



Routing Slip

This routing slip is to be included with your signature pages and is for CIHR's administrative use only.

Funding Opportunity

Collaborative Health Research Projects (NSERC partnered) 2014-10-01

ResearchNet ID 248574

Applicant

Surname	Given Names	PIN
Law	Edith	251160

Title

A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings

Relevant Research Area:

Title of Priority Announcement/Funding Pools:

Linked Programs:

**Participants Signatures**

The participants are in the following order when applicable: Principal Knowledge User, Knowledge Users, Principal Applicant and Co-Applicants, Primary Supervisor and Supervisors.

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and hereby accepted by the participant(s).

Supervisor(s) Signatures (If applicable)

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and are hereby accepted by the applicant's supervisor(s).

The author(s) of the Summary of the Research Project included in the candidate's application also agree that it accurately describes the training program proposed.

Consent to Disclosure of Personal Information

I understand that maintaining public trust in the integrity of researchers is fundamental to building a knowledge-based society. By submitting this application or by accepting funding from CIHR, NSERC and/or SSHRC, I affirm that I have read and I agree to respect all the policies of these Agencies that are relevant to my research, including the *Tri-Council Policy Statement: Tri-Agency Framework: Responsible Conduct of Research* (<http://www.rcr.ethics.gc.ca/eng/policy-politique/framework-cadre/>). In cases of a serious breach of Agency policy, the Agency may publicly disclose my name, the nature of the breach, the institution where I was employed at the time of the breach and the institution where I am currently employed.

I accept this as a condition of applying for or receiving Agency funding and I consent to such disclosure.

Surname	Given Names	Role	Signature
Mateen	Farrah	Knowledge User	x 
Institution	Faculty	Department	Date
The Bhutan Epilepsy Project	Health Sciences		23 Sept. 2014
Surname	Given Names	Role	Signature
Murray	Brian	Knowledge User	x
Institution	Faculty	Department	Date
Sunnybrook HSC Clinical Neurophysiology Laboratory			
Surname	Given Names	Role	Signature
Wennberg	Richard	Knowledge User	x
Institution	Faculty	Department	Date
Epilepsy Program, Toronto Western Hospital			

**Participants Signatures**

The participants are in the following order when applicable: Principal Knowledge User, Knowledge Users, Principal Applicant and Co-Applicants, Primary Supervisor and Supervisors.

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and hereby accepted by the participant(s).

Supervisor(s) Signatures (If applicable)

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and are hereby accepted by the applicant's supervisor(s).

The author(s) of the Summary of the Research Project included in the candidate's application also agree that it accurately describes the training program proposed.

Consent to Disclosure of Personal Information

I understand that maintaining public trust in the integrity of researchers is fundamental to building a knowledge-based society. By submitting this application or by accepting funding from CIHR, NSERC and/or SSHRC, I affirm that I have read and I agree to respect all the policies of these Agencies that are relevant to my research, including the *Tri-Council Policy Statement: Tri-Agency Framework: Responsible Conduct of Research* (<http://www.rer.ethics.gc.ca/eng/policy-politique/framework-cadre/>). In cases of a serious breach of Agency policy, the Agency may publicly disclose my name, the nature of the breach, the institution where I was employed at the time of the breach and the institution where I am currently employed.

I accept this as a condition of applying for or receiving Agency funding and I consent to such disclosure.

Surname	Given Names	Role	Signature
Mateen	Farrah	Knowledge User	X
Institution	Faculty	Department	Date

The Bhutan Epilepsy Project

Surname	Given Names	Role	Signature
Murray	Brian	Knowledge User	X
Institution	Faculty	Department	Date
Sunnybrook HSC Clinical Neurophysiology Laboratory	Medicine	Medicine	September 23 2014
Surname	Given Names	Role	Signature
Wennberg	Richard	Knowledge User	X
Institution	Faculty	Department	Date
Epilepsy Program, Toronto Western Hospital			

Law, Edith
University of Waterloo (Ontario)**Participants Signatures**

The participants are in the following order when applicable: Principal Knowledge User, Knowledge Users, Principal Applicant and Co-Applicants, Primary Supervisor and Supervisors.

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and hereby accepted by the participant(s).

Supervisor(s) Signatures (If applicable)

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and are hereby accepted by the applicant's supervisor(s).

The author(s) of the Summary of the Research Project included in the candidate's application also agree that it accurately describes the training program proposed.

Consent to Disclosure of Personal Information

I understand that maintaining public trust in the integrity of researchers is fundamental to building a knowledge-based society. By submitting this application or by accepting funding from CIHR, NSERC and/or SSHRC, I affirm that I have read and I agree to respect all the policies of these Agencies that are relevant to my research, including the *Tri-Council Policy Statement: Tri-Agency Framework: Responsible Conduct of Research* (<http://www.rcc.ethics.gc.ca/eng/policy-politique/framework-cadre/>). In cases of a serious breach of Agency policy, the Agency may publicly disclose my name, the nature of the breach, the institution where I was employed at the time of the breach and the institution where I am currently employed.

I accept this as a condition of applying for or receiving Agency funding and I consent to such disclosure.

Surname	Given Names	Role	Signature
Mateen	Farrah	Knowledge User	X
Institution	Faculty	Department	Date
The Bhutan Epilepsy Project			
Surname	Given Names	Role	Signature
Murray	Brian	Knowledge User	X
Institution	Faculty	Department	Date
Sunnybrook HSC Clinical Neurophysiology Laboratory			
Surname	Given Names	Role	Signature
Wennberg	Richard	Knowledge User	X <i>R. Wennberg</i>
Institution	Faculty	Department	Date
Epilepsy Program, Toronto Western Hospital	Medicine	Neurology	<i>26 SEPT 2014</i>

**Participants Signatures (Contd)**

The participants are in the following order when applicable: Principal Knowledge User, Knowledge Users, Principal Applicant and Co-Applicants, Primary Supervisor and Supervisors.

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and hereby accepted by the participant(s).

Supervisor(s) Signatures (If applicable)

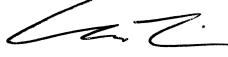
It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and are hereby accepted by the applicant's supervisor(s).

The author(s) of the Summary of the Research Project included in the candidate's application also agree that it accurately describes the training program proposed.

Consent to Disclosure of Personal Information

I understand that maintaining public trust in the integrity of researchers is fundamental to building a knowledge-based society. By submitting this application or by accepting funding from CIHR, NSERC and/or SSHRC, I affirm that I have read and I agree to respect all the policies of these Agencies that are relevant to my research, including the *Tri-Council Policy Statement: Tri-Agency Framework: Responsible Conduct of Research* (<http://www.rcr.ethics.gc.ca/eng/policy-politique/framework-cadre/>). In cases of a serious breach of Agency policy, the Agency may publicly disclose my name, the nature of the breach, the institution where I was employed at the time of the breach and the institution where I am currently employed.

I accept this as a condition of applying for or receiving Agency funding and I consent to such disclosure.

Surname	Given Names	Role	Signature
Lim	Andrew	Principal Applicant	X 
Institution	Faculty	Department	Date
Sunnybrook Research Institute (Toronto, Ontario)	Faculty of Medicine	Medicine/Neurology	September 23, 2014
Surname	Given Names	Role	Signature
Burneo	Jorge	Co-Applicant	X
Institution	Faculty	Department	Date
University of Western Ontario	Faculty of Medicine	Clinical Neurological Sciences	
Surname	Given Names	Role	Signature
Pineau	Joelle	Co-Applicant	X
Institution	Faculty	Department	Date
McGill University/Université McGill		Computer Science	

**Participants Signatures (Contd)**

The participants are in the following order when applicable: Principal Knowledge User, Knowledge Users, Principal Applicant and Co-Applicants, Primary Supervisor and Supervisors.

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and hereby accepted by the participant(s).

Supervisor(s) Signatures (If applicable)

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and are hereby accepted by the applicant's supervisor(s).

The author(s) of the Summary of the Research Project included in the candidate's application also agree that it accurately describes the training program proposed.

Consent to Disclosure of Personal Information

I understand that maintaining public trust in the integrity of researchers is fundamental to building a knowledge-based society. By submitting this application or by accepting funding from CIHR, NSERC and/or SSHRC, I affirm that I have read and I agree to respect all the policies of these Agencies that are relevant to my research, including the *Tri-Council Policy Statement: Tri-Agency Framework: Responsible Conduct of Research* (<http://www.rer.ethics.gc.ca/eng/policy-politique/framework-cadre/>). In cases of a serious breach of Agency policy, the Agency may publicly disclose my name, the nature of the breach, the institution where I was employed at the time of the breach and the institution where I am currently employed.

I accept this as a condition of applying for or receiving Agency funding and I consent to such disclosure.

Surname	Given Names	Role	Signature
Lim	Andrew	Principal Applicant	X
Institution	Faculty	Department	Date
Sunnybrook Research Institute (Toronto, Ontario)	Faculty of Medicine	Medicine/Neurology	
Surname	Given Names	Role	Signature
Burneo	Jorge	Co-Applicant	X
Institution	Faculty	Department	Date
University of Western Ontario	Faculty of Medicine	Clinical Neurological Sciences	Sep 24, 2014
Surname	Given Names	Role	Signature
Pineau	Joelle	Co-Applicant	X
Institution	Faculty	Department	Date
McGill University/Université McGill		Computer Science	

**Participants Signatures (Contd)**

The participants are in the following order when applicable: Principal Knowledge User, Knowledge Users, Principal Applicant and Co-Applicants, Primary Supervisor and Supervisors.

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and hereby accepted by the participant(s).

Supervisor(s) Signatures (If applicable)

It is agreed that the general conditions governing grants and awards, as well as the statement "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and are hereby accepted by the applicant's supervisor(s).

The author(s) of the Summary of the Research Project included in the candidate's application also agree that it accurately describes the training program proposed.

Consent to Disclosure of Personal Information

I understand that maintaining public trust in the integrity of researchers is fundamental to building a knowledge-based society. By submitting this application or by accepting funding from CIHR, NSERC and/or SSHRC, I affirm that I have read and I agree to respect all the policies of these Agencies that are relevant to my research, including the *Tri-Council Policy Statement: Tri-Agency Framework: Responsible Conduct of Research* (<http://www.rer.ethics.gc.ca/eng/policy-politique/framework-cadre/>). In cases of a serious breach of Agency policy, the Agency may publicly disclose my name, the nature of the breach, the institution where I was employed at the time of the breach and the institution where I am currently employed.

I accept this as a condition of applying for or receiving Agency funding and I consent to such disclosure.

Surname	Given Names	Role	Signature
Lim	Andrew	Principal Applicant	X
Institution	Faculty	Department	Date
Sunnybrook Research Institute (Toronto, Ontario)	Faculty of Medicine	Medicine/Neurology	
Surname	Given Names	Role	Signature
Burneo	Jorge	Co-Applicant	X
Institution	Faculty	Department	Date
University of Western Ontario	Faculty of Medicine	Clinical Neurological Sciences	
Surname	Given Names	Role	Signature
Pineau	Joelle	Co-Applicant	X
Institution	Faculty	Department	Date
McGill University/Université McGill		Computer Science	 September 23, 2014



Signature of Institution Paid

Institution Paid Signature

It is agreed that the general conditions governing Grants and Awards, as well as the statements "Meaning of Signatures on Application Forms" as outlined in the CIHR Grants and Awards Guide, apply to any grant or award made pursuant to this application and are hereby accepted by the applicant's institution or the applicant(s) employing Institution(s).

A signature is not required at institutions outside of Canada.

If both your Program and submitting institution are using the Electronic Approval Tool on ResearchNet, a signature is not required for block 1 if the Authorized Official can bind the institution to all obligations outlined in the "Meaning of Signatures on Application Forms". If the Authorized Official cannot bind the institution to all obligations in the "Meaning of Signatures on Application Forms", complete block 2.

1. Signature of Authorized Official: University of Waterloo (Ontario)

Print Name:	Date:
-------------	-------

Signature:

X

2. If the Authorized Official above cannot bind the institution to all obligations outlined in the "Meaning of Signatures on Application Forms", please provide additional signatures below as required.

Print Name:	Date:
-------------	-------

Signature:

X

Print Name:	Date:
-------------	-------

Signature:

X

Signature of Research Institution

Institution Signature at Primary Location of Research (Awards Programs Only)

It is agreed that the general conditions governing Grants and Awards, as well as the statements "Meaning of Signatures on Application Forms for the Authorized Official at the Primary Location of Research" (<http://www.cihr-irsc.gc.ca/e/22630.html#1-G3>) as outlined in the CIHR Grants and Awards Guide, apply to any award made pursuant to this application and are hereby accepted by the Nominated Principal Applicant's institution where the research is to be conducted.

Signature of Authorized Official:

University of Waterloo (Ontario)

Print Name:	Date:
-------------	-------

Signature:

X



Canadian Institutes
of Health Research

Instituts de recherche
en santé du Canada

**PROTECTED WHEN
COMPLETED**

Appl. #

Application Details

Funding Opportunity:

Operating Grant: Collaborative Health Research Projects (NSERC Partnered) – (2014-2015)
(2014-10-01)

Proposed Start Date:

Proposed End Date:

Applicant:

Surname Law Given Names Edith

Institution University of Waterloo (Ontario) Faculty Faculty of Mathematics Department Computer Science

Telephone 519-722-1858 Fax E-mail dr.edith.law@gmail.com

Title:

A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings

Primary location where research to be conducted: University of Waterloo (Ontario)

Faculty: Faculty of Mathematics Department: Computer Science

Institution which will administer project funds (Institution Paid):

University of Waterloo (Ontario)

Location of proposed Activity:

Period of support requested: 3 Year(s) Month(s)

THE FOLLOWING SECTIONS ARE NOT APPLICABLE TO ALL PROGRAMS**Budget section - Amounts Requested from CIHR in the First Full Year:**

Operating: 145607

Equipment: 0

Total Amount Requested: \$145607

New

Renewal

Funding Reference Number (FRN):

Is this application a resubmission of a previously unsuccessful new application?

Yes No

Is this application a resubmission of a previously unsuccessful renewal application?

Yes No FRN #:

Have you applied to this program in the last two years?

Yes No

Is this a multi-center study?

Yes No



Appl. #

Certification Requirements:

- Human subjects Human stem cells Animals Biohazards
- Environmental Impact Containment Level _____
- Clinical Trial
- Contains a randomized trial
- In order to carry out the proposed research in this application, an exemption from Health Canada under Section 56 of the Controlled Drugs and Substances Act is required. Should my application be approved, I understand that I will need to seek an exemption from Health Canada and provide this exemption to CIHR before any funding will be released for this application.

Other Project Information:

- For statistical purposes, does this application propose research involving Aboriginal people?
- Are sex (biological) considerations taken into account in this study?
- Are gender (socio-cultural) considerations taken into account in this study?

Please describe how sex and/or gender considerations will be considered in your research proposal:

We do not anticipate there to be sex or gender related differences in the human EEG recordings that would substantially impact our algorithms.

**Other Applicants**

Surname	Given Names	Role
Mateen	Farrah	Knowledge User
Institution The Bhutan Epilepsy Project	Department	Faculty
Surname	Given Names	Role
Murray	Brian	Knowledge User
Institution Sunnybrook HSC Clinical Neurophysiology Laboratory	Department	Faculty
Surname	Given Names	Role
Wennberg	Richard	Knowledge User
Institution Epilepsy Program, Toronto Western Hospital	Department	Faculty
Surname	Given Names	Role
Lim	Andrew	Principal Applicant
Institution Sunnybrook Research Institute (Toronto, Ontario)	Department Medicine/Neurology	Faculty Faculty of Medicine
Surname	Given Names	Role
Burneo	Jorge	Co-Applicant
Institution University of Western Ontario	Department Clinical Neurological Sciences	Faculty Faculty of Medicine
Surname	Given Names	Role
Institution	Department	Faculty
Surname	Given Names	Role
Institution	Department	Faculty
Surname	Given Names	Role
Institution	Department	Faculty

**Other Applicants**

Surname	Given Names	Role
Pineau	Joelle	Co-Applicant
Institution McGill University/Université McGill	Department Computer Science	Faculty

Surname	Given Names	Role
Institution	Department	Faculty

Surname	Given Names	Role
Institution	Department	Faculty

Surname	Given Names	Role
Institution	Department	Faculty

Surname	Given Names	Role
Institution	Department	Faculty

Surname	Given Names	Role
Institution	Department	Faculty

Surname	Given Names	Role
Institution	Department	Faculty

Surname	Given Names	Role
Institution	Department	Faculty

**Lay title of the research**

A combined machine-learning and crowdsourcing approach to analyzing human brain waves for the diagnosis of epilepsy and sleep disorders

Abstract suitable for preparation of a press release

Electroencephalography (EEG – the measurement of human brain activity using electrodes on the scalp) is a key tool in the diagnosis of epilepsy. It is also a key step in the diagnosis of sleep disorders. Right now, interpretation of EEGs is dependent on specialized neurologists. This limits access to EEG services in smaller communities. Even in large communities, the laborious nature of EEG interpretation and the heavy reliance on specialists imposes substantial costs on the health care system, and can delay diagnosis and treatment. Full automation of EEG interpretation could potentially address these issues. However, attempts to do so have had limited success, in part because some aspects of EEG interpretation such as visual pattern recognition, while relatively easy for trained human experts, are very difficult to automate. Human computing is a field of computer science that aims to combine automated algorithms with judicious application of human input into one framework to leverage the strengths of each while avoiding the limitations of either. Human computing has proven to be a powerful tool to solve many key problems in science that had proven intractable to standard artificial intelligence approaches. We propose to build a system combining state of the art machine learning algorithms and human computing approaches to enable rapid, scalable, accurate interpretation of human EEGs, while minimizing the dependence on experts. We will adapt this system for use in Canadian hospitals and also integrate it with a unique smartphone-based EEG recording device to enable EEG diagnosis in communities without local specialized neurologists. Benefits will include improved timeliness and accuracy of epilepsy and sleep disorder diagnosis, accompanied by reduced costs. For more remote regions in Canada and elsewhere, our smartphone-integrated device will provide local access to accurate and cost-efficient EEG diagnosis avoiding the need to travel to larger centers.

Project Descriptors *

electroencephalography, polysomnography, human computing, machine learning, epilepsy, sleep disorders, mobile devices, telemedicine

Areas of Research *

Primary
NERVOUS SYSTEM

Secondary
HEALTH RESEARCH

Classification Codes *

Primary
EPILEPSY

Secondary
SLEEP DISORDERS

Themes *

1st Clinical

2nd Health systems/services

3rd

4th

Categories *

1st Neurosciences, Mental Health and Addiction

2nd

3rd

4th

Collaborative Health Research Projects (NSERC partnered)/Programme de projets de recherche concertée sur la santé (en partenariat avec le CRSNG) Application/Demande 2014-10-01

Summary of Research Proposal/Résumé de la proposition de recherche

Electroencephalography (EEG – the measurement of human brain activity using electrodes placed on the scalp) is a key tool in the diagnosis of epilepsy and coma. It is also a key component of polysomnography, which is used to diagnose sleep disorders. In current practice, EEG recordings are visually analyzed by specialized physicians. However, this is labour intensive, time consuming, and dependent on the availability of highly trained specialists. This limits the availability of EEG interpretation in rural and remote regions, a significant issue in a country as geographically dispersed as Canada. Even in resource-rich settings such as academic health centres, scarcity of specialist time can lead to delays of hours-days before records are fully analyzed, delaying diagnosis and treatment. Thus, there is a pressing need for scalable, cost-efficient, accurate EEG interpretation that is not heavily dependent on a limited number of highly trained specialists.

