

TRINITY COLLEGE

FACULTY RESEARCH IN NEUROSCIENCE 2008-2009

Prof. Daniel Blackburn - *Functional Morphology & Reproductive Biology of Vertebrates Biology - Neuroscience*

My current research concentrates on the structure, function, and evolution of reproductive specializations in reptiles, particularly features associated with the reproductive pattern of viviparity (live-bearing reproduction). This work draws heavily on microscopic anatomy, and students interested in working with me ideally should gain experience with electron microscopy, before their senior year. Our excellent EM facilities in the LSC and McCook -- and our courses in electron microscopy, especially Biology 210 (Scanning EM) and Biology 220 (Transmission EM) -- offer a wonderful opportunity for Trinity students to learn techniques of immense value to biologists. I also have options for students who wish to focus their attention at the level of light microscopy. Research of several of my recent students has resulted in collaborative research publications and presentations at scientific meetings.

Placental formation and fetal nutrition in live-bearing squamates.

In viviparous lizards and snakes, embryos develop inside the pregnant female, and are sustained by means of placental organs. My main research interest is in understanding the structure, function, and evolution of these placentas. Our current work is focusing on how anatomical characteristics of the placental membranes of viviparous snakes and lizards enhance provision of oxygen, water, and nutrients to the fetus during gestation. This work involves examination of the cytology and development of the uterus and placental membranes, using light and electron microscopy.

Developmental anatomy of extraembryonic membranes of oviparous reptiles

During development, vertebrate eggs are sustained by cellular structures that provide for the respiratory and nutritional needs of the developing embryos. These structures contribute to the placentas of viviparous species. In reptiles and birds, very little is known about the structural composition of these membranes, and how they develop and function. Our current investigations of reproduction in corn snakes (*Pituophis guttatus*) use light and electron microscopy to study the development and cytology of these membranes, as well as the snake embryos themselves. Future work will focus on eggshell anatomy (as seen through electron microscopy) and mechanisms of calcium and water uptake.

Prof. Harry Blaise

Engineering - Neuroscience

Prof. Blaise's research goals are to develop models and tools to advance the study of the biomedical sciences. He currently conducts research at the intersection of biomedical engineering and neuroscience. He has studied the neurophysiology of learning and memory consolidation using his freely behaving mouse and rat model of long-term potentiation (LTP)

and depression (LTD)—two candidate mechanisms accounting for much of the information processing performed by the brain. Dr. Blaise has also investigated the impact of prenatal protein malnutrition and neonatal stress on brain circuits involved in learning. More recently, Dr. Blaise has been conducting research whose ultimate aims are to help better understand the linkages between emotionality and memory. For instance, does one's emotional state alter the ways in which concurrent events and experiences are remembered? Further, stress is known to be mostly harmful to the brain (e.g., as in post-traumatic stress disorders); but are there situations in which stress might be beneficial to brain function? Prof. Blaise's research aims are to answer some of these difficult questions.

Prof. Joseph Bronzino

Engineering - Neuroscience

These students will be given the opportunity to become familiar with electrophysiological techniques, e.g., building electrodes, using recording and stimulating instruments and performing computer analysis of bioelectric events. Upon completion of these skill oriented activities, they will be able to participate in studies investigating the effect of dietary insults on brain plasticity, such as kindling and long-term potentiation.

Prof. William H. Church

Chemistry - Neuroscience

1. Identification of Neurochemical Causes of Nigrostriatal Cell Death

Oxidative stress, with the subsequent generation of oxygen free-radicals, is thought to play a role in the neurodegenerative processes observed in Parkinson's disease. The neuronal sources of these radicals and the endogenous anti-oxidant mechanisms present in brain to control oxidative stress have recently been the focus of intensive investigations. While it has been established that an environment conducive to oxidative stress (deficiencies in anti-oxidant mechanisms and increased levels of iron) exists in the substantia nigra of parkinsonian patients, a fundamental understanding of the chemical reactions responsible for the cell death associated with Parkinson's disease is lacking. The research conducted in my laboratory is designed to provide insight into these reactions. Currently experiments focus on identifying factors associated with susceptibility to various neurotoxins (Church and Rappolt, *Exp. Brain Res.*, 127 (1999) 147-150). Ongoing projects regarding this research area include the manipulation of uric acid levels in a cell culture model, the effect of anti-oxidant deficiencies on neurotoxin-induced apoptosis (in cell culture), and the role of NMDA receptor expression on dopamine cell death (using cell cultures). Techniques utilized in this research include HPLC, spectroscopy, immunochemistry, cell culture, uptake of radioactive isotopes, and histology.

2. Development of Analytical Methods to Monitor Changes in Anti-oxidant Levels

Associated with the projects described above, projects involving utilizing analytical methodology to quantitate changes in the neurochemical milieu and intracellular content of cells exposed to various neurotoxins are ongoing. Techniques utilized in this research include HPLC, spectroscopy, electrochemistry, and solid-phase extraction.

