S.F.N. Tucson Chapter

2010

http://emotion.nsma.arizona.edu/SfnLocal/

THE UNIVERSITY OF ARIZONA

What do we do here to know more about the brain?

University of Arizona Laboratories:

Barnes
Scheres
Gronenberg
Fuglevand
Fellous
Kaszniak
Bedford
Zarnescu
Ritter
Ryan
Edgin
Gerken
Rance

Farley/Koshland
Alexander
Hruby
Gothard
Sanfey
Lukas
Ryan/Bever
Higgins
Stamer
Dussor
Brooks
Fregossi
Barkmeier-Kraemer

Levine
Zinsmaier
Sloviter
Tolbert/Oland
Polt
Wilson
Strausfeld
Allen
Hildebrand
Witter
Narayanan
Falk/Sherman
Ghosh
Eggers

Carol A. Barnes, Ph.D.
Regents' Professor, Psychology and Neurology
Director, Evelyn F. McKnight Brain Institute
Director, ARL Division of Neural Systems, Memory and Aging

The central goal of the research program:

- to understand how the brain changes during the aging process and the functional consequences of these changes on information processing and memory in the elderly

The methods used to study these questions:

- behavioral, ensemble electrophysiological and molecular imaging approaches in awake, behaving young and old rodents and non-human primates

Such research provides a basis for understanding the basic mechanisms of normal aging in the brain and sets a background against which it is possible to assess the effects of pathological changes such as Alzheimer's disease.

Evelyn F. McKnight Brain Institute

NIMA

Evelyn F. McKnight Brain Institute
ARL Division of Neural Systems, Memory and Aging

Examples of experimental findings from the Barnes laboratory:

- Rats, monkeys and humans all show spatial memory deficits that are hippocampal-dependent
- Hippocampal plasticity mechanisms are altered in aged rats and these reductions in plasticity are correlated with cognitive performance
- Ensemble recording studies in rats have revealed hippocampal map retrieval errors and reduced perihinal cortical object fields (e.g., Burke dissertation, 2009) in old animals
- Behaviorally induced immediate early gene activity in hippocampal cells is attenuated (e.g., Penner dissertation, 2008) and this reduced transcriptional response is due to altered DNA methylation

Evelyn F. McKnight Brain Institute

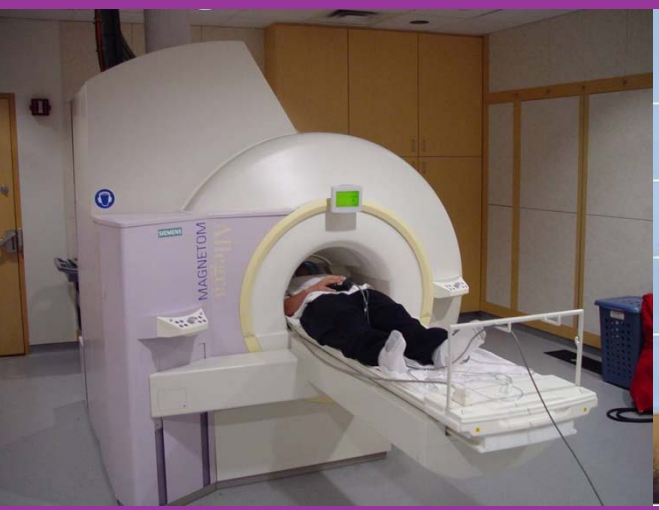
NIA

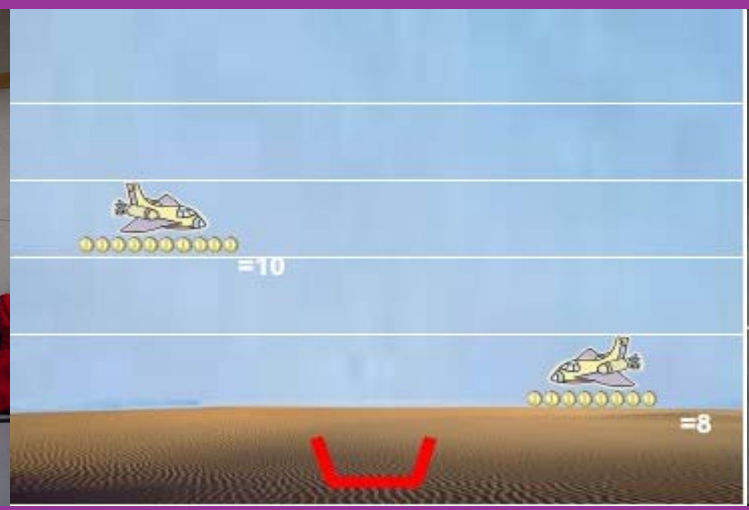
Developmental Cognitive Neuroscience Lab

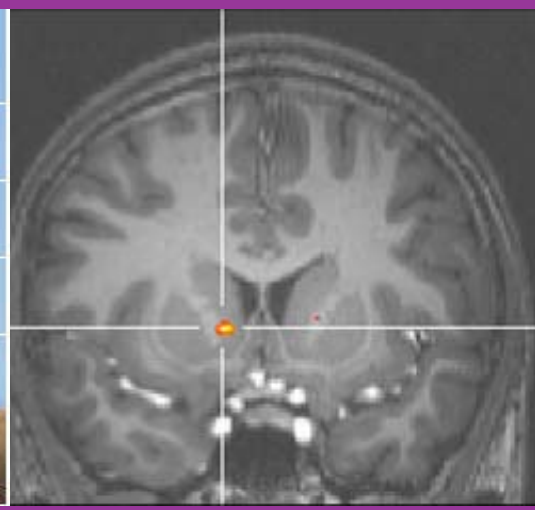
- The main goal of this lab is to learn more about the neural, cognitive, and motivational basis of developmental behavioral disorders such as Attention Deficit Hyperactivity Disorder (ADHD)
- We use game-like computer tasks and brain imaging

Developmental Cognitive Neuroscience Lab

- We found that adolescents with ADHD have less brain activation in the striatum when they expect to win money than adolescents with no ADHD







Developmental Cognitive Neuroscience Lab

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Brain and Behavior in Social Insects: from interneurons to learning and memory

Wulfila Gronenberg

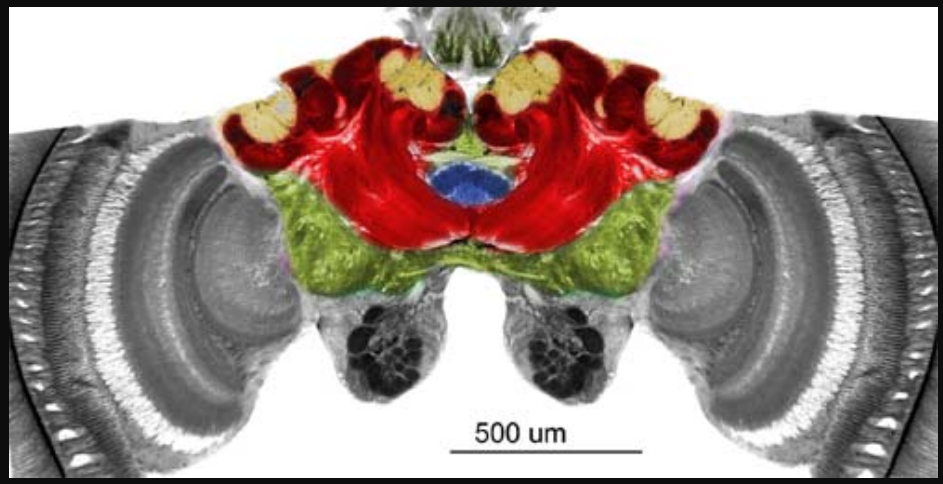
Arizona Research Laboratories

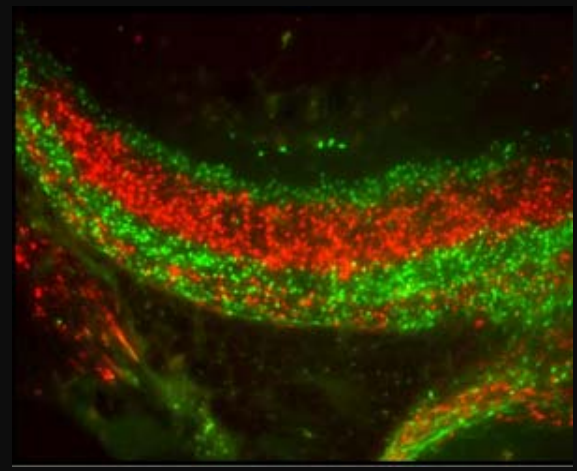
Division of Neurobiology

Bees, ants and wasps can learn colors, landmarks, patterns, odors and other stimuli.

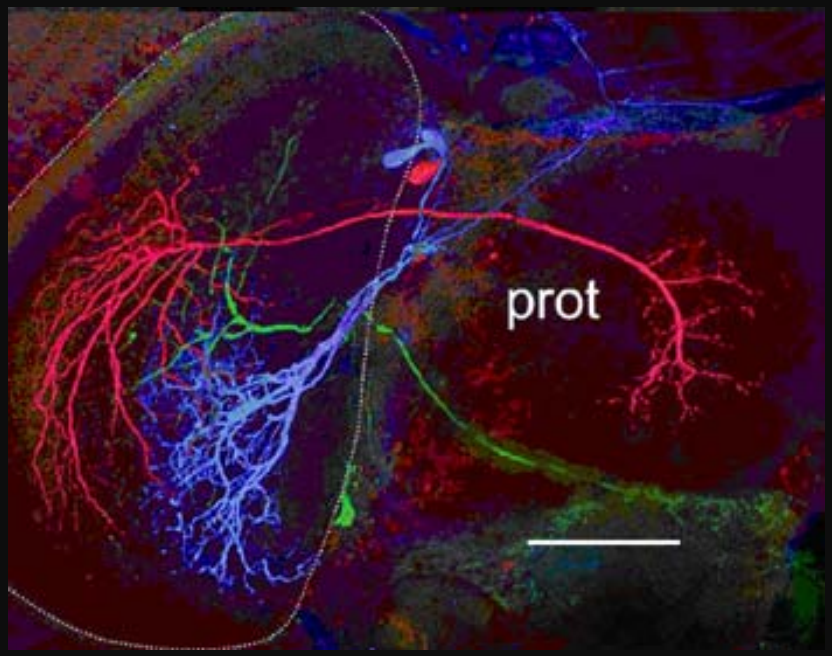
Andre Riveros, PhD 2009

Their brains comprise elaborate sensory processing centers and conspicuous central structures involved in learning and memory.

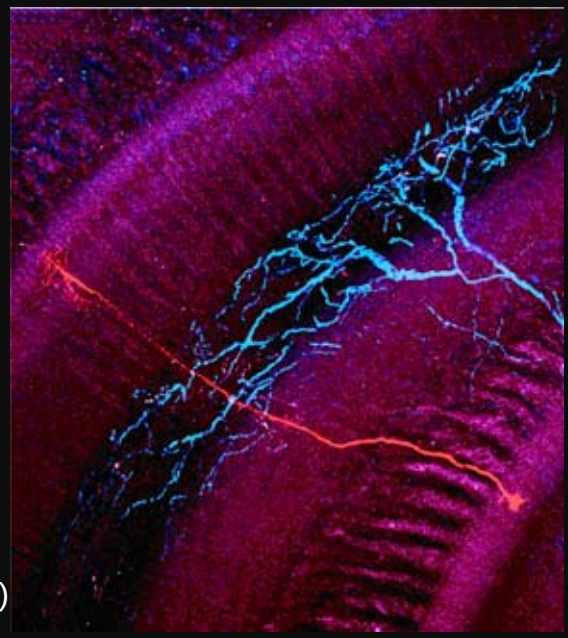


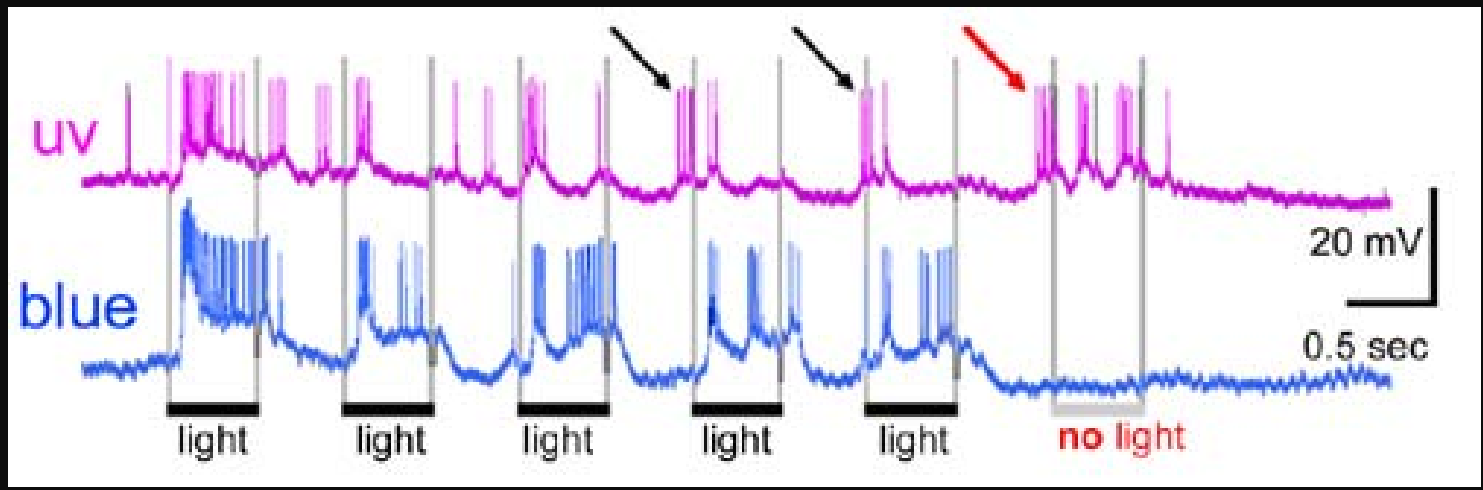


Visual interneurons show complex responses to color and motion and can rapidly entrain to repetitive stimuli



Angelique Paulk (PhD 2008)





Fuglevand Lab

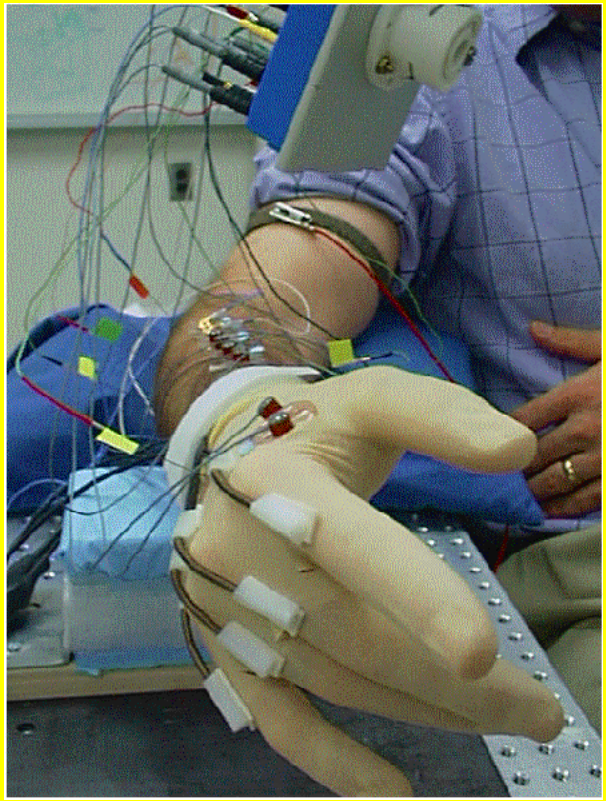
- We use experimental and modeling approaches in an attempt to understand how the nervous system controls movement. Our investigations evaluate interactions among various elements of the motor system, including skeletal muscle, somatosensory afferents, spinal cord, and brain.

Andrew Fuglevand, Ph.D.
Sensorimotor Neurophysiology Lab

Systems Neurophysiology

Cellular Neurophysiology

Applied Neurophysiology



Graduate Students:
Ann Revill
Hilary Wakefield
Lise Johnson
Marco Herrera

UA Collaborators:
Ralph Fregosi
Rick Levine
Fiona Bailey
Katalin Gothard

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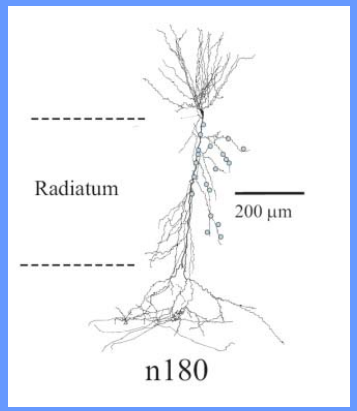
Computational and Experimental Neuroscience Laboratory

Our research interests include:

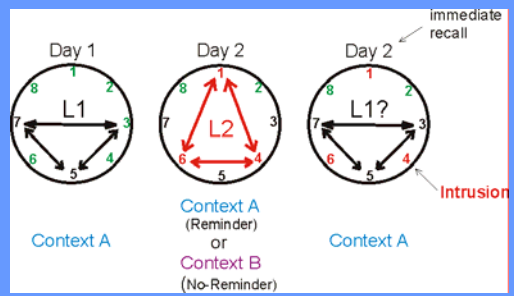
- The neurophysiology of positively motivated **memory reconsolidation** in rodents.
- The neural bases of **Post-Traumatic Stress Disorder.**
- The role of the Ventral Tegmental Area **in memory extinction.**
- **Traveling Sales-rat:** understanding optimal spatial navigation.
- **Computational models** of large neural networks and new measures of neural activity.

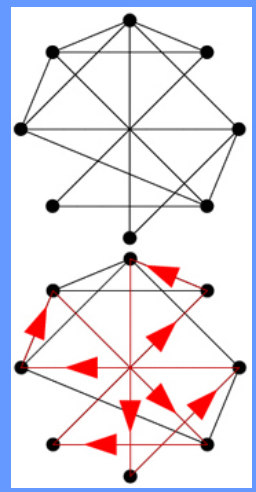
Computational and Experimental Neuroscience Laboratory



Using a computer, we simulate detailed biophysical neuronal models to study the potential for neurons to be reliable and precise signaling devices.

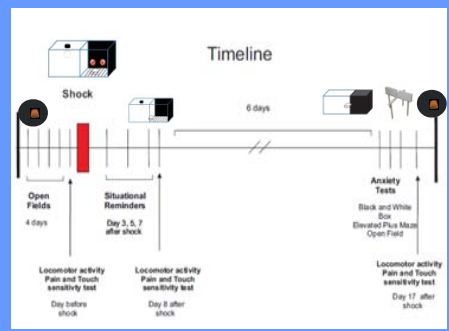
We study how spatial memories are reconsolidated and maintained by the hippocampus and how a rat can teach a task to another rat.





We study how rats optimize spatial navigation and investigate the neural circuitry underlying this behavior.

We study how a traumatic event affects neurons in the ventral tegmental area, specifically dopamine neurons.



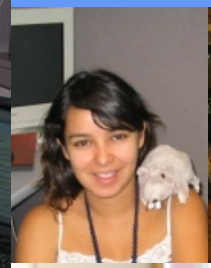
Techniques used: computational models, hyperdrive chronic recordings, pharmacology, in vitro patch clamp recordings.

Computational and Experimental Neuroscience Laboratory


Jean-Marc (PI)


Minryung


David


Nadia


Bethany


Laurel


Brian


Kim


Stevie


Elizabeth

UA Collaborators: L. Nadel, E. French, C. Barnes, Tony Lewis, Ian Fasel
Other Collaborators: B. McNaughton, G. Martin, J.L. Valdes, T. Sejnowski

More information!….. http://emotion.nsma.arizona.edu/lab.html

Neuropsychology, Emotion, and Memory Laboratory

http://emotion.web.arizona.edu/
Director: Al Kaszniak, Ph.D.
Department of Psychology

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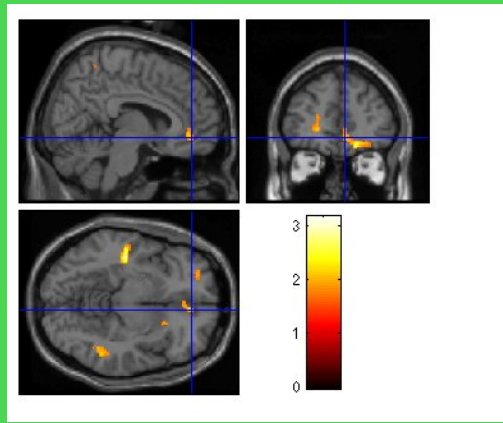
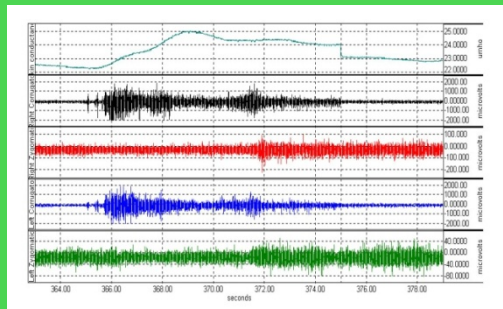
Neuropsychology, Emotion, and Memory Laboratory

- Neuropsychological and functional neuroimaging studies have shown medial frontal brain systems' role in memory self-monitoring
- Studies of memory and emotion in Alzheimer's Disease have contributed to clinical care advances
- Directs Education Core for NIH-funded Alzheimer's Research Center: Studies of Latino and American Indian outreach/ education effectiveness
- Studies of emotion psychophysiology in long-term Buddhist meditators point to meditation's role in emotion regulation





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Neuropsychology, Emotion, and Memory Laboratory

- **Lab Members:**

  Al W. Kaszniak, Ph.D. (Director);

  Marisa Menchola, Ph.D.; Christine Burns, B.A.; Rose Marie O'Donnell, B.A.;

  Dev Ashish, M.A.; Autumn Wiley, B.A.

Phone: (520)621-4003

menchola@u.arizona.edu

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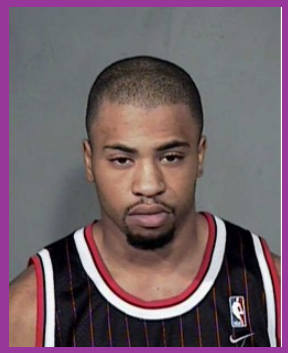
Welcome to the Perceptual Learning Lab

Your mission, should you choose to accept it, is to understand all the ways that experience affects perception

Dr. Bedford
bedford@u.arizona.edu

Learning to Perceive People from other Races

Can you pick him out of the line-up?






We find that studying the eyes leads to improvement, much like attention helps all kinds of *perceptual expertise* (like reading X-rays)

Other Projects in the Perceptual Learning Lab

- If your eyes and your hands disagree with each other, what does your brain do? (New and classic variations on the *prism-adaptation* effect)

- How do we understand the minds of people with challenges about space? (NEW!)

Hey you - do you always get lost? Want to participate in our experiments? Email us at: spacestudy@msn.com

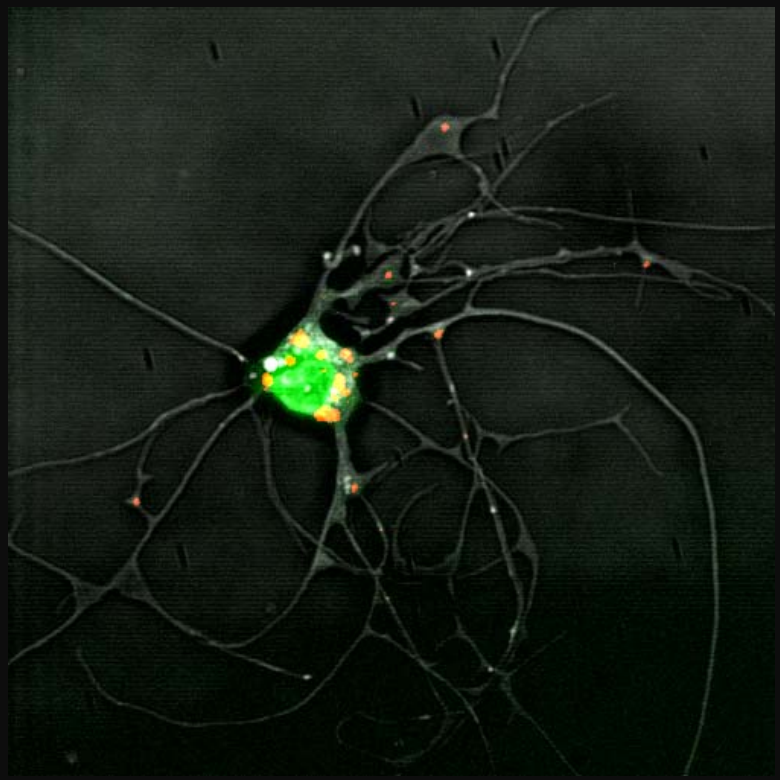
- Effects of visual imagery on healing sickness (NEW!)