These limitations have motivated efforts to develop fully automated algorithms for the interpretation of EEG signals. Unfortunately, these approaches have had limited success, in part because many aspects of EEG interpretation are fundamentally image classification problems that while straightforward for trained humans, are difficult to fully automate. The field of micro-task human computing has developed to address such problems where humans may have some advantages over purely automated approaches. In this paradigm, problems are decomposed into a massive number of very simple, carefully designed, human micro-tasks to be carried out by an array of “human processors” whose answers can be combined with automated algorithms to solve the original problem. This maximizes the advantages of both humans and computers in one algorithm, overcoming the limitations of either.

The overall goal of this project is to design a framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings in both resource-rich and resource-poor health care settings, overcoming the limitations of human visual analysis. In compelling preliminary data, we show the successful application of micro-task human computing to a series of otherwise computationally intractable problems including classifying, locating and describing specific features in scientific images and time series data. Building on these platforms, interfaces and algorithms, and in collaboration with our technology user organizations the Bhutan Epilepsy Project, the Epilepsy Program at the Toronto Western Hospital, and the Clinical Neurophysiology Laboratory at Sunnybrook Health Sciences Centre, we propose to achieve the following aims: 1) Develop a general set of algorithms to decompose EEG analysis into micro-tasks, and integrate the responses of non-expert and expert human processors with automated algorithms to solve EEG-related clinical problems. 2) Develop and validate a general framework to compare these algorithms against fully automated approaches and against human specialist analyses, and an iterative approach to improve these algorithms. 3) Apply the algorithms to the interpretation of clinical EEGs from Canadian hospitals for the diagnosis of epilepsy, coma, and sleep disorders. 4) Integrate these algorithms with a smartphone-based EEG recording device developed by the Bhutan Epilepsy Project to allow recording and interpretation of EEGs in remote settings.

By broadly exploring how to efficiently and accurately apply hybrid human and machine analysis to physiologic time series data in general, and human EEG signals in particular, this work will challenge the status quo of EEG visual analysis and raise interesting questions at the intersection of artificial intelligence and human-computer interaction on how to effectively combine humans and machines to tackle a difficult classification problem.

The end result will be two prototype systems – one for conventional EEG data from large Canadian hospitals, and one integrated with the smartphone EEG recording system developed by the Bhutan Epilepsy Project for use in rural and remote settings by health care professionals without EEG training. For Canadian hospitals, the benefits will include improved robustness, speed, and efficiency of EEG interpretation, resulting in more timely and accurate diagnosis of seizures, epilepsy, and sleep disorders and more efficient utilization of scarce specialist resources. For more remote regions in Canada and internationally, the integrated smartphone-based version will provide access to accurate, scalable, and cost- and time-efficient EEG diagnosis with minimal need for EEG technicians or specialists.

Law, Edith

Collaborative Health Research Projects (NSERC partnered)/Programme de projets de recherche concertée sur la santé (en partenariat avec le CRSNG) Application/Demande 2014-10-01
Lay abstract/Résumé non scientifique

Electroencephalography (EEG – the measurement of human brain activity using electrodes on the scalp) is a key tool in the diagnosis of epilepsy. It is also a key step in the diagnosis of sleep disorders. Right now, interpretation of EEGs is dependent on specialized neurologists. This limits access to EEG services in smaller communities. Even in large communities, the laborious nature of EEG interpretation and the heavy reliance on specialists imposes substantial costs on the health care system, and can delay diagnosis and treatment. Full automation of EEG interpretation could potentially address these issues. However, attempts to do so have had limited success, in part because some aspects of EEG interpretation such as visual pattern recognition, while relatively easy for trained human experts, are very difficult to automate. Human computing is a field of computer science that aims to combine automated algorithms with judicious application of human input into one framework to leverage the strengths of each while avoiding the limitations of either. Human computing has proven to be a powerful tool to solve many key problems in science that had proven intractable to standard artificial intelligence approaches. We propose to build a system combining state of the art machine learning algorithms and human computing approaches to enable rapid, scalable, accurate interpretation of human EEGs, while minimizing the dependence on experts. We will adapt this system for use in Canadian hospitals and also integrate it with a unique smartphone-based EEG recording device to enable EEG diagnosis in communities without local specialized neurologists. Benefits will include improved timeliness and accuracy of epilepsy and sleep disorder diagnosis, accompanied by reduced costs. For more remote regions in Canada and elsewhere, our smartphone-integrated device will provide local access to accurate and cost-efficient EEG diagnosis avoiding the need to travel to larger centers.

A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings

1 Aims

Electroencephalography (EEG) is a key tool in the diagnosis of epilepsy and sleep disorders. In current practice, EEG recordings are visually analyzed by specialist technicians and physicians. However, this is a slow process and dependent on the availability of these expert annotators. This limits EEG as a diagnostic medical tool in smaller communities. Even in larger centers, the time consuming nature of human EEG analysis can lead to backlogs and significant delays in diagnosis and treatment. Thus, there is a need for rapid, scalable, cost-efficient, accurate EEG interpretation that is not heavily dependent on the time of highly trained specialists.

These limitations have motivated efforts to develop fully automated algorithms for the interpretation of human EEG signals. Unfortunately, to date, these approaches have had limited success, in part because many aspects of EEG interpretation are fundamentally image classification problems that while straightforward for trained humans, are difficult to fully automate. The field of human computation developed to address such problems where humans may have some advantages over pure automation. In this paradigm, problems are decomposed into a massive number of very simple, carefully designed, human micro-tasks to be carried out by an array of “human processors,” whose answers can be combined with automated algorithms to solve the original problem. This maximizes the advantages of both humans and computers in one algorithm, overcoming the limitations of either.

The overall goal of this project is to design a framework for hybrid machine and human computation to achieve accurate and scalable analysis of human clinical EEG recordings in both resource-rich and resource-poor health settings. In collaboration with our knowledge organizations the Bhutan Epilepsy Project, the Epilepsy Program at the Toronto Western Hospital, and the Clinical Neurophysiology Laboratory at Sunnybrook Health Sciences Centre, we propose to achieve the following scientific and translational (i.e., knowledge transfer to hospitals and industry partners) aims:

Scientific Aim 1. Develop a general set of algorithms to decompose EEG analysis into micro-tasks, and integrate the responses of non-expert and expert human processors with automated algorithms to solve EEG-related clinical problems.

Scientific Aim 2. Develop a general framework to compare these algorithms against fully automated approaches and specialist analyses, and an iterative approach to improve these algorithms.

Translational Aim 1. Apply the algorithms to the interpretation of clinical EEGs from Canadian hospitals.

Translational Aim 2. Integrate these algorithms with a EEG smartphone-based recording device developed by the Bhutan Epilepsy Project to allow recording and interpretation of EEGs in remote settings.

The outcomes of this work will include two prototype systems freely available for general use by health care organizations – one for analyzing conventional EEG data from large Canadian hospitals, and one integrated with the smartphone EEG recording system developed by the Bhutan Epilepsy Project for use in rural and remote settings by health care professionals (e.g., nurses) without EEG training. For Canadian hospitals, the benefits will include improved robustness, speed, and efficiency of EEG interpretation, resulting in more timely and accurate diagnosis of epilepsy, sleep disorders and other neurological conditions, as well as more efficient utilization of scarce specialist resources. For more remote regions in Canada and internationally, the integrated smartphone-based version will provide access to accurate, scalable, cost- and time-efficient local EEG diagnosis, with minimal need for outside EEG specialists.

2 Background

2.1 EEG Analysis

Electroencephalography is a key neurological test used in many clinical contexts [18, 20]. Routine 20min EEGs (rEEG) are used in both inpatient and outpatient settings to diagnose epilepsy and other neurological conditions. Longer continuous EEGs (cEEG) recorded 24hr a day are used in inpatient epilepsy monitoring units (EMUs) to characterize seizures in patients with epilepsy, and in intensive care units (ICUs) for real-time detection of seizures and neurological deterioration. In the context of polysomnograms (PSGs), 8hr sleep EEGs (sEEG) are used to quantify sleep architecture and diagnose sleep disorders.

There are four main tasks in EEG interpretation (see Figure 3–8): 1) characterizing dominant frequencies, 2) identifying normal features such as K-complexes, sleep spindles etc, 3) using these features to classify segments of the EEG into normal (W, N1, N2, N3, R) or abnormal (e.g. encephalopathy) states, and 4) identifying discrete pathological features, notably interictal epileptiform discharges (IEDs; brief, often <200ms discharges of characteristic morphology) and seizures (runs of abnormal rhythmic brain activity lasting seconds to minutes which can cause loss of consciousness and other neurological symptoms).

Challenges in EEG interpretation include the need to identify relatively brief and rare features (e.g. a single <200ms IED in a 24-hour recording), the presence of signal noise and artifact that can mask or imitate pathological features, the similarity between normal (e.g. vertex waves) and pathological (e.g. IEDs) features, and the desirability in some contexts (e.g. cEEG in the ICU) for near-real-time identification of abnormalities that may indicate neurological deterioration warranting prompt clinical action.

In current practice, specialized technicians and neurologists visually examine EEGs and report their findings. This has several drawbacks. The dependence on large amounts of specialist time (e.g. interpreting 24 hours of cEEG can take 3 hours of technician and 1 hour of neurologist time) limits EEG analysis to centers with these specialists, limits the number of EEGs performed, drives up costs, can delay diagnosis, and takes specialists away from other clinically vital tasks. Meanwhile, the subjective nature of visual analysis leads to inter-rater variability, making it difficult to compare records interpreted by different physicians. Finally, the “needle in a haystack” nature of EEG analysis makes it prone to lapses in attention.

These limitations have led to a desire for automated approaches to EEG analysis. Seizure detection has attracted particular interest, and many automated algorithms [11, 3, 10, 21] have been developed for this purpose. The complexity in creating automated algorithms comes from multiple factors. First, the mechanisms underlying seizure generation are not well understood, resulting in feature engineering challenges. Second, EEG recordings are made from small electrodes that capture a noisy state of the brain activity at a particular location. The electrode placement may not be optimal, yielding weak signals, and the origin of the seizure may be difficult to determine from the ambiguous data. Third, the relatively low rate of occurrence of seizures and their short duration, compared to the amount of between seizures data, makes the EEG recordings highly unbalanced, posing challenges to most standard machine learning algorithms. An automated seizure detection system must address all these challenges in order to be effective.

Another EEG analysis task that has attracted interest is that of identifying normal features such as sleep spindles, and integrating this information into a segment-by-segment classification of behavioral state. Unfortunately, automated algorithms for the detection of specific normal features (e.g. spindles) perform quite poorly compared to human experts, even when relatively artifact-free recordings are used [17]. Meanwhile, automated approaches to segment-by-segment EEG state classification based on frequency analysis have shown some success when applied to relatively artifact-free datasets from healthy individuals or laboratory animals [8, 1], but have not been tested or proven in populations with a high prevalence of neurological diseases or sleep disorders – the individuals most likely to require EEGs.

2.2 Human Computation

EEG interpretation is an example of a larger class of problems that are trivial for human experts but hard for pure artificial-intelligence (AI) systems. A new field of computer science, *human computation* [7], emerged around the idea of harnessing human intelligence to improve upon automated algorithms. In this paradigm, complex tasks (e.g. image classification) are decomposed into many micro-tasks (e.g. identifying shape, color), each of which may take seconds. Micro-tasks amenable to AI are performed by machines, while those that are not are performed by humans. The output of various micro-tasks is then aggregated to solve the original problem. Two key insights underlie human computation. First, by combining AI algorithms with human input, hybrid systems capture the strengths of both while avoiding the weaknesses of either. Second, by efficiently integrating the input of many non-experts and augmenting this with AI algorithms, the accuracy of groups of non-experts can approach or exceed that of experts.

Human computation has been used to solve a host of scientific problems that had proven intractable to pure AI methods, including protein folding [5], object recognition [12, 19], and machine translation [13]. Examples of human computation systems include crowdsourcing marketplaces (e.g., Amazon Mechanical Turk [9]) where workers perform micro-tasks for payment, games with a purpose [15, 6, 14] that generate useful data through gameplay, identity verification systems, e.g., reCAPTCHA [16], which digitize books through billions of users performing computation (e.g. transcribing words) for access to online content. Human computation approaches have been successfully applied to the analysis of some forms of clinical time series data. Zhu et al, in collaboration with China Mobile, have implemented a human computing platform for electrocardiogram (ECG) interpretation for a leading cardiac hospital in Beijing [23]. By efficiently decomposing the task of ECG interpretation and integrating the input of multiple experts using a Bayesian framework, substantial improvement in accuracy is achieved [22].

Most recently, in a paper in *Nature Medicine*, Warby et al [17] applied human computation to the detection of sleep spindles in human EEGs. In their system, the aggregate performance of groups of non-experts exceeded that of even the best automated algorithms, and approached that of trained experts. Moreover, they showed that aggregating the input of groups of experts resulted in performance superior to any single expert. While this work concerns only sleep spindles, it demonstrates the potential superiority of human computation approaches compared to fully automated approaches for EEG feature detection. It also suggests that a carefully designed system combining human computation and automated algorithms for the detection of EEG features may achieve the accuracy of a trained expert, with minimal expert input.

3 Progress to Date

A core component of any hybrid human-machine computing system is a platform to decompose complex tasks into micro-tasks, dynamically delegate these tasks to non-experts, experts, and automated algorithms, and reintegrate their results. PI Edith Law has developed such a platform. The Curio project (Figure 2) is a general platform designed to allow scientists to apply human computation approaches to data processing tasks not easily amenable to pure AI approaches. It includes mechanisms for task decomposition, task delegation and result visualization. In collaboration with co-I Andrew Lim, Dr. Law has begun to adapt the interfaces and algorithms on the Curio platform to handle clinical EEG data.

Co-I Joelle Pineau has previously developed a machine learning toolkit for automating the various phases of building a personalized epileptic seizure detection algorithm. It provides a pool of features and parameterizations, a feature selection module that tailors algorithms to specific patients, high-level machine learning classifiers for detecting seizure events, and a new dataset containing EEG recordings from rats with epilepsy. Our research will further develop ideas on how these algorithms can be combined with human annotations to achieve better performance.

4 Research Plan

4.1 Sources of Clinical Data

Our goal is to design a framework for hybrid machine and human computation for the analysis of human clinical EEGs. Toward this end, we will leverage clinical EEG data from our knowledge organizations:

- 1) The Toronto Western Hospital / University Health Network (UHN) epilepsy program is one of the largest in Ontario, with over 1000 patient-visits per year. A key component is the clinical neurophysiology laboratory and associated inpatient epilepsy monitoring unit. The laboratory performs over 12,500 rEEGs and obtains over 84,000 hours of cEEG recording per year, and has an archived database of over 30,500 rEEGs, and over 680,000 hours of cEEG, all with expert annotation. This will provide fully annotated normal and abnormal rEEG and cEEG recordings from across the clinical spectrum.
- 2) The Sunnybrook Clinical Neurophysiology Laboratory is a major clinical neurophysiology site located at Sunnybrook Health Sciences Centre, a leading Canadian teaching hospital. The laboratory performs over 1300 rEEGs and nearly 1500 sEEGs per year, and has a database of over 6500 sEEGs and 4300 rEEGs. This will give us access to normal and abnormal sEEGs from across the clinical spectrum, as well as an independent set of rEEGs
- 3) The Bhutan Epilepsy Project is a non-governmental multi-national organization that is developing a smartphone-based portable EEG recording device to enable low-cost EEG recordings in remote regions with minimal specialist expertise. The Project is testing prototype devices in Bhutan and is amassing a collection of 200 recordings, to compare with 200 recordings from a conventional EEG device. We will have access to both sets of recordings, enabling us to compare the performance of our algorithms across recording platforms, and to adapt our framework to more resource-limited settings.

4.2 Aim 1: Methodology

Our first aim is to develop a general set of algorithms to decompose clinical EEG analysis into micro-tasks, and coordinate input from experts, non-experts and automated algorithms. We will develop a **first-pass filter approach** whereby each record is analyzed first by automated algorithms. Selected epochs will be passed to non-experts for additional semantic feature annotation. We will then combine the automatically extracted features and features identified by non-experts to generate a classifier. Uncertainty scores from this classifier will determine specific epochs or features to send to experts for further processing.

We aim to develop machine learning algorithms for combining expert labels, features detected by non-experts and automated algorithms, with a particular interest towards algorithms that can provide confidence estimates. Ensemble methods [4], for example, compute confidence based on agreement between multiple classifiers trained on the same data. Co-training [2], on the other hand, derives confidence from the same classifier trained on two different sets of features which are assumed to be conditionally independent given the class label, such as automatically extracted EEG features versus semantic EEG features (e.g. presence and absence of sleep spindles) scored by human annotators. This semi-supervised technique has the added advantage of requiring only a small number of labeled examples from experts to begin with; the algorithm will iteratively add more labeled examples if the two classifiers agree.

We describe here our proposed methodology for integrating automated algorithms, non-expert input, and expert input to solve each of the key tasks in EEG interpretation described in section 2.1.

Frequency Analysis. A key first step in EEG interpretation is the characterization of segment-by-segment dominant frequencies, which can influence how the discrete features identified in the other tasks are interpreted. We propose to fully automate this using standard signal analysis techniques e.g. Fourier analysis.

Identification of Normal Features. The normal EEG is characterized not only by background rhythmic activity, but also by discrete morphological features that define the normal five behavioral states (W, N1, N2, N3, and R) and whose absence may be indicative of an abnormal state (e.g. encephalopathy). We will apply a first pass filter approach here. Initially, machine algorithms will be used to identify the presence of various normal features in 30s epochs. Because these features are common, these algorithms will be biased toward specificity, rather than sensitivity. Where features are detected with high confidence, no further human input will be needed. Epochs with features detected at lower confidence, or epochs with no features detected, will be sent to non-experts for additional feature detection, based on characteristics which will be selected in consultation with Co-I Andrew Lim and knowledge user Brian Murray (both neurologists with board certification in sleep EEG interpretation). Others [17] have shown that, in principle, many such features can be confidently identified by non-experts.

Epoch-By-Epoch Classification of Behavioral State. Automated algorithms will combine information from the background frequency analyses, automated feature detection, and non-expert feature detection, to arrive at a classification of the behavioral state for each non-overlapping 30s epoch of the EEG. For most epochs, these features will be concordant and a classification will be made without expert intervention. For ambiguous epochs, experts will be provided with a visualization of a combination of automatic and non-expert annotations along with the uncertainty of their labels, to arrive at a final classification.

Identification of Abnormal Features. The next task is identification of abnormal discrete features, especially IEDs and seizures, as described in 2.1. As above, we will use a first-pass filter approach. Automated algorithms developed by Co-I Joelle Pineau, as described in section 3 above, will first be deployed to prune the record. These will be biased toward high sensitivity to ensure that no features are missed. Then, the remaining portions of the record will be sent to available non-experts (e.g. nursing staff) to evaluate for specific characteristics, which will be selected in consultation with Co-I Andrew Lim and knowledge user Richard Wennberg (both neurologists with board certification in EEG interpretation). These characteristics may include, as an example, the “sharpness” of a discharge or the extent of “evolution” of a run of rhythmic activity identified by an automated algorithm. The input from non-experts and the automated algorithms will then be integrated to create a confidence score for each feature. Features identified with high confidence and concordance may be classified at this stage. Features that are identified with lower confidence or some discordance will then be sent to experts for disambiguation. The benefit of inserting a layer of non-experts between the algorithms and the experts is that many algorithm misclassifications may be easily *corrected* by available non-expert readers without expert intervention. This is particularly important because in many situations (e.g. overnight care, or in smaller communities) non-experts such as nurses may be available, but EEG trained neurologists may not.

Generation of Final Narrative Report. The final output of our framework will be an automatically generated table, based on automated algorithms and non-expert input, with or without additional expert input, indicating the presence/duration of abnormalities or behavioral state, and the presence/timing of discrete abnormalities such as seizures and interictal discharges. This narrative report, along with a fully annotated record, will be provided to the expert (if available) for further analysis and reporting.

