreta.

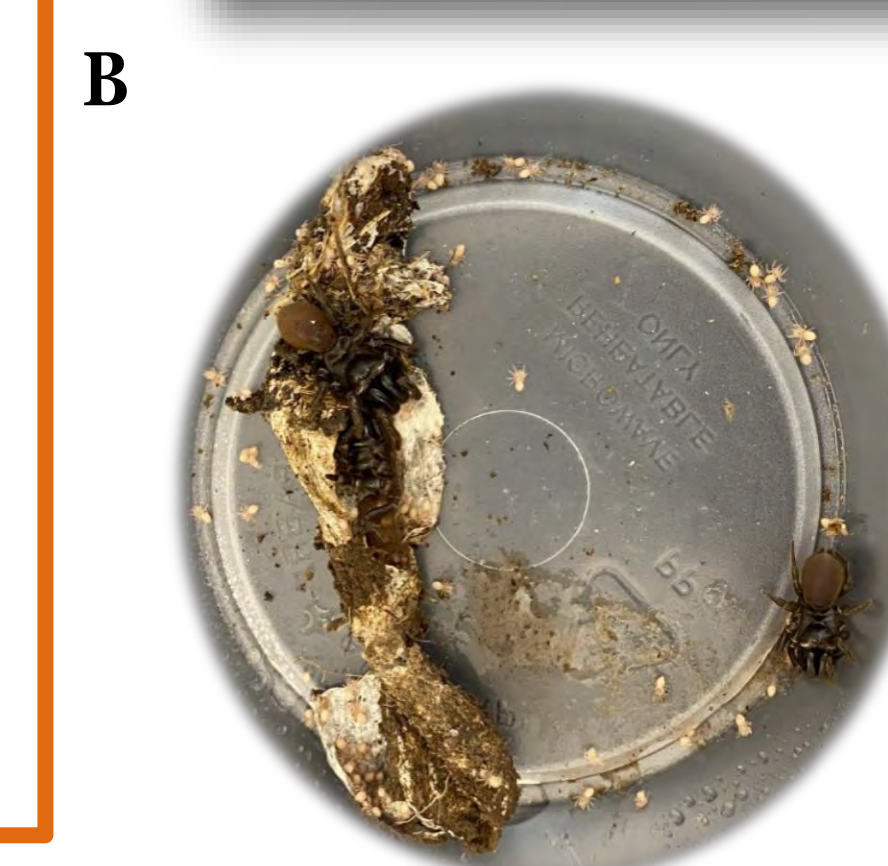
CONCLUSIONS

- Individual purse web spiders as well as populations appear to defecate in the same non-random direction. Along trees, walls, or other continuous borders, they defecate at a right angle relative to the vertical structure behind them. When in open habitat, they produce two axial vectors of excreta that project out at 180 degrees from each other. These linear patterns are consistent with a drift fence and these excreta patterns do change the behavior of at least one possible prey species when encountered. Additional studies using other prey (woodlice) are ongoing. We are also currently conducting a study examining if long term defecation patterns around the web translate into increased encounter rates with prey.



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Figure 4. A. Test subject, female *Pardosa milvina*. B. Multiple adult *Atypus karschi* found living with first instar spiderlings within the same web after excavating the webs at the Tyler Arboretum indicating the species is communal.

Are earthworm body wall synapses both cholinergic and GABAergic?

Fluorescent staining of VIAAT and VACHT

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Background:

GABA is the most common inhibitory neurotransmitter of the central nervous system that works to decrease muscle wall contraction in earthworms

Acetylcholine is the known excitatory neurotransmitter at the earthworm body wall synapses

Vesicular transporters move neurotransmitters and other chemicals into vesicles to be released from the axon

It is unknown if synapses in earthworms are GABAergic, cholinergic, or if the synapses are a combination of both

This project was completed in part of the requirements of a Master of Science degree in biology from Bloomsburg University

Materials and Methods:

An earthworm was dissected from the dorsal side and extra peripheral tissue was trimmed away

The tissue was placed in a paraformaldehyde fixative, rinsed with buffer, and placed in a blocking solution

Primary antibodies were placed on the sample and the sample was placed in a fridge on a shaker overnight

Secondary antibodies were added the next day for two hours at room temperature on a shaker

Sample was stored in fresh PBS

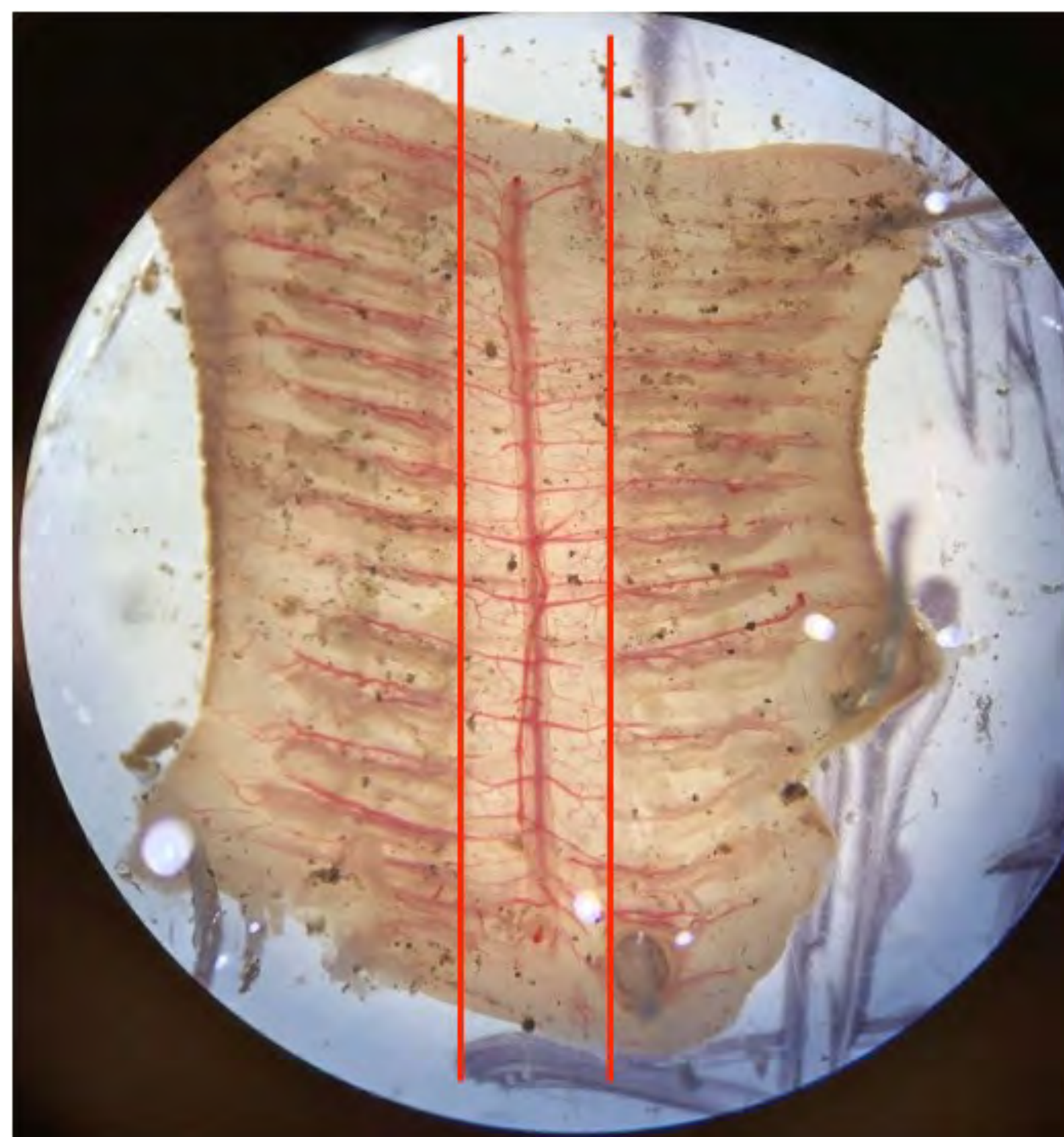
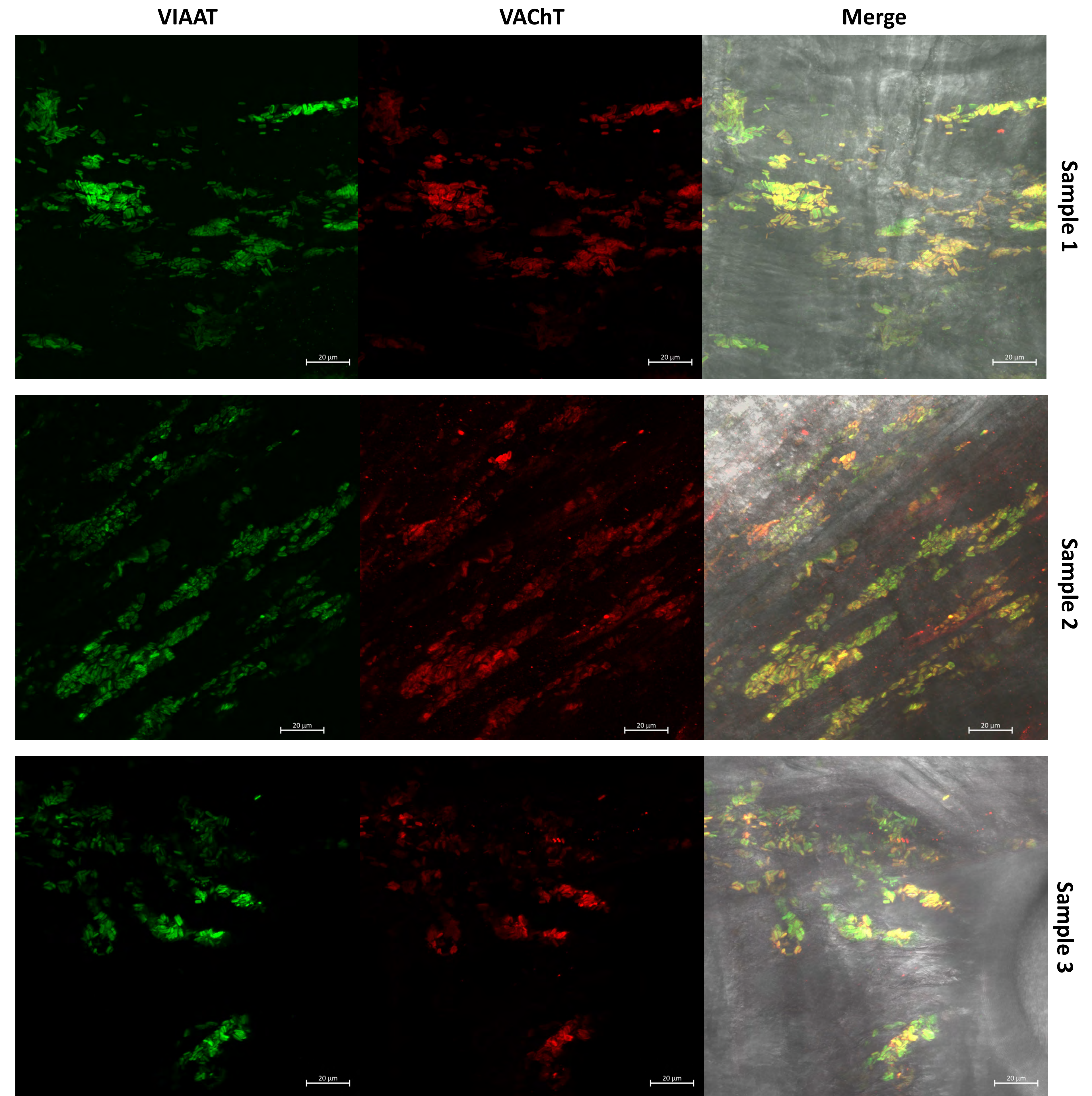


Figure 1 (to the left): Dissection of the earthworm with the ventral nerve cord intact. The peripheral tissue was cut away at the red vertical lines. The tissue in between the red lines was kept and stained. This was done to prevent excessive background staining and to keep only the tissue section we want to visualize under the confocal microscope.

Figure 2 (right): Confocal microscopy images with the double stain for VIAAT and VACHT. The images on the far left in green represent the vesicular inhibitory amino acid transporter, VIAAT. VIAAT allows GABA to enter the vesicle in the axon terminal to be released by the neuron, inhibiting the postsynaptic neuron. The middle images in red represent the vesicular acetylcholine transporter, VACHT. VACHT packages acetylcholine in vesicles to be released by the neuron, providing an excitatory signal to the postsynaptic neuron. The images on the far right with the grey background is the merged image of both VIAAT and VACHT. The yellow indicates that both VIAAT and VACHT are present in the axon terminal, meaning the synapse can send inhibitory and excitatory signals.

Preliminary Results:



Conclusions:

- Many synapses appear to be cholinergic and GABAergic based on the images above, but separation of green and red is still visible in some areas

Future Directions:

- Using synaptogreen with a high and a low GABA concentration and compare to controls
- Using electrophysiology to determine the effect of extracellular GABA on earthworm tissue

Acknowledgements:

- Dr. William Coleman for his guidance and assistance throughout this project
- The Department of Biological and Allied Health Sciences at Bloomsburg University for the use of the laboratory and laboratory equipment
- Susquehanna Valley Undergraduate Research Symposium for allowing me the opportunity to share my thesis research

Introduction

Background

- ❖ In 2020, the Covid-19 pandemic made its way across the world and created devastating consequences on education. Collegiate level education was affected severely due to loss of time in classrooms, loss of experiences, and loss of students both current and future. Nursing education was impacted greatly, but not much research has been completed on these future nurses that allows for a gain of perspective as to what they are/have been going through.
- ❖ The losses to undergraduate nursing education include in-person lab simulations, clinical opportunities, and other hands-on learning opportunities. All these experiences allow for nursing students to gain proper experience and delve deep into their future career.
- ❖ To our knowledge, there have been limited studies completed that seek to gain insight on nursing students' perspectives about their education that also explore alternative methods towards education should another online transition for education need to occur.

Research Questions

- ❖ How do nursing students feel comprehensively about their undergraduate education as a whole?
- ❖ What substitutions/applications were used as supplemental to decrease the overall loss of education?
- ❖ How do nursing students feel about their future as nurses?

Hypothesis

- ❖ We hypothesized that nursing students would feel less prepared to become nurses because of lost experiences and application time due to the pandemic. We also predicted that there would be a heavy increase on specific supplemental resources that were intended to aid students.

Method

Pilot Study

- ❖ Participants will be recruited from a group of Interns and Externs currently at Geisinger Danville that also go to Bloomsburg University.
- ❖ The goal for the pilot study is to obtain feedback about the questionnaire to make any potential changes before completing the final study.
- ❖ The Pilot Study will be completed once IRB approval has been given.
- ❖ Participation in the pilot study will be completely voluntary as there is less likely to be compensation for the participants' time.

Final Study (Fall 2022 semester)

- ❖ Participants in the final study will include Bloomsburg University Undergraduate Nursing majors.
- ❖ Students will be recruited via major nursing classes during the Fall 2022 semester.
- ❖ Students will receive compensation for participating in the form of extra credit, participation points, or another form of compensation for the class that the study is completed in.

Follow-up with PILOT study

Students may give their opinion on the questionnaire

1. What did they think about the questionnaire?
2. Is the questionnaire easy to follow and answer?
3. What could be included to make the questionnaire more comprehensive of feelings and insight as to how much impact the pandemic has had on education?

Questionnaire



- ❖ The questionnaire was composed by including questions from previously created surveys and adding in other prevalent questions that we found to be important to the study.
- ❖ Interns/externs (during the pilot study) and students (during the final study) will access the questionnaire by scanning a QR code that will take them to the Qualtrics survey.
- ❖ The first page that will appear is the informed consent statement. Students must click the box giving consent to participate in the study to be included.
- ❖ Then, the survey questions will appear after the informed consent page for the participant to answer.

Questionnaire

Includes questions about:

1. Demographic information
2. Current healthcare employment?
3. Agree/Disagree questions based on their experiences with pandemic education.
4. Questions about their dealing with online learning due to the pandemic.
5. Questions about resources made available to them by professors and what resources they accessed on their own.