- and many others

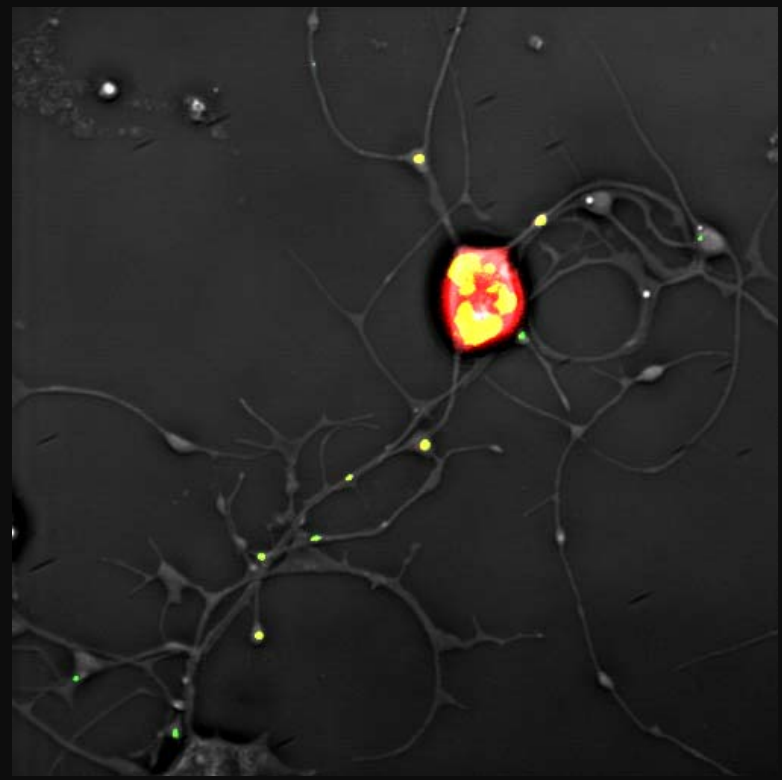
Zarnescu Lab

Molecular and Cellular Biology

http://www.mcdb.arizona.edu/facultyResearchDetail.cfm?netid=zarnescu



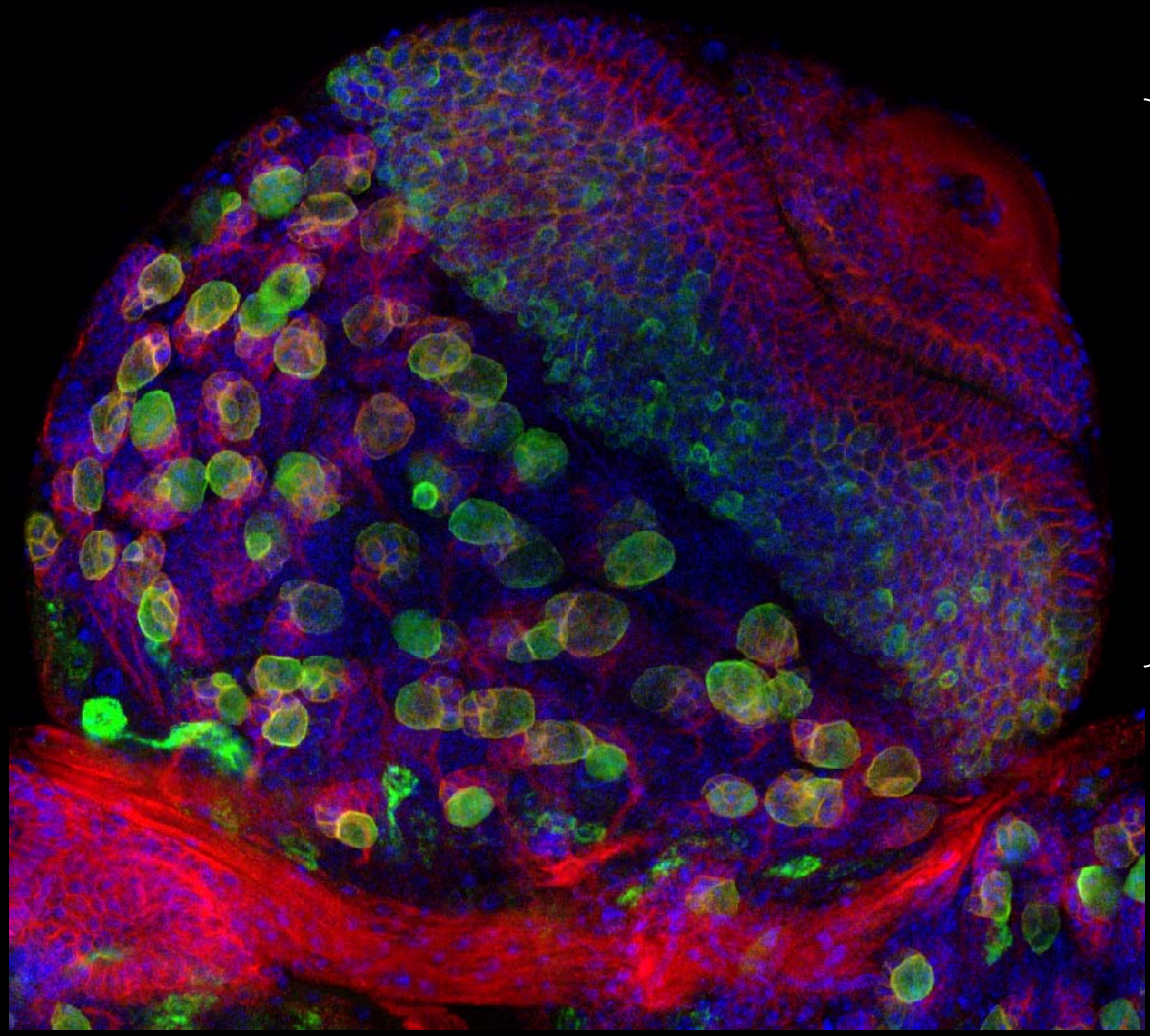
Live imaging studies of mRNA trafficking in *Drosophila* neurons aim to elucidate the role of RNA localization in neural development



RNA granules in *Drosophila* cultured neurons

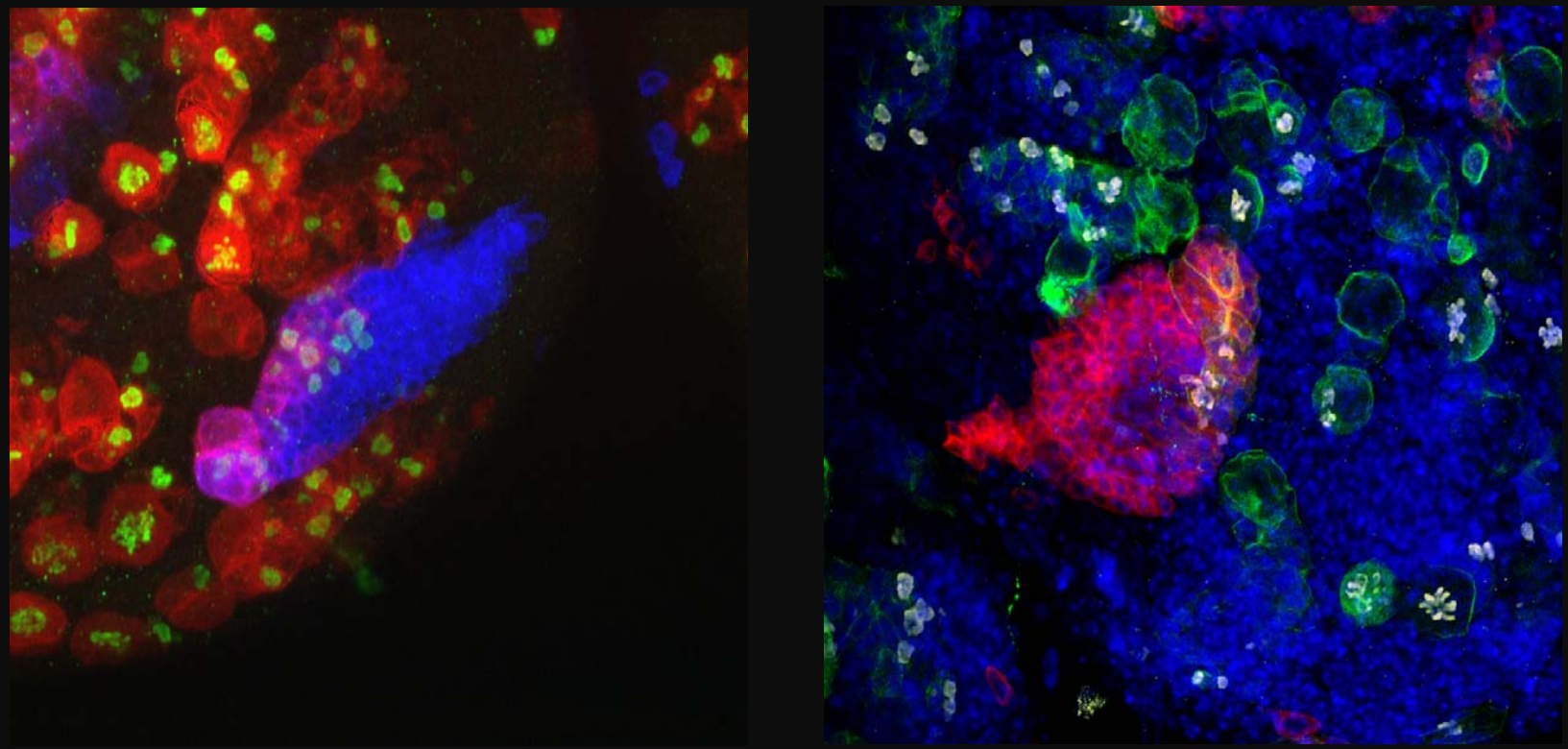
(Research Associate Patty Estes and undergraduate researcher Michele O'Shea)

Neural stem cells in *Drosophila* brains



Large round cells in central brain area (green) are neural stem cells. They generate various types of neurons in the adult brain (graduate student Matt Callan).

Drosophila is an excellent model for *in vivo* studies of neural stem cell development



Blue cells (left panel) and red cells (right panel) are generated by single neural stem cells lacking Fragile X Protein. The rest of the brain cells are wild-type. These studies aim to uncover the disease mechanisms for Fragile X Syndrome and the role of translational control in stem cells (PhD candidate Matt Callan).

Zarnescu Lab current projects:

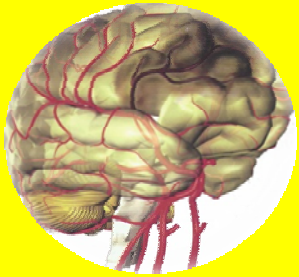
(*) Elucidating the role of RNA localization in neuronal and synaptic development and plasticity using *in vitro* and *in vivo* neuronal models

(*) The role of Fragile X protein and associated mRNAs in neural stem cells

(*) Lethal giant larvae: a tumor suppressor required in neuronal development

Approaches:

We are taking a combined molecular, genetic and live imaging approach in various *Drosophila* neuronal models

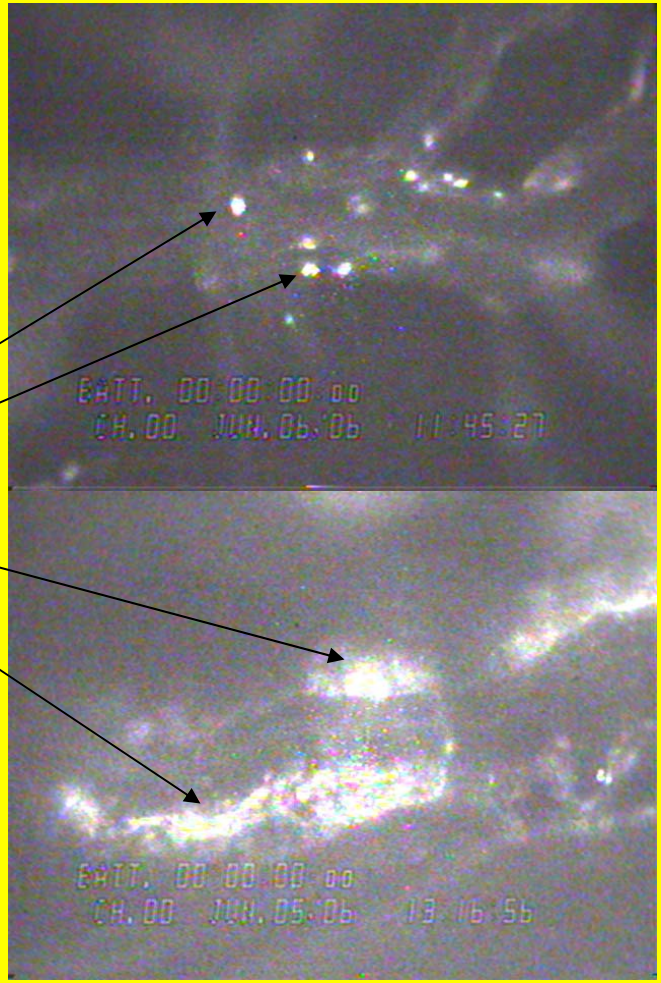


Stroke and Diabetes

Stroke (brain attack) happens when a blood vessel in the brain is blocked. We know that diabetes makes stroke worse. We also know that white blood cells are abnormal in diabetes, and they might be one reason for making stroke worse.

Our laboratory has techniques to find out how white blood cells become “sticky” and how they collect in diabetic brain vessels, making a stroke worse.

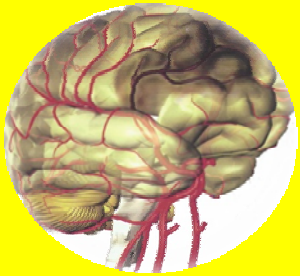
White blood cells in brain blood vessels



White blood cells stick to brain blood vessels after a stroke in *non-diabetics*. These cells release toxic substances that damage the brain, and make stroke worse.

Many more white blood cells stick to brain blood vessels after a stroke in *diabetics*, causing more brain damage, making stroke more severe.

Our goal is to find new ways to decrease white blood cell sticking to diabetic brain vessels, which may decrease brain damage after stroke.



Leslie Ritter, RN, PhD, Principal Investigator

lritter@nursing.arizona.edu

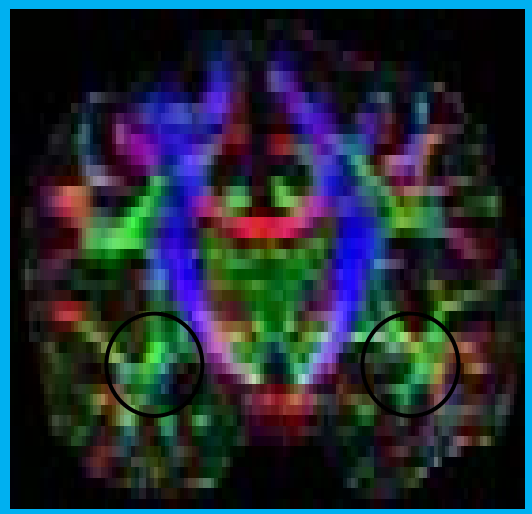
Lee Ryan, Ph.D. Psychology

Cognition & Neuroimaging Laboratory

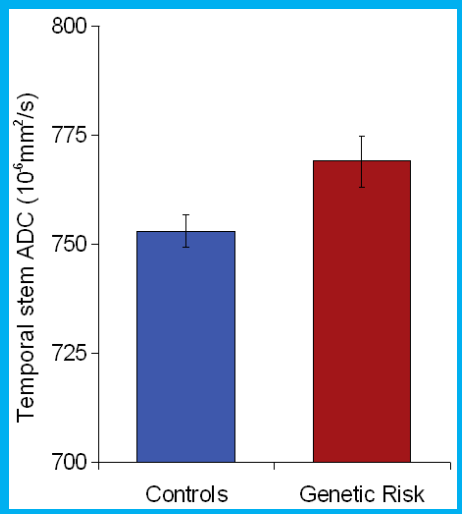
Diffusion Tensor Imaging (DTI) in healthy older adults at risk for Alzheimer's disease (AD)

- Can we detect early changes in the white matter of individuals at genetic risk for AD?

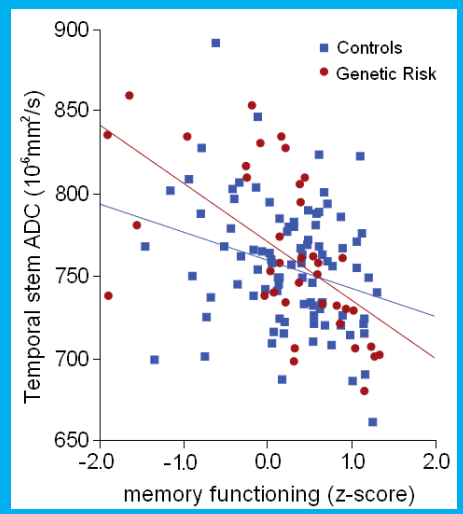
DTI image of the brain



Temporal stem white matter is affected early in AD



Temporal stem ADC is increased in healthy individuals at risk



Temporal stem ADC predicts memory functioning

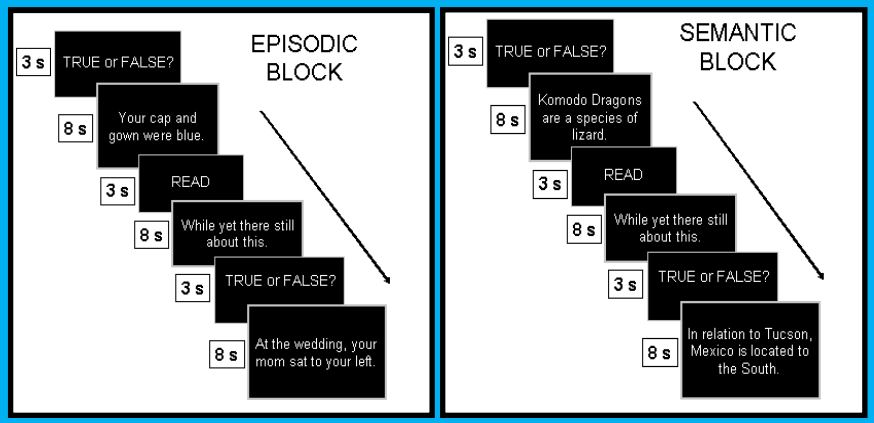
The neural basis of memory

Cognition & Neuroimaging Laboratory

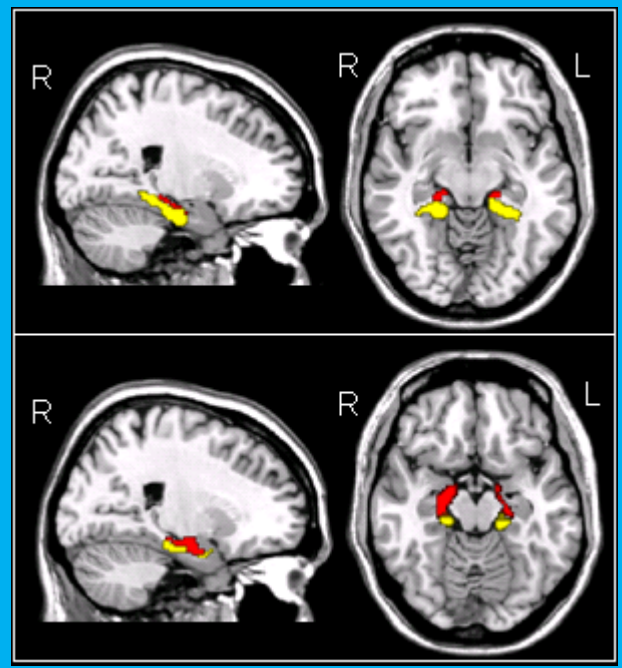
- What is the role of the hippocampus in retrieval of episodic (life events) and semantic (well-known facts) memory?
  - The hippocampus is critical for memory retrieval, particularly spatial information such as location and spatial relations.

Hippocampus: Retrieval of Spatial Information and General Memory.

True/False Recognition Task



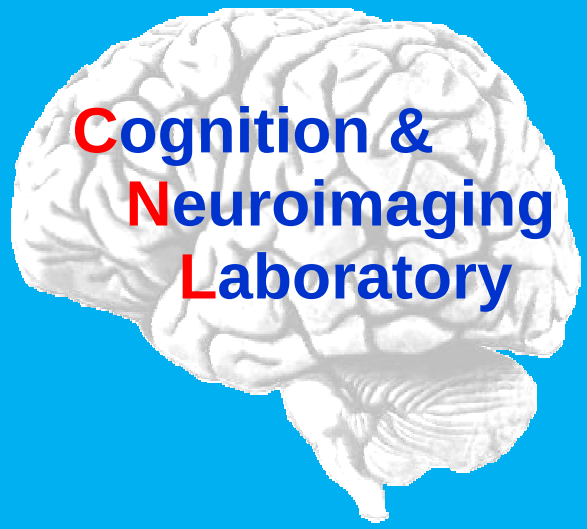
Varied retrieval of space->
spatial content vs. no spatial content



Space

Memory

Hippocampus



Contact:

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UA Department of Psychology
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Email: CNLab@email.arizona.edu

University of Arizona Down Syndrome Research Group

We have active studies aiming to understand cognition in Down syndrome across the entire lifespan (ages infancy-late adulthood).

In the course of this work we also see children without Down syndrome who are 4- 6 years old.

Down Syndrome Research Group
Regents Professor Lynn Nadel
Jamie Edgin, PhD
and several devoted students!

Department of Psychology
Phone: 520-626-0244
Email: jedgin@email.arizona.edu
http://dsrg.web.arizona.edu/

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Down Syndrome Research Group Goals

- Develop a battery of neuropsychological tests that are effective across a range of ages and contexts for individuals with Down syndrome
  - For clinical trials and genetic studies
  - For young and aging individuals
  - For individuals across all levels of function
- Determine sources of variation in cognitive outcome
  - genetic, environmental and medical (e.g., sleep) contributions to cognitive outcome across the lifespan
  - predictors of dementia (35% of individuals with Down syndrome will develop Alzheimer's disease)

Down Syndrome Research Group Findings

Neuropsychology gives us a “window into the brain” by using cognitive assessments closely linked to brain function

– Through this method we know individuals with DS
  - Are strong at immediate visual memory
  - Have difficulty shifting between rules (linked to the prefrontal cortex)
  - Have difficulties with associative memory formation (linked to the hippocampus)

– Despite overall group differences in these domains, a high degree of variability in these and other cognitive functions is evident. We want to understand the factors, both biological and environmental, influencing this variability.

Our laboratory addresses two scientific areas, **basic motor control and clinical rehabilitation**

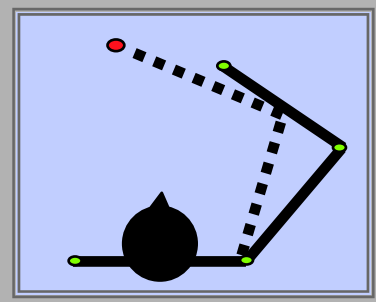
We are presently studying slow movements since many neurological patients move slowly. Control of speed is not as simple as pushing on the gas pedal of a car.

Walking on a carpet that measures foot pressure

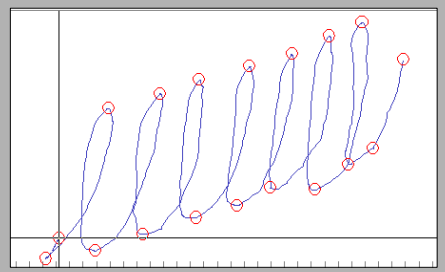
Dual Task -- playing keyboard and counting backwards

We have developed a **clinical research** tool that focuses on physiological and behavioral measures. This tool is useful to test treatment effects, not only of exercise, but also pharmacological, surgical and gene therapy techniques.

Reaching for objects on a table



Handwriting -- repetitive letters - "L"



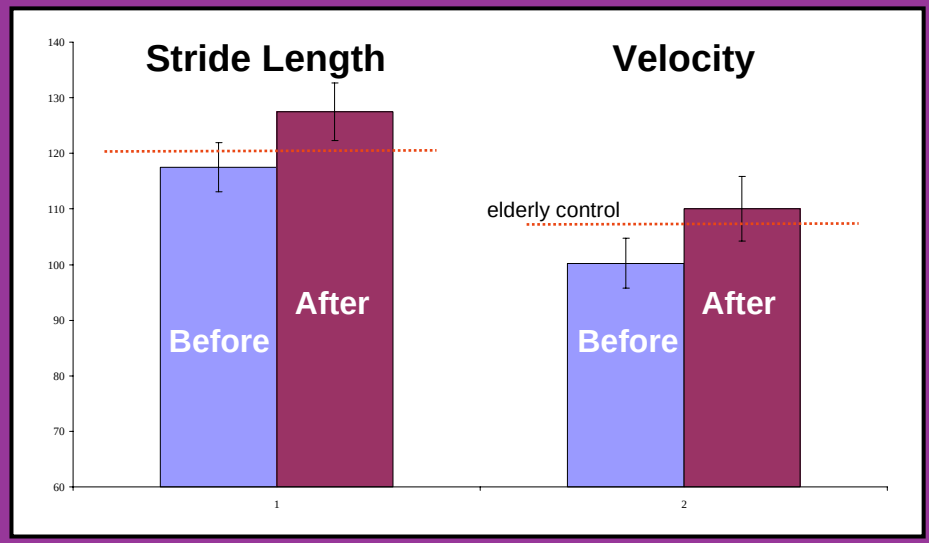
Judging how far to move without watching

Dr. Farley has developed specific exercises for patients with Parkinson's disease that use rules of movement (such as bigger movements are performed faster) to help them move better.

Before exercise treatment

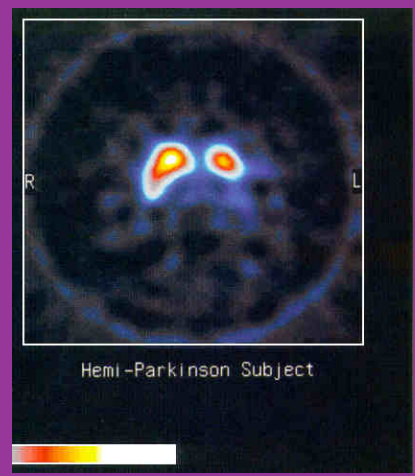
After exercise treatment

After exercise, arm movements become bigger with more hip rotation and better balance



After exercise, steps become bigger (longer stride length) and faster (larger velocity).

We hope to show that these improvements occur because exercise causes changes in activity of cells in the brain



The people in our lab:

Dr. Becky Farley
bfarley@email.arizona.edu

Dr. Gail Koshland
koshland@u.arizona.edu

Both Drs. Farley and Koshland are physical therapists and research scientists (PhD).

Dr. Farley is developing a community wellness program for Parkinson's patients that includes specific exercises as well as ways to approach tai chi, strength training, daily walks, etc.

Dr. Koshland is working on development of the new teaching approach for medical students and also teaches on subjects of muscles, bones, joints, and neural control of movement.

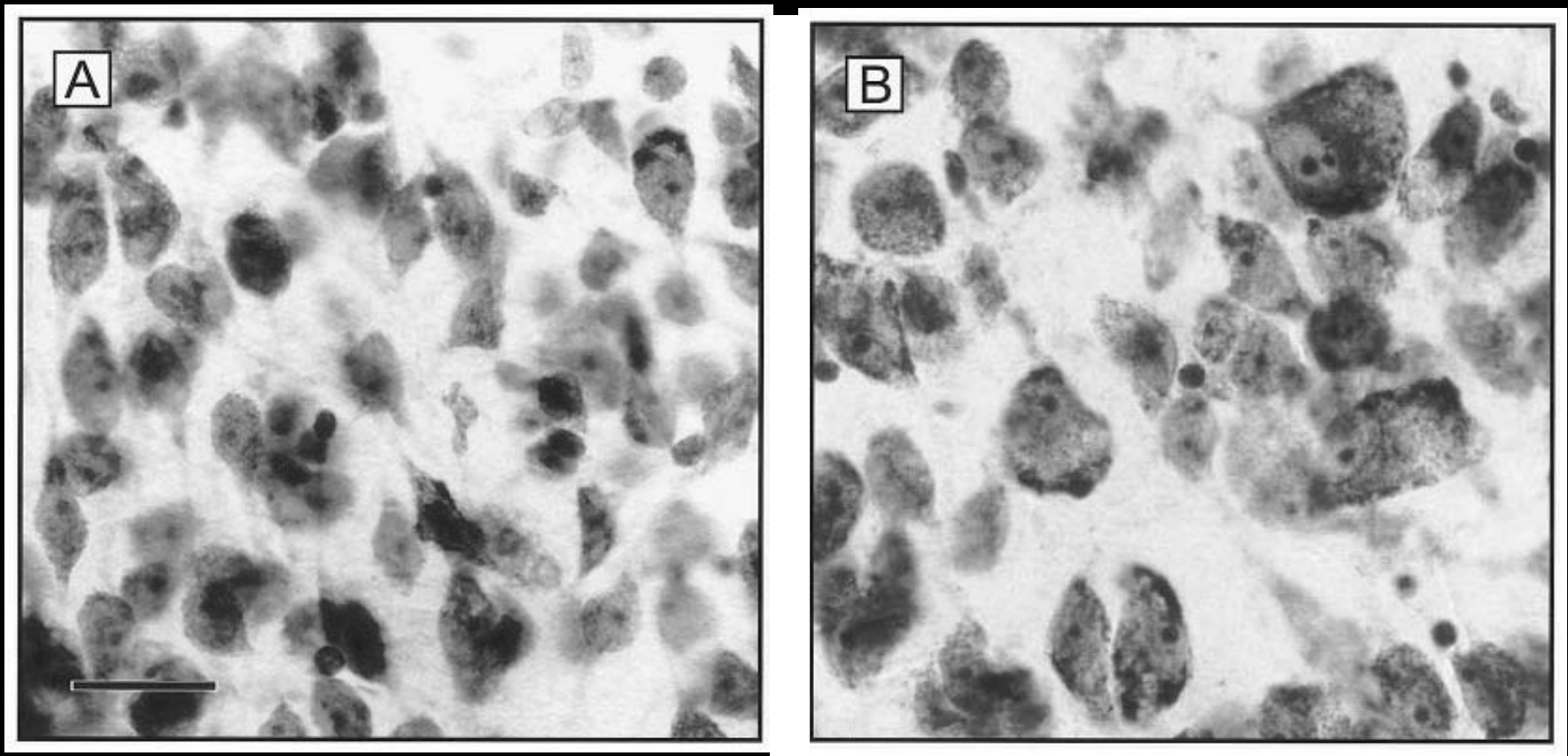
Reproductive Neuroendocrinology Laboratory

Naomi E. Rance, M.D., Ph.D.
nrance@email.arizona.edu

- Effects of estrogen on hypothalamic structure and function.
- Changes in the human hypothalamus associated with menopause.
- Determining the sites and mechanisms of steroid negative feedback on LH secretion.
- Studies on the etiology of menopausal hot flushes.

