

## Outline of Proposed Research

Glasses have been of enormous technological importance for centuries. Although we're most familiar with window glass, most plastics, as well as many aggregate materials such as clays and colloids also fall under this category. Incredibly, there are still many unanswered questions about this mundane material, and the glass transition through which it is formed. When a liquid is cooled below its freezing point then, if crystallization can be prevented, a super-cooled liquid is formed. The viscosity increases rapidly as the temperature is further decreased, and eventually the particle dynamics slow so much that the liquid falls out of equilibrium forming a glass. Glasses have solid-like mechanical properties, however their structure remains disordered like the liquid, and the particles continue to exhibit a surprising amount of mobility. The particle dynamics in a glass are both spatially and temporally inhomogeneous, taking place through the collective movement of small groups of atoms. Through these particle rearrangements, the system slowly finds more favorable conformations and becomes more solid-like. This process is called aging and has effects on all of the physical properties of the system, but especially the mechanical relaxation times.

In this work, we will be studying the dynamics and mechanical response functions in glassy solids using computer simulation. In initial studies [1], we investigated the aging dynamics of glasses using molecular dynamics (MD) simulations of a coarse-grained "bead-spring" polymer at various temperatures and mechanical loads. This technique allowed us to directly correlate the microscopic dynamics of the glass to the macroscopic creep compliance which is the preferred experimental tool for studying this phenomenon, and to look in detail at the distribution of particle displacements. Subsequently, we've revisited a simpler phenomenological "trap" model of glasses [2], which considers the hopping dynamics of non-interacting fictitious particles in a random potential energy landscape at an effective noise temperature. This model shows a glass transition and aging dynamics. We performed preliminary stochastic simulations of this model, and showed that it furthermore exhibits some novel behavior observed experimentally and in our previous MD simulations: mechanical perturbations can cause an erasure of aging (rejuvenation) at large strains, and increased aging (over-aging) at small strains. This simple model contains much of the physics of glasses; however, its predictive ability is limited as it remains difficult to connect the "fictitious" particles in the model to the collective movements that actually take place, and the "noise" temperature to the actual thermodynamics of the system.

In the proposed work, we will investigate the relationship between the trap model and the underlying molecular level processes. We will use the trap model to map the rejuvenation/over-aging phase diagram, and expand it to include particle displacements for direct comparison with the results of our MD simulations. Using molecular dynamics simulations, we will look in detail at fluctuations on the length-scale of the collective rearrangements, and track the distribution of relaxation times. Also, fluctuation-dissipation violations in glasses have been used to define an effective temperature; we will investigate the coarse-grained effective temperature via MD simulations to elucidate the connection between the thermodynamics in the actual glass and the noise temperature. Through this approach we hope to connect the length and time-scales of the trap model and the molecular model, and to improve our ability to predict mechanical behavior through computer simulations.

[1] ██████████ and J. Rottler, Phys. Rev. E **76**, 031802 (2007).

[2] C. Monthus, and J.P. Bouchaud, J. Phys. A: Math. Gen **29**, 3837 (1996).

## Contributions and Statement

### **Part I – Contributions to Research and Development**

#### *a. Articles published in refereed journals*

1. [REDACTED] (2007) Simulations of aging and plastic deformation in polymer glasses. *Physical Review E*. 76: 031802 (Ph.D.).
2. [REDACTED] (2006) A structural, electronic and electrochemical study of polypyrrole as a function of oxidation state. *Synthetic Metals*. 156: 724-730 (M.Sc.).
3. [REDACTED] (2006) Electrochemical switching of conducting polymers: A variable resistance transmission line model. *Journal of Electroanalytical Chemistry*. 590: 76-81 (M.Sc.).
4. [REDACTED] (2005) A structural investigation of polypyrrole as a function of oxidation state. *Organic Thin-Film Electronics, Materials Research Society Symposium Proceedings*. 871E: I6.1 (M.Sc.).