Prof. Kent Dunlap - *Behavioral Physiology of Communication in Electric Fish*
Biology - Neuroscience

I examine sensory mechanisms, hormonal regulation and evolution of communication behavior in electric fish. South American weakly electric fish are nocturnally active and live in muddy waters of the Amazon River basin. They use their electric discharges both for locating objects in the environment and for communicating with each other. Males and females give off distinct electric signals during courtship and aggression, and these sex differences are generated through the actions of steroid hormones such as testosterone and estrogen.

My present research has three components. First, I try to decode their “electric language” used in social interaction by observing fish in different behavioral contexts. I modify specific sensory stimuli and examine how the fish’s electrical signals change. Second, I examine how social interaction influences the production of new brain cells during adulthood. I house fish in pairs and in isolation and determine how this alters cell birth and neuronal differentiation. We also have begun labeling brain sections with markers of neuronal activity to see if these newborn cells become active during the production of electrocommunication signals. Finally, I compare hormonal regulation of the electrocommunication system in various species to address how the endocrine system evolves to generate a diversity of sex-specific electrocommunication behaviors.

Prof. Hebe Guardiola-Diaz - *Biochemistry and Molecular Biology of Nuclear Receptors in the Nervous System*
Biology - Neuroscience

Neuronal development, plasticity and communication depend upon changes in gene expression that often require participation of nuclear receptors. The ligand-activated nuclear receptors PPARs, are present in developing and in adult nervous tissue. There are three PPAR subtypes. PPAR α is best known for its role in liver, where it controls lipid metabolism. PPAR γ has been firmly linked to fat cell development. PPAR δ is most abundant in the nervous system where its function is not well understood. All PPARs are present in the cell nucleus and are normally inactive until specific chemicals (ligands) bind to them and activate them. When active, PPARs bind specific DNA sequences in the regulatory regions of target genes. Therefore, PPARs control gene expression in response to chemical messengers and as a consequence help determine the molecular composition of a cell and the kinds of activities that a cell is capable of participating in. The overarching objective of my research is to investigate the role of PPARs in the nervous system using a model system of cultured neuronal cells. To meet this objective, it is important to discover genes targeted by PPAR. Cytochrome P450 (CYP) monooxygenase gene expression is regulated by PPAR in the liver. The recently discovered *cyp4X1* gene encodes a CYP that appears to be the most abundant CYP in the brain and a likely target for PPAR. In non-neuronal cultured cells, it has been reported that expression of *cyp4X1* mRNA requires PPAR. It is therefore reasonable to hypothesize that *cyp4X1* is one of several PPAR target genes in the brain that are required for proper response to PPAR activation. Utilizing neuronal cells isolated from neonatal rat brain, we aim to determine whether PPAR and CYP4X1 are expressed in the

same neuronal cells, and whether activation of PPAR alters *cyp4X1* gene expression. In addition, this cell culture system permits the investigation of a possible facilitatory role of PPAR/CYP4X1 in the metabolic interplay between neurons and glia, both in healthy cultures and in model cultures for neurodegeneration.

Prof. Dan Lloyd

Philosophy - Neuroscience

I examine aspects of the neural basis of human consciousness. This principally involves the reinterpretation of functional MRI brain scanning data, data that are archived in various research centers and freely available. One main theme of this work is the pervasive human experience of time, which underlies all consciousness. Since temporality always accompanies awareness, it cannot easily be factored out as an experimental variable. Nonetheless the “flow” of time may be a parameter that varies in different tasks and contexts. Looking for evidence of this variable flow is ongoing. All of the analysis is carried on using the powerful computing environment, Matlab. Often students coordinate research under my direction with research opportunities at the Olin Neuropsychiatric Research Center at the Institute of Living. The course “Minds and Brains” (Phil 374 and its lab, Phil 371), provides a philosophical context for understanding functional brain imaging.

Prof. William M. Mace

Psychology - Neuroscience

I. Studies in Vision Science. Students interested in vision research can work in my lab with animated computer displays designed to find out (1) the conditions for seeing surfaces in depth, (2) the conditions for seeing shapes as rigid or not, or (3) the conditions for combining patterns seen by two eyes into a single pattern in depth. This is like studying computer graphics, TV and movie cartoons, and neuroscience.

II. Studies in Movement Science. Students interested in understanding the control of human movement can study (1) the coordination of rhythmic patterns, in rowing and in music, and (2) the perception of tools in sports. For example, what can an athlete feel about a lacrosse stick, hockey stick, ping pong paddle, baseball bat, squash racquet, or tennis racquet without looking? Tools used in sports extend the capacity of the body in ways that are poorly understood and leave room for fascinating research. You hold a tool with your hands, and feel only patterns of pressure on the hands, arms, and body, but you feel a unitary stick or racquet that has length beyond your hand.

