UNIVERSITY *of* WASHINGTON

WRF INNOVATION FELLOWS

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TABLE OF CONTENTS

Innovation Fellows in Clean Energy

- Carl Brozek
- Robert Ireland
- Zhaoxia Qian
- Nirala Singh
- Hao Wang
- Zhibin Yang

Innovation Fellows in Data-Intensive Discovery

- Rahul Biswas
- Sophie Clayton
- Thiago Costa
- Brittany Fiore-Gartland
- Michael Fire
- Jes Ford
- Alexander Franks
- Nick Foti
- Jie Liu
- Xiaofeng Meng
- Allison Smith
- David Williams

Innovation Fellows in Neuroengineering

- Miriam Ben-Hamo
- Hannah Choi
- Nick Foti
- Gabrielle Gutierrez
- Guillaume Lajoie
- Thomas Richner
- Eatai Roth

Innovation Fellows in Protein Design

- Hua Bai
- Ralph Cacho
- Alex Courbet
- Zachary Crook
- A. Gerard Daniel
- Glenna Foight
- Hannah Gelman
- Jason Gilmore
- Karla Herpoldt
- Parisa Hosseinzadeh
- Marc Lajoie
- Anindya Roy
- Daniel Sahtoe
- Franziska Seeger

Clean Energy

Carl Brozek

UW mentor Daniel Gamelin, Department of Chemistry

Education Ph.D., Inorganic Chemistry, Massachusetts Institute of Technology, 2015
S.B., Chemistry, University of Chicago, 2010

The combustion of H_2 releases H_2O as a byproduct, making it a clean alternative to conventional fuels, such as hydrocarbons, that release CO_2 and various environmental pollutants. While these more conventional fuels occur naturally in large quantities, H_2 must be manufactured, requiring an input of energy. Ideally, the process of generating H_2 stores most of this input energy in the H–H chemical bond. In addition to being efficient, the source of input energy should be clean and plentiful. H_2O itself could serve as an abundant source of H_2 through a chemical reaction called water oxidation. But this process comes at a great cost. The required energy to break apart $2H_2O$ and reconstitute $4H^+$ and $4e^-$ into $2H_2$ costs at least 475 kJ/mol. With sunlight as the input energy, these reactions are performed in nature with astounding efficiency and scale. Designing molecules and materials that intake sunlight to catalyze the reduction of protons into H_2 is therefore a promising area of clean energy research.

We study nanoscale materials with exceptional activity for solar-driven proton reduction catalysis. Numerous recent reports hypothesize that protons are reduced to H_2 by metallic nanoparticles, in some cases made of Pt or Ni. The energy input is delivered to these nanoparticles by way of semiconducting nanocrystals whose nanosized dimensions make the absorption of sunlight and the subsequent transfer of energy very efficient. To maximize the communication between the semiconductors and the metal nanoparticles, these two components are interfaced into a single heterostructure.

Rationalizing the activity of these heterostructures requires insight into the bandgap of the semiconductor, how well the bandgap matches the energy of the metal nanoparticle and how the interface of the components differs from the components themselves. Surprisingly few techniques are equipped to measure these properties.

In the Gamelin group, we develop contactless methods to determine the band edge potential energies of nanoscale proton reduction catalysts. Through electrochemical and spectroscopic techniques, we monitor changes in the energy of these materials and how they transfer energy to each other. Tremendous progress has been made in many labs towards realizing H_2 production with these materials, but a solution will require the insight we hope to provide through new measurement techniques.

Robert Ireland

UW mentor Samson Jenekhe, Department of Chemical Engineering

Education Ph.D., Material Science, Johns Hopkins University, 2016
B.S., Materials Science, University of California, Davis, 2011
B.S., Mechanical Engineering, University of California, Davis, 2011

Robert Ireland earned his Ph.D. in Materials Science from Johns Hopkins University. His research focus is to develop molecular, nanoscale, and interface engineering approaches to fully exploit alternative electron transport materials in organic photovoltaic devices. Currently, the fullerene molecule is the dominant acceptor material in organic solar cells, but fullerene-based materials limits solar absorption and open circuit voltage. Robert is developing organic solar materials that could outperform their fullerene counterparts in efficiency and durability. The results of his research could have on for mass produced, low power displays and energy conversion platforms, such as photovoltaics and highly-efficient electronics. He will be working with chemical engineering professor Samson Jenekhe starting in June 2016.

Zhaoxia Qian

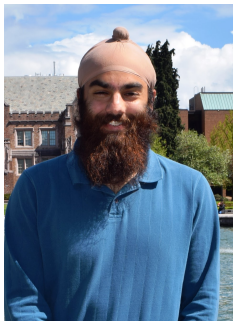
UW mentors David S. Ginger, Department of Chemistry
David J. Masiello, Department of Chemistry

Education Ph.D., Chemistry, University of Pennsylvania, 2014
B.S., Physical Chemistry, University of Science & Technology, China, 2009

The goal of my research is to use plasmonic nanomaterials for solar energy harvesting and conversion. Plasmonic nanomaterials, such as gold and silver nanoparticles, exhibit distinct localized surface plasmon resonance upon light excitation at a frequency that matches the intrinsic oscillation frequency of their surface electrons. This property results in enhanced absorption and scattering of the incident light. Hot charge carriers can also be generated on the surface of plasmonic nanomaterials upon resonant excitation. Compared to semiconductors that are commonly used for light absorption and charge separation in conventional solar energy harvesting devices, plasmonic nanomaterials have widely tunable resonant frequencies and higher absorption and scattering cross sections. Therefore, they are envisioned to be promising candidates for efficient charge separation and solar energy harvesting and conversion.

My current research is to investigate the plasmoelectric effect in plasmonic nanomaterials. The plasmoelectric effect is a newly discovered phenomenon through which the macroscopic charge flow is induced in metal nanomaterials following the excitation of their surface plasmons. As a test case, I have developed a nanoparticle-molecule system in which the molecules undergo photo-oxidation catalyzed by the optical excitation of the nanoparticle surface plasmon. During this process, electrons are injected from the molecules into the nanoparticles; consequently, the electron density and surface potential of the nanoparticles are changed. Currently, I am investigating the detailed mechanism underlying this electron transfer process. I use electrochemical methods to track the electron flow and Kelvin probe

force microscopy to probe the surface potential change of the nanoparticles throughout this photocatalytic process. This study will provide valuable guidelines for designing plasmonic nanomaterials for light harvesting applications. Moreover, I am also fabricating plasmonic nanomaterials with the goal of both increasing and decreasing surface potentials depending on the excitation wavelength. The success of this work will offer a novel route to convert solar energy into electrical energy using metals instead of semiconductors.



Nirala Singh

UW mentor Charlie Campbell, Department of Chemistry

Education Ph.D., Chemical Engineering, UC Santa Barbara, 2015
B.S., Chemical Engineering, University of Michigan, 2009

Nirala Singh earned a Ph.D. in Chemical Engineering from the University of California Santa Barbara. His research interests include catalysis and electrocatalysis for conversion of hydrocarbons, electrocatalyst material characterization and testing, and flow batteries for energy storage. He is currently working with chemistry professor Charlie Campbell to understand surface catalysts of complex molecules and eventually applying the research to solar energy storage in liquid hydrocarbons than can be used for transportation fuels. Prior to joining the University of Washington Nirala was a postdoctoral research scientist at the Pacific Northwest National Laboratory in Richland, Washington.

Hao Wang

UW mentor Baosen Zhang, Department of Electrical Engineering

Education Ph.D., Information Engineering, The Chinese University of Hong Kong, 2015
M.S., Engineering, Shanghai Jiao Tong University, 2010
B.S., Engineering, East China University of Science and Technology, 2007

Hao Wang earned a Ph.D. in Information Engineering from The Chinese University in Hong Kong. His research interests include big data analytics for supporting smart grid planning and operations, as well as long-term investment and short-term (day-ahead & real-time) operation of power systems integrating renewable energy and energy storage. He is also studying new business models and economic mechanisms for incentivizing participation of distributed energy resources, such as renewable energy, storage, electric vehicles in microgrids. He will be working with UW professor Baosen Zhang in electrical engineering starting in June 2016.

