

## CURRICULUM VITAE

Name: Abdallah Mtanios HAYAR, Ph. D.  
Date of birth: 1969  
Citizenship: Lebanese, American  
Marital status: Married to [Souraya](#) (Registered Nurse at the Myeolma Institute UAMS), Children: Tony (born on July 2010), Bernard (born on January 2016).  
Current position: Associate Professor (Tenure)  
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### AWARDED DEGREES

1987: Baccalaureate in Experimental Sciences, Collège des Frères, Tripoli, Lebanon.  
1987-91: Bachelor of Sciences (B.S.) major Biology, [American University of Beirut](#), Beirut, Lebanon.  
1991-92: *Maîtrise de Physiologie Animale*, University Louis Pasteur, Strasbourg, France.  
1992-93: DEA (M.S.) *de Neurobiologie et Physiologie des Systèmes de Communication*. University Louis Pasteur, Strasbourg, France. Director: Prof. Ken Marshall.  
1993-96: Ph.D. in Neurosciences, Department of Physiology, [University Louis Pasteur](#), Strasbourg, France. Director: [Prof. Paul Feltz](#).

**Thesis title:** GABAergic and noradrenergic responses in silent and spontaneously active neurons of the rat rostral ventrolateral medulla *in vitro*. **Committee:** Profs. Alan North, Pascal Bousquet, Jean Champagnat, Rémy Schlichter.

### POSITIONS

1993 : “Cadre de Laboratoire” for 3 months at Sanofi Research, Montpellier, France.  
1997-1999: Research Associate, Dept. of Pharmacology, University of Virginia.  
1999-2003: Research Assistant Professor, Dept. of Anatomy & Neurobiology, University of Maryland.  
2003-2005: Research Assistant Professor, Dept. of Anatomy & Neurobiology, University of Tennessee.  
2006-2008: Associate Professor (Tenure Track), Dept. Neurobiology & Developmental Sciences, University of Arkansas for Medical Sciences.  
2008 (July): Associate Professor (Tenure), Dept. Neurobiology & Developmental Sciences, University of Arkansas for Medical Sciences.

## **LANGUAGES**

English (fluent), French (fluent), Arabic (mother tongue).

## **AFFILIATIONS**

- Society for Neuroscience (U.S.A.), member since 1996.
- Arkansas Chapter of the Society for Neuroscience, member since 2008.
- Association for Chemoreception Sciences (AChemS), member since 1999.
- American Physiological Society (U.S.A.), member (1998-2005, 2014-).
- Société des Neurosciences (France), member (1994-2002).
- International Society for Autonomic Neuroscience, member (1998-2002).
- Graduate Faculty of the University of Maryland Graduate School, member (2001-2003).
- Washington-Baltimore Computational Neuroscience Interest Group, member (2001-2003).
- Graduate Faculty of the University of Arkansas for Medical Sciences Graduate School, member since 2007.

## **HONORS & AWARDS**

- 2015: Nominee, Excellence in Diversity and Inclusion award
- 2010 & 2011: Nominee, Educational Technology Excellence Award (Univ. of Arkansas for Medical Sciences)
- 2010: Nominee, “Secretary” for the Association for Chemoreception Sciences (AChemS)
- April (2006): Young Investigator Award for Research in Olfaction. Prize: \$2000.
- France (1994-1996): University Louis Pasteur scholarship for international doctoral students.
- Lebanon (1988-1991): Fares Foundation scholarship for undergraduate studies.

## **FUNDING / RESEARCH PROJECTS:**

### **Current Funding support**

**1- NSF 1457888** (PI: Steve Stanley, 25% effort)

08/01/2017-07/31/2020

NSF

Title: “RII Track-1: Arkansas Advancing and Supporting Science, Engineering, and Technology (ASSET) III - Multifunctional and Tunable Nanostructured Surfaces”

The primary focus of our thrust is to investigate the viability and differentiation of neural stem cell (NSC) cultures grown on different nanoparticle matrices. The goal is to find an optimal biocompatible surface that promotes cell propagation and differentiation into neurons.

Role: Thrust co-lead

**2- Cancer research proposal** (PI: Abdallah Hayar, 10% effort)

02/01/2016 – 01/31/2019

Seeds of Science Award                      Award amount current year: \$10,000

Title: “Investigating chemotherapeutic drugs using electrophysiological and imaging approaches”

The overall objective of this study is to determine if specific chemotherapeutic agents affect the physiological properties of neurons and whether they can induce neuronal damage by excessively increasing the spiking and synaptic activity of neurons leading to excitotoxicity.

Role: PI

**3- Stroke Grant Proposal** (PI: Abdallah Hayar, 10% effort)

05/01/2017 – 04/30/2019

Fund to Cure Stroke

Title: “Mechanisms of neuroprotection of oxygen carrier molecules in oxygen-deficient conditions such as stroke”

We propose to test dodecafluoropentane and other potential oxygen carrier molecules on the electrophysiological properties of neurons and synaptic transmission in brain slices that are subjected to different hypoxic conditions. The results will help guide clinical trials toward finding the best treatment to protect the brain against hypoxic injury after a stroke.

Role: PI

**4- P30GM110702** (PI: Edgar Garcia-Rill, 5% effort) 05/01/2017 – 04/30/2019

NIH

Title: “Center for Translational Neurosciences”

The major goals of this project are to implement a Career Development Program for five Project Principal Investigators (PIs) who are close to nationally competitive levels using grant support and mentoring activities undertaken by established investigators.

Role: Electrophysiology Core Director

**Recently submitted grants (since 2017)**

**1- R21NS104952** submitted on 2/15/2017 (PI: Abdallah Hayar, 50% effort) 09/01/2017 – 08/31/2019

NIH

Title: “Modulation of synchronous oscillations in dorsal raphe by antidepressants”

The main objective of this study to form a translational research team that includes basic and clinical scientists who use cutting-edge neuroscience techniques to investigate conceptually novel leads into how depression develops and how it can be successfully treated. This research project will provide insight into the fundamental mechanisms leading to alterations in neuronal oscillatory synchrony in depression and how it can be modulated by newly-developed, fast-acting antidepressants.

Role: PI

**2- R21MH117391** submitted on 10/12/2017 (PI: Abdallah Hayar, 50% effort) 07/01/2018 – 06/30/2020

NIH

Title: “A direct neuronal assay for testing a potential link between artificial food dyes and hyperactivity in children”

Our goal is to identify those culprit food dyes that can potentially induce neurotoxic effects and potentially alter behavior. This will allow us to inform the public about their potential impact on mental health and request from food manufacturers to avoid using them because they might constitute a potential neurobehavioral hazard.

Role: PI:

**3- R21DA047525** submitted on 2/15/2018 (PI: Abdallah Hayar, 25% effort) 09/01/2018 – 08/31/2020

NIH

Title “Heart rhythm and cardiorespiratory coupling in conscious restrained mice: Effect of ketamine”

Our goal is to develop a simple method of monitoring cardiorespiratory pattern and HRV, which reflects autonomic regulation, and it could serve as a good approach to dissect the mechanisms by which ketamine induces antidepressant action.

Role: PI

**4- P30GM110702 CTN pilot study** submitted on 12/1/2017 (PI: Abdallah Hayar, 25% effort) 05/01/2018 – 04/30/2019

NIH

\$50,000/ 1 year

Role: PI

Title: “Testing for a potential link between artificial food dyes and hyperactivity in children”

Our goal is to identify those culprit food dyes that can potentially induce neurotoxic effects and potentially alter behavior. This will allow us to inform the public about their potential impact on mental health and request from food manufacturers to avoid using them because they might constitute a potential neurobehavioral hazard.