#### *b. Posters and industrial contributions*

5. [REDACTED] (2007) Simulations of aging and plastic deformation in glassy polymers. Oral presentation at APS March Meeting (international) (Ph.D.).
6. [REDACTED] (2006) Simulations of aging and the plastic deformation of polymer glasses. Poster presented at Boulder School of Condensed Matter (Ph.D.).
7. [REDACTED] (2005) A structural investigation of  $\text{PF}_6^-$  doped polypyrrole as a function of oxidation state. Poster presented at both SPIE and Materials Research Society meetings (international) (M.Sc.).
8. Galian Photonics Inc. Design documents, reports and patent disclosures. May 2001-Feb 2003. (industry)

### **Part II – Most Significant Contributions to Research and Development**

Reference 1 presents a comprehensive exploration of the changes in mechanical response, dynamics, and local order as a function of age, stress, and temperature. The results are the first to make the connection between aging in the mechanical response functions, which are typically measured by experimentalists, and the particle dynamics, which are more frequently used by theorists (see outline of proposed research for background). It also presents evidence for a structural origin to mechanical rejuvenation which is a subject of some controversy right now. I was the primary author of this paper, and all the results are my own. The subject of this paper falls generally under the class of non-equilibrium thermodynamics and statistical physics, which led us to publish in *Physical Review E*.

References 2 and 3 are contributions resulting from my Master's degree (see thesis description). I was given a great deal of freedom in the choice of a topic and how I executed my research on this project. Therefore, the ideas expressed in these papers are largely a result of my own creative effort, and I personally designed and performed all of the experiments. I was the primary author of the publications that resulted from this work. The experimental work [2] was published in *Synthetic Metals*, which is a journal dedicated to conducting polymer research. This is the venue where the original x-ray diffraction work on polypyrrole was presented, which was the primary motivation for publishing in this journal. The paper presenting the electrochemical model of polypyrrole actuators [3] was presented in the *Journal of Electroanalytical Chemistry*. We chose this journal on the recommendation of an electrochemist [REDACTED] as the model presented is of general interest to electrochemists, and this journal frequently presents sophisticated modeling of electrochemical processes.

## Part III – Applicant’s Statement

### Research Experience

My experiences as a graduate student and in industry have made me a confident, independent researcher. I have gained an abundance of practical experience in a number of different working environments: from university and government labs, to a practicing medical physics team, to a telecommunications start-up. I have worked on projects in diverse areas of physics, including condensed matter, photonics, electronics, polymer physics and physical chemistry. This has given me the ability to quickly become familiar with a field and determine where I can best make a contribution, as well as many different perspectives from which to attack a problem. I have also worked in both experiment and theory and I am comfortable with many different techniques in both. My most recent work involves using and creating new modeling tools for simulating non-equilibrium thermodynamics, including molecular dynamics and Monte Carlo algorithms. However because of my background, I have a firm grasp of what experimentalists in the field are doing, and how my research complements their work.

My experiences solving relatively unstructured problems in graduate school and in dealing with the entire product design cycle at Galian Photonics have also given me excellent project management skills. At Galian Photonics, I was responsible for one of the key sub-components of our project, and I was expected to think it through from design to fabrication to testing. I have excellent communication skills, and have attended several conferences to present my results. I am also a regular presenter at various departmental seminar series.

### Relevant Activities

- Director of the Teaching Assistant Training Workshop and Mentor TA Program  
*I spearheaded the TA training workshop and mentor TA program as part of an incentive to improve the level of undergraduate education in this department. I designed the syllabus and managed two other facilitators in organizing and implementing activities for the workshop. I am also the chief administrator of the mentor TA program, whereby experienced TAs share their knowledge and provide feedback to the new TAs.*
- Graduate Student Representative on the Undergraduate Teaching Committee  
*The objective of the committee was to look at ways of improving our undergraduates' education through the use of new teaching methods, and to create a proposal for the Carl Wieman Science Education Initiative. As the graduate student representative, I provided a student's perspective at these meetings, and served as a liaison for the rest of the graduate students to voice their suggestions.*
- Organizing Committee for Biophysical Retreat  
*I was part of the organizing committee for a student-run workshop-style retreat for members of the biophysics community in Vancouver. We were responsible for all aspects of planning, including contacting key-note speakers from outside of our community to speak at the event, registration, and choosing presenters.*
- YWCA Mentor  
*I supported a high school student interested in pursuing physics by being a positive role model and providing information about careers in science.*
- Volunteer for Let's Talk Science  
*I taught a physics lesson to an elementary school class.*
- Teaching Assistant  
*I've taught various undergraduate labs, and held office hours.*