Zhibin Yang

UW mentor Alex K-Y Jen, Department of Materials Science & Engineering

Education Ph.D., Laboratory of Advanced Materials, Fudan University, China 2009-2014
B.E., School of Science, East China University of Science and Technology, China, 2005-2009

My current study focuses on developing high-performance perovskite solar cells (PVSCs) and understanding their internal photophysics behaviors. The exceptional photovoltaic properties demonstrated recently for organic-inorganic halide perovskites, such as CH3NH3PbX3 (X = Cl, Br or I), have attracted great attention from researchers. The promising features of these perovskites including broad and intense absorption spectra, appropriate semiconducting properties, long carrier diffusion length and facile solution processability, enable improved power conversion efficiency from 3.8 percent to 20.1 percent within only a few years. The high efficiencies achieved in these solar cells are already on par with those made from multicrystalline silicon, copper indium gallium selenide, and cadmium telluride. However, most of the PVSCs studied so far are fabricated via a spin-coating method with small area. Moreover, the perovskite crystals are easily degraded due to their sensitivity to humidity in ambient conditions. Therefore, one of my studies is to realize fully printable PVSCs by large-area processing techniques like blade coating or roll-to-roll printing, especially in ambient conditions, to pave the way for future mass production. At the same time, I will try to understand the mechanisms of how moisture affects perovskite crystallization.

Methylammonium lead tri-iodide perovskites (MAPbI3) are the most studied materials with high photovoltaic performance. But MAPbI3 still faces several complex challenges that need to be addressed, such as the thermal and moisture instability, hysteretic current-voltage characteristic, toxic lead contamination, etc. It was found that partial substitution of a cation or an anion will largely change the properties of a new compositional perovskite. Another interest of mine is understanding the detailed roles of organic cations, metal cations and halide anions in perovskites and then developing a better perovskite composition via tuning the three components in the perovksite.

In addition, it is difficult to further improve the power conversion efficiency of commercialized silicon solar cells in a single p-n junction. The efficiency can be further improved with a tandem structure that combines a silicon solar cell with another large bandgap solar cell. Considering the bandgap of a bottom silicon solar cell is about 1.12 eV, an ideal bandgap of a top solar cell is about 1.7-1.8 eV. Therefore, another goal is to develop high-performance large-bandgap perovskite solar cells so as to construct a high efficiency tandem solar cell.

Data-Intensive Discovery

Rahul Biswas

UW mentors Andrew Connolly, Department of Astronomy
Magdalena Balazinska, Dept. of Computer Science & Engineering
Marina Meila, Department of Statistics

Education Postdoctoral researcher, Argonne National Laboratory, 2010-2014
Ph.D., Physics, University of Illinois at Urbana-Champaign, 2010
M.S., Physics, University of Illinois at Urbana-Champaign, 2004
M.S., Physics, Indian Institute of Technology, Kanpur, India, 2001
B.S., Physics (honors), Presidency College, University of Calcutta, India, 1999

My research goals are related to quantifying the phenomenology of the late-time acceleration of the expansion of the universe, which is often described in terms of properties of dark energy, the substance assumed to drive this acceleration. Two of the key challenges to cosmological studies of this type are (a) the data tend to be large and low signal-to-noise and (b) the knowledge of astrophysical objects used to draw cosmological inferences is incomplete (an obviously rich research frontier in itself). My research involves constructing and sharpening probes of cosmology using methods of statistical inferences from large datasets, iterating the models of astrophysical objects used in such inferences by using simulations of data and accounting for the complications arising from the observational system. I also use these tools to forecast performance capabilities of a survey as a step towards optimizing the survey for scientific impact.

Sophie Clayton

UW mentors E. Virginia Armbrust, School of Oceanography
Bill Howe, Department of Computer Science & Engineering and the eScience Institute

Education Postdoctoral researcher, Massachusetts Institute of Technology, 2013
Ph.D., Physical Oceanography, Massachusetts Institute of Technology/Woods Hole Oceanographic Institution Joint Program in Oceanography, 2013
B.Sc. (Hons.), Ocean Sciences, Bangor University, UK, 2007

Microscopic algae (phytoplankton) form the base of the oceanic food chain and are key players in the biogeochemical cycles of many climatically active elements, such as carbon and nitrogen. I use a combination of modeling approaches, field observations and large-scale data analysis techniques to understand how the oceanic environment shapes patterns in phytoplankton ecology. Since joining the UW, I have been working with data collected with the SeaFlow instrument (an underway flow cytometer that describes the community structure of small phytoplankton cells). This represents a rich source of high-resolution (approximately 1 km) data on the physical and biological structure of the surface ocean over a large area. I have recently been applying statistical spatial analysis techniques to identify characteristic scales of variation. Preliminary results show that the influence of physical structures (e.g. ocean eddies) on the distribution of phytoplankton biomass and communities varies across the North Pacific basin.

Thiago Costa

UW mentors Tyler McCormick, Department of Statistics and Department of Sociology
Joshua Blumenstock, Information School

Education Ph.D., Applied Mathematics, Harvard University, 2014
M.S., Mathematics, Institute for Pure & Applied Mathematics, Brazil, 2008
B.S., Computer Engineering, State University of Campinas, Brazil, 2006

My research centers on applications of statistics and network science to social sciences with a focus on exploring massive relational and temporal datasets, such as telecommunications and social networks datasets. During my Ph.D., I worked with a mathematical theory that describes limiting properties of very large networks and I developed a scalable inferential framework to explore applicable aspects of this theory. Now, I am trying to adapt the theory to solve useful real-world problems. One of the applicable perspectives I am exploring is the possibility of developing measures to classify and compare individuals inside the topology of the network. So we identify structural network changes over time both at an individual and at a global level. This can be used, for instance, to model the political identity of individuals and news sources in a social network or to identify and classify real-world events by looking at structural changes in a telecommunication network.

Brittany Fiore-Gartland

UW mentors Cecilia Aragon, Department of Human Centered Design & Engineering
Gina Neff, Department of Communication

Education Ph.D., Communication, University of Washington, 2014
M.A., Sociocultural Anthropology, Columbia University, 2008
B.A., Psychology, University of Pennsylvania, 2003

My research agenda is concerned with the social and organizational dimensions of the data-intensive transformations occurring across many sectors of work. This agenda includes studying how different communities make sense of and value data, and what is organizationally required to support data-intensive practices and collaborations. My previous research pursues these questions of cultural and organizational adaptation to data-intensive technologies in healthcare, global development, and commercial construction. With a team of ethnographers at the UW, NYU and UC Berkeley I am working within the data science environment to understand the cultural and technological changes that are reshaping how data-intensive work is accomplished and the evolution of institutional structures supporting data science in academia.

Michael Fire

UW mentors Carlos Guestrin, Department of Computer Science & Engineering
Josh Blumenstock, Information School

Education Postdoctoral researcher in Telekom Innovation Laboratories, Ben-Gurion University, Israel
Ph.D., Information System Engineering, Ben-Gurion University, Israel, 2013
M.S., Mathematics, Bar-Ilan University, Israel, 2004
B.Sc., Computer Science & Mathematics, Bar-Ilan University, Israel, 2004

I intend to study how social groups form, evolve and dissolve over time. I believe that large-scale spatio-temporal mobile social networks with billions of links can reveal significant insights into how social groups are created and behave. As part of this project, I plan to develop an open and intuitive infrastructure for performing spatio-temporal analyses of large-scale social networks. This infrastructure can then be used by social science researchers to test and validate various hypotheses formulated over the decades.