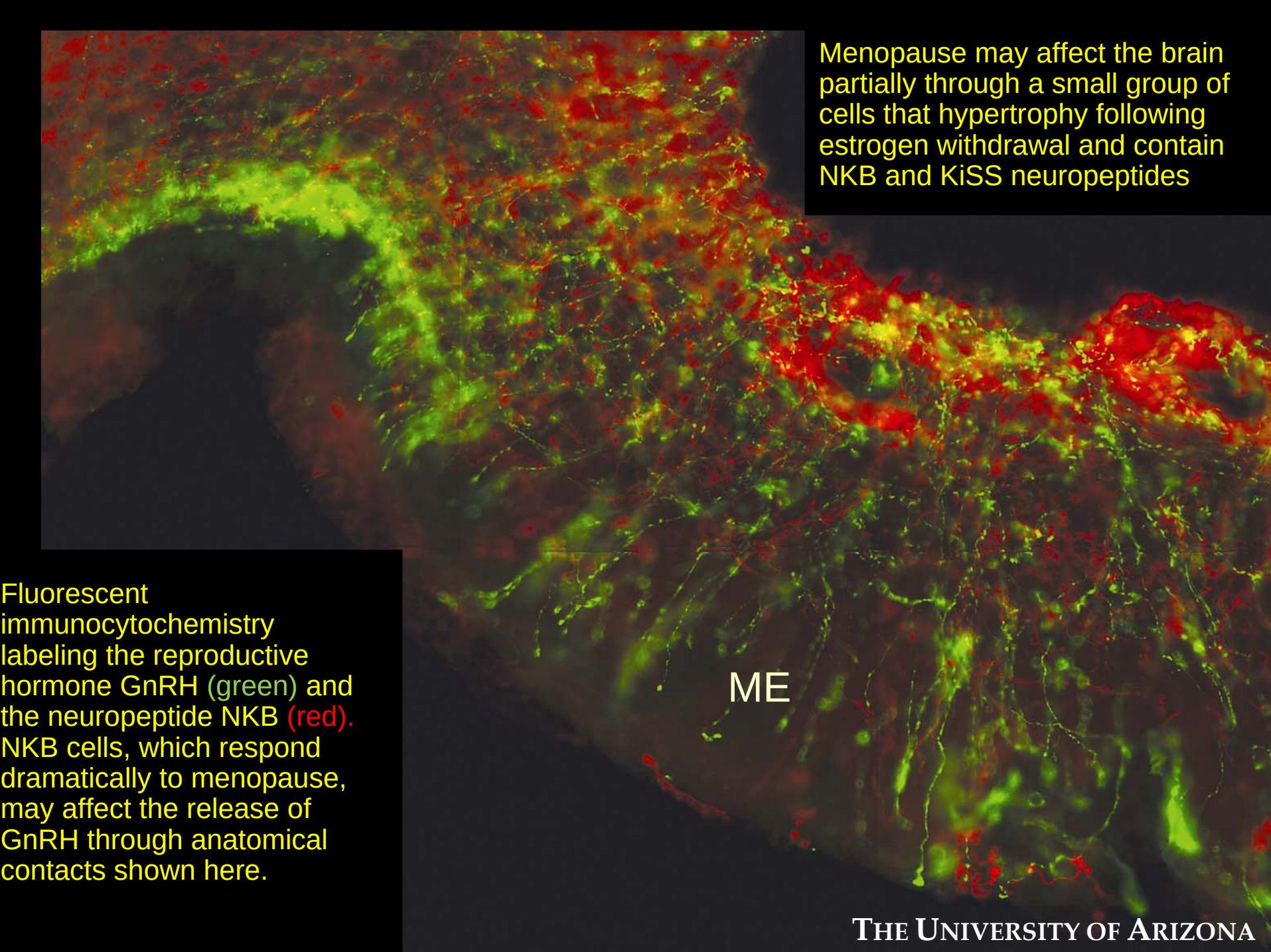
Menopause and the Brain

Following estrogen withdrawal, a small group of neurons in the hypothalamus become larger and express increased neuropeptides (signaling molecules). Shown below are hypothalamic brain slices of pre- and post- menopausal women.



Premenopausal

Postmenopausal


Menopause may affect the brain partially through a small group of cells that hypertrophy following estrogen withdrawal and contain NKB and KiSS neuropeptides
Fluorescent immunocytochemistry labeling the reproductive hormone GnRH (green) and the neuropeptide NKB (red). NKB cells, which respond dramatically to menopause, may affect the release of GnRH through anatomical contacts shown here.
ME
THE UNIVERSITY OF ARIZONA

Dr. Naomi Rance examines how menopause affects the brain's regulation of reproductive hormones and body temperature (hot flushes, anyone??).

Contact: Dr. Naomi Rance, 626-6099,
nrance@email.arizona.edu

THE UNIVERSITY OF ARIZONA

TWEETY LANGUAGE DEVELOPMENT LAB

THE UNIVERSITY OF ARIZONA®

Welcome to the Tweety Lab!

We study how 4- to 18-month-olds find patterns in auditory input, primarily language, and how 2- to 4-year-olds combine complex abilities to become master language users.

In our studies with 4- to -18-month-olds, we familiarize infants for about 2 minutes to a language-like or musical pattern that they have never heard before. We then test to see if they learned the pattern by exposing them on different test trials to new stimuli that are consistent with the familiarized pattern or very similar stimuli that are nevertheless inconsistent with the familiarized pattern. We measure how long infants attend (look toward the source of sound) on consistent vs. inconsistent test trials. A significant difference in listening time means that the infants learned during familiarization.

With 2- to 4-year-olds, we measure the speed and accuracy of children's own utterances or picture selections following target utterances. Differences in speed and/or accuracy reflect

Some recent findings:

Getting better by getting worse: 4-month-olds can detect patterns in musical stimuli that 7.5-month-olds can no longer detect. 7.5-month-olds can detect patterns that don't occur in human languages, but 9-month-olds can no longer detect the same patterns. We hypothesize that infants come to ignore patterns that they deem irrelevant for the domain that they are learning.

Knowing what's knowable: 17-month-olds listen longer to patterns that are learnable than to patterns that are unlearnable. Infants appear to possess a very powerful learning mechanism that allows them to sort problems into those that are worthy of their time and those that are not.

The power of variability: 4-year-olds listened to new words that were played either once or ten times. The words played ten times were either produced by the same person or by ten different people. When children were asked to say the words, they were better at producing the words that they had heard

TWEETY LANGUAGE DEVELOPMENT LAB

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Current Lab Members:

Kara Hawthorne,
Linguistics Ph.D.

LouAnn Gerken,
Ph.D., Director

Brianna McMillan, Lab Manager and soon to be grad student (but where?)

Brittany Linsey,
Post Doc

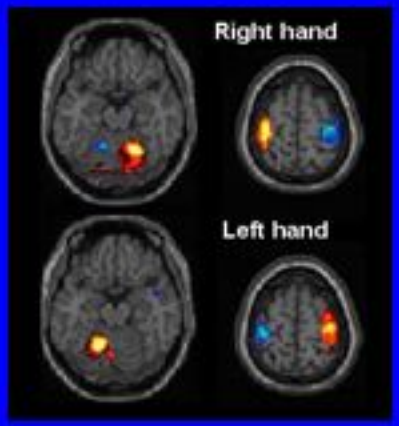
Jaime Parchment,
Linguistics Ph.D

Colin Dawson,
Psychology Ph.D

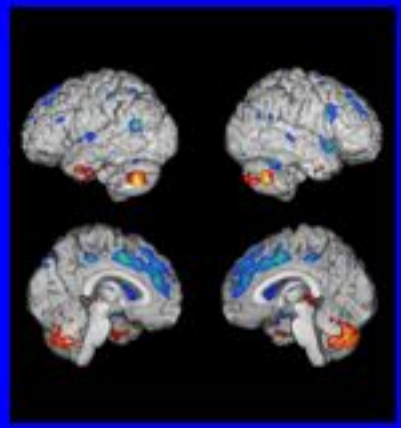
Brain Imaging, Behavior & Aging Laboratory

Dr. Gene Alexander, Director

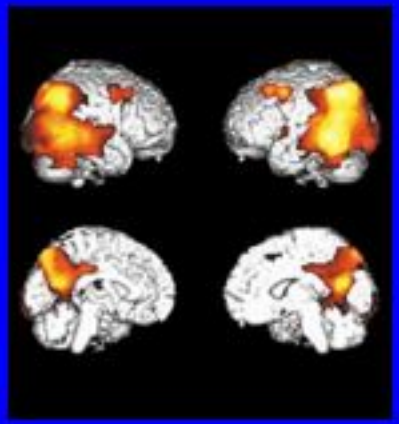
http://biba.arizona.edu



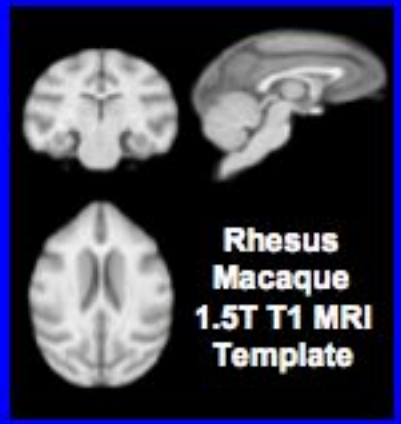
Brain Imaging, Behavior & Aging Lab: Research

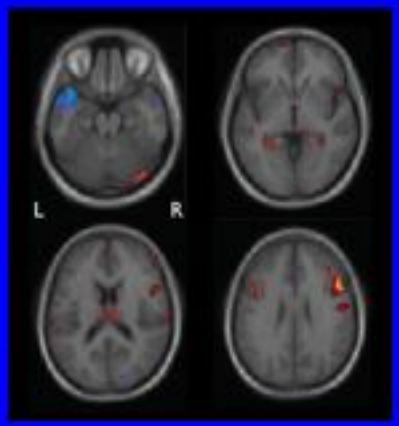


We study brain-behavior relationships in the context of aging and age-related neurodegenerative disease

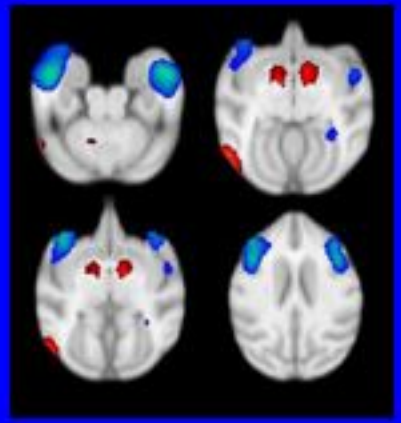


We use neuroimaging techniques, including structural and functional magnetic resonance imaging (MRI) and positron emission tomography (PET), in combination with measures of cognition and behavior





We are also involved in the application of neuroimaging research methods to non-human animal models of aging and age-related disease



Brain Imaging, Behavior & Aging Lab: People

Gene Alexander, Ph.D., Director
Cortney Coxon, M.P.A., Program Coordinator
Marisa Menchola, Ph.D.
Lan Lin, Ph.D.
Dev Ashish, M.A.
Krista Hanson, M.A.
Michelle Valfre, M.A.
Kaitlin Bergfield, B.S.
Iliana Vargas

Hruby Group Interests

- We study the chemistry of human behavior with special emphasis on peptide hormones and neurotransmitters, especially the design, synthesis, and biological and biophysical evaluation of novel ligands with novel biological activities for treatment of disease states (pigmentary, feeding behavior, prolonged and neuropathic pain, cancer, diabetes, etc.).

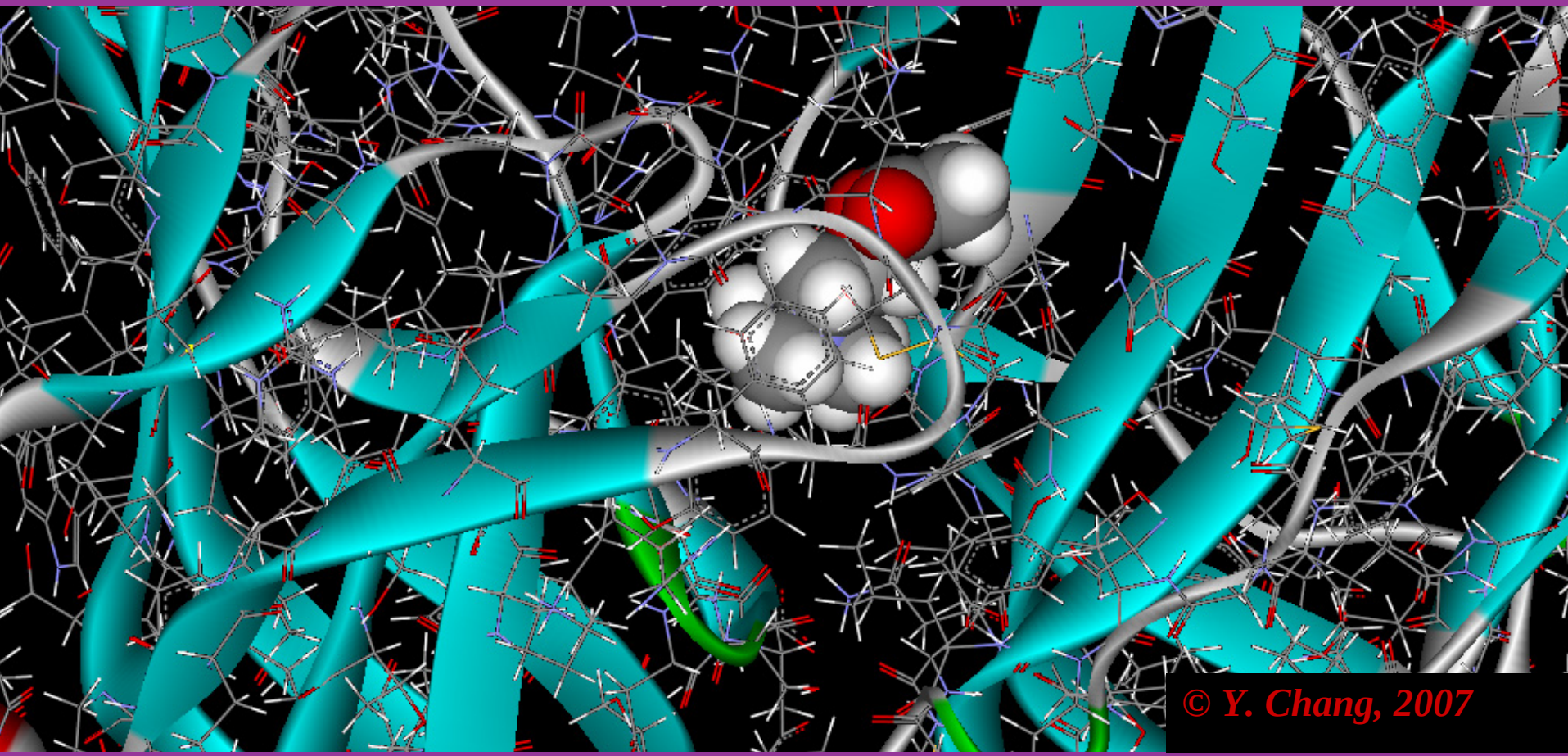
- Multidisciplinary research utilizing asymmetric synthesis; combinatorial chemistry; computer assisted drug design; conformational analysis utilizing NMR, x-ray, and other biophysical methods; molecular pharmacology; molecular biology; cell biology; confocal microscopy and other imaging methods.

Specific Novel Projects—Hruby Group

- **Novel Multivalent Ligands That Can Treat Prolonged and Neuropathic Pain Without Tolerance**
- **Detection and Treatment of Cancer by Addressing Differences on the Surface of Cancer Cells vs. Normal Cells**
- **Novel Ligands That Are Allosteric Effectors of Melanocortin Receptors Involved in Obesity, Anorexia, Pain, Sexual Behavior and Immune Response**

HRUBY LABORATORY – hruby@u.arizona.edu

NICOTINE AND NICOTINIC ACETYLCHOLINE RECEPTORS - TRANSLATION AND DRUG DISCOVERY



Ronald J. Lukas, Division of Neurobiology
Barrow Neurological Institute, Phoenix, Arizona

Lab Members

Dr. Paul Whiteaker, co-PI
Dr. Alain Simard
Dr. Bhagirathi Dash
Brek Eaton
Linda Lucero
Syndia Marxer-Miller
Minoti Bhakta
Terri Murray (ASU Ph.D. candidate)

rlukas@chw.edu
602-406-3399

Projects/Techniques

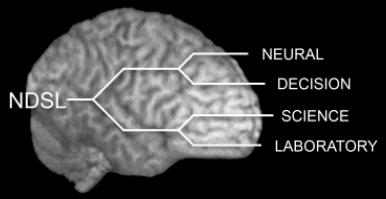
Neuroscience
Molecular and cell biology
Pharmacology
Immunology
Drug discovery
Native and recombinant neurotransmitter receptors
Alzheimer's disease
Multiple sclerosis
Mental illness
Drug dependence

Shi F-D, Piao W-H, Kuo Y-P, Campagnolo DI, Vollmer TL, Lukas RJ (2009) Nicotinic Attenuation of Central Nervous System Inflammation and Autoimmunity. J Immunol, in press.

Studies showing dramatic delay and attenuation of disease symptoms in an animal model of multiple sclerosis upon treatment with nicotine, implicating nicotinic receptors in inflammation and autoimmunity and pointing toward therapeutic opportunities.

Liu Q, Huang Y, Xue F, Simard A, DeChon J, Li G, Zhang J-l, Lucero L, Want M, Sierks M, Hu G, Chang Y-c, Lukas RJ, Wu J (2009) A novel nicotinic acetylcholine receptor subtype in basal forebrain cholinergic neurons with high sensitivity to amyloid peptides. J Neurosci: in press.

Discovery of a new form of nicotinic receptor ($\alpha 7\beta 2$-nAChR) in the part of the brain showing early degeneration in Alzheimer's disease and having high sensitivity to a suspected etiopathogenic agent, suggesting that amyloid-mediated compromise of receptor function could be an early step in the disease.



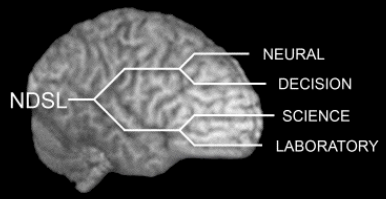
Decision Science Laboratory

What do we do?

People make countless decisions in their lives, from relatively small, daily ones (what will I have for lunch?) to highly consequential ones (where will I go to college?). How do we make these decisions and arrive at good choices? Questions like these are central to our lab's research. Using state-of-the-art neuroscience technologies at the U of A, we examine how the brain responds to decisions and choices and use this knowledge to help us better understand, and improve, our own decision-making abilities.

How do we do it?

To examine the human brain as it makes decisions, we use a technique called Functional Magnetic Resonance Imaging (fMRI). By placing someone inside an MRI machine, we can then examine activation in the brain as people make choices and decisions. For example, we can see what parts of the brain are particularly active when decisions are difficult, or when emotions are involved in the decision.



Decision Science Laboratory

What have we found?

The Decision

Imagine you are playing the following game. You and another person have $100 to divide between you. The catch is that the other person gets to decide how to divide it up. Once they make you an offer, you can either accept or reject their proposal. If you accept, the money is divided as proposed. If you reject, neither of you gets anything. Now, imagine that your partner offers you $1, keeping $99 for themselves. Would you take the dollar, figuring that $1 is better than nothing? Or would you say no, punishing your partner and leaving both of you penniless?

The Behavior

Many people are willing to reject unfair offers, even when it means they will make less money. For example, people often turn down as much as a $10 offer from the $100. This is important, as it show that we have motivations other then money behind our decisions - our reputation and our sense of fairness is an important component of our decision-making.

The Brain

Using fMRI, we find that certain areas of the brain are sensitive to different motivations of the game.

Emotional regions (such as the anterior insula) are particularly active when unfair offers are being made, and this activity can predict whether the person will accept of reject the offer.

More 'rational' regions (such as parts of the frontal lobes) are more active when people take the money, even when the offer is unfair.

By looking at patterns of activation in the brain while people are playing the game, we can begin to see how decisions are made.

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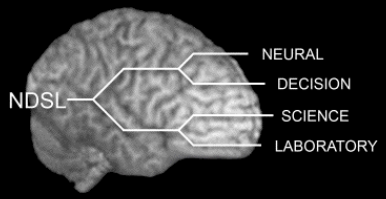

Decision Science Laboratory

Who are we?

Lab Director

Dr. Alan Sanfey

Postdoctoral fellow

Dr. Mascha van 't Wout

Graduate Students

Aaron Tesch
Katia Harle
Bradley Doll
Luke Chang
Trevor Kvaran
Phil Hall

Research Assistants

Erienne Weine
Niko Warner
Lauren Montoya
Julie Shah
Joel McAlister

Contact us!

Email: ndsl@u.arizona.edu
Phone: 520.626.8597
Address: Room 406, Department of Psychology, Tucson, AZ 85721

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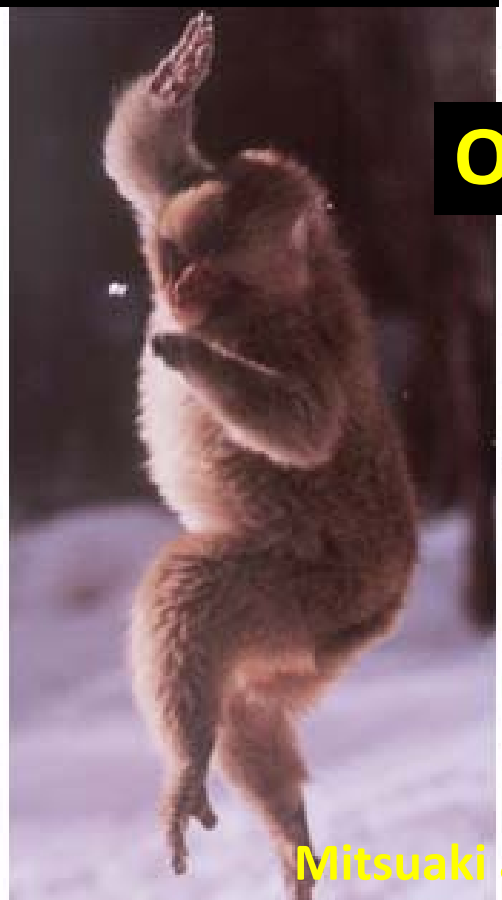
NEUROPHYSIOLOGY

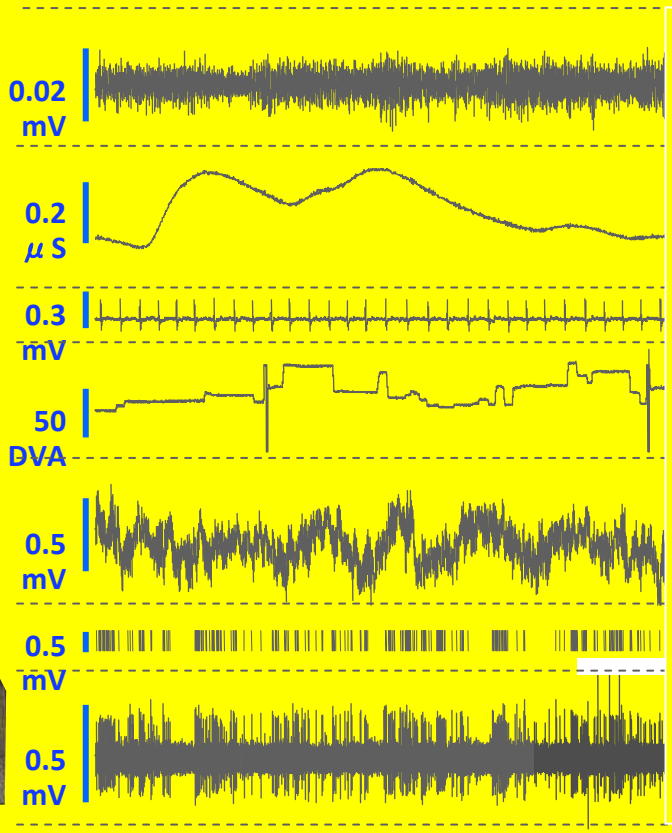


OF

EMOTION & SOCIAL BEHAVIOR

Mitsuaki and Hideko Iwagi – Snow monkeys (1999)

We use behavioral and electrophysiological techniques to monitor emotion-related changes in the brain and in the peripheral organs.



neuromuscular activity in the face

electrodermal activity

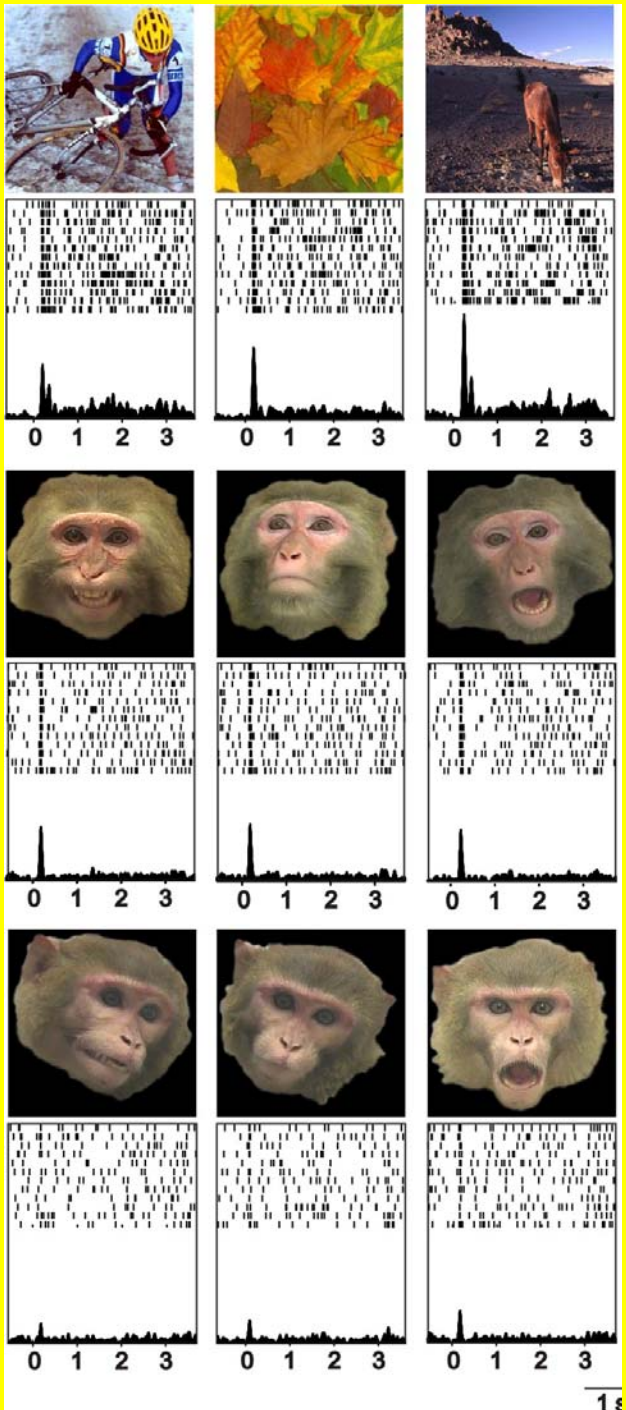
cardiac activity

eye movements

local field potentials

single unit activity

multiunit activity



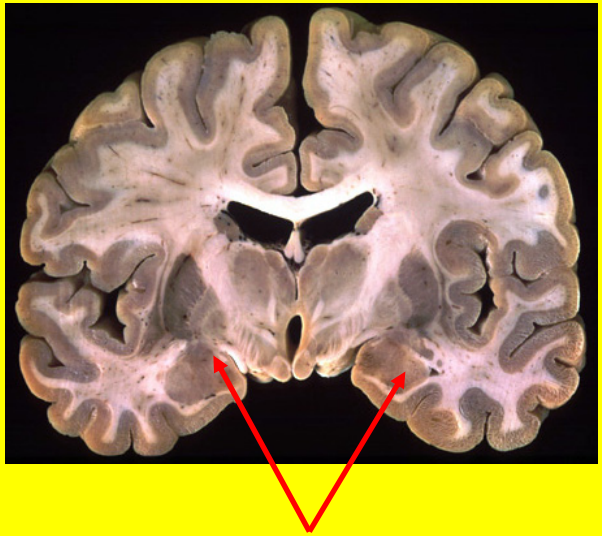
The signals obtained are processed and analyzed

(←)

Neural activity in the **amygdala** encodes information about the **identity of stimulus** (object, their novelty or ambiguity), and the **emotional value** (positive or negative), of as stimulus, especially of a face.