Past funding

1. **Center for Translational Neuroscience Recruitment Funds:** \$100,000 08/1/2006 - 07/31/2007.
2. **239 G1-31595-01-E: UAMS Tobacco Settlement Funds:** \$75,000 07/1/2006 - 06/30/2007.
3. **239 G1-33648-01: UAMS Tobacco Settlement Funds:** \$150,000 07/01/2008 – 06/30/2009.
4. **R03DC006356-04** (PI: Abdallah Hayar) 05/1/2004 – 04/30/2009 3.00 calendar  
NIH/NIDCD \$50,000/year  
Role: PI  
Title: “Synchronous bursting among juxtglomerular neurons” ([NIH RePORTER Abstract](#)).  
The goal of this project is to provide new insight into the intrinsic synaptic organization of the glomeruli and the role of glomerular circuitry in olfactory coding
5. **R01 DC007123-06** (PI: Abdallah Hayar) 07/01/2005 – 06/30/2012 5.36 calendar  
NIH / NIDCD \$187,171/year  
Role: PI  
Title: “External tufted cells coordinate olfactory bulb activity” ([NIH RePORTER Abstract](#)).  
The major goal of this project is to determine the role of external tufted cells in coordinating the activity of glomerular interneurons and output mitral cells via chemical and electrical synapses.
6. **231 G1–35435–01:** (PI: Abdallah Hayar) 01/01/2009 – 12/31/2010 0.00 calendar  
Arkansas Bioscience Institute (ABI) \$38,500/year, UAMS costs: \$14,500.00/year  
Role: PI, co-PI: Roger Buchanan, Arkansas State University  
Title: “Novel treatment for smoking dependence and relapse”.  
The goal of this study is to determine how repetitive trans-cranial magnetic stimulation (rTMS) alters the effects of chronic exposure to cigarette smoke on the rat P13 potential.
7. **P20 GM103425-09** (PI: Edgar Garcia-Rill) 08/01/2009 – 04/30/2014 3.00 calendar  
NIH/National Center for Research Resources \$1,229,518/year  
Role: Electrophysiology Core Director  
Title: “Center for Translational Neuroscience” ([NIH RePORTER Abstract](#)).  
The major goals of this project are to implement a Career Development Program for five Project Principal Investigators (PIs) who are close to nationally competitive levels using grant support and mentoring activities undertaken by established investigators.
8. **R01HL097107-01:** (PI: Sung Rhee) 04/01/2010–03/31/2015, 1.20 calendar  
NIH/NHLBI \$250,000/year  
Role: co-I from 04/01/2010–06/31/2012  
Title: “PSD95 scaffolding of vascular K<sup>+</sup> channels in hypertension” ([NIH RePORTER Abstract](#)).  
This project will investigate a novel scaffolding molecule in the muscle cells of small cerebral arteries that may ensure that potassium channels are expressed in adequate numbers and in the right location in the muscle cells of cerebral arteries to optimize blood flow to the brain.
9. **R01 DC007876-02** (PI: Kathryn Hamilton) 04/01/2009 – 03/31/2012 2.00 calendar  
NIH / NIDCD \$41,400/year  
Role: PI on a subcontract with Louisiana State University.  
Title: “Contribution of EPL interneurons to olfactory processing” ([NIH RePORTER Abstract](#)).

The goal of this project is to characterize the cell types of this external plexiform layer using modern, quantitative anatomical methods and electrophysiological recording methods and to understand the contributions of the cells in this layer to olfactory discrimination.

10. **R01 NS020246-21** (PI: Edgar Garcia-Rill) 12/01/2008 – 11/30/2013 2.40 calendar  
NIH / NINDS \$250,000/year

Role: Co-I from 12/01/2008 – 6/30/2012

Title: “Central Modulation of Rhythms” ([NIH RePORTER Abstract](#)).

The long-term objective of this project is to investigate the mechanisms controlling changes in state mediated by brainstem, particularly mesopontine, mechanisms. The development of neurochemical control of local, ascending and descending pedunculopontine nucleus projections is the main area of study.

11. **P30GM110702 CTN pilot study** (PI: Abdallah Hayar) 05/01/2016 – 04/30/2017 3.00 calendar  
NIH \$50,000/ 1 year

Role: PI

Title: “A mouse model to study the cellular mechanisms involved in dystonia”

This research project will provide insight into the fundamental mechanisms leading to dystonia and it will help us develop strategies to cure or more effectively treat people who are affected by this neurological disorder.

## PUBLICATIONS

**Note:** The number of times each reference was cited was updated on 11/26/2015 using Web of Science database.

- Alexander TC, Kiffer F, Groves T, Anderson J, Wang J, **Hayar A**, Chen MT, Rodriguez A, Allen AR. Effects of thioTEPA chemotherapy on cognition and motor coordination. *Synapse* (in press).
- Dobretsov M, **Hayar A**, Kockara NT, Kozhemyakin M, Light KE, Patyal P, Pierce DR, Wight PA. A Transgenic Mouse Model to Selectively Identify  $\alpha 3$  Na,K-ATPase Expressing Cells in the Nervous System. *Neuroscience*. 2018 Jul 19. pii: S0306-4522(18)30493-7. ([Abstract](#))
- Dobretsov M, Petkau G, **Hayar A**, Petkau E. Clock Scan Protocol for Image Analysis: ImageJ Plugins. *J Vis Exp*. 2017 Jun 19;(124). doi: 10.3791/55819. ([Abstract](#))
- Light KE, **Hayar A**, Pierce DR (2015). Electrophysiological and immunohistochemical evidence for an increase in GABAergic inputs and HCN channels in Purkinje Cells that survive developmental ethanol exposure. *Cerebellum* 14(4):398-412. ([Abstract](#)) ([PDF, 6176 KB](#)). Impact factor: 2.8, cited 0 time.
- Lin XB, Pierce DR, Light KE, **Hayar A** (2013). The fine temporal structure of the rat licking pattern: What causes the variability in the interlick intervals and how is it affected by the drinking solution? *Chem Senses* 38:685-704. ([Abstract](#)) ([PDF, 15374 KB](#)). Impact factor: 3.2, cited 3 times.
- Simon C, **Hayar A**, Garcia-Rill E (2012). Developmental changes in glutamatergic fast synaptic neurotransmission in the dorsal subcoeruleus nucleus. *Sleep* 35:407-417. ([Abstract](#)) ([PDF, 804 KB](#)). Impact factor: 5.9, cited 1 time.
- Simon C, **Hayar A**, Garcia-Rill E (2011). Responses of Developing Pedunculopontine Neurons to Glutamate Receptor Agonists. *J Neurophysiol* 105:1918-1931. ([Abstract](#)) ([PDF, 4434 KB](#)). Impact factor: 3.8, cited 3 times.
- Pierce DR, **Hayar A**, Williams DK, Light KE (2011). Olivary climbing fiber alterations in PN40 rat cerebellum following postnatal ethanol exposure. *Brain Res* 10:54-65. ([Abstract](#)) ([PDF, 1477 KB](#)). Impact factor: 2.5, cited 6 times.

9. Pierce DR, **Hayar A**, Williams DK, Light KE (2010). Developmental Alterations in Olivary Climbing Fiber Distribution Following Postnatal Ethanol Exposure in the Rat. *Neuroscience* 169:1438-1448. ([Abstract](#)) ([PDF, 1753 KB](#)). Impact factor: 3.5, cited 6 times.
10. Simon C, Kezunovic N, Ye M, Hyde J, **Hayar A**, Williams DK, Garcia-Rill E (2010). Gamma band unit activity and population responses in the pedunculopontine nucleus (PPN). ([Abstract](#)) ([PDF, 4643 KB](#)). *J Neurophysiol* 104:463-474. Impact factor: 3.8, cited 24 times.
11. **Hayar A**, Charlesworth A, Garcia-Rill E (2010). Oocyte triplet pairing for electrophysiological investigation of gap junctional coupling. *J Neurosci Methods* 188:280-286. ([Abstract](#)) ([PDF, 1054 KB](#)). Impact factor: 2.5, cited 0 time.
12. Ye M, **Hayar A**, Strotman B, Garcia-Rill E (2010). Cholinergic modulation of fast synaptic transmission of pedunculopontine thalamic projecting neurons. *J Neurophysiol* 103:2417-2432. ([Abstract](#)) ([PDF, 5388 KB](#)). Impact factor: 3.8, cited 17 times.
13. Dong HW, **Hayar A**, Callaway J, Yang X-H, Nai Q, Ennis M (2009) Group I mGluR activation enhances Ca<sup>2+</sup>-dependent nonselective cation currents and rhythmic bursting in main olfactory bulb external tufted cells. *J Neuroscience* 29:11943-11953. ([Abstract](#)) ([PDF, 1836 KB](#)). Impact factor: 7.9, cited 15 times.
14. Heister D, **Hayar A**, Garcia-Rill E (2009) Cholinergic modulation of GABAergic and glutamatergic transmission in the dorsal Subcoeruleus: mechanisms for REM sleep control. *Sleep* 32:1135-1147. ([Abstract](#)) ([PDF, 469 KB](#)) Impact factor: 5.9, cited 13 times.
15. Dong HW, Heinbockel T, Hamilton KA, **Hayar A**, Ennis M (2009) Metabotropic glutamate receptors and dendrodendritic synapses in the main olfactory bulb. *Ann N Y Acad Sci* 1170:224-238. ([Abstract](#)) ([PDF, 539 KB](#)). Impact factor: 2.6, cited 5 times.
16. Ye M, **Hayar A**, Garcia-Rill E (2009) Cholinergic responses and intrinsic membrane properties of developing thalamic parafascicular neurons. *J Neurophysiol* 102:774-785. ([Abstract](#)) ([PDF, 3485 KB](#)) Impact factor: 3.8, cited 4 times.
17. Nai Q, Dong HW, **Hayar A**, Linster C, Ennis M (2009) Noradrenergic regulation of GABAergic inhibition of main olfactory bulb mitral cells varies as a function of concentration and receptor subtype. *J Neurophysiol* 101:2472-2484. ([Abstract](#)) ([PDF, 1033 KB](#)) Impact factor: 3.8, cited 26 times.
18. **Hayar A**, Gu C, Al-Chaer ED (2008) An improved method for patch clamp recording and calcium imaging of neurons in the intact dorsal root ganglion in rats. *J Neurosci Methods* 173:74-82. ([Abstract](#)) ([PDF, 943 KB](#)). Impact factor: 2.5, cited 8 times.
19. Garcia-Rill E, Charlesworth A, Heister DS, Ye M, **Hayar A** (2008) The developmental decrease in REM Sleep: The role of transmitters and electrical coupling. *Sleep* 31:673-690. ([Abstract](#)) ([PDF, 1227 KB](#)). Impact factor: 5.9, cited 35 times.
20. Karpuk N, **Hayar A** (2008) Activation of postsynaptic GABAB receptors modulates the bursting pattern and synaptic activity of olfactory bulb juxtglomerular neurons. *J Neurophysiol* 99:308-319. ([Abstract](#)) ([PDF, 322 KB](#)). Impact factor: 3.65, cited 7 times.
21. Garcia-Rill E, Heister DS, Ye M, Charlesworth A, **Hayar A** (2007) Electrical coupling: novel mechanism for sleep-wake control. *Sleep* 30:1405-1414. ([Abstract](#)) ([PDF, 217 KB](#)). Impact factor: 4.47, cited 50 times.
22. **Hayar A**, Ennis M (2007) Endogenous GABA and glutamate finely tune the bursting of olfactory bulb external tufted cell. *J Neurophysiol* 98:1052-1056. ([Abstract](#)) ([PDF, 209 KB](#)). Impact factor: 3.8, cited 12 times.
23. Dong HW, **Hayar A**, Ennis M (2007) Activation of metabotropic glutamate receptors (mGluRs) enhances synaptic inhibition of olfactory bulb mitral cells (MCs) via actions on GABAergic interneurons in the

