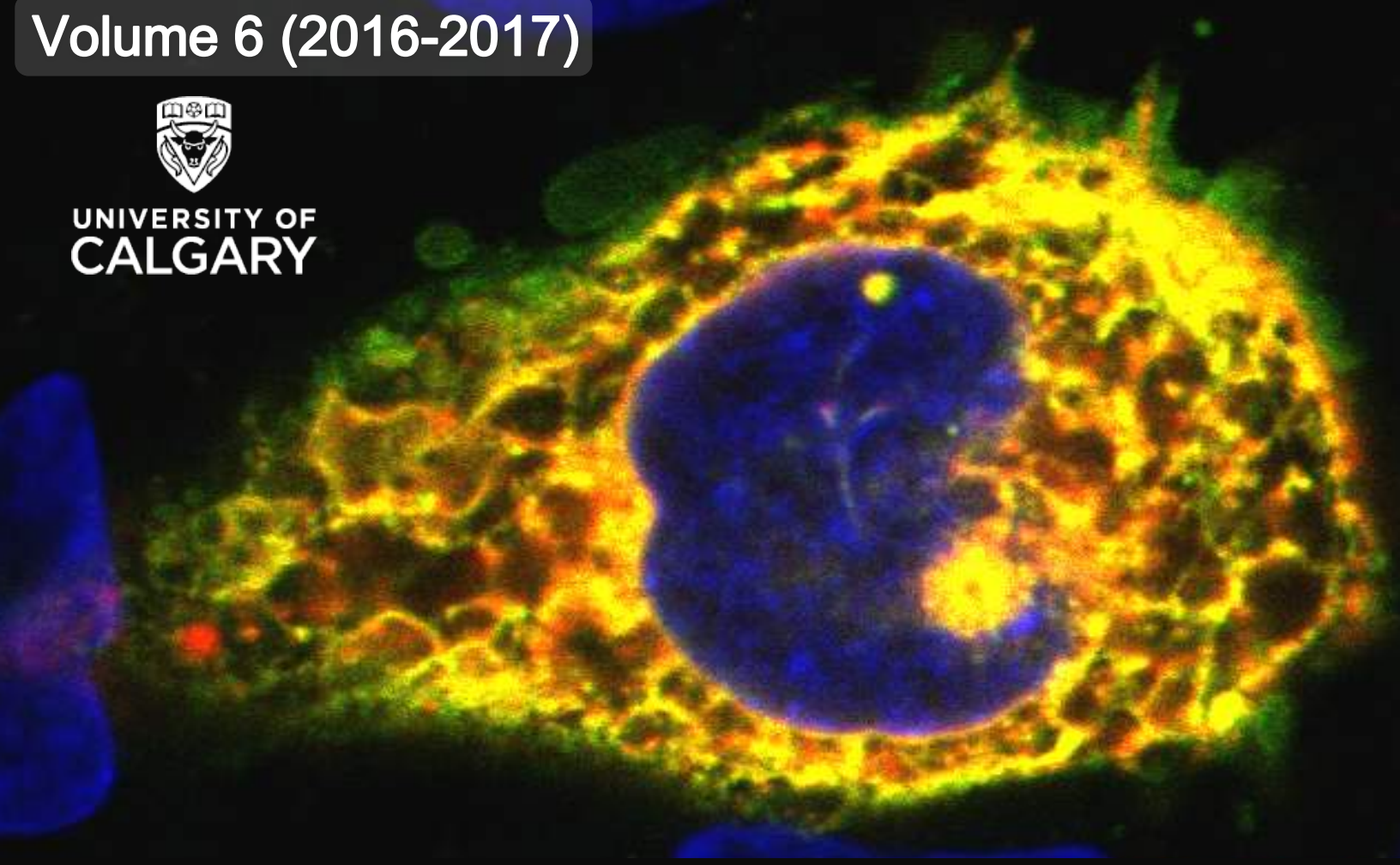
JURA

Journal of Undergraduate Research in Alberta

Volume 6 (2016-2017)

UNIVERSITY OF CALGARY



This Edition of JURA demonstrates the widespread excellence in undergraduate research across the University of Calgary with publications from the Faculty of Public Policy to the Department of Geography and *many* more.

This Issue Only: University of Calgary Faculty reflect on their first publication and early research experiences.

JURA
Journal of Undergraduate Research in Alberta

Volume 6: Contents

This image and the cover image were taken by Stacy Gibson (in Dr. Hollenberg's laboratory) using the Olympus IX81 Laser Scanning Confocal Microscope through the Live Cell Imaging Facility funded by the Snyder Institute at the University of Calgary.

Letter from the Editors

We are pleased to present Volume 6, the 2016-2017 full edition of the Journal of Undergraduate Research in Alberta. This year's edition features excellent contributions of undergraduate authors from a variety of backgrounds including but not limited to Biomedical Engineering, Urban Design, and Business. Accordingly, our multidisciplinary journal offers both reviews on hot political topics such as "Regulation of Biotherapeutics" as well as articles that describe innovation in the area of cell biology and mechanics.

The highly relevant conclusions drawn by our authors underline once again the value of research programs at the undergraduate level. However, JURA's Volume 6 is not the only piece of evidence for the value of undergraduate research. In fact, many qualitative research studies have been performed that clearly pinpoint the benefits of undergraduate research experiences. One particularly thorough study evaluated the experiences of undergraduate students who participated in summer research programs in "core" sciences (DOI: 10.1002/sce.10131). An overwhelming 91% of the interviewed students reported positive gains, starting with personal attributes such as increased confidence and professionalism all the way to improvements in communication skills. Interestingly for us, less than 10% of the reported gains in communication skills were related to skills that are needed for publishing scientific work: Writing skills, reading comprehension skills, and information retrieval. This finding reinforces JURA's motivation to keep promoting undergraduate research articles and emphasizes the need of additional programs that foster the development of writing skills of undergraduate researchers.

For further encouragement of current undergraduate scientists who are considering to publish their work, this year's JURA edition features two novel elements. First, we have initiated the "JURA Best Paper Award", a $250 recognition for the original research article that received the highest ratings from the JURA editors. We are happy to announce that the first JURA Best Paper Award goes to Jared Collette and his research article "Mechanics of Sarcomeres in Series and Instability". Congratulations! Second, JURA Volume 6 includes an interview series with decorated faculty members of the University of Calgary who describe their early career experiences related to undergraduate research and scientific publishing. The reports of our interviewees cover different facets and a wide range of experiences, providing insightful and encouraging advice for undergraduate as well as graduate researchers.

We hope that you enjoy reading our 2016-2017 JURA edition and encourage you to share this journal with your peers. Please do not hesitate to send us any feedback or suggestions for future editions. We would like to acknowledge the support of our peer-reviewers and particularly the continued support of Dr. Walter Herzog, Killam Memorial Chair at the University of Calgary.

Sincerely your JURA Editorial Board,

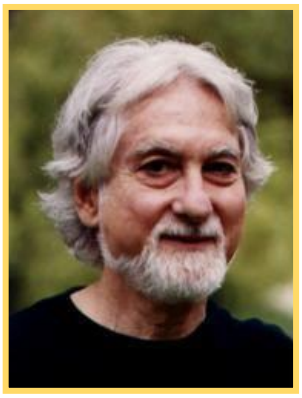
Maurice Mohr, *Editor-in-Chief*;
Yang Yu, *Managing Editor;*
Lindsay Loundagin, *Publishing and Layout Editor;*
Stacy Gibson, *Publishing and Layout Editor*

JURA

Journal of Undergraduate Research in Alberta • Volume 6 • 2017

University of Calgary Faculty Interviews

All great researchers were a novice at some point. The JURA editors have caught up with a few of the great researchers at the University of Calgary to get some insight on their experience writing their 1st first-author publication.



Morley D Hollenberg,
BSc, MSc, PhD, MD
Research interests: Proteinase activated receptors (a type of G-protein coupled receptors) in human disease

Wallace K. MacNaughton,
BSc, MSc, PhD
Research Interests: Gastrointestinal inflammation and epithelial biology

Mark Ungrin,
BSc, PhD
Research interests: Micro-tissue engineering focused on diabetes treaments and macular degeneration

1 JURA: What was the topic of your first published, scientific article and was it related to your current field of study?

MH: My first-authored paper written entirely by me along with my supervisor was data coming from my thesis work. The published topic was the isolation of the multiple oxytocin-vasopressin 'neurophysin' binding proteins from the posterior pituitary gland.

WM: My first first-author paper came out of my MSc work, and involved a study of how mild irritation of the gastric mucosa could confer protection against a subsequent damaging challenge. I still study the gastrointestinal mucosa, so you could say that this was the publication that got me started on a research area that I'm still interested in 30 years later.

MU: Working at Merck-Frosst, I had developed a medium-throughput assay for the activation of certain cell surface receptors, and used it to assess activation of the human EP1 prostanoid receptor. It was not initially related to what we are working on now, but this experience caused me to ask certain questions in our current research, and it looks like we will get at least one paper out of the resulting findings.

2 **JURA: Did your first submission get accepted, require revisions, or get rejected? If rejected, how many attempts did it take until the manuscript was accepted?**

MH: My first submission was accepted with suggestions for revisions. Both manuscripts accepted after revision x 1.

WM: This is a difficult question, because it was so long ago and my supervisor was the corresponding author. As I recall, the manuscript was accepted with revisions. We didn't have to do any extra experiments, so it was accepted rather quickly upon resubmission.

MU: The initial submission was rejected emphatically. Not only did they not like the paper, they questioned why anyone would have wanted to do the work in the first place! In retrospect we had sent it to the wrong journal for the nature of the work, but at the time it was very discouraging. We then sent it somewhere else (Analytical Biochemistry) and it was accepted with very positive reviews and only minor changes requested. The paper has now been cited 57 times and the assay has been used at several Merck sites internationally, and shows up in several patents.

3 **JURA: Looking back, what was the most important skill you learned or improved while writing and publishing your first scientific article?**

MH: The writing skills learned were sitting with my supervisor/collaborator, sketching out the manuscript first; then doing iterative editing, going back/forth between supervisor/collaborators. Persistence in generating a revision responding to the reviewers' critique.

WM: I think I learned three important things when working on my first manuscript. First, you have to tell a compelling story. Just reporting data isn't enough – you have to make it interesting. Second, you need to show the relevance of your work. In biomedical science this means demonstrating clearly how your work is of clinical importance. Third, you have to be honest – don't cut corners and don't publish anything that you don't believe in 100%. These are still important to me in papers I publish now.

MU: It's very important to identify an audience that is predisposed to understand why your work matters; and then to explain clearly what makes it important. The best science in the world, if poorly presented, may not have much impact because no-one pays attention to it. Even though you know how big the potential impact of your work is, that doesn't mean it's as obvious as you think to everyone else.

4 **JURA: What is the main difference in the way you wrote your first scientific article and an article you would write today?**

MH: Today, I sit with my trainees to sketch the manuscript; then let them do the first draft on their own, followed by iterative edits involving all collaborators.

WM: Most articles I write today are actually written by trainees in my lab. My job is to provide oversight and pointers to help grad students and postdocs learn the art of putting together a manuscript. Earlier in my career, I wrote the papers myself and prepared them for submission. It was a longer process then, since figures

had to be prepared by hand and submissions were made by courier, rather than electronically. With the internet, the preparation and submission processes have changed dramatically, but the basic elements of writing a good scientific paper are the same.

MU: Early on I wrote as if I was writing a story – trying to build to the climax and then stun the reader with how interesting the findings are. Now I try to let them know what to expect right from the beginning, so they can decide if they care enough to keep reading. I start with the figures, write the legends, then the results section follows from that. The discussion and materials & methods grow out of that, and then you know what you need to include in your introduction. At the end you know enough to write a clear abstract, and sum the whole paper up in an explanatory titl4. (Note: When I say "I" write a paper now, I mean that in the sense that I make my trainees do it. Then we go back and forth for revisions.)

JURA: What is your most important piece of advice for students who are writing their first scientific article for publication?

MH: Suggestions for writing your 'first' and subsequent articles: 1. Have your working hypothesis, your approach to test the hypothesis and the key data supporting (or disproving) your hypothesis clearly in your mind. THEN 1. Generate a provisional title that captures the essence of what you've discovered. 3. Line up the figures in the sequence you wish to 'tell the story'. 4. Generate a bare-bones point-form outline of the projected manuscript (just the main headings e.g. Intro/Methods/Results/Discussion with point-form topics that will be included in each section. 5. Write the abstract, according to the instructions for your Journal of Choice. The abstract should concisely 'say it all': what was the main issue/background; what was your new hypothesis; how did you test your hypothesis; what did you find; what are the conclusions/implications of your new data. 6. Go on to write the intro based on your abstract information, including ONLY the background and references relevant to the working hypothesis, and the experimental approach used to test the hypothesis. Many authors currently present their 'main findings' in the introductory section; but that information in the intro. is a 'no-no' for many journals; and it takes away from sucking in the reader to read the entire manuscript. 7. Revise ad nauseam; then run by a colleague or other individual for comments, revise again pending comments; read to eliminate final typos etc; then submit online

WM: As mentioned above, be sure you are writing a compelling, interesting story. Use plain language and be very clear. Ensure that your science is excellent. Importantly, involve all of the co-authors in the preparation of the manuscript. Not only is this ethically the right thing to do, but your co-authors can provide lots of insight that will make your paper better. Finally, don't take rejection personally. You will get rejected from time to time, and you will almost always have to do revisions (I've published over a hundred papers, and have only had one accepted without revisions). Being rejected or having to do revisions doesn't mean you're a bad scientist – it's just part of the business.

MU: Science is very specialized. The vast majority of scientists do not have the time or inclination to read your paper. Your title should be clear enough to let the casual reader skimming through their automated PubMed or Google Scholar search results (you all do this, right?) decide quickly whether or not they care enough to read the abstract. Your abstract should summarize the whole paper – I like to think of it as: if someone was willing to trust you completely, all they would need to read is your abstract. The rest of the paper is there because of course they don't.

6 JURA: How did your 1st first author publication positively impact your scientific career?

MH: My 1st first-authored manuscript contained many of the elements of focus and discovery that underpin the direction my research career has followed since that time: Those elements include: 1. peptide hormone biosynthesis, storage and secretion; 2. peptide-protein isolation and characterization; 3. amino acid analysis, 4. protein-protein interactions; 5. protein physical chemistry, 6. smooth muscle tissue bioassay; 7. peptide hormone structure-activity relationships, 8. receptor molecular pharmacology. Many of these elements can be found in a recent manuscript describing the isolation of receptor/PAR-activating proteinases from cockroach extracts (PMID: 28317204). The overview article that follows provides the background for the impact of my manuscript work on my current career follows. In essence, the skills portrayed in my 1st first-authored manuscript were the essential seeds of what has grown to characterize the work I continue to do today.

WM: My first paper was exciting because it showed that I could do good science that others would read and cite. In a way it was a validation of my chosen career path. I still enjoy the thrill of discovery and sharing my findings with colleagues around the world.

MU: The assay system I developed I then went on to use in a second first-author publication. This work combined gave me a portable NSERC entrance scholarship which let me choose where I wanted to go for grad school – I could also have stayed on at Merck if I had wanted a job.

JURA
Journal of Undergraduate Research in Alberta • Volume 6 • 2017

University of Calgary Faculty Interviews continued

A unique perspective on one faculty member's path to a successful research career

Derrick Rancourt is a Professor in the Depts. of Oncology, Biochemistry & Molecular Biology and Medical Genetics, University of Calgary. He received his BSc and PhD in Biochemistry from the University of Guelph and Queens University respectively and postdoc'd in the laboratory of Nobel Laureate Dr. Mario Capecchi. He is the Director of the University of Calgary's Centre for Mouse Genomics, which specializes in the generation of transgenic and knockout mice. His research program revolves around the derivation, expansion, differentiation and genetic manipulation of mouse and human pluripotent stem cells, including embryonic stem cells and induced pluripotent stem cells. Over the past several years he has been developing bioprocesses for generating bone and cartilage tissue from stem cells for transplantation. An important feature of the research is the development of methods for expanding and differentiating murine and human pluripotent stem cells in stirred suspension bioreactors.

Like many, I started in University with the intention of going into Medical School. However, I soon became enamored by the theory of evolution, having not been introduced to it in high school. In my second year, I was inspired by the work of Brinster and Palmiter, who made the first transgenic mouse, demonstrating that forced overexpression of the human growth hormone resulted in animals that were twice the size of their littermates. Seeing opportunities in this brand new field, I made it my mission to become a genetic engineer. After a mind-numbing experience working at a steel plant during the summer after my first year, I decided that the only way I was going to become a genetic engineer is if I procured relevant research experience.

It's funny how we bumble along towards our career goal. Having read Stephen Shapin's *The Scientific Life*, I now know the importance of experimental research, but at the time my instincts told me that research experience would pave my way. People say we are products of our environment and my path to becoming a genetic engineer was a circuitous one. This is largely because in Canada molecular biology, let alone genetic engineering, was in its infancy. At the University of Guelph, there was only one early adopter of molecular biology and getting into his lab seemed next to impossible. Knowing what I know now, I should have engaged him directly and asked him to help me with my plan. But I was gutless at the time. I did not know the importance of network problem solving and how it offered the potential of getting me to my goal faster. Instead I chose the path of least resistance, working for one of his colleagues who had taught me genetics.

I liken my research lab experience to that of the budding artists who worked in the Bottegas of Renaissance Florence. Here, entry level trainees did all the "joe jobs", they cleaned the chicken coups and

collected the eggs used to make the paint for those higher up on the food chain. Similar to cleaning chicken coups, my first lab experience was to prepare "fecalase", an enzyme extract from my own feces. Part of the Ames mutagenicity assay, the theory behind fecalase was that it simulated the conversion of pro-mutagens in the gut. In my project, I used the Ames test to investigate the mutagen content of tannin pigments found in red wine.

Although it wasn't genetic engineering or molecular biology, the project gave me exposure to genetics research and oenology (who knew wine-making/-tasting was a science!). This research experience provided me with an important career entrée. Much like the Florentine Bottega, I was keen to pay my dues as a novice and boy did I pay. I'll never forget how my former boss would snicker whenever it was time to prepare a fresh batch of fecalase. Just to rub it in, he would hand me a box of oatmeal cookies a couple of days beforehand, advising me that enzyme activity would be enhanced if I ate them a day or two before the prep.

Jokes aside, my first academic mentor helped introduce me to academia. He helped me to secure a spot in that molecular biology lab and to get my first genetic engineering position. It was through his kindness and my sacrifice that I am here today.

JURA
Journal of Undergraduate Research in Alberta • Volume 6 • 2017

Mechanics of Sarcomeres in Series & Instability

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JARED COLLETTE

As a recent graduate of Chemical Engineering with a Biomedical Engineering Specialization at the University of Calgary, Jared Collette worked with the Human Performance Lab in his final years under the supervision of Azim Jinha and Dr. Walter Herzog. His research with the Human Performance Lab centered on computational biomechanics focused on sarcomeres. After exposure to many research topics, biomechanics has been his most passionate subject. He plans to pursue an academic career around biomechanics, starting with a Masters and Ph.D. focusing on developing computational models of cell motility.

Abstract

Sarcomeres are the smallest independent unit of force production in the muscle. Current theoretical models of sarcomere in series, i.e. a myofibril, predict instability on the descending limb region of the force-length relationship. However, experimental evidence suggests that sarcomeres can be stable on the descending limb region with non-uniform lengths. The models presented re-evaluates the assumption that sarcomeres are independent units of contraction. Instead, it is hypothesized that there is a dependency between sarcomeres for force generation. Sarcomeres in series were modelled, with force as the dependent variable and sarcomere length and time as the independent variables. Models were developed with both independent and dependent sarcomere force generation. The independent sarcomere models resulted in instability that current theoretical models predict. Two cases of dependent sarcomere models were implemented, both included a shift in the passive force with varying degrees of dependency between adjacent sarcomeres. With these models, there was either stability with non-uniform length, stability with uniform length, or instability on the descending limb region of the force-length relationship. The major finding was that mathematically, sarcomeres with a variable passive force can reach equilibrium at various lengths if a dependency between adjacent sarcomeres is incorporated into the models.

Keywords: Sarcomere, Myofibril, Force-length Relationship, Descending-Limb Region, Instability, Modelling

Introduction

Muscle Anatomy and Physiology

Sarcomeres are the smallest, independent unit of contraction in skeletal muscles. Within each skeletal muscle cell are longs strands of sarcomeres in series called myofibrils, which cause muscle cell contraction. Forces generated by a sarcomere can be broken into active and passive forces. Active forces result from neural stimulation of muscles and are most commonly thought to be generated through cross bridges in accordance with the cross-bridge theory [1]. Passive forces do not involve neural stimulation and are generated from the elasticity contained in sarcomeres, primarily through the protein titin [2]. Early studies have shown that both the active force and the passive force of a single sarcomere depend on the length of a sarcomere, as described by the force-length relationship [3]. The total sarcomere force is the summation of the active and passive forces at any given length.