This is in contrast to older views that the amygdala is mainly concerned with fear.

Gothard Lab:
Neurophysiology of emotion



The primate amygdala

Members

The amygdala plays a major role in translating information from sensations, perceptions, and memories into the bodily responses we associate with emotion. Dysfunction of the amygdala is associated with conditions such as autism, schizophrenia, post traumatic stress disorder, and social phobia.

Language Processing in the Brain

S. Chan, L. Ryan, T.Bever

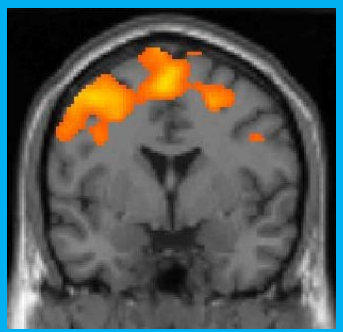
We are interested in finding out whether having left-handed family members would have an effect on the way people process language even if they themselves are right-handed. We asked experimental subjects to carry out a *syntactic order* and *semantic order* task and we measured their brain activity with an fMRI scanner.

Syntactic Task

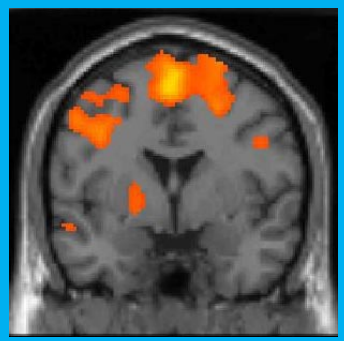
reorder these phrases into a sentence: *upset, the mother, the girl*

Semantic Task

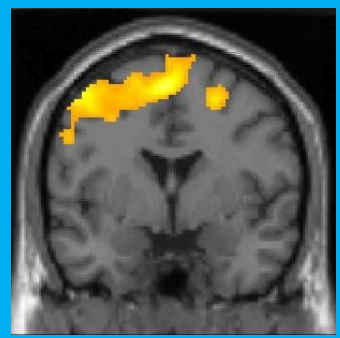
reorder these words in generality: *tree, plant, pine*



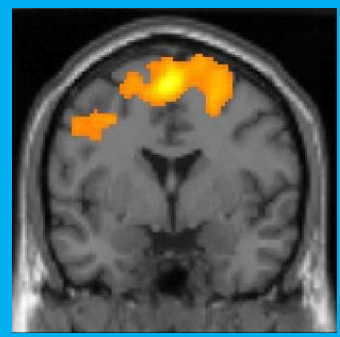
Family all righties



Family with lefties



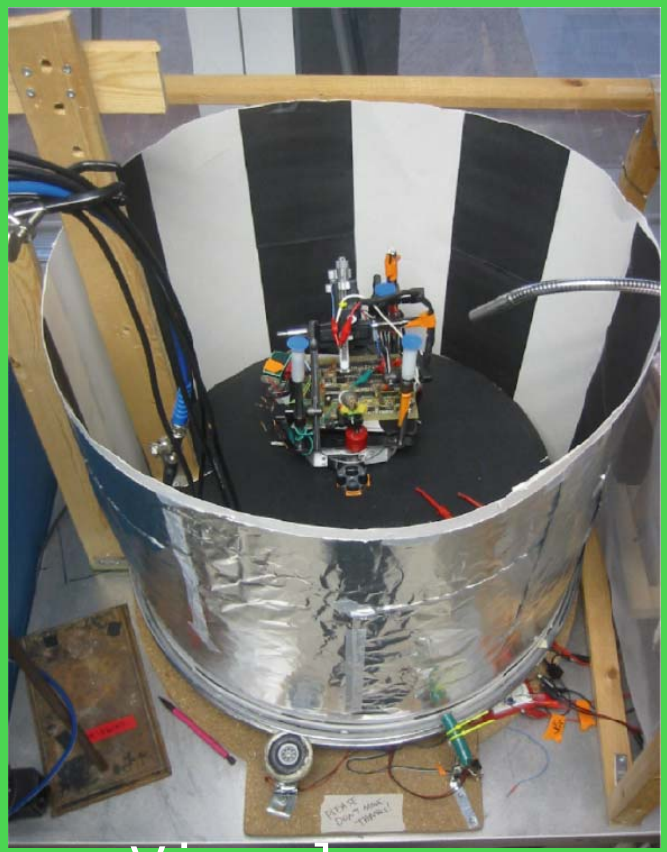
Family all righties



Family with lefties

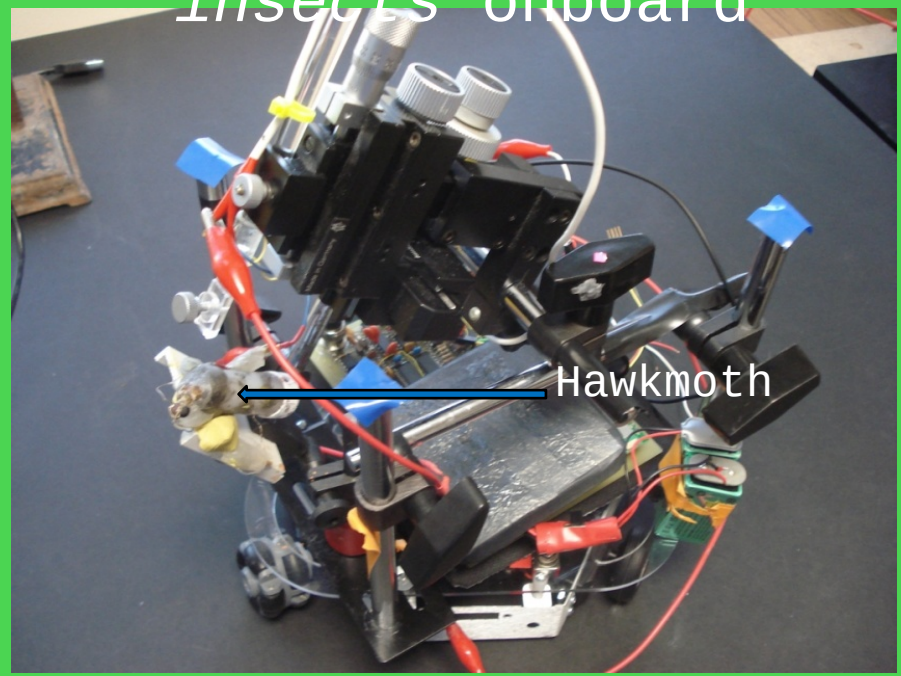
These results show that syntax is mostly in the left hemisphere for everyone, and semantics is in both hemispheres only if you have left handed family members. This is because a left handed family gives you a more evenly balanced brain even if you are right handed.

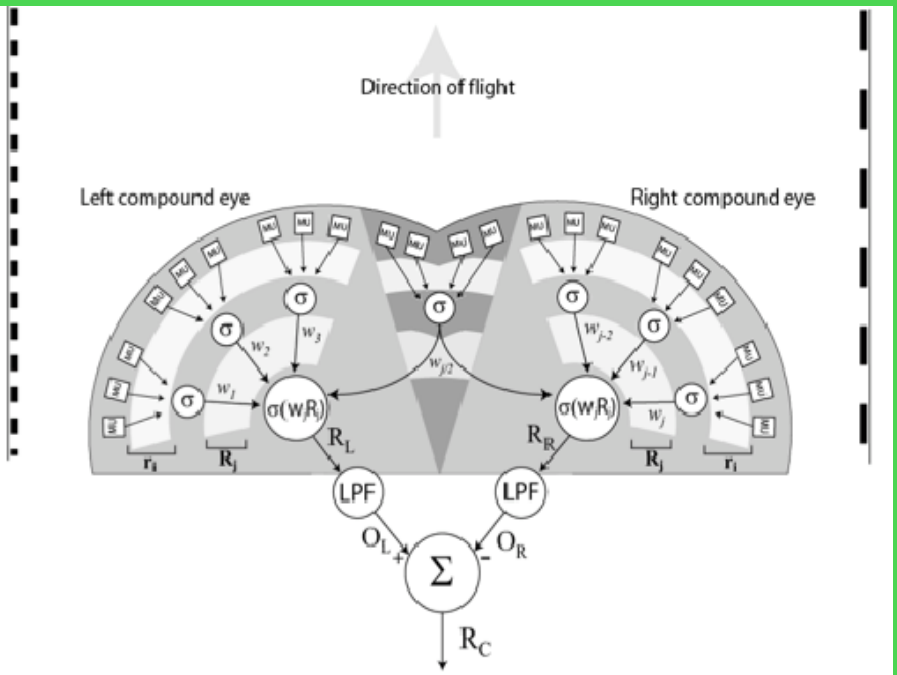
The Higgins Laboratory (Neuroscience/ECE)
Computational Neuroscience and Hybrid BioRobotics



Visual arena experiments

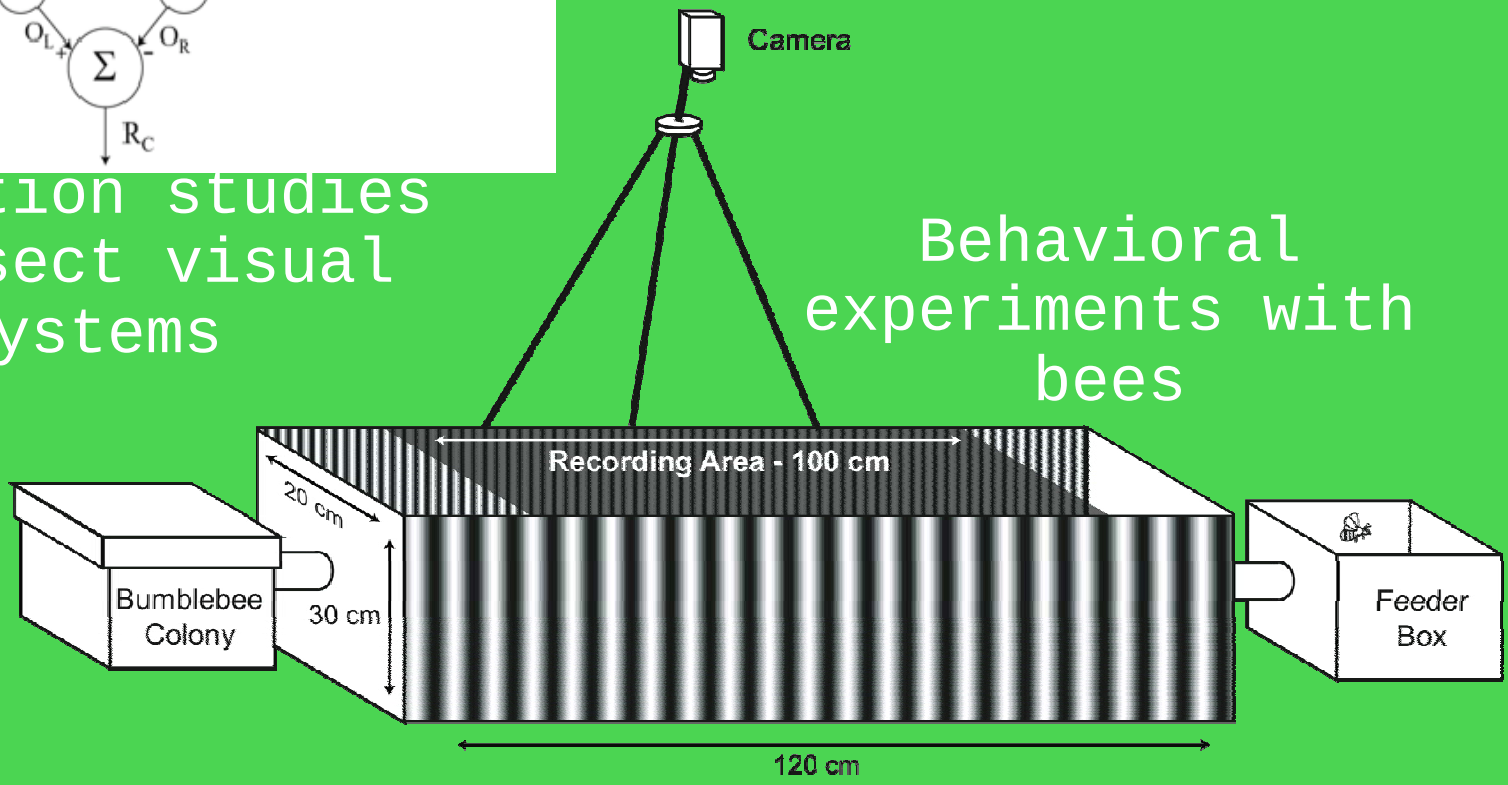
Robots that are guided by the visual system of *live insects* onboard





Simulation studies of insect visual systems

Behavioral experiments with bees



Hard-working graduate students

Contact higgins@neurobio.arizona.edu.

THE GLAUCOMA LABORATORY

Research Program Goal:

- To investigate/understand the molecular and cellular mechanisms that regulate aqueous humor outflow such that novel targets can be identified and used for the development of therapeutics to effectively lower intraocular pressure in people with glaucoma.

- Effective control of intraocular pressure reduces retinal ganglion cell loss and thus blindness over time in those with glaucoma.

THE GLAUCOMA LABORATORY

Laboratory Director

W. Daniel Stamer, Ph.D.
Professor
Departments of Ophthalmology and Vision Science
Department of Pharmacology

dstamer@eyes.arizona.edu

Dussor Laboratory

Greg Dussor: Principal Investigator

520-626-6726 (Office)

dussorg@email.arizona.edu

Location: Life Sciences North, Room 660 (Lab)

Laboratory Members

Jin Yan: Graduate Student, Medical Pharmacology Program
Xiaomei Wei: Graduate Student, Medical Pharmacology Program
Rebecca Edelmayer: Post-doctoral fellow
Ning Qu: Research Associate

Research Interests

The role of ion channels (voltage and ligand-gated) in the pain-signaling pathway, mechanisms of pain signaling from the skin and the cranial meninges. Migraine headache.

Techniques

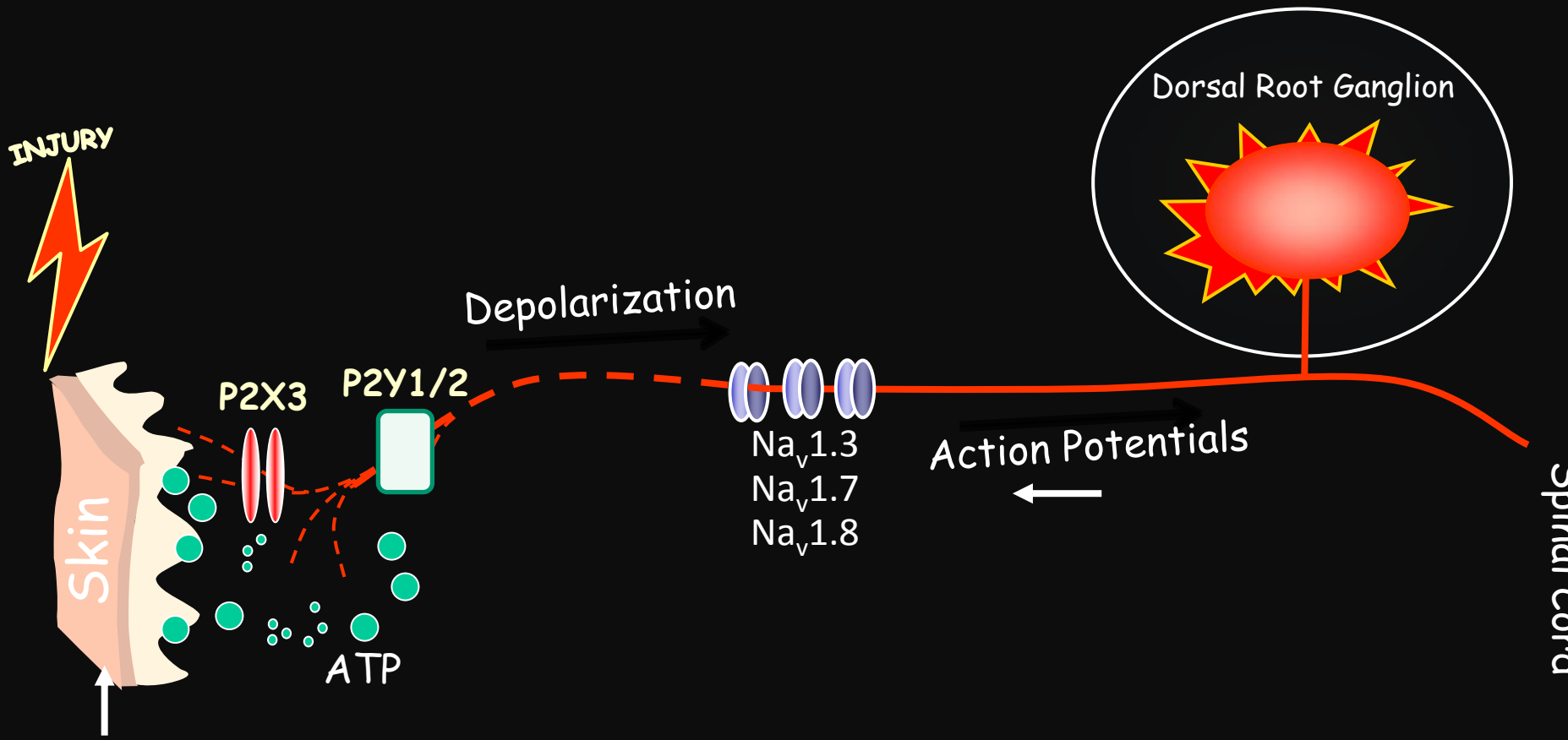
- Patch-clamp electrophysiology
- Ratiometric imaging
- *In situ* hybridization
- Immunohistochemistry
- Animal behavioral assays

Current Projects

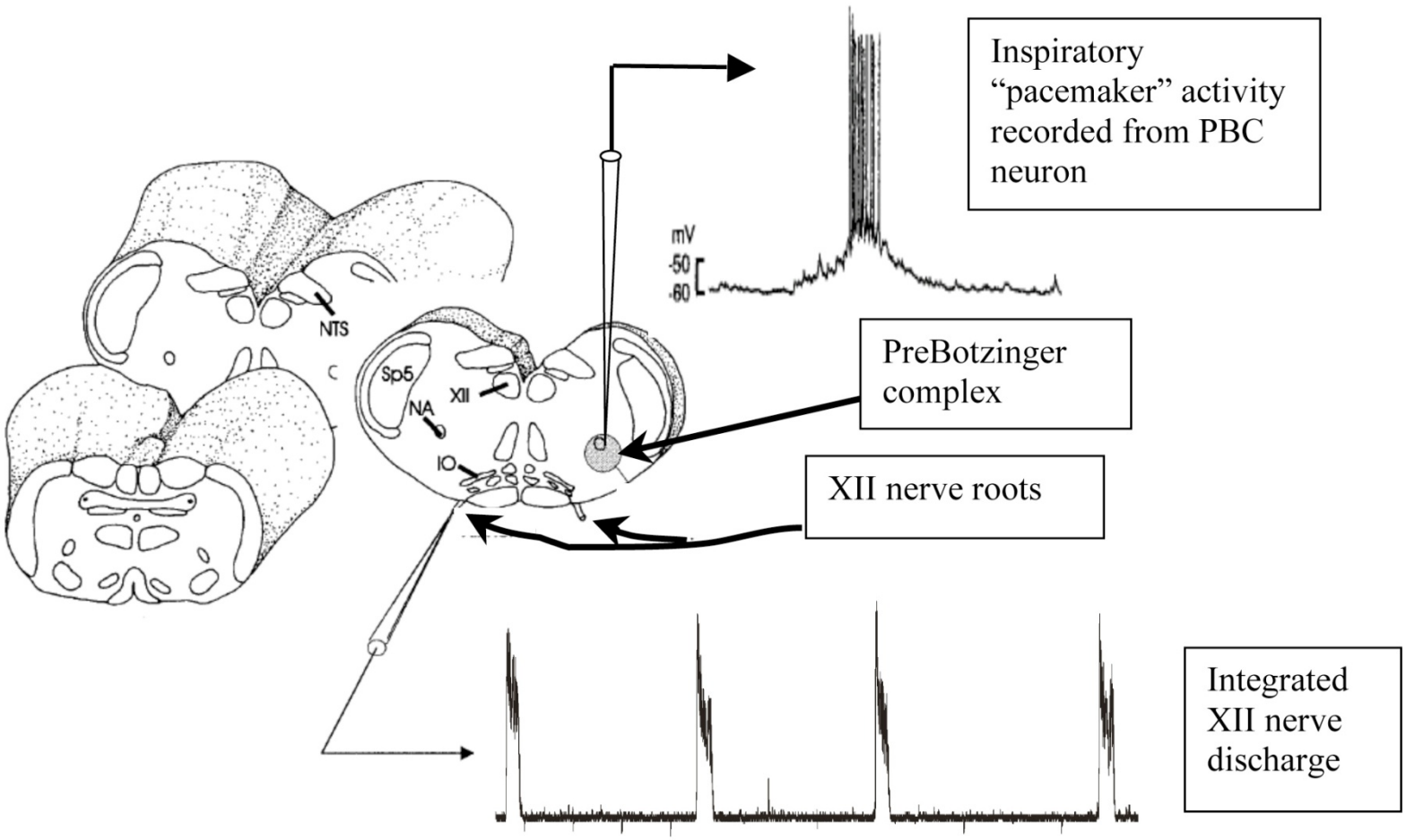
- Investigating the mechanisms by which pain-signaling is initiated in neurons innervating the cranial dura to further understand processes leading to migraine headache.
- Investigating the mechanisms by which pain-sensing neurons innervating the outer epidermis respond to nucleotides released from the skin.
- Investigating the role of the voltage-gated Na^+ channels $Na_v1.3$, $Na_v1.7$, and $Na_v1.8$ in spontaneous pain following nerve injury

Ion Channels on Peripheral Sensory Neurons Contribute to Pain Signaling

1. Peripheral tissues (e.g. skin) release substances such as ATP in response to painful stimuli.
2. ATP activates ion channels and G-protein coupled receptors initiating pain-signaling.
3. Depolarizations are amplified and propagated by sodium channels such as $Na_v1.3$, $Na_v1.7$, and $Na_v1.8$.
4. How do these processes change after nerve injury or inflammation?
5. Do similar processes happen in neurons innervating the cranial dura?



Fregosi Lab, Department of Physiology



Schematic diagram showing how the thick brainstem slice is cut from the medulla. Because the phrenic nerves are not present in the slice, inspiratory activity from a hypoglossal nerve root (which supplies tongue muscles with their respiratory-related discharge) is used as the index of system output by all laboratories that use this method. The preBotzinger complex contains respiratory pacemaker neurons that form a major component of the central pattern generator for breathing in mammals. PreBotzinger complex neurons can be recorded with a low-impedance electrode to obtain the activity of a population of these cells ("population activity"); or, the neurons can be visualized with infrared optics so that whole-cell patch clamp recordings can be made. The inset shows changes in voltage, with inspiratory spiking, in a cell recorded under current clamp conditions. This cell also shows a steady depolarization during the non-spiking phase, indicating that it has "pacemaker like" properties that are presumed to drive the respiratory rhythm. We use these methods to study development of respiratory control, and how development is altered by prenatal exposure to nicotine.