- glomerular layer (GL) and granule cell layer (GCL). *J Neuroscience* 27:5654-5663. ([Abstract](#)) ([PDF, 3304 KB](#)). Impact factor: 7.9, cited 18 times.
24. Heister DS, **Hayar A**, Charlesworth A, Yates C, Zhou YH, Garcia-Rill E (2007) Evidence for electrical coupling in the SubCoeruleus (SubC) nucleus. *J Neurophysiol* 97:3142-3147. ([Abstract](#)) ([PDF, 222 KB](#)). Impact factor: 3.8, cited 28 times.
  25. Karnup SV, **Hayar A**, Shipley MT, Kurnikova MG (2006) Spontaneous field potentials in the glomeruli of the olfactory bulb: the leading role of juxtglomerular cells. *Neuroscience* 142:203-221. ([Abstract](#)) ([PDF, 1454 KB](#)). Impact factor: 3.5, cited 18 times.
  26. Ennis M, Zhu M, Heinbockel T, **Hayar A** (2006) Olfactory nerve-evoked, metabotropic glutamate receptor-mediated synaptic responses in rat olfactory bulb mitral cells. *J Neurophysiol* 95:2233-2241. ([Abstract](#)) ([PDF, 408 KB](#)). Impact factor: 3.8, cited 18 times.
  27. **Hayar A**, Bryant JL, Boughter JD, Heck DH (2006) A low-cost solution to measure mouse licking in an electrophysiological setup with a standard analog-to-digital converter. *J Neurosci Methods* 153:203-207. ([Abstract](#)) ([PDF, 309 KB](#)). Impact factor: 2.5, cited 22 times.
  28. **Hayar A**, Shipley MT, and Ennis M (2005) Olfactory bulb external tufted cells are synchronized by multiple intraglomerular mechanisms. *J Neuroscience* 25: 8197-8208 ([PDF, 934 KB](#)). Impact factor: 7.9, cited 59 times.
  29. Hamilton KA, Heinbockel T, Ennis M, Szabo G, Erdelyi F, **Hayar A** (2005) Properties of external plexiform layer interneurons in mouse olfactory bulb slices. *Neuroscience* 133:819-829 ([Abstract](#)) ([PDF, 544 KB](#)). Impact factor: 3.5, cited 25 times.
  30. **Hayar A**, Karnup S, Ennis M, Shipley MT (2004b) External tufted cells: A major excitatory element that coordinates glomerular activity. *J Neuroscience* 24:6676-6685 ([Abstract](#)) ([PDF, 989 KB](#)). Impact factor: 7.9, cited 105 times.
  31. **Hayar A**, Karnup S, Shipley MT, Ennis M (2004a) Olfactory bulb glomeruli: external tufted cells intrinsically burst at theta frequency and are entrained by patterned olfactory input. *J Neuroscience* 24:1190-1199 ([Abstract](#)) ([PDF, 526 KB](#)). Impact factor: 7.9, cited 104 times.
  32. Aungst JL, Heyward PM, Puche AC, Karnup SV, **Hayar A**, Szabo G, Shipley MT (2003) Center-surround inhibition among olfactory bulb glomeruli. *Nature* 426:623-629 ([Abstract](#)) ([PDF, 798 KB](#)). Impact factor: 32.9 cited 227 times.
  33. Guyenet PG, Stornetta RL, Schreihof AM, Pelaez NM, **Hayar A**, Aicher S, Llewellyn-Smith IJ (2002) Opioid signalling in the rat rostral ventrolateral medulla. *Clin Exp Pharmacol Physiol* 29:238-242. Review. ([Abstract](#)) ([PDF, 58 KB](#)). Impact factor: 2.1, cited 25 times.
  34. Ennis M., Zhou F-M., Ciombor KJ, Aroniadou-Anderjaska V, **Hayar A**, Borrelli E, Zimmer LA., Margolis F, Shipley MT (2001) Dopamine D2 Receptor-Mediated Presynaptic Inhibition of Olfactory Nerve Terminals. *J Neurophysiol* 86:2986-2997. ([Abstract](#)) ([PDF, 195 KB](#)) Impact factor: 3.8, cited 132 times.
  35. **Hayar A**, Heyward PM, Heinbockel T, Shipley MT, Ennis M (2001) Direct excitation of mitral cells by activation of alpha1-adrenergic receptors in rat olfactory bulb slices. *J Neurophysiol* 86:2173-2182 ([Abstract](#)) ([PDF, 199 KB](#)). Impact factor: 3.8, cited 45 times.
  36. **Hayar A**, Guyenet P (2000) Prototypical imidazoline-1 receptor ligand moxonidine activates alpha2-adrenoceptors in bulbospinal neurons of the RVL. *J Neurophysiol* 83:766-776 ([Abstract](#)) ([PDF, 256 KB](#)). Impact factor: 3.8, cited 13 times.
  37. **Hayar A**, Guyenet P (1999) Alpha2-Adrenoceptor-mediated presynaptic inhibition in bulbospinal neurons of rostral ventrolateral medulla. *Am J Physiol: Heart and Circulatory Physiology* 277:H1069-H1080 ([Abstract](#)) ([PDF, 457 KB](#)). Impact factor: 3.7, cited 20 times.

