Section I: Proposal Cover Page

Date of submission: 30 March 2012

Proposed project title:
Towards estimating the position of the leg using sensory information intercepted by neuroprosthetic electrodes

Principle Mentor
Name: Ken Yoshida
Phone number: x 4-9714
Department: BME

Co-mentor
Name: Paul Salama
Phone number: x 8-1682
Department: ECE

Please note that preference will be given to projects that include mentors from multiple disciplines.
Section II: Student Request Page

Total number of students requested: 4-5
(Note: The total number of students must exceed by two the number of mentors)

Total Number of freshmen and/or sophomores to be recruited: 2
(Note: Preference will be given to projects that include at least one freshman and/or sophomore)

Disciplines or majors of students (preference will be given to projects that include at least two disciplines or majors): Biomedical Engineering, Electrical Engineering, Math

Skills expected from students:
Programming skills in Matlab, C, LabView
Understanding of signals and systems, and electrical circuit theory
Coursework in physics, calculus

Names of students you request to work on this project.

(Mentors are invited to recommend students that they would prefer to work on the proposed project. Please provide an email address and a rationale; for example, a student may have an essential skill, may already be working on a similar project, or may be intending to apply to graduate school to pursue the same area of research.)

The Center for Research and Learning will consider the students requested below, but cannot guarantee placement of specific students on teams.

<table>
<thead>
<tr>
<th>Name of Student:</th>
<th>Student’s Email:</th>
<th>Rationale:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Jeremiah Ayres</td>
<td><a href="mailto:jerayers@iupui.edu">jerayers@iupui.edu</a></td>
<td>Systems and math interest</td>
</tr>
<tr>
<td>2) Alec Willard</td>
<td><a href="mailto:aldowill@iupui.edu">aldowill@iupui.edu</a></td>
<td>Labview programming expertise</td>
</tr>
<tr>
<td>3) Daniel French</td>
<td><a href="mailto:dalfrenc@iupui.edu">dalfrenc@iupui.edu</a></td>
<td>Interest in neuroprosthetics &amp; biomechanics</td>
</tr>
</tbody>
</table>
Section III: Body of Proposal

(A maximum of 5 pages is allowed for answers to questions 1-11.)

1) Please list the research objectives for the proposed project.

2) Please identify the specific research question(s) that your proposed project will address.

3) Please describe the significance of the research.

4) Why does this proposal offer a good opportunity for undergraduate researchers to gain substantive research skills?

5) Please describe the research methodology and the specific tasks that students and mentors will undertake.

6) What plan has been designed to ensure effective communication with all co-mentors and undergraduate researchers on the MURI team?

7) What measurable outcomes and benefits do you anticipate this research will provide?

8) What is the timeline for the major tasks associated with this proposal?

9) Please provide a rationale for your budget request. (NOTE: The maximum budget allowance is $2,000 for equipment and/or supplies needed for the research team. Generally speaking, expenditures for computers and/or travel are not approved by the review committee at this time due to financial constraints.)

10) Please describe your plan for sustaining your research beyond the funding that MURI is able to provide. (For example, please list other external grants that have been or will be submitted as a follow-up to your MURI funding.)

11) Please identify any areas relevant to risk management.

All university policies with respect to research must be followed. The usual risk management assurances must be provided where appropriate (animal use, radiation safety, DNA, human subjects protocols) in accordance with the university policies. No funds may be released without risk-management assurances, where needed. Project proposals without required compliance approvals will be reviewed but the funds will not be released until approval is given by the university.

Further information on risk management is available from http://researchadmin.iu.edu/cs.html
Towards estimating the position of the leg using sensory information intercepted by neuroprosthetic electrodes

MURI Mentors: Ken Yoshida (BME), Paul Salama (ECE)

Overview and Objectives

The fluid, graceful and precise movements produced during the normal volitional use of the arms and legs are a marvel of adaptation, tuning and distributed optimal control. Integral in this control scheme are a set of natural sensors distributed throughout the limb's muscles, joint capsules, tendons, fascia and skin. These mechanoreceptors relay the status of the limb and its integral tissues through pathways mediated by the peripheral nervous system, giving the spinal cord, the local optimal controller, continuous feedback information and the brain perceptual information that makes its way to our consciousness as sensory feedback.