Myofibril: Characterizing Sarcomeres in Series

The linearized force-length relationship suffices in describing the isometric force of individual sarcomeres when stimulated at a given sarcomere length. However, the application of this relationship to myofibrils leads to instability on the descending limb region. Consider two sarcomeres in series undergoing an isometric contraction initially at two slightly different lengths (Fig. 1). Applying the force-length relationship, the sarcomere with the shorter length will generate a larger contractile force because of the negative force-length slope. With a larger contractile force, this sarcomere will become even shorter and will generate an even larger force. This positive feedback loop is unstable and would theoretically pull the longer sarcomere to greater lengths until they reach equilibrium with one sarcomere on the ascending limb region (sarcomere length $\lesssim 2.25\,\mu m$) and the other on the passive force region (sarcomere length $\gtrsim 3.65\,\mu m$). Myofibrils do not experimentally behave this way, and there is a gap between theory and experimental evidence. The models developed in this study are aimed at examining this gap by looking at new ways to model myofibrils.

Literature

Empirical Studies on the Myofibril

One discrepancy discovered in activated myofibrils is the idea of uniform sarcomere length at equilibrium. From the force-length relation, if all sarcomeres are in the same region and have the same force, they must have the same length. However, when stretching single, isolated myofibrils on the descending limb of the force-length relationship, great sarcomere length non-uniformities are observed at equilibrium [4]. When the activated myofibrils in this experiment were stretched, all sarcomeres were rapidly stretched and reached equilibrium at various lengths on the descending limb region of the force-length relationship (Fig. 2). In experiments by Telley and colleagues, the dynamics of cardiac myofibrils were monitored through fluorescent tagging, totaling 100 sarcomeres in series [5]. Of the 100 sarcomeres, 11 were dynamically traced over time. These 11 sarcomeres reached equilibrium at non-uniform length on the descending limb region of the force-length relationship. In that same study, a single myofibril with 80 sarcomeres taken from the soleus muscle of a rat was activated and stretched onto the

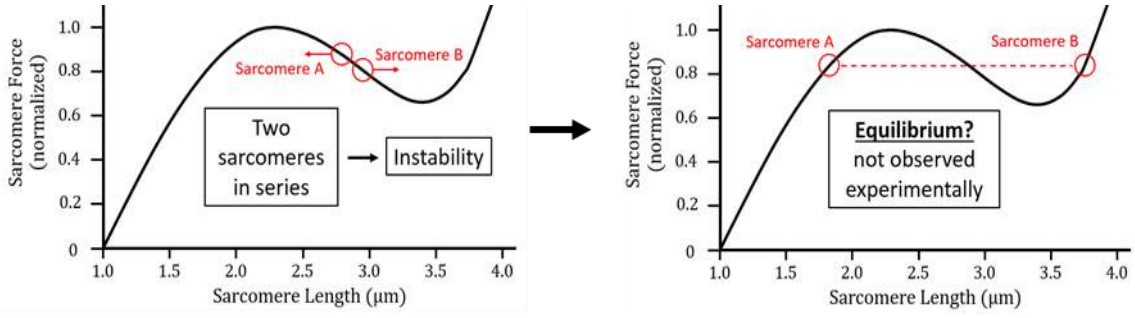


Figure 1: Instability on the force-length curve

descending limb region, and again all sarcomeres reached equilibrium at non-uniform lengths. Other experiments on single myofibril provide similar results as described above [6]–[9].

Theoretical Models on Sarcomeres

To understand the behaviour of sarcomeres, mathematical models have been developed to obtain the force of the sarcomere as a function of length and other factors. A simple empirical model was developed by Gordon et al. in 1966, which is a linearization of the force-length relation (Fig. 3). Passive forces on the force-length relationships can vary greatly between experiments, and those relationships are typically based on approximations of experimentally derived results [10]. However, a first order, linearized relationship can be used to model the passive force.

A frequently used mechanical model of muscle contraction and force production is the Hill's three element model [11]. Hill's model uses a contractile element with two non-linear springs, one in series and the other in parallel with the contractile element. The active force, and corresponding force-length relationship, is represented by the contractile element, while the passive force is represented by the parallel spring. More advanced models have been developed for sarcomeres based on springs and dampers, accounting for more intricate anatomical features [12], [13]. For our purposes, a linearized model proved adequate.

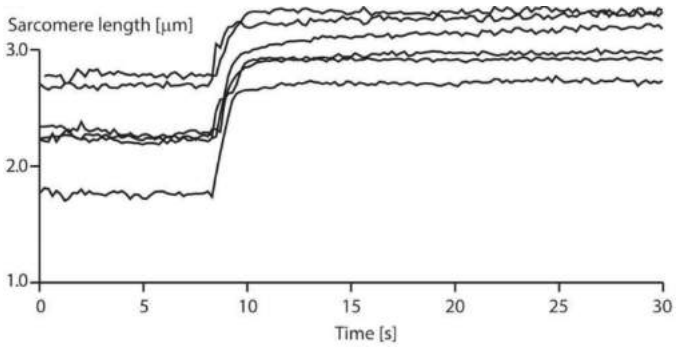
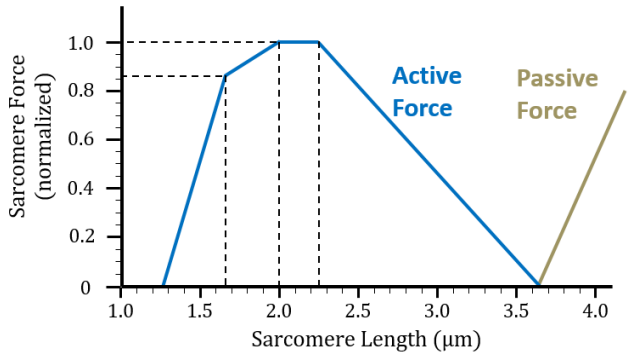


Figure 2: Stability of myofibril on the descending limb region of the force-length curve. Evidence of sarcomere length non-uniformity [4].

Theoretical Models on Myofibrils

Using the simplified, linearized, force-length relationship from Gordon et al. 1966 [3], we developed a theoretical myofibril model of two sarcomeres in series that resulted in instability along the descending limb, contradicting experimental evidence [14]. We then developed two additional models to describe two sarcomeres in series, with the last model incorporating effective stiffness, which tracked experimental data more closely but was limited to two sarcomeres [14].



$$1.27 < L \leq 1.67\ \mu m,\ F^{act} = -2.667 + 2.10 * L$$
$$1.67 < L \leq 2.00\ \mu m,\ F^{act} = 0.04 + 0.48 * L$$
$$2.00 < L \leq 2.25\ \mu m,\ F^{act} = 1.00$$
$$2.25 < L \leq 3.65\ \mu m,\ F^{act} = 2.592 - 0.71 * L$$
$$L \geq 3.65\ \mu m,\ F^{pas} = -5.475 + 1.5 * L$$

Figure 3: Linearized force length relationship.

Zahalak, in response to these models, presented his own model of a myofibril using a comprehensive mathematical formulation of stability of sarcomeres in series, which led back to the issue of instability. [15]. Other models that have been developed for myofibrils include a statistical analysis of sarcomeres ignoring individual degrees of freedom that results in sarcomeres converging at non-uniform lengths only on the ascending-limb region instead of the descending-limb region [16]; a model focusing on stored mechanical energy in sarcomeres using contractile units in series and parallel to represent sarcomeres that does not capture the dynamic nature of sarcomeres [17]; and a model focusing on variable compliance of the sarcomere, but focuses on the forces generated by sarcomeres instead of the resulting lengths

produced [18].

Objective and Hypothesis

The purpose of this study was to develop computational models to improve the understanding of myofibril mechanics by modelling sarcomeres in series with non-uniform length. We hypothesized that force generation by sarcomere units in series are not completely independent of each other. This hypothesis was tested by building a dynamic, computational model where sarcomere force is determined by the length of the sarcomere and the two adjacent sarcomeres. Models were developed for sarcomeres independent of each other, simulating myofibrils with two and six sarcomeres in series. Then, models were developed for sarcomeres that were dependent on each other. These last models were developed with 20 sarcomeres in series.

Methods

Overview

The development of the computational myofibril models are broken into three distinct steps. First, all sarcomeres lengths are initialized to a specific region of the force-length curve. Then, the total forces of each sarcomere are obtained based on the sarcomere lengths. This approach is related to the force-length relationship, and it is this step that will vary from model to model. Finally, the length of the sarcomere is updated over a time interval based on the forces produced by each sarcomere. This is repeated until equilibrium is achieved. The variables used for the models are shown in Fig. 4.

Initializing the Models

The sarcomere lengths are initialized to a certain region in the force-length relationship. For the models, a difference of $0.2 \, m$ was chosen between the minimum and maximum sarcomere lengths. In the models for independent sarcomeres, the sarcomere lengths were initialized randomly within the specified region. In the models for dependent sarcomeres, the sarcomeres lengths are initialized incrementally from the first sarcomere with the minimum length to the last sarcomere with the maximum length. The difference in lengths between two adjacent sarcomeres remain constant.

Models Developed

To develop models of sarcomeres independent of adjacent sarcomeres, the linearized force length relationship from Gordon et al. (1966) was implemented for a 2 and 6 sarcomere myofibril. Each model was tested on the ascending and the descending limb regions of the force-length relationship.

For models in which sarcomeres were dependent on adjacent sarcomeres, myofibrils containing 20 sarcomeres in series were used. Using 20 sarcomeres allowed the models to discern patterns in sarcomeres groups that were lost with 2-6 sarcomeres, while 20 sarcomeres was still a small enough number to manage individual sarcomeres. The dependence of adjacent sarcomeres on each other was represented using a linear passive force that is shifted to the left or right of the force-length curve, depending on the lengths of the adjacent sarcomeres, described as follows:

$$F^{pas} = b + 1.5 * (L - x_{shift}) \quad (1)$$
$$x_{shift} = f(L_{i-1}, L_{i+1})$$

$F = Sarcomere\ Force$
$L = Sarcomere\ Length$
$x = Shift\ Left\ or\ Right$
$b = y - intercept\ of\ passive\ force\ when\ x_{shift} = 0$
$i = i^{th}\ Sarcomere$

It is assumed that this shift is linearly proportional to each of the lengths, and the principle of superposition is imposed to combine the terms. Due to the symmetry on either side of a sarcomere, it is also assumed that the constant of proportionality for each length is the same, so the shift can be written as follows:

$$x_{shift} = C_{1,i-1}L_{i-1} + C_{1,i+1}L_{i+1} = C_1 * (L_{i-1} + L_{i+1}) \quad (2)$$

To use these equations properly, the parameter 'b' from the passive force equation is

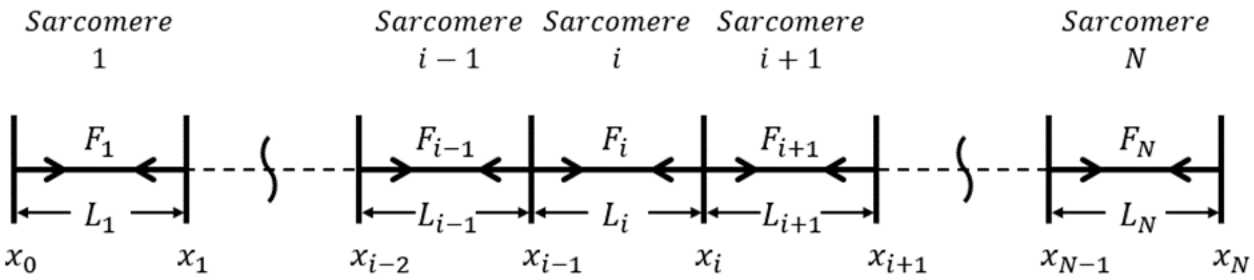


Figure 4: Variable definitions for models. F is the sarcomere force produced from the ith sarcomere, L is the length of the ith sarcomere, and x is the total distance of the ith sarcomere from the start of the myofibril.

required. This 'b' parameter is the y-intercept of the passive force when there is no shift, and is chosen depending on one of two shift methods implemented. In the first method, the constant 'C_1' is a positive value and all shifts occur to the right (i.e. to increasing sarcomere lengths). To choose a b-value, the maximum passive force is chosen for when there is no shift. Based on this curve, the b value is calculated to be b = -2.475, leading to the equation

$$F^{pas} = -2.475 + 1.5 * (L - x_{shift}) \quad (3)$$

Three simulations were run to see the effects of 'C_1' on the model. For these simulations C_1 was equal to 0.1, 0.2, 0.3. In the second method, the constant 'C_1' was given a negative value and all shifts occurred to the left (i.e. shorter sarcomere lengths). To choose a b-value, the minimum passive force is chosen for when there is no shift. Based on this curve, the b value is calculated to be b = -5.475, leading to the equation

$$F^{pas} = -5.475 + 1.5 * \left(L - x_{shift}\right) \quad (4)$$

Three simulations were run to see the effects of 'C_1' on the model. For these simulations, C_1 = -0.15, -0.25, -0.35.

Model Time Evolution

Equilibrium Condition

The following test was used to determine if all sarcomeres were at equilibrium. The average force of all sarcomeres was calculated and was used as a reference value. All forces were compared with the average force and an equilibrium tolerance was set to be ±0.005 units normalized to the maximum active force of 1.0 units. If all forces were within this equilibrium tolerance, then the sarcomeres were assumed to be in equilibrium, otherwise they were not accepted to be in equilibrium.

Sarcomere Length Update

Assuming pseudo steady-state motion (i.e. initial velocity and acceleration are zero at each time interval), a linearized function of the change in length can be derived from Newton's second law.

$$\Delta L_{i,t} = C_2 * \left[F_{i+1,t} + F_{i-1,t} - 2F_{i,t}\right] \quad (5)$$

Where C_2 is an arbitrary constant that determines the speed of convergence. The force term in the above formula matched the simplest numerical definition of a Laplacian.

Boundary Conditions

For sarcomeres in series, the boundary conditions need to be explicitly defined. Here, the two end sarcomeres i.e. L_1 and L_N, were updated based on the boundary conditions of the sarcomere. For isometric contractions, the total length does not change, and can be represented by the following:

$$\frac{dx_0}{dt} = 0; \frac{dx_N}{dt} = 0 \quad (6)$$

Isometric contractions were assumed for all cases. However, a similar method could be implemented for concentric and eccentric contractions. Applying isometric boundary conditions means that sarcomere lengths are updated as follows:

$$L_{1,t+\Delta t} = L_{1,t} + C_2 * (F_2 - F_1); L_{N,t+\Delta t} = L_{N,t} + C_2 * (F_{N-1} - F_N) \quad (7)$$

Results

The results are based on tracking the sarcomere lengths and associated forces over the course of the simulation. For this discussion, stability is defined as sarcomeres that converge to uniform or non-uniform lengths within the descending limb region of the force length relationship, while instability is defined as systems that are not stable.

Sarcomeres Independent of Adjacent Sarcomeres

For the model with two independent sarcomeres in series, initializing the sarcomere lengths in the ascending limb region (1.6-1.8 μm) resulted in stability with uniform sarcomere length. Equilibrium for both sarcomeres was reached at the average initial sarcomere lengths of 1.70 μm and a normalized force of 0.86 (Fig. 5a and Fig. 5b). When initialized on the descending limb region (sarcomere lengths of 2.6-2.8 μm), instability occurred and sarcomere lengths were non-uniform. Equilibrium for the sarcomeres was reached at lengths at 1.52 μm and 3.88 μm and a normalized force of 0.53 (Fig. 5c and Fig. 5d).

For the model with six independent sarcomeres in series, initializing the sarcomere lengths on the ascending limb region (1.6-1.8 μm) resulted in stability with uniform length. Equilibrium for all sarcomeres was reached at a length of 1.68 μm and a normalized force of 0.85 (Fig. 6a and Fig. 6b). When initialized the myofibril on the descending limb region (2.6-2.8 μm), it resulted in instability with non-uniform length. Equilibrium for the sarcomeres was reached with lengths at either 1.52 μm or 3.88 μm at a normalized force of 0.52 (Fig. 6c and Fig. 6d).

Sarcomeres Dependent of Adjacent Sarcomeres

Passive Force Shifted Towards Longer Sarcomere Lengths

With twenty dependent sarcomeres in series, setting C_1 to 0.1 and the initial sarcomere lengths

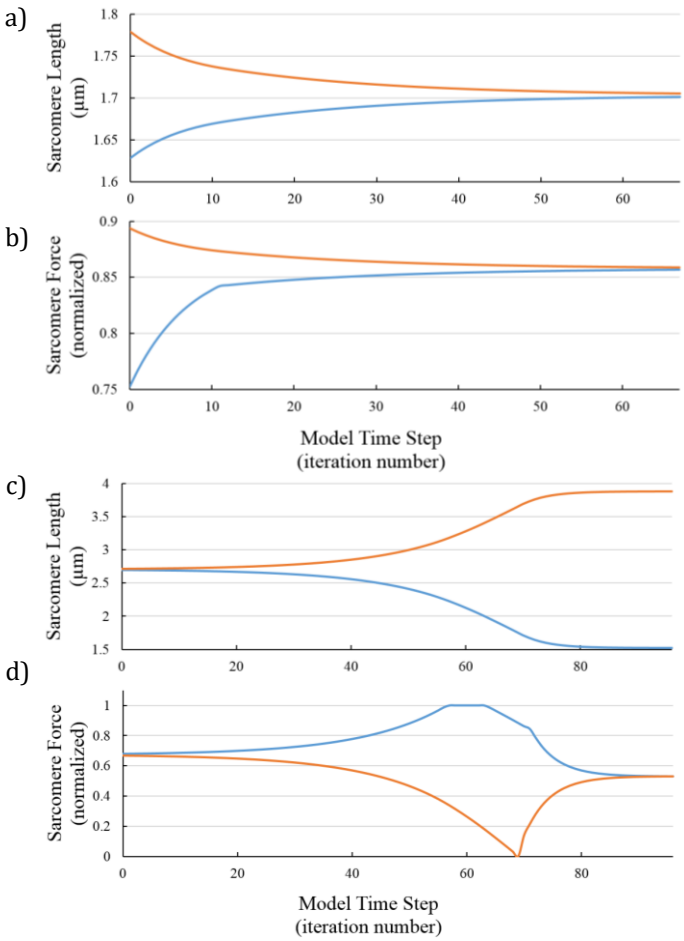


Figure 5: Simulation results for two independent sarcomeres. The ascending limb region simulation of sarcomere lengths (a) and forces (b) over time shows stability while the descending limb region simulation of sarcomere lengths (c) and forces (d) over time shows instability.

to 2.6-2.8 μm resulted in stability with uniform length. Equilibrium for all sarcomeres was reached with lengths at 2.70 μm and a normalized force of 1.44 (Fig. 7a and Fig. 7b).

Setting C_1 to 0.2 and initial sarcomere lengths to 2.6-2.8 μm resulted in stability with non-uniform length. Equilibrium for the sarcomeres was reached with the lengths ranging between 1.65-3.56 μm and a normalized force of 0.80 (Fig. 7c and Fig. 7d).

Setting C_1 to 0.3 and initial sarcomere lengths to 2.6-2.8 μm resulted in instability with non-uniform length. Equilibrium for the sarcomeres was reached with lengths at either 2.00 μm or 3.39 μm at a normalized force of 0.99 (Fig. 7e and Fig. 7f).