38. **Hayar A**, Guyenet P (1998) Presynaptic and postsynaptic effects of methionine-enkephalin on identified bulbospinal neurons of the RVL. *J Neurophysiol* 80:2003-2014 ([Abstract](#)) ([PDF, 319 KB](#)). **Impact factor: 3.8, cited 46 times.**
39. **Hayar A**, Poulter MO, Pelkey K, Feltz P, Marshall KC (1997) Mesencephalic trigeminal neuron responses to gamma-aminobutyric acid. *Brain Res* 753:120-127 ([Abstract](#)) ([PDF, 678 KB](#)). **Impact factor: 2.5, cited 26 times.**
40. **Hayar A**, Feltz P, Piguet P (1997) Adrenergic responses in silent and putative inhibitory pacemaker-like neurons of the rat rostral ventrolateral medulla in vitro. *Neuroscience* 77:199-217 ([Abstract](#)) ([PDF, 722 KB](#)). **Impact factor: 3.5, cited 12 times.**
41. Jung M, Michaud JC, Steinberg R, Barnouin MC, **Hayar A**, Barnouin MC, Mons G, Souilhac J, Emonds-Alt X, Soubrie P, Le Fur G (1996) Electrophysiological, behavioural and biochemical evidence for activation of brain noradrenergic systems following tachykinin NK3 receptor stimulation. *Neuroscience* 74:403-414 ([Abstract](#)) ([PDF, 356 KB](#)). **Impact factor: 3.5, cited 42 times.**
42. **Hayar A**, Piguet P, Feltz P (1996) GABA-induced responses in different electrophysiologically identified neurons in the rat rostro ventrolateral medulla. *Brain Res* 709:173-183 ([Abstract](#)) ([PDF, 1149 KB](#)). **Impact factor: 2.5, cited 8 times.**

## **BOOK CHAPTERS**

43. Ennis M, Hamilton KA, **Hayar A** (2007) Neurochemistry of the main olfactory system, In: [Handbook of Neurochemistry and Molecular Neurobiology](#), 3<sup>rd</sup> Edition (Lajtha A, Editor-in-Chief), Vol. 20, pp 137-204, Sensory Neurochemistry (Johnson DA, Volume Editor), Heidelberg: Springer, ([PDF, 987 KB](#)).
44. Ennis M, **Hayar A** (2008) Physiology of the Main Olfactory Bulb, in Allan I. Basbaum, Akimichi Kaneko, Gordon M. Shepherd and Gerald Westheimer, editors *The Senses: A Comprehensive Reference*, Vol 4, Olfaction and Taste, Stuart Firestein and Gary K. Beauchamp. San Diego: Academic Press; pp. 641-686. (Proof, [PDF 10 MB](#)).
45. Karnup SV, **Hayar A** (2008) Neuronal modules of the olfactory bulb. In: *New Research on Neuronal Networks* (Momoka Yoshida and Haruka Sato, editors), pp 1-54, Nova Science Publishers Inc., New York. ([PDF, 1288 KB](#)).
46. Mennemeier M, Sheffer C, **Hayar A**, Buchanan R (2012) Translational Sstudies using TMS. In: *Translational Neuroscience: A guide to a successful program* (Edgar Garcia-Rill, editor), pp 43-65, Wiley-Blackwell, Oxford, UK.

## **MANUSCRIPTS (IN PREPARATION)**

47. Lin XB, Pierce DR, Light KE, **Hayar A**. Developmental ethanol exposure accelerates the rhythmic pattern of licking (in preparation).
48. **Hayar AM**, Hamilton KA. External plexiform layer interneurons integrate synaptic inputs that are correlated with the bursting activity of surrounding mitral/tufted cells. (in preparation).
49. **Hayar A**, Light KE, Pierce DR Coincident inhibitory inputs induce synchronized pauses in the firing of Purkinje cells. *J Neuroscience* (in preparation).
50. **Hayar A** Center-surround interactions among neighboring olfactory bulb glomeruli revealed by optical imaging of the spatiotemporal propagation of spontaneous population activity. *J Neuroscience* (in preparation).

51. Jeradeh-Boursouliau F, **Hayar A** Ethanol Reduces Olfactory Bulb Output by Reducing Excitatory Drive to Mitral/Tufted Cells. J Neurophysiology (in preparation).

## **MEETING ABSTRACTS AND POSTERS**

1. Marshall K, **Hayar A**, Feltz P. Responses of mesencephalic trigeminal neurons to  $\gamma$ -aminobutyric acid. Can. J. Physiol. Pharmacol. Vol.72 (1994).
2. **Hayar A**, Poulter MO, Feltz P.  $\gamma$ -Aminobutyric acid responses in different electrophysiologically characterized neurons within the rat rostral ventrolateral medulla *in vitro*. (24th Annual Meeting of the Society for Neuroscience, **Miami**, November 1994).
3. **Hayar A**, Feltz P. Réponses pré et postsynaptic GABAergiques dans le noyau rostral ventrolatéral bulbaire de rat *in vitro*. Société des Neurosciences (**France**, Lyon, May 1995).
4. **Hayar A**, Piguet P, Poulter MO, Feltz P. Monophasic and multiphasic GABA responses in neurons of the rat rostral ventrolateral medulla *in vitro*. (25th Annual Meeting of the Society for Neuroscience, **San Diego**, November 1995).
5. **Hayar A**, Piguet P, Feltz, P. Réponses GABAergiques monophasiques et multiphasiques dans les neurones du noyau rostral ventrolatéral bulbaire de rat *in vitro*. (63ème Congrès de la Société de Physiologie, **France**, Strasbourg, December 1995).
6. **Hayar A**, Feltz P, Piguet P. Adrenergic responses in silent and putative inhibitory pacemaker-like neurons of the rat rostral ventrolateral medulla *in vitro*. (European Neuroscience Meeting, **France**, Strasbourg, September 1996).
7. **Hayar A**, Piguet P, Schlichter R. Properties of irregular firing neurons in the rostral ventrolateral medulla *in vitro* and possible involvement in sympathoexcitatory function. (26th Annual Meeting of the Society for Neuroscience, **Washington D.C.**, November 1996).
8. **Hayar A**, Guyenet P. Pre-and postsynaptic inhibitory actions of methionine-enkephalin on identified bulbospinal neurons of the rat rostral ventrolateral medulla. FASEB Journal 12 (5): 4290 Part 2 Suppl. S MAR 20, 1998. (Experimental Biology Meeting, **San Francisco**, April 1998).
9. **Hayar A**, Guyenet P. Presynaptic effects mediated by alpha2-adrenoceptors in the rat rostral ventrolateral medulla *in vitro*. (28th Annual Meeting of the Society for Neuroscience, **Los Angeles**, November 1998).
10. **Hayar A**, Guyenet P. Tyramine releases predominantly serotonin in the lower brainstem of neonate rats *in vitro*. FASEB Journal 13 (4): A473-A473 Part 1 Suppl. S MAR 12, 1999. (Washington D.C., April 1999).
11. **Hayar A**, Guyenet P. Effect of tyramine and other indirectly acting monoamines in the rostral ventrolateral medulla *in vitro*. (29th Annual Meeting of the Society for Neuroscience, **Miami**, October 1999).
12. **Hayar A**, Shipley MT, Ennis M. Direct excitation of mitral cells by activation of alpha1-adrenergic receptors in rat olfactory bulb slices. (**Sarasota**, April 2000).
13. **Hayar A**, Shipley MT, Ennis M. Norepinephrine excites mitral cells by activation of alpha1-adrenergic receptors in rat olfactory bulb slices. Program# 45.3 (30th Annual Meeting of the Society for Neuroscience, **New Orleans**, November 2000, [Abstract](#)).
14. Karnup SV, **Hayar A**, Ennis M, Shipley MT. Morphology & Physiology of juxtaglomerular (JG) cells in rat main olfactory bulb (MOB). Program# 623.8 (31st Annual Meeting of the Society for Neuroscience, **San Diego**, November 2001, [Abstract](#)).
15. Heinbockel T, **Hayar A**, Laaris N, Shipley MT, Ennis M. Metabotropic glutamate receptors shape neuronal excitability and synaptic responsiveness in mouse olfactory bulb slices. Program# 623.5 (31st Annual Meeting of the Society for Neuroscience, **San Diego**, November 2001, [Abstract](#)).

