Comprehension of spoken language is a neurological function that we often take for granted, but the underlying mechanisms are complex. Several brain regions are involved in the span of necessary processes, from parsing the basic auditory structure of syllables, to associating meaning with words and phrases, to appreciating subtle content such as innuendo, irony, and emotion. We propose to study these interrelated mechanisms by recording electrophysiological activity from several regions in the human brain. Neurosurgical procedures sometimes require the placement of electrodes within the brain, and we will use these opportunities to study human language processing with previously unavailable precision. Newly available recording techniques allow the investigation of several brain regions simultaneously, from "low-level" sensory processing to "high-level" cognitive processing. We will employ sophisticated machine learning techniques to tease apart the contributions of these various mechanisms to overall speech comprehension. We hope that the results of these studies will enhance our understanding of the normal physiology of speech processing, and also provide insight for developing therapeutic options for individuals with disorders of speech and language.

Barclay Morrison & Steven Kernie, *A Novel Biomedically-Based Approach for the Treatment of Brain Swelling After Injury*

Patients suffering from traumatic brain injury and stroke often develop elevated intracranial pressure due to brain swelling, which is highly associated with poor outcome and increased mortality. Unfortunately, current therapies to control swelling often fail or are associated with substantial adverse effects. The objective of this study is to fill this gap in critical care by testing an unconventional hypothesis about the causes of brain edema and by testing a novel therapy to control brain edema a preclinical model. Our paradigm-shifting approach targets the intracellular fixed charge density (FCD) of dead cells that we believe is thermodynamically responsible for accumulating fluid from the vasculature.

Virginia Cornish & Robert Kass, *Genetic Encoding of Fluorescently Labeled Membrane Proteins in Mammalian Cells for Live-Cell Imaging*

A fluorescent unnatural amino acid is the smallest possible fluorescent tag for protein labeling in live mammalian cells – 100x smaller than a fluorescent protein. However, the range of fluorescent unnatural amino acids is limited, and fluorescent unnatural amino acid labeling technology in live mammalian cells is unreliable. This project aims to develop the unnatural amino acid technology as a viable, broadly-enabling small fluorescent tag for protein labeling in live mammalian cells. This tag will open up labeling of membrane proteins and enable sophisticated biophysical studies in live mammalian cells, both of which are challenging with current fluorescent protein tags.

Timothy Bestor, Jingyue Ju & James Russo, *Single-Cell, High-Resolution Methylation Profiling for Personalized Medicine*

The information content of the human genome is expanded by the heritable covalent modification of cytosine residues in CpG dinucleotides, a fact that has largely been overlooked in genome biology and in human genetics. Abnormal DNA methylation has long been associated with cancer, and a growing number of other human disorders have been linked to defects in genomic methylation patterns; furthermore, subtle methylation anomalies can cause genotype-independent phenotypic abnormalities. Such methylation anomalies cannot be detected by whole-genome DNA sequencing, and there is no effective means of genome-wide methylation profiling applicable to small amounts
of DNA. We are developing a radically new method for whole-genome methylation profiling. The method involves the enzyme-mediated modification of all unmethylated CpG dinucleotides with an advanced photoactive compound that upon irradiation with non-genotoxic wavelengths of light will convert all unmethylated CpG dinucleotides to TpG dinucleotides. Analysis by whole-genome sequencing of the converted DNA will localize all unmethylated and methylated CpG dinucleotides in quantities of DNA found in single cells. The result will be a powerful new addition to the tools that will be used in the development and application of precision medicine.


For the past 10 years, the Arabian Sea has been experiencing unprecedented blooms of an enigmatic planktonic organism *Noctiluca*, whose recent rise to prominence in the marine food chain is posing a threat to regional fisheries and the long-term health of an ecosystem which supports a coastal population of nearly 120 million. Spatial patterns of ocean phytoplankton viewable from space, have shown that each year *Noctiluca* make its appearance as a small patch off the coast of Oman in December; engulfing the entire northern Arabian Sea by mid-February. Despite the progress in our understanding of *Noctiluca*, further understanding of the dispersal patterns of this organism and its evolution to massive blooms has been hampered by difficulties in separating the influence of abiotic and biotic factors. Here we propose a study transecting the fields of fluid dynamics, phytoplankton physiology and machine learning, to unravel the rich patterns of *Noctiluca* patchiness in ocean color imagery. This hybrid approach could be applied to other ecosystems, especially those along the coast and in lakes that experience massive outbreaks of phytoplankton, which at times could be toxic and detrimental to human health.


Optoelectronic technologies for the deep ultraviolet remain challenging because there are few materials that work as light emitters or sensors. We are developing a new technique to produce nano-engineered boron nitride sensors and light-emitting devices (LEDs). UV sensors will be initially designed for astronomical detection, which has a great demand for highly-efficient, visible-blind, and low-noise detectors, but these same sensors can be used for many other low cost and/or other low UV light level applications. Light emitters in this wavelength range also have a broad applicability, including use as a low-cost/high efficiency source for disinfection, for spectroscopy and fluorescence analysis, and as a low power calibration source for astrophysics.