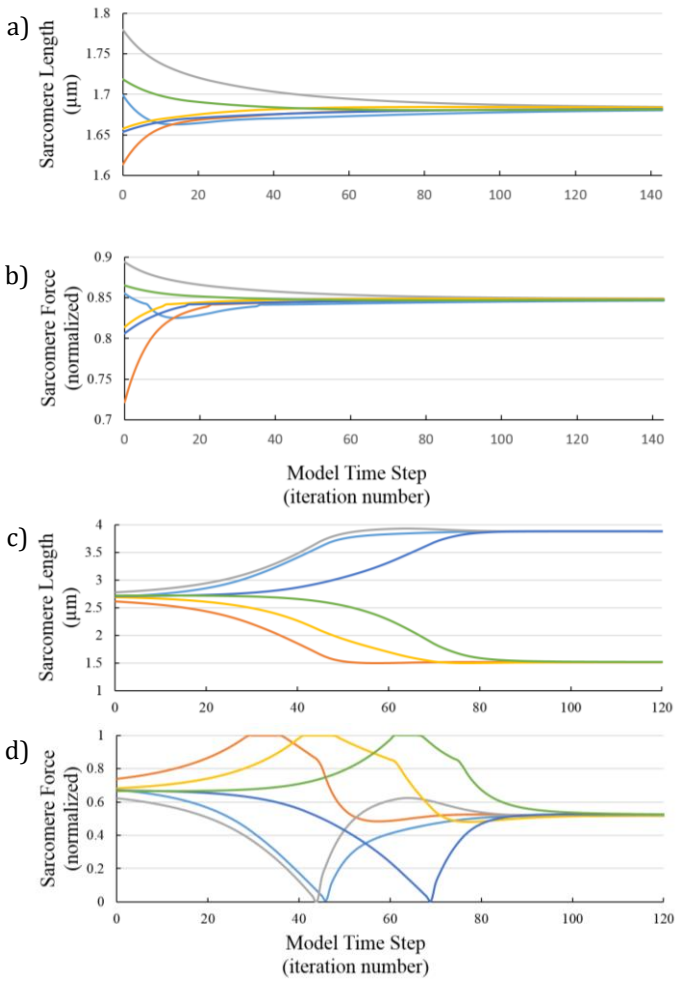


Figure 6: Simulation results for six independent sarcomeres. The ascending limb region simulation of sarcomere lengths (a) and forces (b) over time shows stability while the descending limb region simulation of sarcomere lengths (c) and forces (d) over time shoes instability.

Passive Force Shifted Towards Shorter Sarcomere Lengths

With twenty dependent sarcomeres in series, setting C_1 to -0.15 and initial sarcomere lengths to 2.6-2.8 μm resulted in instability with non-uniform length. Equilibrium for the sarcomeres was reached with lengths at either 1.68 μm or 3.71 μm at a normalized force of 0.84 (Fig. 8a and Fig. 8b). Setting C_1 to -0.25 and initial sarcomere lengths to 2.6-2.8 μm resulted in stability with non-uniform length. Equilibrium for the sarcomeres was reached with the lengths ranging between 2.03-3.97 μm and a normalized force of 1.23 (Fig. 8c and Fig. 8d). Setting C_1 to -0.35 and initial sarcomere lengths to 2.6-2.8 μm resulted in instability with non-uniform length. Equilibrium for the sarcomeres was reached with the lengths ranging between 1.60-4.33 μm and a normalized force of 1.86 (Fig. 8e and Fig. 8f).

Discussion

Sarcomeres Independent of Adjacent Sarcomeres

The purpose of developing the models of independent sarcomeres was to lay the foundations of the model and verify the instability of the descending limb based on current theory. The two sarcomeres in series allowed for easy model development and to show that there was stability on the ascending limb and instability on the descending limb of the force-length relationship. This model was successfully implemented and the results were as expected. The six sarcomere model was implemented to test the generalization of two sarcomere model to an "n" sarcomere model scenario. Models were tested for up to 100 sarcomeres in series and produced the same results as the six sarcomere model, that is, instability on the descending limb region.

Sarcomeres Dependent on Adjacent Sarcomeres

Determining any biological significance of these solutions requires an understanding of the models. The simulations illustrated that there exist mathematical solutions where the sarcomeres are stable and, at equilibrium, have uniform lengths, stable with non-uniform lengths, and unstable. These different outcomes depend on the constant C_1, which is the linear scaling factor used for the shifting of the passive force. C_1 has a different effect depending on whether there is a right (passive force is shifted towards longer sarcomeres) or left (towards shorter sarcomeres) shift.

Passive Force Shifted Towards Longer Sarcomere Lengths

Decreasing C_1 minimizes the contribution of the shifting passive force has on the total sarcomere force, and the passive force remains further to the left on the force-length relationship. If C_1 is too low, as with the simulation using C_1=0.1, the passive force is too large to have

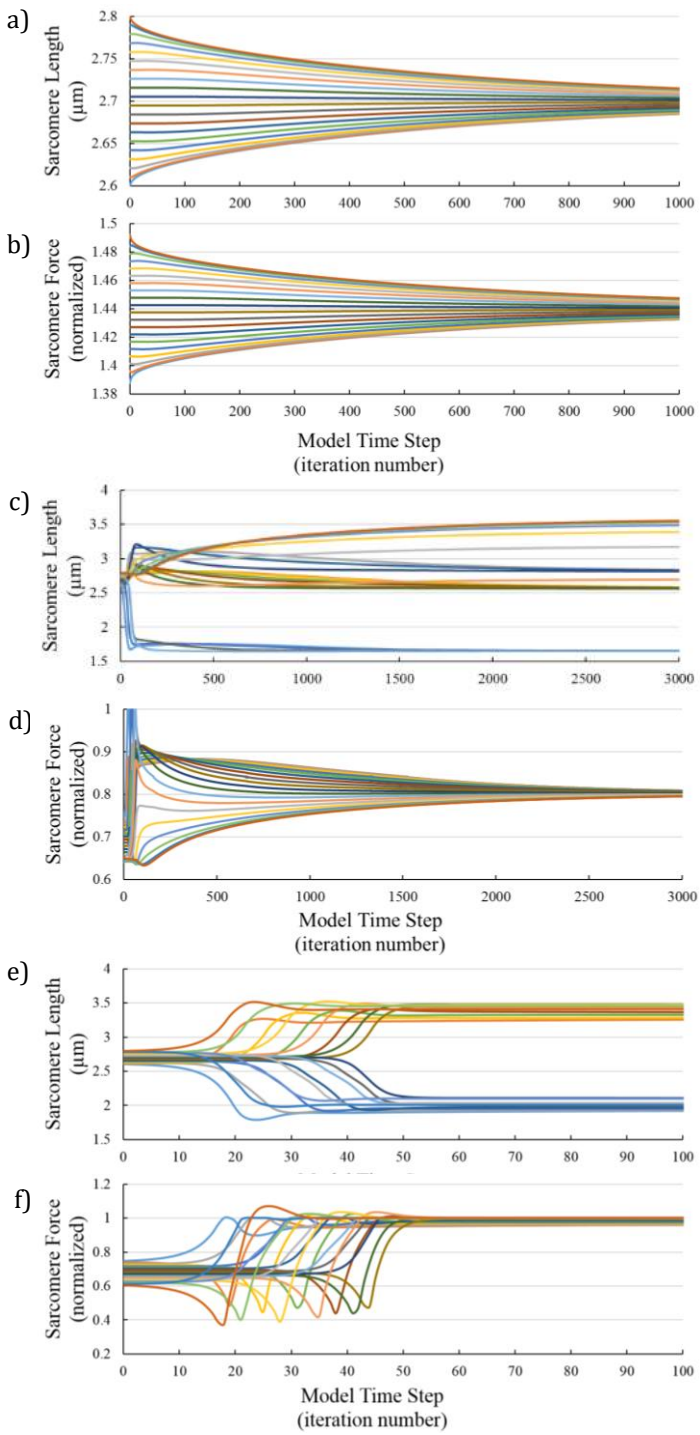


Figure 7: Simulation results for twenty dependent sarcomeres with passive force shifting to the right with constants C = 0.1 with sarcomere lengths (a) and forces (b) over time, C = 0.2 with sarcomere lengths (c) and forces (d) over tine, C=0.3, with sarcomere lengths (e) and forces over time (f).

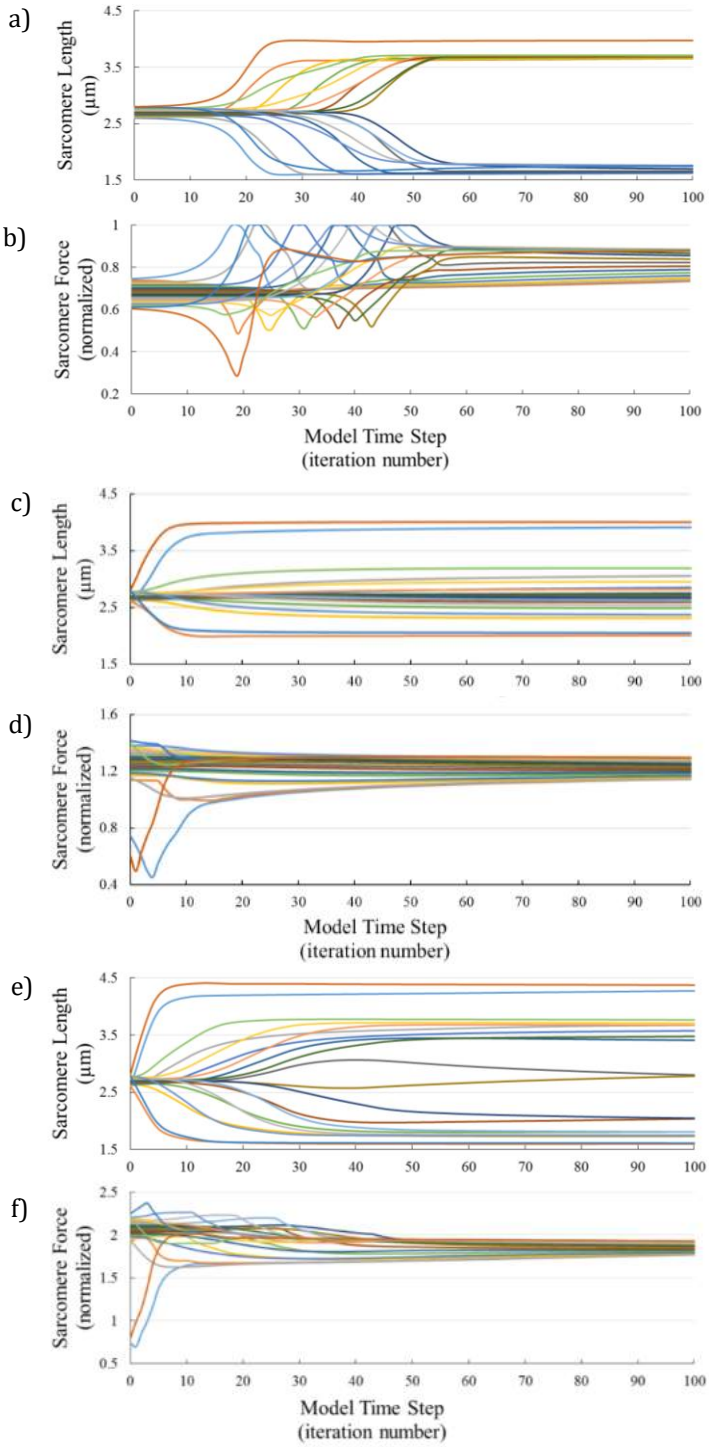


Figure 8: Simulation results for twenty dependent sarcomeres with passive force shifting to the left with constants C = -0.15 with sarcomere lengths (a) and forces (b) over time, C = -0.25 with sarcomere lengths (c) and forces (d) over time, C=-0.35, with sarcomere lengths (e) and forces over time (f).

biological significance. If C_1 is too high, as with the simulation using C_2 = 0.3, the passive force becomes too small resulting in instability

due to the active forces. However, if C_2 is chosen to balance passive and active forces as with C_2 = 0.2, then stability is reached and sarcomere lengths at equilibrium are non-uniform. This

theoretical result matches that observed experimentally in single myofibrils [4].

Mathematically, this result is explained as follows: if *sarcomeres i ± 1* are longer than *sarcomere i*, then *sarcomere i* would have its passive force shifted far to the right, decreasing its passive force. On the descending limb, *sarcomere i* would have a larger active force. This balance between active and passive force creates stability.

Biologically, this result may be interpreted as follows: some mechanism of stretching an adjacent sarcomere causes the passive force of the sarcomere to decrease. Speculatively, there could be some interconnecting structure, a filamentous protein for example, that could achieve the desired interrelation between adjacent sarcomeres. Conclusively, if this interconnecting relation exists, then there is a mathematical solution that creates stability at non-uniform lengths on the descending limb region of the force-length relationship.

Passive Force Shifted Towards Shorter Sarcomere Lengths

Decreasing C_1 minimizes the contribution of the shift of passive force on the total (active and passive) sarcomere force. For this scenario, the passive force remains further to the right on the force-length relationship.

If C_1 is too low, as with the simulation with C_1=-0.15, then the passive force is too small and instability similarly to the independent sarcomere models occurs. If C_1 is too large, as with the simulation with both C_1=-0.25 and C_1=-0.35, then the passive force becomes too large to have biological significance. It is noted that even though the forces are too high, stability with non-uniform lengths can be achieved on the descending limb region.

Mathematically, if *sarcomeres i ± 1* are longer than *sarcomere i*, then *sarcomere i* would have its passive force shifted far to the left, increasing its passive force. However, *sarcomeres i ± 1* still have a larger passive force. On the descending limb, *sarcomere i* would have a larger active force. Therefore, this balance between active and passive forces results in stability. The distribution of sarcomere lengths along the myofibril oscillates symmetrically similar to f(x) = x*sin(x). Similar to the right shift of the passive force, there exists a mathematical solution with stability at non-uniform lengths on the descending limb region of the force-length relationship. However, the total force generated is too high to have biological significance.

Summary

Overall, the independent models behaved as expected with the instability on the descending limb of the force-length relationship. Between the two dependent models, the passive force shifted towards longer sarcomere lengths (i.e. constant C_1 is positive), proved to be a better model because both stability was achieved in the descending limb of the force-length relationship, and the forces produced by each sarcomere was more reasonable (under a value of 1).

Conclusion and Future Work

Sarcomeres in series are theoretically predicted to be unstable on the descending limb region of the force-length relationship. However, experimental evidence has shown that sarcomeres can be stable on the descending limb region, typically with small amounts of non-uniformity between the sarcomeres [4]. The hypothesis was to test the long-held assumptions that sarcomeres are independent units of force generators by developing computational models of dependent sarcomeres in series. The major finding of these models was that mathematically, sarcomeres with a variable passive force can reach equilibrium at different lengths from each other on the descending limb of the force-length relationship. The next stages in this work is to continue developing models for sarcomeres in series. First, a variable passive force slope change will be implemented, which varies the slope of the passive force rather than the sarcomere length at which passive forces is engaged. Then, various initial conditions need to be implemented to further test the models that have already been developed, such as random initial lengths or initial lengths following a normal distribution. Once these models have been developed, they can

be interpreted mathematically, mechanically and physiologically.

Acknowledgements

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References

1. A. F. Huxley, "Muscle structure and theories of contraction," Prog. Biophys. Biophys. Chem., pp. 255–318, 1957.
2. R. Horowits, K. Maruyama, and R. Podolsky, *J. Cell Biol.*, 109**(5)**, 1989.
3. A. M. Gordon, A. F. Huxley, and F. J. Julian, *J. Physiol*., 184**(1)**, 1966.
4. W. Herzog, K. Powers, K. Johnston, M. Duvall, *Front. Physiol*., 6, 2015.
5. I. A. Telley, J. Denoth, E. Stüssi, G. Pfitzer, R. Stehle, B*iophys. J.*, 90**(2)**, 2006.
6. K. S. Campbell, *PLoS Comput. Biol.*, 5**(11)**, 2009.
7. D. E. Rassier, W. Herzog, G. H. Pollack, *Proc. R. Soc. B Biol. Sci.*, 270**(1525)**, 2003.
8. D. A. Martyn, P. B. Chase, M. Regnier, A. M. Gordon, *Biophys. J.*, 83**(6)**, 2002.
9. P. C. Macpherson, R. G. Dennis, J. A. Faulkner, *J. Physiol*., 500, 1997.
10. S. G. Campbell, P. C. Hatfield, K. S. Campbell, *PLoS Comput. Biol*., 7**(9)**, Sep. 2011.
11. A. V. Hill, *Proc. R. Soc. Lond. B Biol. Sci.,* 126 **(843)**, 1938.
12. L. M. Chapin, L. T. Edgar, E. Blankman, M. C. Beckerle, Y. T. Shiu, *Cell. Mol. Bioeng*., 7**(1)**, 2014.
13. C. D. Williams, M. Regnier, T. L. Daniel, *PLoS Comput. Biol.*,8**(11)**, 2012.
14. T. L. Allinger, W. Herzog, M. Epstein, *J. Biomech.*, 29**(9)**, 1996.
15. G. I. Zahalak, *J. Biomech.*, 30**(11-12)**, 1997.
16. S. Givli, *J. Theor. Biol.*, 264**(3)**, 2010.
17. I. Novak, L. Truskinovsky, *Math. Mech. Solids,* 20**(6)**, 2015.
18. P. B. Chase, J. M. Macpherson, T. L. Daniel, *Ann. Biomed. Eng.*,32**(11)**, 2004.

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Community-led planning in(action): the Case of Kingsland, Calgary

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Abstract

This article examines the impacts of the Kingsland Community Plan (KCP), a document prepared by a local neighbourhood group, in shaping the built environment of Kingsland, Calgary. The research methodology combines document analysis with Actor-Network Theory as a theoretical approach. Applications to 'rezone' land within the Kingsland community district, filed from the KCP's creation in October 2009 to December 2016, were analyzed for reference to and conformity with the goals and intent of the KCP. Overall the KCP has not been effective at directing land use change in Kingsland. However, the Plan has acted as an 'informal' intermediary, rendering visible the local neighbourhood group's influence and interests within the planning process. Given recent initiatives to formalize civil society participation in Calgary's planning system, this research may aid decision-makers in determining the appropriate role for neighbourhood groups.

Keywords: Calgary, Neighbourhood Groups, Participation, Community-led Planning, Land use

Introduction

Calgary's Community Associations (CA's) are volunteer-led neighbourhood groups with a degree of influence in the local planning system. The City of Calgary relies on these organizations to provide a 'broad, community perspective' on urban planning matters, allowing them to influence the city's evolving built form [1]. CA's liaise with developers, are circulated by The City for comment on individual planning applications, and advocate (often successfully) for or against change in their neighbourhoods' physical environments.

Over the past several decades Community Associations have become steadily more involved in Calgary's planning system, in line with the ever-increasing emphasis being placed on public participation [2-5]. For example, one study of Calgary's planning process revealed that some local developers felt these groups were far more influential than themselves [6]. Despite this, very little research has been done on Community Associations' actual impacts on planning decisions [3,7-10]. Even the Federation of Calgary Communities, the umbrella organization representing Community Associations, tacitly admits the highly 'informal' and thus unregulated [11] role of these groups. In part due to this informality, The City of Calgary has recently initiated a review of Community Association inputs into the land use and development planning system, with the goal of developing a 'Community Representation Framework' [12]. To establish such a framework it is crucial to better understand how Community Associations currently impact planning outcomes. This research is positioned to serve this end.

Historically CA engagement in planning issues has been in reaction to large-scale private or public sector initiatives, and is often dismissed as "NIMBY-ism" [8,9,13]. In response, some CA's have taken their involvement one step further by producing pro-active and thorough documents that lay out visions for the future development of their neighbourhoods [14-17]. This article explores the materialities of these groups' influence on the planning process by focusing on a single Community Association-produced neighbourhood plan and its impacts.

In 2009, after being informed by the local planning department that an official Area Redevelopment Plan would not be prepared for Kingsland, the Kingsland Community Association created their own 'Kingsland Community Plan' [17]. The Plan was drafted by a committee of residents and addresses a variety of concerns including local parks, rezonings, and public realm concerns. The effects of the Kingsland Community Plan are traced by qualitatively analyzing applications to rezone land within Kingsland, filed from the Plan's creation in 2009 to 2016.

The objective of this research was to examine the materiality of public participation's impact on planning outcomes by analyzing a planning document produced by a neighbourhood group. Overall, the Kingsland Community Plan has negligible influence on land use decisions. However, the Plan does act as an informal intermediary, rendering visible the local Community Association's meagre influence in the land use planning process.

Background

Public participation and neighbourhood plans

Since the 1960's, in North America and around the world there has been growing recognition of public participation's importance within land use planning [2,5,18]. This stems both from normative concerns for democratic decision-making, as well as practical concerns for ensuring community support for planning outcomes. Writing in 1969 and capturing the zeitgeist of her time, Arnstein [19] famously proposed a ladder of participation, ranging from citizen control over program decision-making to various forms of non-participation, such as outright manipulation by authorities.

In Calgary, the 1970's represented a virtual 'golden age' of citizen participation in neighbourhood planning. During this decade residents of many inner-city communities such as Inglewood [9], Victoria Park [13], Hillhurst-Sunnyside [10], and Crescent Heights [8] demanded their voices be heard on community

planning issues. Most often this involved successfully defeating freeway expansion proposals and blanket rezonings. These local examples however, almost exclusively involve reaction against proposals, as opposed to setting forth proactive visions for future neighbourhood development.

In more recent years there have been many high-profile experiments with direct citizen control over planning processes, such as empowering non-expert residents to create proactive strategic planning documents to guide future neighbourhood change. Examples of this include the City of Seattle's neighbourhood plans, prepared by committees of interested citizens in the 1990's [20] and the United Kingdom's experience with plans produced by parish councils (the lowest level of government in that country, at the neighbourhood scale) during the same time period [21]. These plans, produced by non-expert residents, on the surface represent a high degree of citizen control over planning. Outside these well-documented and high-profile examples however, there is a wide gap in the literature on the impacts of these 'grassroots' plans, particularly in Canada.

