ONPRC Summer Undergraduate Fellowships
Position Descriptions
Summer, 2012

Mentors: Fay Horak, PhD/Patty Carlson-Kuhta, PhD
Oregon Health & Science University: Departments of Neurology, Biomedical Engineering, and Physiology & Pharmacology

The Balance Disorders Laboratory has a number of ongoing projects that are potentially suitable for an undergraduate student. These are related to understanding balance and gait problems in people with neurological disorders, such as Parkinson’s disease and multiple sclerosis.

Several of the studies involves challenging a person’s balance while standing on a large movable platform, while measuring muscle activity, surface forces, and whole body motion to quantify how the brain coordinates automatic balancing movements. One ongoing project involves using EEG to look at cortical preparation before postural perturbations. We want to investigate the underlying neurophysiological basis for anticipatory postural control and postural responses in people with Parkinson's disease. Using EEG to measure contingent negative variation (a type of EEG signal) allows us to determine whether there is impaired cortical preparation and modification of ‘central set’ in adults with PD, and could possibly be used to measure response to medication or rehabilitation interventions.

A second project is investigating the mechanism of ‘freezing’ of gait (unintentional stopping of walking or inability to begin walking) in people with Parkinson’s disease using fMRI (functional magnetic resonance imaging). The goal of this study is to investigate the cortical pathophysiology underlying abnormality of postural preparation in people with Parkinson’s disease. We will use the fMRI to examine neural activity during postural preparation for movement and investigate how deficits in cortical activation may contribute to postural problems in PD.

In a third project we are working to create a commercially available, completely wireless sensor system (watch-sized sensors worn on limbs and torso) to make precise measurements of body motion during standing and walking. The system will have a custom-made, user-friendly computer interface that is simple to use and analyzes data for immediate viewing. The system will be usable in clinical and research settings to evaluate a balance and gait problem, follow disease progression, or measure the effectiveness of an intervention in patients with neurological disorders.

While not required, ideal candidates will have a background in physiology, biomechanics, and computer programming.

Learn more about the research being conducted by Drs. Horak and Carlson-Kuhta at http://www.ohsu.edu/xd/research/centers-institutes/neurology/parkinson-center/research/horak-lab-balance/?WT_featured=spotlight&WT_rank=spotlight
Mentor: Sergio Ojeda, DVM  
Oregon National Primate Research Center/OHSU: Division of Neuroscience

The Ojeda lab uses a combination of molecular, physiological, and computational biology approaches to identify networks that, operating within the brain, control the initiation of female puberty. The overarching goal of Dr. Ojeda’s research program is to develop two main concepts: (1) That mammalian puberty is controlled by a genetic network (or set of networks) that, operating within different cell contexts in the neuroendocrine brain, coordinate(s) the activity of GnRH neurons at puberty; and (2) That this network is controlled at the transcriptional level by a repressive mechanism exerted by discrete subsets of gene “silencers.”

Dr. Ojeda and his colleagues are using Systems Biology strategies to gain a new understanding of how mammalian neuroendocrine systems are controlled by gene networks. Because of the challenges posed by this approach, and more importantly, because of the remarkable opportunities for discovery inherent to an emerging field of study such as this, the participation of undergraduate students and highly motivated high-school students is considered to be essential for the establishment of a new generation of young scientists that is as familiar and proficient with the intricacies of Systems Biology as they are with posting on Facebook. It is also anticipated that these young scientists will help deliver new tools to older generations less familiar with bioinformatics. Equally important is the perception that, almost by definition, these young scientists will be more apt than “traditional” researchers to devise new techniques and novel approaches to best address outstanding issues in the mammalian biology of complex tissues.

Learn more about Dr. Ojeda’s research at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/sergio-ojeda.cfm

Mentor: Larry Sherman, PhD  
Oregon National Primate Research Center/OHSU: Division of Neuroscience

The Sherman lab is focused on understanding why the brain often fails to repair itself following damage caused by a number of conditions including multiple sclerosis attacks, stroke, and aging. They recently discovered that a polysaccharide, called hyaluronan, accumulates in areas of brain or spinal cord damage in these conditions and that breakdown products of hyaluronan, generated by an enzyme called PH20, block the ability of stem cells and other cells to repair the damaged nervous system. The Sherman lab is currently testing a number of novel drugs and other agents, both in neural cell cultures and in mice, to attempt to block the activity of PH20 and to test if these agents will promote nervous system repair. The most successful of these agents will be tested in Japanese Snow monkeys that spontaneously develop a multiple sclerosis-like disease. If successful, these drugs will then be tested in human clinical trials. Students engaged in this work will learn primary cell culture and molecular biology techniques while testing how PH20 inhibitors influence neural stem cell differentiation.