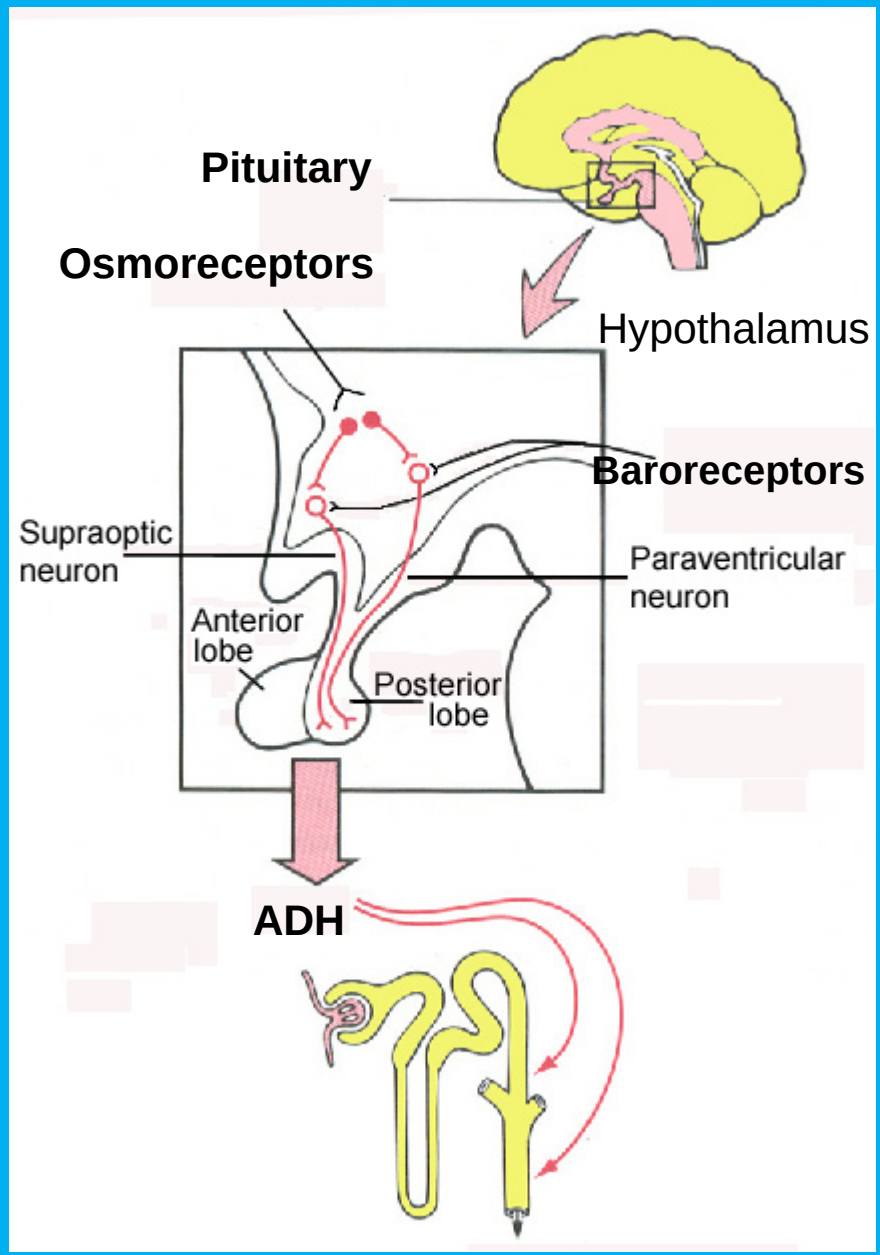
Hormonal regulation (ADH, estrogen) of physiological function

Sex differences in diabetic disease

Dr. Heddwen Brooks
Associate Professor

Arizona Diabetes Program/Department of Physiology
BIO5/Sarver Heart Centre

Posterior Pituitary (ADH): role in fluid homeostasis



Urine is concentrated and flow reduced

SYSTEMS LEVEL- blood pressure and gender differences in physiology

MOLECULAR SIGNALING - GPCR's, aquaporin and sodium channel regulation

Voice and Swallowing Lab

Julie Barkmeier-Kraemer, Ph.D., CCC-SLP
Associate Professor
Department of Speech, Language, Hearing Sciences

Clinical and basic research in this lab addresses normal and abnormal anatomy and physiology of speech & swallowing

Investigation of the connective tissue “packaging” within the recurrent laryngeal nerve (RLN) as a factor in vocal fold paralysis

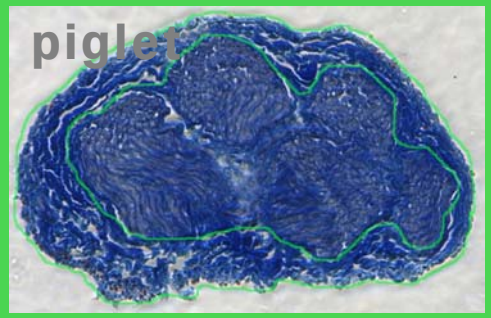
Funded by NIDCD R01 DC05422-01, *Connective Tissues as a Factor in Vocal Fold Paralysis*

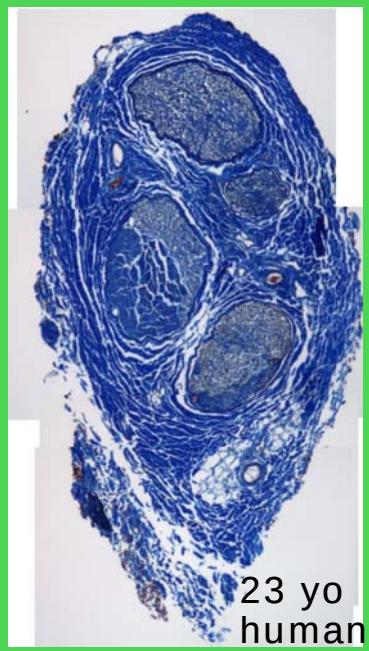
- Purpose of Research is to characterize RLN epineurium in elderly and young humans for comparison to porcine RLN epineurium
  - Proportion of epineurium in RLN cross section
  - Epineurium composition (collagen & adipose)
- Research Questions
  - Are there differences between the left and right RLNs?
  - Are there differences in RLN composition between genders?
  - Are there age group differences?
  - Are there differences along the length of each nerve?

- Findings thus far…
  - Differences in the proportion and composition of RLN epineurium were found between piglets and adult pigs
    - Increased epineurium with age
    - Increased adipose in distal segments of nerve in adult pigs
  - Comparable proportion and composition of epineurium between “young” and “older” humans with the exception of greater quantity of epineurium in the “older” human group
    - Increased adipose associated with increased Body Mass Index (Elderly Human Study)
  - Humans and porcine RLN epineurium appear similar in quantity and composition

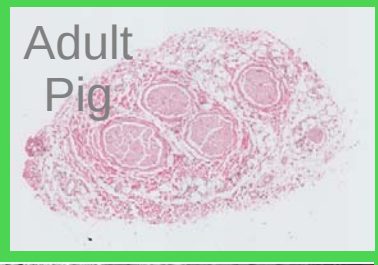
RLN Epineurium studied in younger and older groups

Young Group





Older Group



Current Student Research

- **Undergraduate Research**
  - Salient factors for establishment and maintenance of an interdisciplinary team for evaluation of pediatric feeding, swallowing, and nutrition disorders (Honor's Thesis)
  - The contribution of laryngeal muscle modulation to the acoustic characteristics and perception of vocal tremor (Honor's Thesis)
  - The contribution of lung pressure to the acoustic characteristics and perception of vocal tremor
  - The contribution of pharyngeal wall modulation to the acoustic characteristics and perception of vocal tremor
- **Master's Theses**
  - Recurrent laryngeal nerve epineurium in the adult pig
  - Therapeutic effect of neuromuscular stimulation for treatment of dysphagia in individuals following stroke
- **PhD Student Research**
  - Underlying physiology of neuromuscular stimulation for treatment of swallowing disorders
  - Vocal tremor during connected speech
  - Laryngeal muscle activation patterns associated with glottal configuration in normal adults
  - Recurrent laryngeal nerve epineurium in the piglet

Kaitlyn Cavanaugh

Jessie Liu **Sarah Cook**

Christine Bartelt

Ellen Campbell

Laura Nickerson

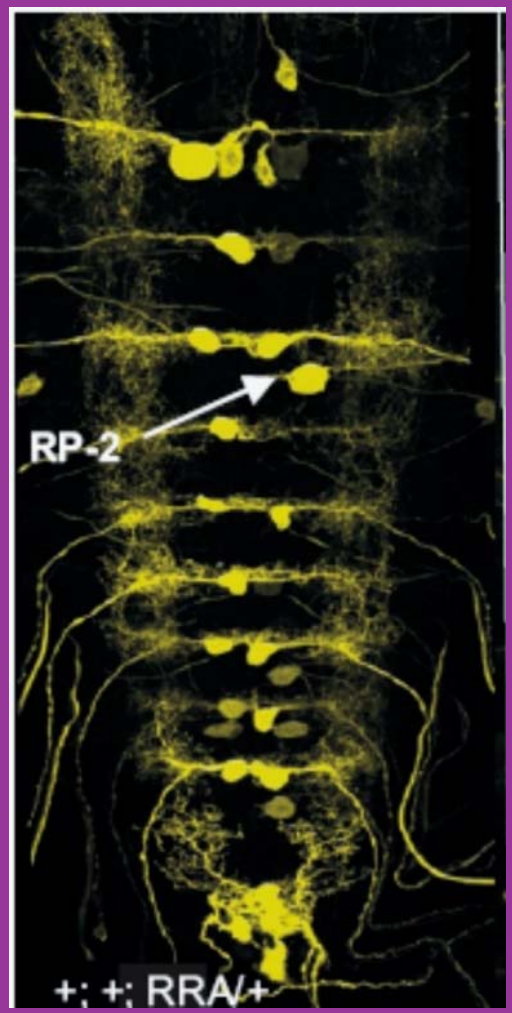
Amy Lederle

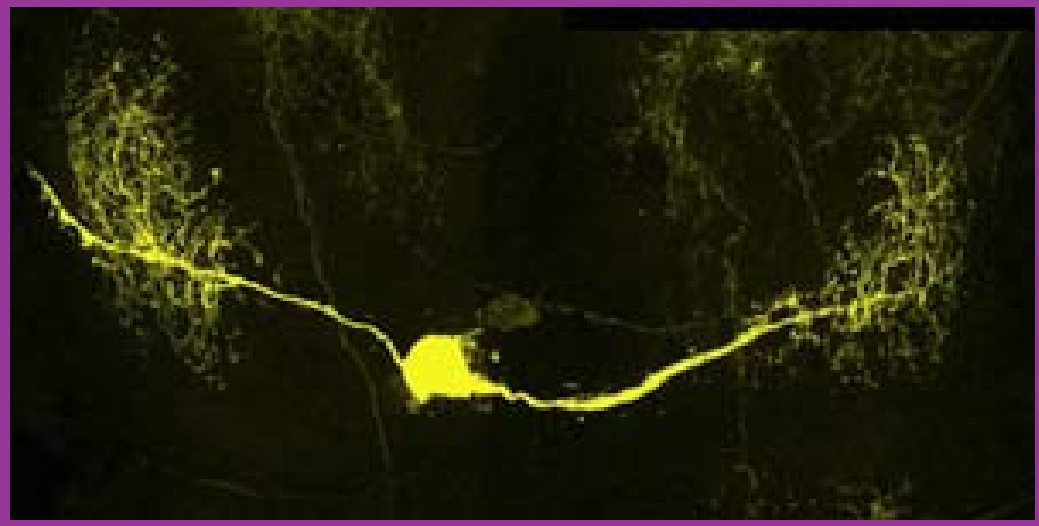
Robin Samlan

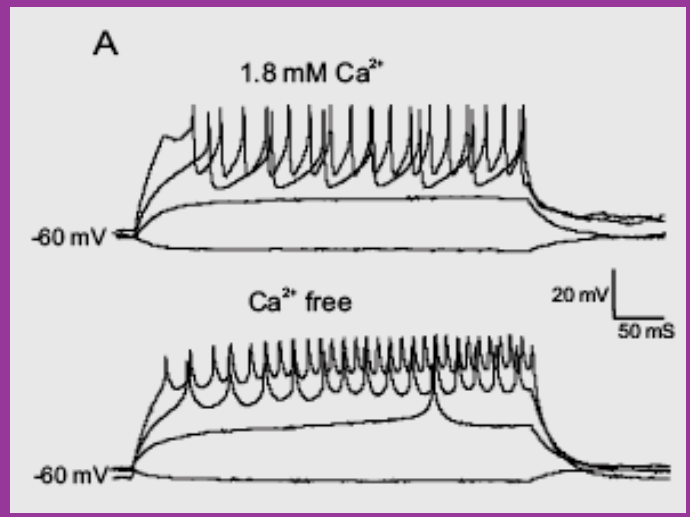
Dr. Rick Levine's Lab

Division of Neurobiology and Dept. Physiology

- **Development and function of motor systems**
- **Regulation and role of specific ion channel expression in motoneurons**
- **Determinants of motoneuron recruitment during rhythmic behavior**


RP-2
+; +; RRA/+




A
1.8 mM Ca2+
-60 mV
Ca2+ free
20 mV
50 mS
-60 mV

Dr. Rick Levine's Lab Members

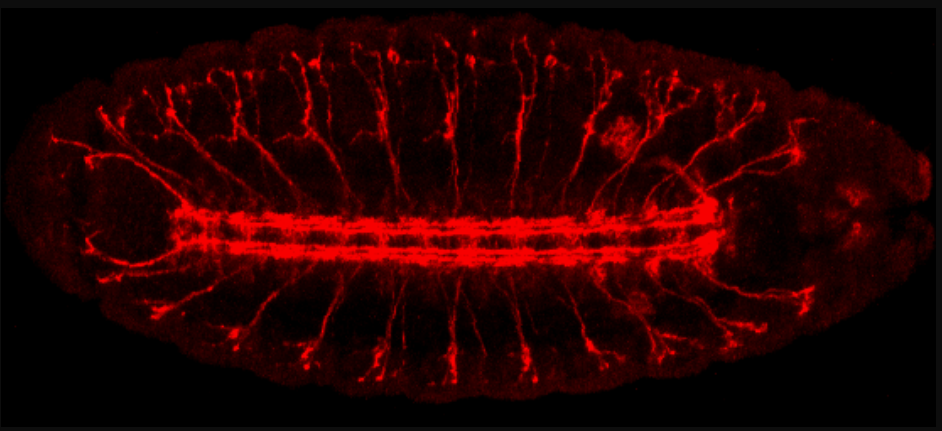
rbl@neurobiology.arizona.edu

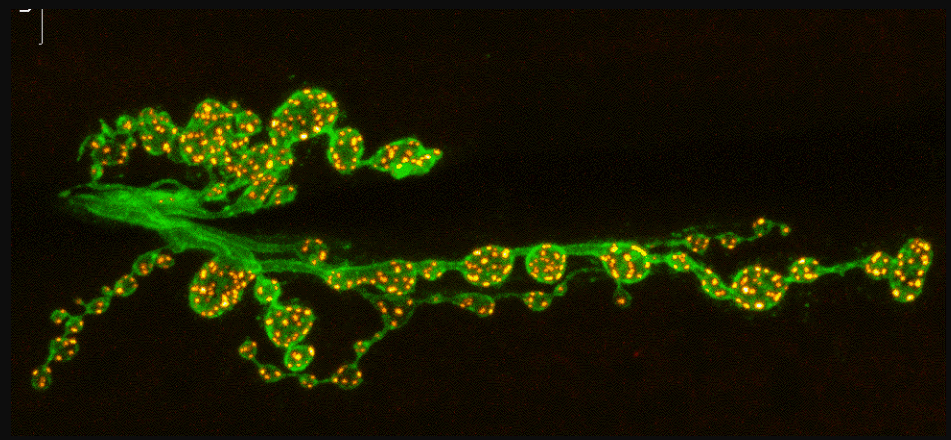
Synaptic Function and Structure

Neurogenetics Laboratory
Konrad E. Zinsmaier

http://www.neurobio.arizona.edu/faculty/zinsmaier/index.php

Arizona Research Laboratories, Division of Neurobiology, University of Arizona



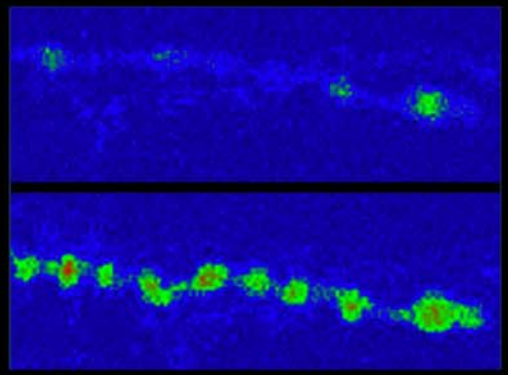


Specialized cell-cell contact sites, called synapses, facilitate communication and computation of information in the brain on a sub-millisecond scale. The accuracy of this process is vital as even subtle changes in synaptic function can disturb neuronal circuits and cause pathological abnormalities that lead to neurological and/or psychiatric disorders.

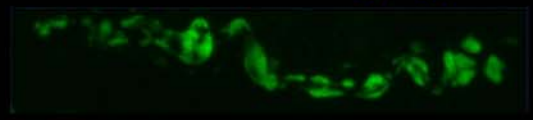
Our laboratory studies the molecular mechanisms that mediate, modulate, and/or maintain synaptic function by employing synapses of genetically modified *Drosophila* (fruit flies) as a model system. Forward and reverse genetics are used to examine effects on synaptic function and structure that are induced by mutations in critical molecules of the machinery.

Our model: The *Drosophila* Neuromuscular Junction

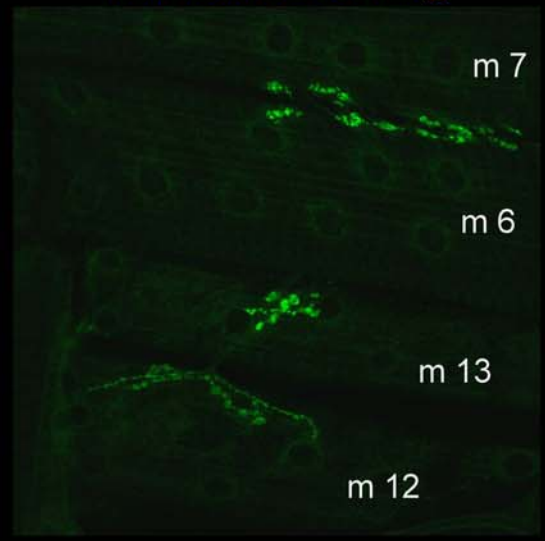
Ca^{2+} Imaging

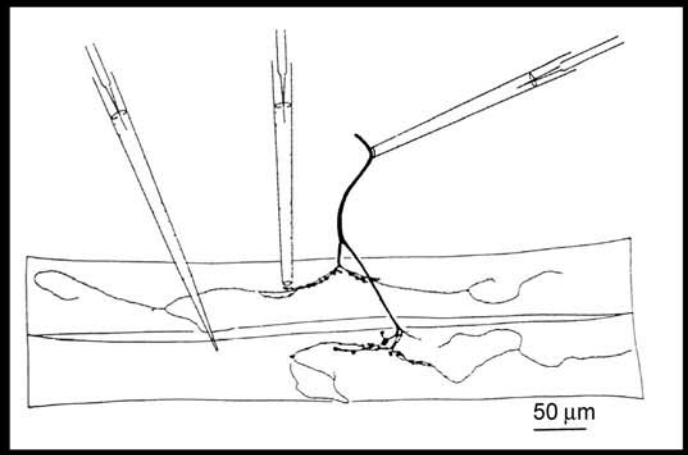


FM1-43 Imaging

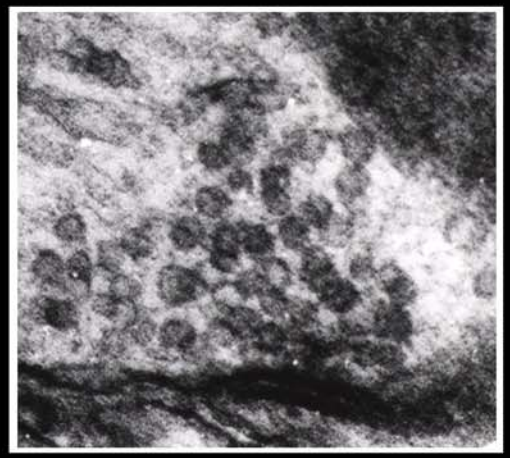


Immunostaining

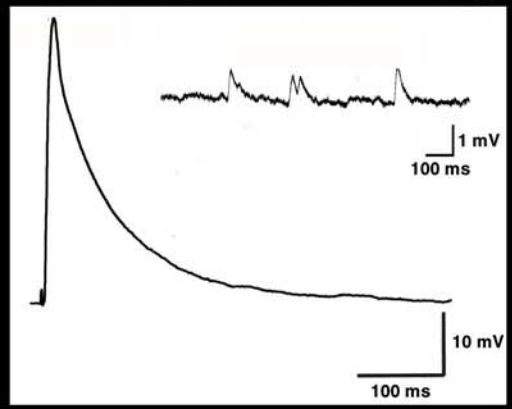




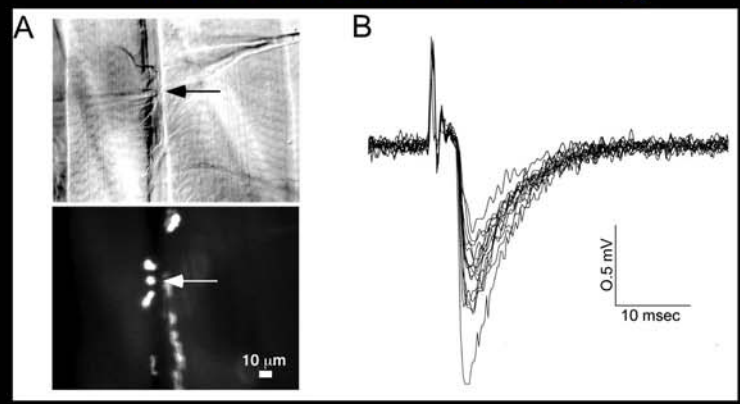
Electron Microscopy



Whole-Cell Recording



Macro-Patch Recording



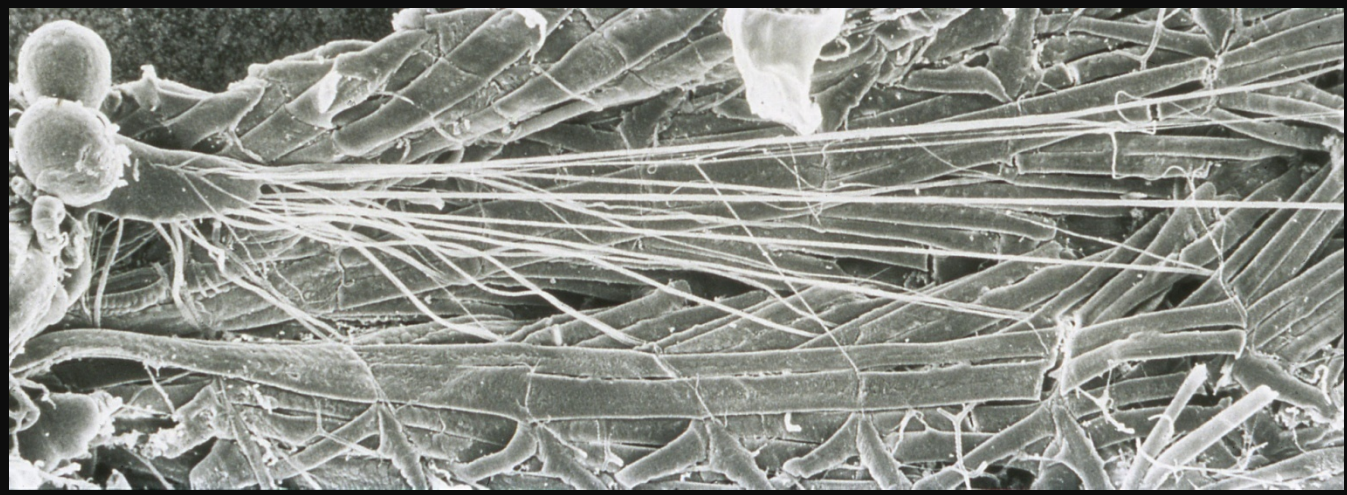
Current Projects

Role of Lipid Transporters.

- Membrane asymmetry
- Synaptic vesicle exo- and endocytosis
- Neurodegeneration
  + Autism, Alzheimer's disease

Role of Serrate/Notch.

- Synaptic growth and maintenance
- Neurodegeneration
  + Mental retardation
  + Alagile syndrome



Axonal Transport of Mitochondria

dMiro (atypical GTPase)

- regulates mitochondrial transport
- likely a Ca^{2+} sensor that controls distribution

New synaptic components

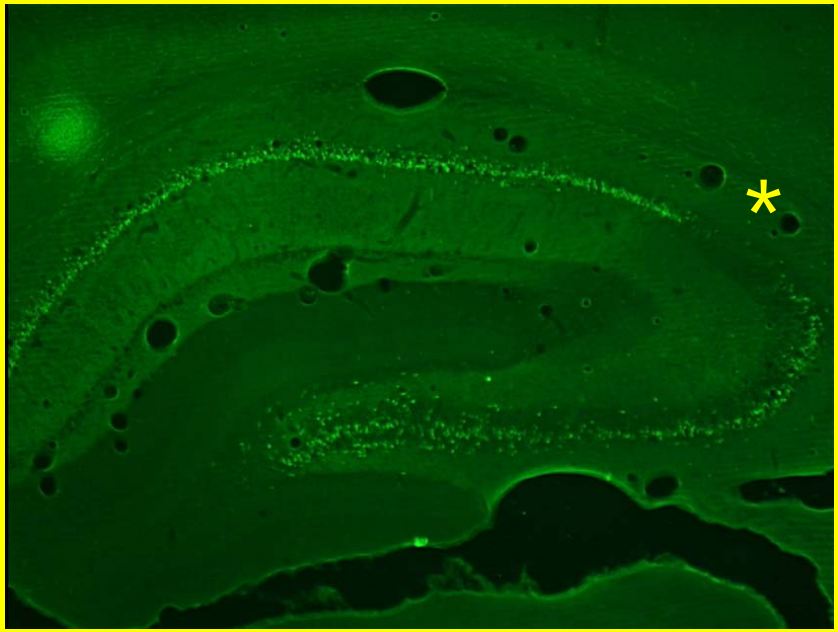
- genetic screen identified ~176 "blind mutations"
- of ~25 analyzed at NMJ, 20 show synaptic function and/or structure

Techniques: Genetics, molecular biology, electrophysiology, live imaging (calcium, synaptic vesicles, mitochondria, proteins), immunocytochemistry, electron microscopy.