4.3 Aim 2: Methodology

The first-pass filter approach developed in Aim 1 will generate an initial set of algorithms and interfaces that will enable a combination of automated algorithms and non-experts to handle a large proportion of most records, routing only ambiguous pages and features to experts. Aim 2 is to develop and validate an **iterative refinement process** to improve these algorithms over time, and increase the proportion of the overall workload that can be handled by the combination of automated algorithms and non-experts.

First, this approach will include algorithms and interfaces to iteratively evaluate and improve the performance of non-experts, experts and automated algorithms. For example, when a non-expert differs from the group consensus or from an expert, the system will present corrective feedback to facilitate improvement. Using the same ground truth data, the accuracy of each non-expert can be re-assessed and recorded, allowing the system to personalize their training. Likewise, experts can improve over time as they are provided with more robust visual aids displaying the crowdsourced features, and the automated algorithms can improve over time due to the addition of training data from experts or the non-expert crowd. Second, a similar iterative refinement approach will be applied to the framework as a whole. As the reliability of non-experts and automated algorithms improves, other algorithms will monitor and re-weigh these different sources of contributions, slowly moving toward a decreasing reliance on human expert input.

To validate the iterative refinement approach, we will engage a group of non-experts and experts in a month-long experiment to evaluate the accuracy and efficiency of each of the components over time, and how the adaptive combination of these components impacts the accuracy of the overall classification and the distribution of the workload.

4.4 Translational Aim 1: Methodology

Translational Aim 1 is to apply our framework to the interpretation of a wide variety of clinical EEGs (rEEG, cEEG, sEEGs) from Canadian hospitals. We will develop an interface between the EEG recording software and our system to allow recordings from consecutive consenting patients (stripped of all personal health information) to be uploaded to a central server in real-time. There, the interpretation of the record will be parsed into micro tasks as described in Aims 1 and 2 above, and distributed to automated algorithms, as well as to non-experts and experts via a web application which can be accessed on participants' own time and from their own locations. For experts, we will use the physicians and technicians at the Toronto Western Hospital Epilepsy Program and the Sunnybrook Health Sciences Centre Clinical Neurophysiology lab, as well as co-I Andrew Lim and a technician from his laboratory, who will provide an independent source of expert annotations. For non-experts, we will use two sources: 1) paid crowdworkers through Amazon Mechanical Turk (as used by [17] in their study of sleep spindle detection) or paid CS undergraduates at the University of Waterloo. All records will also be annotated by experts at the recording site as per the usual clinical workflow to generate gold standard annotations. To ensure that we capture an unbiased representation of EEGs at our knowledge user sites, we will study consecutive recordings, without pre-selecting based on neurological diagnosis, patient features, or recording equipment.

As described in section 5.2, this process will begin with an in-depth needs assessment during which the computer science (CS) team from Dr. Law's lab will embed themselves within the clinical teams at TWH and Sunnybrook to observe the current process of EEG interpretation, identify gaps, and identify key attributes of successful solutions. We will also conduct formal focus groups to allow technicians and neurologists to share perceived problems and solutions with the CS team. Then, as the framework and interfaces are being developed, there will be monthly site visits, during which the technicians and neurologists will use and provide feedback on the latest iterations of the prototype, to ensure a seamless interface between the end users, the clinical workflows, and our system.

To evaluate our approach, we will compare it to standard expert visual analysis. Efficiency criteria will include person-hours of human input needed per recording and at each level of training (non-expert vs. technician vs. neurologist). We will also assess total time to interpretation. For accuracy, we will assess concordance with the expert read on a number of levels - e.g. on the whole record level (e.g. seizure or not anywhere in the recording), on the page-by-page level (e.g. proportion of pages correctly classified as epileptiform or not) or on a feature-by-feature level (e.g. detection of individual IEDs or seizures).

4.5 Translational Aim 2: Methodology

The Bhutan Epilepsy Project (www.bhutanbrain.com) is a new multi-national venture, funded in part by the Government of Canada through the *Grand Challenges Canada* program, developing and evaluating a portable EEG device to allow EEG recordings in rural and remote settings without specialized technicians or neurologists. The focus is initially on Bhutan, as an archetypical under-resourced health care setting, but once validated the developed platform may be applicable to rural/remote settings elsewhere including in geographically dispersed industrialized countries such as Canada. Several prototypes (as seen in Figure 1) have been produced and are being tested in Bhutan. They use an open-source software design, and are compatible with existing mobile devices. The devices cost 250-300 dollars per unit.

The existing prototype device facilitates one aspect of EEG-based diagnostic services in remote settings - obtaining the recordings. However, the system is still reliant on transmitting the recorded data to outside specialists for interpretation. We propose to adapt the human computation framework developed in aims 1 and 2 to a mobile computing setting centered on the smartphone-based recording device developed by the Bhutan Epilepsy Project. This will allow not only recording, but also interpretation of EEGs to occur using available local health care workers, minimizing the need for outside experts. The proposed workflow would depend on the availability of a local internet connection. Where a connection is available, the EEG would be captured using the smartphone-based device and transmitted to our central server in real-time with task decomposition and delegation proceeding as described in section 4.2 above, with local health workers constituting a source of non-experts. Where a connection is not available, algorithms on the recording smartphone itself would begin the process of task decomposition and delegation. Micro-tasks delegated to non-experts could be assigned to local personnel (e.g. local health care workers) for completion right on the recording smartphone, or nearby smartphones communicating wirelessly with the recording smartphone. The input of the local non-experts and algorithms running locally would then be integrated, and the goal is that a substantial proportion of most records could be correctly interpreted using local resources alone. Rare ambiguous features would be flagged. These annotations could be transmitted from the smartphone to remote experts once the phone could be brought within range of an internet connection to complete the interpretative process. Finally, we will apply an iterative refinement process described in section 4.2 to the smartphone based platform in remote settings in the same way as for the hospital based setting. In addition to improving our algorithms, this would have the additional advantage of iteratively improving the performance of local health care workers at EEG interpretation.

Overall, we anticipate several potential advantages of our approach compared to the current reliance on outside experts to read EEGs recorded in remote communities. These include 1) development of the capacity to interpret many if not most EEGs locally using a combination of automated algorithms and local health care workers, 2) gradual improvement of the EEG interpreting capabilities of local workers through the iterative refinement process described in Aim 2, 3) minimization of the need for expert input, meaning that one expert could potentially support EEG interpretation in many communities, 4) allowing for “micro-volunteering” where many experts can contribute meaningfully to EEG interpretation in remote communities one micro task at a time.

4.6 Innovative Aspects

Several key innovative aspects separate this proposal from past attempts to automate EEG interpretation:

Hybrid Human-Machine Computation. To our knowledge, this will be the first application of cutting edge hybrid algorithms to the problem of EEG interpretation. This promises to capture many of the advantages of full automation (speed, efficiency, consistency) while overcoming its disadvantages (difficulty

with ambiguous cases and more subtle pattern recognition tasks).

Task Decomposition. Careful task decomposition carries many advantages, even if all key steps are performed by human processors without automated algorithms. These include the capacity for massive parallel processing resulting in more rapid turnaround, and the ability to engage large communities of potential contributors while requiring minimal input from each individual.

Mobile Computing Environment. Previous attempts at automated EEG interpretation have been targeted toward hospital-based EEG labs, making them poorly suited to resource-poor settings, such as in remote/rural regions of Canada. While the Bhutan Epilepsy Project has developed the hardware to enable EEG recording in remote settings, our work tackles the software and algorithmic aspects needed for a truly scalable and portable solution to the problem of EEG interpretation in such settings.

4.7 Potential Difficulties and Feasibility

Several key attributes enhance the feasibility of this proposal:

Leveraging Existing Datasets and Frameworks. Through our partners, we have access to a truly vast database, ensuring that algorithm development will not be delayed by slow prospective data acquisition. Moreover, development of web-based interfaces on Curio for crowdsourcing time series data annotation is largely complete, allowing us to focus on algorithm development and integration with clinical workflows.

Existing Evidence of Non-Expert Engagement. There already exist pilot projects for training nurses to watch cEEG recordings, and have them call/page a specialist physician when they see something they think is a seizure. The Bhutan Epilepsy Project itself has seen overwhelming support from the local hospital teams, who are not trained in EEG analysis, but nonetheless are willing to help.

Accuracy of Non-Experts and Automated Algorithms. The reliance on non-experts and automated algorithms may introduce bias, or result in missed features. We will address this by continuously comparing the performance of algorithms, non-experts and experts performing the same tasks, and assigning to experts tasks that are consistently poorly performed by non-experts or algorithms, and adaptively flagging or down-weighting poorly-performing non-experts or algorithms.

4.8 Description of Roles

Investigators. As the lead PI and a world expert in human computation, Edith Law will have the overall responsibility of the project and will lead a team of 2 PhD students and 1 MSc student to adapt the time series component of the Curio platform for clinical purposes. She will develop the human computation techniques, including algorithms for routing tasks and aggregating responses, as well as interfaces for non-expert annotations and training. As a board certified neurologist with specialty certification in interpreting EEGs and PSGs, co-I Andrew Lim will provide detailed input into the design of the task decomposition and integration frameworks. He and his technician will coordinate data transfer between the various study sites, and provide an independent source of expert annotations. As an expert in machine learning, Joelle Pineau will be responsible for the development and adaptation of algorithms for seizure detection. She will supervise 1 Ph.D. student (50% time) to extend her existing seizure detection toolbox for this project, and provide support for integration with Curio. As a senior researcher, she will also provide guidance on managing the project. As a neurologist and epidemiologist with expertise in designing and evaluating systems of epilepsy care, co-I Jorge Burneo will play a key role in guiding integration of our technology in the context of epilepsy care, and in evaluating the effectiveness and usability of our tools.

Knowledge Users. Brian Murray, Richard Wennberg, and Farrah Mateen will play key roles in the integrated KT process (see section 5.2) on behalf of the Sunnybrook Clinical Neurophysiology Laboratory, TWH Epilepsy Program, and Bhutan Epilepsy Project, respectively.

5 Impact

5.1 Impact on the Health and Economic Well-Being of Canadians

Approximately 250,000 Canadians, suffer from epilepsy [18]. Meanwhile, the prevalence of sleep apnea, the most common sleep disorder, has been estimated at ~2-4% in adults [20]. EEG is key to the diagnosis of epilepsy, sleep disorders, and other neurological diseases. A large center such as the Toronto Western Hospital can perform over 12,500 EEGs annually. EEG and other tests for epilepsy are estimated to account for > 21% of the direct costs of caring for epilepsy patients [18]. Visual interpretation of EEG by trained specialists has the drawbacks of being slow, costly, and inefficient. Furthermore, these drawbacks make it difficult to provide EEG-based diagnostics in smaller communities in Canada and internationally.

Our project will address these needs by producing two prototype systems - one for conventional EEG data from large Canadian hospitals, and one integrated with the smartphone EEG recording system developed by the Bhutan Epilepsy Project for use in rural and remote settings by healthcare professionals without EEG training. For **large Canadian hospitals**, there will be several benefits: 1) Timeliness. The use of automated algorithms to prune EEG records will reduce the human input needed to review each record. Meanwhile, careful task decomposition may allow much of the required human input to be provided by available non-EEG trained health care workers. Specialists may be called upon to provide input only on ambiguous cases, thus allowing a large proportion of records to be screened in near real-time without specialist input. 2) Accuracy. By decreasing the hours of recording requiring human review, and allowing for parallel review of ambiguous features by multiple experts, the proposed system will minimize errors due to lapses in vigilance, and improve accuracy especially in ambiguous cases. 3) Cost Efficiency. Specialist labour is the main cost associated with EEGs. By decreasing the need for this, our system should decrease EEG costs. 4) Capacity. By decreasing the amount of specialist labour needed to interpret each EEG, a single specialist will be able to review a much larger number of EEGs. For **smaller Canadian communities** the overriding benefit will be the capacity to obtain EEG recordings locally without transferring patients or relying on outside experts, reducing costs, and allowing more rapid diagnosis and treatment.

5.2 Integrated Knowledge Translation Plan

The UHN/TWH Epilepsy Program, the Sunnybrook Clinical Neurophysiology Laboratory, and the Bhutan Epilepsy Project will be deeply involved in every stage of the knowledge translation process.

Needs Assessment. One of the first activities will be for the computer science (CS) team from Dr. Law's lab to embed for several days within the clinical services of the UHN/TWH Epilepsy Program and the Sunnybrook Clinical Neurophysiology Laboratory. In addition to observing the process of recording and interpreting EEGs, hence gaining familiarity with the nature of the data and the challenges of EEG interpretation, they will also follow the neurologists as they treat patients. This will allow the CS team to appreciate the potential real-world clinical impact of faster, more accurate, and more efficient EEG diagnosis. We will also facilitate a series of structured "focus group" sessions between the CS team and the TWH and Sunnybrook EEG staff to more formally assess gaps in the current model of EEG interpretation.

Iterative Development of Technology. Our partners will be deeply integrated into the development process. They will host monthly visits during which they will be able to test and provide feedback on the prototype. The CS team will formally observe the technicians and neurologists interacting with the soft-

ware, and iterate the interface. The TWH and Sunnybrook clinical teams will play a key role in ensuring that our technology is seamlessly integrated into the standard clinical workflow. A similar process of monthly meetings by Skype will occur with the Bhutan Epilepsy Project's front-line workers.

Technology Evaluation. Our partners will play a key role in evaluating the technology. Working closely with Dr. Burneo, the clinical teams at TWH and Sunnybrook will develop and measure clinically relevant benchmarks for accuracy, efficiency, and acceptability while comparing our prototype system with standard visual analysis. Meanwhile, under the auspices of the Bhutan Epilepsy Project, we will formally test the smartphone prototype in the field in Bhutan, evaluating not only accuracy and efficiency, but also acceptability to health care professionals in a resource-limited setting. Drs. Pineau and Law will disseminate these results to the CS community through conference presentations and publications in CS journals, while Drs. Burneo, Lim, Wennberg, Murray, and Mateen will do the same in relevant neurology conferences and publications.

Post-Development Dissemination. Our knowledge users are key to our post-development dissemination plan. The Sunnybrook and TWH programs are located at key academic hospitals in Ontario with a tradition of IT leadership. In addition to integrating our technology into their own programs, serving as an example for other centers, they play a key role in training the next generation of technicians and neurologists, who can serve as ambassadors for the technology at their future employers. Having demonstrated the feasibility of our prototype technology in real world settings in Canadian hospitals and in the field in Bhutan, we anticipate the next stage will be to work with colleagues in health care informatics and software engineering to develop a privacy compliant version of the prototype stably and well integrated into widely used health care informatics systems. While this is being done, our knowledge users will continue to play an important role in building clinical acceptance for the technology. Drs. Wennberg and Burneo are deeply involved with the Canadian League Against Epilepsy as past-president and executive chair for education and will assist with disseminating the technology to key epilepsy professionals through this forum. Dr. Murray is chair of the neurology specialty committee of the Royal College of Physicians and Surgeons of Canada – the body that oversees the training of neurologists in Canada – and is also an executive member of the Canadian Sleep Society, and will help to disseminate our technology through these organizations.

5.3 Training of Highly Qualified Personnel

Training of HQPs is a key component of this project. We will train 2.5 CS PhD students and 1 MSc student in Waterloo and McGill. As described above, these students will have deep and ongoing interactions with the clinical teams at Sunnybrook, TWH, and with the BEP. There will be monthly visits to the Sunnybrook and TWH sites, during which they will embed within the clinical teams, both to formally evaluate clinical needs and iteratively evaluate technology prototypes, as well as to gain a broader appreciation of the impact of potential solutions in the care of patients. They will also have the opportunity to do field work in Bhutan to formally evaluate our technology, and to gain a better appreciation of the unique challenges of providing healthcare in resource-poor settings.

In addition to formally training CS PhD students, this project will also provide valuable training to the next generation of technicians, physicians, and neurologists. The Sunnybrook and TWH labs are major training sites for EEG/PSG technicians and neurologists. These trainees will work collaboratively with cutting-edge researchers in machine learning and human computing, and will not only become familiar with the technology and its capabilities, but also begin to think about how this technology can be applied outside of the EEG setting to other areas of health care.

References

- [1] S. Bastianini, C. Berteotti, A. Gabrielli, F. Del Vecchio, R. Amici, C. Alexandre, T. Scammell, M. Gazea, M. Kimura, V. Lo Martire, A. Silvani, and G. Zoccoli. Scoprism: A new algorithm for automatic sleep scoring in mice. *Journal of Neuroscience Methods*, pages 277–284, 2014.
- [2] A. Blum and T. Mitchell. Combining labeled and unlabeled data with co-training. In *COLT*, pages 92–100, 1998.
- [3] A. M. Chan, S. T. Sun, E. H. Boto, and B. M. Wingeier. Automated seizure onset detection for accurate onset time determination in intracranial eeg. *Clinical Neurophysiology*, 119:2687–2696, 2008.
- [4] T. Dietterich. Ensemble Methods in Machine Learning. In *First International Workshop on Multiple Classifier Systems, Lecture Notes in Computer Science*, 2000.
- [5] C. Eiben, J. Siegel, J. Bale, S. Cooper, F. Khatib, B. Shen, Foldit Players, B. Stoddard, Z. Popovic, and D. Baker. Increased diels-alderase activity through backbone remodeling guided by foldit players. *Nature Biotechnology*, pages 190–192, 2012.
- [6] E. Law and L. von Ahn. Input-agreement: A new mechanism for data collection using human computation games. In *CHI*, pages 361–364, 2009.
- [7] E. Law and L. von Ahn. *Human Computation*. Morgan & Claypool Synthesis Series on Artificial Intelligence and Machine Learning, 2011.
- [8] A. Malhotra, M. Younes, S. Kuna, R. Benca, C. Kushida, J. Walsh, A. Hanlon, B. Staley, A. Pack, and G. Pien. Performance of an automated polysomnography scoring system versus computer-assisted manual scoring. *Sleep*, (4):573–582, 2013.
- [9] W. Mason and S. Suri. A guide to behavioral experiments on mechanical turk. *Behavior Research Methods*, 44(1):1–23, 2012.
- [10] M. Saab and J. Gotman. A system to detect the onset of epileptic seizures in scalp eeg. *Clinical Neurophysiology*, 116:427–442, 2005.
- [11] A. Shoeb and J. Guttag. Application of machine learning to epileptic seizure detection. In *International Conference on Machine Learning (ICML)*, 2010.
- [12] S. Vijayanarasimhan and K. Grauman. What’s it going to cost you? predicting effort vs. informativeness for multi-label image annotations. In *CVPR*, pages 1–8, 2009.
- [13] L. von Ahn. Duolingo: learn a language for free while helping to translate the web. In *IUI*, pages 1–2, 2013.
- [14] L. von Ahn and L. Dabbish. Labeling images with a computer game. In *CHI*, pages 319–326, 2004.
- [15] L. von Ahn and L. Dabbish. General techniques for designing games with a purpose. *Communication of the ACM*, pages 58–67, August 2008.
- [16] L. von Ahn, B. Maurer, C. McMillen, D. Abraham, and M. Blum. recaptcha: Human-based character recognition via web security measures. *Science*, 321:1465–1468, 2008.
- [17] S. Warby, S. Wendt, P. Welinder, E. Munk, O. Carrillo, H. Sorensen, P. Jennum, P. Peppard, P. Perona, and E. Mignot. Sleep-spindle detection: Crowdsourcing and evaluating performance of experts, non-experts and automated methods. *Nature Methods*, (11):385–392, 2014.