Calgary's planning system

Very broadly, urban planning in Calgary (and in the province of Alberta) takes the form of policy planning and implementation planning [11]. In Calgary's case, policy planning includes the statutory Municipal Development Plan, Area Redevelopment Plans (ARPs; which guide change in existing communities), Area Structure Plans/Outline Plans (in new communities), as well as various non-statutory plans such as land use studies. These documents provide normative guidance when planning decisions are being made, either by planners or by City Council itself. Statutory plans (such as ARPs) are legally binding upon the municipality and land owners. When a proposed development does not meet the criteria of the local ARP, the plan must be amended before the proposal can be approved. Non-statutory planning documents provide local context and history, which may (or may not) be deemed relevant to planning decisions.

Calgary's Land Use Bylaw is at the core of implementation planning. The Bylaw defines 'land uses' (e.g. various types of multifamily housing, single detached housing, or commercial uses) and then groups these uses into Land Use Districts, which are then applied to every parcel of land within the municipality. Each Land Use District details what uses are permitted on any given parcel, and often includes other requirements, for example providing a certain number of parking stalls.

If someone wishes to change the Land Use District of their property, they must file an application with The City to do so. A planner analyzes the application, relevant plans and policies, gathers feedback from the local Community Association and any affected landowners, and compiles this information into a report alongside their recommendation to approve or deny. This report is then presented to the Calgary Planning Commission, which then recommends to City Council whether it believes the application should be approved. Before voting to approve or reject a rezoning, City Council holds a public hearing where any person may speak in favour or in opposition. Oftentimes councillors propose changes in response to opposition from community members.

Methods

The research methodology hinges on document analysis and 'close reading', informed by Actor-Network Theory as a general approach. The agendas of all City Council meetings between October 2009 and December 2016 were searched to identify applications to rezone land within the Kingsland community district. Each application includes a report containing the specifics of the land use change being requested, a site analysis, feedback from the public, a summary of applicable legislation and policies, and a rationale prepared by the applicant requesting the land use change; a draft amendment to the Land Use Bylaw; and finally public submissions related to the application. These documents, as well as proceedings of related public hearings and final

council decisions, were analyzed for reference to, and general conformity with, the Kingsland Community Plan.

Land use change was selected as an avenue for examining the effects of the Kingsland Community Plan for a several reasons. As noted above rezoning process generates a significant amount of publicly accessible documentation. This relatively complete record stands in opposition to what some observers have called the otherwise informal nature of planning processes in Calgary [22], which often render them opaque to the public.

Actor-Network Theory (ANT), despite its name, is a methodological approach that calls researchers to 'trace associations' between humans and non-humans [23], and emerged in the 1980's and 1990's in the context of Science and Technology Studies in particular the works of Bruno Latour. Put simply, ANT emphasizes the need to focus on the phenomena under study, as opposed to looking away from said phenomena towards larger organizing forces, for example societal discourses or economic factors such as profit incentives [24].

ANT assigns agency to both humans and non-humans, referred to as 'actants' as opposed to 'actors' to avoid anthropocentricity [23,25,26]. Here, agency is understood as the capacity for one actant to alter another. Actants come together to form complex networks bound together by heterogeneous associations [23]. ANT is interested in tracing these associations, and can do so through a variety of qualitative as well as quantitative methods [27]. ANT has been successfully used to examine the materialities of public participation processes generally, as well as the agency documents and representations of space such as consultant reports [28], low-carbon development guidelines [29], and maps [30] exert within spatial planning processes.

Results

From October 2009 to December 2016, 12 applications to rezone land within Kingsland were filed with The City of Calgary. The majority were to increase permitted density. Table 1 summarizes the details of these applications. Information such as file names, parcel addresses, and names of applicants are omitted for privacy reasons.

Almost all applications involve increasing allowable density of residential parcels of land, which in practice are requests that city council authorize taller developments and/or developments with greater lot coverage. As is noted above, it is often owners of R-C2-zoned parcels who are (with success) requesting land use changes. Despite this, the Kingsland Community Plan (p. 15) does not support rezoning R-C2 parcels for increased density. It appears that the Plan has had virtually no impact on land use change. However, it should be noted that where applications have been approved with amendments residents as well as Kingsland Community Association volunteers had spoken in opposition during their respective public hearings. In all cases these councillor-proposed amendments reduced density increases and/or added conditions to future development. Applications approved outright faced minimal or no opposition at their public hearings.

Discussion and Analysis

The Kingsland Community Plan takes up the bureaucratic "objectifying knowledge practices of documentation" [30, p. 35] as a strategy for enrolling actants into its actor-network. The Plan implements this strategy through highly selective citation and rhetorical arrangement. The Plan draws on the professional expertise of local urban planners: its original 'project chair' was and is currently a planner employed by the City of Calgary [31], it was prepared in consultation with the local planning department [17], and it increasingly viewed as 'legislation and policy' by local officials. In identifying itself as a 'non-statutory' document, a term usually reserved for a class of municipal policies, the Plan asserts that it reflects the community's collective goals for the future (ibid). Further, the political clout of the local councillor is enrolled in that he was explicitly sought out and engaged in the Plan's creation (ibid p. 2-3).

Table 1: Kingsland rezoning applications, 2009-2016

#	Initial Land Use District	Proposed Land Use District	KCP Reference	Status[3]
1	R-C2[1]	M-C2[2]	Yes (applicant submission, Community Association submission)	Approved
2	Direct Control	Direct Control (alter parking requirements)	No	Rejected
3	R-C2	M-CG	Yes (Community Association submission)	Approved with amendments
4	C-COR3	M-H2	Yes (Legislation and policy analysis)	Approved
5	R-C1	M-C1	Yes (Legislation and policy analysis, Community Association submission, applicant submission)	Approved with amendments
6	R-C1	R-C1s	Yes (Public engagement)	Approved
7	R-C2	M-C2	No	Approved with amendments
8	R-C1	R-C2	Yes (Legislation and policy analysis)	Approved
9	R-C2	M-CG	Yes (Legislation and policy analysis)	Approved
10	R-C2	M-CG	Yes (Legislation and policy analysis)	Rejected
11	R-C2	M-CG	Yes (Legislation and policy analysis)	Approved
12	M-H2	M-H2 (correct for clerical error)	No	Approved

Source: The City of Calgary [http://agendaminutes.calgary.ca]

[1] Land Use Districts abbreviated with the letter R denote low-density residential uses, for example single detached homes. The R-C1 Land Use District permits single detached dwellings only, while R-C2 permits single detached dwellings, as well as duplexes and secondary suites.

[2] Land Use Districts abbreviated with the letter M denote higher-density residential uses, for example apartment buildings. Land Use Districts in order from lower to higher densities: M-CG, M-C1, M-C2, M-H1, M-H2.

[3] In response to opposition by community members, city councillors sometimes will propose and vote on changes to rezoning applications.

As a result, the local councillor has both successfully and unsuccessfully introduced changes to rezoning applications, always with the intention to reduce or restrict density increases. In this way, the Plan speaks of the close ties between Calgary's Community Associations, urban planners, and city councillors.

Further, the Kingsland Community Plan attempts to draw on the authority of municipal plans and policies by enrolling them into its actor-network through strategically referencing and interpreting their dictates. The Plan argues that density increases should be directed towards the neighbourhood's periphery, and away from its core of single detached dwellings by citing the city council-approved Glenmore Land Use Study as well as the MacLeod Urban Corridor Study (ibid p. 15). (This however, is a misappropriation of these policy documents as they are intended to guide the City of Calgary's actions as a landowner and as the local authority responsible for roadways, not to regulate privately owned parcels of land.) Further, the minutes of the Kingsland Community Plan Steering Committee, appended to the text of the Plan, discuss the new (in 2009) Municipal Development Plan and opportunities to enrol this document and thus draw on its legitimacy (ibid p. 30-35). Interestingly, the Plan lumps together private actors involved in built environment change (for example real estate agents, landowners, development companies, contractors, etc.) together under the broad

category of 'developers'.

By enrolling other development system actors, the KCP, without much success however, attempts to position itself as a network intermediary and thereby define relationships between actants. Similar to other analyses of document agency [28,29] in urban development processes, absolute statements and 'policy language' is invoked as means to this end:

> *A community traffic study shall be completed by the City of Calgary prior to any major redevelopment projects occurring in Kingsland to ensure the intersections at the periphery of Kingsland can accommodate the additional traffic due to redevelopment. (p. 5; emphasis added)*
>
> *Developers considering redevelopment or densification shall consult this Plan for guidance and discuss their plans with the Planning Committee in advance of submitting an application to the City of Calgary. (p. 9-10; emphasis added)*

The Plan is almost always ignored by City Councillors, who possess final authority to approve or deny rezoning requests. At a recent public hearing for example, one Kingsland resident pleaded with councillors to listen to the KCP's dictates. Council members ignored this plea, and immediately moved on to other matters. Ultimately, rezoning applications are most often approved regardless of the Kingsland Community Plan, barring minor changes in response to individual presentations in opposition.

While the Plan is generally unsuccessful at defining relationships between land development actants, it effectively renders visible the limited influence of the Kingsland Community Association in directing land use change at the neighbourhood scale. Until very recently, the 'informal' [11] role of Community Associations has only existed as administrative convention [1,7]. In our case, the limitations of this influence become strikingly visible by tracing the KCP's movement through individual rezoning applications. This influence takes the form of some minor changes to rezoning applications from time to time, for example through placing additional conditions on future development. Though cited in planning reports, invoked by residents at public hearings, occasionally referenced during council meetings, and at times discussed by applicants in their submissions, congruence with the KCP is almost never a deciding factor when it comes to evaluating land use change in the neighbourhood of Kingsland.

Conclusion

The Kingsland Community Plan attempts to enrol developers, municipal officials, and city councillors to define their mutual responsibilities and relationships, and thereby direct land use change. The Plan works towards this end by drawing on official planning documents, and through the explicit involvement of municipal planners and the local councillor in its 'birth'.

The above analysis of rezoning applications filed from 2009 to 2017 reveals that decision-makers do not consider adherence to the Plan as crucial, or even necessary. Thus, the Plan is ultimately not successful in fulfilling its stated ends. Despite this lack of success however, as measured by its relative inability to direct change, the KCP renders visible the vaguely influential (but in no way determinative) role of the local Community Association within Calgary's planning system. These insights into the current realities of public participation in formal processes of land use change may prove useful to local policy-makers in developing Calgary's so-called "Community Representation Framework", as well as in larger discussions on the role of citizen engagement in planning generally.

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References

1. The City of Calgary, "Roles of Community Association, neighbours, and Ward Councillor". Calgary, 2016.
2. M. Fagence, *Citizen Participation in the Planning Process*. Pergamon Press, Oxford, 1977.
3. I. Townshend, PhD dissertation, University of Calgary, 2009.
4. The City of Calgary, "Public Participation in the Planning Process". Calgary, 1993.
5. M. Hickley, MA thesis, University of Calgary, 2003.
6. D. Rice, MA thesis, University of Calgary, 2000.
7. K. Peterson, PhD dissertation, University of Calgary, 2013.
8. D. Stamm, MA thesis, University of Calgary, 1979.
9. P. Dixon, MA thesis, University of Calgary, 1972.
10. J. Husband, MA thesis, University of Calgary, 1977.
11. Federation of Calgary Communities, "The Community Guide to the Planning Process". Calgary, 2014.
12. The City of Calgary, "Community Representation Framework". Calgary, 2016.
13. H. Hiller H, D. Moylan, *Can. J. Urban Res*. **8**(1), 1999.
14. Ramsay Community Association, "Ramsay Sustainable Neighbourhood Action Plan". Calgary, 2013.
15. Inglewood Community Association, "Inglewood Design Initiative". Calgary, 2011.
16. The City of Calgary, "South Shaganappi Communities Area Plan". Calgary, 2011.
17. Kingsland Community Association, "Kingsland Community Plan". Calgary, 2009.
18. M.B. Lane, *Aust. Geogr*. **36**(3), 2005.
19. S.R. Arnstein, *J. Am. Inst. Plann*. **35**(4), 1969.
20. C. Sirianni, *J. Am. Plan. Assoc*. **73**(4), 2007.
21. N. Gallent, S. Robinson, *Neighbourhood Planning: Communities, Networks and Governance*. The Policy Press, Bristol, 2012.
22. N. Kuzmak, L. Muller, *Can. J. Urban Res*. **19**(2), 2010.
23. B. Latour, *Reassembling the Social: An Introduction to Actor-Network-Theory*. Oxford Univ. Press, Oxford, 2005.
24. B. MacMillan, MA thesis, Carlton University. 2009.
25. A. Smart, J. Smart, *Posthumanism: Anthropological Insights,* forthcoming.
26. K. Ruming, *Aust Geogr*. **40**(4), 2009.
27. D. Cowan, K. Morgan K, M. Mcdermont. *Hous. Stud.* **24**(3) 2008.
28. R. Lippert, *Can. J. Law Soc.* **22**(2) 2007.
29. Y. Rydin, *Plan. Theory*. **12**(1) 2013.
30. M. Hull, *Government of Paper: The Materiality of Bureaucracy in Urban Pakistan*. Univ. of California Press, Los Angeles, 2012.
31. Federation of Calgary Communities, "The Case for Community-Led Planning. Calgary". Calgary, 2012.

JURA
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Enhancing the Efficacy of Human Pancreatic Islet Dissociation

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Keywords: pancreatic islet; dissociation protocol; type 1 diabetes; islet transplantation; pseudo-islet; AggreWell

Introduction

Type 1 diabetes is an autoimmune disease characterized by the destruction of insulin-producing pancreatic beta cells. This condition reduces life expectancy by up to fifteen years and leads to significant health care expenses [1]. In 2015, the global estimates of the number of children living with type 1 diabetes exceeded half a million, and some 86,000 new cases are estimated to occur annually [2].

Currently, a promising treatment for type 1 diabetes is pancreatic islet transplantation. The loss of rich vascular network by native islets during isolation from donors, however, results in the low survival of large islets post-transplantation. A promising proposal is to disperse native islets into single-cell suspensions and aggregate them into smaller, uniform “pseudo-islets”. The recovery of cell mass after dissociation still remains a major challenge that limits the yield and efficacy of pseudo-islet aggregations [3]. As such, the objective of this study is to determine the optimal dissociation protocol for the formation of human pseudo-islets. We hypothesized that by enhancing the dissociation protocol for native human islets, more cells can be recovered and they will form pseudo-islets that function more effectively in terms of insulin secretion and survivability.

Methods

A literature review was conducted to determine the reagents previously used to dissociate native islets. Using the search engine PubMed, we searched the MEDLINE database (1980 to May 2016) to determine the dissociation reagents, concentrations, and time outlined in literature. All trials outlining the methods used to dissociate native rat, mouse, hamster, or human islets were included.

Each of the 3 native post-mortem human islet samples (1 female and 2 male; ages 41, 56, and 75; all negative for HIV, HCV, HBV testing; isolated and supplied by Clinical Islet Laboratory at University of Alberta) were centrifuged at 120 x g for 1 minute in 50 mL centrifuge tubes and after removing the supernatant, resuspended in CMRL-1066 media (containing amino acids, vitamins, and other components). The samples were further divided into several tubes and centrifuged at 120 x g for 1 minute. Two thousand islet equivalents (islets with a diameter of 150 µm) per 1 mL of dissociation reagents (Accutase, Accumax, TrypLE Express, 0.05% Trypsin in phosphate-buffered saline (PBS), 0.05% Trypsin with 0.02% Versene (EDTA) in PBS, and Dispase in PBS ranging from 2 – 5 U/mL) were added with 0.0015% DNase into each of the tubes. Accumax contains the same proteolytic and collagenolytic enzymes as Accutase, but is three times more concentrated. Trypsin is a pancreatic serine protease, while TrypLE Express is a recombinant enzyme. Dispase contains neutral protease from *Bacillus polymyxa*. During the dissociation period, tubes with Accutase or Accumax were left at room temperature due to their sensitivity to heat while the rest of the tubes were put into a 37 °C shaking water bath to speed up the dissociation process. Subsequently, the cells were mechanically dissociated into single-cell suspensions by trituration. After 11-15 minutes, the tubes were topped up with CMRL media to 5 mL in order to stop the dissociation process.

The cells were centrifuged at 280 x g for 1 minute and resuspended in 5 mL of CMRL. Samples were collected from the tubes for cell counting (pre-filtering viability/ cell counts), and the remaining were filtered using cell strainers to obtain uniform cell suspensions. After filtration, cell counting samples were obtained again (post-filtering viability/ cell counts). Samples were analyzed using Trypan Blue and PicoGreen DNA assay to quantify cell loss during islet dispersion and filtration. The cell suspensions were added into 24-well AggreWell plates with CMRL in them and centrifuged at 200 x g for 5 minutes to form smaller, uniform pseudo-islets. The pseudo-islets were cultured in microwells in a cell culture incubator (37 °C, 5% carbon dioxide) up to 5 days (5 day cell viability/ cell counts). During the culture period, samples for cell counting were collected and assessed using PicoGreen DNA assay while the metabolic activity of pseudo-islets was assessed using Alamar Blue assay. Statistical analysis were performed with one-way ANOVA.

Results

Twenty studies met the inclusion criteria, from which we identified the dissociation reagents, concentrations, and time previously used to dissociate native islets [3-22]. These studies employed Trypsin, TrypLE, Accutase, Dispase, and Papain to dissociate native islets with Trypsin being the most common. Dissociation times ranged from 3 to 15 minutes.
In our experiments comparing the dissociation reagents, TrypLE showed the highest percentage of recovered viable cells after filtration (85 ± 43), followed by Accumax (56 ± 22), Trypsin with EDTA (49 ± 5), Accutase (25 ± 2), Dispase 5 U/mL (11), and Dispase 3 U/mL (8). Cell survival during the culture period was found to vary between the trials which may be due to the inherent differences between donor materials (Accumax: 65 ± 19%, Trypsin with EDTA: 64 ± 31%, TrypLE: 57 ± 8%, Accutase: 48%, Dispase 3 U/mL: 59%, Dispase 5 U/mL: 57%).

Overall, TrypLE ranked the highest in terms of the recovery coefficient, followed by Accumax and Trypsin with EDTA (Table 1). The recovery coefficient takes total cells present post-filtration, % viable cells in suspension, and cells remaining post-culture into consideration. Metabolic activity per cell remaining was not

included as the implications are currently unclear.

Table 1 shows the recovery coefficients ± SD, assessed using total number of cells recovered, percentage of viable cells in suspensions, and cell survival post-culture, with equation 1 representing how this was calculated.

Equation 1: *Recovery Coefficient = Total Number of Cells Normalized x % Viable Cells x % Cells Remaining Post-Culture

Table 1. *Ranking of the dissociation reagents.*

	Recovery Coefficient*
Accutase n=1	12.98
Accumax n=2	30.87 ± 8.84
TrypLE n=2	32.80 ± 5.18
Trypsin w/ EDTA n=2	27.73 ± 13.96
Dispase, 3 U/mL n=1	4.83
Dispase, 5 U/mL n=1	6.13

Discussion & Conclusion

Due to the limited supply of donor islets, only 3 trials with different native islet samples were conducted during the study period. In the future, trials will be replicated to increase the reliability of the study. To determine the optimal timing for TrypLE and Accumax, the dissociation times of these most promising dissociation reagents will also be varied. Results from the study are promising and further investigations will allow the results to become applicable to clinical trials, which can directly help increase the number of treatable patients from the limited supply of donor islets.

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References

1. Canadian Diabetes Association, "An economic tsunami, the cost of diabetes in Canada." Canadian Diabetes Association, Toronto, ON, 2009.
2. International Diabetes Federation, in *IDF diabetes atlas*. International Diabetes Federation, Brussels, ed. 7, 2015.
3. H. Callewaert, et al. *Cell Transplant.* **16**(5), 2007.
4. P. Halban, et al. *Endocrinology.* **111**(1), 1982.
5. P. Halban, S. Powers, K. George, S. Bonner-Weir, *Diabetes.* **36**(7), 1987.
6. S. Matta, J. Wobken, F. Williams, G. Bauer, *Pancreas.* **9**(4), 1994.
7. D. Caton, et al. *J Cell Sci.* **116**, 2003.
8. G. Cavallari, R. Zuellig, R. Lehmann, M. Weber, W. Moritz, *Transplant Proc.* **39**(6), 2007.
9. E. O'Sullivan, et al. *Diabetologia.* **53**(5), 2010.
10. J. Hwang, et al. *Macromol Res.* **20**(12), 2012.
11. R. Zuellig, et al. *J Tissue Eng Regen Med.* 2014. doi:10.1002/term.1891
12. A. Chowdhury, O. Dyachok, A. Tengholm, S. Sandler, P. Bergsten, *Diabetologia.* **56**(7), 2013.
13. C. Wittig, M. Laschke, C. Scheuer, M. Menger, *PLoS ONE.* **8**(7), 2013.
14. A. Zaldumbide, et al. *Mol Ther.* **21**(8), 2013.
15. J. Hilderink, et al. *J Cell Mol Med.* **19**(8), 2015.