## **Proposed Research: Factors influencing the vertical distribution and infiltration of fine particles in streams**

Fine particulate matter is an important component of stream systems. Particles deposited on the streambed surface or within the interstices of the bed interact with benthic organisms and bed topography, whereas suspended particles impact free-swimming organisms and water quality. Traditionally, the study of fine particle dynamics has been based on mathematical expressions for the vertical distribution of suspended particles (e.g. Rouse, 1937). However, these classical models are simplified representations of natural systems that have limited predictive ability. Research suggests that several physical and biological mechanisms influence fine particle dynamics, such as turbulent fluctuations generated by channel and streambed morphology, adhesion to surface biofilm (Battin et al., 2003), or particle density (Thomas et al. 2001). My study will test the independent and combined effects of 1) particle density, 2) bed composition, 3) flow condition, and 4) biofilm development on the water-column distribution, deposition, and infiltration of fine particles. Specific hypotheses are as follows:

H1: Low-density particles will be more readily entrained and transported higher in the water column than equal size and shape high-density particles. Deposition and streambed infiltration will be greater and deeper for high-density particles.

H2: A high proportion of fine particles on the bed will increase particle entrainment, producing more uniform vertical profiles than predicted from the mean particle size of the bed. A high proportion of coarse grains will increase form and grain resistance, likely producing less uniform profiles.

H3: Over short durations, low flows will selectively transport fine particles higher in the water column, while high flows will more uniformly distribute particles of different sizes.

H4: 'Sticky' exopolysaccharides of biofilm will enhance particle adhesion and deposition (Battin et al., 2003), particularly for small particle sizes. Due to the decrease in surface friction, very high biofilm coverage may produce more uniform shear stress and particle concentration profiles.

H4A: Filamentous biofilm assemblages reduce near-bed velocities, but do not significantly slow advective velocities into interstitial spaces (Dodds and Biggs, 2002), thus particle deposition and infiltration may be enhanced.

To test these hypotheses, experiments are being conducted in a laboratory flume equipped with highly sensitive instruments to allow for carefully-controlled conditions and detailed measurements. Bed composition experiments test varying amounts of bulk sand fraction using either a 'clean' bed without fines or a 'dirty' bed infiltrated by fines. Biofilm experiments test how the amount and structure of surface biofilm influence particle dynamics. All experiments are run for a long duration under two different flow levels with a supply of either high- or low-density particles. Measurements include short- and long-term velocity, particle concentration, and grain size profiles; streambed infiltration samples; surface deposition samples; and biofilm density and composition analyses. Rates of particle deposition or entrainment are determined from continuous measurements of near-bed particle concentrations. From velocity and shear stress measurements, the influence of each factor on near-bed hydrodynamics is assessed. Suspended particle profiles are compared to theoretical profiles calculated from the classical Rouse equation and the more recently developed Local Exchange Model of McNair et al. (1997). The rate and depth of particle infiltration are measured with bed samplers. Surface samples analysed for ash-free dry mass and ash-mass indicate the areal density of biofilm and the amount of inorganic particle deposition to the bed surface. All results are compared for different particle densities, bed conditions and flow levels to determine the relative importance of each factor.

To date, ~10 experiments have tested the effects of mucilaginous and filamentous biofilm development on particle dynamics relative to a bed without biofilm. Preliminary results demonstrate that particle deposition increases proportionally with biofilm density and is greater for mucilaginous forms. At very high densities, filamentous biofilm significantly reduces near-bed velocities and shear stresses. Furthermore, results suggest that particle deposition and infiltration are more strongly affected by variations in surface condition than by differences in flow level or duration.