Agree/Disagree Question Hypotheses

- ❖ These are our top 4 research questions and our prediction of how participants will answer and what our results will conclude...
- ❖ Question 1: The pandemic has strengthened my desire to become a nurse?
 - We hypothesize that students will agree that they have a stronger desire to become a nurse after seeing and being the healthcare system while the world was in crisis.
- ❖ Question 2: The pandemic has affected at least one of my clinical experiences?
 - We hypothesize that juniors and seniors will generally state that they have had a clinical experience interrupted or taken away by the pandemic because most hospitals were not allowing unnecessary personnel, visitors, or other outside persons be in the hospital or allow students into their clinical experiences to not spread the Covid-19 pandemic.
- ❖ Question 3: I felt adequately prepared to transition to online/remote learning?
 - We hypothesize that students will claim that they did not feel adequately prepared for the transition to online learning because it took many school and educational institutions time to determine how programs were going to continue to run and how to handle the pandemic in general.
- ❖ Question 4: I was easily able to access and transition to using the online resources and materials?
 - We hypothesize that because Bloomsburg is known for being a rural school, students were not as adequately able to access or use online resources due to lack of availability of technology while not in school, as well as the complexity of some of the technology used in favor of in-person classes such as recorded lectures and simulations.

IRB Approval

- ❖ Due to the IRB approval process, the pilot study has not been able to be completed.
- ❖ Therefore, we are not able to have participants complete the questionnaire and gain preliminary insights about the thoughts and feelings of undergraduate nurses or gain insight as to the accuracy of our questionnaire to get into student participants' minds, thoughts, and feelings about learning during the pandemic.

APA Paper

- ❖ While waiting for IRB approval we have begun writing the APA paper with the background information that has been collected and the method section.
- ❖ The goal is for the APA paper to be completed by the end of the Fall 2022 semester.
- ❖ After the paper is written and finalized, we are going to start the publishing process. Our goal is to have the study published in a peer-review psychology or nursing journal.

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Transient Storage Zones & Civil Infrastructure Interactions in Local Streams near Lewisburg, PA

Abstract

Transient storage occurs when solutes enter small pockets of slow-moving water in a stream or river or when they leave the main channel and enter the porous material in the channel bed and banks. While water moves through the main channel of a stream it moves in and out of many transient storage zones along the way. This results in exchanges of solute mass between the main channel and the transient storage zones which affect the water quality and health of the surrounding ecosystem. Infrastructure interrupts this process and as an effect that lasts for a greater distance than the reach directly around the infrastructure. We used ArcGIS to analyze data in the Buffalo Creek Watershed. In addition, field observations helped to verify the ArcGIS data analysis.

Introduction

Transient storage zones are small pockets of slow-moving water that interact with solutes and impact water quality and the surrounding ecosystem (Runkle, 2000; Winter et al., 1998). However, modern infrastructure has changed how streams naturally flow because now there are various forms of bridges and culverts used to prevent streams from flooding roadways. This infrastructure can change flow patterns in the main channel and impact the processes in transient storage zones (Mueller Price et al., 2015). In addition, civil infrastructure creates impervious surfaces near stream systems. Therefore, the presence of infrastructure can create substantial discontinuity in a stream (Bracken et al., 2013).

Research Question:

The specific research question that we focus on is the impact of civil infrastructure, such as bridge crossings, culverts, and other land use changes, on transient storage zone characteristics and processes. We used ArcGIS mapping and data analysis for an initial investigation of the extent of infrastructure impacts on streams. Further research approaches are discussed that could help to determine how the presence of infrastructure impacts the stream processes in more detail.

Methods

ArcGIS Pro is a computer program that can be used to explore, visualize, and analyze data in 2D and 3D maps. This application was used to analyze the overlap of bridges and culverts with local streams in the Buffalo Creek watershed in Pennsylvania. ArcGIS was also used to calculate the surrounding land use and the reach of the stream that is impacted by the civil infrastructure. Data on the PA stream order, bridges, road centerlines, and land cover in the Buffalo Creek Watershed were analyzed to determine infrastructure impact. Our data analysis results were verified by multiple site visitations throughout the duration of the research.

Acknowledgements

ArcGIS Pro was used for analyzing data and Zotero was used to organize sources and create citations. This research was funded by the Bucknell College of Engineering Annual Hymas Gift and the Department of Civil & Environmental Engineering and mentored by Professor Newlin.

Results & Discussion



Figure 1. Images of Buffalo Creek at Strawbridge Road (a) upstream (b) downstream

Bridges and culverts often make a stream wider before and after the infrastructure because vegetation is cleared during construction and a wider opening allows more water to pass under the bridge during high flows. This causes a change in stream flow which creates storage pockets before the structure and influences the interaction time between the surface and subsurface water.

Additionally, the presence of bridges and culverts impacts the depth of the stream. When the velocity of stream flow changes so does the amount of sediment that is transferred and deposited. Due to this change it was found that streams have various depths before the bridge or culvert and a more uniform depth following the infrastructure as seen in Figure 1.

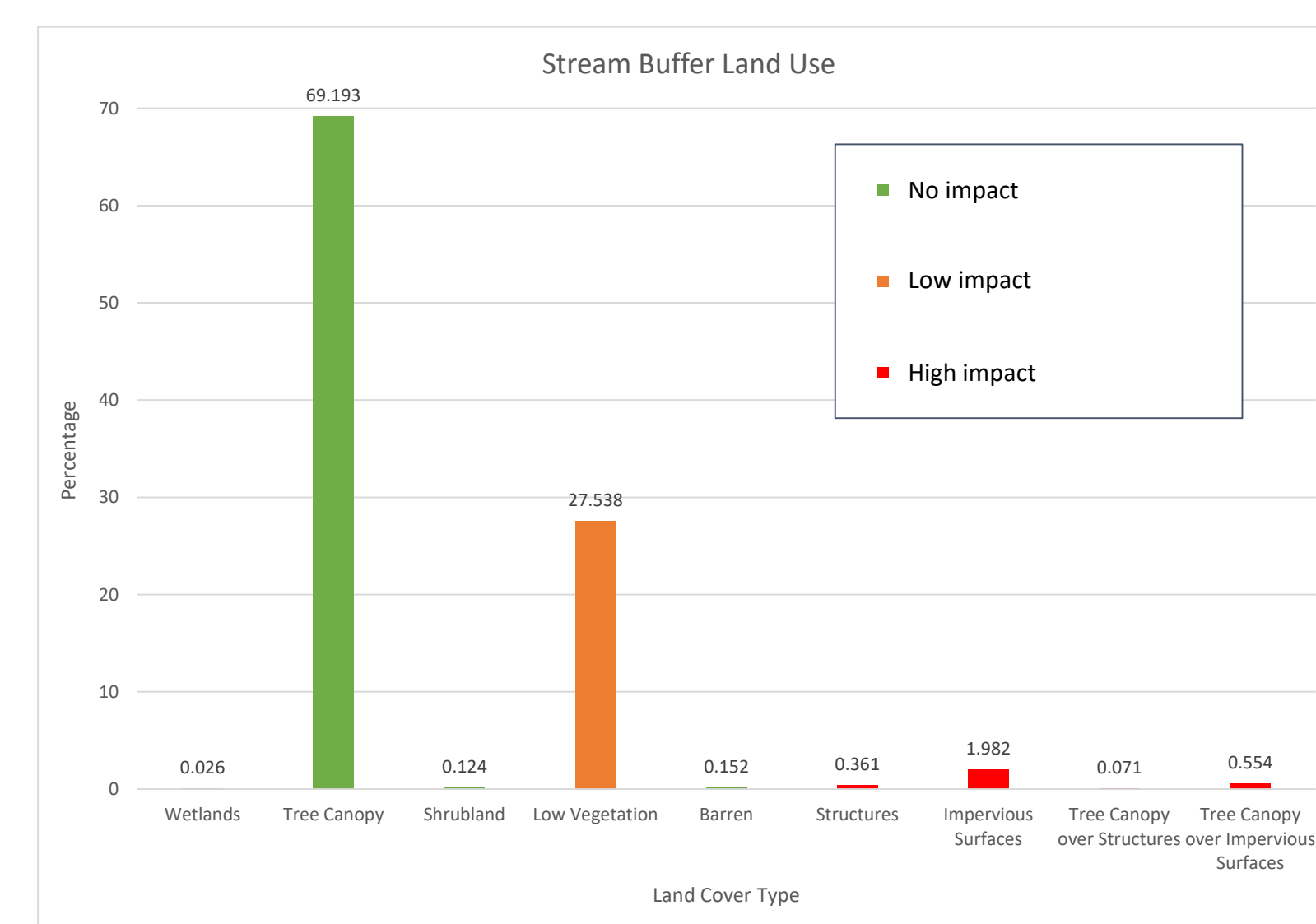


Figure 2. Land Cover in the 100' stream buffer zone in Buffalo Creek. Colors represent impact from infrastructure.

In ArcGIS, Chesapeake Conservancy's high-resolution land cover data was used to calculate the percentages of land cover in the buffer zones surrounding local streams pictured in Figure 2. The largest category is tree canopy which makes up 69.2% of land use in the stream buffer.

Buffalo Creek Watershed Data

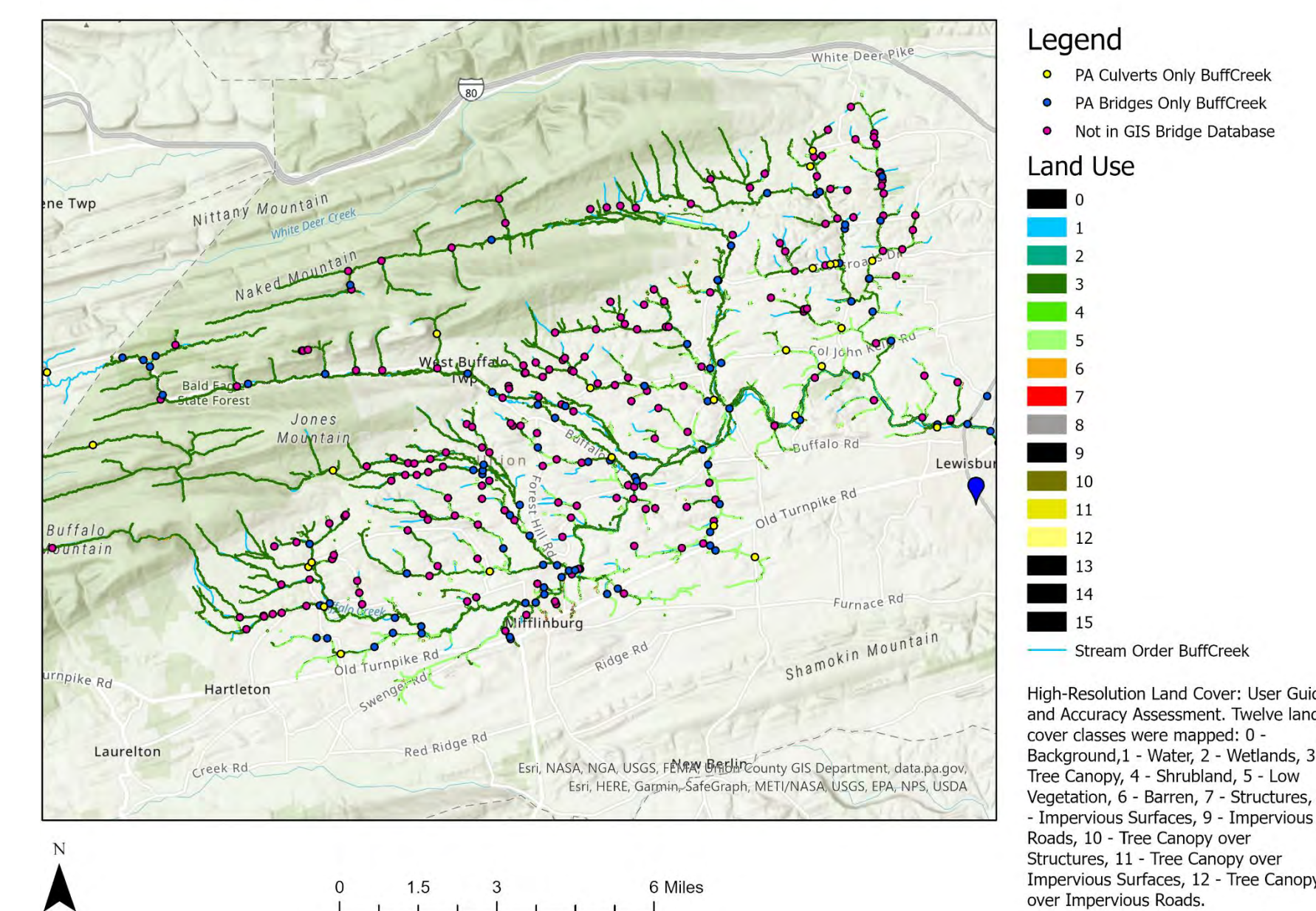


Figure 3. Layout from ArcGIS of an overview of the Buffalo Creek Watershed data

In GIS local and state road data in the Buffalo Creek watershed were overlapped to identify intersections where bridges or culverts should be located. About 200 intersections were missing infrastructure data and of the few that were investigated, culverts were found at all locations Figures 3 and 4. All the intersections that were missing data were located on Township roads implying that these culverts are not regulated or inspected by the state.

Using the average bridge width & typical PennDOT right-of-way measurement of 33' the estimated impacted stream length was 28,130 ft. Compared to the total stream length of 1,319,762 ft, 2.13% of the stream length is impacted by civil infrastructure.

Conclusion

Civil infrastructure in streams such as bridges and culverts impact the natural flow of streams and disrupt the surface subsurface water interactions. The ArcGIS analysis can give us an estimate of the extent of the impact of civil infrastructure on transient storage processes in streams.

Future Research

The data and information collected during this research can be continued in the future to determine the impact that civil infrastructure has on the water quality of streams and interactions with groundwater. Additionally, different methods of determining impacted stream length results can be analyzed for similarities & differences.

Tracer-injection studies can be used in sections of the streams that have the civil infrastructure to estimate the timing, magnitude, and duration of a pollutant cloud. They can also be used to determine the physical characteristics of the stream such as the storage-zone cross-sectional area and the storage-zone exchange coefficient (Buckner, 2020) to identify infrastructure impacts in more detail than the mapping analysis.



Figure 4. Image of a culvert in Buffalo Creek at Gessner Lane

Implementation and Evaluation of a Mail Order Pricing Tool

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Background

- Nearly 1 in 5 adults, aged 40-79 years, use at least 5 prescriptions¹.
- Medication costs can contribute to medication non-adherence leading to worse patient outcomes, increased healthcare costs and even death in some cases².
- Geisinger Health Plan (GHP) provides cost saving incentives for patients utilizing Geisinger Mail Order Pharmacy (MOP) for their prescription fills.
- Prior studies have shown that an outreach program which presents cost savings increased mail order utilization³.
- A MOP pricing tool was developed to allow healthcare team members to readily calculate and compare estimated patient yearly prescription costs for both retail and MOP.
- The objective of this cohort study is to determine the influence this pricing tool has on MOP utilization.**

Intervention

- Excel spreadsheet for healthcare team members to manually choose the patient's GHP GOLD (Medicare Part D) insurance and enter patient-specific medication list.
- Calculates the yearly cost for 30-day retail, 100-day retail, and 100-day mail order, where patient specific cost differences can be seen in real time.
- Only takes into consideration initial coverage phase.