16. Aungst J, Karnup SV, **Hayar A**, Shipley MT, Puche AC. Interglomerular circuits in the main olfactory bulb. Program# 561.10 (32nd Annual Meeting of the Society for Neuroscience, **Orlando**, November 2002, [Abstract](#)).
17. **Hayar A**, Heinbockel T, Karnup S, Ennis M, Shipley MT. Activation of metabotropic glutamate receptors enhances synaptic interactions among juxtglomerular neurons in olfactory bulb glomeruli. Program # 168.4 (33rd Annual Meeting of the Society for Neuroscience, **New Orleans**, November 2003, [Abstract](#)).
18. Shipley MT, Karnup S, Ennis M, **Hayar A**. Olfactory bulb external tufted (ET) cells provide monosynaptic excitatory input to periglomerular (PG) and short axon (SA) cells. Program# 489.14 (33rd Annual Meeting of the Society for Neuroscience, **New Orleans**, November 2003, [Abstract](#)).
19. Hamilton KA, Heinbockel T, **Hayar A**, Szabo G, Erdelyi F, Ennis M. Functional properties of interneurons in the external plexiform layer of the olfactory bulb. Program# 821.7 (33rd Annual Meeting of the Society for Neuroscience, **New Orleans**, November 2003, [Abstract](#)).
20. Li C, **Hayar A**, Smith DV. Patch-clamp recording of medullary taste neurons identified by retrograde labeling from the pons. Program# 594.3 (33th Annual Meeting of the Society for Neuroscience, **New Orleans**, November 2003, [Abstract](#)).
21. **Hayar AM**, Ennis M. Activation of metabotropic glutamate receptors (mGluRs) enhances bursting in external tufted cells of the olfactory bulb. Program# 412.11 (34th Annual Meeting of the Society for Neuroscience, **San Diego**, October 2004, [Abstract](#)).
22. **Hayar A**, Shipley MT, Ennis M. The bursting of olfactory bulb external tufted (ET) cells is coordinated by synaptic and gap junction currents. (27th Annual Meeting of the Association for Chemoreception Sciences, **Sarasota**, April 2005, [Abstract](#)).
23. **Hayar A**, Ennis M. Activation of metabotropic glutamate receptors (mGluRs) enhances bursting in external tufted cells of the olfactory bulb. (27th Annual Meeting of the Association for Chemoreception Sciences, **Sarasota**, April 2005, [Abstract](#)).
24. Hamilton KA, **Hayar A**, Ennis M. Spiking properties of EPL interneurons. (27th Annual Meeting of the Association for Chemoreception Sciences, **Sarasota**, April 2005, [Abstract](#)).
25. **Hayar AM**, Shipley MT, Ennis M. The activity of olfactory bulb external tufted cells (ET) is synchronized by various intraglomerular connections. Program# 614.17 (35th Annual Meeting of the Society for Neuroscience, **Washington DC**, November 2005, [Abstract](#)).
26. Dong HW, **Hayar A**, Ennis M. Activation of metabotropic glutamate receptors (mGluRs1) in the glomerular layer (GL) and granule cell layer (GCL) of the olfactory bulb enhances synaptic inhibition of mitral cells (MCs) (28th Annual Meeting of the Association for Chemoreception Sciences, **Sarasota**, April 2006). Chemical Senses Volume: 31 Issue: 5 Pages: A68-A68 Published: JUN 2006
27. Karnup SV, **Hayar A**, Shipley MT, Kurnikova MG. Spontaneous glomerular field potentials in slices of the olfactory bulb. (36th Annual Meeting of the Society for Neuroscience, **Atlanta**, October 2006, [Abstract](#)). Program# 542.7 Poster# P8.
28. Dong HW, **Hayar A**, Ennis M. Activation of metabotropic glutamate receptors (mGluRs) enhances synaptic inhibition of olfactory bulb mitral cells (MCs) via actions on GABAergic interneurons in the glomerular layer (GL) and granule cell layer (GCL). (36th Annual Meeting of the Society for Neuroscience, **Atlanta**, October 2006, [Abstract](#)). Program# 542.5, Poster# P6.
29. Ennis M, Shipley MT, **Hayar A**. Glomeruli: dynamic portals into the olfactory brain. American Association of Anatomists, **Washington DC**, April 28 - May 2, FASEB Journal 21 (5): A84-A84 APR 2007.
30. Karpuk, N, **Hayar A**. Activation of postsynaptic GABAB receptors directly modulates the bursting pattern and synaptic activity of olfactory bulb juxtglomerular neurons. (29th Annual Meeting of the Association for Chemoreception Sciences, **Sarasota**, April 2007).

31. Hamilton KA, Ennis M, **Hayar A**. Interneuron EPSC bursts are correlated with tufted cell spike bursts in the superficial external plexiform layer of the olfactory bulb. (29th Annual Meeting of the Association for Chemoreception Sciences, **Sarasota**, April 2007).
32. Dong HW, **Hayar A**, Ennis M. mGluR1 Activation Enhances Nonselective Cation Currents and Rhythmic Bursting in External Tufted (ET) Cells. *Chemical Senses* 31 (5): A68-A68 JUN 2006. (29th Annual Meeting of the Association for Chemoreception Sciences, **Sarasota**, April 2007).
33. Heister D, **Hayar A**, Garcia-Rill E. Electrical coupling in whole cell recorded SubCoeruleus neurons. Associated Professional Sleep Societies (APSS). *Sleep* 30: A10-A11 Suppl. S. Meeting Abstract: 30 **Minneapolis**, June 2007.
34. **Hayar A**, Heister D, Garcia-Rill E. Carbachol induces synchronization of IPSCs at theta frequency in whole-cell recorded SubCoeruleus neurons. Associated Professional Sleep Societies (APSS). *Sleep* 30: A12-A12 35 Suppl. S **Minneapolis**, June 2007.
35. Karpuk N, **Hayar A**. Activation of postsynaptic GABA<sub>B</sub> receptors directly modulates the bursting pattern and synaptic activity of olfactory bulb juxtglomerular neurons. (37th Annual Meeting of the Society for Neuroscience, **San Diego**, November 2007).
36. Hayar A. Spontaneous population activity revealed by calcium- and voltage-sensitive dyes in the neuropil of olfactory bulb glomeruli in vitro. (37th Annual Meeting of the Society for Neuroscience, **San Diego**, November 2007).
37. Al-Chaer ED, Gu C, **Hayar A**. An improved method for patch clamp recording of neurons in the intact dorsal root ganglion (DRG). (37th Annual Meeting of the Society for Neuroscience, **San Diego**, November 2007).
38. Dong HW, **Hayar A**, Ennis M. Activation of Group I mGluRs enhances rhythmic bursting and nonselective cation currents in olfactory bulb external tufted cells. (37th Annual Meeting of the Society for Neuroscience, **San Diego**, November 2007).
39. Nai Q, Dong HW, **Hayar A**, Linster C, Ennis M. Activation of  $\alpha 1$  and  $\alpha 2$  noradrenergic receptors differentially regulate GABAergic inhibition of mitral cells in the main olfactory bulb. (37th Annual Meeting of the Society for Neuroscience, **San Diego**, November 2007).
40. Heister D, **Hayar A**, Garcia-Rill E. Differentiating SubCoeruleus neurons by responses to carbachol and developmental changes in resistance. (37th Annual Meeting of the Society for Neuroscience, **San Diego**, November 2007).
41. Ye M, **Hayar A**, Garcia-Rill E. Electrical Coupling in Pedunculopontine (PPN) Nucleus Neurons. (37th Annual Meeting of the Society for Neuroscience, **San Diego**, November 2007).
42. Burkovetskaya M, **Hayar A**, Karpuk N, Kielian T. Characterization of Astrocyte Activation in Acute Brain Slices from Mice Harboring Brain Abscesses. (American Society for Neurochemistry (ASN) annual meeting, **San Antonio**, March 2008). *J Neurochemistry* Volume: 104 Pages: 54-55 Supplement: Suppl.1 Published: MAR 2008.
43. Heister D, **Hayar A**, Garcia-Rill E. Cholinergic modulation of fast excitatory and inhibitory input to the dorsal subcoeruleus. *Sleep* Volume: 31 Pages: A10-A10 Supplement: Suppl. S Meeting Abstract: 31 Published: 2008.
44. Nai Q, Dong HW, **Hayar A**, Linster C, Ennis M. Noradrenergic modulation of GABAergic inhibition of main olfactory bulb mitral cells. *Chemical Senses* Volume: 33 Issue: 8 Pages: S134-S135 Published: OCT 2008.
45. **Hayar A**. Center-surround interactions among neighboring olfactory bulb glomeruli revealed by optical imaging of the spatiotemporal propagation of spontaneous population activity. (38th Annual Meeting of the Society for Neuroscience, **Washington DC**, November 2008).
46. Pierce DR, **Hayar A**, Wiley CA, Light KE. Rat Purkinje cells that survive postnatal ethanol exposure are altered morphologically and physiologically. (32nd Annual Meeting of the Research Society on Alcoholism,