Neural prosthetic interfaces are devices that are implanted within neural tissues that are capable of detecting the activity, i.e. the information flow, within the nervous system. If it were possible to reliably detect and decode the neural traffic, a means to tap into the body's own information stream would be achieved. Such an interface could be used to understand how the body produces precise movements given relatively unreliable signals from sensors and unreliable non-linear muscle actuators. Furthermore, this knowledge could be applied to restore these same movements in those who lost limb function through injury or disease using an artificial controller to activate skeletal muscles using feedback information from natural sensors.

One neural prosthetic interface being developed by our group is the thin-film Longitudinal Intra-Fascicular Electrode (tfLIFE) [1][2][3]. The signals detected by the tfLIFE are on the order of ~100uV, and are usually corrupted by neighboring muscle activity, heart activity, electrode thermal noise, and amplifier flicker noise. As such, they must be processed to purify, detect, and track the neural signal stream from single nerve fibers before the information it carries can be demodulated. Once demodulated, interpretation of the information can only take place by correlating the demodulated signal with an external event or conditioning stimulation.

In the context of sensory-motor neural information for limb control, the neural data stream is contained within motor nerve fascicles. Experimentally, nerve activity is generated by changing the limb position, changing the joint angles, and thereby stretching or shortening muscles. Sensory fibers within the muscles react to stretching and can be correlated to joint angles and limb positions. In 1996, the LIFE was applied as the neural interface to the artificial control problem outlined above. Yoshida and Horch [4][5] successfully demonstrated that the ankle joint could be controlled using a modified classical feedback controller that activated the ankle plantar flexors in response to natural sensory information from muscle mechanoreceptors to achieve a target ankle joint trajectory. The demonstration is relatively simple in that only one joint with one degree of freedom was controlled using a muscle group that acts largely on that single joint. Similarly, the sensory feedback was monitored close to the muscle, ensuring that the information contained was coherent. The next step of extending this demonstration to the entire limb has not been successfully shown to date.

The two critical steps needed to expand the earlier work controlling the ankle joint to the more realistic case of trying to monitor and control a multi-degree of freedom, multi-joint limb, such as the leg are the two major aims in this MURI project:

1. Develop the means to process the raw data stream to detect, separate and track the activities of multiple single nerve fibers.
2. Develop a means to move and manipulate the leg while measuring the kinematics and biomechanics to enable interpretation of the neural data stream.

Development and convergence of these two objectives will enable us to collect pilot data in the acute rabbit hind limb model, and process it to demonstrate that the biomechanical and kinematic parameters of the leg can be accurately predicted using only signals originating from natural sensors in the leg. This demonstration will form pilot data to support a future grant application to the National Institutes of Health.

**Approach**

This project aims to merge two lines of research taking place within the Yoshida lab:

1. Development of a robotic end point effector
2. Development of neural signal processing algorithms.

The first phase of the research will concentrate on work with the robotic end-effector. The second phase of the research will concentrate on the analysis of the neural signal processing algorithm. To accomplish this, a multi-disciplinary team with interest in mechanics, signal processing, computer programming, neural electrophysiology, and rehabilitation is required.

**Robotic non-exoskeleton end-point effector**

The robotic, non-exoskeleton device used for end-point manipulation of the arm or leg is a means to generate nerve activity while simultaneously collecting the biomechanical and limb kinematics needed to interpret the neural data stream. A conceptual diagram of the ultimate system is shown above (Figure 2). The robotic device is necessary to manipulate a multi-degree of freedom, multi-joint system of segments, such as the arm or leg while measuring the end point position and end point forces. The measurement of the end point position with apriori knowledge of the hip joint position and limb segment length enables the estimation and reconstruction of the position of all the limb segments in the leg. Measurement of the end point forces and torques at the junction between the the foot and the robotic arm further enables us to estimate the internal joint torques and forces at the hip, knee and ankle.

The current implementation of the robotic device is shown in Figure 1 consisting of an industrial 5 degree-of-freedom robot, a 6 degree-of-freedom endpoint sensor, simulating manipulation of the rabbit’s hind limb.
mounting shoe and control software. The specific aim for the MURI group for this phase of the project is to develop a testing paradigm and software to enable rapid, consistent manipulation of the rabbit’s foot, and to validate and calibrate that paradigm. The robotic device and developed software will be used, once validated and calibrated, during an acute experiment to measure the nerve activity resulting from the manipulation and movement of the hind limb. The recordings will form the data set used in the off-line analysis and neural signal processing algorithms.