## Part 1: Contributions to research and development

### Articles published or accepted in refereed journals

- [REDACTED] Reply to Discussion by Potyondy and Sylte of 'Assessment of Methods for Measuring Embeddedness: Application to Sedimentation in Flow Regulated Streams', *J. Am. Water Resources Assoc.*, In Press. Accepted 20 Aug. 2007. 7 pp. (M.Sc.)
- [REDACTED] (2007) Suspended sediment dynamics at high and low storm flows in two small watersheds. *Hydrological Processes*, Accepted 6 Mar 2007. 39 pp. (Ph.D.)
- [REDACTED] (2007) The use of short-lived radionuclides to quantify transitional bed load transport in a regulated river. *Earth Surf. Processes Landforms*, 32(4): 509-524. (M.Sc.)
- [REDACTED] (2006) Short and long-term changes to bed mobility and bed composition under altered sediment regimes. *Geomorphology*. 76: 43-53 (M.Sc.)
- [REDACTED] (2006) Assessment of methods for measuring embeddedness: application to sedimentation in flow-regulated streams. *J. Am. Water Resources Assoc.*, 42(6):1671-1682.
- [REDACTED] (2006) Evaluating the impacts of impoundment on sediment transport using short-lived fallout radionuclides, In: *Sediment Dynamics and The Hydromorphology of Fluvial Systems*, The International Association of Hydrological Sciences (IAHS) Special Publication 306, IAHS Press, Wallingford, UK. In Press. 12 pp. (M.Sc.)

### Other refereed contributions

- [REDACTED] (2007) Fine particles in streams: physical, ecological, and human connections. In *Land Management Impacts on Coastal Watershed Hydrology*. WIT Press Royal. (Ph.D./invited contribution)

### Non-refereed contributions

- [REDACTED] The use of fallout radionuclides to quantify downstream trends in sediment transport below dams. Geological Society of America, Nov. 2004, Denver, CO. Poster presentation. International conference. (M.Sc.)
- [REDACTED] (2006) Timescales of streambed stabilization due to altered flow and sediment regimes below dams. American Geophysical Union Annual Meeting, December 2005, San Francisco, CA. Poster presentation. International conference. (M.Sc.)
- [REDACTED]. Suspended sediment dynamics at high and low flows in two small watersheds. American Geophysical Union Annual Meeting, Dec. 2006, San Francisco, CA. Poster presentation. International conference. (Ph.D.)

### One poster removed on account of room

## Part 2: Most significant contributions to research and development

1) My M.Sc. thesis resulted in three publications that address the complex and variable effects of flow regulation on streambed condition and sediment transport. Each manuscript focused on a different method of analysis, including modeling of long-term bed elevation and discharge data [REDACTED] (2006), embeddedness measurements [REDACTED] (2007), and sediment tracing by short-lived radionuclides [REDACTED] (2007). The latter manuscript presents a novel and innovative technique in which the short-lived fallout radionuclide  $^7\text{Be}$  is used to independently quantify transitional bed material load transport rates over short temporal and spatial scales. The ability to independently measure transitional bed material load as distinguished from suspended and bulk bed load transport is critical for assessing the impact of increased sediment loads on aquatic systems. This information will have highly practical applications, aiding assessment of fine sediment infiltration into spawning habitat, for example, and the conditions under which this material is mobilized. Because of its multi-faceted, interdisciplinary

approach, my research is relevant to a wide audience that includes both scientific researchers in the fields of geomorphology and ecology as well as watershed managers and restoration directors in applied fields. For two of these three papers, I independently collected and analysed the data, created the figures, wrote the first draft and edited subsequent drafts. I also acted as field assistant, mentor, and co-author to a senior honours student whose thesis was later published (2007).

2) During my first year as a Ph.D. student at UBC, I wrote a literature review of fine particle dynamics for a peer-reviewed chapter in the book *Land Management Impacts on Coastal Watershed Hydrology*. My paper integrates and compares knowledge obtained via the diverse and often disparate methods used in the ecological and physical sciences. I present a conceptual framework that links these two fields, a novel approach that will benefit scientists in hydrology, geomorphology, ecology, and watershed management. My review demonstrates that the mechanisms and rates of particle entrainment and deposition are highly complex and ill-represented by theoretically-based models. My dissertation research is intended to elucidate the dominant factors influencing vertical particle movement.