- [18] S. Wiebe, P. Camfield, N. Jette, and J. Burneo. Epidemiology of epilepsy: prevalence, impact, comorbidity and disparities. *Journal of Neurological Sciences*, 36(2):7–16, 2009.
- [19] Kyle W. Willett, Chris J. Lintott, Steven P. Bamford, Karen L. Masters, Brooke D. Simmons, Kevin R. V. Casteels, Edward M. Edmondson, Lucy F. Fortson, Sugata Kaviraj, William C. Keel, Thomas Melvin, Robert C. Nichol, M. Jordan Raddick, Kevin Schawinski, Robert J. Simpson, Ramin A. Skibba, Arfon M. Smith, and Daniel Thomas. Galaxy Zoo 2: detailed morphological classifications for 304122 galaxies from the Sloan Digital Sky Survey. *Monthly Notices of the Royal Astronomical Society*, September 2013.
- [20] T. Young, M. Palta, J. Dempsey, J. Skatrud, S. Weber S, and S. Badr. The occurrence of sleep-disordered breathing among middle-aged adults. *New England Journal of Medicine*, 328(17):1230–1235, 1993.
- [21] A. Zandi, M. Javidan, G. Dumont, and R. Tafreshi. Automated realtime epileptic seizure detection in scalp eeg recordings using an algorithm based on wavelet packet transform. *IEEE Transactions on Biomedical Engineering*, 57:1639–1651, 2010.
- [22] T Zhu, AEW Johnson, J Behar, and G D Clifford. Crowd-sourced annotation of ecg signals using contextual information. *Annals of Biomedical Engineering*, 2014.
- [23] T. Zhu, M. Osipov, T. Papastylianou, J. Oster, D. A. Clifton, and G. D. Clifford. An Intelligent Cardiac Health Monitoring and Review System. In *Appropriate Healthcare Technologies for Low Resource Settings (AHT), The 8th International Conference - Promoting access to healthcare through technology*, 2014.

Appendix



Figure 1: The Bhutan Epilepsy Project

Curio

All Projects elaw

Projects

What organic molecules are the most efficient for use in solar cells?
Professor Alan Aspuru-Guzik
Tell Me More

What are the characteristics that distinguish different species of nematocysts?
Professor Meg Daly
Tell Me More

How does the brain control sleep and wakefulness?
Dr. Andrew Lim
Tell Me More

How has climate changes affected flowering times in New England over the last 160 years?
Professor Charles Davis
Tell Me More

Figure 2: Curio: A Platform for Mixed-Expertise Crowdsourcing

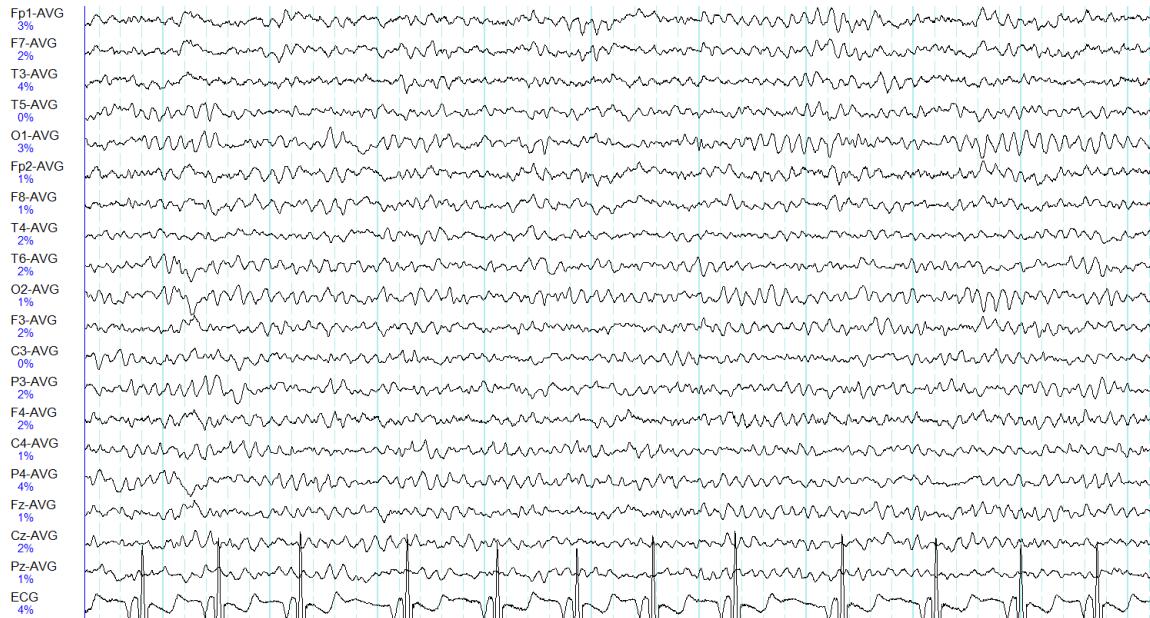


Figure 3: Normal wake EEG. Note the 8Hz dominant background frequency.

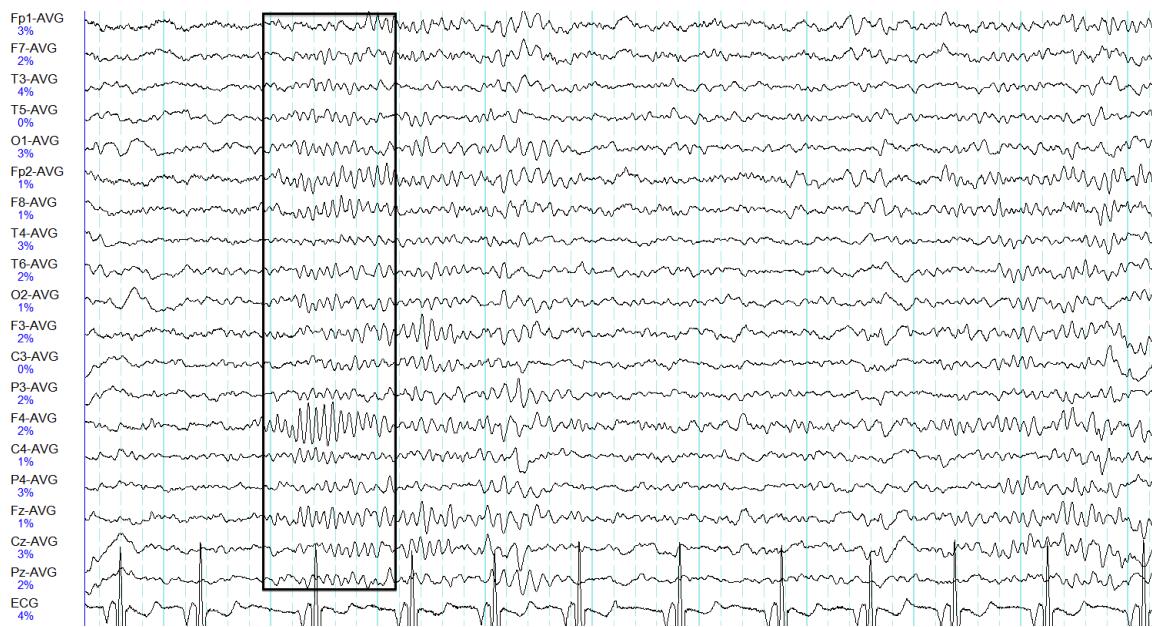


Figure 4: EEG in stage N2 sleep. Note the prominent sleep spindles (black box) and the dominant frequency <8 Hz.

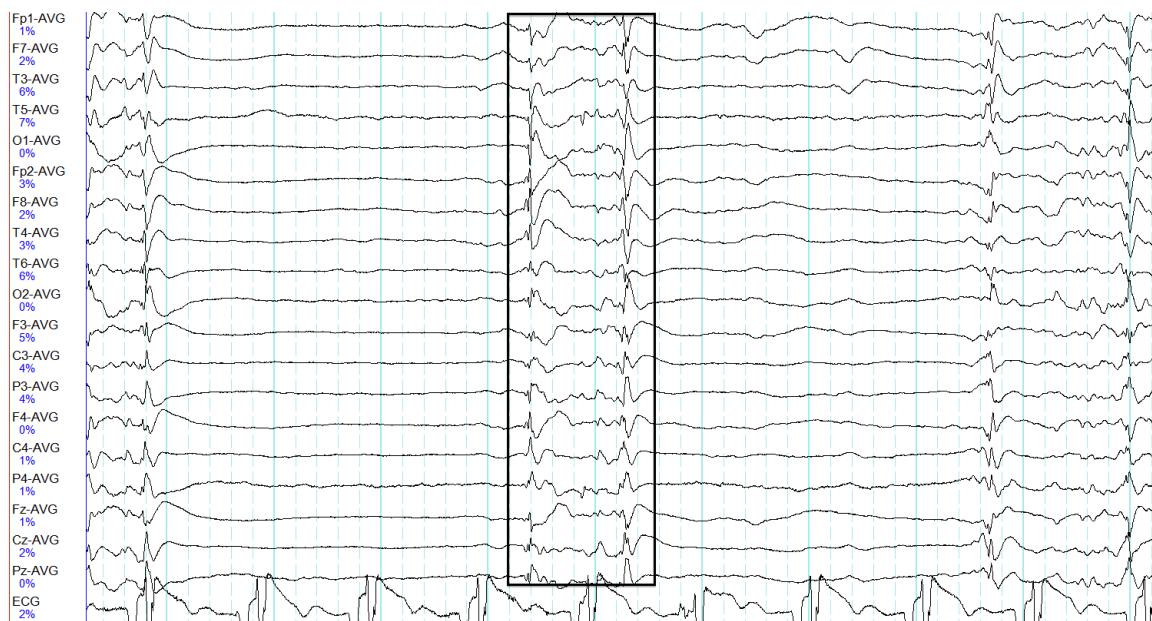


Figure 5: Abnormal burst-suppression background with brief bursts (box) punctuated by long periods of suppression. Note the interictal epileptiform discharges contained within the bursts.

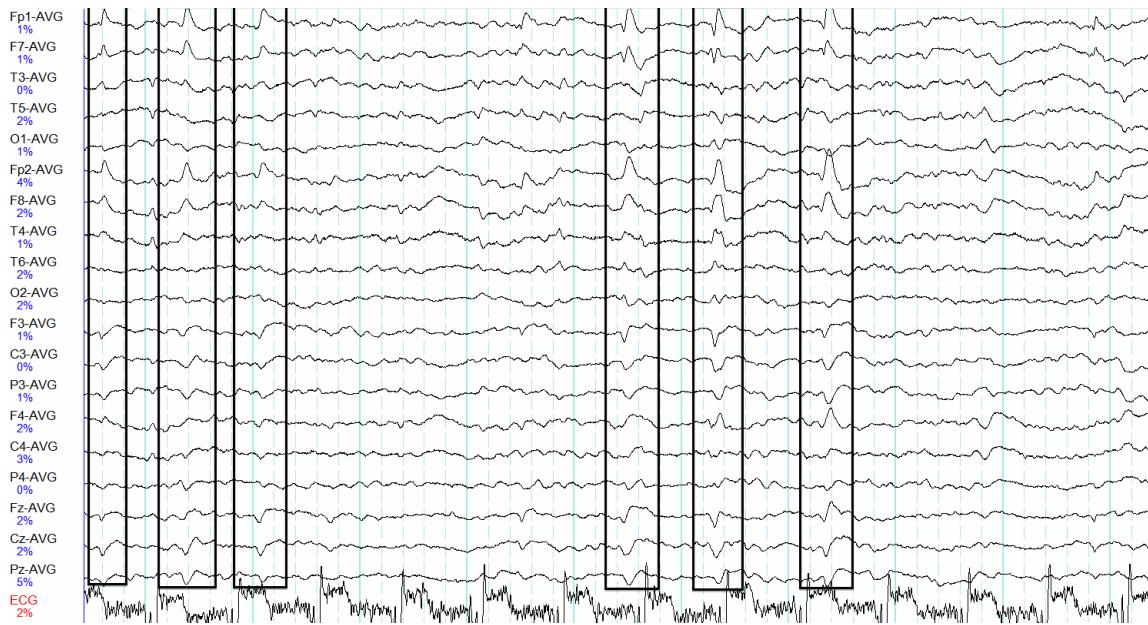


Figure 6: Interictal discharges (black boxes) on a slow (<8Hz) background.

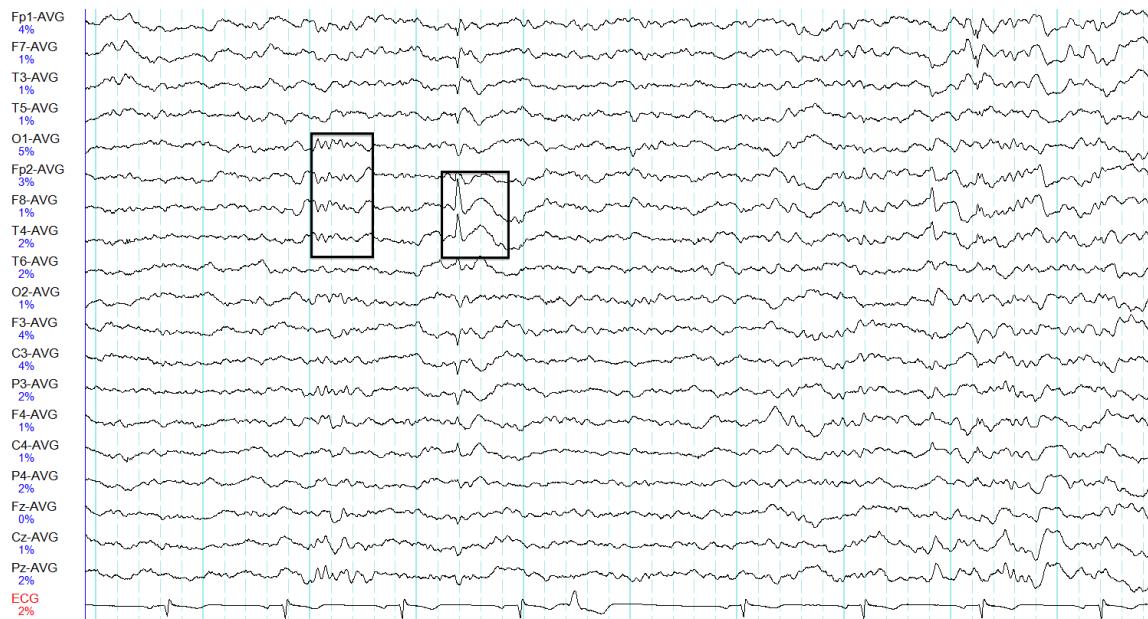


Figure 7: Single focal interictal discharge preceded by a normal spindle (black boxes) occurring in the context of otherwise normal stage N2 sleep.

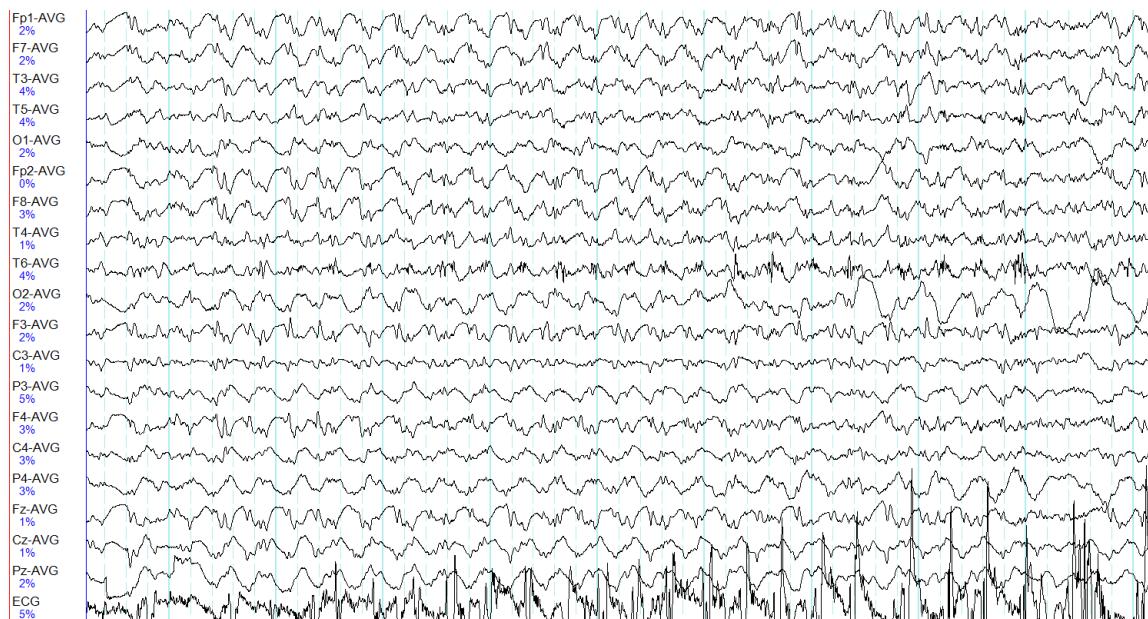


Figure 8: Middle of a generalized seizure (the beginning and end are not seen on this page).

Activities Schedule

Milestones	Description of Activity	Anticipated start date	Anticipated completion date
Preparation	In consultation with Brian Murray, Richard Wennberg and Farah Mateen, Computer Specialist will work with Dr. Law to create a preliminary data pipeline, which will transfer and prepare a labeled dataset from each of the knowledge organizations. MSc1 will adapt the existing time series annotation interfaces on Curio for EEG annotation.	04/01/2015	08/31/2015
Formative Study	Edith Law's team will visit the hospitals on a weekly basis, to gain an understanding of how clinicians and technicians currently process EEGs. This will involve in-person meetings with the knowledge users, with the goal of developing an initial scheme for allocating feature detection tasks to non-experts, experts, and automated algorithms.	09/01/2015	11/01/2015
(Translational) Aim 1 <i>State Classification</i>	Edith Law's team will work with Andrew Lim and Brian Murray to develop for sleep EEG analysis (a) automated algorithms for frequency analysis, (b) automated algorithms for detecting normal features, (c) annotation interfaces for non-experts to detect normal features, (d) an algorithm for classifying behavioral state by combining non-expert, expert and machine contributions, (e) a visual aid for experts to review crowdsourced results.	11/01/2015	02/01/2016
Aim 1 <i>Evaluation</i>	Edith Law's team will perform an analysis, comparing our algorithm against purely automated techniques or expert analyses. They will also run several user studies to understand experts' use of the visual aid, and its effects on their sleep staging workflow.	02/01/2016	03/01/2016
Aim 2 <i>State Classification</i>	Edith Law and PhD1 will develop an iterative refinement approach, which will repeatedly assess the quality of each component of our hybrid system, and dynamically changes how the tasks are allocated. We will evaluate the iterative refinement approach against a static approach.	03/01/2016	08/01/2016
(Translational) Aim 1 <i>Seizure and IED Detection</i>	Edith Law's team will work with Joelle Pineau and PhD3 to develop a set of hybrid algorithms for seizure and IED detection. In particular, we will develop a new set of algorithms and interfaces for non-experts to tackle the “needle-in-a-haystack” search problem.	08/01/2016	12/01/2016
Aim 2 <i>Seizure and IED Detection</i>	Edith Law and PhD2 will apply the iterative refinement approach developed earlier to the IED and seizure detection problem. PhD2 will also design new interfaces for routing expert and crowd feedback to non-experts for training purposes. We will evaluate the effects of the iterative refinement approach and the feedback interfaces on the overall performance of the system.	12/01/2016	04/01/2017
Translational Aim 2 <i>Bhutan Epilepsy Project</i>	Andrew Lim, Joelle Pineau and Edith Law will work with Farrah Mateen to incorporate the hybrid epilepsy detection algorithm into the mobile EEG recording devices. We will also work with Jorge Burneo to identify rural Canadian sites for field studies.	04/01/2017	12/01/2017
Translational Aim 2 <i>Evaluation</i>	We will conduct field studies in Bhutan and small rural communities in Canada.	12/01/2017	04/01/2018

London, September 24th 2014

Dear Dr. Law and Dr. Lim:

RE: Support for the proposed CIHR-NSERC project "A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings"

I am delighted to offer my full support to your innovative proposal to apply hybrid human-machine computational approaches to the analysis of human electroencephalographic signals.