- San Diego**, June 2009). Alcoholism-Clinical and Experimental Research, Volume: 33 Issue: 6 Special Issue: Sp. Iss. S1 Pages: 168A-168A.
47. **Hayar AM**, Light KE, Pierce DR. Coincident inhibitory inputs induce synchronized pauses in the firing of Purkinje cells (39th Annual Meeting of the Society for Neuroscience, **Chicago**, October 2009, [Abstract](#)). Program # 622.3, Poster # F4.
  48. Ye M, **Hayar A**, Strotman B, Garcia-Rill E. Cholinergic modulation of fast synaptic transmission of pedunculo pontine thalamic projecting neurons (39th Annual Meeting of the Society for Neuroscience, **Chicago**, October 2009, [Abstract](#)). Program # 375.16, Poster # FF16.
  49. Jeradeh-Boursoulia F, **Hayar A**. Ethanol Reduces Olfactory Bulb Output by Reducing Excitatory Drive to Mitral/Tufted Cells (32<sup>nd</sup> Annual Meeting of the Association for Chemoreception Sciences, **St Petersburg, Florida**, April 2010).
  50. Yadlapalli K, **Hayar AM**, Al-Chaer ED. Differential Effects of ATP on the Electrophysiological Properties of Postsynaptic Dorsal Horn Neurons in the Rat. (40<sup>th</sup> Annual Meeting of the Society for Neuroscience, **San Diego**, November 2010, Abstract).
  51. Myal S, **Hayar AM**, Buchanan R, Garcia-Rill E. Effect of repetitive transcranial magnetic stimulation (rTMS) on nicotine-induced suppression of P13 auditory evoked potential (41<sup>st</sup> Annual Meeting of the Society for Neuroscience, **Washington DC**, November 2011). Program # 397.01, Poster # WW59
  52. Simon C, **Hayar A**, Garcia-Rill E. Responses of developing pedunculo pontine neurons to glutamate receptor agonists. (41<sup>st</sup> Annual Meeting of the Society for Neuroscience, **Washington DC**, November 2011). Program # 397.04, Poster # WW62.
  53. Watts JL, Yadlapalli K, **Hayar AM**, Al-Chaer ED. Minocycline alters neuronal plasticity in rats with colon inflammation. (41<sup>st</sup> Annual Meeting of the Society for Neuroscience, **Washington DC**, November 2011). Program # 494.03, Poster # SS7.
  54. Pierce DR, **Hayar A**, Light KE. Increased HCN1 expression at Basket cell innervation of rat Purkinje cells surviving postnatal ethanol exposure. (34<sup>th</sup> Annual Meeting of the Research Society on Alcoholism, June 25-29, 2011, **Atlanta**, Georgia). Abstract # 0127, published in Alcoholism: Clinical and Experimental Research. Vol. 35, Issue Supplement s1, page 42A.
  55. Pierce DR, Lin XB, Light KE, **Hayar AM**. Rhythmic licking behavior is altered in adult rats that received postnatal ethanol exposure. (35<sup>th</sup> Annual Meeting of the Research Society on Alcoholism, June 23-27, 2012, **San Francisco**, California).
  56. **Hayar AM**, Hamilton KA. External plexiform layer interneurons integrate synaptic inputs that are correlated with the bursting activity of surrounding mitral/tufted cells. (42<sup>nd</sup> Annual Meeting of the Society for Neuroscience, **New Orleans**, October 2012). Session # 339.
  57. Lin XB, Pierce DR, Light KE, **Hayar AM**. The Fine Temporal Structure of the Rat Licking Pattern: What Causes the Variability in the Interlick Intervals and How is it Affected by the Drinking Solution? (35<sup>th</sup> Annual Meeting of the Association for Chemoreception Sciences, **Huntington Beach, California**, April 2013).
  58. Pierce DR, **Hayar A**, Light KE. Ethanol exposure to rat pups days 4-6 decreases Purkinje cell number but appears to increase axonal innervations from Basket cells. (37<sup>th</sup> Annual Meeting of the Research Society on Alcoholism, June 21-25, 2014, **Bellevue**, Washington). Abstract # 1015, published in Alcoholism: Clinical and Experimental Research. Vol. 38, Issue Supplement s1, page 254A.
  59. Dobretsov M, Petkau G, **Hayar A**, Eugen P (2016) Clock-scan protocol for image analysis: ImageJ plugins. (Submitted to the American Society for Neurochemistry meeting on March 2017 in Little Rock, AR).
  60. Salomon RM., Golden K, Mhyre J, Eads L, James AJ. Clothier J, **Hayar A**, Delgado DL, Larson-Prior L. Resting state fMRI of raphé nucleus activity following ketamine. Society of Biological Psychiatry, 72nd Annual Meeting, May 18-20, 2017, San Diego, California.

## **SEMINAR PRESENTATIONS**

### **Local seminars**

- 01/25/2007: Presentation for candidacy for joint appointment at the Dept. of Physiology and Biophysics. Title: "Synaptic transmission and gap junctions synchronize the bursting activity of olfactory bulb neurons"
- 04/02/2007: Presentation of the progress report for the Center of Translational Neurosciences External Advisory Committee.
- 06/15/2007: Training seminar for CTN summer students. Title: "How to record from single neurons?"
- 05/20/2008: Dean's Research Forum. Title: "Neuronal synchronization: The olfactory bulb model"
- 05/22/2009: Training seminar for CTN summer students. Title: "Introduction to Patch-Clamp Electrophysiology in Brain Slices"
- 03/18/2010: Dept. of Pharmaceutical Sciences. Title: "Alcohol-induced alterations in cerebellar circuits"
- 09/27/2010: Center for Translational Neuroscience, Mini-Symposium on Transcranial Magnetic Stimulation. Title: "TMS investigations in rodents"
- 03/15/2016: Dept. of Neurobiology and Developmental Sciences seminar series. Title: "The Brain, Space-time and the Universe"
- 11/22/2016: Dept. of Neurobiology and Developmental Sciences seminar series. Title: "Depression: A Loss of Slow Oscillations in Serotonin Function?". This seminar was presented in collaboration with Dr. Ronald Salomon, Professor, Psychiatric Research Institute.

### **National seminars**

1. **Hayar A**, Guyenet P. (Slide talk) Pre- and postsynaptic inhibitory actions of methionine-enkephalin on identified bulbospinal neurons of the rat rostral ventrolateral medulla. (Experimental Biology Meeting, **San Francisco**, April 1998).
2. **Hayar AM**, Karnup S, Shipley MT, Ennis M. ([Slide talk](#)) Synchronous activity among juxtglomerular neurons of the rat main olfactory bulb (MOB) in vitro. Program# 459.4 (31st Annual Meeting of the Society for Neuroscience, **San Diego**, November 2001).
3. **Hayar A**. ([Seminar](#)) Pre- and postsynaptic inhibitory actions of methionine-enkephalin and norepinephrine on identified bulbospinal neurons of the rat rostral ventrolateral medulla. (Univ. of Wyoming, **Laramie**, June 2002).
4. **Hayar A**. ([Seminar](#)) Synchronous bursting among juxtglomerular neurons of the olfactory bulb is mediated by synaptic and non-synaptic interactions. Developmental Neural Plasticity Unit, NINDS (**NIH, Bethesda**, June 2003).
5. **Hayar A**. Invited speaker for the "Satellite symposium to the 2004 Computational Neuroscience meeting ([CNS\\*04](#))" July 17, 2004, **Baltimore**.
6. **Hayar A**. ([6 Seminars](#), faculty candidate) Synaptic transmission and gap junctions synchronize the bursting activity of olfactory bulb neurons. 2004-2005, 1- Univ. of Drexel, **Philadelphia**, 2- Univ. of Illinois, **Rockford**, 3- Univ. of Texas, **Galveston**, 4- Univ. of North Dakota, **Fargo**, 5- Univ. of Mississippi, **Jackson**, 6- Univ. of Arkansas for Medical Sciences, **Little Rock**.
7. **Hayar A**. (3/14/2011) Correlated Activity in Neuronal Networks: Olfactory Bulb vs. Cerebellum. Department of Cellular Biology and Anatomy, Louisiana State University Health Sciences Center, 1501 Kings Highway, Shreveport, LA 71103.

### **International seminars**

07/01/1996: **Hayar A.** GABAergic and noradrenergic responses in the rat rostral ventrolateral medulla (RVL) *in vitro*: Relevance to cardiovascular regulation and vasomotor rhythmogenesis. International School for Advanced Studies ([SISSA](#)), 2-4, via Beirut, **Trieste, Italy**.

09/02/2010: **Hayar A.** Neuronal Interactions and Synchrony. Invited talk at the Basic Medical Science Departments and Biology Department, American University of Beirut, **Beirut, Lebanon**.

### **RESEARCH TECHNIQUES AND EXPERTISE**

- Autoradiography in rat brain slices
- Intracellular pH measurement by micro-fluorimetry using the BCECF probe
- Intracellular dye labeling
- Immunocytochemical staining for biocytin and tyrosine hydroxylase
- In situ hybridization (GABA mRNA subunits)
- Intracellular, extracellular and field potential recordings in brain slices
- Patch-clamp technique: whole-cell, outside-out, and single channel recordings
- Analysis of the properties of evoked, spontaneous, and miniature postsynaptic currents
- Recordings from bulbospinal neurons identified with retrograde tracing of fluorescent dyes
- Simultaneous whole-cell recordings from pairs of neurons in olfactory bulb slices
- Auto- and cross-correlation analysis of spike trains and waveforms
- Calcium and voltage-sensitive dye imaging, confocal microscopy
- Ultraviolet light laser uncaging of glutamate in brain slices
- Laser Doppler measurement of cerebral blood flow
- High speed spinning disk confocal microscopy at 2000 frames/s

### **TEACHING**

Despite the dedication of most of my effort to research, I have been involved in significant teaching and training in my Department as well as in other Departments. I have also organized Journal Club presentations that involve students, postdoctoral fellows, and faculty, during which we discuss recently-published articles in different areas of Neurophysiology.