The MURI project group will spend its first month on this phase of the project completing this phase of the project.

**Neural Signal Processing**

This phase of the project focuses on the development of signal processing algorithms necessary to extract the information contained in the peripheral nerve. Figure 3 schematically illustrates the information carried by the peripheral nerve and what can be detected through the tfLIFE. The peripheral nerve contains hundreds to thousands of nerve fibers that link the end organ to the central nervous system. Each fiber is uniquely connected to a single end organ, such as a motor unit in a muscle or a natural sensor. In general, the nerve bundle is mixed, containing fibers that carry sensory information to the CNS, afferent fibers, and fibers carrying information to activate muscle fibers, efferent fibers. The nerve fiber transmits the information as a series of impulses called action potentials, which propagates down the fiber, from the end organ in the case of afferent fibers (sensory) or to the end organ in the case of efferent fibers (motor). Similar to Pulse Code Modulation used in modern digital communication, the frequency of the action potentials encodes magnitude information. The shape and magnitude of the action potentials themselves do not carry any information. They are akin to the carrier wave in electronic communications.

Electrodes, such as the tfLIFE are able to detect the action potentials, however, they detect

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**Figure 3: Illustration of the mixing of**

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the mixed electrical activity from all nearby fibers, corrupted by the electrical activity of nearby muscles, the heart, and external noise sources. The example shown in Figure 3 is a typical raw recording from the neural interface. Complicating matters further the amplitude of the signal from the single fiber action potential (SFAP) is only 2-3x larger than the theoretical background noise of the amplifier and electrode. This leads to a challenging signal processing problem.

The steps for processing the signal are summarized in figure 4, and consist of 1) denoising, 2) unit identification, 3) unit tracking, 4) unit demodulation and 5) decoding.

Denoising maximizes the available signal to noise ratio, and simplifies the identification step. Although the SFAP of any given fiber at the fiber is identical to that of any other fiber in the bundle, the electrical coupling between each fiber to the detecting electrode interface is different. The difference in coupling distorts the shape of the SFAP detected by the electrode such the shape of the action potentials can be used to identify and discriminate the activity of one fiber from another. Once the SFAPs are all nearby fibers are identified and discriminated, their pulse trains can be unmixed from one another, tracked, and demodulated to reveal the magnitude of the information they carry.

It is worth mentioning that since we rely on the shape to discriminate the activity of one fiber from another, the denoising step must not distort the shape of the SFAPs. Although simple band pass filtering will improve the signal to noise ratio, the filter will distort the SFAP, minimizing differences that existed before filtering. Current work [6] in the lab has developed a denoising algorithm that does not distort the SFAP shape, retaining differences between units.

In this project, raw electroneurograms will be collected from tLIFEs implanted in the sciatic nerve of the acute anaesthetised rabbit using the robotic end-effector system and automated movement control software developed in the first phase of the MURI project.

These raw signals will be denoised to form the data set to be used by the MURI project, to develop algorithms to identify, unmix and track single unit activity.

The MURI team will spend the second half of the project period on this phase of the project.

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Figure 4: Summary of signal processing steps to purify, unmix and demodulate the signal to enable access to the information contained in the neural data stream.
MURI Project Management

To facilitate communication between the co-mentors and the undergraduate researchers, an Oncourse project site will be requested and used as the project information repository and primary communication tool. The Forum tool will be used as the official communication pathway and communication archive in the project. All participants will be required to enable forum notifications and watch for all threads and postings. The undergraduate researchers will be requested to assign 3 officers amongst themselves: a general project leader to coordinate management of the research activities, a project accounts manager to administer the research budget and purchases, and communications officer to act as the single point of contact for external communications. Biweekly meetings with the co-mentors will take place on Mondays and Fridays during the project period. Monday meetings will be used to plan activities for the week, while Friday meetings will be used to report upon progress during the week.

The project is designed to develop and reinforce team group work in research. The participation in both parts of research, management and technical, will be imposed upon the group. The technical skills of mechanics (statics and dynamics), computer programming, signals and systems will be reinforced and integrated within the context of motor control neurophysiology. These activities will aim to produce as deliverables a project report consisting of the technical and management activities in the project, and participation in the Undergraduate Research Day with a poster presentation of the project. We will aim to publish the results of the research activities, initially as a conference paper at either the IEEE-EMBS or BMES meeting. As with the previous MURI project, it is anticipated that the preliminary work developed by the MURI team will become the seed of a Masters or PhD thesis project. We also hope to identify potential future candidates to take graduate research positions for future projects within the lab.