Zinsmaier Lab

Sloviter lab

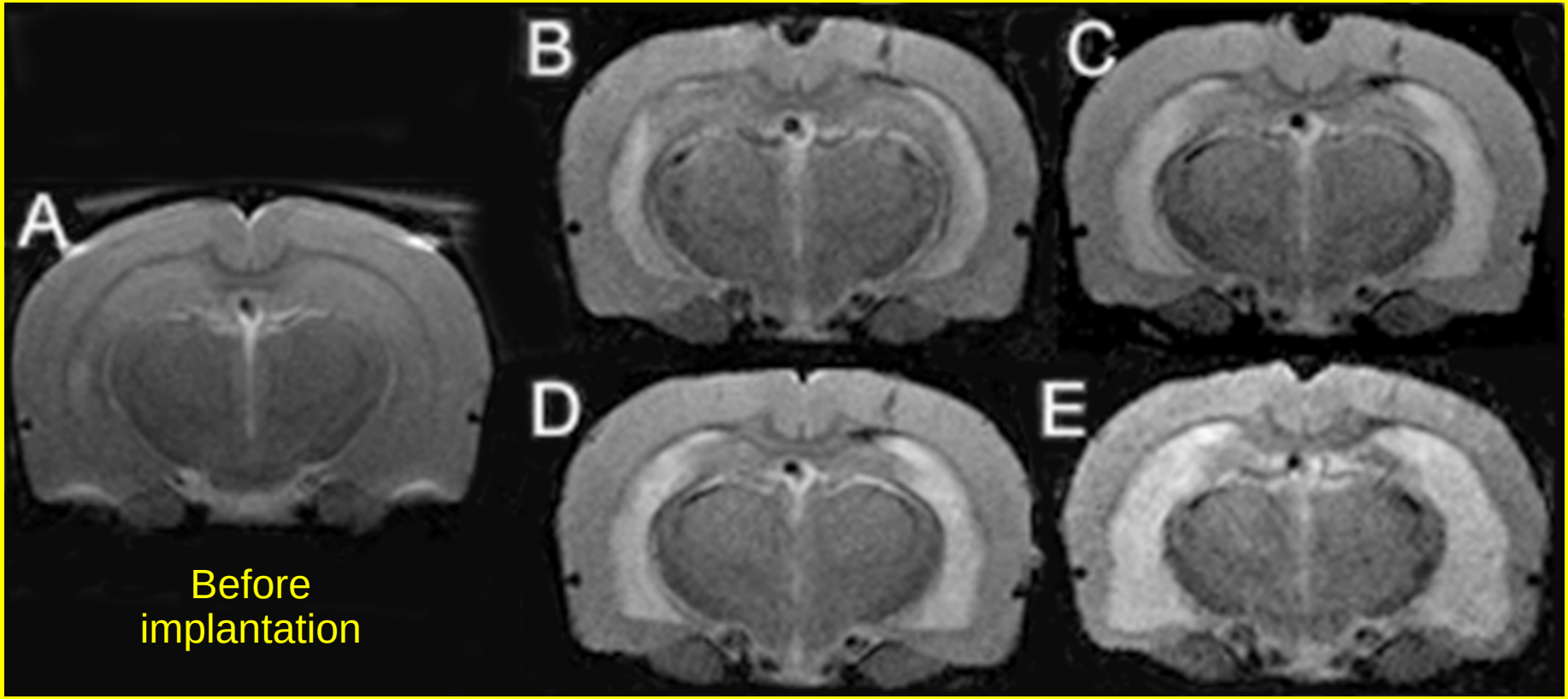
Trying to understand hippocampal structure and function, and the nature of hippocampal malfunction in temporal lobe epilepsy



Prolonged focal excitation causes selective neuron loss identical to the human pathology
(fluorescent cells are acutely dying- FluoroJade B stain)

PhD candidate Braxton Norwood

Sequential MRI images after perforant pathway stimulation in an awake rat



With Fabene PF, Marzola P, Nicolato E, Sbarbati A. MR Imaging Lab, Univ. Verona

Sloviter lab- current projects

1. Producing temporal lobe epilepsy in rats

2. Elucidating the role of neuron loss in the development of spontaneous hippocampal seizures

3. Understanding the role of fever and decreased GABA-mediated inhibition in the exacerbation of neuron loss after a brain insult

4. Developing treatments that decrease neuron loss in response to neuronal insult.

Tolbert/Oland Laboratory, Department of Neuroscience

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Regents' Professor
Laboratory Head
tolbert@vpr.arizona.edu

Lynne A. Oland, PhD
Research Scientist
Lab Director
lao@neurobio.arizona.edu

Students (front row):

Jane Lim, Emily Ricq, Mounir Koussa

Mark Higgins, Sr. Staff Specialist
mrh@neurobio.arizona.edu

Patty Jansma, Staff Scientist and Manager, ARLDN Imaging Facility
plj@neurobio.arizona.edu

Nicholas J. Gibson, PhD
Staff Scientist
njgibson@neurobio.arizona.edu

James Pearson, Research Technician
jpearson@neurobio.arizona.edu

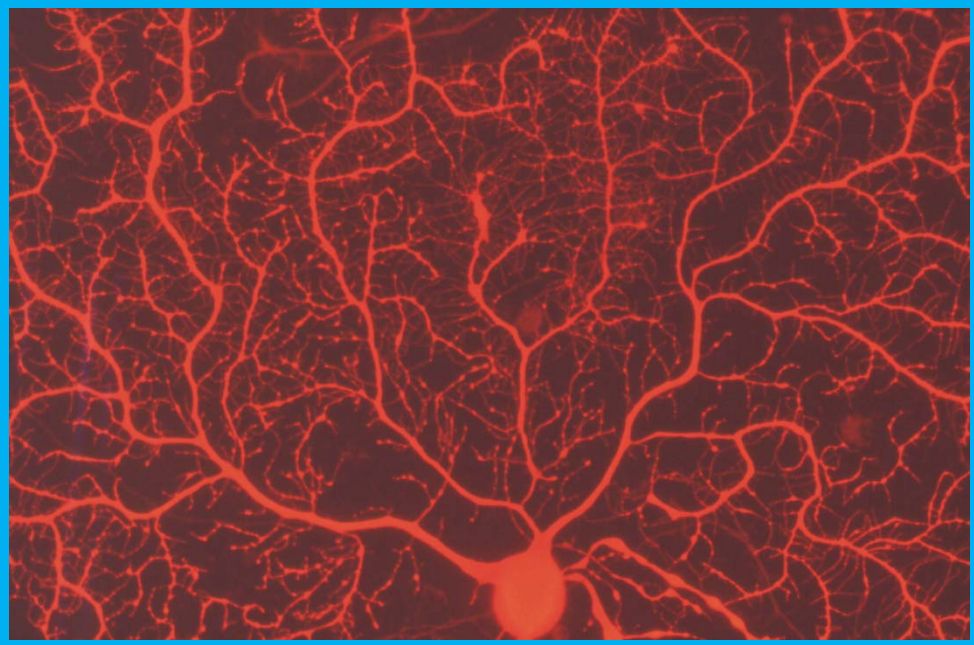
www.neurobio.arizona.edu/faculty/tolbert

Tolbert/Oland laboratory

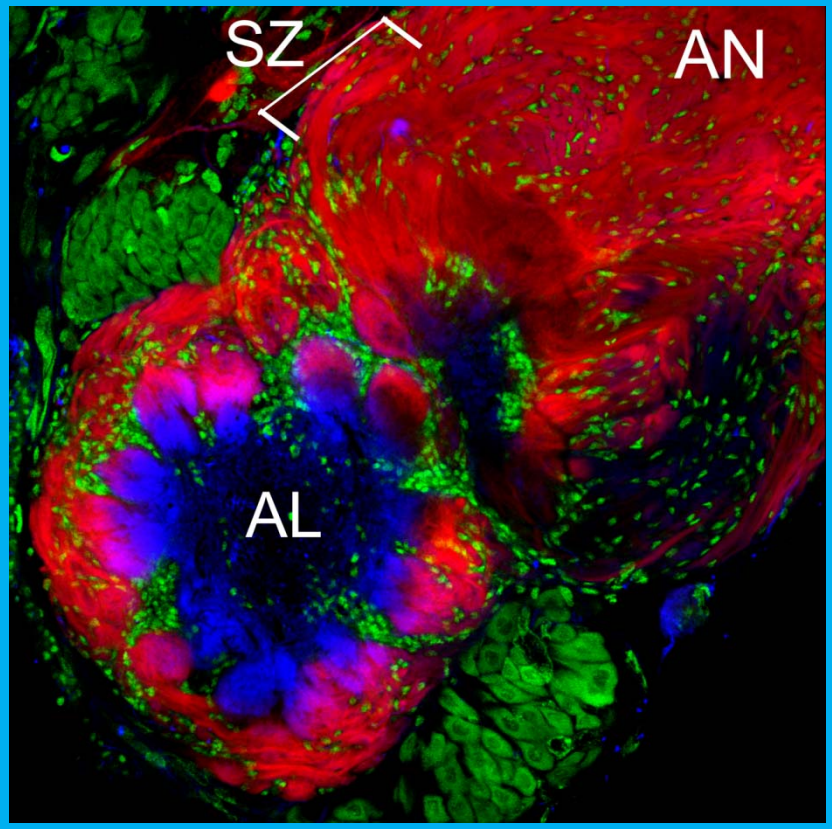
Research in the lab focuses on:

- Development of the olfactory system
- Neuron-glial cell interactions in axon targeting

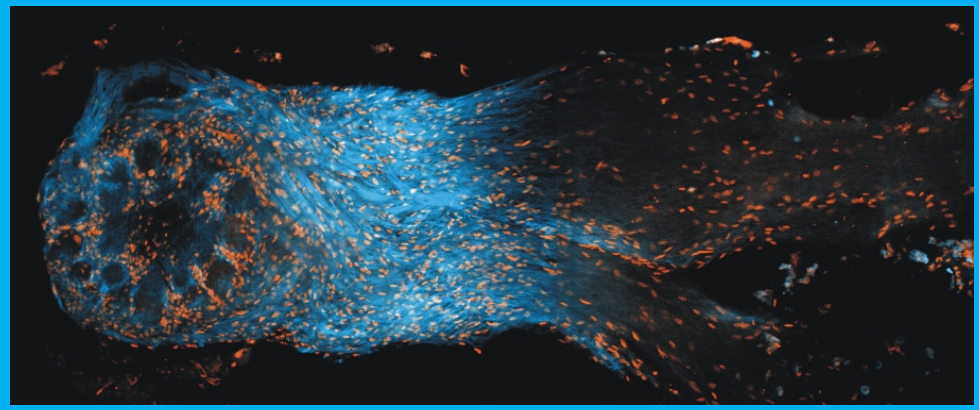
We use the large moth *Manduca sexta*, for ease in surgical and pharmacological manipulation, and the tiny fruitfly *Drosophila melanogaster,* for its genetic power.

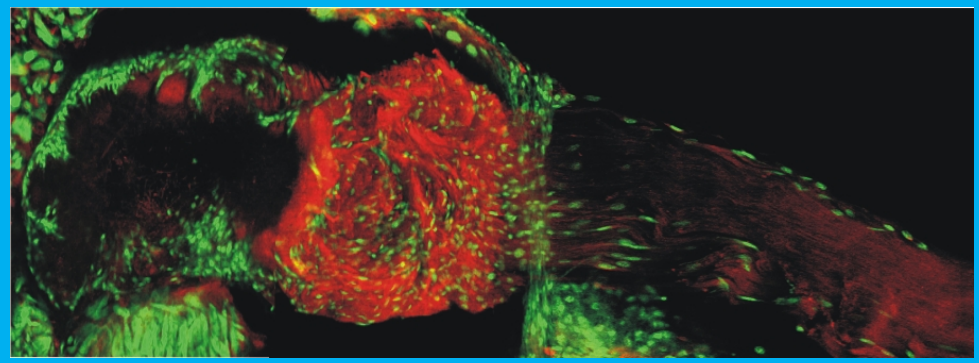


Glia-neuron interactions in the developing olfactory pathway

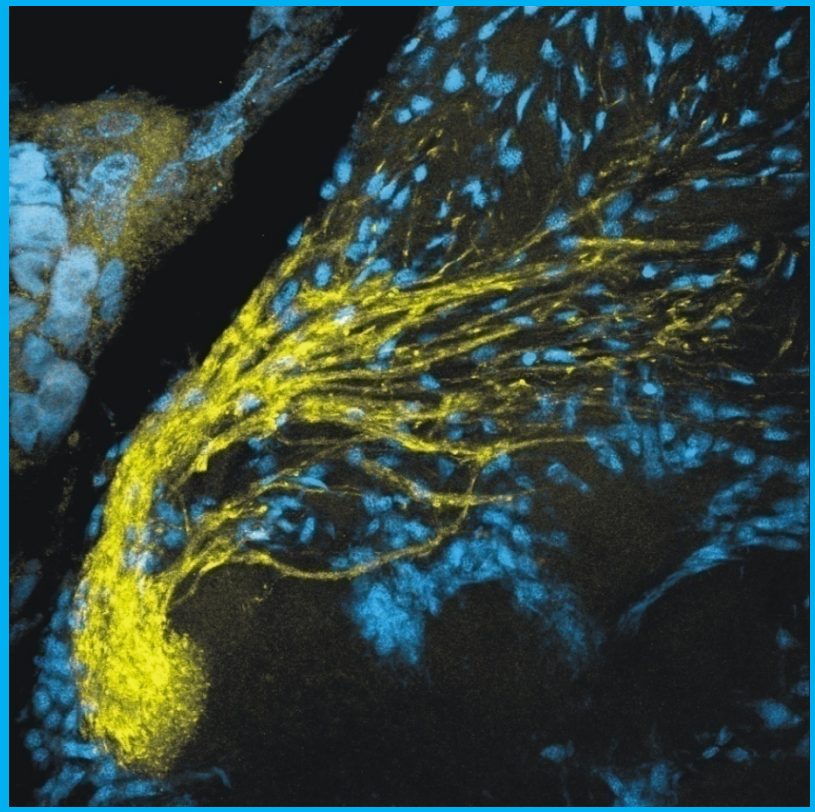


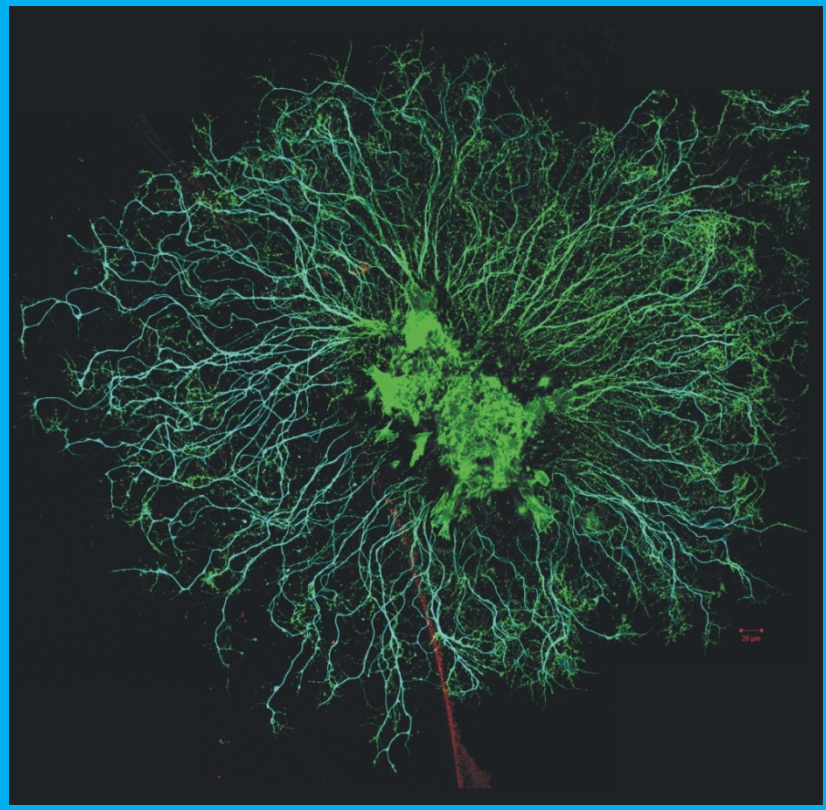
The first part of the brain receiving odor information in the moth. *Red,* olfactory axons; *blue*, dendrites of AL neurons; *green*, cell bodies of neurons and glial cells. Round structures are olfactory glomeruli.

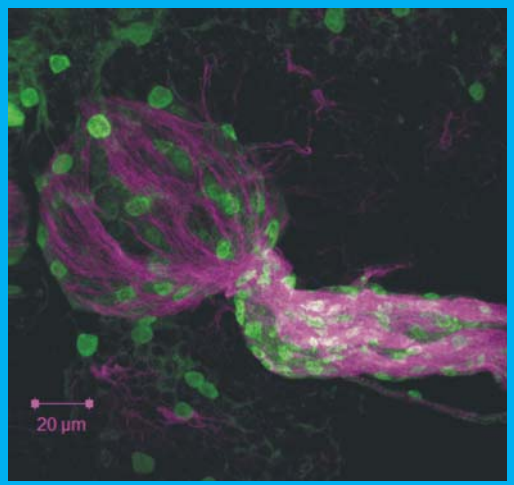




Signaling molecules in the sorting zone region of the nerve where receptor axons change direction. *Blue*, neuroglian; *red*, activated epidermal growth factor receptor.







Left above, receptor axons (*yellow*) targeting a glomerulus.

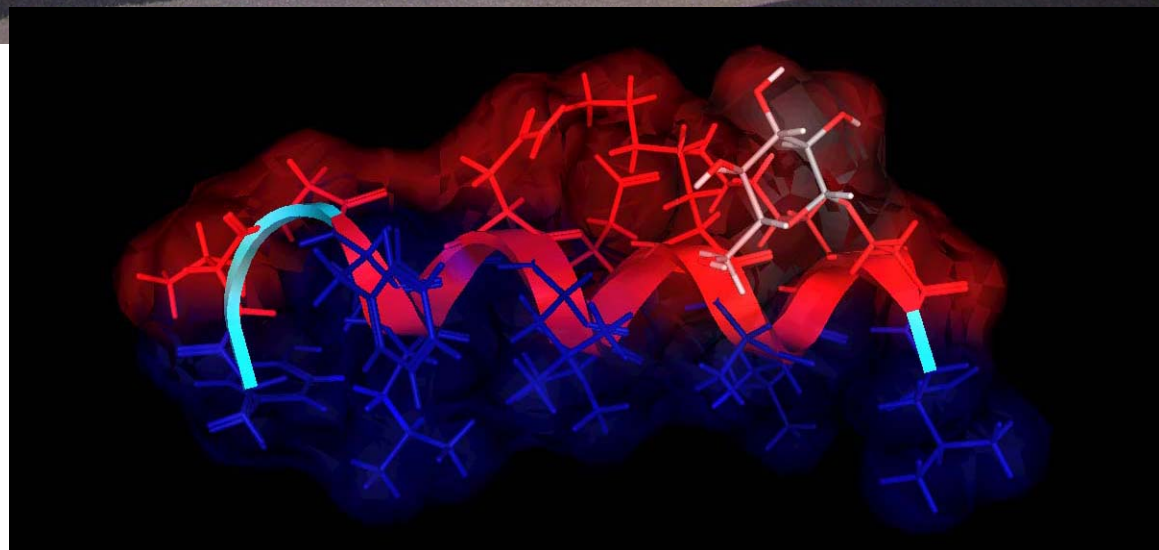
Right above, receptor axons growing in a dish from a small piece of the antenna.

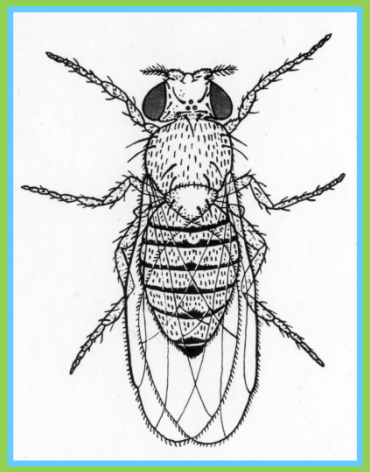
Left, Neuroglian (*magenta*) labels olfactory sensory axons in the nerve and in the nerve layer of the *Drosophila* antennal lobe. Glial cells (*green*).

Polt Group

polt@u.arizona.edu

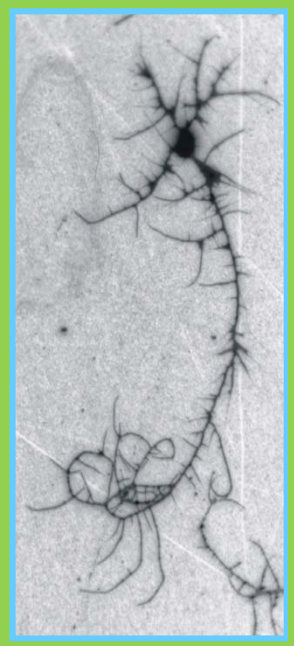
Glycobiology, Neuropeptides, Drug Design





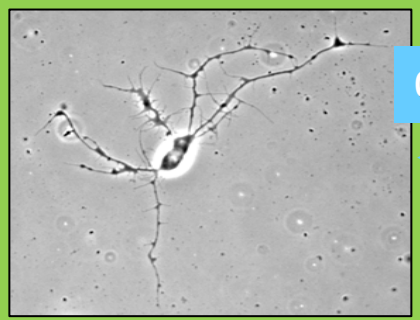
Linda L. Restifo, M.D.,Ph.D.

ARL Division of Neurobiology
Department of Neurology
McKnight Brain Institute
BIO5 Collaborative Research Institute

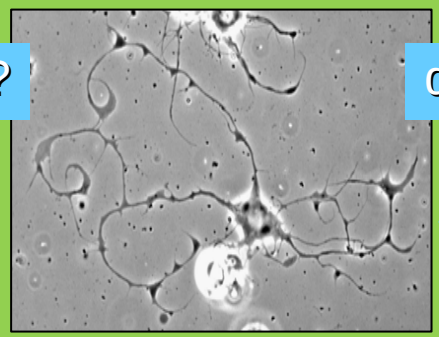


Research foci:

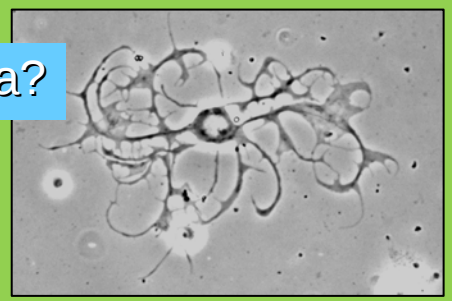
- Genetics and cell biology of brain development: morphogenesis and neuronal remodeling
- Cellular bioassays for drug discovery for neurological disorders, including gliomas and mental retardation/autism



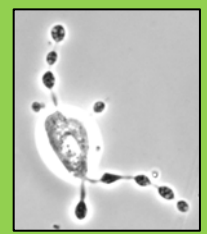
drugs for MR?



drugs for glioma?



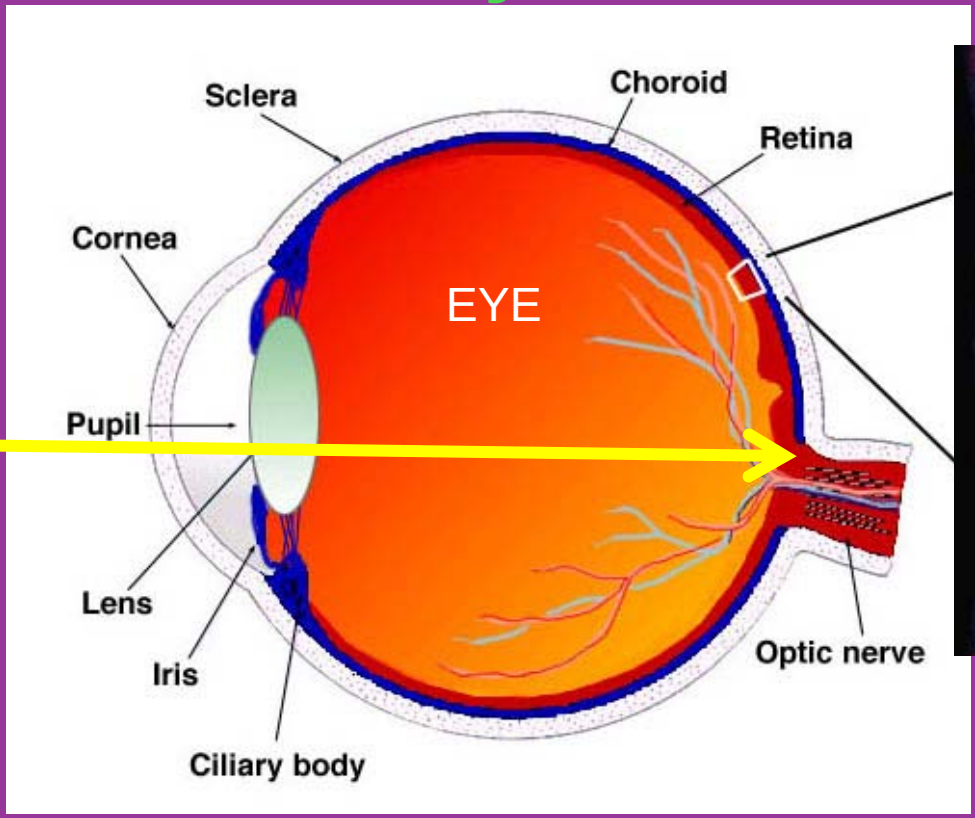
neurotoxic drugs

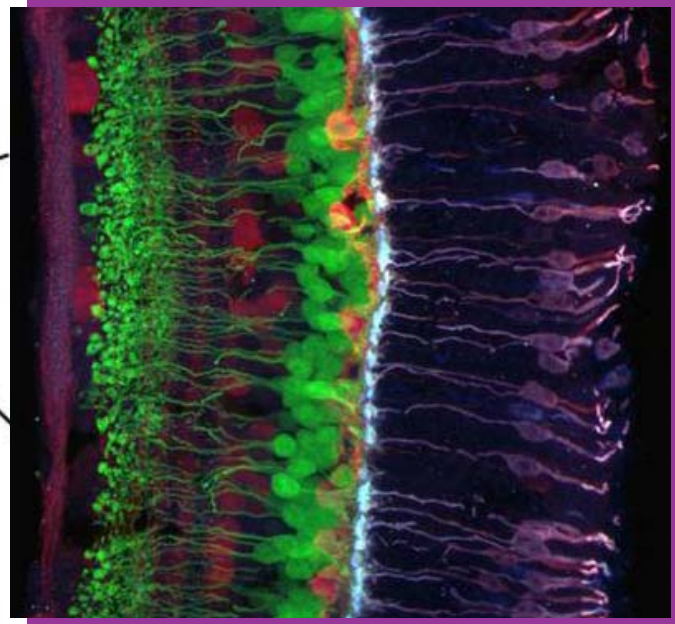


Coming soon:

- Cellular bioassays for neurotoxicity
- Genetic links between brain development & brain aging

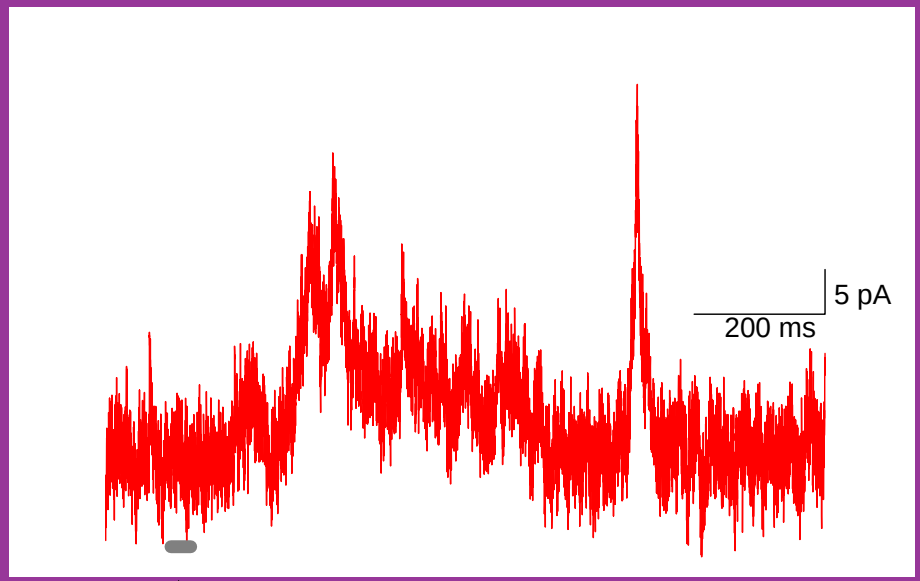
Eggers Laboratory of Retinal Neurophysiology





- The retina is the neural layer at the back of the eye responsible for sensing light
- It can be removed from the eye, intact and stimulated with light.
- Understanding retinal circuitry is important for understanding how we see and understanding what goes wrong in retinal diseases such as glaucoma and diabetic retinopathy.
- Also, the retina is a good neuronal model system that can be stimulated with its natural stimulus – light, while being experimentally manipulated.

Light-evoked inhibitory current



Light turned on

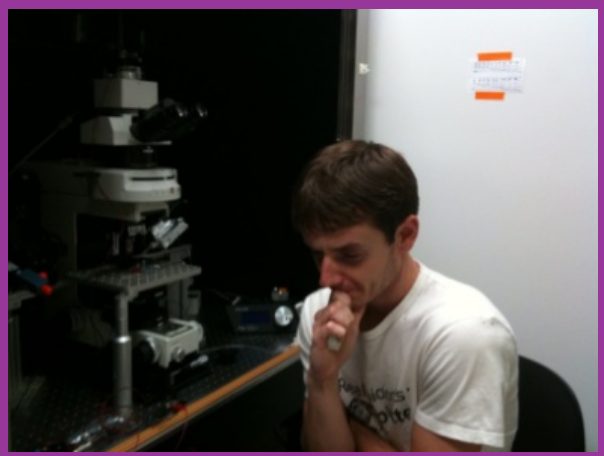
- We can record the electrical response to light from individual cells in the retina (like this bipolar cell shown here).

- During recordings these cells are filled with a dye and their morphology is identified.

- From this information you can make a circuit diagram of the retina correlating anatomy and function.