3) In my second year at UBC, I analysed a long-term dataset of suspended sediment and discharge measurements from the Goodwin Creek Experimental Watershed, Mississippi. I compared discharge-SSC relationships from two small streams of widely different bed compositions (one dominated by sand, the other by gravel), using bed composition as representative of in-channel sediment supply. I analysed both high flow events and low flow periods in order to distinguish external from in-channel sources of sediment and to assess the relationship between low flows and sediment supply. A major contribution of this research is the discovery that in-channel storage plays an important role in the mobilization and transport of fine sediment, a concept that is typically neglected in the study of suspended sediment dynamics. My manuscript based on this analysis is being published in *Hydrological Processes*.

### **Part 3: Applicant's statement**

#### **a. Research experience**

Over the last eight years, I have worked on a wide range of research projects, including laboratory and field studies in ecology, soil science, geomorphology, and hydrology. As an undergraduate student at Dartmouth College, I took part in two intensive and rigorous field courses in the fields of tropical and marine ecology and earth sciences. I also worked as a research assistant for the U.S. Geological Survey Biological Division in deserts of the U.S. southwest, where I took part in long-term plant monitoring studies, and as a research technician for two Ph.D. students in aquatic ecology and soil science at Dartmouth. For my M.Sc. thesis, I independently collected and analysed data on sediment transport, morphology, and streambed condition in small streams of eastern Vermont. From these experiences I gained an extensive set of observational, experimental, and analytical research skills in several different disciplines and geographical locations. My multi-disciplinary background has provided me with an expertise that is unique and far-reaching.

#### **b. Relevant activities**

Since my teens, I have worked as a teacher, waterfront lifeguard, swim and climbing instructor, and outdoor trip leader. As an undergraduate, I was chair of the Dartmouth Mountaineering Club, organizing trips, purchasing equipment, and recruiting new members. I also instructed climbing classes and led outdoor orientation trips for Dartmouth Outdoor Programs and Outing Club. During the same period, I co-managed a seven-person crew at Moosilauke Ravine Lodge, a food service and overnight rest spot for hikers and families, where I was responsible for ordering and preparing food for more than 100 guests each night, scheduling crew work projects, and performing regular maintenance on the nearly 70-year old lodge. As a graduate student, I have worked as a teaching assistant for several undergraduate courses on a range of topics, including hydrology, environmental change, and physical geography, for which I give lectures, run laboratory sessions, tutor students, and design and mark course examinations. These roles have taught me that an effective leader is one who is responsible, organized, attentive, and proud of the work being done. I believe that the skills I've gained in these positions will be essential to successfully undertaking the rigours and challenges of a Ph.D. research project.

PIN: [REDACTED]

The basic approaches to a programming solution – top-down or bottom-up – apply to how we examine biological problems. We can start from a high level and investigate the macro: characterize the behaviors of a black-box population without detailing its internals. Alternatively, we can build up to a complete model of a biological system by considering its components at different modular levels: nucleic acids and proteins, series of chemical reactions, or networks like gene regulation. We define the modules, assemble them into complex structures, and inspect the system as a whole. My interests lie in a bottom-up view of the cell that exposes its elements, their interactions, and the results of those relations.

Systems biology describes the cell as a system of biological networks consisting of protein interactions, metabolic reactions, transcriptional interactions that lead to gene expression, gene regulation, and other pathways [1]. Research in identifying these pathways is rapidly evolving. As a first stage, existing data on protein-protein interactions, transcriptional regulation, and other gene information was combined into a Bayesian network. The probabilistic confidence of the interactions in the network was then used to identify other interactions in other pathways [1]. Next, networks of protein-protein interactions, in which each protein pairs with a series of others, were modelled to reveal a snapshot of the network in different states [1]. I want to take this one step further by performing such an analysis on biological networks affected by mutations or some form of disease. I want to examine how the components of a diseased network change over time and space compared to a healthy network. This dynamic approach shows great promise though has not been explored as extensively as static approaches with no temporal aspect [2]. Understanding networks, as complex yet key components of the cell, requires interdisciplinary insight. I plan to use both computational and mathematical tools for their modelling and simulation.