Jes Ford

UW mentors Mario Juric, Department of Astronomy
Jake VanderPlas, eScience Institute

Education Ph.D., Physics, University of British Columbia
B.Sc., Physics, University of Nevada, Reno, 2008

My research interests include cosmology, galaxy clusters and the evolution of large-scale structure. For my Ph.D., I worked on gravitational lensing magnification, comparing measurements with the much more common shear technique, in order to study the distribution of dark matter in the halos of galaxy clusters. All matter in the universe bends light, a phenomenon known as gravitational lensing, and this effect can be used to study the properties of galaxies, clusters and the mysterious dark matter and dark energy that make up most of the universe. I am interested in improving the characterization of galaxy clusters in large astronomical surveys and in promoting open and reproducible science. Currently I split my time between the UW's Department of Astronomy and the eScience Institute, and hope to make useful contributions to open source projects for gravitational lensing and galaxy cluster analyses, as well as become proficient with machine learning and handling big data.

Nick Foti

UW mentors Emily Fox, Department of Statistics
Adrian KC Lee, Department of Speech & Hearing Sciences

Education Ph.D., Computer Science, Dartmouth College, 2013
B.S., Computer Science and Mathematics, Tufts University, 2007

My research focuses on the development of Bayesian nonparametric statistical methods applied to machine learning. In particular, I develop models and scalable inference algorithms applicable to data arising from various dynamic complex phenomena, including finance, genomics and neuroscience, among others. As a joint UW Institute for Neuroengineering and eScience WRF Postdoctoral Fellow, I will develop statistical models to learn the effective connections between the auditory sensory areas of the brain and the attentional network from high-dimensional time series of magnetoencephalography (MEG) recordings.

Alexander Franks

UW mentors Peter Hoff, Department of Statistics
Daniel Promislow, Department of Pathology

Education Ph.D., Statistics, Harvard University, 2015
Sc.M. Applied Mathematics, Brown University, 2010
B.A., Computer Science and Applied Mathematics, Brown University, 2009

I am primarily interested in improving the statistical sophistication of research in systems biology. At the UW, I plan to develop a Bayesian statistical methodology for handling large and heterogeneous metabolomic data. The wealth of large-scale data in biology has made it possible to investigate many new questions about the metabolome. The metabolome consists of the set of small molecules involved in the chemical reactions that make organisms function in their environments. Importantly, metabolomic data differs from genomic or proteomic data in scale and scope. The metabolome consists of as many as 100,000 molecules, of which many metabolites are still unclassified. The molecules also may react in complex ways with exogenous metabolites from the environment. While recent techniques have made it possible to measure tens of thousands of metabolites simultaneously in a variety of conditions, truly understanding the various roles of these molecules requires new statistical techniques for assessing variability in array data as well as tools for data integration and ways of handling missing data.

Jie Liu

UW mentors Bill Noble, Department of Genome Sciences
Jeff Bilmes, Department of Electrical Engineering

Education Ph.D., Computer Science, University of Wisconsin-Madison, 2014
M.S., Statistics, University of Wisconsin-Madison, 2011
M.S., Computer Science, University of Wisconsin-Madison, 2009
M.S., Signal and Information Processing, Peking University, China, 2007
B.S., Information Management and Information Systems, Beijing University of Posts and Telecommunications, China, 2004

In aggressive and metastatic breast cancer, genomic aberrations quickly evolve and metastasize, resulting in extreme spatial and temporal heterogeneity that makes the cancer extremely difficult to treat. As a result, multiple biopsies over different locations and at different time points need to be collected and sequenced to monitor the oncogenic processes within individual patients. In my research project, we aim to jointly analyze these different types of genomic aberration events from multi-location/multi-time biopsies in metastatic breast cancer using an integrated probabilistic model. This approach will allow us to accurately characterize genomic aberrations and understand oncogenic processes at a significantly larger scale, which are critical to making progress in cancer genome research. In addition, the proposed project solves many data science challenges in this data-rich, computation-intensive “Big Data” problem, such as handling noisy data, scaling and speeding up, inference under uncertainty and incremental analysis. The proposed approach will greatly facilitate the transformation of terabytes of DNA sequencing data into the actual knowledge we need to understand and cure breast cancer.

Xiaofeng Meng

UW mentors John Vidale, Department of Earth & Space Sciences
Jake VanderPlas, eScience Institute

Education Ph.D., Geophysics, Georgia Institute of Technology, 2015
B.Sc., Physics, Beijing Normal University, China, 2008

My research interests include the responses of fault systems to stress perturbations, the physics of earthquake nucleation and interaction, improved detection of micro-earthquakes and seismic hazard assessment. While I was at Georgia Tech, I helped develop a graphics-processing-unit-based matched filter technique that effectively uses waveforms of known earthquakes as templates to search for similar signals within continuous data. For my research with the eScience Institute, I will develop an auto-correlation technique that is capable of detecting repetitive seismic signals (e.g., earthquakes and nonvolcanic and volcanic tremors) through multi-year-long waveforms recorded in Cascadia. The proposed work is not only vital for better understanding the fundamental physics of fault rupture and volcanic eruption, but is also useful for seismic and volcanic hazard forecasting and mitigation.

K. Allison Smith

UW mentors Curtis Deutsch, School of Oceanography
Jeffrey Heer, Department of Computer Science & Engineering

Education Postdoctoral researcher, Atmospheric and Oceanic Sciences Program, Princeton University, 2010-14
Ph.D., Biological Sciences, University of South Carolina, 2010
M.A., Ecology and Evolutionary Biology, University of California, Los Angeles, 2005
Fulbright student, Marine Sciences, University of Auckland, New Zealand, 2002
B.S., Biology, with distinction, Duke University, 2001

My research focuses on understanding and predicting the distribution of species in coastal and open ocean ecosystems. My hypothesis is that animals maintain geographic position in the open ocean by migrating to deeper depths during the day where the horizontal current speeds are slower. In the course of this research, I am using and developing mechanistic models of organisms and ecosystems that incorporate physiology, chemistry and physics. Results from my research will help determine the effects of climate change on marine ecosystems. I have additional interests in reproducibility and data visualization. After releasing my own code for the first time, I decided to do a systematic study of code and software in ecological journals. My computer science advisor, Jeffrey Heer, and I will report these findings in a forum article.

C. David Williams

UW mentors Thomas L. Daniel, Department of Biology
Magdalena Balazinska, Department of Computer Science & Engineering

Education National Science Foundation Postdoctoral Fellowship in Mathematical Biology, Harvard University, 2012-2014
Ph.D., Physiology and Biophysics, University of Washington, 2012
B.A., Physics, Reed College, 2006

Muscle is a uniquely regulated system. We are used to thinking of biological processes as primarily controlled by chemical signals. The processes in which these chemical signals are coupled to mechanical stresses and strains, such as bone growth, typically occur over time periods of days to months. My work focuses on the physical regulation of muscle contraction, a process controlled by forces on the sub-millisecond time scale. This field has traditionally relied on expert hand digitization of experiment images. I'm increasing replicability, throughput and the questions we can ask about muscle regulation through the introduction of automated analysis techniques drawn from cross-discipline collaborations. We have developed a processing tool chain, described in an accepted conference paper, which first segments the diffraction image into regions of interest using highly conserved features and then samples possible parameter values with a Markov chain Monte Carlo approach. We are applying this tool chain to our first high-temporal resolution data set and we will further refine it in the coming year.

Neuroengineering

Miriam Ben-Hamo

UW mentors Horacio de la Iglesia, Department of Biology
Matthew Reynolds, Department of Electrical Engineering

Education Ph.D., Animal Physiology, Ben-Gurion University of the Negev, Israel, 2013
M.Sc., Animal Physiology, Ben-Gurion University of the Negev, Israel, 2009
B.Sc., Biology, Hebrew University of Jerusalem, Israel, 2007

Electrocorticographic (ECoG) techniques revolutionized the study of the function and regulation of sleep. ECoG studies in laboratory animals have established the association of sleep with critical physiological and behavioral processes, including learning and memory, immune response, energy balance and growth. However, the technical limitations imposed by ECoG equipment have so far presented an insurmountable challenge to the science of sleep: ECoG recording requires implanting transcranial electrodes that are connected via tethered wires to an amplifier. In primates, this technique typically requires immobilization, which induces significant stress, limits the duration of the studies and is known to modify sleep amount and the temporal distribution of sleep stages known as sleep architecture. Furthermore, the use of wired implants is particularly problematic in group-housed animals with good hand dexterity as they can grab each other's implants. Thus, the lack of appropriate primate models stems mainly from technological limitations.