#### **Courses I am currently directing and teaching:**

**1- Cellular and Developmental Neuroscience (NBDS 5114).** Course director and lecturer of more than half of the course (46 hours, 3 credit-hour course, 7-14 graduate students, 1/1/2011- until present).

For more information, see the course website which I have designed: <http://hayar.net/NBDS5114>

**Course description:** This course is required for all Neuroscience track graduate students. It consists of lectures, assigned readings and student presentations that cover the structure, function and development of cells of the nervous system, the basic principles of the physiology of excitable cells, and synaptic transmission.

**Lectures:** Neuronal Network Construction, Autonomic Nervous System, Central Control of the Cardiovascular System, Membrane Potential and Action Potential, Release of Neurotransmitters, Neurotransmitters, Neuroreceptors, Postsynaptic Potentials and Synaptic Integration, Synaptic Plasticity & Memory Formation, Cellular & Developmental Aspects of Olfaction, Alcohol-induced alterations in cerebellar circuits, Lab: Electrophysiology & Imaging, Neuroscience of Pain, Neuroscience of Addiction, Neuroscience of Depression, Critical Discussion of a scientific article, students' article presentation.

**2- Neuronal Signals (NBDS 5123).** Course director and lecturer of the entire course (18 hours, 1 credit course, graduate students, 06/01/2010- until present)

For more information, see the course website which I have designed: <http://hayar.net/NBDS5123>

**Course Description:** This condensed one credit summer course consists of teaching the theoretical aspects of modern analytical methods to study neuronal activity. It focuses on the study of brain signals and describes several methods for recording and analyzing neuronal activity using modern techniques such as patch clamping and imaging neuronal networks using calcium- and voltage-sensitive dyes. The course is to be taught annually in June-July, during a 7-week period on Tuesdays and Thursdays. It consists of 12 sessions: 9 lectures (80 min each), 1 laboratory demonstration (80 min) and 2 article presentations (80 min each) by the instructor. The goal of the course is to help graduate and medical students pursuing a career in neuroscience or neurology to become familiar with the cutting edge techniques for monitoring brain activity. The students were allowed to use all the resources in my lab so that they can get practical experience in how research is performed, and how experimental data is analyzed and published in scientific journals.

**Lectures:** Design of an electrophysiology setup, Neural population recordings, Single cell recordings, Analyzing synaptic activity, Data acquisition and analysis, Analyzing and plotting data using OriginLab, Detecting electrophysiological events, Writing algorithms in OriginLab, Imaging neuronal activity, Laboratory demonstration of an electrophysiology and imaging experiment, Article presentation I: Electrophysiology, Article presentation II: Imaging, Exam and students' survey about the course.

**3- Basic Neuroscience (NBDS 5106).** (4 x 1.5 hrs lectures, graduate students, 1/1/2013- until present)

**Course Description:** This course consists of lectures that cover the structure, function and development of the central nervous system.

For more information, see the course website which I have designed: <http://hayar.net/NBDS5106>

**Lectures:** "Chemical Senses: Taste", "Autonomous Nervous System", "Central Control of Respiration", and "Central Control of Digestive System".

**4- Human Structure** for M1 medical students (8/14/2018 - ): Gross Anatomy labs 12 sessions of 2-3 hours

**5- Embryology** lectures for M2 medical students (2018 - ) (2 lectures on embryology of the heart and congenital diseases, 1 lecture on pulmonary embryology, 1 lecture on embryology of the gastrointestinal tract)

**6- Grand Rounds/Neurology Residency Integrated Didactic Curriculum** (4 x 1 hr lectures, ~12 neurology residents, 9/16/2013- until present).

Lectures: "Ion channels", "The action potential", "Synaptic Integration", "Neurotransmitters".

**7- Ultrasound Anatomy** for Medical Students (M1 and M2, 13 X 3 hr sessions, 3/19/2018-present)

### **Previous teaching experience:**

- 1992-1996: Experience in training graduate students for electrophysiological techniques at the Univ. Louis Pasteur, France.
- 2001-2003: Teaching in Medical Neuroscience courses at the Univ. of Maryland: The role of the RVL in hypertension, synaptic physiology, synaptic communications in glomerular circuits.
- 2004-2005: Teaching in Morphological Neuroanatomy: Limbic system, olfactory system (Univ. of TN).
  
- 08/18/2006: Neurosurgery Lecture Series/Grand Rounds, Olfactory System.
- 08/25/2006: Neurosurgery Lecture Series/Grand Rounds, Neuroreceptors.
- 08/28/2006 - 12/11/2006: Physiology Journal Club Series: supervise 8 student presentations
- 09/06/2006: Systems Neuroscience (NBDS 5153), Neurotransmitters I.
- 09/08/2006: Systems Neuroscience (NBDS 5153), Neurotransmitters II.
- 09/11/2006: Systems Neuroscience (NBDS 5153), Channels and Currents I.
- 09/13/2006: Systems Neuroscience (NBDS 5153), Channels and Currents II.
- 10/27/2006: Systems Neuroscience (NBDS 5153), Olfactory system.

- 01/12/2007: Medical Neuroscience, Neurotransmitters I, Neurotransmitters II.
- 04/03/2007: Cellular & Develop. Neurosci. (NBDS 5103), Membrane Potential and Action Potential.
- 04/12/2007: Cellular & Develop. Neurosci. (NBDS 5103), Postsynaptic Potentials and Synaptic Integration.
  
- 03/06/2008: Cellular & Develop. Neurosci. (NBDS 5103), Membrane Potential and Action Potential.
- 03/07/2008: Medical Neuroscience, Neurotransmitters I, Neurotransmitters II.
- 04/03/2008: Cellular & Develop. Neurosci. (NBDS 5103), Postsynaptic Potentials and Synaptic Integration.
  
- 03/05/2009: Medical Neuroscience, Neurotransmitters I.
- 03/06/2009: Medical Neuroscience, Neurotransmitters II.
- 03/30/2009: Cellular & Develop. Neurosci. (NBDS 5103), Postsynaptic Potentials and Synaptic Integration.
- 04/06/2009: Cellular & Develop. Neurosci. (NBDS 5103), Cellular and Developmental Aspects of Olfaction.
  
- 02/22/2010: Cellular & Develop. Neurosci. (NBDS 5103), Membrane Potential and Action Potential.
- 03/05/2010: Medical Neuroscience, Neurotransmitters I.
- 03/08/2010: Cellular & Develop. Neurosci. (NBDS 5103), Postsynaptic Potentials and Synaptic Integration.
- 03/09/2010: Medical Neuroscience, Neurotransmitters II.
- 04/09/2010: Cellular & Develop. Neurosci. (NBDS 5103), Cellular and Developmental Aspects of Olfaction.
- Medical Neuroscience NeuroAnatomy Lab: Lab1: 3/2/10 (Whole Brain), Lab2: 3/3/10 (Half Brain), Lab3: 3/8/10 (Gross Brain Stem), Lab4: 3/16/10 (Spinal Cord), Lab5: 3/30/10 (Internal Medulla), Lab6: 4/6/10 (Internal Pons and Midbrain), Lab7: 4/21/10 (Coronal Sections), Lab8: 4/27/10 (Neuroradiology), Lab9: 4/28/10 (Motor System), Lab10: 4/28/10 (Upper Brain Stem).
- Medical Neuroscience Clinical Conferences: CC1: 3/17/10 (Spinal Cord Diseases), CC2: 4/5/2010 ( Brain Stem Diseases), CC3: 4/16/10 (Vision System), CC4: 4/30/10 (Motor Diseases), CC5: 5/7/10 (Higher Brain Diseases)

## **MENTORING AND TRAINING**

- Thesis director of the following graduate Ph.D. students
  - Xiong Bin Lin (7/1/2011 – 12-31-2014, candidacy exam: 10/23/2013, graduated on 12/9/2014)
  - Martin Watts (co-director with Dr. Elie Al-Chaer, candidacy exam: 4/19/2010, graduated on 4/1/2014)

Mentoring and training for electrophysiological techniques the following:

