## Application for CTSI Pre-Doctoral Training in Translational Research

## Preamble:

The CTSI Pre-Doctoral Training Positions in Translational Research are designed to provide promising pre-doctoral students with the opportunity to be mentored in research-intensive multi-disciplinary settings toward the goal of developing careers in translational research. Translational research consists of either "T1 research" (basic biomedical research, e.g. study disease at a molecular or cellular level, as it progresses to the development of new treatment options at the clinical level) or "T2 research" (enhancing access to and the adoption of evidence-based strategies in clinical and community practice, institutionalizing programs, products, and services to improve health). To that end, pre-doctoral training through this CTSI program is viewed as a collaborative endeavor between the primary mentor, co-mentor and the trainee. Therefore the application must be completed by both the primary mentor and the applicant.

## Opportunities available for CTSI Predoctoral Trainees

- Annual stipend comparable to other pre-doctoral training positions (\$24,000)
- Partial tuition and fees for coursework relevant to the applicant's research
- Mentoring with a faculty member whose research program includes, peer reviewed, extramurally funded clinical or translational research
- Networking with other pre and post-doctoral fellows, program mentors and allied researchers from multiple institutions to develop a cross-disciplinary community of scientists
- Attendance at a national meeting that involves similar trainees from 40 other medical schools and research institutions
- Funding is for one year and is renewable for one additional year based upon progress attained

## Criteria for a successful application include:

- Candidate must have completed at least one year of a predoctoral training program (i.e., applicants must be in at least the 2<sup>nd</sup> year of their predoctoral program when they apply) at IUPUI, Indiana University at Bloomington, or Purdue University, West Lafavette.
- Candidate must have dual mentorship from a clinician-scientist and a non-clinician scientist. This means there must be at least two mentors (i.e. one person cannot fill both roles).
- > Candidate must have interest in multi- and inter-disciplinary scientific training in translational research consistent with the ongoing work of the primary and co-mentors.
- ➤ The primary mentor must have a research program that includes, peer reviewed, extramurally funded research.
- Applicant must be U.S. Citizen or permanent resident status.

Applications must be received no later than 4:00 PM, February 15, 2009.

## CTSI Predoctoral Training Position in Translational Research

# Submission deadline is 4:00 PM, February 15, 2009. Include all materials listed on the last page.

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chael Heinz, PhD	
ta Krishnan, PhD, CCC-A	
oril 29, 1980	
: African American/Black <_ White, Non-Hispanic Hispanic; Latino(a) Other (please specify) _ Prefer not to respond	Asian-American Pacific Islander Native American; Alaskan Native
	chael Heinz, PhD  ta Krishnan, PhD, CCC-A  oril 29, 1980  African American/Black White, Non-Hispanic Hispanic; Latino(a) Other (please specify)

State and federal laws pertaining to civil rights require the University to report ethnic data. Only U.S. citizens and permanent residents should complete this section. Applicants who select Other should specify ethnic status in the space provided. Applicants who choose to submit this application without ethnic data should select the "Prefer Not to Respond" option.

## **Brief Statement of Research Plan**

In the space below please provide a brief description of the proposed research.

This research proposal addresses the need for hearing aids that are effective for an increased percentage of the hearing-impaired population. Hearing aid prescriptions are currently based on simple threshold measurements and do not consider the various physiological configurations that could result in similar audiometric thresholds. This research project will result in the development of a new prescriptive technique based primarily on the underlying physiology. A computational model of the ear will be matched to individual patients and used to determine the optimal hearing aid parameters for that particular patient. These customized parameters are expected to improve speech intelligibility for patients that might otherwise not benefit from hearing aids. A behavioral evaluation of speech perception in noise will be used to verify the effectiveness of this approach.

#### Personal Statement

Please try to answer each question in the space provided.

1. Please describe your proposed research. Include sections on specific aims, design, brief description of methods, and expected outcomes.