Learn more about the Sherman lab at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/larry-sherman.cfm
Mentors: Elinor Sullivan, PhD and Kevin Grove, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

The Grove Laboratory examines the impact of maternal nutrition and obesity on the physiology, behavior and brains of offspring. A non-human primate model is used to compare offspring from obese mothers consuming a high fat diet and lean mothers consuming a low-fat diet. The impact of maternal obesity is being examined in a number of different parts of the body including the brain, cardiovascular system, liver and pancreas. The student will have the opportunity to participate in ongoing studies which examine the consequences of maternal obesity and high-fat diet consumption on the offspring’s body weight regulation, food preference and behavioral responses to novelty and stress. The student will assist in measuring the food intake, physical activity, food preference and behavior of juvenile monkeys. This will require the collection and analysis of video recordings to examine behavior and characterization of energy balance regulation by measuring food intake, metabolic rate and physical activity.

Learn more about the research being conducted by Drs. Grove and Sullivan at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/kevin-l-grove.cfm

Mentor: Martha Neuringer, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

Dr. Neuringer’s lab is involved in two areas of research. The first examines the effects of aging and hormones on learning, memory and motor function in rhesus monkeys, as a model for human brain aging. These changes are correlated with noninvasive evaluation of brain structure and function obtained by magnetic resonance imaging (MRI). The second area of research is studying the effects of aging on the retina, the contributions of nutritional and genetic factors to age-related macular disease, and the development of gene and stem cell therapies for retinal degenerative diseases. Candidates must be willing to work closely with animals. Biology and/or psychology background is preferred.

Learn more about Dr. Neuringer’s research at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/martha-d-neuringer.cfm

Mentors: Amanda Vinson, PhD and Anne Lewis, PhD, DVM
Oregon National Primate Research Center/OHSU: Division of Neuroscience

How much heredity affects the development of certain diseases in humans is an important question in modern medicine and genetics. Macaques naturally develop many diseases that are similar to those that affect humans. Whether or how much genetic factors may influence these diseases is not known. The goal of this project is to characterize animals for a familial study of disease that affects both macaques and humans, such as endometriosis or chronic colitis/inflammatory bowel disease, in order to test hypotheses of familial aggregation that would demonstrate genetic effects on disease. This summer undergraduate student would be co-mentored by Anne Lewis, DVM, PhD, and Amanda Vinson, PhD. The student would work
with Drs. Lewis and Vinson to learn to recognize normal and diseased tissues at both the gross and microscopic levels, using state of the art equipment, and to apply this knowledge to the identification of appropriate affected and unaffected animals and their families.

Learn more about Dr. Vinson’s research at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/amanda-vinson.cfm

Mentors: Kathleen Grant, PhD/Christa Helms, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

The Grant Laboratory has many projects that are suitable for undergraduates that are related to studying risk factors for excessive alcohol drinking and the physiological consequences of alcohol drinking.

Ongoing studies in the lab involve monkeys that have access to alcohol and water 22 hours per day. One project measures the extent to which physiological systems that respond to stress adapt during chronic alcohol drinking. In these studies, the monkeys are administered synthetic hormones typically used in human clinical tests both before and during alcohol drinking. Blood samples are collected repeatedly during the test so that stress hormones can be measured. These studies allow us to characterize changes in activity of the hypothalamus, pituitary and adrenal gland during alcohol drinking that could relate to why alcoholics have difficulty abstaining from alcohol.