	A	B	C	D	E	F
1	Insurance					
2	Classic Complet	Medication	30 day retail	100 day retail	100 day mail order	
3		Metformin	\$3.00	\$7.50	\$0.00	
4		Lisinopril	\$3.00	\$7.50	\$0.00	
5		Jardiance	\$47.00	\$117.50	\$70.50	
6		Albuterol	\$20.00	\$50.00	\$0.00	
7		Atorvastatin	\$3.00	\$7.50	\$0.00	
8		Trelegy	\$47.00	\$117.50	\$70.50	
9		Omeprazole	\$3.00	\$7.50	\$0.00	
10		Hydrochlorothiazide	\$3.00	\$7.50	\$0.00	
11		Ozempic	\$47.00	\$117.50	\$70.50	
12						
13						
14		Yearly Total	\$2,112	\$1,760	\$846	
15						\$1,266
16						\$914
17		*Cost savings are our best ESTIMATE but do not take into account other coverage, deductibles, or coverage gaps*				
18						
19						

Figure 1. Mail Order Pricing Tool Example

Methods

Cluster randomized, stepped-wedge pre-post study

- Geisinger Medication Therapy Disease Management (MTDM) pharmacists' access to MOP tool

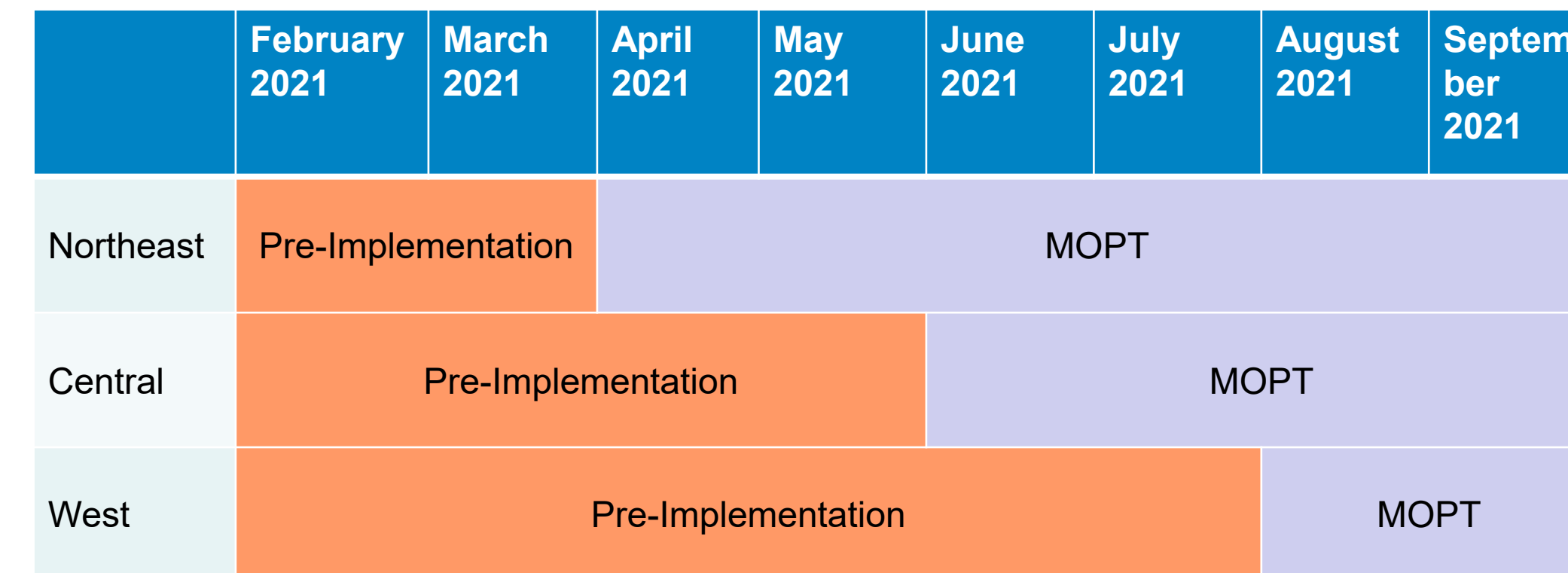


Figure 2. Stepped-Wedge Design

Survey

- Users of the tool were interviewed to determine barriers and facilitators to tool use

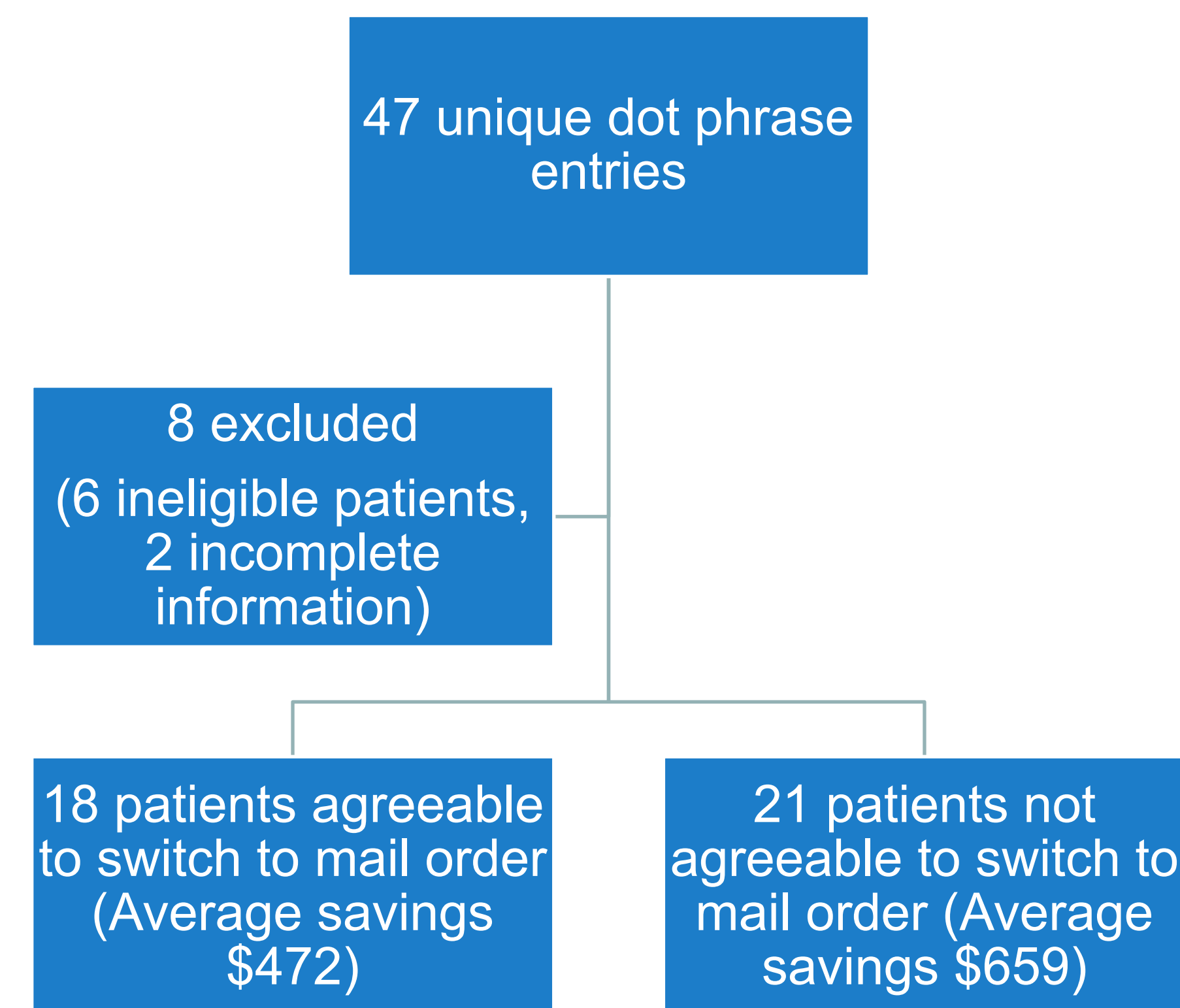


Figure 3. Dot Phrase Results

- There was no association between cost savings and patients' willingness to switch to mail order
- Documented 7 patients who would consider switching in the future

Survey Results:

- 11 responses, 82% (9) used for MOPT.
- Top reasons for not using tool: "did not think about tool during encounters, not enough time in visits."

Inclusion criteria:

- Patients with at least 1 MTDM appointment and GHP Gold insurance

Data Collection:

- Dot phrase ".MOPT"
- Electronic Health Record (Prescription Orders)
- Survey

Statistical Analysis

- Descriptive statistics (Proportions, Medians, etc.)
- Inferential statistics (Fisher's Exact test & McNemar's test)
- SAS & R Studio

Results

	Pre-period	Post-Period
# of Patients	3972	3971
# of Prescriptions	48452 (57%)	35861 (43%)
# of Prescriptions Per Patient Median (IQR)	12 (19)	15 (22)

Table 1. Patients and Prescriptions in the Pre and Post Periods

Therapeutic Class	# Prescriptions n(%)
N= 84312	
Cardiovascular Agents	28870 (34.24%)
Endocrine & Metabolic Agents	23147 (27.45%)
Hematological Agents	6315 (7.49%)
Central Nervous System Agents	5560 (6.59%)
Gastrointestinal Agents	5212 (6.18%)

Table 2. Top 5 Most Common Therapeutic Classes

- A higher proportion of prescriptions were sent to Mail Order in the post-period, after the implementation of the MOP tool, than those of the pre-period.
- The risk of a prescription being sent to mail order was 7% higher than being sent to another pharmacy (RR 1.07, 95% CI 1.05-1.10)
- Patients in the post-period were 2x more likely to stop using mail order than to switch to mail order.

Discussion

- Use of the mail order pricing tool was voluntary and manual. Documented use of the tool was low.
- Despite a higher proportion of prescriptions being sent to mail order, patients were more likely to stop using mail order than to start using mail order
 - This may suggest that patients with higher prescription burden and thus higher cost savings were more likely to switch to mail order
- Concerns about the security and reliability of mail order prevent patients from switching to mail order
 - Delays in mail during COVID may have contributed to patients leaving or fewer patients transiting to mail order.
- We performed an intention-to-treat analysis therefore not all patients analyzed were exposed to the tool.
 - Examining only those who were exposed to the tool may give a better understanding of the effect of the tool, however, better implementation strategies may be needed to improve pharmacist use.

Conclusion

A manual mail order pricing tool did not increase the number of patients who used mail order. A better implementation strategy may need to be employed for a mail order pricing tool to have an effect on the number of mail order users.

Acknowledgements

Thank you to Geisinger and the Center for Pharmacy Innovation and Outcomes for hosting me as a summer undergraduate research student this past summer.

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Effect of Subthalamic Nucleus Deep Brain Stimulation on Levodopa and Dyskinesia Reduction in Parkinson Disease

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Introduction

- Parkinson disease (PD) is caused by the death of dopamine releasing neurons
- Levodopa, a precursor of dopamine, is a medication for treating PD
- Dyskinesia, involuntary and uncontrollable movements, is a side effect of levodopa
- Deep brain stimulation (DBS) is a surgical option for PD patients when levodopa loses overall effectiveness
- Volume of tissue activation (VTA) modeling is used to determine stimulation location [1]
- The subthalamic nucleus (STN) is a standard stimulation target for improving PD motor symptoms
- DBS reduces levodopa and dyskinesia, but it is still unknown whether their stimulation locations overlap

Objective: Determine optimal stimulation location for the greatest levodopa and dyskinesia reduction

Methods

- 40 PD patients received bilateral STN DBS
- VTAs were calculated using patient-specific tissue activation modeling [1] for 72 hemispheres (Figure 1)
- Activation in the dorsal-ventral, medial-lateral, and anterior-posterior directions was calculated in the STN and external to the STN
- Levodopa-equivalent daily dose (LEDD) was recorded at pre-/post-operation
- Dyskinesia scores (MDS UPDRS-IV) were recorded pre-/post-operation
- Statistical analysis was performed comparing stimulation location and LEDDD and dyskinesia reduction

$$\text{STN activation (\%)} = \frac{\text{Number of VTA voxels in STN}}{\text{Total number of STN voxels}} \times 100$$

$$\text{External activation (\%)} = \frac{\text{Number of VTA voxels not in STN}}{\text{Total number of VTA voxels}} \times 100$$

$$\text{LEDD reduction (\%)} = \frac{\text{LEDD}_{\text{pre-op}} - \text{LEDD}_{\text{post-op}}}{\text{LEDD}_{\text{pre-op}}} \times 100$$

$$\text{Dyskinesia reduction (\%)} = \frac{\text{Dys score}_{\text{pre-op}} - \text{Dys score}_{\text{post-op}}}{\text{Dys score}_{\text{pre-op}}} \times 100$$

VTA Modeling

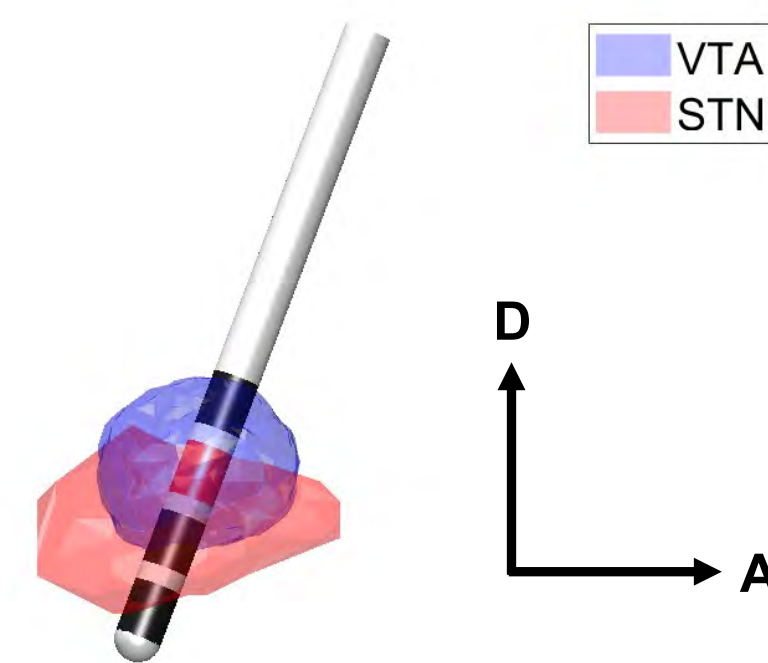


Figure 1. Sagittal view of VTA (blue), STN (red), and DBS lead. D is dorsal and A is anterior.

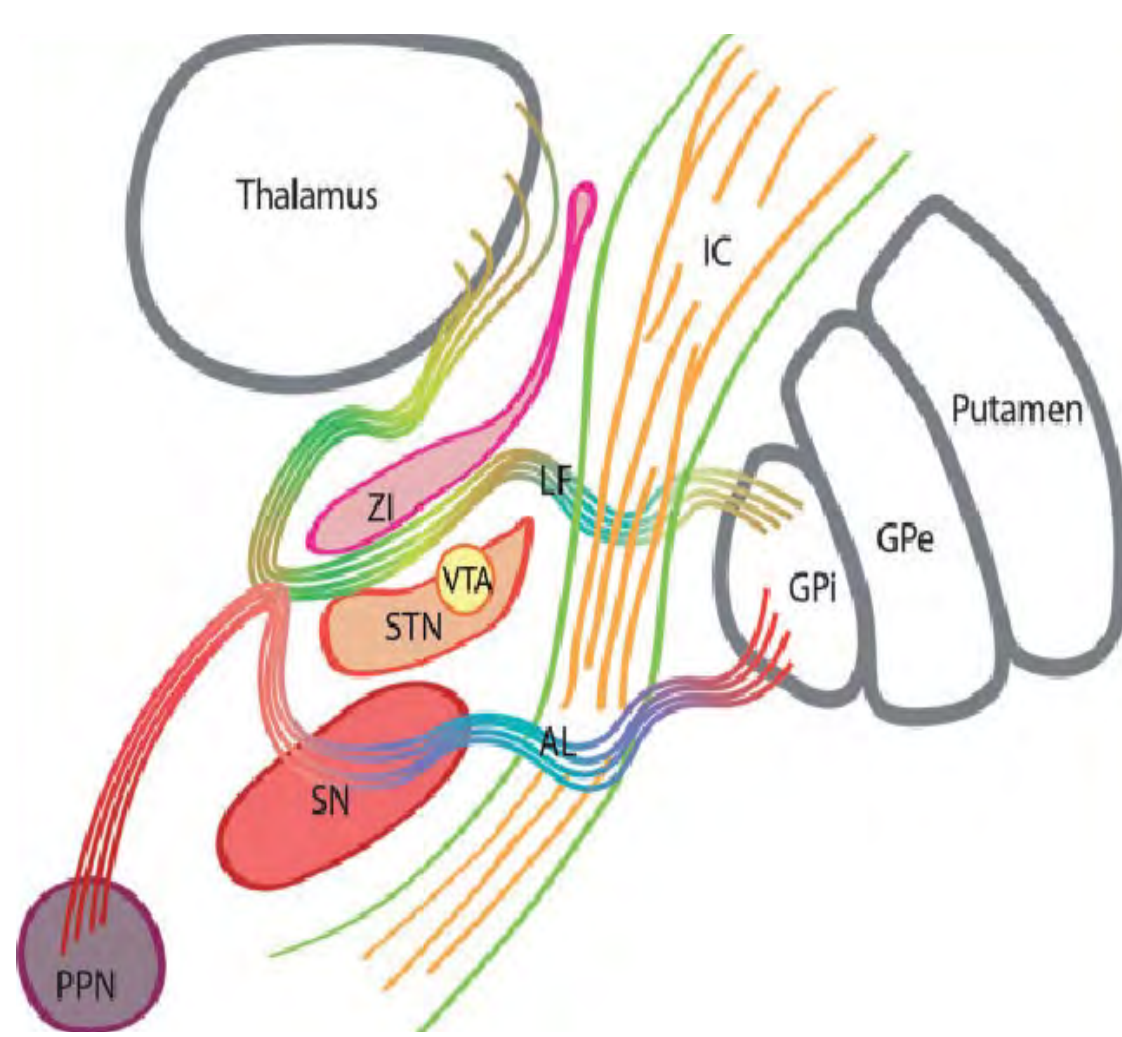


Figure 5. Structures and tracts surrounding the STN, which may also be stimulated by DBS [3]