The World Health Organization estimates that 278 million people currently have a disabling hearing loss, and this number is expected to increase as the population ages. These impairments can severely limit communication, and have been shown to significantly reduce quality of life. Although hearing aids have been tremendously successful at restoring some functionality for those with hearing impairments, 50% of patients are not satisfied with their hearing aid performance when background noise is present. Unfortunately this is likely due, in part, to fitting procedures that do not take into consideration the physiological differences among patients. Recent research suggests that these differences may critically determine what acoustic information is presented to the brain, as encoded in the auditory nerve. This research also suggests that precise timing ('fine structure') in the neural system is important for representing critical sounds in noisy environments. A hearing aid strategy that accounts for individual differences can be designed to improve temporal coding of the neural signals, thus improving speech perception in noisy conditions.

The first aim of the proposed research is to develop a prescriptive software program for use in clinical settings. This software will be used to calculate optimal hearing aid parameters for an individual patient, based on his/her unique physiological impairment. Using a set of clinically viable behavioral metrics (e.g. audiograms and masking functions) and non-invasive physiological metrics (e.g. auditory brainstem responses and otoacoustic emissions), the patient's hearing abilities will be measured. measurements will be used to create a computational model of the patient's underlying physiology based on an automatic fitting procedure that matches the performance of the model to the behavioral performance of the patient. The resulting parameter set is a prediction of the underlying cochlear damage, in terms of inner and outer hair cell damage along the length of the cochlea. This model can be used to predict the difference in neural coding between a normal ear and the parameterized impaired ear. Three different measurements of neural coding will be used – envelope coding (known to be very important for speech perception), fine structure coding (thought to be particularly important for understanding speech in the presence of background noise), and spatiotemporal coding (thought to be important for signal detection and localization). The software will identify the hearing aid parameters (gain, compression ratio, time constants, etc.) that best restore overall neural coding to normal, and provide these optimal settings for the clinician to apply to the patient's amplification device.

The second aim of this proposal is to test the hearing aid prescription software with hearing impaired patients. The audiology clinic at Purdue University is open to the public and regularly sees patients with varying degrees of hearing impairment, many of whom also volunteer for listening experiments. Our lab has a sound-isolated listening booth, which we currently use for conducting experiments with hearing impaired subjects and which will be available for the proposed experiments. Subjects' abilities to understand speech in noise will be evaluated without any amplification and with a conventional hearing aid (using a standard fitting strategy). The customized hearing aid settings generated by the software for each individual subject will then be applied to a hearing aid system and each subject's speech perception in noise will again be evaluated. It is expected that the customized settings will significantly improve speech perception in noise for some patients – those whose customized prescriptions differ greatly from the standard prescription.

This design approach, based primarily on the underlying physiological impairments rather than strictly behavioral metrics, is a relatively new idea and has tremendous promise for improvements in the field of auditory prostheses. In summary, recent computational models of the auditory nerve will be used to model the physiology of individual patients and calculate optimal hearing aid parameter settings for that person. These optimal parameters will be implemented in a digital hearing aid system and a series of behavioral experiments will then be used to evaluate the effectiveness of this approach.

2. Summarize in the space provided your research experience/interests to date. Speak specifically to any research progress made to date in your current program of research.

Including my final year of undergraduate study and the time I spent working on my Masters degree, I have nearly 5 years of academic research experience in the field of auditory perception (including the publication of three papers). After completing my B.S. in Electrical Engineering from the University of Illinois and a M.S. in Music Engineering from the University of Miami, I worked in industry for 2 years as a software engineer, developing devices that improve audio quality. During this time, I had the opportunity to conduct many behavioral experiments and soon came to the realization that a thorough understanding of neurophysiology could be used to significantly improve the quality of hearing devices. I decided to return to school full-time so that I could study neural coding and apply this knowledge to the creation of new technologies for the hearing impaired.

Since I began my research at Purdue, I have learned a tremendous amount about the physiology of hearing impairment. During the first year of my PhD studies, I worked on three projects – psychoacoustics of simultaneous vowel identification (showing that pitch differences are very important), neural correlates of loudness (showing that auditory nerve firing rates alone do not account for loudness perception and that precise timing may be important), and a preliminary study of hearing aid time constants (showing that fast time constants may in fact improve neural coding of temporal fine structure). I have spent the past several months specifically working toward the research proposed here. I recently used a computational model of the auditory nerve to predict normal and impaired responses to speech sounds. I calculated the optimal amplification for various hearing impaired systems and the results suggested that patients with primarily outer hair cell damage would likely benefit most from the current hearing aid prescriptive methods. However, for patients with primarily inner hair cell damage (possibly from acoustic trauma, ototoxic drugs, etc), the optimal gains were often less than the standard prescribed gains, indicating that these patients would likely benefit more from a hearing aid that used this new fitting strategy.