One of my mentors, Dr. Matt Reynolds, has designed the latest generation in telemetric recording systems. It consists of a microchip with several electrode leads that can be connected in vivo for recording neuronal activity. In its current form, the chip has been successfully used to record single-unit neuronal activity from free-flying dragonflies. I am currently working on customizing this recording system to specifically record sleep stages from free-behaving group-housed primates. The innovative aspect of this chip is that it contains all the necessary elements (electrodes, amplifier, transmitter and batteries) and can communicate telemetrically with a receptor station that can be placed in the animals' cage. Importantly, the battery that this chip carries is charged by radio waves. The entire implant is approximately 1.5 mm thick and is as big as the area defined by the electrodes. Thus, this autonomous recording device can remain in an animal's body indefinitely and with minimal effect on its behavior.

My overall goal is to provide proof-of-principle experimental evidence for the continuous high-frequency recording of ECoG and electromyography (EMG) data in free-behaving group-housed monkeys. Most studies of sleep in nonhuman primates have been limited to experiments that last only a few hours. Although these studies have allowed the characterization of circadian and homeostatic regulatory processes of sleep in monkeys, they all measured ECoG and EMG activity in animals that are either restrained, isolated or both. No studies thus far have assessed long-term changes in sleep architecture in non-stressed individuals that are living in meaningful social environments. It is my hope that our telemetric recording system will provide a significant step forward in sleep-research technology.

Hannah Choi

UW mentors Eric Shea-Brown, Department of Applied Mathematics
Wyeth Bair, Department of Biological Structure

Education Ph.D., Applied Mathematics, Northwestern University, 2014
M.S., Applied Mathematics, Northwestern University, 2010
B.A., Applied Mathematics, University of California, Berkeley, 2007

The goal of my research is to understand the circuit mechanisms underlying adaptable responses in the visual system. Neurons in the visual system, like in many other sensory systems, do not have a unique mapping of input stimuli to output responses. Rather than being shaped solely by the target stimuli, visual system responses are modulated by contextual information. For example, visual responses and the resulting motor outputs can depend on other visual stimuli near the target, on attention levels or on motivation. In order to fully understand how neural circuits in the visual system integrate and interpret sensory inputs, the biological mechanisms underlying context-dependent computation of sensory information need to be investigated.

My current research investigates the mechanisms responsible for discriminating shapes that are partially occluded (hidden) in collaboration with Anitha Pasupathy. The primate visual system has an exceptional ability to recognize objects in natural scenes even though most objects appear partially occluded. This ability has yet to be matched in computer vision. We are studying neural mechanisms of shape discrimination under partial occlusion using a computational model. Recent recordings of the macaque brain from the Pasupathy lab indicate that feedback signals from the prefrontal cortex (PFC), a higher-level brain area involved in executive control of behavior, are sent to cortical area V4, a mid-level visual cortical area that contributes to the discrimination of partially occluded shapes. The responses of V4 and PFC neurons were measured while monkeys discriminated pairs of shapes under varying degrees of occlusion. In V4, neurons showed decreased shape selectivity early in their responses as the occlusion was increased. Interestingly, about 200 milliseconds after the stimulus was presented, there was a second peak in V4 responses, and the amplification of shape selectivity was more prominent for the stimulus under intermediate levels of occlusion. Many neurons in the PFC, which are known to receive signals from V4, responded strongly to occluded stimuli but weakly to unoccluded stimuli. These observations are consistent with the hypothesis that the PFC provides feedback modulation responsible for the later increase in shape selectivity in V4 under occlusion.

To better understand the underlying neural circuitry, we constructed a computational model of neurons in V4 and PFC. The V4 neurons in the model send excitatory signals to groups of PFC neurons, whose responses are also modulated by an occlusion-dependent gain function. The PFC output is fed back to V4 neurons. The model outcome matches the experimental results, predicting initial low V4 shape selectivity under occlusion that increases later. The model also predicts equally robust shape selectivity with a gain function that either detects the presence of occlusion or gradually increases as the degree of occlusion is increased. In addition, analysis of the model-based reward rate suggests that it is more advantageous to wait until the second peak of V4 neuron activity to discriminate shapes when the level of occlusion is high, in spite of the delay involved.

Furthermore, we are currently developing a model to examine whether the observed responses in V4 and the PFC can emerge under the assumption of predictive coding, in which the PFC makes predictions of V4 activity via feedback signals and only the unpredicted error signals are transmitted from V4 to the PFC via feed-forward projection.

Nick Foti

UW mentors Emily Fox, Department of Statistics
Adrian KC Lee, Department of Speech & Hearing Sciences

Education Ph.D., Computer Science, Dartmouth College, 2013
B.S., Computer Science and Mathematics, Tufts University, 2007

My research focuses on the development of Bayesian nonparametric statistical methods applied to machine learning. In particular, I develop models and scalable inference algorithms applicable to data arising from various dynamic complex phenomena, including finance, genomics and neuroscience, among others. As a joint UW Institute for Neuroengineering and eScience WRF Postdoctoral Fellow, I will develop statistical models to learn the effective connections between the auditory sensory areas of the brain and the attentional network from high-dimensional time series of magnetoencephalography (MEG) recordings.

Gabrielle Gutierrez

UW mentors Eric Shea-Brown, Applied Mathematics
Fred Rieke, Physiology and Biophysics

Education Ph.D., Neuroscience, Brandeis University, 2012
B.A., Physics, Barnard College, Columbia University, 2006

Gabrielle Gutierrez works in collaboration with Eric Shea-Brown in Applied Mathematics and Fred Rieke in Physiology and Biophysics. Her research is aimed at understanding how neural circuits implement functional computations using the rich assortment of biophysical mechanisms available to them. These studies are based in the retina; a profoundly complex circuit that may hold the key to understanding how local neuron properties contribute to global circuit function. Gabrielle seeks to address these issues using a combination of experimental electrophysiology techniques, and normative theories and computational modeling. This work will provide insight into the multiple solutions that allow neural circuits to adapt to the immensely complex stimuli encountered in nature. Gabrielle has a doctoral degree in Neuroscience from Brandeis University. She received her bachelor's degree from Barnard College, Columbia University, where she majored in physics and minored in applied math. Gabrielle was awarded an IGERT training fellowship at Brandeis.

Guillaume Lajoie

UW mentors Adrienne Fairhall, Department of Physiology and Biophysics
Eb Fetz, Department of Physiology and Biophysics

Education Bernstein Research Fellow in Computational Neuroscience, Max Planck Institute, Germany, 2014-2015
Ph.D., Applied Mathematics, University of Washington, 2013
M.S., Applied Mathematics, University of Washington, 2010
M.S., Mathematics, University of Ottawa, Canada, 2007
B.S., Mathematics, University of Ottawa, Canada, 2004

My main project is aimed at linking experimental research and theory by building mathematical models of the neural dynamics of artificially induced plasticity in the brain's motor cortex. Experimental results have shown that neural implants that stimulate parts of a macaque motor cortex can strengthen synaptic connections between otherwise uncorrelated neural populations.

The models I am developing will capture relevant biophysical features of artificially stimulated cortical dynamics and will provide insights into the relationship between neural dynamics and function in the motor cortex. Furthermore, the models will provide a theoretical testbed that can be used for future brain-machine interface experiments in the Fetz Lab.

So far, progress has gone well. Since the start of my appointment in January 2015, I have implemented a large-scale network model of localized motor cortex areas using spiking integrate-and-fire-type neurons. Importantly, I have added some rudimentary plasticity rules to the network dynamics, a nontrivial task due to challenges introduced by the interactions of dynamics on multiple time scales. This model has yielded some fascinating preliminary data. We plan to use the model to test the stability of plastic changes under different regimes of cortical dynamics.