Conclusion

- LEDD reduction does not predict dyskinesia reduction
- STN activation may lead to the greatest LEDD reduction
- Anterior STN activation may provide beneficial outcomes for LEDD reduction
- Dorsal external activation may lead to the greatest dyskinesia reduction
- Stimulation of the pallidothalamic fibers, specifically the lenticular fasciculus originating from the globus pallidus internus (GPi), may explain dyskinesia reduction [2,3]

Results

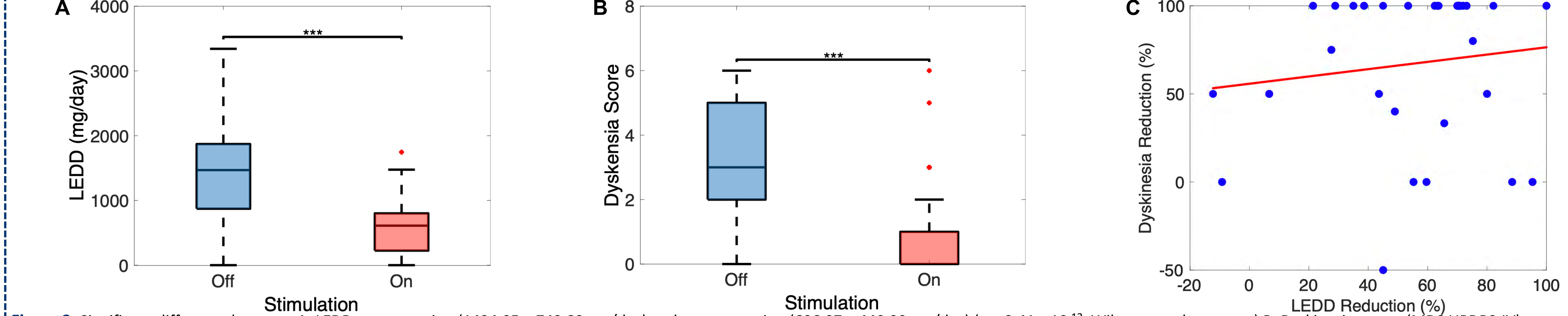


Figure 2. Significant difference between A. LEDD pre-operation (1434.05 ± 743.82 mg/day) and post-operation (606.07 ± 440.90 mg/day) ($p = 3.41 \times 10^{-12}$, Wilcoxon rank sum test) B. Dyskinesia scores (MDS UPDRS-IV) pre-operation (3.04 ± 1.93) and post-operation (0.90 ± 1.48) ($p = 1.57 \times 10^{-9}$, Wilcoxon rank sum test). C. Dyskinesia reduction and LEDD reduction had no significant relationship ($r = 0.12$, $p = 0.34$, Pearson's linear correlation).

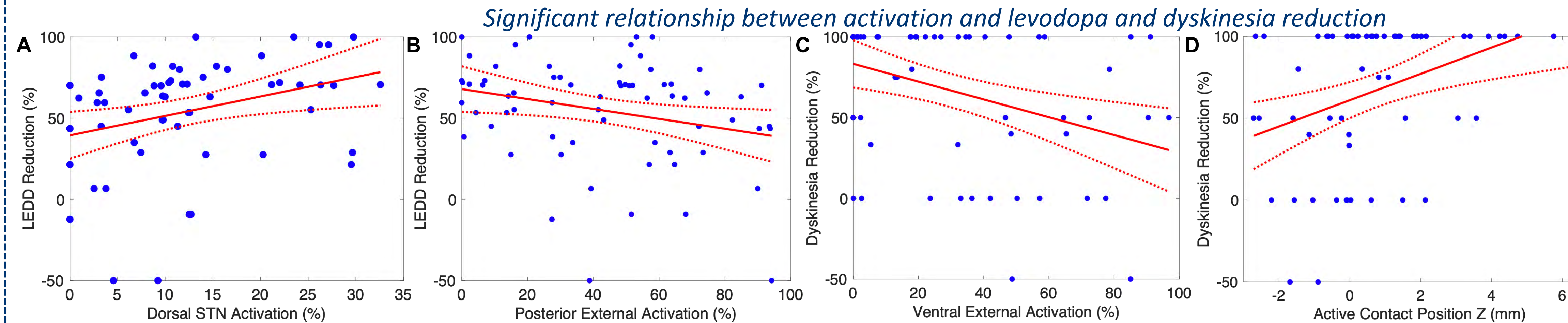


Figure 3. Significant relationship between A. Dorsal STN activation and LEDD reduction ($p = 0.013$) B. Posterior external activation and LEDD reduction ($p = 0.030$) C. Ventral external activation and dyskinesia reduction ($p = 0.003$) D. Active contact position (Z coordinate) and dyskinesia reduction ($p = 0.003$). Stepwise regressions were performed.

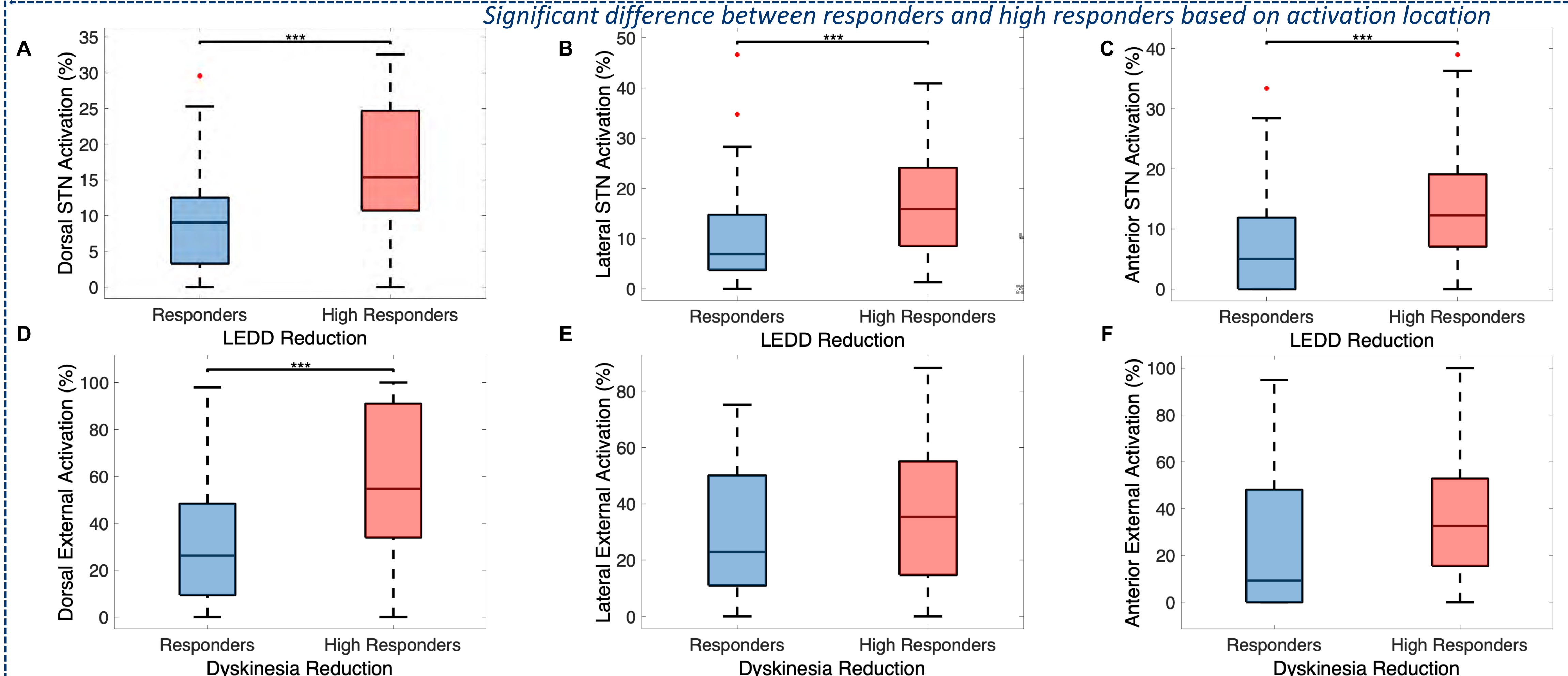


Figure 4. A. High responders (17.03 ± 8.71%) had significantly greater dorsal STN activation than responders (9.26 ± 7.76%) ($p = 0.0007$). B. High responders (17.10 ± 10.49%) had significantly greater lateral STN activation than responders (7.82 ± 9.28%) ($p = 0.0197$). C. High responders (55.73 ± 33.16%) had significantly greater dorsal external activation than responders (32.80 ± 30.57%) ($p = 0.0057$). D. High responders (55.73 ± 33.16%) had significantly greater dorsal external activation than responders (32.80 ± 30.57%) ($p = 0.0057$). E. No significant difference between lateral external activation in responders (28.98 ± 21.81%) and high responders (36.31 ± 23.97%). F. No significant difference between anterior external activation in responders (24.27 ± 29.13%) and high responders (37.44 ± 28.51%). Kruskal-Wallis tests was performed.

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Effect of Epigallocatechin-3-gallate (EGCG) and PPAR β/δ Activation in a Human Carcinoma Cell Line

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Abstract

Skin carcinoma remains a consistently studied cancer due to human's continual exposure to ultra-violet (UV) radiation and subsequent mutagenesis. Therefore, innovative new therapeutic approaches are of great importance. Emerging evidence suggests that ligands for peroxisome proliferator-activated receptor- β/δ (PPAR β/δ) inhibit carcinogenicity and are potential agents for skin carcinoma. Epigallocatechin-3-gallate (EGCG), a major polyphenol component of green tea, has also shown promise as a cancer therapeutic. Thus, the present studies examined the effects of combining EGCG and a PPAR β/δ ligand (GW0742) in the A431 human skin carcinoma cell line. Control cells cultured with EGCG exhibited reduced proliferation in a dose-response manner, and A431 cells with over-expression of PPAR β/δ were more sensitive to this effect. EGCG had no effect on anchorage-independent spheroid growth in any A431 cell line. EGCG reduced cell proliferation in A431 control cell lines, but co-administration of EGCG and GW0742 did not further influence this effect. Interestingly, A431 cells over-expressing PPAR β/δ were highly sensitive to GW0742; however, co-administration of EGCG and GW0742 did not inhibit proliferation greater than EGCG alone. Ligand activation of PPAR β/δ did not modulate the effects of EGCG on clonal expansion in control A431 cells, but an additive effect was observed between GW0742 and EGCG in A431 cells over-expressing PPAR β/δ . EGCG and GW0742 had no effect on spheroid formation. Collectively, these studies demonstrate that A431 cells over-expressing PPAR β/δ are sensitive to the anti-proliferative effects of either EGCG or a PPAR β/δ ligand. These studies provide evidence suggesting that EGCG and ligand activation of PPAR β/δ could be combined for human skin carcinoma therapy.

Introduction

Skin carcinoma remains a dangerous and consistent cancer due to repeated UV radiation exposure, and basal cell carcinoma is the most common cancer type in Caucasian patients (Reviewed in [1]). Basal cells are cuboid-shaped cells that form in the deepest layer of the epidermis and attach strongly to the basement membrane (Reviewed in [2]). The layer of the basal cells is also referred to as the stratum germinativum due to the capacity of the basal cells to rapidly undergo cell division and eventually differentiate and replace the squamous cells found on the top layer of the epidermis (Reviewed in [3]). Consequently, it is because of this property, under constant exposure of UV light, that basal cells develop cancer-initiating mutations. Importantly, models like the A431 basal cell carcinoma cell line have been developed to study carcinoma. It is therefore imperative that new therapeutic approaches be examined in appropriate models.

Among several beverages, teas have been a long-standing and essential remedy in Chinese medicine to reduce inflammation, tumorigenesis, and cardiovascular disease (Reviewed in [4]). The presence of polyphenolic biomolecule flavonoids remains the primary support for these positive health benefits (Reviewed in [5]). The flavonoids continue to be an area of investigation for anti-cancer molecules due to their reported anti-oxidant free radical scavenging activities (Reviewed in [6, 7]). Of the over 8,000 flavonoids identified, the most prevalent in human diets are catechins (Reviewed in [5-6]). One important efficacious green tea catechin is epigallocatechin-3-gallate (EGCG), and literature indicates that this molecule exerts strong anti-oxidant and anti-cancer activities (Reviewed in [6,7]), including impacts on colorectal adenoma, prostate cancer, breast cancer, and carcinoma (Reviewed in [8]). Specifically, the administration of EGCG on the skin cell lines A431 and SCC13 have confirmed the anti-carcinogenic and cytotoxic effects (Reviewed in [9]). While the studies of EGCG in skin carcinomas are limited, there is nascent evidence that the molecular signaling pathways targeted by EGCG could be partnered with other therapeutic approaches (Reviewed in [10,11]).

This investigation focuses on the EGCG and the modulation of peroxisome proliferator-activator receptors (PPAR) - a class of nuclear hormone receptors. Currently, there are three known PPAR isoforms (α , β/δ , and γ). Each one expresses unique ligand-specificity and tissue distribution (Reviewed in [11, 12]). Recently, evidence has suggested that targeting of PPAR β/δ may be utilized in the prevention and treatment of skin cancers (Reviewed in [13, 14]). The present study thus investigated whether PPAR β/δ expression and/or ligand activation modulates the reported anti-carcinogenic effects of the green tea flavonoid EGCG in the A431 human malignant carcinoma cell line. By examining the dose response effects of EGCG with the presence and absence PPAR β/δ ligand (GW0742) through several assays of tumorigenesis (cell proliferation, anchorage-dependent clonal expansion, and anchorage-independent spheroid growth), these studies aim to analyze how EGCG and PPAR β/δ can be co-targeted as part of future skin carcinoma therapeutic strategies.

Methods

Cell Counting: A431 cell lines were plated to a density of 25,000 cells/well in 12-well dishes twenty-four hours prior to cell counting at time 0. The time 0 plates were counted, and the remaining plates were treated with the indicated concentration of compound. The number of cells per well was measured every twenty-four hours for a total of seventy-two hours. There were N = 3 independent samples for each treatment group and each well was measured in duplicate at each timepoint.

Clonogenics: A431 cell lines were plated at 200 cells/well in 60-mm dishes. Six hours post-plating, fresh media containing the indicated concentration of compound was added. The cells were grown undisturbed for fourteen days prior to staining (0.5% w/v crystal violet, 6.0% v/v glutaraldehyde). Plating efficiency (# colonies/200) and surviving fraction (% of colonies/plate efficiency) were calculated from the quantification of visualized colonies. There were N = 3 independent samples for each treatment group.

Spheroids: A431 cell lines were plated at 500 cells/well in Corning 96-well spheroid plates. Tumor spheroids were allowed to form for twenty-four hours prior to imaging at time 0. Media was added to obtain the indicated concentration of compound. Spheroids were then imaged at 72-, 120-, and 168-hours post-treatment. Spheroid volume was calculated using the NIS-Elements D software at a 100x magnification. There were N = 5 independent samples for each treatment group.