16. N. Mullooly, W. Vernon, D. Smith, P. Newsholme, *Exp Physiol.* **99**(3), 2014.
17. F. Pagliuca, et al. *Cell.* **159**(2), 2014.
18. D. Penko, et al. *Islets.* **3**(3), 2011.
19. A. Wojtusciszyn, M. Armanet, P. Morel, T. Berney, D. Bosco, *Diabetologia.* **51**(10), 2008.
20. S. Tsukiyama, et al. *Tissue Eng.* **12**(1), 2006.
21. S. Tsukiyama, et al. *Artif Organs.* **32**(3), 2008.
22. K. Ramachandran, S. Williams, H. Huang, L. Novikova, L. Stehno-Bittel, *Tissue Eng Part A.* **19**(5-6), 2013.

JURA
Journal of Undergraduate Research in Alberta • Volume 6• 2017

Examining the relationship between biomechanics and GMFCS level in children with cerebral palsy

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Nicole has completed her third year in Mechanical Engineering with a Biomedical Specialization at the University of Calgary. Picking a specific research interest is difficult for Nicole as all the research areas she has been exposed to have appealed to her. However, her summer research experience in biomechanics has strengthened her resolve to pursue research in the biomedical field and she ultimately hopes to become a professor someday.

Introduction

Cerebral palsy (CP) is a non-progressive lesion of the developing central nervous system that affects the development of posture and motor control [1]. Gait analysis is used clinically to assess differences in body function in patients with CP and to inform clinical decision making [2,3]. Classification of the severity of disability is commonly performed using the Gross Motor Function Classification System (GMFCS, www.canchild.ca) or classifications of the severity of gait abnormality (e.g. Gait Deviation Index [4]). The GMFCS categorizes patients based on their functional competence using five levels ranging from least severe (I) to most severe (V) gross motor disability. Given the heterogeneity of motor outcomes in children with CP, it is important to understand differences in body function across levels of disability. Biomechanical analysis provides a quantitative approach that may allow for patient-specific functional classifications [5] to support clinical decision-making and to assess the efficacy of therapy interventions [6]. The objective of this project is to develop novel strategies for determining clinically meaningful biomechanical patient clusters. The specific aim of this study was to determine the differences in gait biomechanics (kinematics and kinetics) for children diagnosed with hemiplegic or diplegic CP categorized as either GMFCS level I or II.

Methods

Gait biomechanics of 24 children with hemiplegic or diplegic CP were analyzed as part of a secondary data analysis approved by the local ethics committee. Participants were classified according to GMFCS: Level 1 (n=12) - 12.2±1.9 yrs, 1.54±0.07 m, 46.4±12.5 kg; Level 2 (n=12) - 13.6±1.6 yrs, 1.56±0.03 m, 47.8±10.5 kg. All data were collected as part of a clinical consult over the past seven years. All biomechanical data were collected using a 12 camera motion analysis system (Motion Analysis, USA) recording at 120 Hz and 4 force plates (OR6-6, AMTI, USA) recording at 1200 Hz. Small reflective markers were affixed to the skin of the lower and upper limbs of the participants using the Helen-Hayes markerset and participants walked at their preferred pace along a raised wooden walkway.

Raw marker data were processed using Evart (Motion Analysis, USA). All kinematics and kinetics calculations were performed using Visual 3D (C-Motion, USA) to determine local coordinate systems for each lower limb segment and define mass and inertial properties of the segments using the regression equations by Dempster [7]. Joint angle and moment data were computed for five steps of the left leg across all participants. Inclusion of the right leg was not feasible across all participants due to data limitations. All data were then normalized to stance phase from heel-strike to toe-off (101 data points). Joint moments were normalized to body mass.

Statistical analyses of kinematic and kinetic waveforms were conducted in MATLAB (MathWorks, USA) using statistical parametric mapping (SPM, spm1d.org). SPM computes a t-statistic at each time point of the waveform across groups. Thereafter, Random Field Theory is used to estimate a critical threshold above which group data may be assumed to be significantly different from one another. For this analysis alpha for the critical threshold was set to 5%. The advantage of this approach was that the entire waveform could be interrogated for group differences and differences could be identified with regards to the time period during the stance phase of walking. Further, differences in gait velocity were assessed using Student's t-test in SPSS (IBM, USA).

Results

In examining the biomechanics of the hip, knee and ankle joints, two significant differences in hip joint moments were identified with respect to GMFCS levels. GMFCS level I participants displayed significantly greater hip abductor ($p=0.002$, Figure 1) and hip internal rotation ($p=0.047$,) moments between 17-26% and 18-21% of stance phase respectively. No significant differences were observed for the knee or ankle kinetics. No significant differences in joint kinematics were observed for the hip, knee or ankle joints. Further, children with GMFCS Level I walked slightly but significantly faster than those with GMFCS Level II ($p=0.009$, level 1 1.1±0.1ms^{-1}, level 2 0.9±0.2 ms^{-1}).

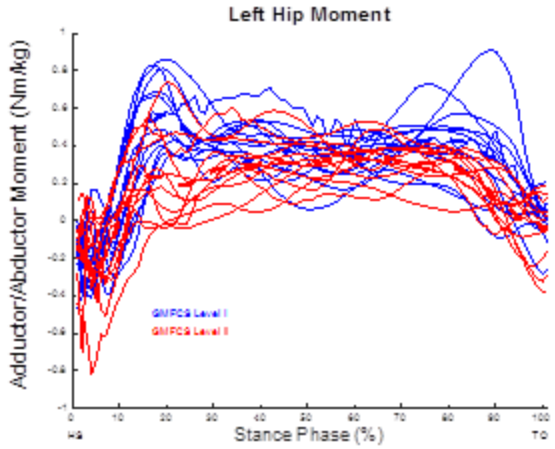

Figure 1: Left hip adductor/abductor moment. The x-axis represents the stance phase from heel strike (HS) to toe off (TO) and the y-axis is the moment in Nm/kg. The blue lines represent GMFCS Level I participants (12) and red are Level II (12). The thin lines indicate individual participants (the mean of five trials) and the thick dashed lines denote the mean of the corresponding GMFCS level.

Discussion & Conclusion

The results of this investigation demonstrated few between-group differences in gait biomechanics. The differences found at the hip abductor and internal rotation moments could be due to a number of contributing factors. They could be related to greater abductor muscle weakness in participants with lower functional competence, differences in walking speed, or due

to the effects of spasticity. Spasticity is commonly seen in children with CP and presents as increased muscle tone in response to stretch that results in resistance to movement [8]. However, the influence of spasticity on gait kinematics and kinetics for participants in this study was not determined.

Interestingly, most lower limb kinematic and kinetic measures were not significantly different with respect to GMFCS level. The primary role of the GMFCS is to predict gross motor function of children with CP with respect to their future motor function with an emphasis on sitting, walking and wheeled mobility [9]. Within this study, participants with GMFCS levels I and II displayed substantial heterogeneity with respect to the biomechanical strategies employed in the performance and control of walking. Consequent lack of distinct biomechanical patterns within GMFCS groups provide supporting evidence for a poor association between GMFCS level and subject-specific gait deviations. Confirmation of this lack of consistent biomechanical deviations within this specific population is important since all participants in this study were referred as part of a clinical consult, which could have led to unexpected results due to selection bias.

Implications

It is evident from these results that a delineation of body function in children with CP is not supported by an a priori grouping strategy using GMFCS. Indeed, a specific focus on assessing kinematic and kinetic data biomechanics using specific classification tools [e.g. 4] may be more appropriate, in line with current clinical practice [10].

Future Directions

Further research will be conducted to identify strategies for determining clusters in kinematic and kinetic data. These approaches will include unsupervised machine learning to determine optimal data clusters and supervised learning to identify appropriate criteria to classify new patients within clinically meaningful groups of body function. Sensitive and specific clustering may benefit clinical practice by providing unbiased assessment criteria and reducing the analysis burden on the clinician. Further, it may be instrumental in assessing the associations between biomechanical outcomes and clinical measures of functional capacity (e.g. spasticity and fatigue).

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References

1. Palisano et al. *DMCN.* 39:214-223, 1997.
2. Lofterod et al. *Dev Med Child Neurol*. 50: 503–09, 2008.
3. Wren et al. *Gait Posture*. 34: 364–69, 2011.
4. Schwartz and Rozumalski *Gait Posture*. 28(3):351-7, 2008.
5. Dziuba et al. *Acta Bioeng Biomech.* Vol. 15, No. 2, 2013.
6. Gage J.R. *Clin Orthop Relat Res.* 288:126-134, 1993.
7. Robertson et al. *J Sports Sci Med. 2nd edition*. 2014
8. van den Noort et al. *Arch Phys Med Rehabil*.91(4): 615-23, 2010.
9. Wood and Rosenbaum. *Dev Med Child Neurol.* 42: 292-96, 2000.
10. Nieuwenhuys et al. *Dev Med & Child Neurol*. 306-313, 2015.

JURA
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A Review of the Effect of Nurses' Use of Smartphone to Improve Patient Care

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Yoon is a 2017 graduate of University of Calgary's Bachelor of Nursing program who is currently working as a Registered Nurse with the Alberta Health Services. In the past, he has obtained BSc-biology degree at the University of British Columbia. As a nursing student, Yoon was curious about how the use of new technology by nurses, such as Smartphones, can influence patient care. Furthermore, he has interests in discovering new innovative ways for nurses to integrate new technology to effectively deliver care to their patients. He hopes to continue his endeavors in this field while working as an RN under AHS.

Abstract

Nurses in the acute-care setting use touchscreen smartphones (eg. iPhones) to facilitate patient care. However, on-duty nurses also use smartphones to access social media, text, and shop online. The overall benefit of nurses' use of smartphones to patient care is unclear. We conducted a systematic review to examine the use of smartphones by acute-care nurses and how that influences patient care. We searched Embase, MEDLINE, PsycINFO, CINAHL, and PubMed databases using the keywords "smartphone," "nurse," "patient care" and "quality of care" to identify articles focusing on smartphone use by nurses in acute care setting. Only 274 articles were initially identified. Fourteen articles remained after applying inclusion criteria such as nurses in acute care setting, written in English, and excluding those addressing the use of smartphones by non-nurses. We identified six themes encompassing advantages and disadvantages of smartphone use by nurses in the acute care setting. Theme 1: enhanced interprofessional communication. Theme 2: easy and quick access to clinical information (e.g. medications). Theme 3: improved time-management. Theme 4: reduction of work stress. Disadvantages included Theme 5: distraction from work, and Theme 6: the appearance of unprofessionalism. Smartphone use by nurses in the acute care setting impacts how they provide daily care to their patients. Benefits of smartphone use include improved patient safety, more efficient communication between healthcare providers, and better time-management. Disadvantages found involved distraction of nurses at work and the perceived appearance of unprofessionalism. We believe there is an unmeasured risk of smartphones as potential vectors of infection. We support the use of smartphones in a limited manner to aid their work performance but recommend that education is necessary for the appropriate use of smartphones to mitigate risks such as infection, distraction, and accountability of personal use.

Keywords: Nurse, Smartphone, Patient care, Patient outcome, Quality of care.

Introduction

As touchscreen smartphones have become more popularized in the general public since the introduction of Apple's iPhone™ less than a decade ago, there has also been a more spontaneous use of smartphones by bedside nurses in acute care settings. However, there does not seem to be a clear consensus as to whether or not nurses in acute care facilities should use smartphones during their clinical practice. Some nurses have discouraged the use of smartphones due to the risk of compromising patient privacy, distracting the nurse, and the appearance of unprofessionalism [1]. However, other nurses believe that smartphones can be utilized to quickly search for information relevant to their practice (e.g. drug information), communicate more efficiently with others in the healthcare team, and facilitate safe clinical decisions at the point of care [2,3]. As such, it became apparent that there were risks and benefits associated with nurses using smartphones within the acute care setting. However, it is unclear if there is an overall benefit concerning the provision of better care to patients. We conducted a systematic review of current evidence to examine how smartphone use can influence nurses providing patient care, and also to determine how the smartphones technology can be best integrated by nurses to improve their performance in patient care.

Methods

In order to gain insight regarding how nurses' smartphone use can impact patient care, we searched CINAHL, PubMed, Embase, MEDLINE, PsycINFO database using a combination of the following keywords: "smartphone," "nurse," "patient care," and "quality of care." Based on this search, 274 articles were initially identified across all databases and from this, we removed 46 duplicate queries. We excluded articles that focused on patients using information from smartphone apps to better manage their disease and nurses encouraging patients to use their smartphones as part of their care. We also excluded articles that involved non-nurses such as physicians using smartphones for their practice and articles that were irrelevant to nurses using smartphones within the acute care clinical context. From this initial screening process, we were able to eliminate 190 articles, leaving 38. We then narrowed the selection criteria to studies that focused on bedside nurses using smartphones and studies about how the nurses' smartphone use impacted practice, resulting in selected ten articles (Fig 1) [4]. Using similar methods above and Google Scholar database, we identified four additional articles to include in our review. We examined the fourteen articles and focused on the identification of key themes regarding how smartphone use could impact the delivery of care by acute care nurses.

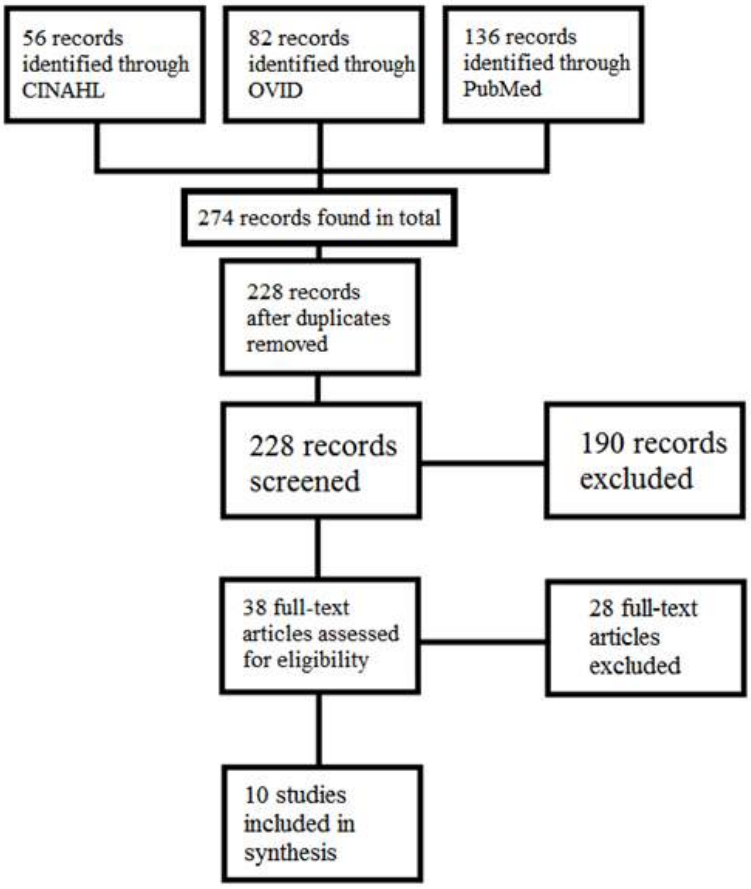

Figure 1: PRISMA diagram illustrating how articles were excluded and included for the systematic review. Embase, Medline, and PsycINFO were searched through OVID.

Results

We identified six major themes regarding how smartphones can impact nursing practice: 1)

Communication, 2) information access at the point of care, 3) time management, 4) stress relief, 5) distraction, and 6) the appearance of unprofessionalism (Fig 2).

Communication

Nurses experienced improved communication when they used smartphones to communicate with others on the healthcare team compared to using traditional methods of communication, such as pagers. In one study, nurses were able to receive a quicker response from other healthcare providers (HCPs) (p = 0.001) and also experience fewer interruptions to patient care (p = 0.002) when 35 nurses used smartphones to communicate with healthcare providers (HCP) [5]. In other studies, nurses believed that smartphone use resulted in better communication and collaboration amongst all healthcare professionals [6,7]. Using the pager system, the nurses were only capable of one-way communication with physicians, however, using smartphones enabled nurses to engage in a two-way communication. Two-way communication enabled quicker communication of simple messages as nurses did not need to wait for return calls, which led to fewer interruptions from patient care. Using smartphones in this manner also had an added effect of ensuring accountability of practice between nurses and other HCPs as information that was sent and received could be stored [8]. The nurses reported that improved communication increased patient outcomes and satisfaction, but there were no measured patient outcomes [5,7]. However, some nurses, especially nurses from the older generation, did not experience enhanced communication as result of smartphone use. These nurses thought that communicating with doctors were easier with a pager, or that they did not know how to take full advantage of the assigned smartphones [6,7].

Information Access at the Point of Care

Nurses can access information related to patient care efficiently and quickly using smartphones. Bedside nurses used smartphones' mobile application feature to access clinical information such as medication parameters, patient education, and wound-care [7,9]. The nurses surveyed in other studies also reported that smartphones allowed ease of access to clinical information during their care of the patient. These nurses commonly sought clinical knowledge from formularies and textbooks via smartphone applications and web browsers on the smartphones [10,11]. Some nurses have used smartphones to inquire as well as share clinical expertise with their colleagues to support each other's practice [12]. Six nursing students using smartphones to search drug and other information found the device helpful to them in providing quick, safe, and confident care to their patients [13]. The student nurses claimed that patient care was easier and faster with smartphones, and the authors believed that having an appropriate resource available to students and boosting their confidence in the provision of care increased patient safety and satisfaction [13,14]. In a survey of student nurses and registered nurses, the respondents believed that smartphones were helpful in learning clinical information, which allowed them to provide safer and better quality of care, and thus, they wanted to be allowed to use smartphones while on duty [11]. In a different survey, British nurses who used smartphones at work reported that smartphone applications were easy to use, would increase patient safety, would be useful in patient care, and save time [10]. Although nurses have reported the advantage of integrating smartphone use in their clinical practice, the specific patient outcome has not been determined nor measured.

Time management

Nurses can improve time efficiency using smartphones as part of their practice. In one study, nurses in a 26-bed medical unit were able to conserve a total of 160 minutes within a 12-hour shift when they used smartphones instead of pagers. The nurses were able to save time as there was less need for nurses to physically reach the landline phone to return the call as well as having

less interruption to patient care. And having fewer interruptions, the nurses reported enhanced time efficiency and workflow [5]. Nurses in China who used smartphones to receive call-bell requests from their patients were able to respond quicker than those who relied on the Public Announcement system (6 seconds with smartphone vs. 3.8 minutes with PA system, $p < 0.001$). Furthermore, the nurse could communicate with the patient and respond directly rather than visit and inquire why the patient called [15]. The prompt response time to the call-bell request could also reduce the occurrence of adverse events such as falls. This also means the nurses would have to spend less time addressing the adverse events that had occurred [16]. In another study, 29 nurses surveyed felt that smartphones led to fewer interruptions during patient care and more time to care for their patients. Some of these nurses stated that this has resulted in better patient outcome and satisfaction [6].