Starting with a wide literature search, I will first explore different models for dynamic biological networks, such as dynamic Bayesian networks or Boolean networks [2]. I will also collect data on diseased networks or extrapolate missing structure from other networks showing the same functions. This generalization is possible to a certain extent when networks are modeled using nodes (biological elements) and connecting edges (interactions between elements). Many biological networks exhibit similar degree distributions [1], the existence of high-degree nodes representing elements that dominate a process [1], and common graph motifs [3]. My next step is to extract the strengths of different models and combine them into my own. A strong model will be efficient and accurate, and elucidate important features of a diseased network. Finally, if two elements are similar, one can apply the set of rules that one element obeys to the other, to find new interactions that may arise in the network. Algorithmic approaches such as expectation maximization [4] can be used to predict these new pathways.

Besides contributing an important module to a comprehensive, bottom-up model of the cell, identifying diseased networks has obvious therapeutic applications. If we understand the mechanisms by which such a network operates, we can understand how normal cell activity is affected and how it can be corrected.

- [1] Zhu, X., Gerstein, M., and Snyder, M. (2007) Getting Connected: Analysis and Principles of Biological Networks. *Genes & Development*. 21: 1010-1024.
- [2] d'Alchi-Buc, F. and Schachter, V. (2005) Modeling and Identification of Biological Networks. In Proceedings of *International Symposium on Applied Stochastic Models and Data Analysis (ASMDA)*.
- [3] Milo, R., Shen-Orr, S., Itzkovitz, S., Kashtan, N., Chklovskii, D., and Aloni, U. (2002) Network Motifs: Simple Building Blocks of Complex Networks. *Science*. 298: 824-827.
- [4] Dempster, A.P., Laird, N.M., and Rubin, D.B. (1977) Maximum Likelihood from Incomplete Data via the EM Algorithm. *Journal of the Royal Statistical Society, Series B*. 39: 1-39.

PIN: [REDACTED]

I. Contributions to Research and Development

*c. Other refereed contributions*

[REDACTED] 7<sup>th</sup> Workshop on Algorithms in Bioinformatics (WABI) (international). To appear in *Lecture Notes in Bioinformatics (LNBI)*. 4645: 323-334 (USRA work).

*d. Non-refereed contributions (talks and posters)*

[REDACTED] RiboWest 2007 (regional) (USRA work).

[REDACTED] \* (March 3, 2007) [REDACTED] UBC Multidisciplinary Undergraduate Research Conference (institutional) (undergraduate thesis work).

[REDACTED] (July 24-25, 2006) [REDACTED] RiboWest 2006 (regional) (USRA work).

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III. Applicant's Statement

*a. Research experience:* Introduced to research in my first undergraduate year, I worked under an NSERC USRA investigating the Ramanujan property of graphs. Gaining experience in Matlab and graph theory, I then took on two USRAs in bioinformatics. With two other students, I looked at how an RNA strand folds on itself – or secondary structure prediction. We implemented, in Haskell, a prediction algorithm handling complex “pseudoknotted” structures. To solidify and publish my understanding, I wrote a tutorial on implementing such algorithms with the new technique of algebraic dynamic programming. Rejoining the project in 2007, I wrote C++ programs to manipulate algorithm input, learned Perl to automate testing, and set up a program needed for tuning the parameters of the energy model underlying the algorithm. Independently, I also analyzed a new energy model from the literature, enhanced it with a comprehensive treatment of “coaxial stacking” interactions, and added it to a heuristic prediction algorithm. To understand the structural motifs of RNA, I turned to articles as well as books on atomic structure and polymer physics. The same thorough literature search was important in a BioMEMS course, for which I wrote a review of DNA sequencing using biological and synthetic nanopores. To my proposed research, I further bring experience in modelling and simulation of a type of regulatory system in biological networks: for my final-year undergraduate project, I analyzed and applied two computational tools to simultaneously determine the initial conditions and parameters of the differential equations characterizing tryptophan regulation dynamics. Rooted in algorithmic knowledge, versed in the relevant biological concepts, I have the strengths to succeed in my future research.