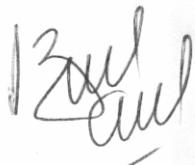
I am a neurologist and epileptologist with a particular interest in the development and evaluation of systems to provide epilepsy care in underserviced areas. One of the greatest barriers to efficiently provide such care is the necessity of highly trained experts to properly record and interpret electroencephalograms (EEGs) - the key test in the diagnosis of epilepsy. This is a particularly pressing problem in more rural and remote health regions, which often have a high proportion of aboriginal citizens, and where risk factors for epilepsy such as low socioeconomic status are more common, while specialists in EEG are rare. This results in the need to transport patients to larger centers to obtain EEG services, at great cost, and with potential delays in diagnosis.

Your proposal to develop a combined human and machine computation approach for interpreting human clinical EEG recordings, and to integrate this with a Smartphone-based EEG recording device, has the potential to address this gap by lessening the dependence on scarce highly trained experts to record and interpret EEGs, allowing cost-efficient and timely diagnosis of epilepsy to happen closer to home for thousands of at-risk Canadians in rural and remote communities, not to mention millions of at-risk individuals in the rural areas of developing countries.

I am happy to be a co-investigator on this project, and will lend my expertise in the development and evaluation of systems of epilepsy care in resource-limited settings. I will provide input into the development of the human-computer interface to ensure applicability to available healthcare personnel and resources in rural/remote settings in Canada and elsewhere, and will provide assistance in developing a program to properly evaluate the completed prototype in such settings and eventually integrate it into a wider epilepsy care framework. Finally, in my capacity as education chair of the Canadian League Against Epilepsy, I will be able to promote more widespread adoption of any successful prototype system in the broader Canadian epilepsy community.

I wish you success in your application, and look forward to working with you on this exciting project.

Yours truly,



Jorge G Burneo, MD, MSPH, FAAN
Associate Professor of Neurology, Biostatistics and Epidemiology
Epilepsy Programme
Department of Clinical Neurological Sciences
Western University - London Health Sciences Center
339 Windermere Rd, B10-118
London, ON, N6A5A5
Phone: (519) 663-3464
Fax: (519) 663-3498
E-mail: jorge.burneo@lhsc.on.ca



FORM 183A

Information Required from Organizations Participating in Research Partnerships Programs

Read the instructions before completing the Form.

GENERAL INFORMATION ON THE ORGANIZATION					
Name of organization The Bhutan Epilepsy Project			Name and title of contact person at the organization Dr. Farrah Mateen		
Mailing address The Bhutan Epilepsy Project c/o Dr. Farrah Mateen Thompson Hall, 25 University Private Ottawa, ON K1N 7K4			Mailing address for the contact person (only if different)		
Telephone number 613-562-5800	Facsimile number 617-562-5632	Telephone number	Facsimile number		
E-mail address fmateen@uottawa.ca			E-mail address		
Is your organization <input checked="" type="radio"/> Private sector? <input type="radio"/> Government owned? <input type="radio"/> Government agency/department?				Industry/Products and Services Code	
Is your organization <input type="radio"/> Profit-motivated? <input checked="" type="radio"/> Not-for-profit?		Web site http://www.bhutanbrain.com/			
Canadian ownership (in percentage) (If Applicable) %	Date of incorporation in Canada (If Applicable)			Total number of employees in Canada 3	
Types of products sold and/or services offered Smartphone-based EEG recording device				Total annual sales for previous year (If Applicable)	
				Net profit (loss) for previous year (If Applicable)	
Is your organization <input type="radio"/> a parent company? <input type="radio"/> a subsidiary of? (specify)					
RESEARCH AND DEVELOPMENT ACTIVITIES					
Does your organization have an R&D department?		Yes <input type="radio"/>	No <input checked="" type="radio"/>	Annual R&D expenditures (previous/ current / next year)	
If not, does it undertake R&D within the organization's premises?		Yes <input checked="" type="radio"/>	No <input type="radio"/>		
Number of R&D staff in Canada Scientists and technicians: 4		R&D staff with a PhD: 1		\$150,000	/\$150,000
APPLICANT INFORMATION					
Family name Law	Given names Edith			Initial(s) of all given names	
Title of proposal A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings				Personal identification no. (PIN)	
				Appl ID (for NSERC use only)	
ORGANIZATION'S CONTRIBUTIONS					
Contributions to the direct costs of research	Year 1	Year 2	Year 3	Year 4	Year 5
a) Cash contribution	\$0	\$0	\$0		
b) In-kind contribution	\$19,360	\$38,400	\$52,800		
Has your organization received publicly-funded support for R&D directly related to the proposed project?		Yes <input checked="" type="radio"/>	No <input type="radio"/>	Are the applicant and co-applicant(s) at arm's length from your organization?	
Name, title and telephone number of authorized representative of the organization Dr. Farrah Mateen, Project Lead, 613-562-5800/617-726-2383			Signature 		Date 09/18/2014



18 September 2014

To the Members of the Review Panel:

I am writing on behalf of the Bhutan Epilepsy Project to express our support for Dr. Law and Dr. Lim's exciting proposal to develop a hybrid human-computer platform for EEG interpretation, and our enthusiasm for partnering with them to integrate this technology with a smartphone-based mobile EEG recording device we are developing.

The Bhutan Epilepsy Project is a non-governmental multi-national organization that is developing a smartphone-based portable EEG recording device to enable cost-efficient EEG recordings in remote regions of the world with minimal specialist expertise. We are funded in part by a grant from Grand Challenges Canada <http://www.grandchallenges.ca/grantee-stars/0338-04/>, and a number of key members of our research staff are based in Canada. We have an annual research and development budget of \$150,000. We are initially testing our device in Bhutan, a particularly striking example of a low-resource health care setting, but anticipate that the device and work may eventually play an important role in meeting EEG diagnostic needs in other settings without epilepsy specialists, including in geographically dispersed populations in high-income countries such as Canada.

The smartphone-based device we are developing solves one of the key difficulties in providing EEG diagnostic capabilities in settings without expert technicians and physicians - that of obtaining adequate quality recordings. However, the problem of accurately and efficiently interpreting the recordings remains. Presently, we remain dependent on the effort of specialists who volunteer their time to interpret the recordings obtained using our device, and relay their interpretations back to the recording site. This can result in delays in diagnosis and treatment. Limitations in the number of voluntary experts and the amount of time to volunteer limit the number of recordings that can be analyzed. This is precisely where the collaboration with Dr. Law and Dr. Lim has so much promise. Successful completion of the proposed project and integration with our smartphone-based EEG recording apparatus would have several tangible benefits for us including:

1. ***Broadening the pool of volunteer experts*** by a) decreasing the time required for any single expert to make a meaningful contribution. This drops the barriers to volunteering (i.e. opening the door to "micro-volunteering") and b) breaking down the EEG interpretation task into simple micro tasks that might be tractable for less highly trained individuals (e.g. medical students) or even local health care professionals (e.g. nurses) so that not all human interpreters need be EEG-trained neurologists. This would allow a far greater number of records to be interpreted.

2. **Decreasing the time required** of the limited pool of highly trained specialists so that each specialist can effectively interpret a far greater number of recordings per unit time

3. **Building local capacity** of local non-EEG-trained professionals (e.g. nurses) may begin with relatively straightforward interpretative tasks, but through iterative feedback develop their skill to the point that input from a pool of such professionals, when combined with automated algorithms, may approach the accuracy of a highly trained specialist. This would have the benefit of better timeliness of diagnosis since EEG data would not have to be relayed to outside experts for interpretation.

In order to facilitate integration of Dr. Law and Dr. Lim's algorithms with our hardware, we will work with them right from the beginning. We will provide them with 2 working prototypes of our hardware as well as access to the necessary code to assure interoperability. Our engineering and software development team will work closely with Dr. Law and Dr. Lim's teams. Members of Dr. Law's and Dr. Lim's laboratories will be invited to visit our technical development facilities in Denmark and Boston as well as in Ottawa to facilitate technical interchange. We will provide access to the wealth of data already collected with our device (approximately 200 recordings, paired with recordings from a conventional EEG device). Altogether, over three years, we estimate that this will involve 1152 hours of time from our technical research staff, at \$80 per hour, and 48 hours of physician time at \$300 per hour plus the manufacturing cost of our two prototypes which constitutes a total in-kind contribution of \$110,560.

Once performance benchmarks are met using locally collected and archived data, members of Dr. Law's and Dr. Lim's laboratories will join us for fieldwork in Bhutan to get input about the human-computer interface from front line Bhutanese health care professionals and to further refine the algorithm. The ultimate goal will be to fully incorporate their prototype algorithms with our smartphone-based EEG system to allow seamless recording and interpretation in a single system.

I have reviewed this proposal and am in full agreement with it, including the proposed role of the Bhutan Epilepsy Project.

We at the Bhutan Epilepsy Project are thrilled to have the opportunity to partner with Dr. Law and Dr. Lim, whose promising technology has the potential to meet a very real need both vis à vis our product, and vis à vis the global health implications of access to EEG diagnosis in remote regions.

Sincerely, with thanks,



Farrah J. Mateen, MD, PhD
Project Lead, The Bhutan Epilepsy Project
Adjunct Professor, Interdisciplinary Faculty of Health Sciences, University of Ottawa

The Bhutan Epilepsy Project is a multinational non-governmental organization with researchers based in Canada, the United States, Denmark, and Bhutan whose goal is to develop and validate technologies for the cost-efficient diagnosis of epilepsy in remote settings. Its current focus is development of a smartphone-based device to enable low cost accurate EEG recordings with minimal specialized expertise, with plans to initially field-test the device in Bhutan, as a prototypical under-resourced remote setting. However, the same technologies are potentially applicable to other settings without EEG specialists, including smaller communities in industrialized countries like Canada.

Through an affiliated entity, the SoundMind Project, it is registered as a 501(c)(3) nonprofit organization in the United States. Over 20% of its core workforce of 15 individuals is based in Canada. The project lead, Dr. Farrah Mateen, has an academic appointment at the University of Ottawa in addition to her role with the Bhutan Epilepsy Project. It is supported by private donations, as well as a grant from Grand Challenges Canada and currently has a research and development budget of \$150,000 per year.

The Bhutan Epilepsy Project (BEP) is a multinational non-governmental organization with researchers based in Canada, the United States, Denmark, and Bhutan whose goal is to develop and validate technologies for the cost-efficient diagnosis of epilepsy in remote settings. Although nominally registered in the United States as a 501(c)(3) non-profit organization, it has a strong Canadian presence. Over 20% of its core workforce of 15 researchers is based in Canada, and the project lead, Dr. Farrah Mateen, has an academic appointment at the University of Ottawa in addition to her role in the BEP. The BEP is supported by a grant from Grand Challenges Canada in addition to private donations.

The BEP's key product is a smartphone-based device to enable low-cost accurate EEG recordings with a minimum of specialized technical expertise. The device is being field-tested in Bhutan as a prototypical remote and under-resourced setting. However, this could just as easily be a cost-effective way of providing EEG services to Canadian communities that currently lack EEG specialists, or provide more rapid access to EEG services even in larger Canadian centres. Widespread adoption of this inexpensive technology, augmented by the algorithms that are the subject of the current proposal, could result in substantial cost savings by avoidance of the need to either bring specialized technicians, equipment, and physicians to remote regions, or alternatively bring patients to urban centers to obtain EEGs. Moreover, this would have a substantial impact on health by decreasing delays to diagnosis associated with travel. In so doing, the potential for both economic and health benefits to Canadians is substantial.

In this proposal, we are partnering with 2 fully Canadian technology transfer partners – the epilepsy program at the Toronto Western Hospital, and the clinical neurophysiology laboratory at Sunnybrook Health Sciences Centre. The BEP brings a number of unique strengths as an additional technology transfer partner: 1) most importantly, the BEP is developing a unique piece of technology, a smartphone-based EEG recording apparatus, that would magnify the health and economic impacts of our technology by extending its applicability to low-resource health care settings 2) the BEP has expertise in clinical evaluation of EEG technology in remote and low-resource settings and will be able to assist with field testing our technology in a challenging remote environment. No fully Canadian organization has access to the same technology and expertise, hence our decision to partner with the BEP. Besides, although nominally registered as a US non-profit, the BEP has strong Canadian connections – the project lead Dr. Farrah Mateen has a University of Ottawa academic appointment, several key R&D staff are based in Canada, and the project is funded by Grand Challenges Canada.



FORM 183A

Information Required from Organizations Participating in Research Partnerships Programs

Read the instructions before completing the Form.

GENERAL INFORMATION ON THE ORGANIZATION					
Name of organization			Name and title of contact person at the organization		
Mailing address			Mailing address for the contact person (only if different)		
Telephone number	Facsimile number		Telephone number	Facsimile number	
E-mail address			E-mail address		
Is your organization Private sector? Government owned? Government agency/department?				Industry/Products and Services Code	
Is your organization	Profit-motivated?	Not-for-profit?	Web site		
Canadian ownership (in percentage) (If Applicable)	%	Date of incorporation in Canada (If Applicable)	Total number of employees in Canada		
Types of products sold and/or services offered				Total annual sales for previous year (If Applicable)	
				Net profit (loss) for previous year (If Applicable)	
Is your organization	a parent company?	a subsidiary of? (specify)			
RESEARCH AND DEVELOPMENT ACTIVITIES					
Does your organization have an R&D department?	Yes	No	Annual R&D expenditures		
If not, does it undertake R&D within the organization's premises?	Yes	No	(previous/ current / next year)		
Number of R&D staff in Canada Scientists and technicians:	R&D staff with a PhD:		/	/	/
APPLICANT INFORMATION					
Family name	Given names		Initial(s) of all given names		
Title of proposal				Personal identification no. (PIN)	
			Appl ID (for NSERC use only)		
ORGANIZATION'S CONTRIBUTIONS					
Contributions to the direct costs of research	Year 1	Year 2	Year 3	Year 4	Year 5
a) Cash contribution					
b) In-kind contribution					
Has your organization received publicly-funded support for R&D directly related to the proposed project?	Yes	No	Are the applicant and co-applicant(s) at arm's length from your organization?		
Name, title and telephone number of authorized representative of the organization	Signature			Date	



Brian James Murray, MD FRCP(C) D,ABSM
Director of Integrated Medical Education
for the University of Toronto Department of Medicine
Associate Professor, Neurology and Sleep Medicine
Chair – Research Ethics Board
Sunnybrook Health Sciences Center
Room M1-600; 2075 Bayview Avenue Toronto, Ontario,
Canada, M4N 3M5
phone (416) 480-6100x2461, fax (416) 480-6092
brian.murray@utoronto.ca



Sept 21 2014

To the Members of the Review Panel:

I am writing to express my enthusiasm and full support of the Sunnybrook Clinical Neurophysiology Laboratory for Dr. Law and Dr. Lim's exciting proposal to apply hybrid human-computer algorithms to the analysis of human electroencephalogram (EEG) and polysomnogram (PSG) data. The full protocol details a novel practical approach to a significant problem, and I am eager to support their efforts to get this work realized given the potential benefits to our society.

The Sunnybrook Clinical Neurophysiology Laboratory is a major neurophysiology site in Canada at Sunnybrook Health Sciences Centre, one of the leading academic teaching hospitals in Canada. Here I have directed the clinical neurophysiology services of EEG and PSG. The lab is responsible for generating over 1300 clinical EEGs and nearly 1000 PSGs per year. As it stands now, each of these over 2000 records is reviewed in its entirety by one of our highly trained technicians, and then again by one of our specialist physicians, a laborious and time-consuming process. This has several negative implications. First, it often results in delays of days to weeks before records can be formally reviewed, leading to delays in diagnosis and treatment. Second, it takes highly trained and highly specialized professionals away from other clinically important tasks, such as seeing patients. Third, it increases the unit costs of providing PSG and EEG services since labour costs are the primary costs in any clinical neurophysiology laboratory, including ours.

Sunnybrook hospital is at the leading edge of integrating novel computing solutions into clinical care. For example, Sunnybrook was one of seven health care providers in Canada to receive a LEADING practice award from Canada Health Infoway for demonstrating

leadership in the advanced use of technology in clinical practice. We are always on the look out for innovative technologies for the potential to benefit patient care and increase cost efficiency. If successful, this project has the potential to revolutionize the way clinical EEG and PSG recordings are handled at our hospital and hospitals across Canada and internationally. By decreasing technician time and specialist physician time necessary to interpret each recording, this project will allow these highly trained professionals to devote more time to other clinical duties, to the benefit of patient care. This proposal has the potential to substantially decrease costs in our laboratory, a key benefit in a time of scarce resources and pervasive upward cost pressures in our health care system. Most importantly, by decreasing the time required to interpret EEGs and PSGs, it will result in less waiting for patients, and more timely diagnosis and treatment of seizures, epilepsy, and sleep disorders. These disorders have huge economic impact, and efforts to mitigate these problems have significant financial implications.

The Sunnybrook Clinical Neurophysiology Laboratory will be involved at every stage of this project. Our technicians will facilitate access to our vast digital database of over 6500 PSGs and 4300 EEGs which have been meticulously archived over 10 years. This resource is an exceptional opportunity. Our group will test and provide feedback on elements of the prototype throughout the development process, and will contribute gold-standard expert annotations. We will invite members of Dr. Law and Dr. Lim's laboratories to spend time in our lab to better understand the current clinical workflow, and the current standard approach to visual PSG and EEG interpretation. Our laboratory will serve as a real-world test site to evaluate the accuracy and efficiency of the finished product. We estimate that in total, our technicians will provide 398 hours of time in year 1, 382 in year 2, and 478 in year three. In addition, we estimate our physicians will provide 100 hours of time in years 1, 2, and 3. At \$50/hour including benefits for technicians, and \$300/hour including benefits for physicians, we estimate that this constitutes an in-kind contribution of \$49,900 in year 1, \$49,100 in year 2, and \$53,900 in year 3.

Given the history of IT innovation in our laboratory and at at Sunnybrook

more generally , if the project achieves all of its 5-year goals, our laboratory is well-placed to integrate a working prototype into our clinical workflow and to evaluate the impact on financial and clinical outcomes. Finally, after the project is done, as a key training centre for technologists, medical students, physicians, and EEG/PSG specialists in the Province of Ontario (hundreds of trainees pass through our laboratory each year), our laboratory will be able to train a new generation of health care professionals in the use of this exciting technology. Moreover, as the Chair of the Neurology specialty committee of the Royal College of Physicians and Surgeons of Canada, an executive member of the Canadian Sleep Society, and Director for integrated medical education at the University of Toronto, I will be personally well placed to extend the reach of this technology well beyond our institution to clinical neurophysiology laboratories and hospitals around the country and beyond. Our group can facilitate the training of a new generation of medical professionals, through our national-level lectures and publications, and by our influence on curricular changes at the university and national levels.

I look forward to being able to support Dr. Law and Dr. Lim on this exciting project, and look forward to a successful review.

Sincerely,



Brian Murray,

Chair of the Neurology Specialty Committee, Royal College of Physicians and Surgeons of Canada
Director of Integrated Medical Education, University of Toronto



FORM 183A

Information Required from Organizations Participating in Research Partnerships Programs

Read the instructions before completing the Form.