Stress relief

Smartphone use by nurses for personal non-work reasons may provide some degree of stress relief. Over three quarters (78%) of 825 nurses reported using personal smartphones while caring for patients for non-work related activities such as using social media, playing games, doing online shopping and keeping in touch with families and friends [17]. In a similar study, the authors found that 46% of 312 nursing students in South Korea reported using smartphones during clinical their practice connect and socialize with their families and friends. These social activities may have provided the students with social and emotional support [18]. Nurses have

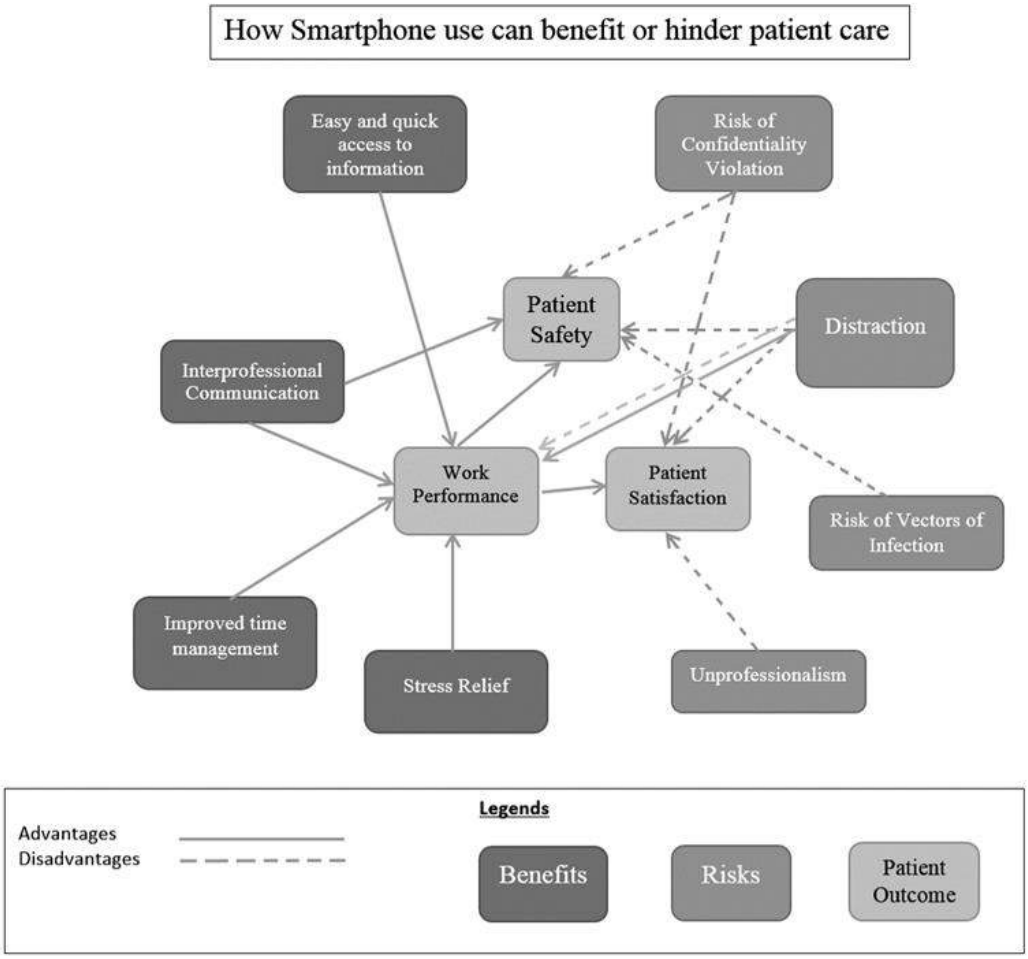

Figure 2: Concept map illustrating how each major themes related to nurse's smartphone use can impact nursing and patient outcomes.

also used smartphones to communicate with their colleagues to engage in non-work related conversations [12]. While there is speculation that nurses can use smartphones to help alleviate their stress during work-time, there is a lack of quantitative data on the magnitude of this stress reduction and if the benefits outweigh the risks.

Appearance of unprofessionalism

While some nurses deemed smartphones as useful tools for patient care, they were hesitant to use smartphones in front of patients and families, fearing they would appear unprofessional. It was reported that 31% of 111 registered nurses and 51% of 287 nursing students surveyed in Sweden felt that using smartphones in front of the patients and families would lead them to believe that the nurse may have insufficient clinical knowledge. They also felt that they were being perceived to be playing games or were using the smartphone for other non-work related purposes [11]. Although the nurses provided rationales of using smartphones to patients, they still felt that they appeared unprofessional and rude when accessing information or answering phone calls while providing care [6,7]. One nurse stated that using a smartphone would appear to patients as "doing your own personal stuff on work time". Furthermore, some nurses did not carry smartphones to patients' rooms as they were concerned they might be interrupted during care and appear unprofessional receiving incoming phone calls [7]. The nurses' perception towards using smartphones as appearing unprofessional would be a barrier to their adaptation to a new system of better communication modes and information source [6].

Distraction

When nurses and nursing students used smartphones during their practice, it has distracted them while caring for their patients. Based on a survey of nursing students in South Korea, student nurses stated they were sometimes distracted by smartphones and also witnessed other staff nurses being distracted by smartphones [18]. There is a potential hazard to patients when nurses are distracted by smartphones during patient care. However, there is uncertainty as to how much of an impact this distraction had on the patient outcome, Specifically, there was no quantitative association between nurses' distraction of smartphone use and its effect on patient care [17]. It is worth mentioning that when unit-issued smartphones were used by nurses and other healthcare staff in lieu pagers for work-related purposes, none of the 103 participants raised the issue that distraction was a significant factor during their work. Researchers also found that distractions were decreased during patient care when nurses used smartphone communication over pagers [5,6].

Discussion

Evidence to support nurses' use of smartphones within clinical practice was enhanced communication, ease of access to clinical information, and improved time management. Evidence against using smartphones include a potential source of distraction and displaying unprofessional appearance. Furthermore, we believe there are unmeasured risks of smartphones being vectors of nosocomial infection as well as being a cause of a potential breach of confidentiality. However, when appropriate strategies are implemented to mitigate these risks, we believe that the potential benefits of using smartphones can easily outweigh the risks associated with using these devices.

Nurses experienced improved communication when they used smartphones to communicate with others compared to using traditional methods of communication, such as pagers and landline phones. The improved communication was as a result of nurses having a more efficient tool for communication, being able to communicate with others quickly, and having to deal with fewer interruptions and delays associated with other methods of communications. By allowing nurses to engage in a two-way communication using smartphones, nurses can communicate with other HCPs quickly, use their smartphones to communicate with

others at any location in the unit, and easily access important contact information such as the patient's physician via the contact list on the phone [5,6,7]. Similarly, a direct two-way communication between the nurse and the patient allows greater depth of information to be shared between them, such as the reason for requesting assistance as well the level of urgency. This may, in turn, allow the nurses to prioritize their tasks better and can help reduce the occurrence or the severity of an adverse event such as falls [15].

Using smartphones as a tool to obtain clinical information at the point of care not only provides direct and instantaneous access to information but that this may also help reduce the barrier for nurses to seek pertinent clinical information as they need it. The reason for reduced barrier is because that when many bedside nurses require certain information, they would in most cases be required to physically find materials such as a computer or a book to access the information. As such, for many nurses with time constraint due to heavy workload, having a hand-held device to which they can access information instantly on the spot could be a critical determining factor as to whether or not they can integrate relevant clinical information, such as medications, into their care [19]. This can potentially impact patient safety, and outcome as nurses can make a better-informed decision during their care. Furthermore, nurses can also use other features of smartphones such as a calculator, a notepad, and task-reminder functions to assist them in their day to day care of their patients. Thus, we believe that many of these features that are available on smartphones would have an additive effect in not only aiding the nurse in carrying out their day to day tasks but saving time and also promoting patient safety. Other prospective usages of smartphones may include using smartphones and their accessories as a tool to visually document the progression of wound healing as well on the spot electronic documentation of any pertinent nursing actions such as medication administration [21,22]. We believe this would be conducive to reducing medication errors as bed-side nurses would have the information at their point of care to verify the medication orders rather than simply relying on memories, which may be susceptible to errors from distractions they face during their care.

While there are benefits to nurses using smartphones during their care, smartphones can cause safety hazards to patient care when nurses are distracted from using them. When nurses were using their personal smartphones for non-work related purposes while caring for their patients, they were distracted from focusing their attention on caring for patients [17,18]. And although using smartphones to reduce work-related stress may have been beneficial, the magnitude stress reduction relative to possible hazards to patients caused by distraction is not clear [5,6]. Other risk associated with smartphone use includes the device being a potential vector for infectious disease as well as there being a chance of it being used to leak confidential patient information. So while there may appear to be real risks associated with nurses using smartphones, we believe that it is possible to mitigate some of these risks through various strategies. One of them may be to encourage nurses only use unit-issued smartphones for work-related reasons. While using smartphones for personal non-work related reasons caused distractions, nurses reported less distraction compared to using pagers when unit-issued smartphones were used solely for patient care [5,6]. We believe that this may be the case because when nurses use unit-issued smartphones, they most likely use the unit smartphones for work-related purposes rather than for personal use, hence leading to less distraction as well as patient confidentiality issues associated with non-work related use. As for other risks, frequently cleaning the device using antiseptic agents, and ensuring that access to the devices is secured and kept within the nursing unit will help mitigate the risks of infection and confidentiality, respectively. To effectively implement this, setting and enforcing these rules as well as periodic education on proper use of smartphones may ensure that the benefits of using smartphones to assist nurses in

their day to day care would outweigh the potential risk of using them.

With regards to barriers to implementing this plan, some healthcare organizations have policies that discourage the use of smartphones by healthcare staff during clinical setting. However, these policies mainly focus on staff using smartphones for personal non-work related reasons. The formation of these policies may have likely been as a result of healthcare staff bringing own smartphones to hospitals for their personal use after the device became popularized. It may have also been because that as smartphone technology, which became popularized less than a decade ago, is a relatively new phenomenon in the healthcare context, as such; there is lack of documented use compared to other technologies such as personal computers. Hence, while there is growing evidence with regards to benefits and risk of smartphone use within the clinical context by nurses, they are not as widespread and well-known as other technologies that have existed for some time. Another significant barrier to nurses using smartphones was the fear that they would appear unprofessional to patients as well as the probable perception of patients and families that the nurse may seem unprofessional while using smartphones in their line of duty [6]. We believe that given the lack of wide-spread adaptation of smartphone use into not only nursing care but also healthcare in general, it would be plausible to state that individual patients and families may perceive smartphone use as being for personal use only. However, if smartphones use in healthcare becomes more widespread than now, this may shift the perception of the public with regards to the role of smartphones in the healthcare setting. It is also worth noting that while many nurses, especially young nurses suggested that smartphones were better than the pagers, other nurses, especially older nurses preferred pagers over smartphones [6,10]. The difference of opinion between the generations could be because while younger nurses were already familiar with basic smartphone functionality from their day to day personal use, older nurses who were unfamiliar with this new technology may have faced challenges in integrating the device with their clinical care. Other barriers to smartphone use are financial costs associated with obtaining the phones, programming the phones for nurses to use, and linking the phones to existing computer systems at each unit [20].

Based on our systematic review, smartphones can assist nurses in their day to day care. However, there is a lack of research on direct measures of patient outcomes from nurses' smartphone use including, but not limited to, the number of adverse events (e.g. falls, medication errors), the effectiveness of patient education and overall patient satisfaction. Further research may be needed on this to help clarify if smartphone use may significant benefit patients. However, if nurses are able to manage their time as well as better coordinate their day to day tasks using smartphones, this can also benefit patients. Presently, nurses in various units are restricted from using smartphones during work-time due to reasons such as perceived risk of distraction and unprofessional appearance. But based on our systematic review, we believe that there may be overall benefits to nurses' clinical performance when they are permitted to use unit-issued smartphones for work-related purposes. However further studies may be needed to verify if the advantages of using smartphones outweigh the risks for patients. While there are nurses who opposed smartphone use in the clinical setting, there are also nurses who supported its use. As such, we believe that nurses should be given the opportunity to decide for themselves whether or not they should utilize smartphones to facilitate their clinical practice.

Conclusion

Based on our systematic review, we would recommend smartphone use by acute-care nurses under specific conditions, such as using unit-issued smartphones after providing appropriate education as well as having usage rules to nurses who are accountable for their practice. While this tentative recommendation may be beneficial in promoting nursing practice,

we believe that further research can expand our understanding of the extent of positive and negative impact on patient care, as few research papers directly measured any quantifiable change to the patient outcome when smartphone uses were implemented. The use of smartphones by nurses is a relatively new phenomenon, and there may be in the near future, newer innovative approaches that nurses can utilize using this tool to enhance further how they deliver care to their patients.

References

1. P. S. Gill, A. Kamath,, *Risk Mag Healthc Policy*. **5**(1), 2012.
2. C.D. Parker. *Am nurse today*. **9**(11), 2014.
3. C.L. Ventola, *P T.* **39**(5), 2014.
4. 4.D. Moher et al. *Ann. Intern. Med.* **151**(4), 2009.
5. M.L. Whitelow et al. *Comput Inform Nurs..* **32**(7), 2014.
6. A. Nagler et al. *Tech Learn Med.* **26**(3), 2014.
7. M. Farrell. *JMIR Mhealth Uhealth.* **4**(2), 2016.
8. R. Wu et al. *J Hosp Med.* **10**(2), 2015.
9. W.R. Bischoff, R.H. Hinojosa. *Comput Inform Nurs.* **31**(11), 2013.
10. S. Moore, D. Jayewardene. *J Nurs Manag*. **21**(4), 2014.
11. P. Johansson, G. Petersson, B.I. Saveman, G. Nilsson. *Health Informatics J.* **20**(3), 2014.
12. M. Koivunen, A. Nieme, M. Hupli. *J Adv Nurs*, **71**(3), 2014.
13. R.A. Wittmann-Price, L.D Kennedy, C. Godwin. *J Nurs Educ.* **51**(11), 2012.
14. S. Izumi, J.G. Baggs, K.A. Knafl. *Res Nurs Health.* **33**(4), 2010.
15. S.T. Chuang et al. *Telemed J E Health*, **21**(2), 2015.
16. R. Digby, M. Bloomer, T. Howard. *Nurs Older People*, **23**(6), 2011.
17. D.L, McBride, S.A. Levasseur, D. Li. *JMIR Mhealth Uhealth,* **13**(1), 2015.
18. S. Cho, E. Lee. *Nurs Educ Today*, **40**(1), 2016.
19. J. Jones, K. Schilling, D. Pesut. *Open Nurs J* **5**(1), 2011.
20. F. Ehrler et al. *JMIR Mhealth Uhealth*, **1**(1), 2013.
21. G. Aldaz et al. *PLoS One*, **10**(4), 2015.
22. L. Wang et al. *IEEE Trans Biomed Eng.* **62**(2), 2015.

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A Critical Look at Food Security in Social Work: Applying the Socio-ecological Lens

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Elisabeth Ragan is a 4th year BSW student at the University of Calgary. Her passion for nutrition developed early on and has carried throughout her academic and professional endeavor's. Her research interests focus on the impact of food security and nutrition on child and family development. Elisabeth is currently involved in a research study which examines the practical application of food security interventions in frontline social work. In future, she plans to continue her studies at the graduate level. She hopes to use her research to bring awareness to social work about the importance of food security in social development.

Abstract

One in six children under the age of 18 in Canada lives in a food insecure household. This is deeply concerning as the presence of food insecurity can disrupt developmental trajectories potentially impacting the lifespan of a child. However, when compared to other social problems such as housing or mental health, food security takes a backseat. Twenty-four years ago, a call to action was issued to social workers to make food security a priority within their practice. The literature demonstrates a slow but encouraging rise in the number of social workers heeding that call. This paper provides a critical analysis of 21 articles investigating social work and food security interventions. The articles were published in peer-reviewed, academic journals between 1993 and 2016. The socio-ecological model was used to guide the review of the articles to help extrapolate how social workers can address food security at the MIC, MES, EXO, MAC and CHR level of practice. Forty-four interventions were identified. Most of the interventions considered the EXO and MAC, highlighting the importance of building strong communities and implementing policies for "food justice". The results also indicate that front-line social workers are well suited for food security interventions, but comprehensive research on how MIC, MES and CHR level strategies are best executed would help bring them to fruition. Furthermore, implementing food security into social work curriculum and becoming food conscious themselves was highly recommended.

Keywords: Food security (having access to sufficient, safe and nutritious food that meets dietary needs and food preferences for an active and healthy life); Intervention (providing programs and resource to individuals and families to help them achieve greater health and well-being); Socioecological model (An approach which considers the intersectionality between individual, family, groups, and community when assessing for intervention).

Introduction

In 2014, a University of Toronto interdisciplinary research group monitoring food insecurity in Canada found twelve percent of households experienced a certain level of food insecurity over the past year, representing 3.2 million individuals [1]. Per their report, Household Food Insecurity in Canada, 2014 one in six children under the age of 18 in Canada lives in food insecure households [1]. Children in food insecure households have a higher risk for physical and behavioral deficiencies than children in households which are food secure. Household food insecurity (HFI) in Canada is a result of a lack of financial resources, and program and policy development. Finding workable solutions will help reduce social and health inequities perpetuated by food insecurity [2].

The socio-ecological model seeks to understand the intersectionality between multiple levels of society and is helpful when designing health interventions [3]. Bronfenbrenner's ecological model, introduced in the 1970s, conceptualizes the ecological environmental as five nested structures: the microsystem (MIC); the mesosystem (MES); the exosystem (EXO); the macrosystem (MAC); and the chronosystem (CHR) [4]. The MIC encompasses the pattern of activities, roles, and interpersonal relations in the immediate familial environment; the core of the MES are the interactions between two or more microsystems in which the developing person actively participates; the EXO looks to 'the linkages and processes taking place between two or more settings, at least one of which does not contain the developing person, but in which events occur that indirectly influence processes" (e.g. communities and organizations); the MAC includes overarching pattern of MAC, MES, and EXO, culture and subculture, and the underpinning beliefs, knowledge, lifestyles, customs, opportunities, barriers, and material resources; and lastly, the CHR focusses on the impact of change over time (e.g., changes in life course due to family structure, employment, location, coping mechanisms, or disease) [4]. The socio-ecological model has been used before in social work theory, research and intervention [5-7]. Two such previous discussions of social work and food security have also drawn on the socio-ecological perspective [8,9]. These articles, both of which are included in this analysis, focus on EXO and MAC in the context of community 'food justice' and promoting food justice as part of social work education.

Definition of Food Security and Household Food Insecurity

We use the current definition which state "food security exists when all people, at all times, have physical, social and economic access to sufficient, safe and nutritious food which meets their dietary needs and food preferences for an active and healthy life. HFI is the application of this concept to the family level, with individuals within households as the focus of concern"[10].

The physical, social and economic access to food security varies significantly between countries and between individuals living in those countries. The articles included in this review originated from western countries, therefore we employed a western definition of HFI to contextually reflect our findings. In Canada, HFI is defined as "the inadequate or insecure access to food due to financial constraints. HFI negatively impacts physical, mental, and social health, and costs our healthcare system considerably" [2]. This paper will use the terms "food security" and "food insecurity" to capture all situations, including HFI. We acknowledge that countries with low food security contain people with high food security, and countries with high food security contain people with low food security, and this points to a problem with distribution rather than a lack of food. However, the dynamics of inequality and inequity in global food distribution is beyond the scope of this discussion. The focus of this paper will be on food security in families with children and/or youth, and the role of social work.

Food security is necessary for healthy physical, mental and emotional development,

especially in children [11]. Food insecurity related physical complications include diarrhea and cough [12]; stunted growth, respiratory infections [13]; physical disabilities [14]; and anaemia [15]. Ironically, food insecurity has been found to be a factor in obesity [16]. Mental and emotional consequences include learning disabilities [14]; poor cognitive and emotional development [17]; poor academic and psychosocial development [18]; compromised language expression and understanding in children as young as 18 months [19]; repeating a grade and lower reading scores [18]; and problems with relationships, mood, and externalizing in grade five students [20].

Research has shown living in a food insecure home may be associated with disorganization and chaos [21,22]. Moreover, food insecurity is associated with maternal depression [23,24]; chronic illness; divorce [14]; and adult smokers in the family home [21]. Additionally, some parents may be aware of the impact that food insecurity has on their children, and become anxious and depressed as they desire to protect their children [18,25]. Food insecurity has been found to raise the level of stress in the home, and as stress increases so might the use of alcohol, cigarettes, and consumption of carbohydrates [26]. As individuals with food insecurity tend to require more medical intervention, the cost of health care also increases [27].

Social workers are well positioned to intervene in situations of food security, however, there are no guidelines stating what social workers could or should be doing. A cursory look at the social work literature reveals that food security is not as high on the priority list as other social problems, such as housing and mental health, and we feel this is a detriment to our profession and the individuals we are called to serve. This socio-ecological critique of the literature sheds light on what social workers can and must do.

Objectives

The primary objectives of this paper are:

1) To critically analyze the social work literature on multi-level food security intervention
2) To determine what social workers can and must do to enhance food security for families and communities

Method

This critical analysis involved selecting articles that discussed food security and the role of social work. Eight electronic databases were searched using search terms “food security”, “food insecurity,” and “social work”. Medline, Psycinfo, Social Service Abstract, Social Work Abstracts, PubMed, and SocIndex, SCOPUS, and CINAHL were the databases selected, as they have been used in similar literature reviews [see 28, 29]. We expanded the search by using “social work” and “nutrition”, which generated a large number of abstracts, however only three abstracts fit the criteria. Google was also used with no additional results. Finally, bibliographies of selected articles were reviewed by hand to capture any suitable articles not picked up by the electronic searches.