Erika Eggers
Assistant Professor Physiology
and Biomedical Engineering
Joined University of Arizona in 2009

Eggers Laboratory



Justin Klein –
Research Technician

Jilian Frieder & Dan Shtutman
Undergrad Researchers

Wilson Lab

Control of neuritogenesis, with emphasis on membrane trafficking

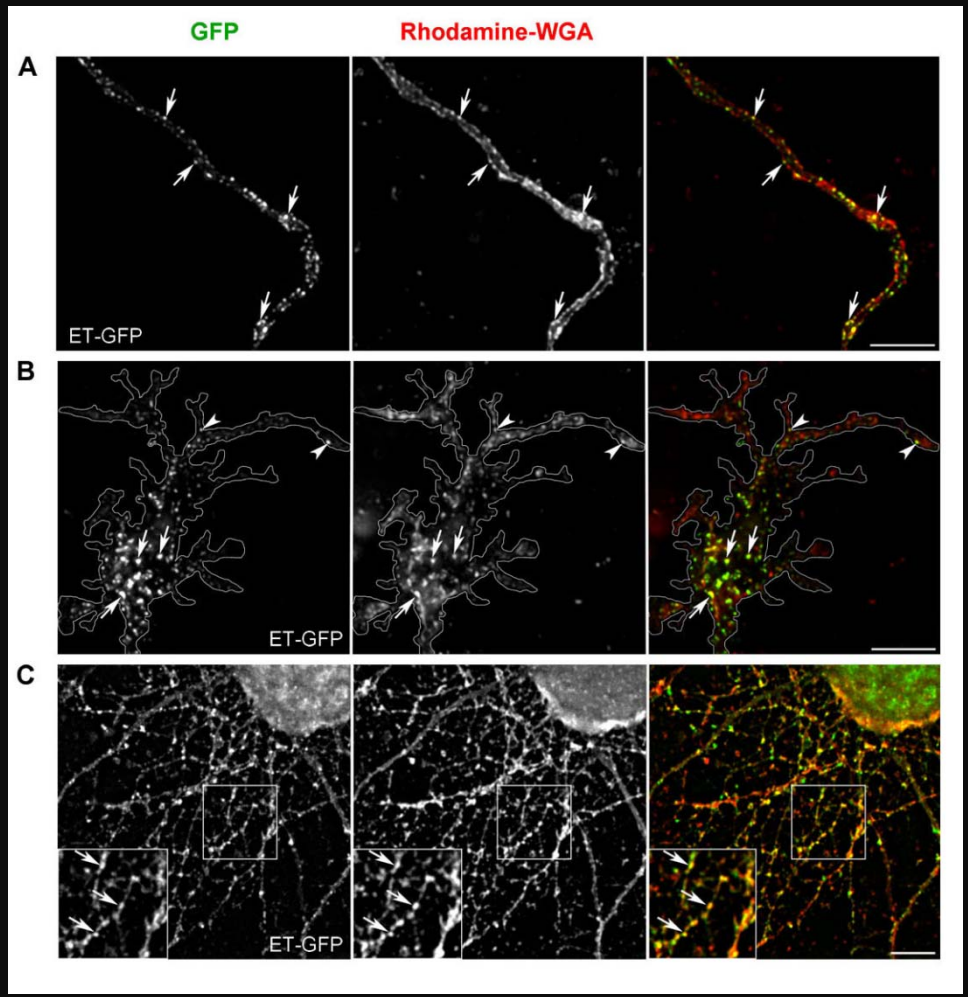
Jean Wilson

Department of Cell Biology and Anatomy

jeanw@email.arizona.edu

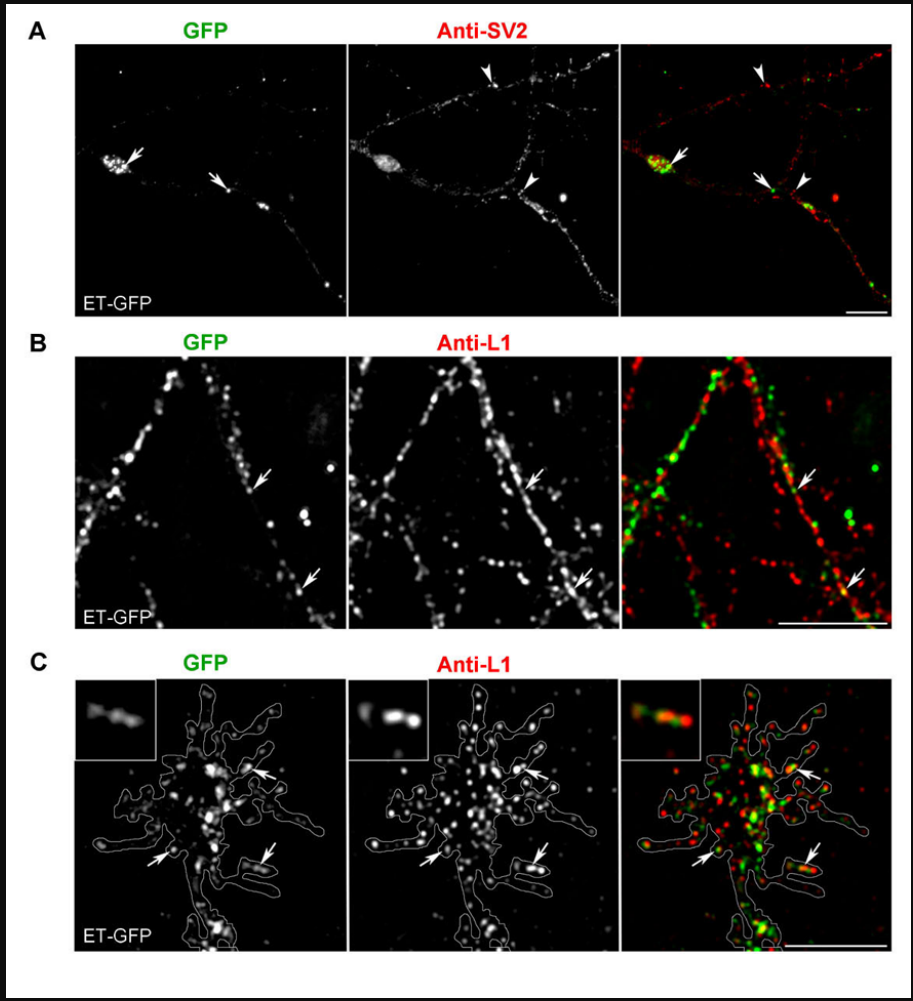
626-2557

Endosomal compartments in hippocampal neurons

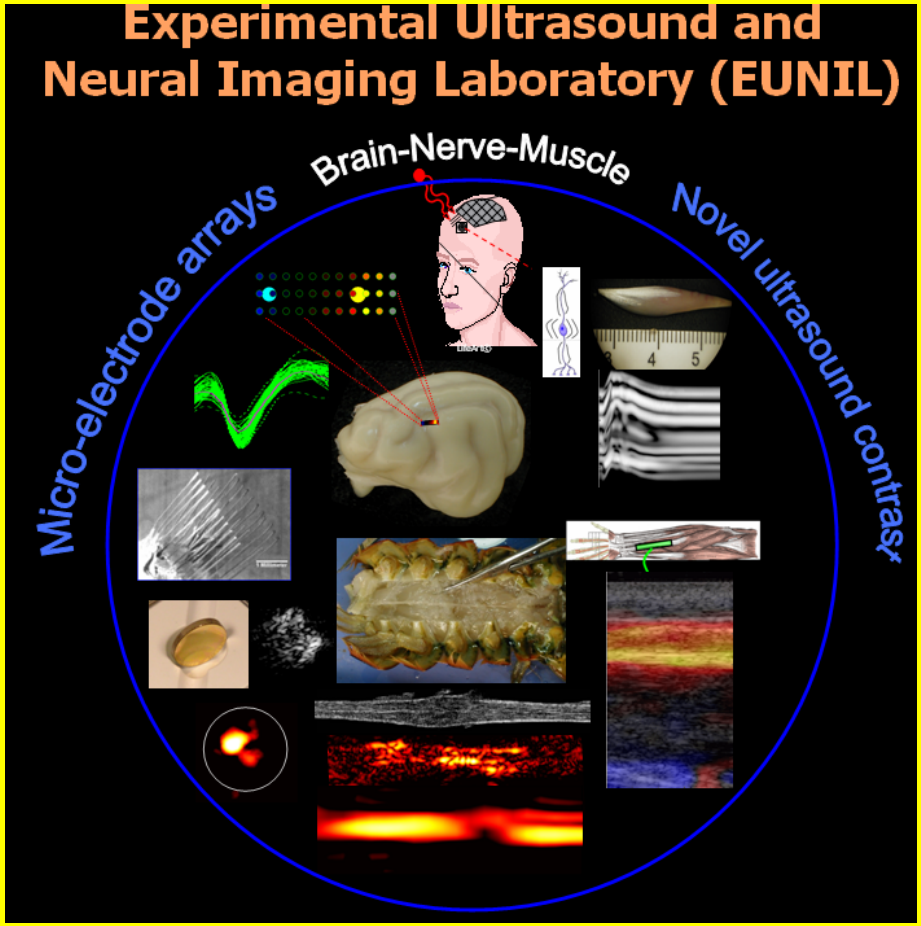


Internalized Rhodamine-WGA colocalizes with expressed endosomal marker (ET-GFP) in axons (A), growth cones (B), and dendrites (C).

Endosomal marker (ET-GFP) largely targets to compartments distinct from SV2 and L1 containing compartments.



These compartments are differentially regulated, allowing the cells to respond to different extracellular cues.



Russell Witte, PhD
Assistant Professor

Radiology
Biomedical Engineering
Optical Sciences
rwitte@radiology.arizona.edu

The Experimental Ultrasound and Neural Engineering Laboratory (EUNIL) develops novel imaging techniques for biomedical applications. These techniques exploit ultrasound, light and/or radio frequency and potentially impact a myriad of diseases from *epilepsy* to *cancer*.

- **Photoacoustic Imaging**
- **Smart Contrast Agents**
- **Novel Imaging of Bioelectricity**
- **Elasticity Imaging**

Russell Witte, PhD

Principal Investigator

Ragnar Olafsson, PhD

Postdoctoral Fellow

Zhaohui Wang, M.S.

Graduate Student

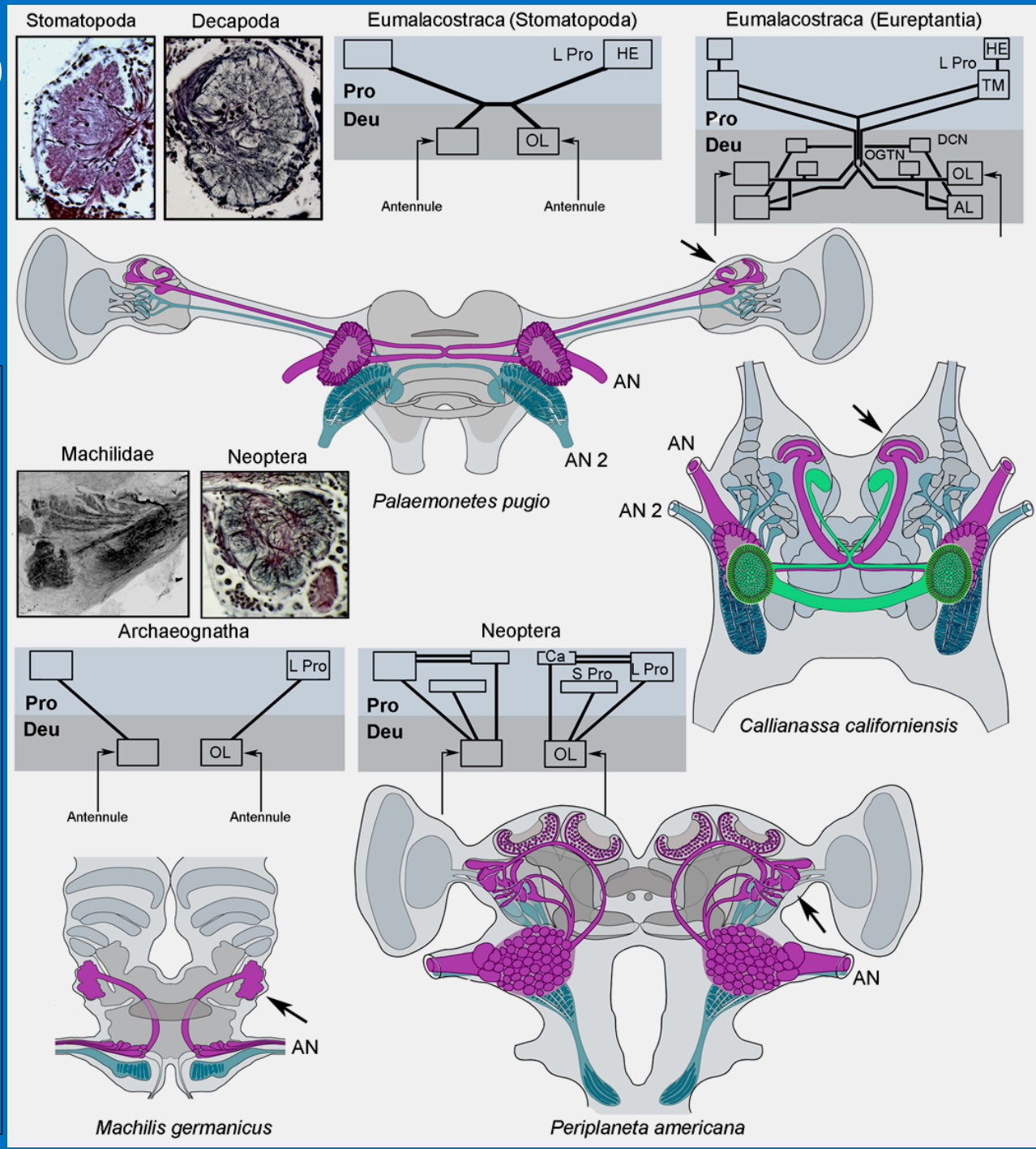
Leo Montilla, B.S.

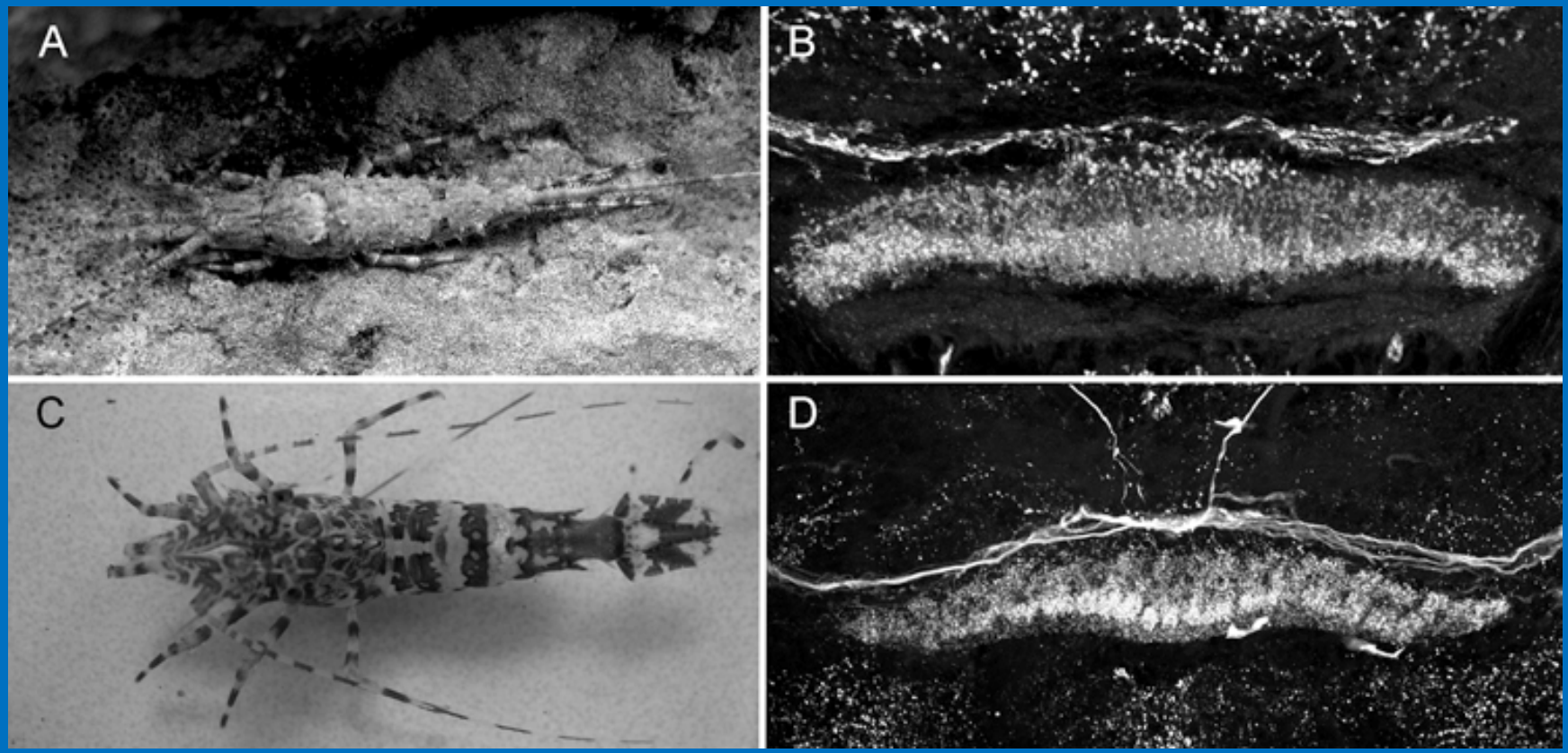
Graduate Student

Strausfeld Lab

ARLDN

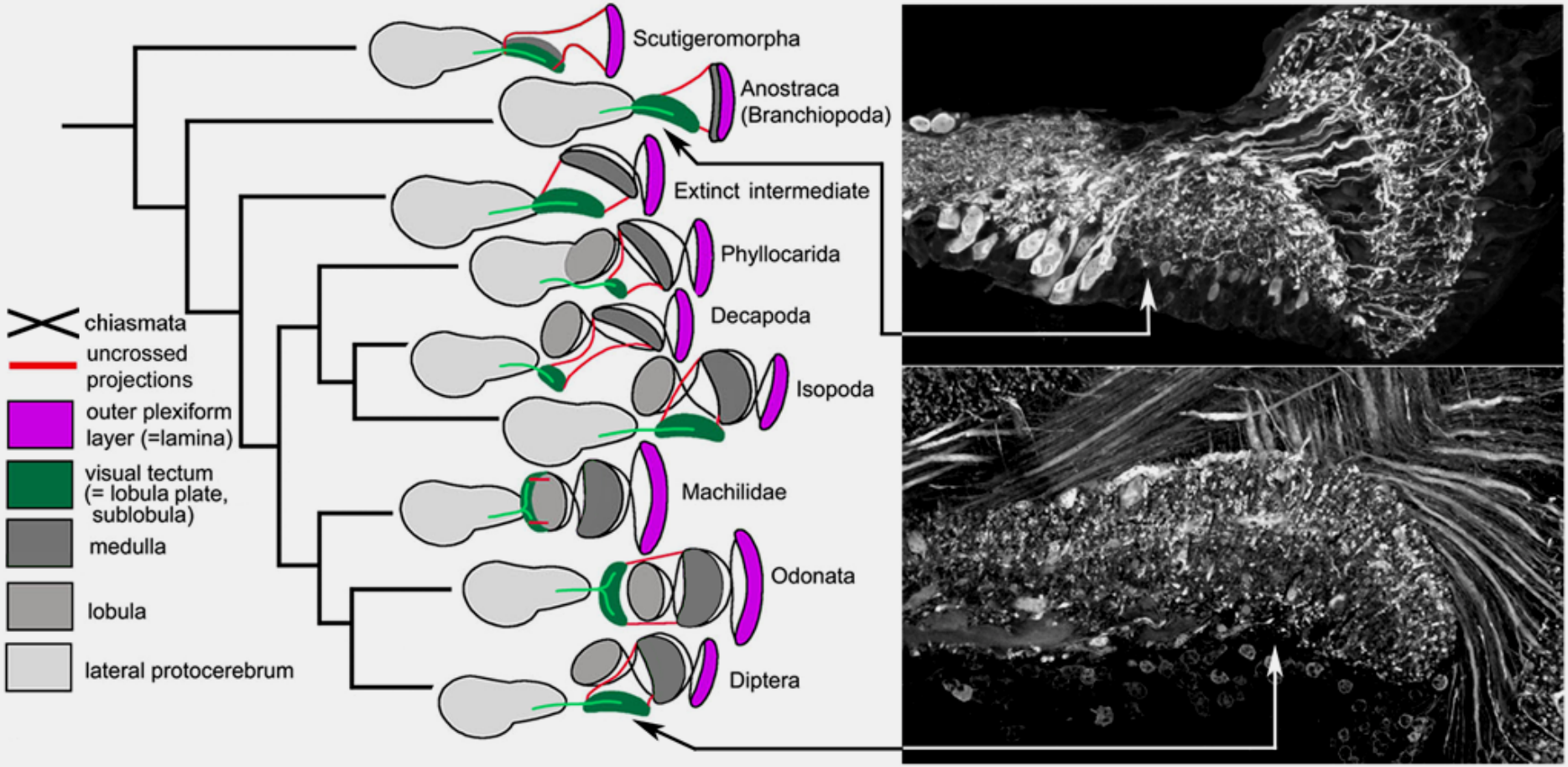
Common evolutionary traits of olfactory lobes and pathways in decapod crustaceans (*P. pugio*, *C. californiensis*) and insects (*M. germnanicus*, *P. americana*). The trend is towards elaboration in advanced group[s (e.g. Reptantia, Neoptera). However, commonalities of basal eumalcostracans and insects suggest common origins as do the glomerular structure of their olfactory lobes.





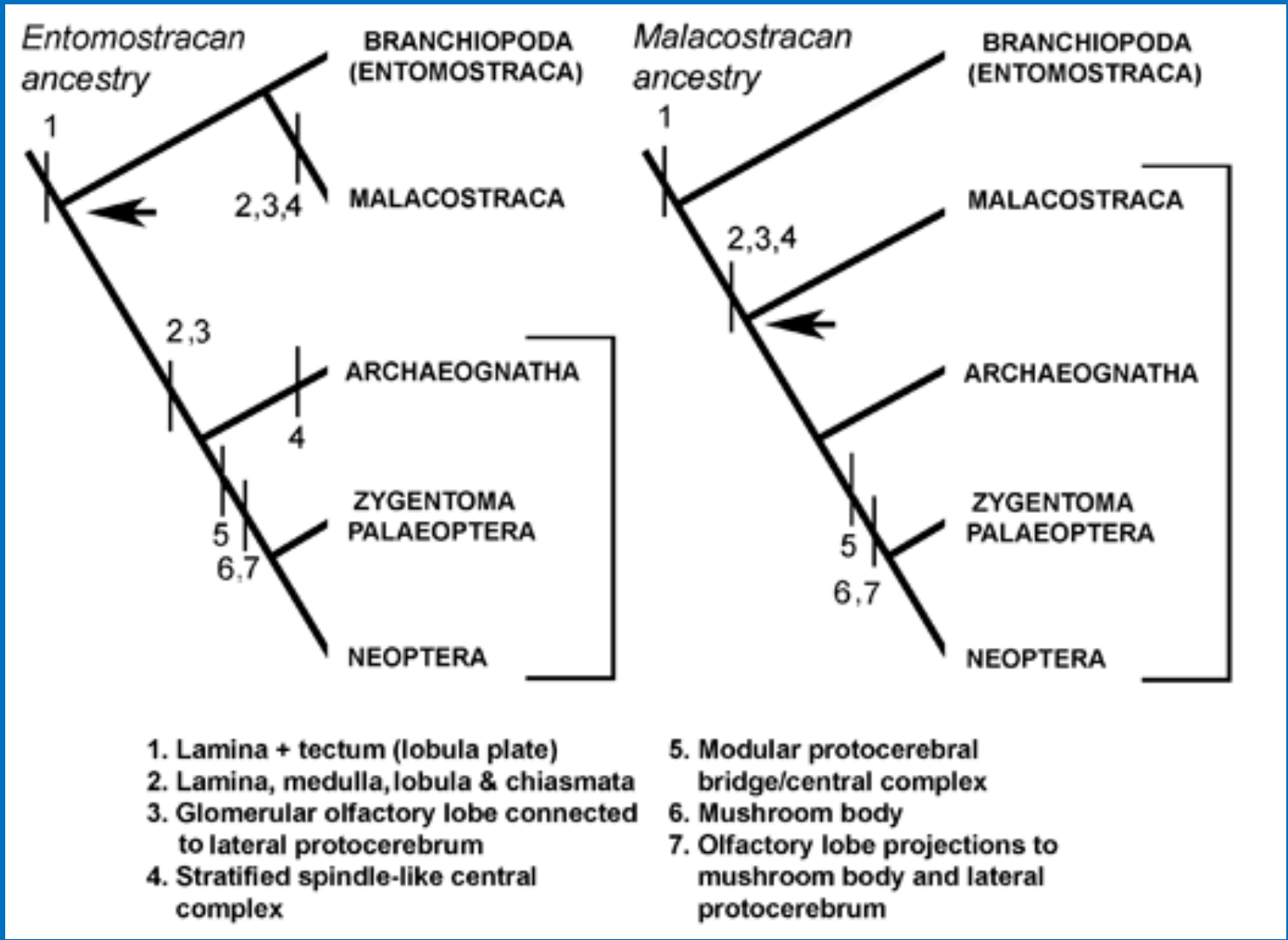
The most primitive insect (*Machilis*, A) possesses a mid-line central complex neuropil (B) that is essentially a “carbon copy” of that (D) typifying a decapod crustacean (C). Such neuroanatomical similarities strengthen the hypothesis that insects originate from a malacostracan stem lineage

Strausfeld Lab



Organization of optic lobe neuropils suggests closer affinities of insects and malacostracans than with entomostracans (Branchiopoda) or chilopoda (Scutigeromorpha). Notably, insects and crustaceans all have four nested optic lobe centers and two chiasma.

Strausfeld Lab



Neural characters 2-7 are shared by malacostracans and insects. An entomostracan origin of the Malacostraca (left) implies convergent evolution of characters 2, 3, 4. A common malacostracan-like ancestor of Malacostraca and Insecta supports one time evolution of these three characters.