Results

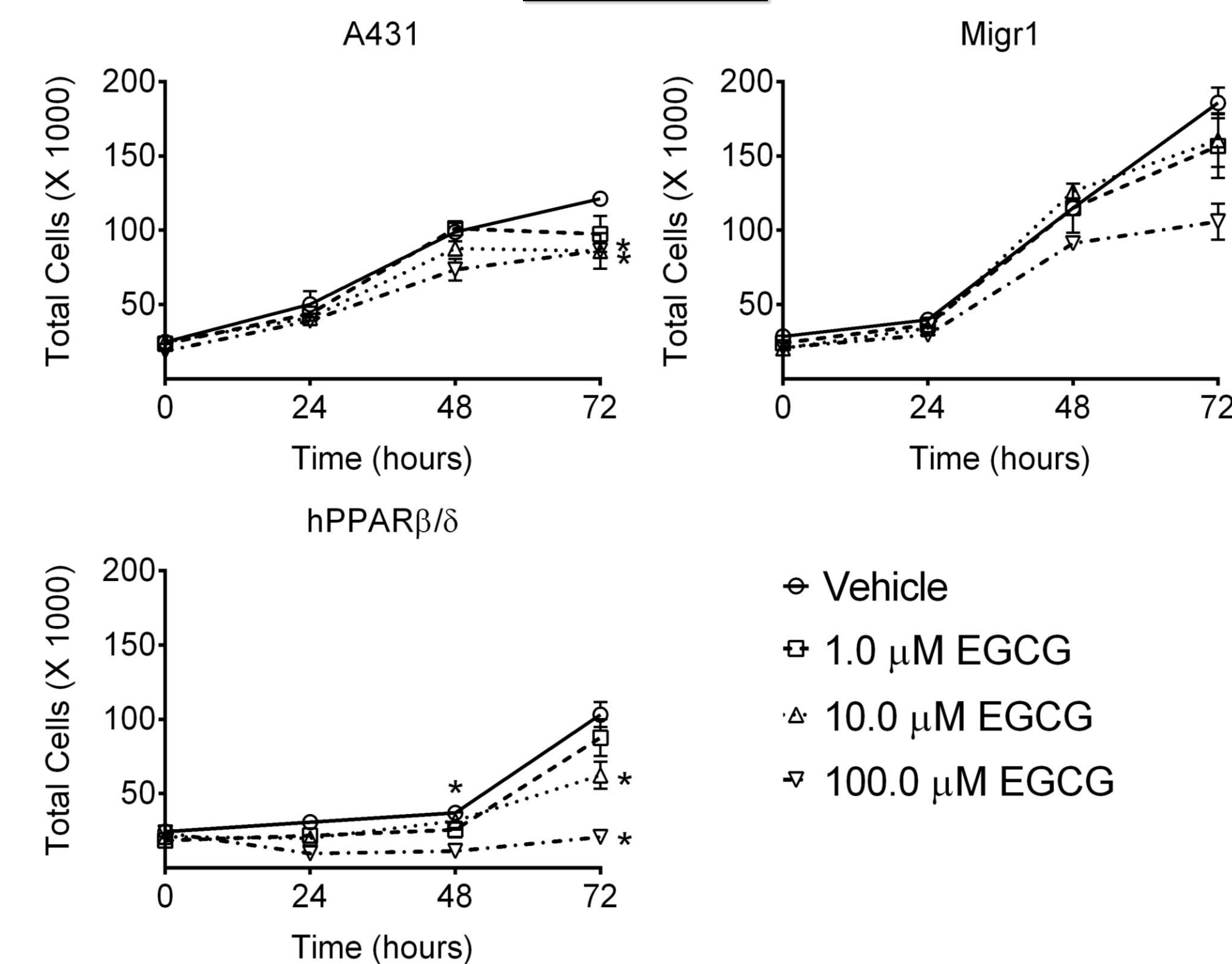


Figure 1: Effect of EGCG on cell proliferation in the A431 cell lines. Values represent the mean \pm SEM of each treatment group. An asterisks (*) indicates significantly different values from vehicle by analysis of variance (ANOVA) with Bonferroni's multiple comparison test ($P < 0.05$).

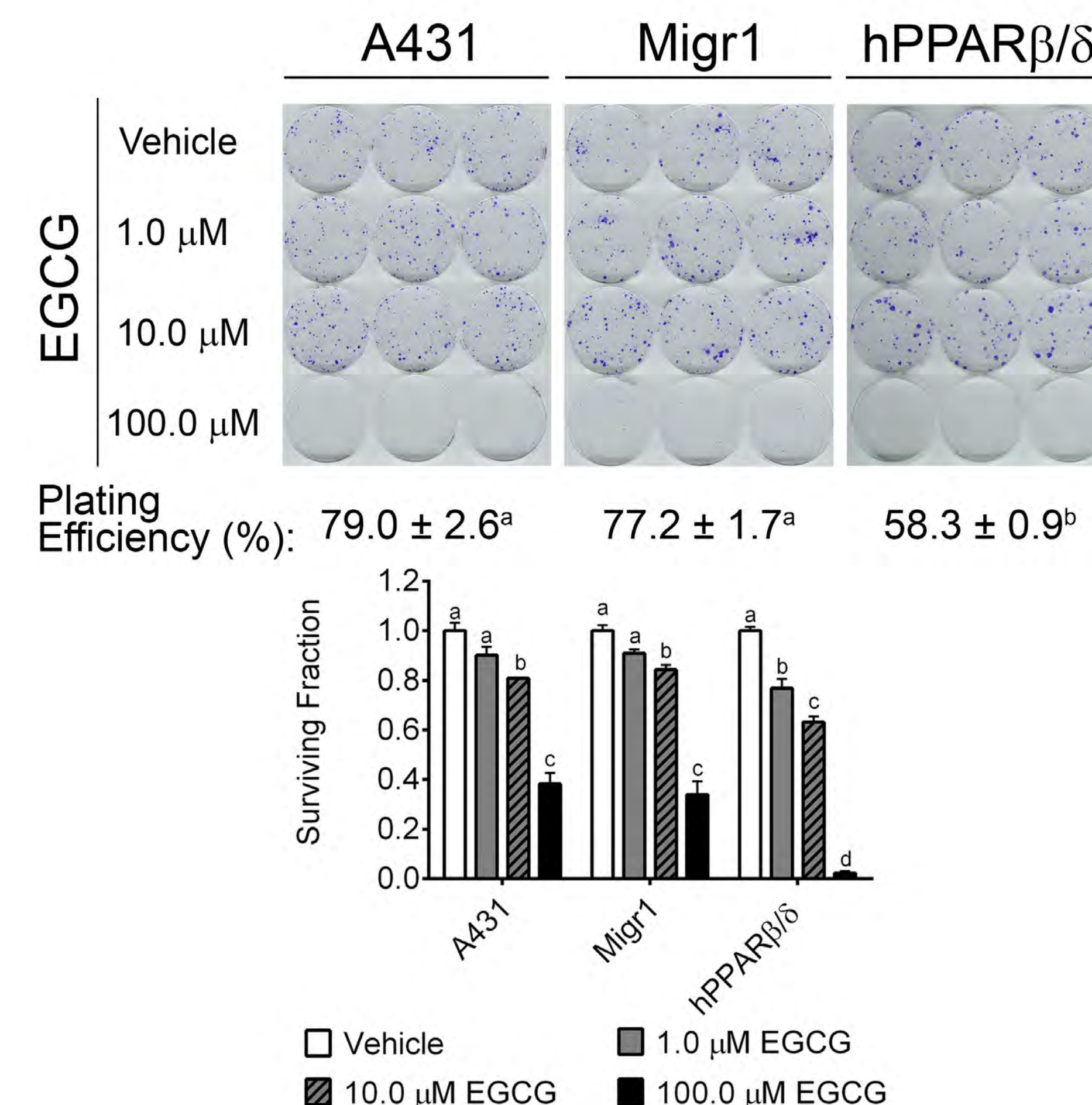


Figure 2: Effects of EGCG on clonal expansion. Plating Efficiency and Surviving Fraction are represented as mean \pm SEM. Different letters indicate significant difference between group means by analysis of variance (ANOVA) with Bonferroni's multiple comparison test ($P \leq 0.05$).

Results

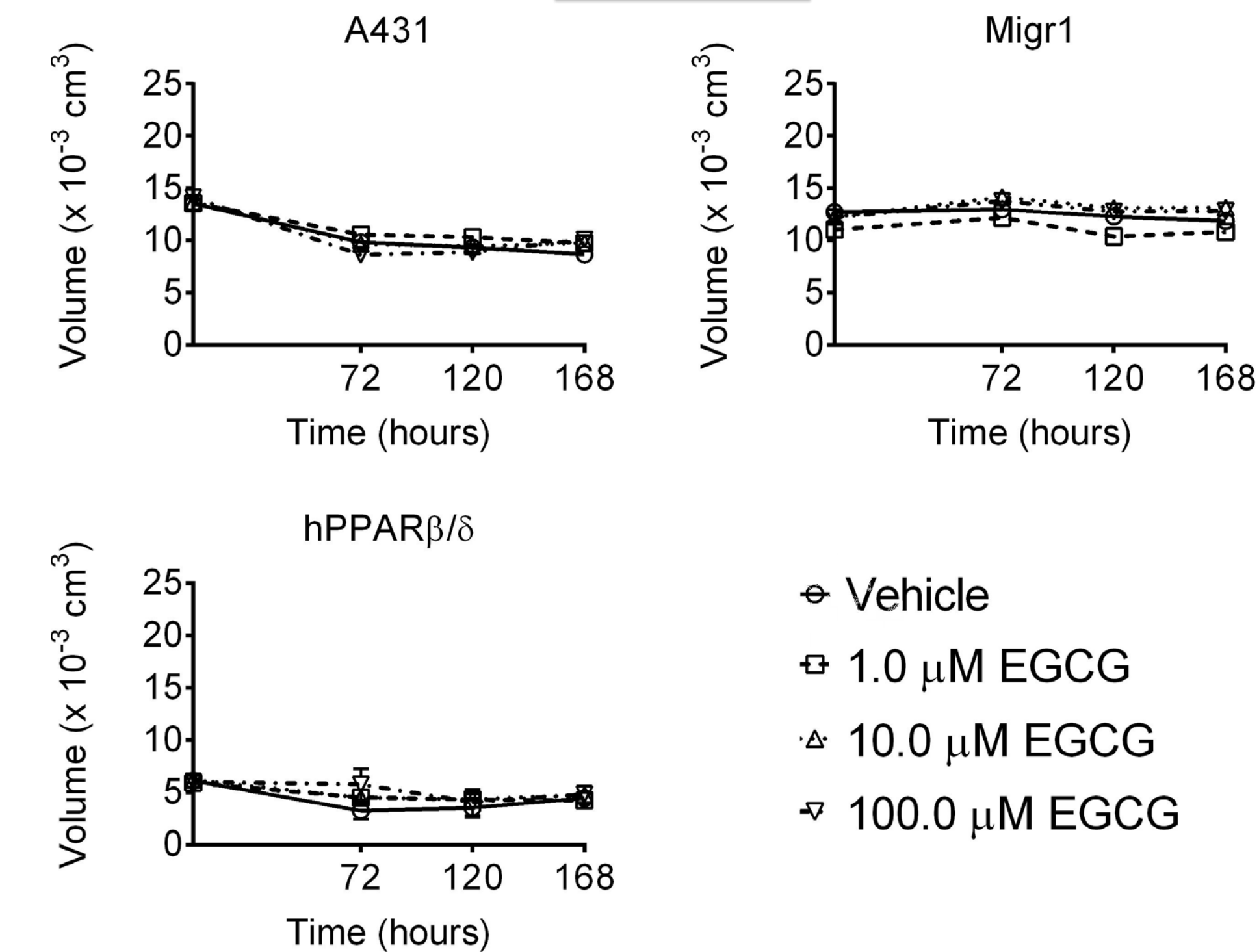


Figure 3: Effect of EGCG on spheroid growth in the A431 cell lines. Values represent the mean \pm SEM of each treatment group. An asterisks (*) indicates significantly different values from vehicle by analysis of variance (ANOVA) with Bonferroni's multiple comparison test ($P < 0.05$).

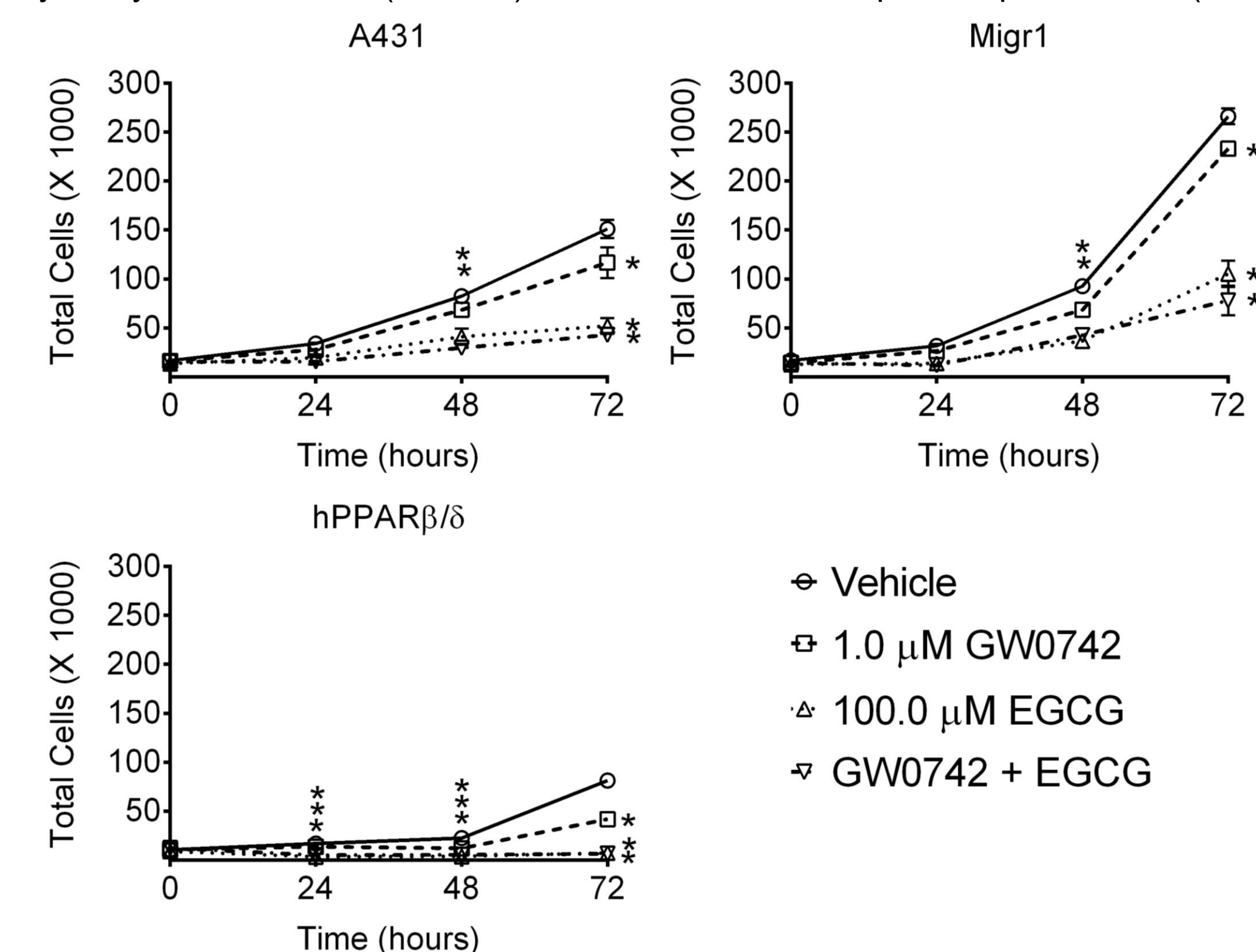


Figure 4: Effect of EGCG and a PPAR β/δ ligand on cell proliferation in the A431 cell lines. Values represent the mean \pm SEM of each treatment group. An asterisks (*) indicates significantly different values from vehicle by analysis of variance (ANOVA) with Bonferroni's multiple comparison test ($P < 0.05$).