GENERAL INFORMATION ON THE ORGANIZATION

Name of organization The Toronto Western Hospital, Epilepsy Program		Name and title of contact person at the organization Dr. Richard Wennberg	
Mailing address Clinical Neurophysiology Laboratory, Toronto Western Hospital 399 Bathurst St. - West Wing 5th Floor, Suite 444 Toronto, ON M5T 2S8		Mailing address for the contact person (only if different)	
Telephone number 416-603-5402	Facsimile number 416-603-5768	Telephone number	Facsimile number
E-mail address richard.wennberg@uhn.ca		E-mail address	
Is your organization <input type="radio"/> Private sector? <input checked="" type="radio"/> Government owned? <input type="radio"/> Government agency/department?			Industry/Products and Services Code
Is your organization <input type="radio"/> Profit-motivated? <input checked="" type="radio"/> Not-for-profit?		Web site http://www.uhn.ca/KNC/PatientsFamilies/Clinics_Tests/Epile	
Canadian ownership (in percentage) (If Applicable) %	Date of incorporation in Canada (If Applicable)	Total number of employees in Canada 20	
Types of products sold and/or services offered Diagnosis and treatment of patients with epilepsy		Total annual sales for previous year (If Applicable)	
		Net profit (loss) for previous year (If Applicable)	

Is your organization a parent company? a subsidiary of? (specify)

RESEARCH AND DEVELOPMENT ACTIVITIES

Does your organization have an R&D department?	Yes <input type="radio"/> No <input checked="" type="radio"/>	Annual R&D expenditures (previous/ current / next year)		
If not, does it undertake R&D within the organization's premises?	Yes <input checked="" type="radio"/> No <input type="radio"/>	\$100,000 / \$100,000 / \$100,000		
Number of R&D staff in Canada Scientists and technicians:	10	R&D staff with a PhD:	4	

APPLICANT INFORMATION

Family name Law	Given names Edith	Initial(s) of all given names
Title of proposal A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings		Personal identification no. (PIN)
		Appl ID (for NSERC use only)

ORGANIZATION'S CONTRIBUTIONS

Contributions to the direct costs of research	Year 1	Year 2	Year 3	Year 4	Year 5
a) Cash contribution	\$0	\$0	\$0		
b) In-kind contribution	\$51,200	\$50,400	\$55,200		

Has your organization received publicly-funded support for R&D directly related to the proposed project?	Yes <input checked="" type="radio"/> No <input type="radio"/>	Are the applicant and co-applicant(s) at arm's length from your organization?	Yes <input type="radio"/> No <input checked="" type="radio"/>
--	---	---	---

Name, title and telephone number of authorized representative of the organization Dr. Richard Wennberg, Director, Clinical Neurophysiology Laboratory, 416-603-5402	Signature 	Date 25 Sep 2014
--	---	-------------------------



Toronto Western Hospital

University Health Network

RICHARD WENNBERG, MD, PhD, FRCPC
Neurology and Electroencephalography
Professor of Medicine, University of Toronto

5W - 444, 399 Bathurst St., Toronto, Ontario M5T 2S8
Telephone: (416) 603-5402 Fax: (416) 603-5768
E-mail: Richard.Wennberg@uhn.on.ca

25 September 2014

To the Members of the Review Panel:

On behalf of the Epilepsy Program and the Clinical Neurophysiology Laboratory at the University Health Network (UHN), Toronto Western Hospital, it is with great enthusiasm that I am writing in support of this proposal to apply combined human-computing and machine learning approaches to the analysis of human EEG data.

The UHN Epilepsy Program is one of the largest of its kind in Ontario with over 1000 patient-visits per year. A key component of the program is our Clinical Neurophysiology (EEG) laboratory and inpatient epilepsy monitoring unit (EMU). Altogether, we perform over 2,500 routine EEGs and obtain over 84,000 hours of continuous inpatient EEG recordings per year - a truly massive amount of data. In our current clinical workflow, each minute of each recording is visually reviewed by one of our 10 specialized EEG technologists followed by a second stage of review by one of our specialized epileptologists. This is an extremely time consuming process which limits the number of records that can be read, takes our highly trained staff away from other clinically important duties, and can potentially result in delays in diagnosis and treatment. Moreover, in its reliance on the time of highly trained specialists, it is an extremely cost-inefficient process.

Faced with these facts, it has long been a holy grail of the EEG field to develop a reliable, accurate, efficient, fully-automated approach to EEG interpretation. However, the sea of automated approaches to EEG interpretation is littered with wrecks of many failed attempts. Dr. Law's proposal to combine task decomposition, automated algorithms, and judicious use of human input is a promising approach that may achieve many of the benefits of full automation (speed, accuracy, minimization of the need for highly trained specialized professionals) while overcoming the difficulties encountered by fully automated algorithms in doing some aspects of visual analysis. If this can be made to work seamlessly, it could potentially have a huge impact on clinical EEG workflows in our epilepsy program and programs like it across the country, including faster and more accurate diagnosis, ability to redirect scarce human resources to other tasks in epilepsy care, and cost savings.

The Clinical Neurophysiology Laboratory at the UHN is deeply integrated with every step of this proposal. We will provide access to our archive of >30,000 interpreted EEG recordings, and access to our unique archive of >60,000 hours of EEG recordings obtained from continuous monitoring studies performed in our EMU. I and other physicians and technicians will participate in fine-grained record annotation, which will serve 2 purposes: 1) provide a clinical gold-standard annotation 2) facilitate development of the user interface. Scientists and graduate students involved in the design of the prototype framework will have the opportunity to "embed" within the Clinical Neurophysiology Laboratory and Epilepsy Program to learn about the entire

process of epilepsy care, from initial clinical encounter, to EEG, to treatment and follow-up. In so doing, they will appreciate first-hand how the project will enhance clinical care, and gain insights into key attributes of any computer-human interface in a busy clinical setting. Once the prototype is completed, our program, through the real-time recordings of the EMU, will serve as the main test-bed for the component of the proposal concerning real-time or near-real-time EEG interpretation. Altogether, we anticipate contributing 1336 hours of technologist time and 300 hours of physician time over the 3-year course of this project, which constitutes an in-kind contribution \$156,800 using a rate of \$50/hour for technician time and \$300/hour for physician time.

If tests are successful, then we will serve as a site for the side-by-side comparison of the proposed hybrid human-machine paradigm vs. standard human visual analysis, using metrics of accuracy of diagnosis, time efficiency, and cost efficiency. In addition to incorporating this technology into our own epilepsy program, we are a major training site for health care professionals at many levels (technologists, neurologists, epileptologists) and in training these professionals in the use of the new technology will be able to achieve impact well beyond our institution.

I have reviewed this proposal and am in full agreement with it, including the proposed role of the TWH Clinical Neurophysiology Laboratory.

I look forward to working with Dr. Law and Dr. Lim on this promising and novel technology.

Yours truly,



Richard Wennberg, M.D., M.Sc., Ph.D., F.R.C.P.C.
Professor of Medicine (Neurology), University of Toronto
Director, Clinical Neurophysiology Laboratory
Director, Magnetoencephalography Unit
University Health Network, Toronto Western Hospital



Appl. #

Application for Funding – Budget**Funding Opportunity**

Collaborative Health Research Projects (NSERC partnered) 2014-10-01

ApplicantLast Name
LawFirst Name
EdithInstitution
University of Waterloo (Ontario)**Financial Assistance Required****Year 1**

Research Staff (excluding trainees)	No.	Salary	Benefits	CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Research Assistants	0.0	\$0	\$0	\$0	\$0	\$0	\$0
Technicians	0.9	\$67,430	\$20,230	\$31,200	\$0	\$56,460	\$87,660
Other personnel (as specified in Employment History)	0.6	\$70,154	\$17,206	\$27,360	\$0	\$60,000	\$87,360
Research Trainees	No.	Stipend	Benefits	CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Postdoctoral Fellows (post PHD, MD, etc.)	0.0	\$0	\$0	\$0	\$0	\$0	\$0
Graduate Students	3.5	\$70,663	\$0	\$70,663	\$0	\$0	\$70,663
Summer Students	0.0	\$0	\$0	\$0	\$0	\$0	\$0
Materials, Supplies and Services				CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Animals				\$0	\$0	\$0	\$0
Expendables				\$7,500	\$0	\$4,000	\$11,500
Services				\$6,200	\$0	\$0	\$6,200
Other (as specified in the Details of Financial Assistance Requested)				\$0	\$0	\$0	\$0
Travel				CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Total Operating				\$2,684	\$0	\$0	\$2,684
Total Equipment				\$145,607	\$0	\$120,460	\$266,067
Total Request				\$145,607	\$0	\$120,460	\$266,067

**Application for Funding – Budget****Funding Opportunity**

Collaborative Health Research Projects (NSERC partnered) 2014-10-01

ApplicantLast Name
LawFirst Name
EdithInstitution
University of Waterloo (Ontario)**Financial Assistance Required****Year 2**

Research Staff (excluding trainees)	No.	Salary	Benefits	CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Research Assistants	0.0	\$0	\$0	\$0	\$0	\$0	\$0
Technicians	1.1	\$83,923	\$25,177	\$31,200	\$0	\$77,900	\$109,100
Other personnel (as specified in Employment History)	0.6	\$70,154	\$17,206	\$27,360	\$0	\$60,000	\$87,360
Research Trainees	No.	Stipend	Benefits	CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Postdoctoral Fellows (post PHD, MD, etc.)	0.0	\$0	\$0	\$0	\$0	\$0	\$0
Graduate Students	3.5	\$70,663	\$0	\$70,663	\$0	\$0	\$70,663
Summer Students	0.0	\$0	\$0	\$0	\$0	\$0	\$0
Materials, Supplies and Services				CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Animals				\$0	\$0	\$0	\$0
Expendables				\$0	\$0	\$0	\$0
Services				\$6,200	\$0	\$0	\$6,200
Other (as specified in the Details of Financial Assistance Requested)				\$0	\$0	\$0	\$0
Travel				CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Total Operating				\$2,684	\$0	\$0	\$2,684
Total Equipment				\$138,107	\$0	\$137,900	\$276,007
Total Request				\$138,107	\$0	\$137,900	\$276,007

**Application for Funding – Budget****Funding Opportunity**

Collaborative Health Research Projects (NSERC partnered) 2014-10-01

ApplicantLast Name
LawFirst Name
EdithInstitution
University of Waterloo (Ontario)**Financial Assistance Required****Year 3**

Research Staff (excluding trainees)	No.	Salary	Benefits	CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Research Assistants	0.0	\$0	\$0	\$0	\$0	\$0	\$0
Technicians	1.1	\$91,308	\$27,392	\$31,200	\$0	\$87,500	\$118,700
Other personnel (as specified in Employment History)	0.65	\$81,231	\$20,529	\$27,360	\$0	\$74,400	\$101,760
Research Trainees	No.	Stipend	Benefits	CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Postdoctoral Fellows (post PHD, MD, etc.)	0.0	\$0	\$0	\$0	\$0	\$0	\$0
Graduate Students	3.5	\$70,663	\$0	\$70,663	\$0	\$0	\$70,663
Summer Students	0.0	\$0	\$0	\$0	\$0	\$0	\$0
Materials, Supplies and Services				CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Animals				\$0	\$0	\$0	\$0
Expendables				\$0	\$0	\$0	\$0
Services				\$6,200	\$0	\$0	\$6,200
Other (as specified in the Details of Financial Assistance Requested)				\$0	\$0	\$0	\$0
Travel				CIHR	Other Funding Sources		Total
					Cash*	In-Kind*	
Total Operating				\$17,609	\$0	\$0	\$17,609
Total Equipment				\$153,032	\$0	\$161,900	\$314,932
Total Request				\$153,032	\$0	\$161,900	\$314,932



Human Resources

Research Personnel

EEG Technicians: We are requesting support for an EEG technician (0.4 FTE/year) for 3 years to be based at Dr. Lim's laboratory. This individual will perform several functions including a) liaising with technicians at the three partner organizations to organize and transfer data between sites b) providing additional fine-grained expert annotation of EEG records independent of the recording laboratory. The amount requested is based on a base salary of \$60,000 per year plus 30% benefits x 0.4 effort. Other technician support will be provided as in kind from the 3 partners (0.6 FTE in total per year). Physician time totaling approximately 0.2 FTE will be provided in kind by the participating sites.

Computer Specialist: We are requesting support for a computer specialist (0.4 FTE/year) for 3 years to be based on PI Dr. Law's laboratory in Waterloo, who will develop a pipeline for transferring data from Canadian hospitals and from Bhutan, and automatically processing the data into a web-ready format for crowdsourcing. The amount requested is based on a base salary of \$60,000 per year plus 14% benefits.

Research Trainees

Graduate Students: We are requesting support for 3 PhD students and 1 MSc student for 3 years. 2 PhD students and 1 MSc student will be based at Dr. Law's laboratory in Waterloo. PhD1 will focus on the development of the task decomposition, delegation, and iterative refinement framework for the epoch-by-epoch behavioral state classification problem. PhD2 will do the same for the seizure and IED detection problem. MSc1 at Waterloo will handle interface design and human-computer interface questions. PhD3 (0.5 effort) at McGill will develop Dr. Pineau's automated IED and seizure detection algorithms for use in this project. The amount requested reflects a base of \$21,865 per year for PhD students and \$16,000 per year for MSc students.

Expendables

Laptop Computers: We are requesting \$1500 each for laptop computers for the 4 graduate students, and 1 technician who will be devoted to this project.

Service

Non-Expert Annotations: We are requesting \$5000 per year for 3 years to provide compensation for representative non-expert annotators who will be recruited through advertisements, as well as through the Amazon Mechanical Turk platform.

Data Hosting for Time Series Data: We are requesting \$100 per month to cover costs of hosting our data.

Travel

Waterloo-Toronto: We are requesting funds to cover costs for monthly visits for PI Dr. Law and one of the Waterloo graduate students to travel to Toronto where they will be hosted by our technology transfer partners at Sunnybrook and Toronto Western Hospital. Activities at these visits will include embedding in the clinical teams to better understand the needs of these clinical services and the potential for technology to meet these needs, more formal focus group needs assessment, iterative interface development, and evaluation and testing of prototypes. Costs are based on standard CIHR per-diem costs for meals (\$73.65 per person) plus GO-bus fares (\$32.20 per person return) plus subway fare (\$6 per person) for 2 people.

Bhutan: In year 3, we are requesting funds for 2 graduate students and 2 PIs to travel to Bhutan to field-test the finished smartphone-integrated prototype. This is essential to assess how the prototype functions in the hands of front-line health workers in the setting in which it is intended to be used. Performing similar testing in the laboratory environment would likely not be sufficient. The budget is based on \$2000 for air travel, the standard CIHR per-diem meal rate of \$73.65 per day for 14 days, and \$50 per day for accommodations.



Appl. #

Partnership Details

Applicant

Last Name Law First Names Edith

Title

A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings

Partner Details

Name of Partner Sunnybrook Hospital Clinical Neurophysiology Lab

Acronym Name of Partner (if applicable)

Contact Last Name	Contact First Names
Murray	Brian

Telephone	Email
416-480-4475	brian.murray@sunnybrook.ca

Full Mailing Address	Fax	416-480-4674
Clinical Neurophysiology Laboratory,		
Sunnybrook HSC		
2075 Bayview Ave - Room M1-600		

Website Address	http://sunnybrook.ca/glossary/item.asp?g=2&i=939&page=
-----------------	---

Expected Period of Support : 3 Year(s) 0 Month(s)

	Partner Contribution	
	Cash	In-Kind
Year 1	\$0	\$49900
Year 2	\$0	\$49100
Year 3	\$0	\$53900
Year 4		
Year 5		
TOTAL	\$0	\$152900
Total Cash + In-Kind =	\$152900	

Non - Leveraged Contribution (if applicable)	
Year 1	
Year 2	
Year 3	
Year 4	
Year 5	
TOTAL	\$0
Total Non-Leveraged =	\$0

Signature of Responsible Partner Officer:

The responsible Partner Officer has the authority to bind the Partner to the final support of the grant and/or award.

Surname	Given Name(s)	Title
Date	Signature	



Appl. #

Partnership Details**Applicant**

Last Name Law First Names Edith

Title

A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings

Partner Details

Name of Partner Sunnybrook Hospital Clinical Neurophysiology Lab

Acronym Name of Partner (if applicable)

Contact Last Name Murray Contact First Names Brian

Telephone 416-480-4475 Email brian.murray@sunnybrook.ca

Full Mailing Address
Clinical Neurophysiology Laboratory,
Sunnybrook HSC
2075 Bayview Ave - Room M1-600Website Address
<http://sunnybrook.ca/glossary/item.asp?g=2&i=939&page=>

Expected Period of Support : 3 Year(s) 0 Month(s)

	Partner Contribution	
	Cash	In-Kind
Year 1	\$0	\$49900
Year 2	\$0	\$49100
Year 3	\$0	\$53900
Year 4		
Year 5		
TOTAL	\$0	\$152900
Total Cash + In-Kind =	\$152900	

Non - Leveraged Contribution (if applicable)	
Year 1	
Year 2	
Year 3	
Year 4	
Year 5	
TOTAL	\$0
Total Non-Leveraged =	\$0

Signature of Responsible Partner Officer:

The responsible Partner Officer has the authority to bind the Partner to the final support of the grant and/or award.

Surname	Given Name(s)	Title
MURRAY	Brian	MD FRCPC DABSM
Date	Signature	
Sept 21 2014		



Appl. #

Partnership Details**Applicant**

Last Name Law First Names Edith

Title

A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings

Partner Details

Name of Partner Toronto Western Hospital Epilepsy Program

Acronym Name of Partner (if applicable)

Contact Last Name Wennberg Contact First Names Richard

Telephone 416-603-5402 Email richard.wennberg@uhn.ca

Full Mailing Address
Epilepsy Program, Toronto Western
Hospital
399 Bathurst St. - West Wing 5th FloorWebsite Address
http://www.uhn.ca/KNC/PatientsFamilies/Clinics_Tests/Epilepsy_Clinic

Expected Period of Support : 3 Year(s) 0 Month(s)

	Partner Contribution	
	Cash	In-Kind
Year 1	\$0	\$51200
Year 2	\$0	\$50400
Year 3	\$0	\$55200
Year 4		
Year 5		
TOTAL	\$0	\$156800
Total Cash + In-Kind =	\$156800	

Non - Leveraged Contribution (if applicable)	
Year 1	
Year 2	
Year 3	
Year 4	
Year 5	
TOTAL	\$0
Total Non-Leveraged =	\$0

Signature of Responsible Partner Officer:

The responsible Partner Officer has the authority to bind the Partner to the final support of the grant and/or award.

Surname Given Name(s) Title

Date Signature



Canadian Institutes
of Health Research

Instituts de recherche
en santé du Canada

PROTECTED B WHEN COMPLETED

Appl. #

Partnership Details

Applicant

Last Name Law First Names Edith

Title

A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings

Partner Details

Name of Partner Toronto Western Hospital Epilepsy Program, Clinical Neurophysiology Laboratory

Acronym Name of Partner (if applicable)

Contact Last Name Wennberg Contact First Names Richard

Telephone 416-603-5402 Email richard.wennberg@uhn.ca

Full Mailing Address Epilepsy Program, Toronto Western Hospital
399 Bathurst St. - West Wing 5th Floor, TORONTO, ON M5T 2S8

Website Address http://www.uhn.ca/KNC/PatientsFamilies/Clinics_Tests/Epilepsy_Clinic

Expected Period of Support : 3 Year(s) 0 Month(s)

	Partner Contribution	
	Cash	In-Kind
Year 1	\$0	\$51200
Year 2	\$0	\$50400
Year 3	\$0	\$55200
Year 4		
Year 5		
TOTAL	\$0	\$156800
Total Cash + In-Kind =		\$156800

Non - Leveraged Contribution (if applicable)	
Year 1	
Year 2	
Year 3	
Year 4	
Year 5	
TOTAL	\$0
Total Non-Leveraged =	
<b">\$0</b">	

Signature of Responsible Partner Officer:

The responsible Partner Officer has the authority to bind the Partner to the final support of the grant and/or award.