*b. Relevant Activities:* To be inspired – in research and in general – is to first inspire others, to lead, and continue to learn. I apply this when I design events for the UBC Physics Olympics, volunteer at the PIMS Elementary Grades Math Contest, and return annually to my high school's graduation ceremonies as technical support. With several other bright women, I initiated the Calliope Network to connect girls to artists and innovators, and helped organize its inaugural conference. I am currently designing the first-of-its-kind “Distinguished Student Lecture Series” at the UBC branch of the Golden Key International Honor Society. As a forum for sharing student work, it will promote research and mutual learning. I also loved applying my university-level knowledge as a teaching assistant for two math courses. My skills in communication have evolved at various venues: an open house highlighting electrical and computer engineering research, at which I was invited to present; the UBC Bioinformatics Reading Group, which I attended and presented at; and the RiboWest RNA conference, where I presented a poster and a talk.



██████████ – Training Expectations

1. **Master's and Doctoral Research Award Candidates:** Provide an overview describing how the training you expect to acquire will contribute to your productivity and to the research goals you hope to achieve.
2. **Fellowship Award Candidates:** Provide an overview of how your previous research training relates to the present proposal and elaborate on your career goals. Describe how the training you expect to acquire will contribute to your productivity and to the research goals you hope to achieve and how this award will enable you to establish yourself as an independent investigator. Indicate why you decided upon the training location and what you expect to learn from the training experience. In addition, if you are planning to hold this award in the same institution where you completed your PhD, please justify.
3. **Clinician Scientist (Phase 1) Award Candidates:** In addition to the information requested of a Fellowship Award Candidate: indicate how you will eventually combine research and clinical practice; and describe your career expectations at the completion of the training and the contribution you plan to make at the Nominating Institution.

My scientific interests lie in the Neurosciences, with an emphasis on neurological disorders, neurodegeneration and nervous system injury. These areas of Neuroscience are interesting to me not only because they satisfy my scientific curiosity but also because they have a direct biomedical and clinical application. In other words, I am interested in undertaking research that not only can advance our knowledge of the natural world, but can also provide us with practical solutions to health issues. In particular, I am interested in using technology-based approaches to address such issues.

To pursue my interests, I have undertaken Masters level studies in Neuroscience at the University of British Columbia, working on Parkinson's disease at the Pacific Parkinson's Research Centre (PPRC), which is also a National Parkinson Foundation Center of Excellence. I believe that my research training at the PPRC, under the guidance of ██████████, will allow me to deepen my knowledge of the Neurosciences and of Parkinson's disease, and will enable me to utilize and sharpen the quantitative skills needed to bridge the gap between technology and biomedical as well as clinical issues.

During my undergraduate experience at the University of British Columbia I learned to appreciate the value of interdisciplinarity and collaboration across fields, and the notion that novel research ideas and approaches often arise when the boundaries of different disciplines are crossed. In particular, my undergraduate degree, which integrated Neuroscience, Mathematics and Genetics as part of the Honours Integrated Sciences Program, allowed me to build both solid mathematical skills as well as a foundation in the Neurosciences. Specifically, I gained research experience on the study of Parkinson's disease (PD) while working at the PPRC on my Honours thesis, which focused on the use of cell transplantation as a potential treatment for the disease.

My Masters research project will thus build on the skills that I acquired during my undergraduate training, as it requires both an understanding of biological and clinical issues related to PD, as well as mathematical and analytical skills. The latter will be especially beneficial in the analysis of electrophysiological data and the design of virtual environment (VE) based experiments. Moreover, ██████████ unique background in Engineering and Medicine, as well as the interdisciplinary nature of his research and collaborations, will provide the necessary guidance for me to become a successful and well-rounded neuroscientist.