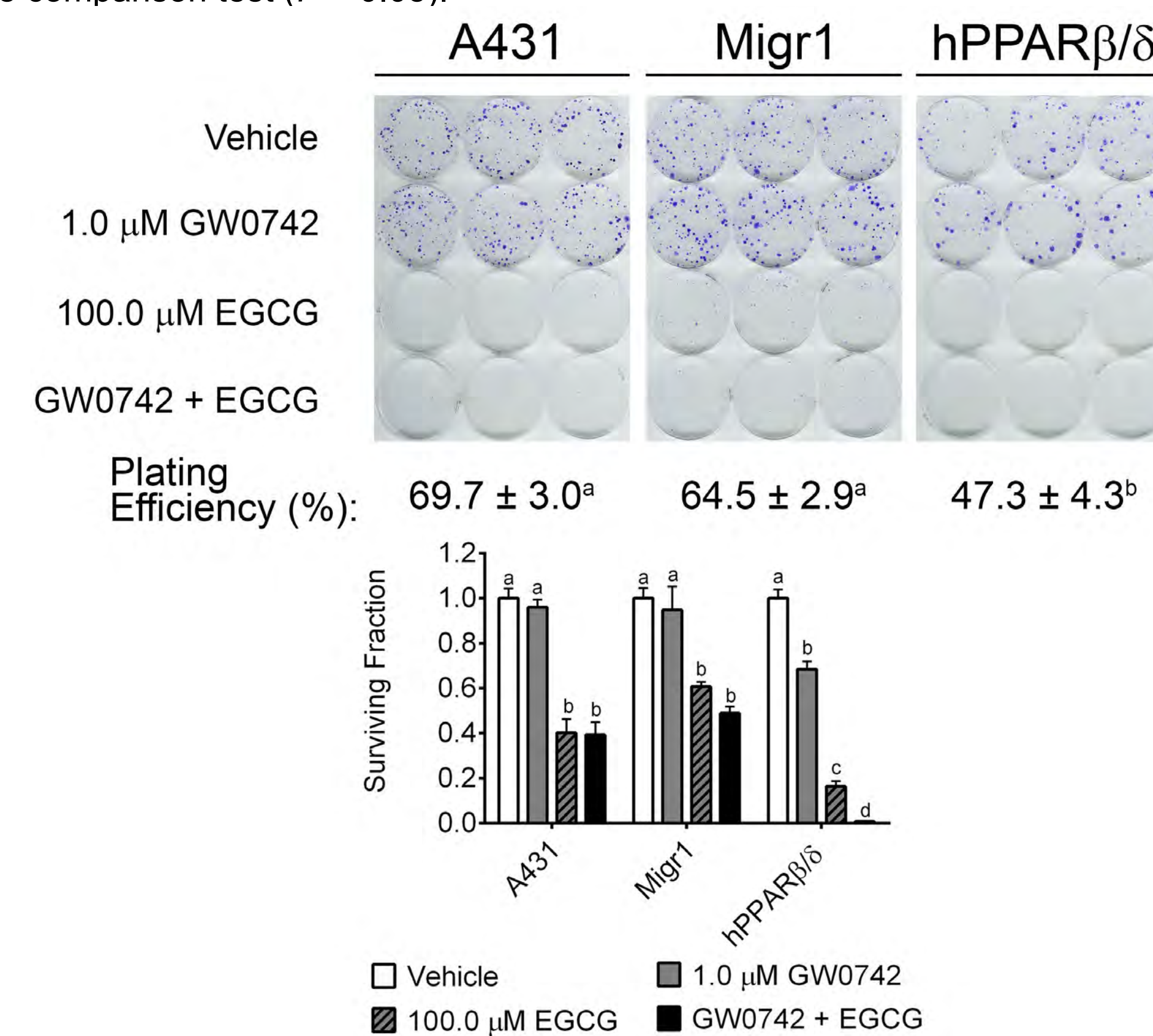


Figure 5: Effect of EGCG and a PPAR β/δ ligand on clonal expansion. Plating Efficiency and Surviving Fraction are represented as mean \pm SEM. Different letters indicate significant difference between group means by analysis of variance (ANOVA) with Bonferroni's multiple comparison test ($P \leq 0.05$).

Results

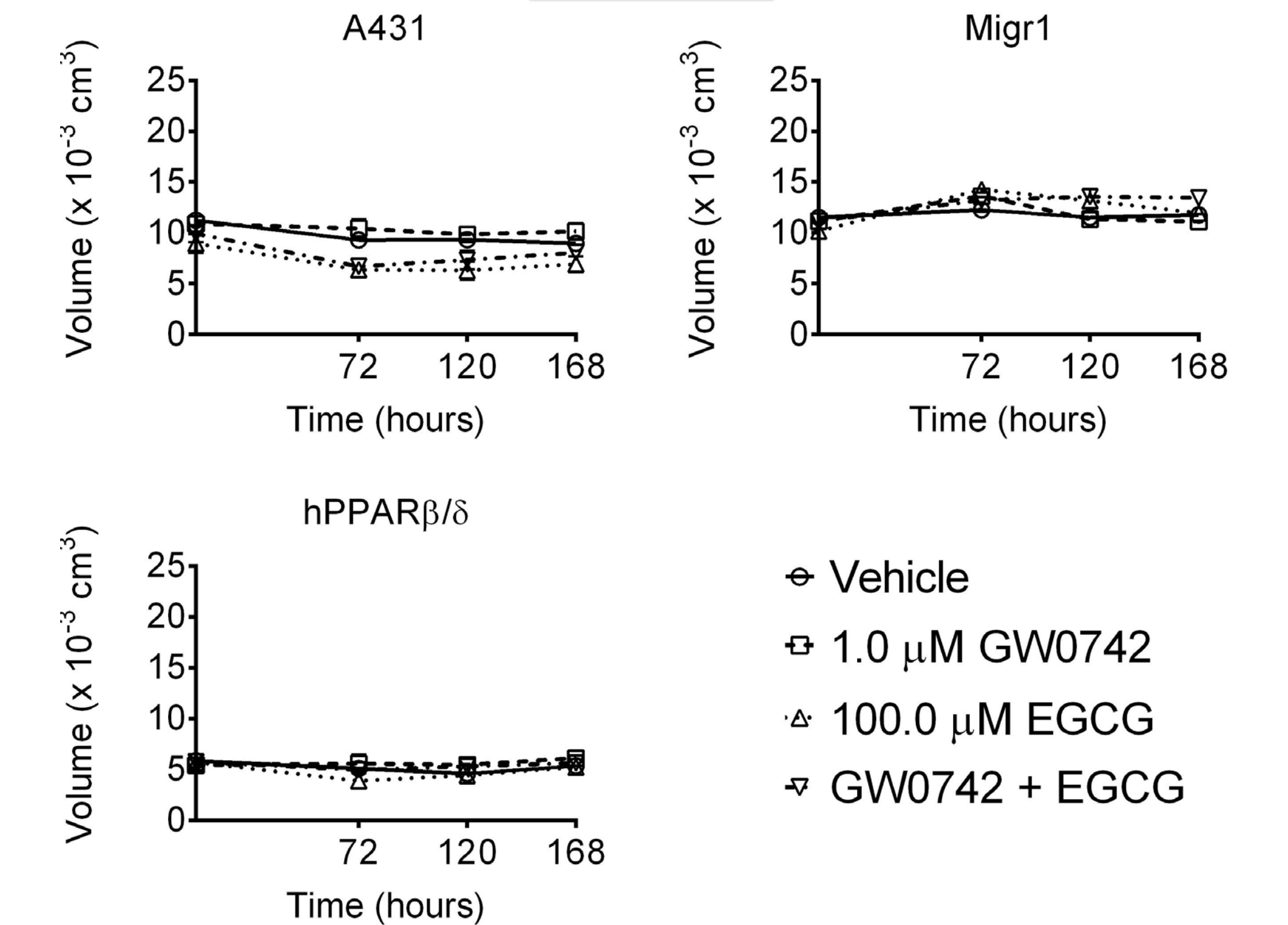


Figure 6: Effect of EGCG and a PPAR β/δ ligand on spheroid growth in the A431 cell lines. Values represent the mean \pm SEM of each treatment group. An asterisks (*) indicates significantly different values from vehicle by analysis of variance (ANOVA) with Bonferroni's multiple comparison test ($P < 0.05$).

Conclusions

- EGCG reduced cell proliferation in a dose-dependent manner in all A431 cell lines. These effects were enhanced in cells over-expressing PPAR β/δ .
- EGCG inhibited clonal expansion in all A431 cell lines. The cell line over-expressing PPAR β/δ exhibited an increased sensitivity.
- Spheroids generated from the A431 cell lines did not grow during the study. Furthermore, EGCG had no further influence on spheroid size. Spheroids from the cell line over-expressing PPAR β/δ retained a smaller spheroid size.
- Ligand activation of PPAR β/δ enhanced the anti-proliferative effects of EGCG only in A431 cells that over-express PPAR β/δ .
- PPAR β/δ ligand activation reduced clonal expansion only in A431 cells over-expressing PPAR β/δ . GW0742 enhanced the anti-tumorigenic effects of EGCG only in A431 cells that over-express PPAR β/δ .
- Neither EGCG, PPAR β/δ ligand, or combination had any further influence on spheroid size.
- Further studies are warranted to clarify the biological effects and underlying mechanism(s) by which PPAR β/δ can be utilized to treat skin carcinomas.

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INTRODUCTION

- Get-2-Goal is a medical application available on Android and iOS platforms that allows people with diabetes to track their weight changes and receive surgical recommendations.
- The latest version of Get2Goal contains five user pages, including
 - My Progress page which records daily weights
 - Goals page which helps users keep track of their weight loss progress
 - Tools page which includes three functions that help patients estimate surgery risks and offer surgery suggestions
 - Stories page where other patients share their personal experience
 - Settings page where users could customize preferential colors and reset profiles and logs.

APP Testing and Debugging

- A number of bugs still remain in this app, and these bugs have an adverse effect on the user experience. For instance, users were unable to scroll down the My Progress page, which prevented them from viewing their historical records beyond page one (see Figure 1).
- The app now has a rating of 2.5 out of 5 in the Apple Store and 2.2 out of 5 in the Google Store, with most users commenting that there are bugs in the design of the app that affect normal use.
- My part of project is first to identify the potential bugs that could affect users' experience and unjustifiable design of bugs. Then, I need to fix the problems as much as possible.



Figure 1. Screenshot: My Progress page

SUMMARY

- Identify and record bugs and potential illogical design.
- Fix bugs and optimize user experience.
- Check the grammar of existing code

APPROACH

- Learn Javascript, HTML, CSS
- Draft debugging plan (see Figure 2).
- Search online grammar checking tools.
- Install Cordova and Android Studio.
- Implement testing functions in JS file.
- Test the application and record the result.
- Present weekly meetings with Geisinger Obesity Institute.

Profile input testing:

1. Try different BMI ranges. Considering the starting weight may affect chart rendering, take three different start points:
 - a. Low weight: weight 100 height 36 (both the lowest value) BMI 54.25
 - b. High weight: weight 900 height 80 BMI 98.86
 - c. Medium weight: weight 400 height 60 BMI 78.11
2. Try different ages in the range of 18 and 75:
 - a. Lowest value: 18
 - b. Highest value: 75
 - c. Middle value: 50
3. Try different biological sex:
 - a. Female
 - b. Male
4. Try different historical surgery options:
 - a. Yes
 - i. Time close to today
 - ii. Time far to today
 - b. No
5. Try different answers to medical conditions questions, especially tests on different answers of type2 diabetes.
6. Diabetes:
 - a. Time: test four different options and n/a
 - b. Yes or No questions: try different answers
 - c. HbA1c: test five different options and n/a

Figure 2. Screenshot: part of Debugging plan

```
function testWeightEntry() {
    //good weight ranges inclusively from 100 to 10000
    //weigh too low
    document.getElementById('weightEntry').value = 99;
    document.getElementById('dateEntry').value = "2021-10-08";
    if (checkBlurWindow()) {
        alert("ERROR: weigh too low is fine");
    }

    //weigh too lhigh
    document.getElementById('weightEntry').value = 1006;
    document.getElementById('dateEntry').value = "2021-10-08";
    if (checkBlurWindow()) {
        alert("ERROR: weigh too high is fine");
    }

    //weigh lowest but good 100
    document.getElementById('weightEntry').value = 100;
    document.getElementById('dateEntry').value = "2021-10-08";
    if (checkBlurWindow()) {
        alert("ERROR: low but good weight is rejected");
    }

    //weigh highest but good
    document.getElementById('weightEntry').value = 1000;
    document.getElementById('dateEntry').value = "2021-10-08";
    if (checkBlurWindow()) {
        alert("ERROR: high but good weight is rejected");
    }

    // date in future is bad
    var today = new Date();
    var tomorrow = new Date(today);
    tomorrow.setDate(tomorrow.getDate() + 1);
```

Figure 3. Screenshot: part of weight entry test function

RESULTS SUMMARY

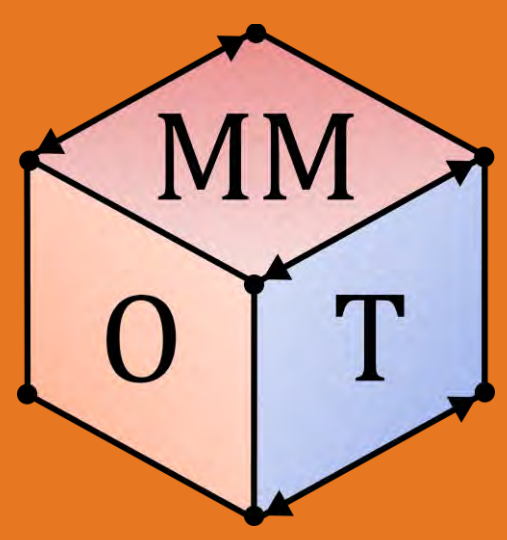
- Created and ran My Progress Page test functions
- Identify bugs:
 - Users cannot scroll down the pages **FIXED**
 - Users are allowed to input a future date **FIXED**
 - Users are able to input duplicated weights on the same day **FIXED**
 - Cumbersome design of the separate, single-deletion button. Users need to click on the delete buttons several times to delete several weight records. **IN PROGRESS**

FUTURE CONSIDERATIONS

- Optimize user experience with improved button design that enables users to select several records and delete them at one time
- Finish Stories Page test

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Modeling the Effects of Femoral Anteversion on Joint Loads in the Hip

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Introduction

- Femoral anteversion is the inward torsion of the femur bone, typically 12° to 20° (Fig. 1)
- Excessive profiles exceed ~40° and cause gait impairment and joint pain
- Kinematics and muscle activity patterns are variables that cause varying joint loads [1]
- Musculoskeletal models can estimate joint loads (Fig. 1)

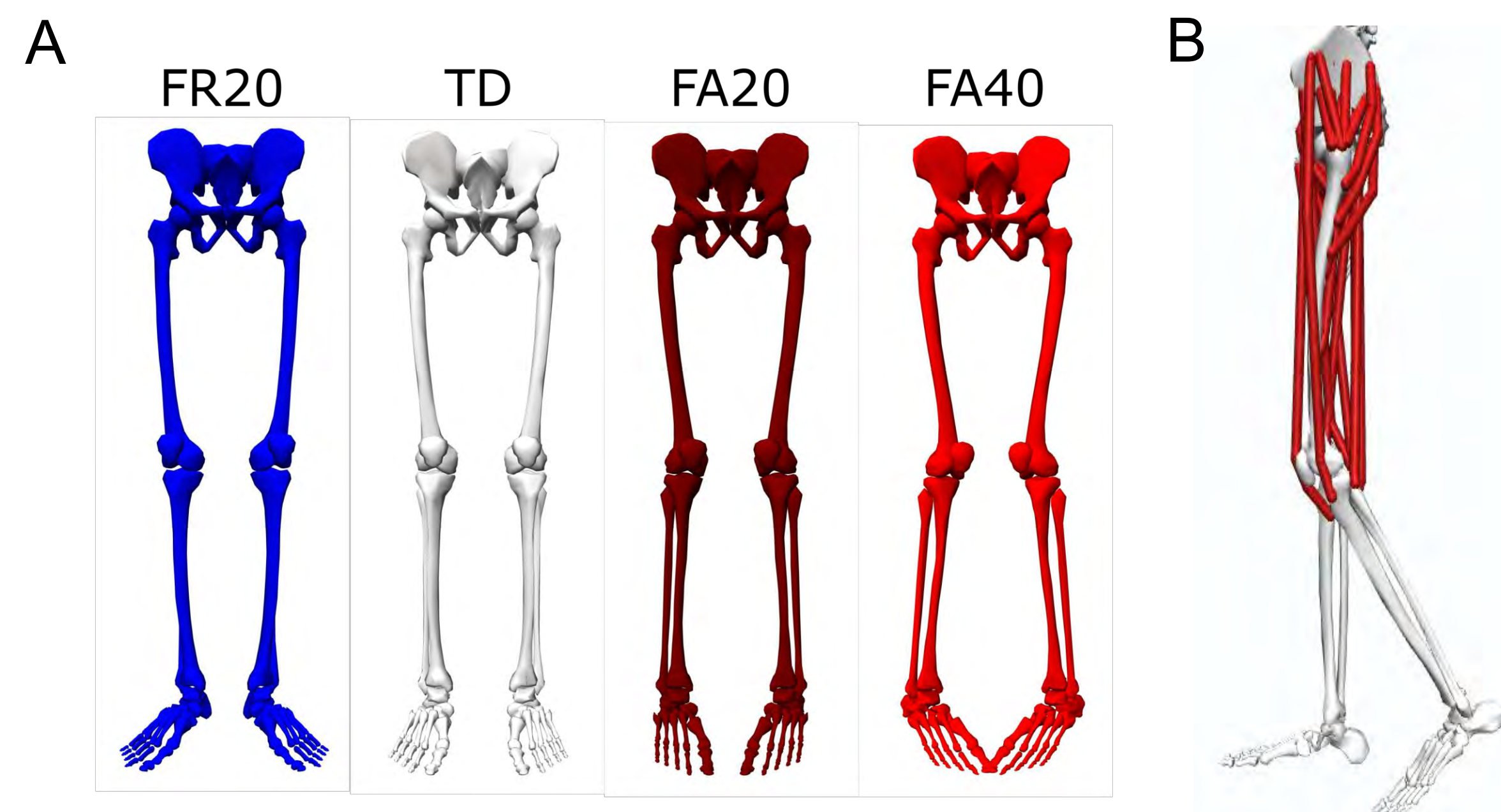


Figure 1. A) Models that represent different degrees of femoral anteversion. B) Model with muscles adjusted to the hip joint.