Surname Given Name(s) Title
WENNBERG RICHARD Director, Clin. Neurophysiology
Date Signature Laboratory
25 SEPT 2014 *RICHARD WENNBERG, PhD, FRCPC*



Appl. #

Partnership Details

Applicant

Last Name Law First Names Edith

Title

A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings

Partner Details

Name of Partner The Bhutan Epilepsy Project

Acronym Name of Partner (if applicable)

Contact Last Name Mateen	Contact First Names Farrah
-----------------------------	-------------------------------

Telephone 613-562-5800 / 617-726-2383	Email fmateen@partners.org
--	-------------------------------

Full Mailing Address Interdisciplinary Faculty of Health Sciences University of Ottawa Thompson Hall, 25 University Private	Fax 613-562-5632 / 617-726-2353
--	---------------------------------

Website Address
<http://www.bhutanbrain.com/>

Expected Period of Support : 3 Year(s) 0 Month(s)

	Partner Contribution	
	Cash	In-Kind
Year 1	\$0	\$19360
Year 2	\$0	\$38400
Year 3	\$0	\$52800
Year 4		
Year 5		
TOTAL	\$0	\$110560
Total Cash + In-Kind =	\$110560	

Non - Leveraged Contribution (if applicable)	
Year 1	
Year 2	
Year 3	
Year 4	
Year 5	
TOTAL	\$0
Total Non-Leveraged =	\$0

Signature of Responsible Partner Officer:

The responsible Partner Officer has the authority to bind the Partner to the final support of the grant and/or award.

Surname Given Name(s) Title

Date Signature



Appl. #

Partnership Details

Applicant

Last Name Law

First Names Edith

Title

A framework for hybrid machine and human computation for the accurate and scalable analysis of human clinical EEG recordings

Partner Details

Name of Partner The Bhutan Epilepsy Project

Acronym Name of Partner (if applicable)

Contact Last Name Mateen Contact First Names Farrah

Telephone 613-562-5800 / 617-726-2383 Email fmateen@partners.org

Full Mailing Address Interdisciplinary Faculty of Health Sciences
University of Ottawa
Thompson Hall, 25 University PrivateWebsite Address
<http://www.bhutanbrain.com/>

Expected Period of Support : 3 Year(s) 0 Month(s)

	Partner Contribution	
	Cash	In-Kind
Year 1	\$0	\$19360
Year 2	\$0	\$38400
Year 3	\$0	\$52800
Year 4		
Year 5		
TOTAL	\$0	\$110560
Total Cash + In-Kind =		\$110560

Non - Leveraged Contribution (if applicable)	
Year 1	
Year 2	
Year 3	
Year 4	
Year 5	
TOTAL	\$0
Total Non-Leveraged =	
<b">\$0</b">	

Signature of Responsible Partner Officer:

The responsible Partner Officer has the authority to bind the Partner to the final support of the grant and/or award.

Surname	Given Name(s)	Title
Mateen	Farrah	Adjunct Professor
Date	Signature	
18 Sept 2014		

Game Mechanisms for Attribute Learning

Games with a Purpose are games that people play, and as a by-product, generate useful data. I introduced a new game called TagATune, which implements a novel mechanism for incentivizing truthful annotations. TagATune has been played by tens of thousands of players, generated more than 1 million high quality annotations, resulting in a research dataset that is still being widely used today.

E. Law and L. von Ahn. (2009) Input-agreement: A New Mechanism for Data Collection using Human Computation Games. CHI, 1197-1206. (Best Paper Honorable Mention).

E. Law, B. Settles and T. Mitchell. "Learning to Tag using Noisy Labels." In ECML 2010.

Hybrid Human-Machine Computation

I developed a hybrid human and machine computation approach which decomposes complex classification tasks into something that non-experts can do, and uses machine learning algorithms to combine non-expert and expert contributions to achieve the original task. I studied this approach within the context of bird species classification. Results show that a hybrid categorization approach – using machine intelligence to enable non-experts to complete an expert classification task – outperforms asking non-experts to classify birds directly, both in terms of achieving better classification results and motivating participation.

E. Law. Attribute Learning using Human and Machine Computation. Ph.D. Thesis, Carnegie Mellon University, 2012.

A Framework for Studying Human Computation

I wrote a book on human computation, which has been distributed to over 100 attendees at the AAAI and IUI conference, downloaded more than 280 times, and widely used in courses at many universities, including Cornell, Harvard, Rutgers, UT Austin, Carnegie Mellon and McGill. I also co-organized the Human Computation Workshops (HCOMP) from 2009-2012, and co-founded the first AAAI Conference on Human Computation and Crowdsourcing in 2013.

E. Law, L. von Ahn. (2011) Human Computation. Synthesis Lectures on Artificial Intelligence and Machine Learning, 1-105..

Collaborative Interfaces for Crowdsourcing Complex Tasks

An important class of complex problems are those that demand the solution to satisfy a set of global requirements. I demonstrated, through the creation of two collaborative interfaces for itinerary planning and text summarization, that such complex tasks can be solved using a social computing approach, with participants making bite-size contributions using a shared interface and with algorithms coordinating the computational process.

H. Zhang, E. Law, R. Miller, K. Gajos, D. Parkes, E. Horvitz. Human Computation Tasks with Global Constraints: A Case Study. In CHI, 2012. (Best Paper Honorable Mention).

E. Law, B. Grosz, L. M. Sanders, and S. H. Fischer. Simplyput: Leveraging a mixed-expertise crowd to improve health literacy. In AAMAS Workshop on Human-Agent Interaction Design and Models, 2013.

Curio: A Mixed-Expertise Platform for Crowdsourcing Scientific Tasks

I built Curio, a citizen science platform (<http://www.crowdcurio.com>) that enables researchers, who are domain experts but not necessarily technically savvy or familiar with crowdsourcing, to more easily create and manage crowdsourcing projects.

E. Law, C. Dalton, N. Merrill, A. Young, and K. Z. Gajos. Curio: A platform for supporting mixed-expertise crowdsourcing. In HCOMP, 2013.

E. Law and K. Gajos. Crowdsourcing Science: Opportunities, Challenges and Design Implications. In Submission.

1 - Five Most Significant Contributions

Chair of the Royal College Specialty Committee in Neurology

April 2014-

-After 5 years service on the examination board of the Royal College of Physicians and Surgeons of Canada for neurology I was appointed as chair of the Specialty Committee in neurology. This committee has representation from across Canada. I am responsible for providing leadership to advance the discipline in Canada by focusing the committee on specialty education matters. We are engaging on a massive restructuring of medical education based on a move towards competency based education.

Chair of the Research Ethics Board of Sunnybrook Health Sciences Centre

October 2013-

-After several years service on the board and as vice-chair I assumed this leadership position. As one of Canada's largest teaching hospitals, I lead a board of over 20 members in the ethical review of research protocols. We have over 1360 active studies, and the numbers are increasing. Some of our emergency protocols are breaking new ground in the practice of research ethics, and have been featured in publications such as the Globe and Mail.

Director of Integrated Medical Education for the University of Toronto

2011-

-The University of Toronto sought to expand its medical school and has established a campus at Mississauga that would be the size of many independent medical schools. I am responsible for leading the integrated medical education strategy in the Department of Medicine and guide and support the development of community-affiliated internal medicine and sub-specialty medicine experiences in undergraduate, postgraduate medicine and continuing education.

Winkelman JW, Henderson JH, Kotagal S, Lee-Chiong TL, Lichstein KL, Murray BJ, Schenck, CH as **editors for the American Academy of Sleep Medicine: The Sleep Medicine Case Book-A learning companion to the International Classification of Sleep Disorders, 2nd ed., Diagnostic and Coding Manual**. Westchester, Illinois: American Academy of Sleep Medicine

2008

-I was an invited member of the nosology committee of the American Academy of Sleep Medicine, and co-edited this textbook, which was a major educational resource for this society. This book has sold 1198 copies in the first year and represents a publication of "major impact" for the field. This publication was developed as a teaching resource for many levels, and required a broad survey of topics, incorporating authors from around the world.

Establishment of the Sleep Laboratory at Sunnybrook Health Sciences Centre

2004-

-I established a sleep laboratory at Sunnybrook that has a focus in neurological aspects of sleep medicine. We have an advanced laboratory for video/neurophysiological monitoring with all digital information archived from 2004. The laboratory facilitates the work of several investigators with over \$500,000 in peer-reviewed funds, over 50 publications in the last 5 years, and international recognition with trainees from across the world.

1. Identification of the first common human genetic variant to be associated with the circadian timing of human behavioural rhythms and with clock time of death
Lim et al., *Ann Neurol.* 2012; 72:324-34

Using novel actigraphic and statistical methods, I identified the first common genetic variant to be associated with the timing of human behavioural rhythms and with clock time of death. This polymorphism is associated with a >1 hour difference in human circadian phase and a >5 hour difference in mean clock time of death, and appears to regulate expression *PER1*, a canonical “clock” gene, in cerebral cortex. This finding may inform the individualization of the timing of medical tests and therapies, and the broader scheduling of work, school, and social activities.

2. Demonstration that sleep fragmentation is associated with the risk of Alzheimer’s disease and the development of Alzheimer’s disease pathological changes in older persons.

Lim et al., *Sleep.* 2011; 34:1569-81

Lim et al., *Sleep.* 2012; 35:633-40.

Lim et al., *Sleep.* 2013; 36:1027-32.

Lim et al., *JAMA Neurol.* 2013; 70(12):1544-51.

I developed a novel transition-probabilistic approach to the quantification of sleep fragmentation from actigraphic data and demonstrated that so measured, sleep fragmentation predicts the risk of incident Alzheimer disease and Alzheimer’s disease (AD) pathology in older individuals, and magnifies the effects of the APOE4 allele, the main genetic risk factor for AD. This provided the first practical objective way to measure sleep fragmentation in large cohorts in their usual environments, and established the clinical significance of sleep fragmentation to the risk of AD..

3. Demonstration of cell loss in the human intermediate nucleus of the hypothalamus as an important cause of sleep disruption in aging and Alzheimer’s disease.

Lim et al., *Brain.* 2014; 137(10):1847-61.

This provided an anatomical explanation for sleep disruption in aging and Alzheimer’s disease - a key contributor to poor quality of life. This may open the door to targeted pharmacologic or anatomic therapies for sleep disruption and insomnia in aging and AD.

4. Demonstration of circadian rhythms of gene expression and DNA methylation in the human cerebral cortex.

Lim et al., *J Biol Rhythms.* 2013; 28(2):117-29.

Lim et al., *PLoS Genetics.* In Revision.

I developed novel analytic tools to extract information about circadian rhythms of gene expression and DNA methylation from post-mortem human tissue. I used these tools to demonstrate for the first time in any mammalian species circadian rhythms of DNA methylation and their relationship to RNA expression, illuminating a novel role for dynamic circadian rhythms of DNA methylation in the control of human neocortical gene expression.

5. Demonstration that deep brain stimulation can modulate human sleep

Lim et al., *Ann Neurol* 2009; 66:110-114.

This work was the first demonstration that deep brain stimulation can fundamentally modulate human sleep architecture. This opened the door to the use of DBS to therapeutically modulate human sleep, and highlighted anatomical homology between brainstem circuits regulating human and animal REM sleep

Andrew Lim	Activities and Contributions
<u>Research Supervision</u>	
2014 May - 2014 Aug	Role: Primary Supervisor. Student: Shahmir Sohail (BSc summer student). <i>Disrupted Circadian Rest-Activity Rhythms in Older Adults are Associated with Adverse Metabolic and Cardiovascular Consequences</i> . Awards: Supported by a summer studentship from the Canadian Stroke Network. Awards: D&D SRI Summer Student Research Competition – 2nd Place.
2014 Mar	Role: Thesis Examiner. Student: Bojana Gladanac (MSc University of Toronto). <i>Effects of filtering visual short wavelengths on circadian photic phase resetting</i> .
2011 Jul - 2014 Feb	Role: Thesis Committee Member. Student: Mark Boulos (MSc student) <i>Restless Legs Syndrome and Periodic Limb Movements in Sleep Following TIA or Minor Stroke</i> .
2013 May - 2013 Aug	Role: Primary Supervisor. Student: Shahmir Sohail (BSc summer student). <i>A Genome-Wide Association Scan Identifies a Common Genetic Variant Near the KCTD2 Gene Associated with a Biomarker of Parkinson Disease</i> . Awards: D&H SRI Summer Student Research Competition - 1st Place.
2013 May - 2013 Aug	Role: Primary Supervisor. Student: Naveed Islam (visiting MSc student). <i>Circadian Rhythms of DNA Methylation in the Human Cerebral Cortex</i> .
<u>Grant Reviews - International</u>	
2014 Jan - 2014 Feb	National Institutes of Health (USA), Cardiovascular and Sleep Epidemiology Study Section, Number of Reviews: 2
2013 Nov - 2013 Nov	Medical Research Council (United Kingdom), Fellowships, FEC, Career Development Awards, Number of Reviews: 1
<u>Grant Reviews - National</u>	
2013 - 2014	Canadian Institutes of Health Research, Doctoral Research Awards A, Number of Reviews: 13
2012 - 2013	Canadian Institutes of Health Research, Behavioural Sciences B, Number of Reviews: 1
<u>Manuscript Reviews</u>	
2014	Canadian Journal of Neurological Sciences, Number of Reviews: 1
2013 - 2014	European Journal of Neurology, Number of Reviews: 1
2013	International Journal of Neuroscience, Number of Reviews: 1
2013	Journal of the American Aging Association, Number of Reviews: 1
2013	Movement Disorders, Number of Reviews: 1
2012 - 2014	Chronobiology International, Number of Reviews: 4
2012	Alzheimer Disease and Related Disorders, Number of Reviews: 1
2012	International Journal of Epidemiology, Number of Reviews: 1
2012	PLoS One, Number of Reviews: 1
2011 - 2012	Proceedings of the National Academy of Sciences, Number of Reviews: 1
2010 - 2014	Annals of Neurology, Number of Reviews: 1
2010 - 2014	Journal of Neuroscience Methods, Number of Reviews: 1
2010 - 2014	Sleep, Number of Reviews: 3
2010	Journal of Comparative Neurology, Number of Reviews: 1

Published Original Research Articles In Peer-Reviewed Journals (Last 5 Years)

1. **Lim AS**, Ellison B, Wang J, Yu L, Schneider JA, Buchman AS, Bennett DA, Saper CB. Sleep is related to neuron numbers in the ventrolateral preoptic/intermediate nucleus in older adults with and without Alzheimer's disease. **Brain (IF 10.2)**. 2014; 137(10):1847-61. **Contribution:** 80% (developed and carried out immunohistochemistry and stereological cell counting protocol; developed MATLAB algorithms for actigraphy analysis, carried out all analyses, wrote manuscript)
2. **Lim AS**, Yu L, Kowgier M, Schneider JA, Buchman AS, Bennett DA. Modification of the Relationship of the Apolipoprotein E ε4 Allele to the Risk of Alzheimer Disease and Neurofibrillary Tangle Density by Sleep. **JAMA Neurology (IF 7.7)**. 2013; 70(12):1544-51. **Contribution:** 80% (conceived of hypothesis, developed MATLAB algorithms for actigraphy analysis, carried out all analyses, wrote manuscript)
3. **Lim AS**, Kowgier M, Yu L, Buchman AS, Bennett DA. Sleep Fragmentation and the Risk of Incident Alzheimer's Disease and Cognitive Decline in Older Persons. **Sleep (IF 5.1)**. 2013; 36(7):1027-32. **Contribution:** 80% (conceived of hypothesis, developed MATLAB algorithms for actigraphy analysis, carried out all analyses, wrote manuscript)
4. **Lim AS**, Myers AJ, Yu L, Buchman AS, Duffy JF, De Jager PL, Bennett DA. Sex difference in Daily Rhythms of Clock Gene Expression in the Aged Human Cerebral Cortex. **Journal of Biological Rhythms (IF 3.2)**. 2013; 28(2):117-29. **Contribution:** 80% (conceived of hypothesis, developed R algorithms for genetic analysis, carried out all analyses, wrote manuscript)
5. Park M, Buchman AS, **Lim AS**, Leurgans SE, Bennett DA. Sleep Complaints and Incident Disability in a Community-Based Cohort Study of Older Persons. **The American Journal of Geriatric Psychiatry (IF 4.1)**. 2013; 12:123-6. **Contribution:** 20% (provided important input into analysis and interpretation and contributed to drafting manuscript)
6. Buchman AS, Nag S, Shulman JM, **Lim AS**, VanderHorst VG, Leurgans SE, Schneider JA, Bennett DA. Locus caeruleus neuron density and parkinsonism in older adults without Parkinson's disease. **Movement Disorders (IF 4.6)**. 2012; 27(13):1625-31. **Contribution:** 20% (provided important input into analysis and interpretation and contributed to drafting manuscript)
7. **Lim AS**, Chang AM, Shulman JM, Raj T, Chibnik LB, Cain SW, Rothamel K, Benoit C, Myers AJ, Czeisler CA, Buchman AS, Bennett DA, Duffy JF, Saper CB, De Jager PL. A common polymorphism near PER1 and the timing of human behavioral rhythms. **Annals of Neurology (IF 11.2)**. 2012; 72(3):324-34. **Contribution:** 80% (conceived of hypothesis, developed MATLAB algorithms for actigraphy analysis, carried out all actigraphic and genetic analyses in R, PLINK, and MATLAB, wrote manuscript)
8. **Lim AS**, Yu L, Costa MD, Leurgans SE, Buchman AS, Bennett DA, Saper CB. Increased fragmentation of rest-activity patterns is associated with a characteristic pattern of cognitive impairment in older individuals. **Sleep (IF 5.1)**. 2012; 35(5):633-40. **Contribution:** 80% (conceived of hypothesis, developed and carried out all analyses, wrote manuscript)
9. **Lim AS**, Yu L, Costa MD, Buchman AS, Bennett DA, Leurgans SE, Saper CB. Quantification of the fragmentation of rest-activity patterns in elderly individuals using a state transition analysis. **Sleep (IF 5.1)**. 2011; 34(11):1569-81. **Contribution:** 80% (conceived of hypothesis, developed R algorithms for genetic analysis, carried out all analyses, wrote manuscript)
10. **Lim AS**, Moro E, Lozano AM, Hamani C, Dostrovsky JO, Hutchison WD, Lang AE, Wennberg RA, Murray BJ. Selective enhancement of rapid eye movement sleep by deep brain stimulation of the human pons. **Annals of Neurology (IF 11.2)**. 2009; 66(1):110-4. **Contribution:** 80% (I conceived of and designed the study protocol, cared for the subjects clinically, analyzed the data, and wrote the manuscript)

Published Editorials in Peer-Reviewed Journals (Last 5 Years)

1. **Lim AS**, Saper CB. Sleep, circadian rhythms, and dementia. **Annals of Neurology (IF 11.2)**. 2011; 70(5):677-9. **Contribution:** 90% (I wrote the editorial)
2. **Lim AS**, Scammell TE. The trouble with Tribbles: do antibodies against TRIB2 cause narcolepsy? **Sleep (IF 5.1)**. 2010; 33(7):857-8. **Contribution:** 90% (I wrote the editorial)

Submitted Original Research Articles In Peer-Reviewed Journals

1. **Lim AS**, Srivastava GP, Yu L, Chibnik LB, Xu J, Buchman AS, Schneider JA, Myers AJ, Bennett DA, De Jager PL. 24-Hour Rhythms of DNA Methylation and Their Relation with Rhythms of RNA Expression in the Human Dorsolateral Prefrontal Cortex. **PLoS Genetics (IF 8.2)**. 2014 Sep 5. In Revision. **Contribution:** 80% (I developed the hypotheses, processed and analyzed the data, and wrote the manuscript)

Selected Published Abstracts (Last 5 Years)