Strausfeld Lab

Psychophysiology Laboratory

Department of Psychology

Faculty

John J.B. Allen, PhD

Post Doctoral Researchers

Jie Pu, PhD

Mike Cohen, PhD

Graduate Students

James Cavanagh

Andrew Bismark

Anya Povzer

Jay Sanguinetti

Laura Zambrano-Vazquez

Affiliated Researchers

Jamie Velo

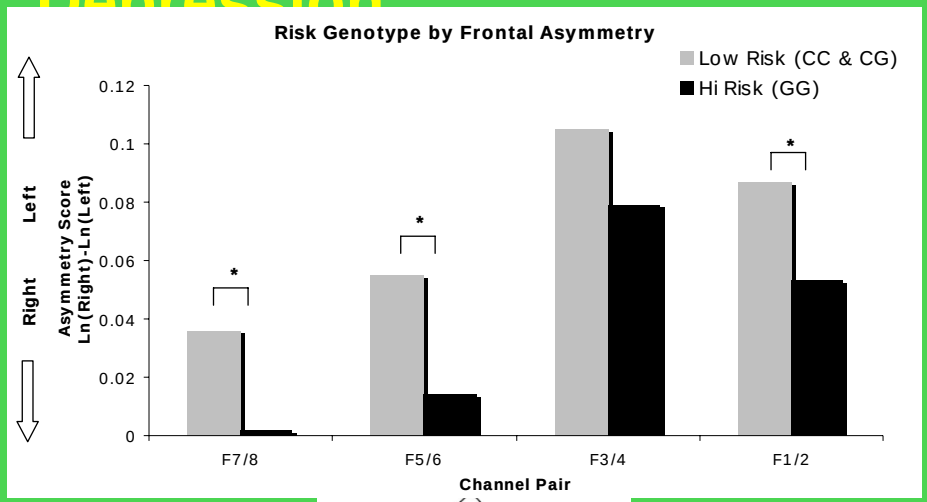
Adam Lester

Web: www.psychofizz.org

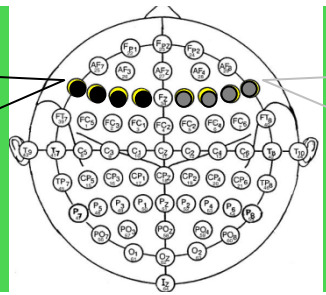
Using a wide variety of physiological measures, our laboratory's research focuses on the following major themes:

- Identifying risk for depression and anxiety disorders
- Examining how emotion and emotional disorders alter how individuals perceive and process information
- Examining processes of self-regulation, in both cognitive and emotional domains

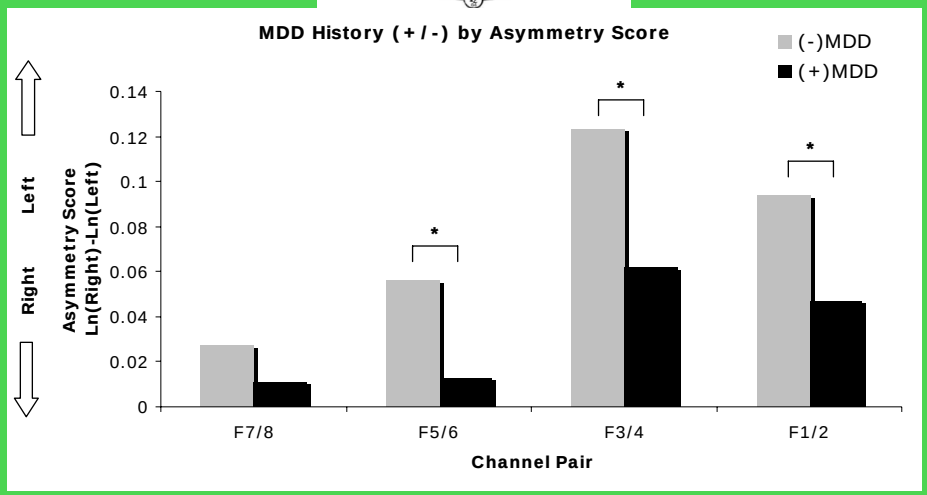
Genetic & Neurophysiological Associations with Depression



Approach Behaviors



Withdrawal Behaviors

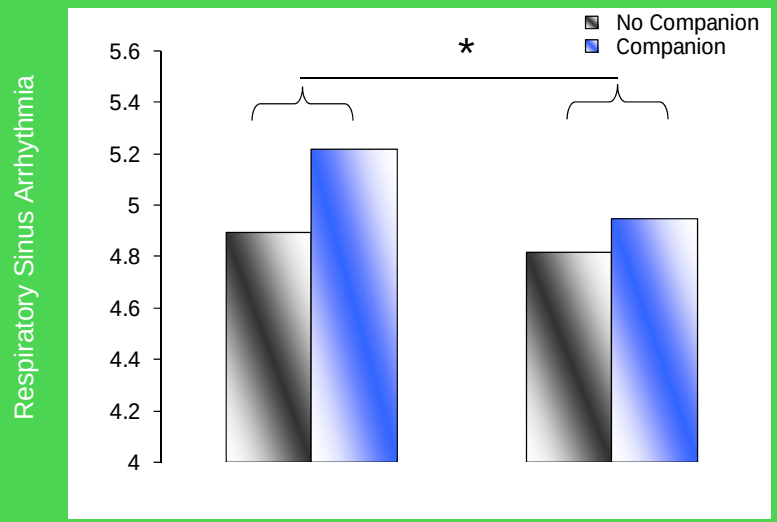


- A pattern of asymmetrical brain activity (called frontal EEG asymmetry) may index risk for depression. Lower panel shows that across 4 frontal brain regions, less left frontal activity is related to any lifetime history of major depression.
- Variations in the neurotransmitter Serotonin also are thought to relate to risk for depression
- We find that the pattern of brain asymmetry relates to a risk-related variation in a Serotonin receptor gene (5HT1A) as shown in the top panel across 4 frontal brain regions
- Genetically conveyed risk may operate via alterations in frontal brain activity to increase risk for major depression

Resting Cardiac Vagal Control and Quality of Partner Relationship in Women Newly Diagnosed with Breast Cancer

Figure 1. Physical touch is associated with reduction in RSA.

Note: * indicates a significant comparison ($p < .01$).



In the subsample of participants who brought companions to the visit (N =16), there was a trend for moderational effect of relationship quality, with those participants reporting better relationship quality showing less reduction in RSA during physical touch condition (F = 3.83 (1, 13), p = .07).

Figure 2. Higher RSA is associated with better relationship quality.

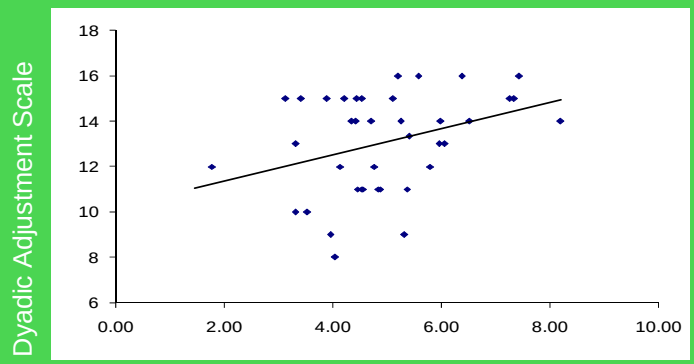
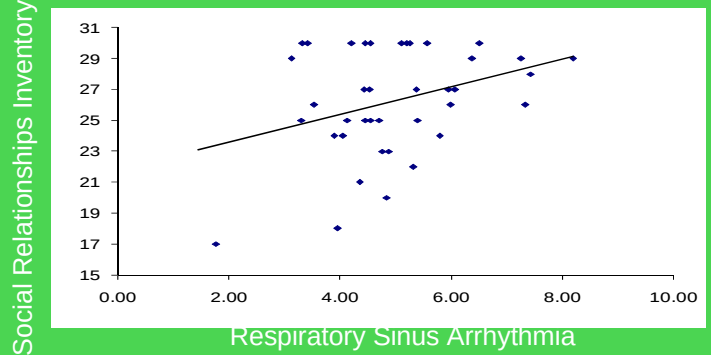


Figure 3. Higher RSA is associated with more positive partner interactions.



Povzner, A., Allen, J.J.B., O'Donnell, R., Brody, A.E., & Weihs, K.L. (2009). Resting Cardiac Vagal Control and Quality of Partner Relationship in Women Newly Diagnosed with Breast Cancer. *Psychophysiology*, *46*, S80

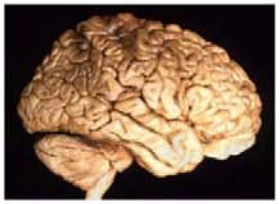
An introduction to ……..

Arizona Research Laboratories
Division of Neurobiology

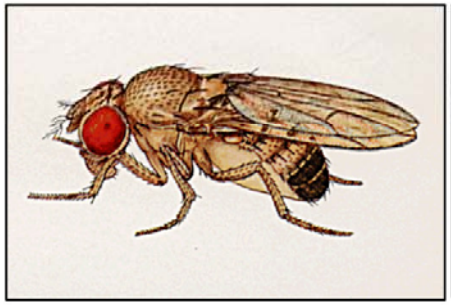
- Founded 1985
- Current faculty:
  - Norman Davis
  - Wulfila Gronenberg
  - John Hildebrand
  - Richard Levine
  - Alan Nighorn
  - Lynne Oland
  - Linda Restifo
  - Nicholas Strausfeld
  - Leslie Tolbert
  - Konrad Zinsmaier

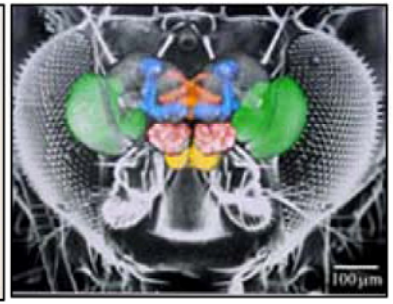
Joint-appointee faculty:
- Ralph Fregosi *(Physiology)*
- Andrew Fuglevand *(Physiology)*
- Katalin Gothard *(Physiology)*
- Charles Higgins *(Elec. & Computer Engineering)*
- Daniela Zarnescu *(Molecular & Cellular Biology)*

- ~100 personnel (students, postdoctoral associates, staff, faculty)
- 10 adjunct faculty (from other universities)

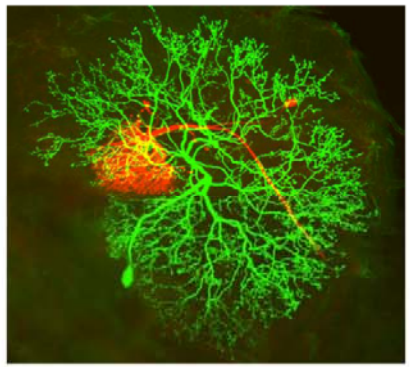


Examples of Research Themes in the ARL Division of Neurobiology



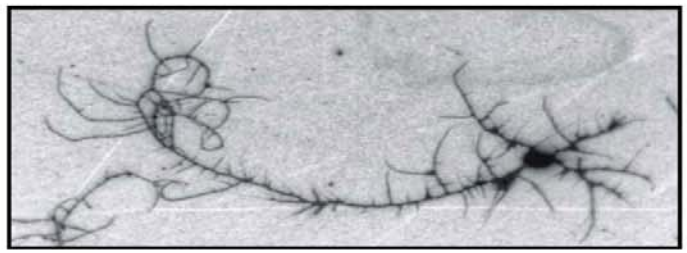


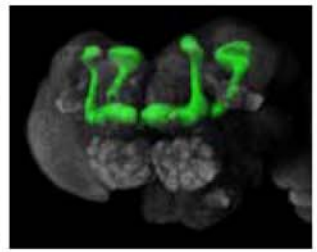
Insect nervous systems: experimental models for explorations of neural, glial & synaptic development & function



Neuroethology: sensory, motor, & integrative mechanisms underlying natural behavior

Insect-host interactions: sensory bases



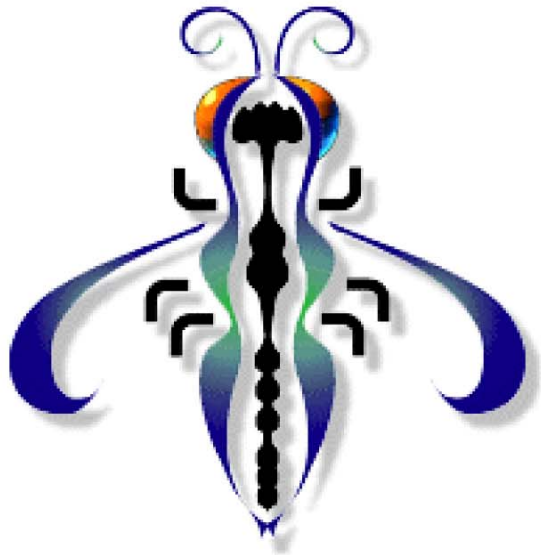


Neurogenetics: models of neural, muscular & mental disease

A short overview of the Hildebrand lab…….

We live in……..

Arizona Research Laboratories
Division of Neurobiology



Contact: John G. Hildebrand
Regents Professor of Neurobiology
jgh@neurobio.arizona.edu
http://neurobio.arizona.edu/faculty/hildebrand.html

Main research themes

Olfaction
- functional organization of glomeruli
- physiology & structure of olfactory neurons
- synaptic wiring & processing of olfactory information within & among glomeruli
- functional plasticity in olfactory pathway

Aaron Beyerlein, Hong Lei, Josh Martin, Carolina Reisenman, Jeff Riffell

Chemical ecology and behavior
- moth-hostplant interactions (feeding, oviposition)

Pablo Guerenstein, Carolina Reisenman, Jeff Riffell

Kissing bugs: insect vectors of human disease
- behavior and sensory neurobiology
- vector competence of local species

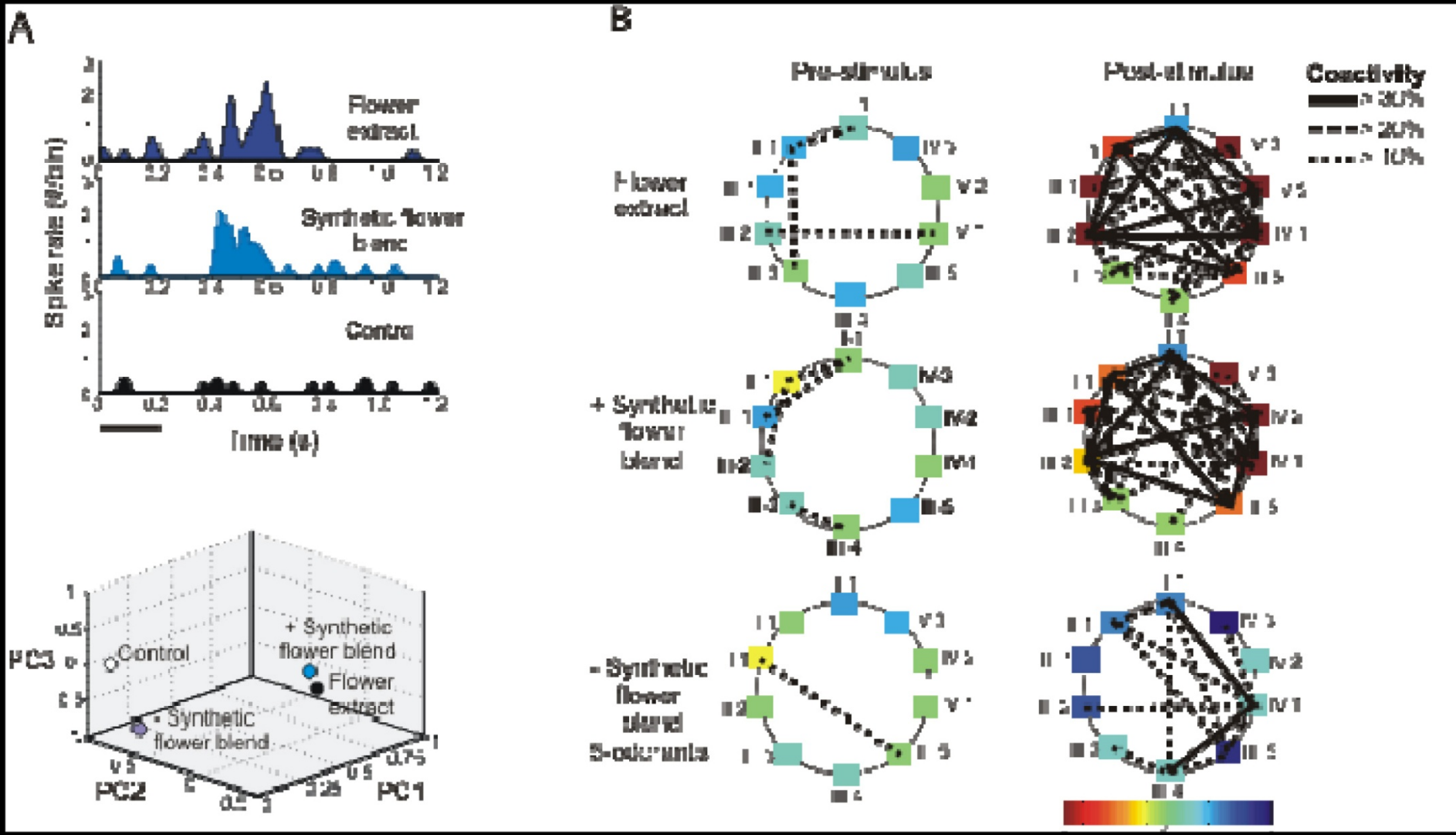
Teresa Gregory, Pablo Guerenstein, Kayla Peck, Carolina Reisenman,

CNS neurosecretion & neuromodulation

Norm Davis

Hybrid insect-MEMS systems ("cyborg moth project")
- neural control of flight
- development, surgical implantation, and testing of electronics for remote control of flight

Recent finding: Coincident firing of glomerular output neurons encodes salience, context, and/or behavioral significance of odor stimuli



Riffell *et al., in progress*

Hildebrand Lab

How Moths Do It: Probing the Brains Behind Natural, Olfaction-Dependent Behaviors (and some other stuff)

Current Group Members

Aaron Beyerlein *(Ph.D. Student GIDP–Insect Science)*
Eleni Constantopoulos *(Undergrad. Research Student)*
Norman Davis, Ph.D. *(Research Professor)*
Teresa Gregory *(Research Technician)*
Hong Lei, Ph.D. *(Staff Scientist)*
Josh Martin *(Ph.D. Student GIDP–Neuroscience)*
Kayla Peck *(Undergrad. Research Student)*
Carolina Reisenman, Ph.D. *(Assoc. Staff Scientist)*
Jeff Riffell, Ph.D. *(Research Associate)*
Alice Stone *(Senior Research Specialist)*

March 2008

Recent Lab Alumni

Andrew Dacks, Ph.D.
Pablo Guerenstein, Ph.D.
Jordanna Sprayberry, Ph.D.

Our Favorite Study Animals

Triatomine bug

Manduca sexta

Funding: **NIH (NIDCD, NINDS), NSF, USDA, DARPA, Monsanto**

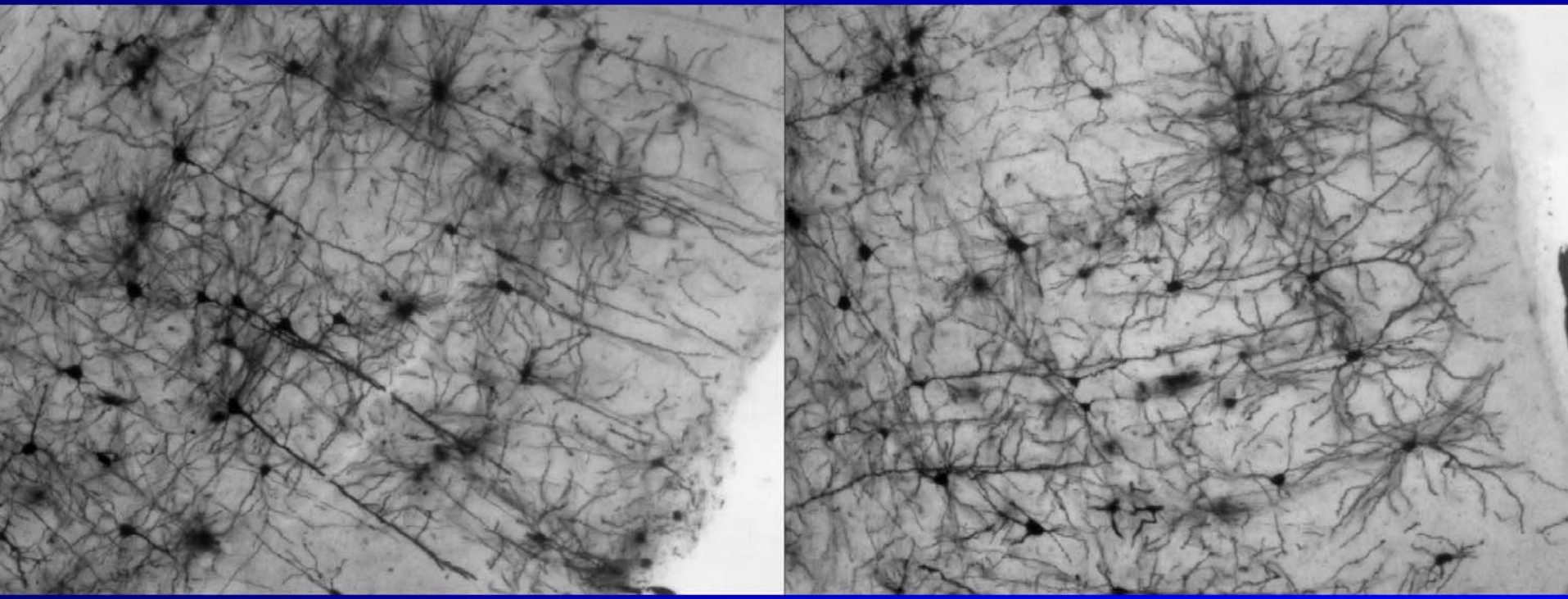
Developmental Neurogenetics Lab
Barrow Neurological Institute
Phoenix, AZ

Contact: Vinodh.Narayanan@chw.edu; 602-406-3130

Projects

- Overall Goal: Pathogenesis of Cognitive Impairment in Neurogenetic Disease
  - Rett syndrome
  - Neurofibromatosis 1 (NF1)
  - Tuberous Sclerosis Complex (TSC)
- Project 1: Characterization of a new model (MeCP2 A140V knock-in) of Rett syndrome
- Project 2: Role of Allelic Expression Imbalance in Variable Expressivity (TSC and NF1)
- Project 3: Axonal transport defects in the Nf1 k/o mouse (in vivo imaging)

Dendritic arbor in A140V mouse



A140V

WT

Garilyn Jentarra, PhD

Parkinson 's disease: New directions for the treatment

Torsten Falk[1] and Scott J. Sherman [1,2]

College of Medicine, University of Arizona, Departments of Neuro logy [1] and Physiology [2], Tucson, AZ 85724

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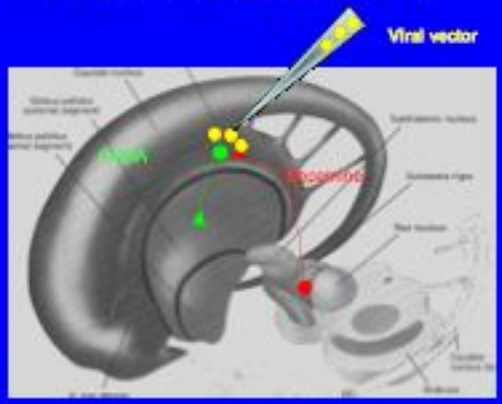
Our laboratory is focused on transiational research geared toward better therapies for Movement Disorders, especially Parkinson's disease.

Techniques commonly used in the lab are:

- *In vitro*: primary neuronal cell culture, immunocytochemistry, electrophysiology, molecular biology
- *In vivo*: stereotaxic injection into the striatum and *behavioral characterization of rat models of Parkinson's disease*

(A) Gene Therapy Approach

Restoring the balance of the basal ganglia circuitry that is disturbed in PD with a new type of gene therapy may treat PD symptoms with less side effects.



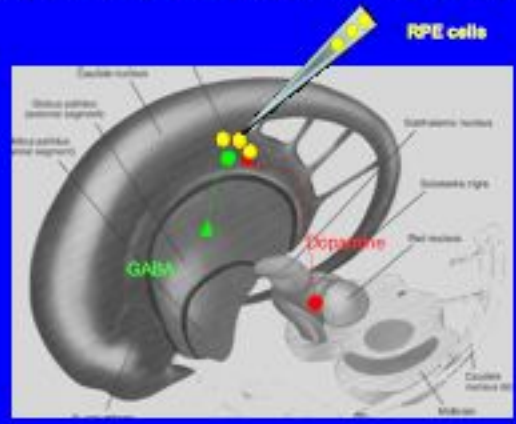
Parkinson's disease (PD) results from the progressive loss of dopamine-producing brain cells in an area named substantia nigra. While the reason for this process of cell death is unknown, the impact of their loss on the circuitry of another brain area, the basal ganglia, is well defined: in PD, there is an imbalance between the "*direct*" (GO) and "*indirect*" (NOGO) circuits in these basal ganglia with a relative over-activity of the *indirect* or NOGO pathway. This study is aimed at setting the stage for the development of a gene therapy that can be applied to selectively control the direct pathway of the basal ganglia, the pathway that has reduced activity in PD.

In order to increase neuronal activity in the direct pathway, we will employ a mutant K+ channel (the Kir2.3-AAA channel) that can knock down naturally occurring Kir channels. This is a powerful tool to reduce endogenous Kir currents and make neurons more excitable. With this gene transfer vectors, we will have the tool in hand to increase the excitability of the dopamine 1 receptor positive neurons, the cells that comprise the *direct or GO* pathway of the basal ganglia.

The knockdown of endogenous Kir channels is expected to alleviate the PD motor impairment by bringing the basal ganglia circuits back in balance.

(B) Cell -based Therapy Approach

Tissue -type Retinal Pigment Epithelial (RPE) cells may treat PD symptoms AND slow disease progression.



Transplantation of retinal pigment epithelial (RPE) cells in the basal ganglia could provide a novel cell-based therapy for Parkinson's disease, by providing a constant source of dopamine replacement via the melanin synthetic pathway enzyme tyrosinase. A human phase II trial is currently already under way to test the effect of RPE cell transplantation as a dopamine source on PD.

We now have demonstrated that human RPE cells can produce another effect, a neurotrophic effect (enhancement of growth).

These results indicate that transplantation of properly differentiated RPE cells could potentially provide a dual benefit in Parkinson's disease producing both dopamine and helping growth of the neurons of the basal ganglia, the brain area affected in PD.

DEPARTMENT OF BASIC MEDICAL SCIENCES

GHOSH LABORATORY

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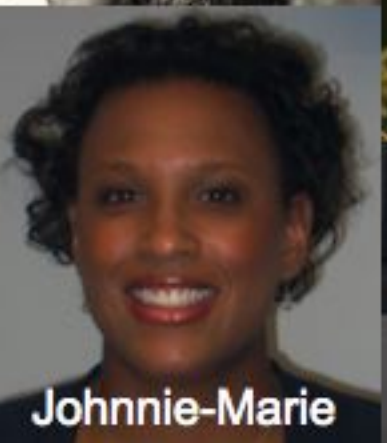
Josh


Robert


Johnnie-Marie


Sourav


Lisa

THE UNIVERSITY OF ARIZONA.
COLLEGE OF MEDICINE ▪ PHOENIX

in partnership with
Arizona State University

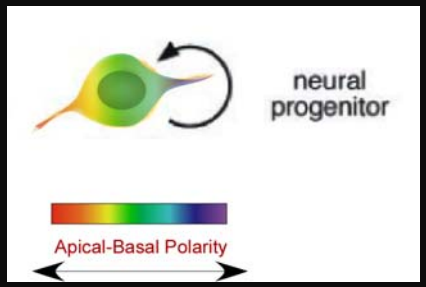
ASU ARIZONA STATE UNIVERSITY

TGEN

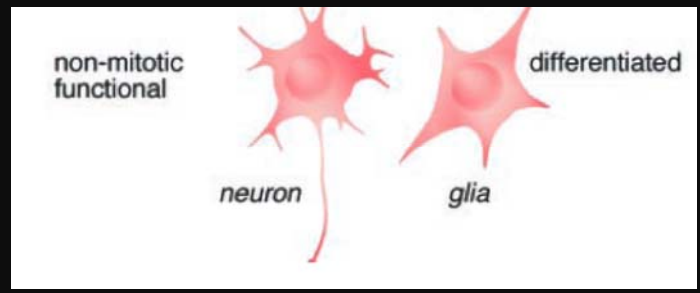
We study protein kinase genes that regulate apical-basal polarity (asymmetry of protein, RNA and organelles along an apical-basal axis within the cell) in neural stem cells.

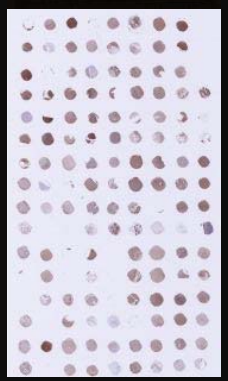
These genes are fundamental for neurodevelopment

Knowing how these genes function will lead us to
better therapeutic strategies for regenerative medicine



For example, we can induce adult Neural Stem Cells to proliferate and make neurons to replace lost ones





Abnormal function of these gene products are associated with brain tumors