In addition to this work, I am currently implementing a simpler model that uses a statistical description of neuronal spike trains to probe the effect of artificial stimulation of motor cortical areas under specific learning rules. The reasons for using this model are twofold. First, it provides an analytically feasible framework to ask basic questions about the functioning of neural implants from the Fetz Lab. Second, it complements existing studies from a previous collaboration of Eb Fetz.

I believe that these two approaches are complementary in that the latter, the more simplistic one, will inform us on important directions to take in the former study, where more complex biologically realistic mechanisms are modeled.

Thomas Richner

UW mentors Chet Moritz, Department of Rehabilitation Medicine
Adrienne Fairhall, Department of Physiology and Biophysics

Education Ph.D., Biomedical Engineering, University of Wisconsin, 2014
B.S., Biomedical Engineering, Washington University in St. Louis, 2008
B.S., Mathematics, Northland College, 2006

As a jointly funded WRF and Center for Sensorimotor Neural Engineering (CSNE) and UW Institute for Neuroengineering fellow, I continue to work on two projects: cortical coding of proprioception and motor decoding for spinal reanimation.

Proprioception is the sense of where your body is in space and how it is moving. Proprioception is essential for coordinated limb movements, such as reaching and walking. Even with our eyes closed, we know where our limbs are. Thus, there must be a neural representation of limb states within the brain. We hypothesize that proprioception, like other senses, is encoded in the sensory cortex. Little is currently known about how proprioception is coded in the brain. Do cortical neurons represent individual muscle lengths, joint angles, muscle synergies, endpoint position or a more complex abstraction? Our approach to answering this question uses calcium imaging to survey a large population of cortical neurons while a robotic manipulator directs the limb through a sequence of movements. Through a collaboration with the Allen Institute for Brain Science, we are obtaining transgenic mice that express GCaMP6f, the latest genetically encoded calcium indicator. A small implanted window over the cortex provides microscope access, allowing us to record videos of sensory neurons lighting up in response to limb movement. The limb is tracked in 3D with two motion capture cameras So that muscle lengths and joint angles can be estimated with a muscle and bone kinematic model. We will conduct initial investigations in lightly sedated mice to help disentangle sensory inputs from concurrent motor signals, but future investigations will transition to awake passive movement and then active movement. Capturing the interplay of the sensory and the motor cortex during reaching could inform other research collaborations between the Moritz and Fairhall labs. Understanding the cortical encoding of proprioception is the first step towards developing proprioceptive neuroprostheses.

Brain-controlled spinal reanimation is another important area in which I am working. The goal of this research is to use signals decoded from the motor cortex to trigger spinal stimulation to cause a paralyzed limb to move. This work is being developed in the rat animal model in Professor Moritz's laboratory in collaboration with Professor Fairhall. I have implemented a generalized linear model (GLM) that uses motor signals from the cortex to predict lever presses in real time. The algorithm currently runs on external digital signal processors, but will eventually be ported to an implanted wireless device currently being collaboratively developed by Center for Sensorimotor Neural Engineering faculty. While the GLM is lightweight enough to run on implanted computing hardware, fitting the model requires the computational power of an external computer. The model can be updated in a co-adaptive framework as more information is gathered and the user becomes more practiced. The GLM is a broadly applicable algorithm that is more commonly used to model sensory systems and could be further applied to studying proprioception.

Eatai Roth

UW mentors Tom Daniel, Department of Biology
Kristi Morgansen, Department of Aeronautics and Astronautics

Education Ph.D., Mechanical Engineering, Johns Hopkins University, 2012
B.S., Mechanical Engineering, University of Pittsburgh, 2005
B.F.A, Fine Arts, Washington University, 2001

Animal locomotor behavior is largely multisensory, using information from multiple sensory modalities to control action. Decoding the computations by which these streams of information are combined to modulate behavior — the sensory integration problem — is a key challenge of neurobiology and neuroengineering. In my research, I investigate the individual roles of and the interplay between visual and mechanosensory information using insect flight as a model system. I examine two behaviors in the hawkmoth *Manduca sexta*: flower following during feeding and active pitch control during forward flight. Both studies require a reverse engineering approach to unravel the complex interplay between multiple sensory modalities in movement control.

During feeding, the nectivorous hawkmoth hovers in front of a flower while its long proboscis probes for nectar. As a flower sways in the breeze, the moth must also weave reactively to stay with the flower. It was long believed that this behavior was mediated predominantly by visual cues. However, the moth probosicis is more than just a drinking straw; it is richly adorned with mechanoreceptive bristles. In order to disentangle the contributions of visual and mechanosensory information, we use a robotically actuated, two-part 3D printed flower that can simultaneously deliver independent visual and mechanosensory stimuli to the hovering moth. By leveraging sensory conflict, we are able to simultaneously model the individual contributions of the two sensory pathways. We discovered that both modalities contribute to the tracking behavior and that their contributions sum linearly. And, contrary to held beliefs, the mechanosensory pathway is the dominant contributor in this behavior. This work is currently in preparation for publication.

Mechanoreceptive bristles can be found all over the insect body. In the second part of my work, I ask how this distributed mechanosensory system plays a role in encoding body orientation for the purpose of flight control. I also investigate how the nervous system uses different streams of sensory information to maintain robust behavior while compensating for both external perturbations (such as wind gusts) and changes to the animal body (especially mass change due to feeding). To explore this question, I am developing a virtual reality system capable of delivering independent visual and mechanical rotational stimuli to a tethered moth. Measuring the torque exerted on a tethering pin, the visual scene and tether angle can be modulated in a closed loop to simulate free flight. In this preparation, we can play games with the physics that govern the visual and mechanical feedback: isolating a single modality, imitating wind gusts or simulating rotational dynamics as if the animal were suddenly heavier. This system promises a flexible platform for exploring questions about the interplay between neural processes and the biomechanical systems they control.

Animals are agile and robust agents interacting with dynamic and uncertain environments. I am translating tools from control theory and robotics to uncover the underlying control principles that afford this adept performance. This is an open problem in both biology and engineering.

Protein Design

Hua Bai

UW Mentors David Baker, Department of Biochemistry & Institute for Protein Design
David Galas, Pacific Northwest Diabetes Research Institute

Education Ph.D., Department of Neuroscience (physiology emphasis), University of Wisconsin-Madison, 2015
B.Sc., Biological Sciences, Peking University, China, 2005

To restore auto-antigen tolerance in autoimmune disease models, especially in the Type 1 Diabetes model, I will work under the guidance of Dr. David Galas at the Pacific Northwest Diabetes Research Institute and Dr. David Baker at the Institute for Protein Design to design and validate therapeutic peptides (or small proteins) that can interfere with the recognition of auto-antigen/MHC complexes by T-cells receptors and hence inhibit the activation of pathogenic T-cells. By exploiting self-assembling nanoparticle design methods, I will design tolerogenic MHC-peptide complexes that can promote the proliferation of regulatory T-cells and then induce auto-antigen tolerance. This project can potentially create novel tolerogenic therapeutics, and it can lead to a better understanding of immune tolerance mechanisms as well.

I obtained a B.S. degree in Biological Sciences in Peking University, China. Later, I went to the University of Wisconsin-Madison to pursue a Ph.D. degree in physiology. After two years of working on metabolism using animal models and five years of studying membrane trafficking using various *in vitro* biochemistry and biophysics techniques, my career objective to be an outstanding protein engineer is getting clearer and more determined. I will be dedicated to addressing metabolic syndromes and related disorders by using powerful protein design and engineering methods.