A second project is measuring impulsivity in monkeys before and during alcohol drinking. The goal of this study is to determine the extent to which impulsive behavior in monkeys is a risk factor for excessive alcohol drinking, and whether alcohol drinking makes monkeys more impulsive. We will use operant behavior techniques to train the monkeys to choose between a small, immediate reward and a large, delayed reward. We expect to be able to compute a quantitative measure of impulsivity in each monkey at different times in the experiment. These studies are expected to provide information about the role of decision-making processes in excessive alcohol drinking.

A third project determines the extent to which a very high dose of alcohol in young animals could chemically alter their DNA, thereby affecting the expression of genes. This project involves working with DNA samples obtained before and after alcohol administration to compare the levels of methylation. The goal of this project is to evaluate whether binge drinking in adolescence could alter DNA in a way that increases the risk of future alcohol abuse.

While not required, ideal candidates will have a background in psychology, physiology and Excel.

Learn more about the research being conducted by Drs. Grant and Helms http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/kathleen-a-grant.cfm
The focus of research in Dr. Reddy's lab is on understanding the molecular and cellular bases of aging and age-related neurodegenerative diseases, including Alzheimer's disease (AD), Huntington's disease (HD) and Parkinson's disease (PD). Currently, Reddy and colleagues are investigating whether mitochondrial dysfunction triggers mitochondrial gene expression, and whether mutant APP and A-beta cause oxidative damage, synaptic pathology and cognitive deficits in AD mice. Reddy and colleagues are also investigating whether mitochondrially targeted antioxidants (MTAs) reduce oxidative damage and A-beta pathology, increase neurite outgrowth and ameliorate cognitive deficits in APP transgenic mice. This project is being conducted in two ways in order to study mitochondrial function/dysfunction, A-beta pathology, cognitive behavior and extended lifespan: (1) by treating APP mice with MTAs and (2) by genetic crossing of APP mice with mitochondria-targeted catalase transgenic mice.

The Reddy lab is also investigating the mechanisms of selective neuronal loss in patients with HD, and also studying the transport of mutant huntingtin aggregates and oligomers into nucleus and other subcellular organelles in neurons affected by HD. Using primary neurons from transgenic mouse models of Aging, AD, HD and PD and live-cell imaging tools, Reddy and colleagues are extensively investigating axonal transport of organelles, including mitochondria, mitochondrial biogenesis, mitochondrial dynamics (fission and fusion balance) and synaptic activity. Further, using primary neurons/mammalian cells and high throughput screening tools, the Reddy lab is also screening the small molecule libraries in order to determine the molecules that protect neurons from patients with AD, HD, PD and other neurodegenerative diseases.

In another project, the Reddy lab is studying the mitochondrial DNA changes and mitochondrial dynamics, mitochondrial biogenesis, mitochondrial transport and synaptic degeneration in the brains of male and female, and young and aged nonhuman primates, and nonhuman primates fed with alcohol, in order to determine the effect of age, gender and alcohol, in mitochondrial structure and function, and cell survival.

The Reddy laboratory uses a variety of techniques and approaches, including molecular biology and cell biology, in situ hybridization, immunofluorescence, confocal/electron microscopy, live-cell imaging tools, and state-of-the-art gene expression techniques.

Learn more about Dr. Reddy's research at [http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/hemachandra-reddy.cfm](http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/hemachandra-reddy.cfm)

Mentor: Christopher Kroenke, PhD
Oregon National Primate Research Center/OHSU: Division of Neuroscience

A major focus for the Kroenke laboratory is to understand the cellular and biophysical underpinnings of image contrast that can be observed by magnetic resonance imaging (MRI). One particular MRI procedure, termed “diffusion weighted MRI” can potentially be used to characterize changes in the shapes of neurons as they form new circuits in the developing brain, or as they respond to environmental stressors such as exposure to alcohol. A firm understanding of the cellular-level determinants of MRI signal intensity could make it possible
to monitor cellular changes with development and pathology in living individuals rather than requiring analysis using a microscope on post mortem tissue.

The project available for the summer of 2012 will involve performing histological measurements on tissue that has previously been characterized by MRI. Over recent years, a mathematical model relating the MRI signal intensity to specific aspects of neuronal morphology has been proposed. The histological measurements will be quantitatively compared to the MRI data to assess the accuracy of the proposed mathematical relationship, which will be of value in guiding the interpretation of future diffusion weighted brain MRI measurements.