3. How is your proposed research translational (either T1 or T2)? Describe how you have or will interact with your co-mentors (i.e. what is your mentorship plan?).

My research is focused on interfacing basic neuroscience with human studies to improve the design of auditory prostheses in a way that is clinically viable. To accomplish this goal, I am combining knowledge of impaired neurophysiology (from animal studies) with behavioral studies (in humans) through the use of computational models. Although similar methods have been used to show the relationships between physiology and behavioral performance, they have not yet been implemented for clinical use. The proposed research will provide a clinical tool for evaluating the health of a patient's inner ear and prescribing a hearing aid parameter set that is customized for that individual. This approach has the potential to make hearing aids beneficial to a much larger population of hearing impaired patients, particularly in adverse listening environments. This research may also have implications for the design of neural prostheses such as cochlear implants and brainstem/midbrain implants, which often use hearing aid strategies in their processors.

My primary mentor, Dr. Michael Heinz, has expertise in the basic science of auditory coding and in digital signal processing. His research has included the use of neural models to predict behavioral performance, and he is recognized as an expert on coding schemes in the auditory nerve. Through Dr. Heinz, I have access to a wealth of physiological data, several computational models, and the use of a psychoacoustics lab for performing behavioral research. My clinical mentor, Dr. Lata Krishnan, is the director of the MD Steer Audiology Clinic at Purdue University. She has expertise in clinical evaluation and hearing aid fittings, as well as behavioral research. Dr. Krishnan has allowed me to observe a number of hearing aid fittings and consultations with patients over the past year. I will work with Dr. Heinz on the physiology, modeling, and signal processing aspects. I will work with Dr. Krishnan on developing the hearing aid prescription strategies and other practical details (e.g., limitations of clinical measurements, minimizing patients' time in clinic, etc.). Dr. Krishnan will also advise me on conducting the behavioral assessments of hearing impaired subjects. The three of us have recently begun meeting on a monthly basis, and both mentors will receive weekly updates on the research progress.

## 4. Please state in the space provided why you are applying for this fellowship.

I am interested in developing new strategies for auditory prostheses that improve speech intelligibility in noisy environments, and this fellowship will help provide the resources to concentrate on developing a clinically viable solution. As an experienced software engineer with a passion for studying auditory perception, I believe I am in a unique position to apply basic science research to technologies for the hearing impaired.

I came to Purdue University for two primary reasons. The first was the fact that Dr. Heinz, who has a joint appointment in Biomedical Engineering (BME) and Speech, Language, and Hearing Science (SLHS), is conducting some very useful basic research into auditory impairment (using both animal and human studies). The second reason was the fact that the audiology clinic is well integrated with the SLHS department and the research being done there. In the first two years of my PhD studies, I have had the opportunity to learn about the latest hearing science research and to start work on a system that will combine behavioral and physiological data to improve speech intelligibility for many people. With the successful completion of this work, I plan to continue in my research career, but to also start a company to further develop and market this system.

Support from CTSI will allow me to focus my efforts on developing a truly viable system that could be easily used in clinics world-wide. It will allow me to present this work at conferences and discuss the results with scientists, but also with the engineers and clinicians that care most about implementation and patient interaction.

#### PROCEDURES FOR SUBMISSION

## Please use the following checklist with your application:

## Applicant:

- 1. Completed Application
- 2. Curriculum Vitae
- 3. Transcript from current graduate program (computer printout is sufficient)
- 4. Two letters of recommendation (one should be from the clinician-scientist mentor and one from the non-clinician scientist mentor)

## Primary Mentor:

- 1. Brief curriculum vitae (NIH 4-page Biosketch would be sufficient. The intent is to indicate research publications and grant support.)
- 2. Letter of support (counts as one of the two letters of recommendation required above)

### Please return materials to: (paper or electronic submission is acceptable)

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Applications must be received by 4:00 p.m. February 15, 2009.