The preliminary search of the literature yielded 35 abstracts from 1993 to 2016. To address the research question specifically, the yield was further refined to include only those articles that met the inclusion criteria. We selected twenty-one articles, 15 opinion-based and six research-based. These articles were then analyzed to determine whether the intervention strategies discussed were MIC, MES, EXO, MAC or CHR strategies, or some combination thereof. Interrater reliability was established by having both authors independently reviewing the articles for selection and thematic analysis [30]. The authors then applied the socio-ecological framework to classify MIC, MES, EXO, MAC and CHR interventions and found agreement 90 per cent of the time.

Results

A shift in the number of publications over the past several years may signal an increase in awareness of food security among social workers or that food insecurity is growing (Fig. 1). Sixteen

articles were published in the U.S., two from Israel, and one each from Australia, Brazil, Canada, and New Zealand. Thus, mainly western social and political experiences are represented in this review. Forty-four social work interventions were identified in total (Table 1). Most articles included EXO and MAC interventions, 10 addressed MIC; six addressed MES; 14 addressed EXO; 19 addressed MAC; and three addressed CHR (Table 2).

Microsystems

MIC interventions include: conducting mental health assessments [31,32]; implementing family-based food assessments [32-36]; helping with meal plans and food budgets [37]; developing and distributing recipe books [31]; linking clients to services and programs [34,36,37]; assisting in filling out forms [33,36]; arranging transportation [33]; educating on nutrition and health [9,38] and empowering clients [9,32,37,39,40].

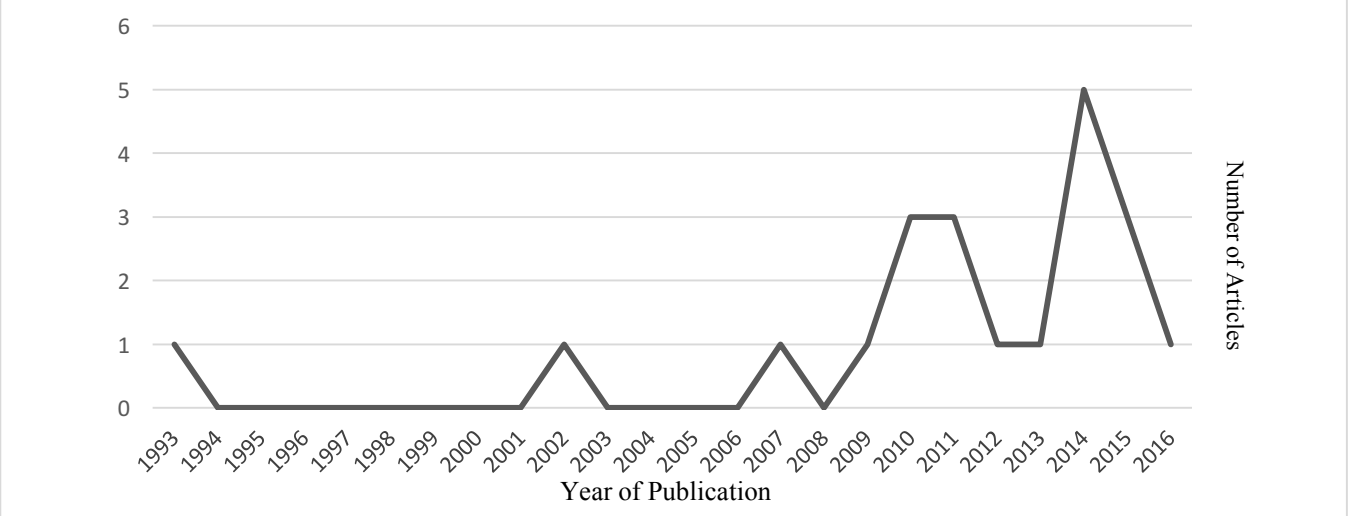

Figure 1: Number of articles published on food security and social work over the last 24 years.

Table 1: Typology matrix for mapping food-security intervention effort

System	Social Work Focus for Intervention
MIC	• Mental health assessment • Family-based food assessments • Meal planning and budgeting • Developing and distributing recipe books • Linking clients to services and programs • Assistance in filling out forms • Educating on nutrition and health • Empowering efforts for self-reliance • Arranging transportation
MES	• Empowering relationships • Broadening social support • Community gardens and community kitchens • Food sharing networks • School-based food distribution programs • School-based lunch programs and peer support

EXO	• Enhance opportunities and reduce barriers to CFS • Food rescue and redistribution • Small-scale farm promotion (i.e., urban and vertical farms) • Facilitating relationships between community members and ethnically diverse groups • Creating new innovative programs • Coalitions between consumers and producers • Community food and needs assessment • Participatory action research (PAR) • Partner with local dieticians and horticulturalists • Enhance personal nutrition consciousness • Access to grocery stores and healthy food options
MAC	• Implement food security policies at all levels of government • National food security movements • Advocacy roles • Welfare reform • Living wage policy • Tax incentives for neighbourhood farms • Methods to reduce costs of healthy food • International and feminist social work • Sustainable agriculture and food systems • Human rights and social justice • Commodification of food in a culture of convenience • Awareness of the commoditization and marketing of low-nutrient food • Gender and cultural influences • Food security and nutrition embedded in social work education • Collaborate with other health care professionals (i.e., dieticians) • Bridging the work done by governments, NGOs, and institutions
CHR	• Investing in current nutrition programs for the future • Re-grounding family food practices with healthy habits

Table 2: Final Articles Included in Critical Analysis

Authors and Date	**Title**	**Intervention**
Lombe, Nebbitt, Sinha, and Reynolds (2016)	Examining effects of food insecurity and food choices on health outcomes in households in poverty	MIC, EXO, MAC
Kaiser and Hermsen (2015)	Food acquisition strategies, food security, and health status among families with children using food pantries	MIC, EXO
Kaiser, Himmelheber, Miller, and Hayward (2015)	Cultivators of change: Food justice in social work education	MIC, MES, EXO, MAC
Kiehne and Mendoza (2015)	Migrant and seasonal farmworker food insecurity: Prevalence, impact, risk factors, and coping strategies	MES, EXO, MAC

Deepak (2014)	A postcolonial feminist social work perspective on global food insecurity	
Hirai (2014)	Food security and sustainability	MAC
Himmelheber (2014)	Examining the underlying values of food security programming: Implications for the social work profession	MIC, MES, EXO
Libal, Tomczak, Spath, and Harding (2014)	Hunger in a "land of plenty": A renewed call for social work action	EXO, MAC
Martinez and Kawam (2014)	A call to action for social workers: food insecurity and child health	MIC, MES, EXO, MAC, CHR
Besthorn (2013)	Vertical farming: social work and sustainable urban agriculture in an age of global food crises	EXO, MAC
Lessa and Rocha (2012)	Regrounding in infertile soil: Food insecurity in the lives of new immigrant women	EXO, MAC, CHR
Apaitia-Vague (2011)	Social work and food: A discussion	MIC, MES, EXO, MAC
Conway and Lassiter (2011)	Opportunity knocks: The intersection of community social work and food justice praxis	EXO, MAC
Kaiser (2011)	Food security: An ecological-social analysis to promote social development	MES, EXO, MAC
Juby and Meyer (2010)	Child nutrition policies and recommendations	MIC, MAC, CHR
Shor (2010a)	Interdisciplinary collaboration between social workers and dieticians in nutrition education programs for children-at-risk	EXO
Shor (2010b)	Children-at-risk from poor nutrition: Advancing the approach and practice of students of social work	MIC, MAC
Phillips (2009)	Food security and women's health: A feminist perspective for international social work	EXO, MAC
Jacobson (2007	Food matters: Community food assessments as a tool for change	EXO, MAC
Biggerstaff, Morris, and Nichols-Casebolt (2002)	Living on the edge: An examination of people attending food pantries and soup kitchens	MIC, MES, EXO, MAC
Whitaker (1993)	A charity/justice partnership for U.S. food security	EXO, MAC

Mesosystems

MES interventions include: empowering relationships [32]; broadening social support [8,32,41]; establishing community kitchens [8,37,40] and community gardens [8,37]; supporting food banks and soup kitchens [9,33,36,37,40]; promoting food sharing networks [31]; coordinating school-based food distribution programs [40]; and installing lunch programs and peer support at school [36,40].

Exosystems

EXO interventions include ways to enhance opportunity and reduce barriers to community food security (CFS) [8,9,31-33,36-38,40-45]. Specific interventions include: small-scale farm promotion [8] including neighbourhood vertical farms [45] and urban farms [9]; facilitating relationships between community members and ethnically-diverse groups [31,45,47]; creating new, innovative programs [36,44]; building coalitions between producers and consumers [8,45,47] promoting food rescue and redistribution [37], conducting community food and needs assessments [40,41,45] and participatory action research (PAR) [40]; becoming more food conscious themselves [32,41], collaborating with other food professionals such as dieticians [46] and horticulturalists [9]; and securing access to

grocery stores and healthy food options [43-45]

Macrosystems

MAC interventions include the development of food security policies [9,34,36,38-40,45,47,48]; national food security movements [49]; advocacy roles [33,38]; welfare reform [33]; living wage policy [40]; tax incentives for neighbourhood farms [45]; methods to supplement cost of healthy food [34]; international and feminist social work [39,42]; sustainable agriculture and food systems [8,39,43,45,47]; human rights [31,47,48]; social justice [48,49]; awareness of how low-nutrient food products are commoditized and marketed [43]; gender and cultural influences [31,38,39,42,44]; food security and nutrition embedded in social work education [9,35,41,48]; and bridging the work done by governments, NGOs, and institutions (i.e., places of worship and schools) [31].

Chronosystems: Interventions over time

CHR interventions include: investing in sustainable food security programs [34,36] and re-grounding family food practices to help shape lifelong eating habits [44].

Discussion

Twenty-one articles discussing food security and the role of social worker were analyzed for this review. Our findings suggest that social work, with its broad-based scope and focus on helping, is ideally suited for the promotion of food security. The socio-ecological model assists in contextualizing the different systems in which social workers can provide interventions. Gustafsson and Draper (2009) understood the importance of context in deciding what to eat:

> *Our food choices are not the result of irrational prejudices and of ignorance. But structured by a series of influences many of which are social in nature. We should consider people's lives and behaviors in the social contexts in which they are embedded and which influence them* [50].

MIC interventions focused on the inclusion of mental health and food assessments, provision of resources, and empowerment strategies. Findings suggest that social workers should not be hesitant to ask questions even when there are no obvious signs of deficiency [34] and determine whether food insecurity is the result of neglect or a lack of resources [32]. Factors that could lead to neglect, such as depression and social isolation, correlated with mothers who were food insecure [51]. Such situations should be approached with sensitivity, as parents may feel uneasy, thinking that food insecurity could be considered a sign of neglect [33]. Meal planning can be an effective strategy to reduce stress, moreover, a lack of family mealtime could indicate food insecurity [22]. Social workers should ask about family meals, and consider using assessment tools as part of the overall treatment plan. For example, the Socio-Economic Empowerment Assessment (SEEA), an ecological multi-systems perspective, can situate the family financial situation within their psychological, cultural, and life-experience contexts [51]. Another helpful tool is the Household Food Security Survey Model (HFSSM) that can be used with adults and a shorter version with children to determine the level of HFI [52]. Self-reliance is considered a more ethical and sustainable solution than emergency food provisions, and social workers can help guide their clients in practical ways of attaining this goal [37]. However, social workers need to be mindful of the structural barriers that continually challenge self-reliance, and that social workers can help by strengthening communities and advocating for government resources to enhance MIC and MES intervention. Emergency food services are vital for individuals, families, and communities when facing sudden economic or environmental hardship but should never been looked upon as long term solutions to systemic

problems.

MES interventions focused on the importance of healthy relationships and the availability of social food network's (i.e., community gardens, food exchanges, emergency provisions). Social networks can be a source of food (i.e., meal sharing) [32]. Low social cohesion, reduced trust between neighbours, and less interaction and support were linked to food insecurity [54]. Social workers can help enable their clients to create strong bonds between friends, neighbours, or co-workers. Schools can help social workers to stay informed [35], as a social worker may be referred to a student with behavioral challenges and find out they have not eaten [31]. In addition, by growing a garden at school, students can feel more connected to their food source [9].

EXO interventions revolved around building strong, self-sufficient communities with safe and accessible means of acquiring food. CFS is a situation in which "all community residents obtain a safe, culturally acceptable, nutritionally adequate diet through a sustainable food system that maximizes community self-reliance and social justice" [55]. Social workers can help build CFS using their skills of advocacy and collaboration to encourage the availability and affordability of healthy food options. A lack of access to nutritious food has been found to increase the consumption of fast food [44,45]. Research has shown that in urban centers in Canada, some poorer neighbourhoods are referred to as "food swamps", characterized by high access to sources of minimally nutritious food coupled with low access to nutritionally dense food, an important consideration in policy and program planning [56].

MAC interventions emphasized human rights and social justice, and the establishment of food security policies on access, availability and marketing strategies. School-based lunch programs are instrumental in alleviating problems associated with food insecurity [34]. Canada has been criticized for being the only G8 country without a national food program [57]. Canada's neoliberal ideology may explain both the lack of school-lunch program and national food policy. In Brazil, social workers observed how their neoliberal government was ignoring food insecurity in parts of the country and successfully advocated for a Food Security and Nutritional Policy [47]. Michael McCain, president and CEO of Maple Leaf Food, is hoping the new federal government will develop a Canadian food strategy and states "the challenge of food insecurity is one of the great issues of our time" [58]. Nutrition professor Valerie Tarasuk also considers government intervention as the solution to food insecurity but claims "What's hard is breaking the sound barrier with governments" [59]. Government supported food policies centered around human rights and social justice could address the inequality and inequity of food distribution.

Concerns regarding how gender and ethnicity impact food security were also noted. Research shows that women are left with the burden of feeding older family members [42] and the first to go hungry in times of food insecurity [31,42]. New immigrant women in Toronto reported racism, discrimination, and bullying as impacting their food choices [44]. In addition, the mothers stated how their children felt pressure from classmates to eat western food (i.e., fast food) and they no longer felt safe to eat food from their culture [44]. As recommended by Apaitia-Vague (2011) [31], Lessa & Rocha (2013) [44], and Lombe et al. (2016) [38] social workers should be mindful of different racial and ethnic needs, and the challenges in locating culturally appropriate food.

Finally, schools of social work should investigate ways in which food security can be included in the curriculum. The American Council on Social Work Education (ACSW) suggests four ways food security can be added to the curriculum: 1) teach the importance of nutrition and the right to food security; 2) advocate for vulnerable groups that experience discrimination against their right to nutritious food; 3) intervene

in ways that enhance food security in vulnerable communities, like community gardens; and 4) build coalitions with key stakeholders locally, nationally, and internationally [60]. Social workers may fail to ask questions about food simply because they do not consider it part of an assessment. Educators of social work educators should consider including information on the importance of food security in their coursework. Research has shown that health professionals with a certain level of nutritional competency are better equipped to help children at risk of malnutrition [61].

CHR interventions consider the cyclical nature of food insecurity. Food insecurity can promote a cycle of poverty [43] which can last for multiple generations. Women who experienced poverty and food insecurity in childhood often grow up with unhealthy relationship with food leading to obesity, which is further complicated by stresses such lone parenting, social isolation, and chronic disease [62]. Adverse childhood experiences of the mother were positively associated with current food insecurity [51]. Exposure to adversity in childhood, like food insecurity, can lead to depression and emotional problems that directly affect education and employment outcomes [51]. Juby and Meyer (2010) state "a country that cares about its future generations will legislate adequate nutrition for all children" [34].

Limitations

There are several limitations to this critical review. First, no external peer-reviews were conducted, which may call into question the interrater reliability [30]. Second, only five of the articles included results from a quantitative or qualitative research design. Sixteen of the articles were opinion based, written for and by social workers who favour the inclusion of food security in social work. The inclusion of disconfirming evidence enhances research validity [30] although we did not find any articles that disputed our findings. Third, most articles were from the U.S., as such, some of the interventions prescribed may not be effective in other countries. For example, urban farms, community gardens and vertical farming that rely on warm weather may not be an effective food security strategies in places with a shorter growing season, like northern Canada. Fourth, we used the terms food security, food insecurity, household food security, HFI, food justice and nutrition interchangeably throughout our analysis, and this may not have been the intention of the original authors.

Conclusion

In 1993, William Whitaker issued a call to action for social workers to include food security as part of their practice [49]. Whitaker recognized that social work had the capacity both in theory and practice to develop multi-level interventions to reduce food insecurity and the problems that result. Since that time there has been a slow but encouraging answer to that call seen especially in CFS and advancing food policy. More comprehensive research should focus on MIC, MES, and CHR assessment and intervention, detailing the ways in which front-line social workers can be helpful to families with children and/or youth facing food insecurity. Finally, the inclusion of food security in social work education can encourage new social workers to become food conscious themselves thus incorporating food security strategies into their personal and professional aspirations.

Significance and Application

This review has significant implications for practice and social work education. Front-line social workers whose clients are families with children and/or youth should conduct food and mental health assessments using measurement tools, like the Socio-Economic Empowerment Assessment and The Household Food Security Survey Model, to identify patterns of food insecurity in the home. Social workers should increase their knowledge of food security and be willing to discuss menu planning and meal

preparation with their clients. Further support in filling out forms, accessing the resources and transportation to purchase food may also be required.

Social workers should be knowledgeable of the risk factors of food insecurity. People who lack both economic and social resources are particularly vulnerable. Social workers can help clients enhance their food security by helping to create relationships within the community and secure income sources. Community gardens and food sharing networks should be promoted over the use of food banks. Collaborating with schools can help identify and provide support to children who are food insecure. Social workers should become involved in the development of school-based meal programs and food distribution systems, research, community needs assessments, creating innovative programs and evaluation strategies, linking with dieticians and horticulturalists that can offer professional support in their initiatives, and developing a personal food consciousness.

Social workers should lend their voice to groups that support food security policies like school-lunch or national food programs. Food security is foremost a human right that needs to be considered in all areas of practice. In addition, social workers should familiarize themselves with the ways gender and ethnicity can impact issues of food security. Finally, current and future social workers should come to understand the importance of food security in our developmental trajectory, especially that of children. The potential benefits to both our profession and society are immeasurable.

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References

1. V. Tarasuk, A. Mitchell, N. Dachner, "Household food insecurity in Canada, 2014." PROOF. Apr. 5, 2016. Last retrieved June 16, 2017. http://proof.utoronto.ca.
2. E. Power, "Individual and Household Food Insecurity in Canada: Position of Dieticians of Canada." Dieticians. 2015. Last retrieved June 16, 2017.
3. B. Haughton, *Fam Community Health.* **29**(1), 2006.
4. U. Bronfenbrenner, in *Readings on the Development of Children,* M. Gauvain and M. Cole, Eds. Freeman, New York, NY, , ed. 2, 1993, p.p. 37-43.
5. B. Berkman et. al, *Soc Sci Med.* **31**(1), 1990. http://dx.doi.org.ezproxy.lib.ucalgary.ca/10.1016/0277-9536(90)90005-D
6. C. Germain, *Soc Work Health Care.* **3**(1), 1977.
7. C. Meyer, in *Clinical Social Work in an Ecosystems Perspective*, C. Meyer Ed. Columbia University Press, New York, NY, 1983, p.p. 6-34.
8. M. Kaiser, *J Community Pract.* **19**(1), 2011.
9. M. Kaiser, S. Himmelheber, S. Miller, R. Hayward, *J Soc Work Educ*. **34**(5), 2015.
10. Food and Agriculture Organization of the United Nations (FAO). "Chapter 2: Food Security Concepts and Measurement." FAO. 2015. Last retrieved June 16, 2017. http://www.fao.org/docrep/005/y4671e/y4671e06.htm.
11. R. Rose-Jacobs et. al, *Pediatr.* **121**(1), 2008.
12. M. Reis. *Health Econ.* **21**, 2012.
13. M. Hackett, H. Meglar-Quinonez, M. Alverez, *Rev Panam Salud Public*. **25**(6), 2009.
14. E. Racine, K. Jemison, L. Huber, A. Arif, *Public Health Nutr.* **12**(9), 2008.
15. K. K. Schmeer, B. A. Piperata, *Matern Child Nutr.* **13**(2), 2016.
16. A. Metallonis-Katsaris, K. Must, J. Gorman, *Acad. Nutr. Diet.* **112**(12), 2012.
17. M. Chilton, D. Rose, *Am J Public Health*. **99**(7), 2009.