Learn more about Dr. Kroenke’s research at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/christopher-kroenke.cfm

**Mentor:** Ilhem Messaoudi, PhD  
*Oregon National Primate Research Center/OHSU: Division of Pathobiology & Immunology*

The emphasis of the Messaoudi laboratory is to further understanding of how the immune system changes with age and its impact of the response to infectious diseases. More specifically, we focus on understanding why varicella zoster virus (VZV) reactivates in the elderly to cause shingles, a debilitating disease that sometimes results in mortality in the elderly. The immunological and virological bases for VZV reactivation are poorly understood, and the currently available vaccines against VZV are not very efficacious. We have developed the first nonhuman primate animal model that recapitulates hallmarks of VZV infection in humans. We are using this animal model to identify aspects of immune senescence that contribute to herpes zoster. Furthermore, we are identifying viral genes that can either be used in subunit vaccines against herpes zoster, or be deleted to create a safer attenuated vaccine.

*Learn more about Dr. Messaoudi’s research at [http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/messaoudi.cfm](http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/messaoudi.cfm)*

**Mentor:** Jonah Sacha, PhD  
*Oregon National Primate Research Center/OHSU: Division of Pathobiology & Immunology*

With more than 20 million dead and greater than 30 million currently infected with HIV, the development of a prophylactic HIV vaccine is a top global health priority. However, despite 30 years of intense research there is no vaccine and new approaches are urgently needed. Viral sequence diversity is the Achilles’ heel of traditional vaccine approaches to HIV and poses one of the greatest hurdles to vaccine development. The Sacha laboratory aims to determine which antigens should be targeted to overcome the formidable obstacle of HIV viral sequence diversity. In addition to HIV vaccine studies, the Sacha laboratory is embarking on a new line of research investigating the role of macrophages as latent reservoirs of HIV during highly active antiretroviral (HAART) treatment. The successful candidate will be expected to actively participate both experimentally and conceptually in these experiments and will be included on any publications arising from their time in the laboratory.

*Learn more about the Sacha lab: [http://www.ohsu.edu/vgti/Sacha_Lab/Welcome.html](http://www.ohsu.edu/vgti/Sacha_Lab/Welcome.html)*
Mentor: Andrew Sylwester, PhD [Picker Lab]
*Oregon National Primate Research Center/OHSU: Division of Pathobiology & Immunology*

The Picker Lab is focused on understanding how adaptive memory works, and applying that knowledge towards understanding HIV pathogenesis, and in the rational development and testing of new vaccines. This work is conducted with rhesus macaque monkeys as our experimental model of the human immune system. Currently, we are most occupied by large scale testing of prototype HIV vaccines (for monkeys) and therapies for those already infected. The projects we can offer would be related to adapting or developing new assays to meet our ever-more-demanding needs for quality and throughput. Possible projects include (but are not limited to) transferring an established assay for measuring immunological memory to another format; elucidating the causes of cell death induced by certain peptides used as regular study antigens; transferring established flow cytometry staining panels from a three-color laser platform to a four-color analyzer. The student fellow will be trained to conduct her/himself in a laboratory that routinely works with pathogens and will become proficient in standard laboratory processes, including the use of a flow cytometer.

*Learn more about the research underway in the Picker lab at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/louis-picker.cfm*

**Mentors: Richard Stouffer, PhD; Cecily Bishop, PhD**
*Oregon National Primate Research Center/OHSU: Division of Reproductive & Developmental Biology*

The Stouffer laboratory’s current focus is to characterize and explore ovarian function regulation by steroid hormones, in particular progesterone. Studies involve identifying the contribution of progesterone-regulation of immune cell processes, as well as signaling by progesterone receptors in the primate ovulatory follicle and corpus luteum. Projects involve characterization of immune cell cohort in rhesus monkey corpus luteum by cell-sorting analysis, gene expression (real-time PCR), and immunohistochemistry. There will also be an opportunity to observe gene silencing, and possibly ultrasound and MRI experiments depending on timing of arrival and duration of rhesus macaque menstrual cyclicity.

*Learn more about research in the Stouffer lab at http://www.ohsu.edu/xd/research/centers-institutes/onprc/scientific-discovery/scientists/richard-stouffer.cfm*