Ralph Cacho

UW mentors David Baker, Department of Biochemistry and Institute for Protein Design
Michael Gelb, Department of Chemistry

Education Ph.D., Chemical and Biomolecular Engineering, University of California, Los Angeles, 2015
B.S., Biochemistry, University of California, Los Angeles, 2010

The anticancer agents salinosporamide A and rebeccamycin, the antifungal griseofulvin and the antibiotic vancomycin all contain carbon-halogen bonds. The presence of the halogen atom in these compounds is vital to the activity of the respective molecules. A lack of specificity and regioselectivity (a process that favors bond formation at a particular atom) has hampered classical synthetic chemistry methods for carbon-halogen bond formation. But enzymes evolved a variety of elegant mechanisms to catalyze this synthetically challenging reaction. Hence novel methods for the introduction of carbon-halogen bonds in advanced synthetic or biosynthetic intermediate with complex molecular scaffolds can be developed by engineering these halogenating enzymes.

My project aims to apply computational protein design to redesign a chlorinase enzyme with a modified substrate scope. To demonstrate the potential of computational protein design to efficiently change the substrate scope of the enzyme, I will design the chlorinase to catalyze the conversion of dechlorogriseofulvin to griseofulvin. Griseofulvin is an antifungal compound used in the treatment of skin and scalp infections caused by dermatophytes like *tinea capitis* and *tinea pedis*.

While previous engineering approaches have been performed on chlorinase enzymes, previous examples use indole-containing substrates (such as tryptamine) or aryl rings with nitrogen substituents (such anthranilic acid or kyneurine). While these examples highlight the plasticity of the substrate scopes of this class of enzymes, they also highlight the deficiencies of the current approaches used to modify the specificity of flavin-dependent chlorinases. My project aims to supplement these current methods with computational design by targeting a reaction involved in the synthesis of a medically relevant compound.

Alexis Courbet

UW Mentors David Baker, Department of Biochemistry and Institute for Protein Design
Joshua Smith, Department of Computer Science and Engineering
Luis Ceze, Department of Computer Science and Engineering

Education Ph.D., University of Montpellier, 2015
Pharm.D., University of Montpellier and University of Paris Sud, 2015
M.S., University of Montpellier, 2012
M.S., University of Paris Sud, 2011

Research

Computers have revolutionized our understanding and relation to the world. Automating the manipulation of information, they transfer human labor to machines and augment human capabilities. While science and engineering have placed increasing demands on computation, miniaturization of silicon-based electronics has been the main driving force behind its enhancement. However, physical limits of CMOS technology are announcing the end of Moore's law. Further advancing computers to achieve ever-higher densities of useful computational work under specified quantity of time, material, space, energy and cost, remains a critical challenge in the 21st century.
Novel approaches relying on biological substrate (*i.e.* biocomputing) have the potential to outperform conventional silicon. Indeed, living systems are incredibly efficient three dimensional computers capable of solving hard computational problems. Synthetic biologists are thus considering the possibility of engineering computing systems where input, output, software, and hardware are made of biological molecular-scale machinery to store and perform operation on data.
This approach holds promising advantages: high density of data storage, massive parallelization and ultra-low power signal processing. Biocomputers are biosynthesized and self-assembling, ensuring a low cost and high scale of production. By nature biocompatible, they could support the monitoring, control and electronic interfacing of biological systems. Therefore, the engineering of biological computing machines could pave the way towards unprecedented scientific opportunities, offering powerful solutions for computer sciences, biotechnology and molecular medicine. Yet, developing functional biocomputers with a scalable architecture remains elusive since tools are lacking to perform precise assembly of biomolecular components at nanoscales.

In this project, we identified proteins as versatile and modular components constituting a vast engineering playground. Proteins self-assemble in a sequence dependent way and are capable of information processing, which we intend to exploit for the rational design of complex three dimensional biocomputers. Although proteins rely on complex folding, allosteric mechanism and interfaces of non-covalent interactions, recent advances in the development of Rosetta software allowed computational design of protein nanomaterials with unprecedented accuracy and design space. *De novo* protein components can now be generated *in silico* to self-assemble into specified symmetric scaffolds, which we suggest could support high-order biocomputing architectures. This project thus proposes to harness advances in computational protein design as a systematic methodology to engineer universal nanoscale biocomputers. We propose to investigate how massively parallel computing architectures can be built using self-assembling 3D arrays of protein logic gates, ultimately implementing any given Boolean function. There are two engineering challenges to realizing such systems: first, methods for designing

protein nanomachines need to be developed; and second, because of non-conventional substrate, mechanism of information processing, programmability of the computer and interfacing will need to be overcome. The proposed research intends to *i)* investigate machine architectures and programmability *in silico ii)* explore design rules, experimental and computational methods for designing 3D self-assembling protein logic gate arrays *iii)* develop methods for designing digital protein information carriers (*i.e.* switches). Such computers designed with 10 nm nodes could theoretically accommodate 10^{15} layered logic gates within a single microliter, while achieving energy requirements orders of magnitude below those of silicon computers.

Zachary Crook

UW mentor Jim Olson, Fred Hutchinson Cancer Research Center

Education Ph.D., Department of Biology, Massachusetts Institute of Technology, 2013
B.A., Molecular, Cellular, and Developmental Biology, University of Colorado, 2007

I am interested in novel therapeutic applications for cysteine knotted peptides. While the Olson Lab has a strong interest in their potential uses for cancer treatment, I come from a research background in neurodegeneration and wish to investigate the means for getting these natural drug-like peptides across the blood-brain barrier. Efforts toward this will make use of Rosetta and several known structures. I will use both the knotted peptides that the Olson Lab routinely produces and several receptor proteins that facilitate transcytosis of natural signaling proteins to identify potential knotted peptides that can bind these receptors and efficiently transport them into the brain. This has the potential to make the blood-brain barrier a little less imposing for therapeutic applications, including for neurodegenerative diseases and brain cancer.

I attended college at the University of Colorado in Boulder and graduated with honors in molecular, cellular, and developmental biology. Then I entered the Ph.D. program at MIT where I studied mouse models of Huntington's disease under David Housman and developed assays to rapidly and accurately determine the effect of test therapeutics. The idea of drug design using naturally stable bio-available knotted peptides and their potential utility in diseases of the central nervous system drew me to the lab of Jim Olson where I bring knowledge of screening assays in mouse disease models to mix with the biochemical and drug design expertise of the Olson Lab and collaborators at the Fred Hutchinson Cancer Research Center.

A. Gerard Daniel

UW mentors Thomas Spiro, Department of Chemistry
Karen Goldberg, Department of Chemistry
David Baker, Department of Biochemistry & Institute for Protein Design

Education Ph.D., Chemistry, Virginia Commonwealth University, 2013
M.Sc., Pondicherry University, Pondicherry, India, 2005
B.Sc., University of Madras, Chennai, India, 2003

Natural enzymes are remarkable in achieving chemical transformation with extraordinary efficiency and high specificity. The repertoire of these enzymes is clearly self-sufficient for sustenance and progress of life. However, their function is limited by the abundance and bio-availability of the substrates and essential cofactors. For instance, earth-abundant first row transition metals, as cofactors, catalyze several critical biological processes. On the other hand, modern synthetic needs to perform challenging organic transformations are often met by organometallic catalysts of nonbiological, late transition metals. There is an increasing interest in bringing together the rather complementary benefits of the protein environment and organometallic catalysts, which is manifested as the design of artificial metalloenzymes. De novo design of protein for direct incorporation of nonbiological metals at the active site presents greater challenges and by far remains unexplored. In an exploratory effort, the rational design of a metalloenzyme for photocatalytic reduction of CO2 at (Ru,Zn)-bimetallic active site using the unnatural amino acid bipyridyl-alanine (Byp-Ala) as a ligand for Ru is being attempted using the Rosetta protein design suite. Given the increasing rates of CO2 in the atmosphere and its adverse effect on climate change, CO2 capture and conversion to useful reagents and fuel would be an elegant method for sustainable energy production. Hence, based on previously established chemistry, an active site consisting of a Ru center for catalyzing the reduction of CO2 and a Zn center, acting a dual role, for positioning of CO2, in the form of bicarbonate anion, and to facilitate the hydrolysis of the intermediates formed after the reduction is being designed.