## **[REDACTED] – Training Expectations**

As Neuroscience is now more than ever developing into a very diverse and interdisciplinary field, I believe that this type of training will prove very beneficial for my career. Not only will I be able to look at biological issues from a different perspective, but I will also further develop the necessary skills to collaborate with scientists from diverse backgrounds, an ability which is very valuable in today's research world. During my training I will learn widely applicable approaches to investigate brain electrical activity such as EEG and EMG analysis, as well as novel, cutting edge techniques such as the use of VE technology. Moreover, the nature of the project entails that I will be able to interact with PD patients, thus being in direct contact with the clinical reality of the disease. I am looking forward to this aspect of my future research, as I am convinced that it is always important for a good scientist to keep in mind the broader scope of one's research, which in this instance is the development of practical solutions to improve the life of individuals living with PD.

Overall, I believe that the training environment I will be exposed to during my Master's degree will be very challenging and stimulating, as it will provide me with a solid set of research skills that will be beneficial not only during the rest of my graduate experience, but also during my academic career. In the future I in fact envisage using the knowledge and expertise that I have developed throughout the course of my education to engage in independent, interdisciplinary Neuroscience research at a Canadian university.

## - Proposed Training Program.

1. **Project Title.** 2. **Summary of the research project.** Include the specific hypothesis of the research and describe the candidate's role on the project. This summary should be written in general scientific language. For Master's Awards, Doctoral Research Awards and Fellowships no additional pages may be added (one page total). For Clinician Scientists (Phase 1), Senior Research Fellowships (Phase 1) and Operating Fellowships, a minimum of 3 pages is required and a maximum of 6 pages is allowed. Page limits include references.

### Suppression of pathological brain oscillations in Parkinson's disease with visual stimuli

Parkinson's disease (PD) is characterized by the motor symptoms of tremor, rigidity, slowness of movement and postural instability. Surgical treatments or pharmacotherapy are currently available for PD patients, but often result in serious side effects [7]. **Alternative, non-invasive treatments are thus needed.** Recent research has shown that lack of dopamine (DA), characteristic of PD, results in an abnormal synchronization of neuronal activity within the basal ganglia and related cortical loops [5]. These beta-band, pathological oscillations are prominent in the subthalamic nucleus (STN) and the globus pallidus external (GPe), and appear to suppress movement. High frequency deep brain stimulation (DBS) of the STN has been shown to result in motor improvements in PD patients [5], possibly by disrupting abnormal neuronal synchronization [6]. However, disruption of pathological oscillations need not be invasive, as visually guided movements can dampen and desynchronize oscillatory activity in the STN of PD patients [2], even with low-amplitude (but appropriately timed) stimuli [8]. Other work in normal subjects has inferred direct cortical → STN effects during a number of behavioral responses such as a go/stop paradigm [1]. **We hypothesize that suppression of abnormal oscillations in PD can be achieved with the use of appropriately-timed visual stimuli and/or motor tasks.** In order to have maximum flexibility and effectiveness of visual stimuli, we will utilize Virtual Environments (VE).

The current proposal examines the direct effects of visual stimuli and motor behavior on synchronized beta brain activity in PD, as opposed to prior studies that have only looked at the relation between visual stimuli and gross behavioural performance such as gait [3,4]. In order to assess the effect of specifically-timed visual stimuli and behavioural paradigms on the pathological oscillations seen in PD, we will first use a suite of paradigms that have been shown to activate the STN in normal subjects. We will then proceed to see if specific visual stimuli alone, in the absence of motor movements, can achieve the same effect on suppressing oscillations. The research will build on previous work in our group showing that coupling patterns in EEG recordings can be used to infer stimulus-induced changes, and that these patterns are different in PD subjects. We will also test whether levodopa medication affects the sensitivity to stimuli. The study will include ten healthy volunteers as well as ten levodopa-treated patients with clinically defined, mild-moderate PD, recruited from the Pacific Parkinson's Research Centre at UBC. The candidate's role will involve (1) recruiting and obtaining consent from subjects, applying electro-physiological electrodes and supervising the collection of data; (2) designing a set of experiments using visual stimuli that can be repetitively applied and analyzing the resulting data. The proposed research is an essential part of the long-term goal of providing an effective, non-invasive treatment for PD.

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