Budget

The project involves programming and signal processing using Matlab and LabView. Research licenses for these two software titles are requested to complete this project.

<table>
<thead>
<tr>
<th>Software Title</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matlab (base)</td>
<td>$100</td>
<td>Stat Math Center</td>
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<tr>
<td>Signal processing toolbox</td>
<td>$30</td>
<td>Stat Math Center</td>
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<tr>
<td>Wavelet toolbox</td>
<td>$30</td>
<td>Stat Math Center</td>
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<tr>
<td>System Identification toolbox</td>
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<td>Control toolbox</td>
<td>$30</td>
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<td>Optimization toolbox</td>
<td>$30</td>
<td>Stat Math Center</td>
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<tr>
<td>LabView Pro</td>
<td>$1,507</td>
<td>National Instruments</td>
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</table>

Total $1,757

Risk management

This project will involve application of the robotic end-point effector to an animal model, and the use of that model to generate data for analysis and algorithm development. The animal work will be conducted under the LARC approved acute rabbit protocol MD-3492-R. Because of the limited duration of the project and time required to obtain inclusion of the student researchers into the protocol, the student researchers will not directly participate in the study.
Please check any risk assurances that apply to this proposal:

☐ Animals (IACUC Study #): MD3492R
☐ Human Subjects (IRB Study #): ____________________
☐ r-DNA (IBC Study #): _____________________
☐ Human Pathogens, Blood, Fluids, or Tissues must be identified if used: ______
☐ Radiation : ______
☐ Other : ______

12) The center for Research and Learning generally shares the text of funded proposals on the web so that prospective students can learn about available MURI projects. Please let us know if it is OK with you to post your proposal on the CRL MURI webpage by checking one of the following answers:

☐ YES   ☐ NO
Section IV: References/Bibliography (insert 1-2 pages as needed)
References
Section V: CVs/Resumes (insert 2 pages per mentor for a maximum of 6 pages)

Section VI: Support Letters (insert 1-2 pages as needed)

Section VII: Appendix

<table>
<thead>
<tr>
<th>Title of Past MURI Project:</th>
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<tbody>
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<td>Development of a biofeedback testing platform for evaluating sensory feedback and volition through an advanced neuroprosthetic device</td>
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<tbody>
<tr>
<td>Oct 2007</td>
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<table>
<thead>
<tr>
<th>Date Completed:</th>
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<tr>
<td>Dec 2008</td>
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<table>
<thead>
<tr>
<th>Description:</th>
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<tr>
<td>The project aims to design, develop and implement a psychophysical testing protocol and instrumentation to efficiently quantify and map the volitional intentions and sensory feedback perceived by a subject following multi-channel surface stimulation and recording. The system will be the first step towards developing a method to be used to evaluate an amputee subject interacting with a neuroprosthetic electrode implanted in the amputee’s peripheral nerve. It further aims to introduce tools and concepts across disciplines to the MURI scholars through cross pollination and group work on a multidisciplinary project involving psychophysics, bioinstrumentation, and object oriented software design</td>
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</table>

<table>
<thead>
<tr>
<th>Outcomes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>The protocol, instrumentation and software developed by the MURI team served as the basis of a successful application to the European Commission (TIME) 2008-2012. It formed the initial starting point for a PhD student thesis project. Bo Geng, the PhD student from Aalborg University is co-mentored by Dr. Yoshida and Dr. Jensen (Aalborg University), and has published 2 full papers, and 5 conference papers.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Publications:</th>
</tr>
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<tbody>
<tr>
<td>Title: Development of a biofeedback testing platform for evaluating sensory feedback and volition through an advanced neuroprosthetic device</td>
</tr>
<tr>
<td>Date: 12/18/2008</td>
</tr>
<tr>
<td>Students Involved: David Semsrott, Brandon Brungard, Sriharsha Muttineni, Magali Carret</td>
</tr>
</tbody>
</table>
NSF Biographical Sketch
Ken Yoshida

Professional Preparation
University of California, San Diego, 9/84-6/86 Pre-AMES
University of California, Los Angeles, 9/86-6/89 B.S. Engineering (Biocybernetics)
University of Utah, Salt Lake City, UT 8/89-12/94 Ph.D. Biomedical Engineering
University of Alberta, Edmonton AB Canada 12/94-4/98 Postdoctoral Fellow, Neuroscience