Glenna Foight

UW mentor Dustin Maly, Department of Chemistry

Education Ph.D., Biology, Massachusetts Institute of Technology, 2015
B.S., Biochemistry, North Carolina State University, 2009

Cellular signaling pathways are complex networks of protein and enzymatic interactions. Understanding their contributions to disease states is an important goal. The development of protein inhibitors through computational design and directed evolution is a powerful approach for specifically targeting individual elements of signaling pathways. Small-molecule inhibitors offer temporal control and cell permeability, but the development of small molecules that specifically target only one protein in the cell is a difficult and lengthy process. The Maly lab has combined the power of protein and small-molecule inhibitors in a

system known as a chemical genetic switch. This involves the fusion of two components of a protein-protein interaction to a protein of interest such that a small molecule that disrupts the interaction will allow activation of the protein. The first part of my research will involve creating a new chemical genetic switch system by designing a protein interaction partner for an existing protein and small-molecule inhibitor. The new system will use components that are foreign to mammalian cells, thus offering compatibility with future studies of mammalian signaling pathways.

My second project will focus on developing inhibitors of the oncogenic protein Ras. Ras is an important signaling protein in numerous cellular processes, and the Ras family is the most frequently mutated protein family in human cancers. I will design protein inhibitors that specifically target individual oncogenic mutants and family members of Ras. These inhibitors will aid in dissecting the complex functional differences between different mutants and variants of Ras. Furthermore, I will use the successfully engineered chemical genetic switch developed in my first project to confer small-molecule-based, temporal control over these Ras inhibitors in cells.

I did my undergraduate degree in biochemistry at North Carolina State University where I performed X-ray crystallography research, coincidentally, on structures of oncogenic Ras mutants in the lab of Dr. Carla Mattos. My interest in protein structure led me to the lab of Dr. Amy E. Keating at MIT, where I studied the determinants of protein-protein interaction specificity in my graduate work. My interest in studying signaling processes controlled by protein-protein interactions led me to the lab of Dr. Dustin Maly at the UW. Designing specific protein interactions and using my designs to disrupt cellular interaction networks will be an exciting combination of my expertise and interests.

Hannah Gelman

UW mentors Doug Fowler, Department of Genome Sciences
David Baker, Department of Biochemistry & Institute for Protein Design

Education Ph.D., Physics, University of Illinois at Urbana-Champaign, 2015
B.A., Physics, Dartmouth College, 2006

Guiding protein design with comprehensive maps of mutant function
Computational protein design — in which new protein sequences are developed to perform a specific function — promises efficient generation of biological molecules that can carry out novel functions. Designed proteins could be ideal for the treatment of rare or emerging diseases and potentially mitigate the side effects of more broadly acting classes of drugs. This method is hampered by the difficulty of predicting the effect of mutations on protein function, especially if the mutation affects protein stability or structure, and by our incomplete understanding of how protein physical properties like thermodynamic stability affect protein function.

The efficiency of a designed protein can be significantly enhanced with deep mutational scanning (DMS), in which a library of mutants based on the designed sequence is expressed and subjected to weak functional selection (e.g., binding to the targeted ligand). The change in the distribution of sequences over the selection — enrichment of some sequences and depletion of others — is measured and used to

determine the relative function of every sequence. This strategy refines the sequence found by computational design to find a better performing variant, but does not address the underlying mismatch between the performance predicted by the design algorithm and that measured in the real world. Integration of DMS and computational design can be pushed even further so that data from DMS is used to improve design algorithms at the outset instead of to refine the algorithm's output.

Incorporating the large-scale DMS data into the development of protein design algorithms will require us to quantitatively and accurately measure specific biophysical and biochemical properties rather than rely on the more easily obtained relative measurements of mutant function that are currently used. A limited number of assays have been developed to measure these properties in a high throughput manner, but each is highly targeted to a specific protein target. We will expand and combine them in a unified platform that can reproducibly characterize libraries of protein mutants across many of the properties that may be correlated to overall function. For each mutant we will analyze how the measured physical properties correlate with each other and with mutant function. We can then compare these measurements to the predictions of the design algorithm and use the quantitative data obtained to improve the algorithm's ability to accurately predict physical properties and how these properties affect protein function.

Our method can guide the implementation of additional design constraints that better represent the key contributions to a protein's ability to function. A more complete and accurate design algorithm will streamline the design process as it will reduce the need for multiple rounds of computational design and functional screening. In addition, more accurate design algorithms will open the door for more ambitious targets for protein design — for example, the design of novel functions or modes of action — that are currently out of reach.

Jason Gilmore

UW mentors Michael MacCoss, Genome Sciences
David Baker, Department of Biochemistry & Institute for Protein Design

Education Ph.D., Genetics, Dartmouth College, 2014
B.A., Biology, University of Pennsylvania, 2007

I will work jointly with Michael MacCoss and David Baker to develop high-throughput, highly sensitive screens to accelerate experimental validation for *de novo* protein design. The first aim of this project will use liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) to simultaneously quantify hundreds of protein designs expressed together in pooled cultures as opposed to the traditional methods that require individual expression and confirmation of new designs. Additionally, this project will extend software and experimental techniques for MS-based protein chemical crosslinking experiments to rapidly evaluate disulfide linkages in small *de novo* designed proteins. Together, these mass spectrometry methods will improve the productivity of protein design protocols and accelerate the development of novel protein-based therapeutics.

During my undergraduate summers, I worked at the Pacific Northwest National Laboratory in Richland, WA where I helped implement automated quality control metrics for the proteomics core facility. After graduating from the University of Pennsylvania in 2007, I returned to PNNL for one year and wrote a software tool for predicting protein-protein interaction probabilities. My dissertation at Dartmouth College, in the proteomics laboratory of Dr. Scott Gerber, focused on the detection and quantification of phosphopeptide species by mass-spectrometry-based shotgun sequencing. This included a publication on sequential digestion by complementary proteases to survey previously inaccessible regions of the proteome in complex biological mixtures. Subsequently, I developed a computational technique to improve the sensitivity and precision of peptide quantification in cases where isotopically labeled standards failed to fully complement endogenous peptide profiles.

Karla Herpoldt

UW Mentors Patrick Stayton, Department of Bioengineering
David Baker, Department of Biochemistry & Institute for Protein Design
Neil King, Department of Biochemistry and Institute for Protein Design

Education Ph.D., Imperial College London
M.Phys., University of Oxford

Protein-based nanoparticles have been designed and used for a variety of drug-delivery systems. These drug carriers are based on naturally self-assembled protein subunits which form a cage that can be used to trap pharmaceutical compounds. The use of naturally derived proteins offers benefits in terms of their biocompatibility, biodegradability, low toxicity and relative abundance. Despite these advantages, they remain limited in their use, being repurposed from their original biological application. In contrast, the computational design of protein nanomaterials has created the ability to design self-assembling cages which incorporate additional synthetic functionalities into their structure.

Working with the Baker/King labs Karla is working on using computational design to develop ‘smart’ protein cages that exhibit a strong response to environmental pH. In collaboration with the Stayton group these materials can then be loaded with polymer-prodrug carriers. It is hypothesized that the polymer therapeutics can be loaded via pH-dependent assembly of the cages, and subsequently their higher molecular weight will lead to intra-cage retention. In this way she hopes to develop targeted drug delivery vehicles which release their cargo inside the tumor microenvironment, minimizing chemotherapy dosage levels.

Karla obtained her MPhys in physics from the University of Oxford where she studied laser-plasma interactions and space dust formation before discovering a love of biological physics. She then carried out her PhD research in the lab of Prof. Molly Stevens at Imperial College London where her main focus was on the study of phage-derived peptides for use in diagnostics and therapeutics for HIV. She is also interested in peptide-protein interactions and the rational design of protein ligands. During her PhD Karla held a sabbatical fellowship at the UK Parliament's Office of Science and Technology and was heavily involved with educational outreach.