Prof. Susan Masino

Psychology - Neuroscience

A major focus of my research is the neuromodulator adenosine. Adenosine is the core molecule of the cell energy molecule ATP, and it also participates in controlling brain activity. Adenosine

is widely regarded as a neuroprotective molecule under pathological conditions such as stroke, but the ongoing role and regulation of adenosine is less well understood. By combining techniques such as imaging, electrophysiology, and behavior, we are revealing more of the underlying cellular mechanisms which regulate adenosine and recording their effects on brain activity. With its dual role in cell energy and brain activity, we are particularly interested in the relationship between metabolism and brain activity. Current projects are focused on new ways to regulate the inhibitory potential of adenosine and develop novel strategies to help conditions such as epilepsy.

Another aspect of my research is sensory processing in the rodent somatosensory cortex. Termed “barrel cortex,” the cortical area representing the large whiskers on the rodent snout is an unparalleled model system to study sensory processing, plasticity, and learning and memory. The whisker system is highly developed in rodents, and its development, anatomy and functional organization are well characterized. Specifically, the interaction between adenosine, sensory discrimination, and learning and memory is largely unexplored. This is extremely surprising in that caffeine is an adenosine receptor antagonist, and 80% of the population worldwide ingest this psychoactive substance on a regular basis.

My students and I are developing a novel sensory discrimination task that demands a behavioral choice and is known to involve the barrel cortex. During initial training, rats whisk surfaces of different textures in a maze environment and learn to turn in the direction of the rougher texture. As the rats learn the task, the discrimination becomes more difficult by making the textures more similar. Training rats in this task allows us to explore the limits of discrimination within the whisker system, and ultimately can be used to determine the effects of genetic and pharmacological manipulations (knockout models or drugs) on sensory discrimination. Currently, most knockout animals are characterized behaviorally on a simple battery of tasks which neither engage cortical processing nor sophisticated sensory discrimination.

Prof. Sarah Raskin

Psychology - Neuroscience

My research primarily involves examining behavioral methods to facilitate changes in human brain structure following damage to the brain. It has been demonstrated in animal studies that enriched environments lead to greater brain complexity. It has also been well documented that repeating particular tasks (such as simple motor movements) causes increases in the number of brain cells involved in coordinating that task. Finally, we know that without certain experiences (like having cataracts so that you cannot see) there is a lack of development of the usual brain systems involved in that function.

Given these findings in rats, cats, and monkeys, it is worthwhile to ask whether the right experiences might similarly effect increased brain specialization in humans. Early studies using positron emission tomography suggest that indeed, repetitive practice does cause a greater area of the brain to be used for the function that is being practiced. Our research is an attempt to determine which types of practice are most effective and whether they can be effectively used to help people who have had brain damage.

People with brain injury experience several types of cognitive deficits. Often they have trouble paying attention. One particular function that is often lost is memory. This is a complex function that involves large systems in the brain. As such, virtually no treatments for memory loss have been effective. More specifically, the type of memory that people with brain damage find most troubling is prospective memory. This is the ability to remember to do things in the future (for example, remember to buy milk at the store on your way home). We are currently working on creating measures that more effectively test prospective memory.

We have developed a set of exercises that seem to be effective at improving attention skills and a set of exercises that improve prospective memory in people with brain damage. We continue to work at refining these tasks. In addition, we are very interested in how success in this area of research is defined. It is not enough that the person get better in the lab. So we also look at whether they seem better in their daily lives.

Moreover, we are interested in whether these effects truly represent change in brain organization. To measure change in brain organization we use electrophysiological methods. We measure the electrical activity in the brain both before and after treatment. The specific activity we measure most often involves event-related potentials. These are characteristic waveforms that occur after a particular event takes place. For example, 100 ms after you hear a tone you generate an electrical potential that reflects the working of the auditory system. We look at later potentials thought to reflect the working of attention and memory. Specifically we measure the novel P300 (a positive waveform that occurs at 300 ms) and the contingent negative variation. Both are generated in the frontal lobes of the brain.

Prof. Chris Swart

Biology - Neuroscience

As laboratory coordinator my main area of interest currently is developing lab modules for use in several neuroscience courses here at Trinity. My goal is to provide students with artificial and animal models, computer software, and cognitive exercises that demonstrate the concepts discussed in neuroscience lecture courses. These laboratory exercises span the range from anatomy to behavior, electrophysiology, chemistry, psychology, and cognitive science. I am very interested in allowing students to experiment with novel animals, models, or apparatus that will foster the skills necessary to promote the pursuit of original thesis research or post-graduate study.

In addition to my main focus on developing new neuroscience labs I am currently involved in two research projects. I have started a series of experiments aimed at describing the structure and function of the Cerebral Ganglion of the freshwater snail, *Cipangopaludina chinensis* using a variety of techniques including histological techniques, electron microscopy, and electrophysiology. My second area of research interest is in insect morphology and sensory nerve signaling. I am currently working with Dr. Smedley of the Biology Department to describe the variation in the morphological structures that caterpillars use to produce defensive chemicals.