Professional Appointments
04/98-12/00 Research Asst Prof., Center for Sensory-Motor Interaction, Aalborg Univ, Denmark
01/01-09/01 Asst Prof., Center for Sensory-Motor Interaction, Aalborg Univ, Denmark
10/01-10/06 Assoc Prof., Dept. of Health Science and Technology, Aalborg Univ, Denmark
10/06-pres Assoc Prof., Dept of Biomedical Engineering, Indiana Univ.-Purdue Univ. Indianapolis (IUPUI).

Related Publications 5 related


Other significant publications


**Synergistic Activities**

Grant Reviewer for the VA RR&D grant panel on rehabilitation engineering
Ad hoc reviewer for 12 journals
Editorial board for Frontiers in Neuroengineering
Board of directors member for the International Functional Electrical Stimulation Society
2003 Sygekassernes Helsefond Young Investigator Award
2002 Hede-Nielsens Family Foundation Award
Non-EU participant with the European Union ICT TIME project

**Graduate and Post-Graduate Advisors**
Kenneth W. Horch (Ph.D. Advisor, Univ Utah), Richard B. Stein (Post-doc. Advisor, Univ Alberta)

**Advisees**

*Post-Doc.:* Jing Xiong (IUPUI, pres), Kristian Hennings (Aalborg U, 2006, currently an Engineer at Terma A/S), Christine Azevedo-Coste (Aalborg U, 2004, currently a Research Scientist at INRIA), Winnie Jensen (Aalborg U, 2003, currently an Assoc Prof at AAU)


*Masters:* Muller Soliman (IUPUI, pres), David Semsrott (IUPUI, pres), Kevin Mauser (IUPUI, pres), Smitha Murthy Jayaram (IUPUI, 2009) Shaoyu Qiao (IUPUI, 2009, currently a PhD student at Purdue U)

*Undergraduate Interns and Practicums Hosted:* 3 (IUPUI), 10 (Aalborg U), 1 (U Alberta)

*High School Interns Hosted:* 1 (IUPUI)

**Collaborators**

Kevin Otto (Purdue Univ), Paul Salama (IUPUI, Indianapolis), Winnie Jensen (Aalborg U., Denmark), Thomas Stieglitz (U. Freiburg, Germany), Xavier Navarro (UAB, Barcelona, Spain), Silvestro Micera (SSSA, Pisa, Italy), Paolo Dario (SSSA, Pisa, Italy), David Guiraud (LIRMM, Montpellier, France), Christine Azevedo-Coste (LIRMM, Montpellier, France), Dario Farina (Georg-August Univ Göttingen, Germany), John Schild (IUPUI, Indianapolis), Jeffery Hendrix (Biotectix LLC), Benedict Kjærgård (Aarhus Univ Hosp, Denmark), Flemming Besenbacher (Aarhus U., Denmark), Michael Grey (U. Birmingham, UK)
NAME
Paul Salama, Ph.D.

eRA COMMONS USER NAME
psalama

POSITION TITLE
Associate Professor

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purdue University, West Lafayette, IN, USA</td>
<td>MSEE.</td>
<td>1992-1993</td>
<td>Electrical Engineering</td>
</tr>
<tr>
<td>Purdue University, West Lafayette, IN, USA</td>
<td>Ph.D.</td>
<td>1994-1999</td>
<td>Electrical Engineering</td>
</tr>
</tbody>
</table>

A. Positions and Honors.

Professional positions
  1999-2005: Assistant Professor of Electrical and Computer Engineering, Department of Electrical and Computer Engineering, Indiana University – Purdue University, Indianapolis, IN
  
  2005 – Present: Associate Professor of Electrical and Computer Engineering, Department of Electrical and Computer Engineering, Indiana University – Purdue University, Indianapolis, IN, Indianapolis, IN

Awards and other professional activities
Award: Senior Member of the IEEE, 2005
Associate Editor: IEEE Transactions on Circuits and Systems for Video Technology
Ad hoc reviewer: NSF

B. Selected peer-reviewed publications (in chronological order).


Section VIII: Signature

Name and Signature of the Principal Mentor:
(typing in the full name suffices as signature for electronic copies)

Ken Yoshida  
30 March 2012