18. K. Alaimo, C. Olson, E. Frongillo, *Pediatr.* **44,** 2001.
19. K. Saha, F. Tofail, E. Frongillo, J. Hamadani, *Child Care Health Dev.* **36**(3), 2010.
20. S. Kirk et. al, *Public Health Nutr.* **18**(16), 2014.
21. M. Kursmark, M. Weitzman, *Curr Opin Clin Nutr Metab Care.* **12**(3), 2009.
22. B. Fiese, C. Gunderson, B. Koester, B. Jones, *Econ. Hum. Biol*. **5**(21), 2016.
23. P. Casey et. al, *Pediatr.* **113**(2), 2004.
24. M. Zaslow et. al, *Matern Child Health J.* **13**(1), 2009.
25. M. Knowles, J. Rabinowich, S. Ettinger de Cuba, D. Cutts, M. Chilton, *Matern Child Health J.* **20**, 2016.
26. J. Mikkonen, D. Raphael, "Social determinants of health: the Canadian facts". The Canadian Facts. 2010. Last retrieved June 16, 2017. http://www.thecanadianfacts.org/the_canadian_facts.pdf.
27. V. Tarasuk et. al, *CMAJ.* **187**(14), 2015.
28. I. Weiss-Gal, *Int. J. Soc. Welf.* **25**, 2016.
29. M. J. Pack, *Int. Soc. Work.* **56**(5), 2013.
30. J.W. Creswell, in *Research Design: Qualitative, Quantitative, and Mixed Methods Approaches.* SAGE Publications, Thousand Oaks, CA, 2014.
31. T. Apaitia-Vague, *ANZASW.* **23**(3), 2011.
32. M. Kaiser, J. Hermsen, *Fam Soc.* ***96***(2), 2015.
33. M. Biggerstaff, P. Morris, A. Nichols-Casebolt, *Social Work*. **47**(3), 2002.
34. C. Juby, E. Meyer, *J. Soc. Work.* **11**(4), 2010.
35. R. Shor, *Soc Work Educ.* **29**(6), 2010.
36. M. Martinez, E. Kawam, *NASW.* **59**(4), 2014.
37. S. Himmelheber, *JPHS.* **25**(2), 2014.
38. M. Lombe, V. Nebbitt, A. Sinha, A. Reynolds, *Soc Work Health Care.* **55**(6), 2016
39. A. Deepak, *Affilia.* **29**(2), 2014.
40. E. Kiehne, N. Mendoza, *Soc Work Public Health.* **30**(5), 2015.
41. M. Jacobson, *J Community Pract.* **5**(3), 2007.
42. R. Phillips, *Int. Soc. Work*. **52**(4), 2009.
43. P. Conway, K. Lassiter, *Arete*. **32**(2), 2011.
44. I. Lessa, C. Rocha, *CASWE.* **29**(2), 2012.
45. F. Besthorn, *Aust Soc Work.* **66**(2), 2013.
46. R. Shor, *Soc Work Health Care.* **49**(4), 2010.
47. W. Hirai, in *Social Work-Social Development: Global Social Transformation and Social Action: The Role of Social Workers: Social Work-Social Development Volume III*. S. Hessle, Ed. Routledge, Farnham, GB, 2014, p.p. 47-50.
48. K. Libal, T. Tomczak, R. Spath, S. Harding, *Social Work.* **59**(4), 2014.
49. W. Whitaker, *Social Work.* **38**(4), 1993.
50. U. Gustafsson, A. Draper, *J Hum Nutr Diet.* **22**(2), 2009
51. M. Chilton, M. Knowles, J. Rabinowich, K. Arnold, *Public Health Nutr.* **18**, 2015.
52. R. L. Hawkins, E. J. Kim, *Clin Soc Work J.* **40**, 2012.
53. Health Canada, "The Household Food Security Survey Model (HFSSM)." Health Canada. July 25, 2012. Last retrieved June 16, 2017. http://www.hc-sc.gc.ca/fn-an/surveill/nutrition/commun/insecurit/hfssm-mesam-eng.php.
54. M. Carter, L. Dubois, M. Tremblay, Taljaard, M, *BMC Public Health.* **12**, 2012.
55. M. Hamm, A. Bellows, *J Nutr Educ Behav.* **35**(1), 2003.
56. L. Minaker et. al, *Can J Public Health.* **107**(1), 2016.
57. G. Bellett, "Canada the only G8 Country without national school meal plan". *Vancouver Sun,* May 9, 2016. Last retrieved December 30, 2016 from: http://vancouversun.com/news/local-news/canada-the-only-g8-country-without-national-school-meal-plan
58. M. McCain, "Canada Can, and Should, Tackle Domestic and Global Food Insecurity". *Globe and Mail,* December 28, 2015. Last retrieved December 30, 2016. http://www.theglobeandmail.com/report-on-business/rob-commentary/canada-can-and-should-tackle-domestic-and-global-food-insecurity/article27941122/.
59. V. Tarasuk, "Basic Income a Solution to Food Insecurity, say Professor". *CBC News*, November 18, 2016. Last retrieved April 6,

2017. http://www.cbc.ca/news/canada/toronto/programs/metromorning/food-banks-food-insecurity-basic-income-1.3857066C.

60. Council on Social Work Education (CSWE), "Understanding Food Insecurity: Human Rights and Social Work Implications." CSWE. 2016. Last retrieved June 16, 2017. http://www.cswe.org/CentersInitiatives/KAKI/50754/77835.aspx.
61. B. Sunguya et. al, *Front Public Health.* **1**, 2013.
62. A. Papan, B. Clow, *Gen Dev.* **23**(2), 2015.

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Policy Review: Addressing the Complex Challenges of Regulating Biotherapeutics

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University of Calgary IGEM Team

University of Calgary iGEM team is composed of 15 undergraduate students from the faculties of science, medicine, and engineering. Each year they tackle solutions to real-world problems using synthetic biology. They present their work annually on the global stage amongst 250 teams at the International Genetically Engineered Machines (iGEM) competition.

Abstract

The advancing industry of biotherapeutics is providing the public with new promising and innovative drugs which may pose risks if their production, distribution, and marketing are not directly governed by legislation. Apart from international agreements, such as the Cartagena Protocol that governs the migration of biotherapeutics between countries, there are no specific and direct laws or regulations governing manipulated cell-based therapeutics in Canada. The introduction of these laws and regulations in Canada will allow for the safe research and use of biotherapeutics in a proactive manner.

Keywords: Biotherapeutics; cell-based therapeutics; regulations; Health Canada

Introduction

The emerging biotechnology sector in the global economy combined with the vast amount of research efforts into engineered cell-based therapeutics alludes to the imminent creation and marketization of engineered cell-therapy drugs (hereby referred to as biotherapeutics) [1]. Effective planning of regulations and economics will be necessary to better prepare for the introduction of these biotherapeutics into the market. Specific regulations can both serve to encourage expansion in this novel field, deter misuse of this technology, and prevent potential incidents that elicit risks from the use of this group of drugs.

In the research community, biotherapeutics have been appraised as the emerging "third pillar" of pharmaceuticals after synthetic chemicals and biologics [1]. Biologics are large molecules products that are manufactured from living systems (live cells), whereas biotherapeutics involve the use of these live cells directly [1]. The use of live cells on site of the human body offers detection, production, and administration of therapeutics in a responsive manner [1]. This offers completely novel solutions to drug administration with a lot of therapeutic potential. For instance, the treatment of type 1 diabetes can be revolutionized by planting engineered cells in the body which can secrete insulin specifically after detection of high blood glucose levels [1]. This would eliminate the need for attaching extraneous electronic devices to the bodies of diabetics. Other applications of this novel technology include the use of engineered bacterial cells to treat disorders of the human microbiome (such as *Clostridum difficile* infections), B lymphocytes to combat Epstein-Barr viral cancers, or providing regulated production of lactase for individuals who are lactose intolerant [1].

Previous literature reviews have extensively covered the therapeutic potential of biotherapeutics.[2][3] In the scientific field, there is a surge of promising therapeutics that emerged from cells modified using genetic engineering technologies.[4,5] Many of these technologies are expected to enter clinical trial stages in the upcoming years. North America has experienced tremendous growth in the biotechnology sector in the last 5 years, with the number of biotechnology companies increasing by 400% since 2011 [6]. The biotechnology sector currently totals $108.8 billion annual revenue [7]. Furthermore, 68.4% of biotechnology companies focus mainly on human health technologies, which is evidence for the increasing availability and prevalence of biotherapeutics [7]. Thus, an appropriate policy framework would need to be installed to ensure these technologies are properly regulated and contained. Policy frameworks will also serve to streamline the process of bringing biotherapeutics to the market.

The current Health Canada regulatory frameworks (and international standards) are shaped to address potential incidences with chemically synthesized drugs, some biologic products, and some stem cell therapy applications [8,9]. These Health Canada regulations give some mention to synthetic biology/genetically engineered products, but these are descriptive at best [8,9]. Prior experiences pertaining to the introduction of biologics has elucidated the importance of parallel development of technological discoveries and policy to avoid accidents [10]. Early planning for preventative purposes is particularly important for biotherapeutics due to the rapid and far-reaching consequences that could occur if they are misused [11].

The fragmentation of applicable regulatory policies in separate guidance documents, the dispersion of responsibilities across ministries and agencies, and a limited infrastructure appropriate for manufacture of this novel technology could pose potential challenges in its implementation. Biotherapeutics are governed by many separate guidance documents under the current framework, particularly through a combination of cell-based therapeutics and gene therapy documents [9]. This separation leaves many

regulatory gaps where the interactions between separate genes, as well as between genes and cell types are not considered. This absence of specific guidelines also deters individuals from entering the field of biotherapeutics as a whole, which impedes its growth.

This policy brief presents strategies that can build an effective policy framework for biotherapeutics and develop a comprehensive knowledge base to guide, accelerate and improve action.

Strategies for Action

The introduction of specific regulations pertaining to the development, manufacturing, and ongoing surveillance of biotherapeutics is pertinent to facilitate the safe and effective use of this drug technology. For such regulations to be practical, they must:

- build off of existing framework;
- involve the coordinated efforts of relevant ministries, academic institutions, companies, and other relevant partners;
- require the financial and technical support of governmental institutions, and;
- acquire political confirmation and support of international institutions.

The strategies outlined below should be seen as complementary to one another, but should be implemented concurrently for maximum impact.

Existing Policy

Currently, Health Canada has separate categories of regulation for gene-engineering products, including genetically modified foods and drug products[12], and cell-based therapeutic products, which includes guidance on cell, tissue, and organ transplantation.[13] Under the select agent compliance program of Canada, risk classification of each cell type/gene type is conducted based on origin and intended use.[14] With risk considerations in mind, the therapeutic is then given an overall risk-benefit score to determine approval. The assessment of a genetically engineered cell-product would warrant first a risk assessment of the cell type, as well as an assessment of the gene origin separate from one another under the current policies.[11] Although this approach is effective in filtering out certain agents of the high-risk variant, it leaves gaps where the cell-genetic interaction is not considered. For example, transformation of select genes from ebola virus into low risk organisms may not warrant high-risk classification even though the gene of ebola origin would be considered high risk. Or perhaps interaction between a low risk gene and a low risk organism, for example the introduction of antibiotic resistance genes in certain gut bacteria for probiotic applications, could warrant higher risk classifications as a therapeutic.

Adaptive Drug Assessment Process

The United States Environmental Protection Agency has classified intergeneric microorganisms as being distinct from other microorganisms and has created regulations specific to them [15]. Canada should adopt a similar policy regarding modified microorganisms that account for their unique properties, namely the likelihood of emergent properties. Emergent properties refer to the possibility of unpredictable phenotypes arising due to the interactions of exogenous genes with endogenous genes, other cellular components, or other cells. Because of the unpredictability of these emergent properties, it will be necessary to improve current risk assessment procedures as well as introduce long term plans for effective monitoring of manipulated cells once they are released to the market [16].

The translation of research for biotherapeutics (particularly from research in model organisms to clinical research in humans) is not as linear as drugs currently on the market, due to these emergent properties [11]. Thus strategies to mitigate adverse effects during translational research is compulsory. Consequently, the research ethics board will need to take extra precaution when assessing present research for clinical studies involving biotherapeutics, as well as set up frequent

monitoring of adverse effects while clinical trials are conducted. This may require the government to impose additional measures in authorization of such translational research.

Standard Indicators

Although there is no single standard that can reveal the entire complexity of whether a biotherapeutic will have undesired side effects, a number of design specifications of a biotherapeutic technology should be considered when assessing the safety of the technology. These design specifications include, but are not limited to:

- the presence of kill-switch technology (genes incorporated such that certain environmental exposure causes the cell to commit to apoptosis);
- the presence of auxotrophy (knocking out genes for essential nutrients of the cell so that it cannot survive without an abundance of said nutrient in its immediate surroundings);
- reporting on reproductive capabilities of cell product;
- whether the cell type is likely to retain integrated genes for an extended period of time (linked to the insertion site of gene, *e.g.* plasmid *vs.* chromosome)
- promoter strength (how likely gene is to be transcribed and translated into product, as it relates to dosage);
- reporting on therapeutic cells' localization and migration abilities;
- cell type and origin; (with reference to existing cell-therapy regulations)
- gene type and origin, and; (with reference to existing select agent compliance regulations)
- the differentiation of *in vivo vs. ex vivo* transformations.

Users should be aware that any one of these points would not be sufficient to assess the safety of a biotherapeutic product; instead, reference to multiple standardized indicators may be required. Benefit-risk analysis should be conducted with reference to standardized indicators on a case-by-case basis. Standardized indicators could offer a fast way to review incoming biotherapeutic proposals, although it will need to work in conjunction with current assessments to inform decision regarding drug approvals.

Improving Pharmacovigilance Practices

To best implement biotherapeutic technologies for use in the future, it is important for pharmacovigilance practices to be up to the same standards as the drug approval process [17, 18]. This is especially important for biotherapeutics due to the proliferative and adaptive properties of cells, which makes even the smallest contamination issue potentially far-reaching and detrimental [19]. Although Canada currently has mandates for pharmacovigilance under section C.05.010(f) of the Food and Drug Regulations, numerous systematic reviews have cited the pitfalls of Canada's current pharmacovigilance system, particularly the issues of under-reporting of adverse drug events and long processing times [9]. A qualitative study of Canadian pharmacovigilance identified that only 3% of all adverse reactions get reported, and the overall reviewing times take months after the actual occurrence of said adverse drug events [9, 10]. Under these circumstances, even modest modifications could yield significant results. The proposed modifications to consider include:

- an increase in reporting frequency by encouraging participation of both community and institutional pharmacists, physicians, and affiliated institutions as well as giving individual patients the option of reporting of adverse drug events;
- imposing accountability measures for companies and professionals that do not report adverse events in compliance with good pharmacovigilance practices, including the mishandling or intentional release of products;

- an intuitive online reporting system with categorical data that is easily compiled for reviewing purposes, and;
- a coordinated effort between epidemiologic personnel in the Public Health Agency of Canada and the pharmacovigilance review board to react quickly to adverse events or leaks.

Optimal use should be made of the above strategies, but there are certain limitations to each and alternative or fastidious strategies might be necessary. These modifications are meant to be restricted to any future biotherapeutic products, as implementation for all drugs could be costly and cumbersome.

Building Local Expertise and Know-How

Historically, the release of any novel technology has faced opposition from the public and lobby groups due to a lack of understanding. Often, individuals who might benefit from the technology miss opportunities due to misconceptions and stigmas. For these reasons, training and public education are particularly vital to avoid misuse and to obtain maximum benefit. Training with these new technologies should be extended to relevant ministries, authorized health professionals, and community advocates. In terms of content, the training should involve both theoretical science and physical handling skills of each biotherapeutic. Individuals should know its basic operation as well as troubleshooting and emergency reaction protocols upon training completion. Public education concerning the science involved in genetically engineered devices is equally vital to prevent stigmatization. This involves an integrated effort between education boards and health ministries. The advantages of professional training and public education include the access of biotherapeutics by individuals who need them to maximize societal benefit, as well as minimizing incidence of misuse.

International Harmonization

Biotherapeutics also offer many advantages in foreign settings, including but not limited to ease of use, minimal maintenance, and self-reproducibility [1]. With increasing international travel and migration, there is a resulting increasing demand for the pharmaceutical industry to be regulated on the global scale, as the development in the biotechnological industry is occurring around the globe. Local, national, and international efforts are needed to gain more insight on the potential ways to increase safety and efficacy of biotherapeutics; this may include specific international guidelines established through the International Conference of Harmonization (ICH) [20].

Building Innovative Research Networks

Ensuring the safety and efficacy of biotherapeutics should involve coordinated efforts across many sectors – the health, education, labor, civil service and private sectors – and the Canadian regulatory system, academic institutions and other stakeholders. It is therefore important to distinguish and strengthen mechanisms that bring together producers, regulators, and end users of biotherapeutic products. This could be achieved by increasing awareness and funding of biotherapeutics in government. Potential benefits include increasing drug research innovativeness, consolidation between the lab bench and the public, and higher ability to better address health demands while still being strict on issues such as bioterrorism.

The Cartagena Protocol is a step that the international community has taken to get closer to increasing cooperation between sectors by governing the movement of biotherapeutics from one country to another, and it has valid points regarding the development of biotherapeutics [16]. In practice, such a network does not yet exist on the international scale. Canada, as an international leader of progressive health policies, should develop strategies toward this end.

Conclusion

The advancing industry of biotherapeutics is supplying society with novel, promising drugs which may pose risks if their production, distribution, and marketing are not governed by legislation. As there are no specific regulations in Canada governing manipulated cell-based therapeutics, the introduction of these laws and regulations in Canada will be beneficial in authorising the safe research and use of biotherapeutics.

Strategies attempting to address this gap in therapeutic regulation should include an adaptive drug licensing process which makes use of existing standard indicators commonly used by researchers, a cooperative pharmacovigilance strategy for post-market monitoring, as well as a local and international research network which increases access to biotherapeutics for those who need it while preventing misuse and bioterrorism acts.

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References

1. M. Fischbach, J. Bluestone, W. Lim, *Sci. Transl. Med*. **179**(5), 2013.
2. R.M. Dudek, Y. Chuang, J.N. Leonard, *Adv. Exp. Med. Biol.* **844**, 2014.
3. D.J. Woodsworth, R. Holt, *Trends Mol. Med.* **23**(2), 2017.
4. M. Mimee, R. Citorik, T. Lu, *Adv. Drug Deliv. Rev.* Article in press, 2016.
5. J.R. Bagõ, A. Alfonso-Pecchio, O. Okolie, et al. *Nature Comm.* **7**, 2016.
6. Synthetic Biology Project Group, "U.S. Trends in Synthetic Biology Research Funding". Wilson Centre, Pennsylvania, WA, 2015. http://www.synbioproject.org/publications/u.s-trends-in-synthetic-biology-research-funding/
7. J. Curran, "IBIS World Industry Report NN001. Biotechnology in the US". IBIS World, 2016. http://www.ibisworld.com/industry/default.aspx?indid=2001
8. Government of Canada, "Food and Drugs Act". Minister of Justice, Ottawa, ON, 2016.
9. N. Yeates, D. Lee, M. Maher, *CMAJ*. **176**(13), 2007.
10. V. Nichols, I. Theriault-Dube, J. Touzin, J. Delisle, D. Lebel, et al. *Drug Safety*. **32**(7), 2009.
11. "Biotechnology: Product Life Cycle". Health Canada, Ottawa, ON, 2015. http://www.hc-sc.gc.ca/sr-sr/tech/biotech/health-prod-sante/prod_life-vie-eng.php
12. "Biotechnology". Health Canada, Ottawa, ON, 2015. http://www.hc-sc.gc.ca/sr-sr/tech/biotech/index-eng.php
13. Ministry of Health, "Guidance Document: preparation of clinical trial applications for use of cell therapy products in humans". Health Products and Food Directorate. Ottawa, ON, 2015
14. Minister of Justice Canada, "Human pathogens and toxins act". Canadian Ministry of Justice. Ottawa, ON, 2009. http://laws-lois.justice.gc.ca
15. "Toxic Substance Control Act". US Environmental Protection Agency, Washington, DC, 1976.
16. CBD (Secretariat of the Convention on Biological Diversity), "Cartagena Protocol on Biosafety to the Convention on Biological Diversity: text and annexes". Secretariat of the Convention on Biological Diversity, Montreal, QC, 2000.
17. Health Products and Food Branch Inspectorate, "Good Pharmacovigilance Practices (GVP) Guidelines GUI-0102". Health Canada, Ottawa, ON, 2013.
18. Health Products and Food Branch Inspectorate, "Inspection Strategies for Good Pharmacovigilance Practices (GVP) for Drugs POL-0041". Health Canada, Ottawa, ON, 2013.
19. H. Meisel, T. Ganey, W. Hutton, J. Libera, Y. Minkus, O. Alasevic. *Eur. Spine J*. **15**, 2006.
20. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, "Pharmacovigilance Planning E2E Step 4". ICH Harmonized Tripartite, Geneva, Switzerland. 2004.