Research Question: How do different torsional profiles, muscle activity patterns, and kinematic patterns affect the joint loads of the hip?

Methods

- Rajagopal full body model for studying gait [2] (Fig. 2)
- Modenese bone deformation tool applied to femur [3]
- OpenSim Moco tracking and inverse problems [4] to solve for gait kinematics and muscle forces
- Recorded root mean square (RMS) of hip joint loads during stance phase of gait.

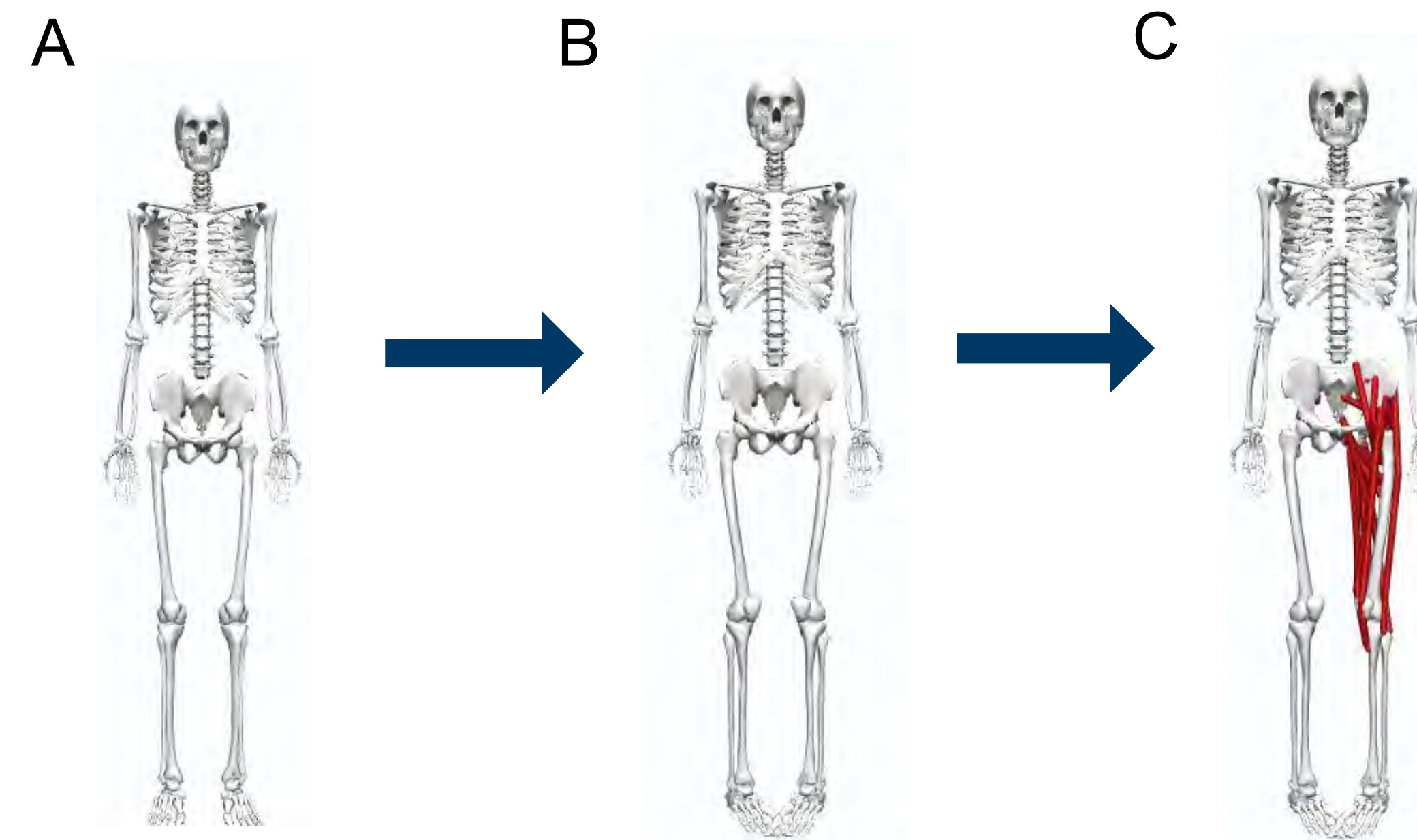


Figure 2. A) The Rajagopal model for studying gait. B) A 30° femoral torsion using the bone deformation tool. C) Rotated model with the muscles that cross the hip joint.

Results

- Joint loads increased in the anterior-posterior and superior-inferior directions, decreased in the medial-lateral direction (Fig. 3)
- Largest force in the superior-inferior direction

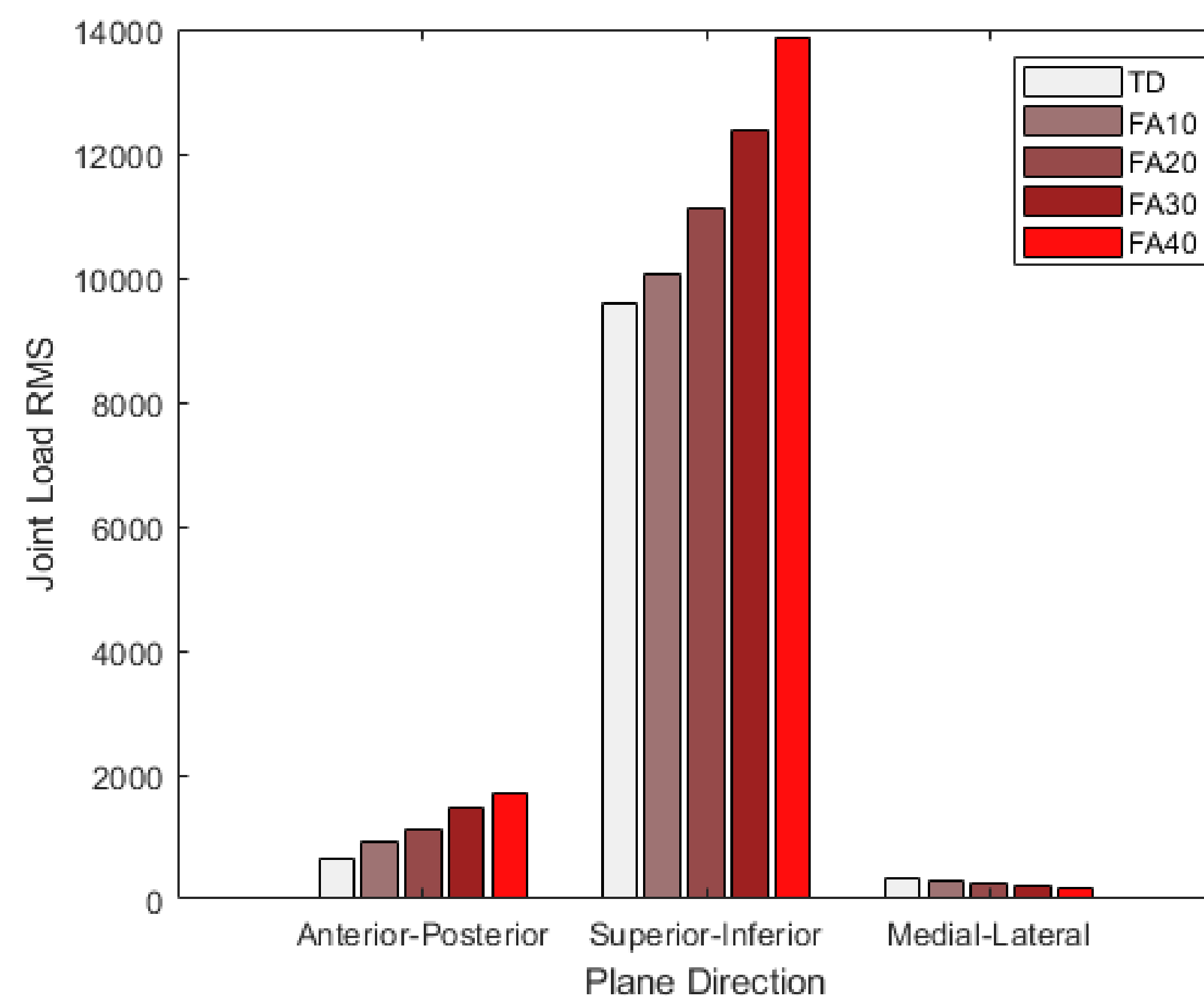


Figure 3. Plot of RMS values of joint loads calculated for varying degrees of femoral anteversion. TD refers to typically developing, FA10 refers to an addition 10 degrees of femoral anteversion.

Discussion

- Results show that as the degree of femoral anteversion increases, hip joint loads increase
- Few studies discuss hip implications and femoral anteversion only
- Similar studies have shown that there has not yet been a significant effect on the hip during gait with femoral anteversion [5]

Future Work

- Modeling miserable malalignment – torsion of femur and tibia –to study interactions between torsional profiles, muscle activity patterns, gait kinematics, and joint loads

- Ongoing - collect data on typically developing subjects and those with femoral anteversion using motion analysis and surface electromyography (Fig. 4)
- Run kinematics and simulations collected data
- Perform statistical analysis on both data sets in order to form comparisons

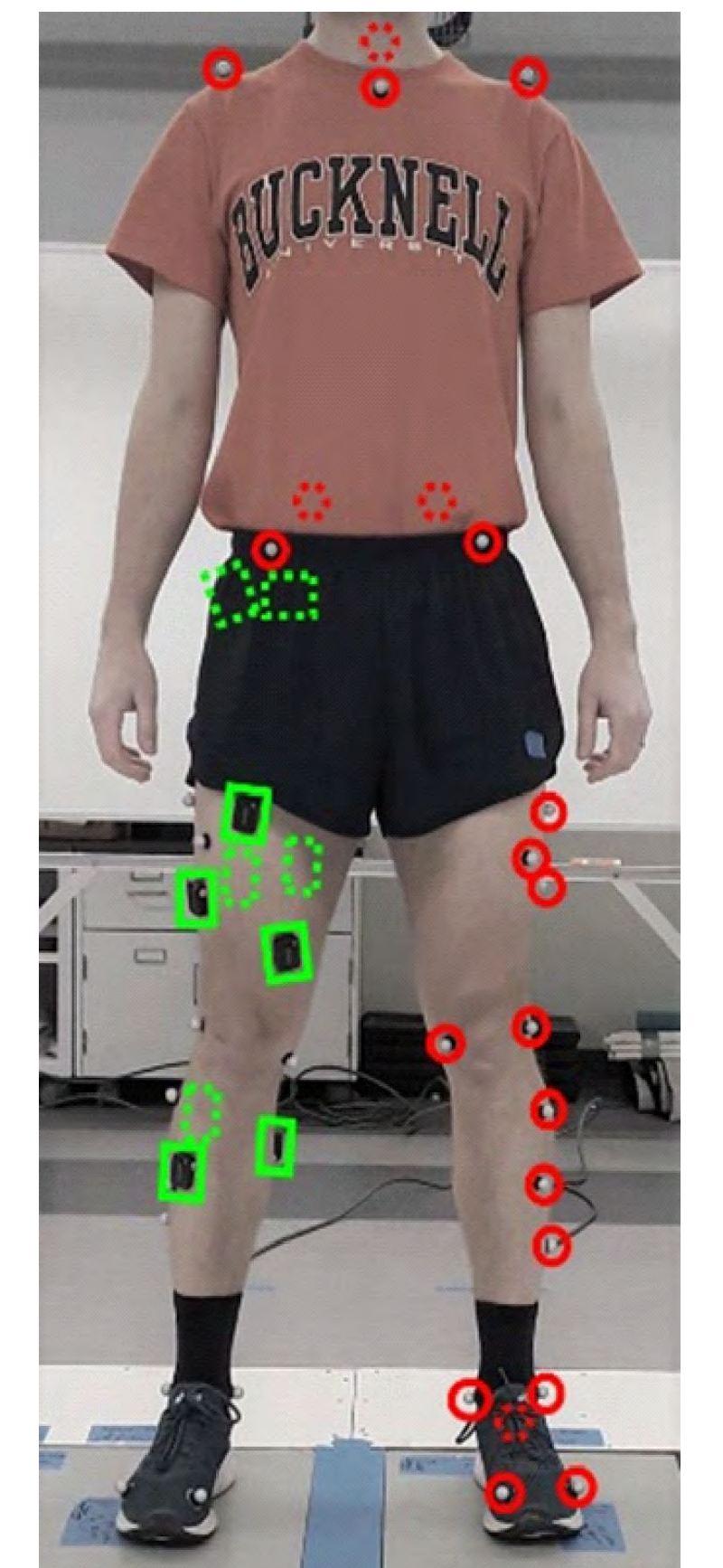


Figure 4. Location of motion capture markers (red) and EMG sensors (green).

Acknowledgements and References

The authors would like to thank the Program for Undergraduate Research (PUR) at Bucknell University for funding this study.

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Genome Wide Association Studies of Quantitative Traits in MyCode Cohort

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Abstract

A Genome Wide Association Study (GWAS) identifies gene loci and variants associated with specific diseases or traits. Knowing which genetic variants are associated with a disease or trait may help us understand the mechanism of disease, and potentially create treatment options. We performed GWAS on height and BMI (Body Mass Index), as well as 12 lab measures collected from electronic health records from the MyCode cohort at Geisinger. Specific lab measures were selected since they are markers for specific diseases. We focused on markers of cardiometabolic diseases such as type 2 diabetes, hyperlipidemia, hypertension, and chronic kidney disease. We use stringent criteria for our GWAS. We authenticate our findings with those from previous published GWAS data. Future goals are to identify novel genetic variants for these traits in the MyCode population and potentially find novel mechanisms and therapeutic targets for these diseases

Background

While all humans are mostly genetically identical, the small degree of genetic variation gives rise to phenotypic differences amongst individuals. By collecting larger genetic data sets, we can more accurately pinpoint which genetic variations are responsible for specific traits.

At Geisinger, we have performed three types of genetic analysis on approximately 175,000 participants in the MyCode cohort. These analyses include imputed genotype data, array genotyping, and exome sequencing. Imputed genotype data is the most widely used genetic data when performing a GWAS and involves inferring missing genotypes in a patient's genetic data. Using imputed data can be beneficial to a GWAS because the data is fast and cost effective. Exome data only captures regions of the genome that code for protein, called the exons, and mostly excludes non-coding regions or introns. Exome data captures data most likely to contain variants that alter proteins. However, it captures only about 2% of the genome making it faster and more cost effective than whole genome sequencing. Genotype data includes the entire genome, capturing the exon and the intron regions, however, it only detects previously identified genetic variant.

Geisinger also has extensive electronic health record (EHR) data on patients. These data are maintained in a scalable and readily searchable database that is available in a de-identified manner. The deidentified data can be conveniently used for GWAS analyses on traits such as BMI or specific lab results like cholesterol levels.