1. **Lim AS**, Srivastava GP, Yu L, Buchman AS, Schneider JA, Myers AJ, Bennett DA, De Jager PL. Diurnal Rhythms of Clock Gene DNA Methylation and their Relationship to Rhythms of Clock Gene Expression in the Human Cerebral Cortex. ASHG Abstract Supplement. 2013 Oct 24:2. The 63rd Annual Meeting of The American Society of Human Genetics, Boston, MA, October 23-26. **Contribution:** 80% (conceived of hypothesis, carried out all analyses, designed poster)
2. **Lim AS**, Myers AJ, Yu L, Buchman AS, Duffy JF, De Jager PL, Bennett DA. Sex Difference in Diurnal Patterns of Clock Gene Expression in the Human Cerebral Cortex. **Sleep**. 2013 Jun 2;36(S1):A47-A48. 2013; 36(S1):A47-48. The 27th Annual Meeting of the Associated Professional Sleep Societies, Baltimore, Maryland, June 1-5, 2013. **Contribution:** 80% (conceived of hypothesis, developed R algorithms for genetic analysis, carried out all analyses, gave platform presentation)
3. **Lim AS**, Simpson N, Nemeth E, Scott-Sutherland J, Mullington JM, and Haack M. Self-Reported Spontaneous Pain is Increased in Insomnia with Objective Sleep Impairment. **Sleep**. 2013 Jun 2;36(S1):A218-A218. 2013; 36(S1):A218. The 27th Annual Meeting of the Associated Professional Sleep Societies, Baltimore, Maryland, June 1-5, 2013. **Contribution:** 80% (conceived of hypothesis, developed R algorithms for genetic analysis, carried out all analyses, designed poster)
4. **Lim AS**, Yu L, Kowgier M, Buchman AS, Bennett DA. Sleep Fragmentation Modifies the Impact of the ApoE4 Allele on the Risk of Incident Alzheimer Disease and Cognitive Decline in Older Persons. **Neurology**. 2013; 80(A1):S24-004. The 65th Annual Meeting of the American Academy of Neurology, San Diego, CA, March 16-23, 2013. **Contribution:** 80% (conceived of hypothesis, developed MATLAB algorithms for analysis, carried out all analyses, gave platform presentation)
5. **Lim AS**, Kowgier M, Yu L, Buchman AS, Bennett DA. Rest/Activity Fragmentation and the Risk of AD in Older Adults. **Annals of Neurology**. 2012; 72(S16):46. The Annual Meeting of the American Neurological Association, Boston, MA, October 7-9, 2012. **Contribution:** 80% (conceived of hypothesis, developed MATLAB algorithms for analysis, carried out all analyses, designed poster)
6. **Lim AS**, Haack M, Simpson N, Mullington JA. Fragmentation/Consolidation of Rest-Activity Patterns Correlates with Subjective Sleep Quality in Chronic Primary Insomnia. **Sleep**. 2012; 35(S):A231. The 26th Annual Meeting of the Associated Professional Sleep Societies; Boston, MA, June 12, 2012. **Contribution:** 80% (conceived of hypothesis, developed R algorithms for genetic analysis, carried out all analyses, designed poster)
7. **Lim AS**, Simpson N, Haack M, Mullington JA. Experimental Sleep Deprivation is Associated with an Increased Tendency to Sustained Spontaneous Motor Activity in Healthy Human Subjects. **Sleep**. 2012; 35(S):A119-20. The 26th Annual Meeting of the Associated Professional Sleep Societies; Boston, MA; June 11, 2012. **Contribution:** 80% (conceived of hypothesis, developed R algorithms for genetic analysis, carried out all analyses, designed poster)

8. **Lim AS**, Yu L, Costa MD, Leurgans SE, Buchman AS, Bennett DA, Saper CB. The local continuity of rest-activity patterns is associated with cognitive function in old age. *Neurology*. 2011; 76(9):A118. The 63rd Annual Meeting of the American Academy of Neurology, Honolulu, HI, April 9-16, 2011. **Contribution:** 80% (conceived of hypothesis, developed MATLAB algorithms for analysis, carried out all analyses, designed poster)
9. **Lim AS**, Saper CB, Buchman AS, Bennett DA, and De Jager, PL. A common genetic variant near PER1 is associated with objectively measured circadian phase in humans. *Annals of Neurology*. 2010; 68(S14):S67. The 135th Annual Meeting of the American Neurological Association, San Francisco, CA, October 12-15, 2010. **Contribution:** 80% (conceived of hypothesis, developed algorithms for actigraphy analysis, carried out all analyses, delivered platform presentation)

Presentations as a Guest Speaker – Conference Presentations (International; Last 5 Years)

- 2013 Jun 2 **Invited Speaker.** Diurnal Patterns of Clock Gene Expression in the Human Cerebral Cortex. 27th Annual Meeting of the Associated Professional Sleep Societies. Baltimore, Maryland, United States. Presenter(s): Lim AS. Platform Presentation.
- 2013 Mar 20 **Invited Speaker.** Sleep Fragmentation Modifies the Impact of the ApoE4 Allele on the Risk of Incident Alzheimer Disease and Cognitive Decline in Older Persons. 65th Annual Meeting of the American Academy of Neurology. San Diego, California, United States. Presenter(s): Lim AS. Platform Presentation.

Presentations as a Guest Speaker – Invited Lectures (International; Last 5 Years)

- 2013 Jun 25 **Invited Lecturer.** Sleep Disruption and Sleep Disorders as Potentially Modifiable Risk Factors for Vascular Cognitive Impairment. International Society of Vascular, Behavioural, and Cognitive Disorders. Toronto, Ontario, Canada. Presenter(s): Lim, A.S. Invited lecture at the 6th International Society of Vascular, Cognitive and Behavioural Disorders Congress.
- 2013 May 30 **Invited Speaker.** Sleep and Circadian Biology in the Rush Memory and Aging Project. ROS/MAP Investigators' Meeting. Chicago, Illinois. Invited round.
- 2012 Jun 15 **Invited Speaker.** Sleep and Circadian Biology in the Rush Memory and Aging Project. ROS/MAP Investigators' Meeting. Chicago, Illinois. Invited round.
- 2012 Mar 19 **Invited Lecturer.** Sleep and Circadian Biology in the Rush Memory and Aging Project. Rush Alzheimer Disease Center Neuroepidemiology Course.
- 2011 Mar 30 **Invited Speaker.** Sleep and Circadian Biology in the Rush Memory and Aging Project. ROS/MAP Investigators' Meeting. Chicago, Illinois. Invited round.

Presentations as a Guest Speaker – Invited Lectures (National; Last 5 Years)

- 2013 Nov 2 **Invited Speaker.** Genetic and epigenetic dissection of human neocortical, behavioral, and clinical circadian rhythms. CIHR New Principal Investigators Meeting. Mont Gabriel, Quebec, Canada. Presenter(s): Lim AS. Platform Presentation.
- 2010 Sep **Invited Speaker.** Parasomnias. Fraser Health Region Medical Grand Rounds. Maple Ridge, British Columbia. Invited round. (Continuing Education).
- 2010 Sep **Invited Speaker.** A common genetic variant near PER1 associated with human circadian phase. University of British Columbia Neurosciences Grand Rounds. Vancouver, British Columbia. Invited round. (Continuing Education).

Presentations as a Guest Speaker – Invited Lectures (Regional; Last 5 Years)

- 2013 Oct 30 **Visiting Professor.** Genetic and epigenetic dissection of human neocortical, behavioral, and clinical circadian rhythms. Thrombosis and Atherosclerosis Research Institute, Hamilton, ON. Hamilton, Ontario, Canada. Presenter(s): Lim, A.S. Visiting Professor.
- 2013 Feb 1 **Invited Speaker.** "Sleep Fragmentation and the Risk of Alzheimer Disease in Older Adults". Province-Wide Sleep Grand Rounds. Toronto, Ontario, Canada. Presenter(s): Lim AS. University of Toronto Invited Presentation.

Presentations as a Guest Speaker – Invited Lectures (Local; Last 5 Years)

- 2012 Oct 12 **Invited Speaker.** "Sleep Fragmentation and the Risk of Alzheimer Disease in Older Adults". City-Wide Sleep Grand Rounds. Toronto, Ontario, Canada. Presenter(s): Lim AS. University of Toronto Invited Round.
- 2012 May 25 **Invited Speaker.** Sleep Fragmentation, Cognition, and Dementia in Older Persons. University of Toronto City-Wide Neurology Grand Rounds. Ontario, Canada.
- 2011 Dec **Invited Speaker.** "Rest-Activity Fragmentation and Cognitive Impairment in Older Individuals". Sunnybrook Brain Sciences Rounds.

- 2011 Nov **Invited Speaker.** “A common polymorphism near PER1 and the timing of human behavioural rhythms”. University of Toronto Division of Neurology Research Day. Toronto, Ontario.
- 2011 Oct 11 **Invited Speaker.** “A common polymorphism near PER1 and the timing of human behavioural rhythms”. Sunnybrook Health Sciences Centre Medical Grand Rounds. Toronto, Ontario.
- 2011 Sep **Invited Speaker.** “A common polymorphism near PER1 and the timing of human behavioural rhythms”. City-Wide Sleep Grand Rounds. University of Toronto Invited Round.
- 2011 Sep **Invited Speaker.** “A common polymorphism near PER1 and the timing of human behavioural rhythms”. Sunnybrook Brain Sciences Rounds. University of Toronto Invited Round.

Media Appearances (International; Last 5 Years)

- 2014 Aug 20 **Interviewee.** Neuron loss in the intermediate nucleus and sleep disruption in older adults with and without Alzheimer's disease. Interviewer: James Tuck. CBS radio news KNZ. Los Angeles, California, United States. Radio Interview.
- 2014 Aug 20 **Interviewee.** Neuron loss in the intermediate nucleus and sleep disruption in older adults with and without Alzheimer's disease. Interviewer: Anne Winburry. CBS radio news. New York, New York, United States. Radio Interview.
- 2013 Dec 1 **Interviewee.** Sleep alleviates AD-related neuropathological processes. Interviewer: Hemi Malkki. Nature Reviews Neurology. United Kingdom. Presenter(s): Hemi Malkki. Magazine Article.
- 2013 Oct 25 **Interviewee.** From ApoE to Zzz's - Does Sleep Quality Affect Dementia Risk? Interviewer: Esther Landhuis. Alzforum.org. San Francisco, California, United States. Presenter(s): Esther Landhuis. Online Article. Available from: [www.alzforum.org/new/detail.asp?id=3627&utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+alzforum%2FPpcR+\(Alzforum+News\)](http://www.alzforum.org/new/detail.asp?id=3627&utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+alzforum%2FPpcR+(Alzforum+News)).
- 2013 Oct 21 **Interviewee.** Poor sleep tied Alzheimer's like brain changes. Interviewer: Genevra Pittman. Reuters Health. United States. Presenter(s): Genevra Pittman. Online Article. Available from: www.reuters.com/article/2013/10/21/us-poor-sleep-alzheimers-idUSBRE99K0WV20131021.
- 2013 Jul 31 **Interviewee.** Wish you were a morning person? Try a camping trip. Interviewer: Cari Nierenberg. livescience.com. United States. Presenter(s): Cari Nierenberg. Online Article. Available from: www.livescience.com/38604-camping-resets-circadian-rhythms.html.
- 2013 Feb 6 **Presenter.** Night Owls and Morning People. Interviewer: Bradley Cornelius. WAMC Academic Minute, WAMC Radio. Albany, New York, United States. Radio Segment. Available from: wamc.org/post/dr-andrew-lim-university-toronto-night-owls-and-morning-people.
- 2012 Nov 27 **Interviewee.** Gene determines early risers, time of death. Interviewer: J Chadbourne. Cosmos Magazine. Sydney, New South Wales, Australia. Presenter(s): Chadbourne J. Magazine Article. Available from: <http://www.cosmosmagazine.com/news/genetic-basis-found-body-clock/>.
- 2012 Nov 20 **Interviewee.** The Joan Lea Show; Interviewer: Jean Lea. The Joan Lea Show. Dublin, Dublin, Ireland. Radio Interview.
- 2012 Nov 19 **Interviewee.** You are most likely to die at 11 a.m.". The Atlantic. Washington, District of Columbia, United States. Magazine Article. Available from: <http://www.theatlantic.com/health/archive/2012/11/you-are-most-likely-to-die-at-11-am/265427/>.
- 2012 Nov 19 **Interviewee.** Gene that predicts what time of day we'll die. Daily Mail. London, London, City of, United Kingdom. Newspaper Article. Available from: <http://www.dailymail.co.uk/health/article-2235014/Gene-predicts-time-day-DIE-discovered.html>.
- 2012 Nov 19 **Interviewee.** Gene can tell time of death. Times of India. Mumbai, Maharashtra, India. Newspaper Article. Available from: http://articles.timesofindia.indiatimes.com/2012-11-19/science/35204497_1_gene-variant-shift-work-internal-biological-clock.
- 2012 Oct 11 **Interviewee.** Sleep fragmentation tied to risk of Alzheimer's disease. Interviewer: Genevra Pittman. Health24.com. Cape Town, South Africa. Online Article. Available from: www.health24.com/Medical/Alzheimers/News/Sleep-fragmentation-tied-to-risk-of-Alzheimers-disease-20130210.

Media Appearances (National; Last 5 Years)

- 2014 Sep 4 **Interviewee.** Poor Sleep Linked to Shrinking Brain. Interviewer: Avril Favaro. CTV National News, CTV. Toronto, Ontario, Canada.
- 2013 Aug 1 **Interviewee.** Bonjour: how to become a morning person. Interviewer: Devon Scoble. theloop.ca. Canada. Presenter(s): Devon Scoble. Online Article. Available from: www.theloop.ca/living/article/-/a/2626145/How-to-become-a-morning-person.
- 2013 Jan 28 **Interviewee.** The world at Six; Interviewer: Pauline Dakin. Interviewer: Pauline Dakin. CBC Radio. Toronto, Ontario, Canada. Radio Interview.
- 2012 Nov 26 **Interviewee.** CTV Canada AM; Interviewer: Jeff Hutcheson. Interviewer: Jeff Hutcheson. CTV. Toronto, Ontario, Canada. Television Interview.
- 2012 Nov 22 **Interviewee.** CTV News Channel; Interviewer: Marcia MacMillan. Interviewer: Marcia MacMillan. CTV. Toronto, Ontario, Canada.
- 2012 Nov 22 **Interviewee.** The Richard Brown Show; Interviewer: Richard Brown. Interviewer: Richard Brown. The Richard Brown Show, AM650. Toronto, Saskatchewan, Canada. Radio Interview.
- 2012 Nov 20 **Interviewee.** The Charles Adler Show; Interviewer: Charles Adler. AM640. Toronto, Ontario, Canada. Radio Interview.

Media Appearances (Regional; Last 5 Years)

- 2014 Mar 13 **Interviewee.** Tips for Good Sleep. CTV News at 6:00, CTV. Toronto, Ontario, Canada.
- 2014 Feb 18 **Interviewee.** Smartphones, Sleep, and Work Performance. Global News at 5:30, Global. Toronto, Ontario, Canada.
- 2012 Nov 26 **Interviewee.** London in the Afternoon; Interviewer: Alan Coombs. Interviewer: Alan Coombs. AM1290. London, Ontario, Canada. Radio Interview.

Media Appearances (Local; Last 5 Years)

- 2012 Nov 19 **Interviewee.** University of Toronto professor discovers gene that predicts time of death. Toronto Star. Toronto, Ontario, Canada. Presenter(s): N. Scallan. Newspaper Article. Available from: http://www.thestar.com/news/gta/2012/11/19/university_of_toronto_professor_discovers_gene_that_predicts_time_of_death.html.

1) Influence of seizures on stroke outcomes: a large multicenter study.

Burneo et al, Neurology. 2014 Mar 4;82(9):768-76.
Burneo et al, Eur J Neurol 2010; 17(1): 52-8

In this work, we assess the influence of seizures and epilepsy in the outcomes following strokes.

2) A collaborative effort to establish a comprehensive epilepsy program in Peru.

Burneo et al, Epilepsy Behav. 2013 Jan;26(1):96-9

This work is based on an initiative to develop a comprehensive epilepsy program in Lima, Perú, the first of its kind in that country.

3) An assessment of the disparities in epilepsy care in North America.

Burneo et al, Epilepsia. 2009 Oct;50(10):2285-95
Burneo et al, J Can Dent Assoc 2009 Jul;75(6):450
Burneo et al, Epilepsy Behav 2006 Feb; 8(1): 299-302
Burneo et al, Epilepsy Behav 2005 Nov; 7(3): 486-90
Burneo et al, Neurology 2005 Jan; 64(1): 50-4

I formed and lead a Task Force on Disparities in Epilepsy Care, supported by the North American Commission of the International League Against Epilepsy to identify/assess the disparities in Epilepsy Care in the region. I have also studied that independently.

4) Development of an international collaborative research in neurocysticercosis and epilepsy.

Burneo et al, Epilepsy Curr 2014 jan;14(1 suppl):23-8
Burneo et al, Neurology 2013 Oct; 81(16):1474
Burneo et al, Epilepsia 2013 May; 54(5):783-92
Burneo et al, Epilepsia. 2009 May;50(5):1289-90
Burneo et al, CMAJ 2009; 180(6): 639-42

This work is based on the development of a network of researches worldwide for the study of Neurocysticercosis-related Epilepsy, which is endemic in many regions across the globe.

1. Development & validation of intelligent robots for personalized health-care.

Kim&Pineau'14; Rushton et al.'14; Kim&Pineau'13; Boucher et al.'13; Kairy et al.'13; Png et al.'12; Pineau et al.'11; Honore et al.'10; Kaplow et al.'10; Atrash et al.'09.

I am a founding member of two multi-disciplinary ventures aimed at developing prototype robotic assistants for elderly and disabled individuals. In both the Nursebot and SmartWheeler projects, I have been a leading contributor to the design and validation of complex robotic systems, and their validation with the target population. Results were presented in top journals and conferences.

2. Reinforcement learning: theory, algorithms and empirical analysis.

Barreto et al.'14; Paduraru et al.'13; Fard et al.'13; Hamilton et al.'13; Ong et al.'13; Doshi-Velez et al.'12; Barreto et al.'12; Fard et al.'12; Ross et al.'11; Barreto et al.'11; Fard et al.'11; Fard et al.'10

This work tackles the problem of defining new scalable algorithms for optimal learning and planning in stochastic domains. We propose tractable approximate solutions based on sampling methods and online search. The work generalizes known results in the RL and classical control literature, and applies to a large class of discrete/continuous and fully/partially observable problems. The results have been presented at a number of top journals and conferences (JMLR, NIPS, ICML, UAI, ICRA).

3. Adaptive learning&optimization of treatment strategies for chronic disease.

Shortreed et al.'14; Panuccio et al.'12; Bush et al.'12; Shortreed et al.'11; Vincent et al.'11; Pineau et al.'09; Deng et al.'11; Bush et al.'10

I have developed unique expertise in applying reinforcement learning techniques to the problem of sequential treatment optimization for chronic disorders using clinical data. Recent papers, appearing in a number of journals (Drug and Alcohol Dependence, Neural Networks, Machine Learning), propose frameworks for optimizing treatment strategies for chronic mental illnesses, using data from two of the largest US randomized clinical trials for mental illness (STAR*D and CATIE), and for treating medically-resistant epilepsy using deep-brain stimulation.

4. Point-based approximate algorithms for fast, scalable POMDP planning.

Shani et al.'13; Pineau et al.'08; Pineau et al.'03

I developed a class of anytime approximate algorithms for solving discrete POMDPs, based on a selective sampling of the information state to provide a bounded approximation to the optimal strategy. This technique improved state-of the-art POMDP planning by many orders of magnitude. The original paper (IJCAI'03) has been cited by over 600 publications, spawning a number of follow-up work by researchers worldwide (incl. 5+ PhD theses). The most recent survey paper (Shani et al.'13) has already received over 40 citations.

5. Program chair (2012), General chair (2015), International Conference on Machine Learning (ICML). *Langford & Pineau'12*

ICML is the premier international meeting for machine learning research. In 2012, it received 890 submissions (up 50% from previous years), of which 27% were selected for oral and poster presentation after a rigorous reviewing process involving 50 area chairs, 450 reviewers, and extensive discussions. With my co-chair (John Langford), I oversaw the reviewing process and was responsible for the final selection of papers, tutorials, workshops, and invited speakers. I am now the general chair for 2015.