Parisa Hosseinzadeh

UW Mentors David Baker, Department of Biochemistry and Institute for Protein Design
Michael Gelb, Department of Chemistry

Education Ph.D., Biochemistry, University of Illinois at Urbana-Champaign, 2015
B.S., Biotechnology, University of Tehran, Iran, 2010

As a WRF fellow, my goal is to develop new computational tools to design cyclic peptides and to use these peptides as specific inhibitors/binders to target enzymes/proteins. Cyclic peptide binders have the advantages of both proteins and small molecules: they can offer specificity through providing more contacts and they are small and usually more stable. Design of cyclic peptides is an exciting new addition to the field of protein design.

In particular, I am working with Dr. David Baker and Dr. Michael Gelb to design new cyclic peptide binders for specific inhibition and study of different members of secreted phospholipase A family of enzymes. These enzymes are known to be important in inflammatory disease states including asthma; however their exact roles remain elusive. While there are small molecule inhibitors for some members of these enzymes, similarly specific small-molecule based inhibitors have not been identified for all members of this family of enzymes hampering their study. This project is aimed to use the designed cyclic peptide to address this issue and provide better understanding of secreted phospholipases.

I was trained as a molecular biologist in my undergrad. My interest in proteins led me to do my graduate research on rational design of metalloproteins in the lab of Dr. Yi Lu. I was mainly focused on altering second shell interactions to tune the activity of proteins. My research provided a general guideline for tuning the redox potential of metal centers.

Marc Lajoie

Dr. Lajoie's salary is funded by a Cancer Research Institute Fellowship; Protein production and other research expenses are supported by the WRF Innovation Fellows Program at the Institute for Protein Design.*

UW mentors David Baker, Department of Biochemistry and Institute for Protein Design
Nora Disis, Department of Medicine

Education Ph.D., Chemical Biology, Harvard University
B.A., Biophysical Chemistry, Dartmouth College

As a WRF Innovation Fellow at the Institute for Protein Design, I am working with the Baker, King and Disis labs to develop next-generation vaccines for cancer treatment and prevention. Antigen-presenting cells determine how the immune system responds to antigens. To exploit this control point, I am developing protein nanorobots capable of delivering immunogens directly to sub-compartments of dendritic cells in order to control how the immunogen is presented to naive T-cells. Cytosolic targeting could specifically activate CD8+ T-cells that destroy cancer cells, and endosomal targeting could specifically activate CD4+ Th1 cells that promote a strong, sustained immune response.

After receiving a B.A. in biophysical chemistry from Dartmouth College, I completed my Ph.D. in chemical biology under the mentorship of George Church at Harvard Medical School. During my dissertation research, I developed genome engineering technologies to reassign the genetic code. My graduate research has implications for enabling virus resistance, improving biocontainment of recombinant organisms and expanding the amino acid repertoire for industrial organisms. I received a National Defense Science and Engineering Graduate Fellowship in 2009 and was named to Forbes' "30 under 30" in science in 2012.

Anindya Roy

Mentors David Rawlings, Immunology, Seattle Children's Hospital
David Baker, Department of Biochemistry and Institute for Protein Design

Education Ph.D., Department of Chemistry and Biochemistry, Arizona State University
M.S., Chemistry, Indian Institute of Technology, India
B.Sc., Chemistry, Calcutta University, India

As a WRF fellow, I work with Dr. David Rawlings and Dr. David Baker to develop APRIL- and BAFF-specific inhibitors for the development of therapeutics for autoimmune diseases and cancer. Both these ligands have been shown to play critical roles in maintaining humoral immunity, and the signaling network pertaining to this ligand axis is highly exploited in cancer and autoimmune diseases. Current therapeutic approaches rely on using the soluble extracellular domain of the receptor for these ligands to block the signaling network. However, initial clinical trial results show that an extracellular receptor decoy might not be a safe therapeutic agent, presumably due to the complexity and shared ligand space of this signaling network under normal conditions. This project under the WRF fellowship aims to design orthogonal binding partners for BAFF and APRIL with high affinity and specificity.

I started my scientific career with a special interest in chemical biology and protein biochemistry. I studied protein-small-molecule interactions using biophysical techniques and received my M.Sc. from the Indian Institute of Technology Kharagpur. In 2008, I moved to the US and received my Ph.D., under the guidance of Dr. Giovanna Ghirlanda, from Arizona State University where I worked on de novo design of artificial metalloproteins. In this work, I laid the foundation for designing multicofactor redox proteins that go beyond naturally existing systems.

Danny Sahtoe

Dr. Sahtoe's salary is funded by a European Molecular Biology Organization (EMBO) Long Term Fellowship; Protein production and other research expenses are supported by the WRF Innovation Fellows Program at the Institute for Protein Design.*

Mentors David Baker, Department of Biochemistry and Institute for Protein Design
Andrew Scharenberg, Seattle Children's Research Institute

Education Ph.D., Erasmus University Rotterdam and Netherlands Cancer Institute
M.S., Vrije Unversiteit Amsterdam
B.S., Leiden University

Franziska Seeger

Mentors Mohamed Oukka, Seattle Children's Hospital
David Baker, Department of Biochemistry and Institute for Protein Design

Education Ph.D., Chemistry, Department of Chemistry and Biochemistry, University of Maryland, Baltimore County, 2014
B.Sc., Biochemistry, Technical University of Munich, Germany, 2009

The goal of my research is to computationally design high-affinity binders to the cytokine IL-17 and inhibitory mimetics of the cytokine IL-23 p19 to improve our understanding and treatment options for autoimmune diseases.

Autoimmune diseases, such as multiple sclerosis and Crohn's disease, have posed a major medical challenge — elucidating their molecular mechanisms as well as finding effective therapies have been formidable. Current treatments have severe side effects and merely delay disease onset. Th17 cells, which areIL-17 factories, induce autoimmune disease and trigger the pathogenicity of multiple sclerosis and Crohn's disease. In multiple sclerosis, elevated levels of IL-17 lead to migration of auto-reactive Th17 cells from the peripheral lymph nodes, across the blood-brain barrier into the central nervous system. In the central nervous system, elevated IL-17 levels initiate an exaggerated inflammatory response, which is characteristic for autoimmune diseases. Another cytokine player, IL-23, spurs inflammation by stabilizing Th17 cells and promoting their expansion. Multiple genes regulating the IL-23–Th17 pathway have been associated with the development of inappropriate levels of inflammation in inflammatory bowel diseases. Monoclonal antibody (mAb) and non-antibody therapies that target IL-17 and IL-23 are currently being developed in pre-clinical and clinical trials; nevertheless, monoclonal antibodies bear challenges in their biodistribution and non-antibody scaffolds are limited to their starting topology. Thus, the capability to engineer entirely novel proteins de novo _ with a particular structure to fulfill a desired therapeutic function — would be a major advancement in the field of drug development.

In this project, we aim to design stable and effective IL-17 binders and IL-23 cytokine mimetics with minimal immunogenicity and favorable biodistribution to explore and test the role that computationally designed proteins can play as novel therapies for the treatment multiple sclerosis and Crohn's disease.

Specifically, we will apply a Rosetta interface design approach to design high-affinity binders to the IL-17A cytokine. Our IL-23-p19 mimetic design strategy will preserve crucial interface residues that ensure binding to the private IL-23R while deleting the interface between the p19 and the p40 subunit as well as the IL-12β1 receptor. We expect that our high-affinity IL-23-p19 mimetic will efficiently compete with its wild-type equivalent and block IL-23 mediated signaling in human Th17 cells and prevent development of inflammation in murine experimental colitis and multiple sclerosis. We Furthermore, we expect to address open questions about the bona fide IL-23 signaling complex. Additionally, our IL-17 binders will inhibit the IL-17-mediated inflammatory response in multiple sclerosis model animals. In combination, our IL-17 binder and Il-23 mimetic will bear enormous potential for the understanding and treatment of chronic autoimmune diseases, such as multiple sclerosis and Crohn's disease.

Several of the WRF Innovation Fellows in Protein Design have been awarded highly competitive external fellowship awards. These individuals continue to receive the mentorship, training, and other non-monetary benefits of their position in the WRF Innovation Fellows program, and the program continues to provide support for some of their non-salary research expenses such as supplies and protein production services, as allowed by their respective fellowships.

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