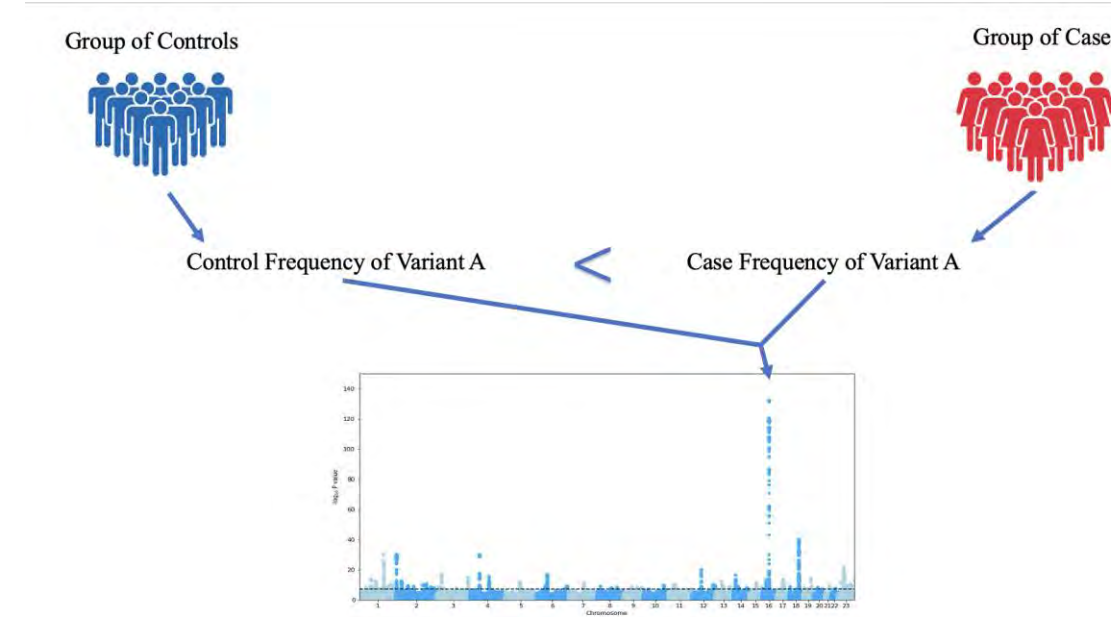
Here, we tested twelve traits obtained from the EHR, against four genetic data sets (Imputed, Exome, Genotype OMNI, Genotype GSA), totaling forty-eight GWAS aiming to identify known and novel genetic loci associated with each trait.

Methods

Median phenotype files were created using Geisinger's patient records, which contains 175,000 patient's genetic data and their medical history. Plink 2.0 software was used to run linear regressions of a genotype file against a phenotype file. Confounding variables such as age, race, sex, ancestry, patient relationships, and linkage disequilibrium had to be properly accounted for before running the regression.

In order to visualize the results, two plots were created for each GWAS, a Manhattan plot and a Quantile-Quantile plot (QQ plot). A Manhattan plot represents the statistical significance of variants' affects on a disease or trait per chromosome. The threshold for significance for a GWAS is widely accepted and set at a p-value of 5×10^{-8} . The QQ plot shows the accuracy of the linear regression by comparing the inflation of the p-values from the linear regression with a normal distribution.

1 What is a Genome Wide Association Study?



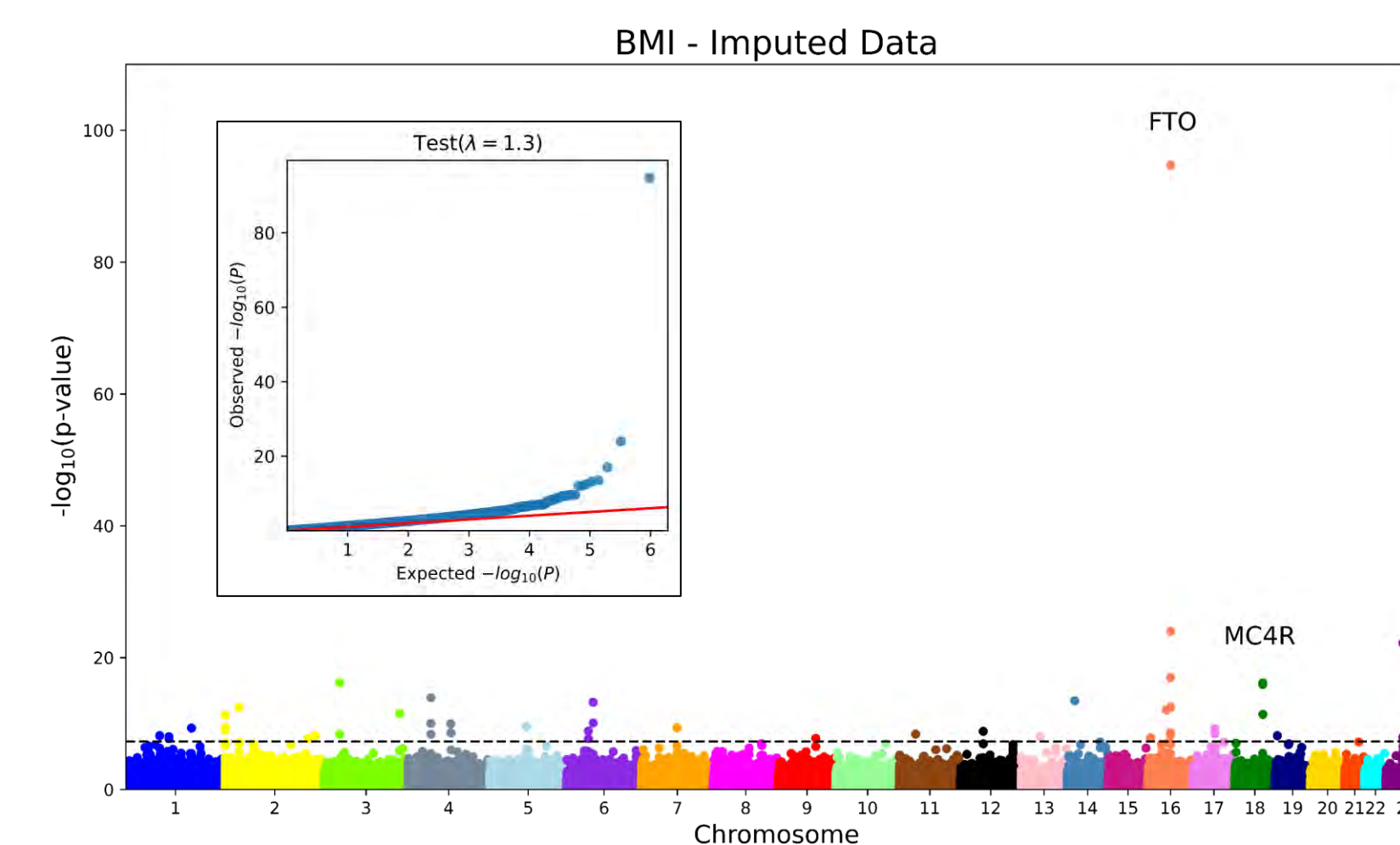
This illustration shows the concept of a GWAS. When there is a higher frequency of a variant in affected patients than control patients, it will result in a peak on the Manhattan plot.

2 Data Used for a GWAS

	Imputed	Genotype OMNI	Genotype GSA	Exome
Variants	604,713	142,780	230,282	86,559
Number of Patients				
BMI	108,992	33,920	21,558	109,405
Height	108,992	33,920	21,558	109,405
Systolic Blood Pressure	105,550	33,231	21,147	105,890
Diastolic Blood Pressure	105,224	33,126	21,086	105,554
Estimated Glomerular Filtration Rate	105,855	33,619	20,975	106,197
Fasting Blood Glucose	69,393	25,212	14,298	69,489
Fasting Insulin Levels	5,014	2,450	976	5,023
Hemoglobin A1c	57,697	20,990	11,254	57,851
HDL Cholesterol	74,198	26,890	15,246	74,307
Total Cholesterol	73,662	26,703	15,163	74,044
LDL Cholesterol	74,662	26,703	15,163	73,763
Triglycerides	74,215	26,912	15,252	74,321

Summary of the number of variants per genetic data set and the number of patients per trait and genetic data set. Each variant is analyzed against each patient in a GWAS for any particular trait.

3 Example GWAS with Body Mass Index



A Manhattan plot of body mass index, created using imputed genomic data. The peaks on the graph represent significant genes, most notably *FTO* on chromosome 16 and *MC4R* on chromosome 18. The black dotted line represent a significance threshold set at a p-value of 5×10^{-8} . Anything above this line is considered a significant association. These results have been corroborated by multiple previous studies.

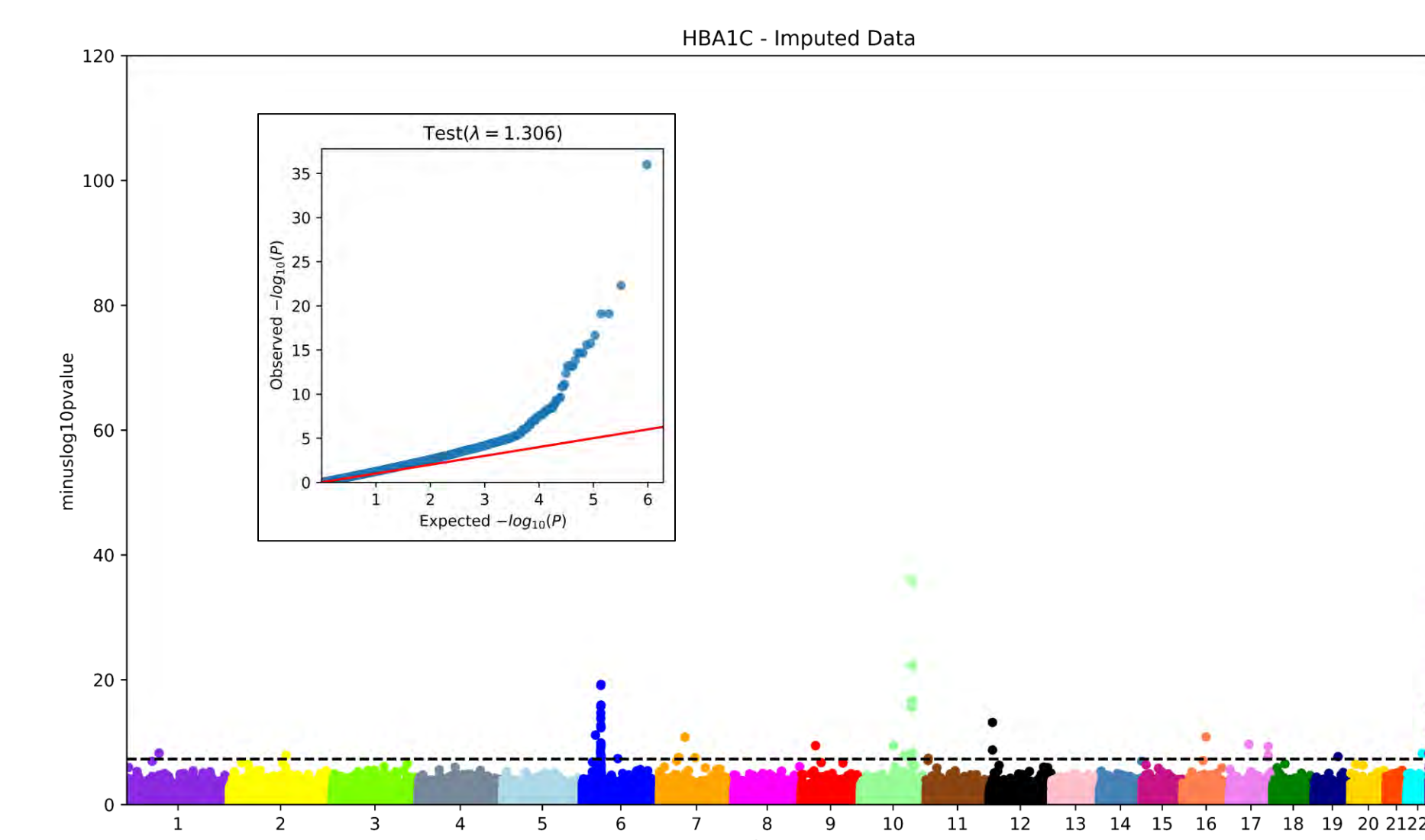
The graph inside the Manhattan plot is a Quantile-Quantile plot (QQ plot). The QQ plot shows the accuracy of the linear regression by comparing the inflation of the p-values from the linear regression to a normal distribution.

4 Comparison of Significant Association in Public Domain

	Variants from GWAS Catalog	Variants from Geisinger GWAS
BMI	5003	22
Height	5087	1866
Systolic Blood Pressure	2674	65
Diastolic Blood Pressure	1684	29
Estimated Glomerular Filtration Rate	1595	20
Fasting Blood Glucose	142	21
Fasting Insulin Levels	63	0
Hemoglobin A1c	719	35
High Density Lipoprotein	3534	109
Cholesterol	2336	63
Low Density Lipoproteins	2536	63
Triglycerides	2912	119

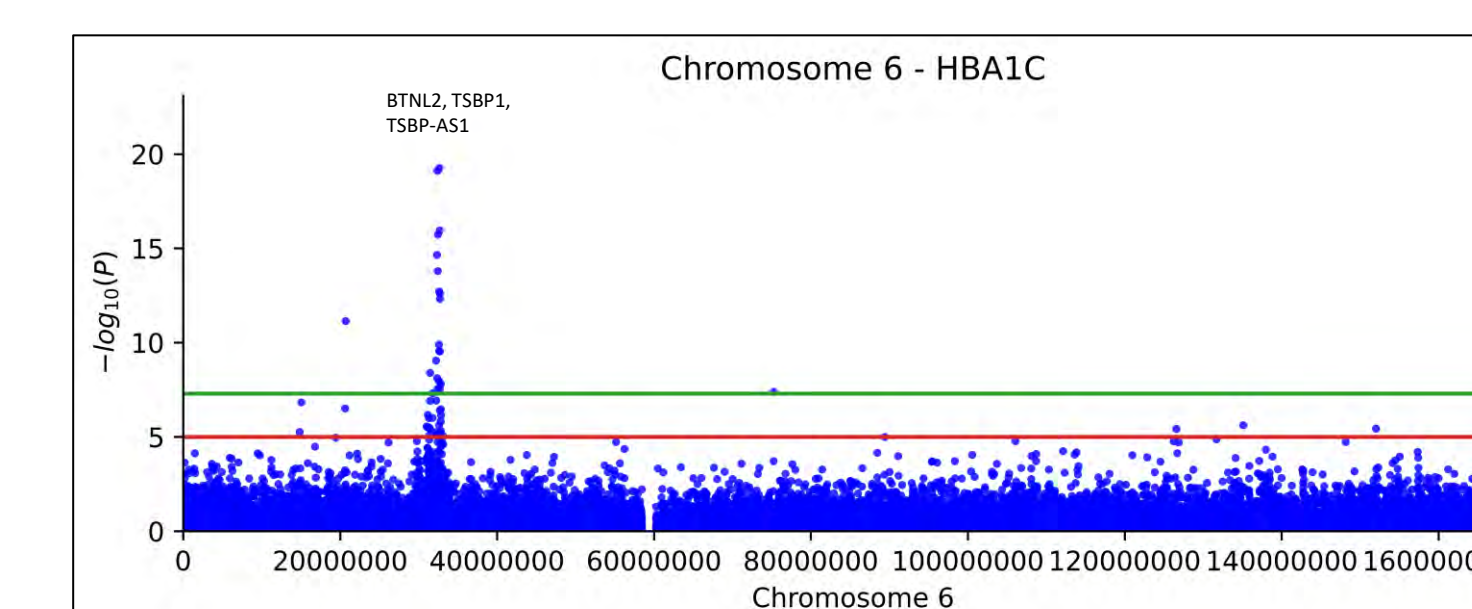
Founded by the NHGRI in 2008, GWAS Catalog is a large public database of variant-trait associations containing eligible, published GWAS. This table shows the variant count in GWAS Catalog's cohort per trait and the variant count in Geisinger's imputed cohort per trait. GWAS Catalog has a much larger sample size than Geisinger does. It is important to note that multiple variants can point towards the same loci.

5 GWAS for Hemoglobin A1c



A Manhattan plot of Hemoglobin A1c, created using imputed genomic data. Hemoglobin A1c measures the average amount of sugar attached to the hemoglobin in blood cells over three months. Hemoglobin A1c measurements are usually used as a diagnostic tool for prediabetes and diabetes.

6 Chromosome 6 GWAS



This figure shows the enlarged Manhattan plot from Figure 5 on chromosome 6. Three significant genes were found on chromosome 6: *BTNL2*, *TSBP1*, and *TSBP1-AS1*. The red and green lines represent significance thresholds, red representing a p-value of 9×10^{-6} , and green representing a p-value of 5×10^{-8} .

Summary

- Use large data sets to perform large scale association
- Associate lab measurements and genetic data
- Compare findings to GWAS data in public domain
- Identify common genetic variants between previous work and Geisinger's population
- Try to identify possible genetic variants unique to Geisinger's population

Conclusions

Combining a large genetic data set with a large clinical data set that can be linked together allows for identifying unique genetic contributors to a disease or trait. It is important to note that the data sets that were used in these studies had very stringent constraints placed on them, which could have affected the identification of loci.

Future Direction

- Assess the significance of possible novel variants for all traits and genomic data sets
- Begin to assess possible novel gene's location and functionality against a trait
- Change our parameters to capture additional loci, possibly lead to identifying novel loci

Funding

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