- Graduate students:
  - David Heister (8/1/2006 – 4/15/2008) - My role: co-mentor
  - Meijun Ye (8/1/2006 – 4/21/2009) - My role: co-mentor
  - Nebojsa Kezunovic (8/1/2009 – present) - My role: co-mentor
  - Christen Simon (8/1/2009 – present) - My role: co-mentor
  - Samuel Carus (7/1/2010 – 9/1/2010) - My role: mentor (lab rotation)
  - Aminiel Awichi (1/1/2013- 4/21/2013) - My role: mentor (lab rotation)
  
- Research assistants:
  - Parul Soni (4/1/2006 – 3/1/2008)
  - Maria Burkovetskaya (11/1/2006 – 6/30/2008)
  - Madhvi Patel (5/10/2009 – 8/1/2009)
  - Julius Franz (8/1/2009 – 5/15/2010)
  - Krishnapraveen Yadlapalli (3/1/2008 – present)
  - Margarita Escovedo (5/10/2009 – 12/31/2011)
  - Stephanie Myal (8/2/2010 – 12/31/2011)

- Nelson Piper (training in collaboration with Dr. Sung Rhee, 4/1/2011-present)

• Postdoctoral fellows:

- Dr. Nikolay Karpuk (7/1/2006 – 6/30/2008)
- Dr. Feras Jeradeh-Boursouliau (5/1/2009 – 6/30/2010)
- Dr. Nikhil Kamalnath Parelkar (training in collaboration with Dr. Sung Rhee, 12/1/2010-3/31/2011)

• Medical students:

- James Scott Steele (5/17/2010 – 8/1/2010)

• High school students:

- Brennon Luster (6/11/2007 – 6/22/2007)
- Shatterica Dawson (6/11/2007 – 6/22/2007)
- Michael Smith (6/1/2010 – 8/6/2010)
- Konstantin Gruenwald (6/1/2010 – 8/13/2010)

## **ADMINISTRATION AND SERVICE**

### **Community service**

- Jury Duty (Pulaski County Circuit Court): 5/1/2015 - 8/31/2015
- As a vice president of the Arkansas Chapter of the Society for Neuroscience, I continue to help the society's officers to organize our yearly scientific meeting to promote awareness about Neuroscience research. For example, each year in March, we organize the Brain Awareness Day at the Museum of Discovery. Our neuroscience exhibits attracted to the discovery museums additional visitors who were curious to learn more about the way the brain functions in animals and human being. This Brain Awareness Day event is of important value to the chapter vitality because it directly addresses the Society's outreach goal of promoting novel initiatives linked to neuroscience literacy, education or training. The Brain Awareness Day event at the Museum of Discovery has demonstrated to be a very effective method of introducing school-age children as well as adults to the world of neuroscience and the brain. I am also the webmaster of the Chapter's website: <http://www.ar-neuro.org>

### **Administrative & Academic Committees**

- Vice-President of the UAMS chapter of the American Association of University Professors (AAUP) (7/5/2017-present) <http://www.hayar.net/AAUP>
- Chair of the Academic Senate Communications Committee (12/1/2017-present)
- Member of the Dept. of Neurobiology and Developmental Sciences Faculty Development committee (12/1/2016-present)
- Member of the admissions committee for the new Graduate Program in Biomedical Sciences (GPIBS) and Neuroscience Track representative (11/2/2015-present)
- Member of the Exit Survey Committee of the UAMS Faculty Senate (10/17/2015-present)
- President of the Arkansas Chapter of the Society for Neuroscience (11/8/2011-12/31/2012)
- President-elect of the Arkansas Chapter of the Society for Neuroscience (11/10/2010-11/8/2011)
- Member of the Institutional Animal Care and Use Committee (7/1/2010-present): Obtained IACUC101 and IACUC201PLUS certificates on 9/19/2012 -9/20/2012
- Member of the Dept. of Neurobiology & Developmental Sciences Graduate Advisory Committee (9/1/2009 – present)
- Member of the Academic Senate Communications Committee (12/1/2010-12/1/2017)
- Member of the Strategic Planning Committee (Chair of Research Subcommittee) of the Dept. of Neurobiology & Developmental Sciences (8/20/2008 – 12/31/2008)

- Member of the Recruitment Committee of the Dept. of Neurobiology & Developmental Sciences (5/7/2009 – 2010)
- Member of ResNet proposal Committee (4/1/2011-6/30/2012)

### **Graduate student thesis committees**

Member of the thesis committees of the following graduate students:

1. David Heister (Mentor: Dr. Edgar Garcia-Rill, candidacy exam: 4/12/2007, graduated on 4/15/2008)
2. Meijun Ye (Mentor: Dr. Edgar Garcia-Rill, candidacy exam: 10/2/2007, graduated on 4/21/2009)
3. Kyongmin Kim (Mentor: Dr. Z. Jimmy Zhou, candidacy exam: 9/10/2007, did not graduate)
4. Hamdan Hamdan (Mentor: Dr. Patricia Wight, candidacy exam: 4/11/2008, graduated on 5/7/2012)
5. Jennifer Watts (Mentor: Dr. Elie Al-Chaer, candidacy exam: 5/26/2009, graduated on 6/28/2011)
6. Christen Simon (Mentor: Dr. Edgar Garcia-Rill, candidacy exam: 5/18/2010, graduated on 10/28/2011)
7. Nebojsa Kezunovic (Mentor: Dr. Edgar Garcia-Rill, candidacy exam: 11/30/2010, graduated on 3/6/2012)
8. James Hyde (Mentor: Dr. Edgar Garcia-Rill, candidacy exam: 4/11/2012, graduated on 4/26/2013)
9. Paige Beck (Mentor: Dr. Edgar Garcia-Rill, candidacy exam: 4/18/2012, graduated on 4/30/2013)
10. Naveen Babu Kandavalli (Mentor: Dr. Steve Barger, did not graduate)
11. Martin Watts (Mentor: Dr. Elie Al-Chaer, candidacy exam: 4/19/2010, graduated on 4/1/2014)
12. Gwendolyn Carter (Mentor: Dr. Mark Mennemeier, candidacy exam: 5/1/2012, graduated on 4/28/2015)
13. Tonisha Kearneyramos (Mentor: Dr. James G. Andrews, candidacy exam: 8/23/2013, graduated on 5/22/2015)
14. Xiong Bin Lin (Mentor: Dr. Hayar, candidacy exam: 10/23/2013, graduated on 12/9/2014)
15. Brennon Luster (Mentor: Dr. Edgar Garcia-Rill, candidacy exam: 11/19/2013, graduated on 4/5/2015)
16. Stasia D'Onofrio (Mentor: Dr. Edgar Garcia-Rill, candidacy exam: 11/26/2013, graduated on 4/12/2015)
17. Cristy Philips (Mentor: Dr. Edgar Garcia-Rill, did not graduate)
18. Helen Hayes (Mentor: Dr. Mark Mennemeier)
19. Thomas Grove (Mentor: Dr. Antino Allen, candidacy exam: 8/9/2016, graduated on 4/19/2018)
20. Tyler Alexander (Mentor: Dr. Antino Allen, candidacy exam: 8/9/2016, graduated on 4/26/2018)
21. Seung Hyun Jung (Mentor: Dr. Michael Borrelli, candidacy exam: 5/24/2018)
22. Frederico Kiffer (Mentor: Dr. Antino Allen, candidacy exam: 8/10/2018)

### **Grant review and study sections**

- **2010: NIH Study Section:** Ad hoc reviewer for the NTRC “Neurotransporters, Receptors, Channels and Calcium Signaling Study Section” at the NIH
- **2010: NIH Study Section:** Ad hoc reviewer for R03 Chemical Senses review meeting, National Institute on Deafness and Other Communication Disorders Special Emphasis Panel (ZDC1 SRB-R (37))
- **2012:** UAMS Translational Research Institute: TRI Pilot Grant Study Section Meeting (8/20/2012)
- **2013:** External reviewer for The University of Alaska's IDeA Network of Biomedical Research Excellence (INBRE) internal Seed Grant Competition (11/13/2013).
- **2018:** The Arkansas IDeA Network of Biomedical Research Excellence (Arkansas INBRE) study section (reviewed 3 grants)

I revised, made suggestions and/or helped in providing preliminary data for the following grants

#### **At the University of Arkansas for Medical Sciences:**

- Dr. Z. Jimmy Zhou: R01 EY010894-11, Title: “Physiology of the vertebrate retina”. Funded on 8/1/2007
- Dr. Elie Al-Chaer: R01 DK077733-01, Title: “Sex Hormones and Visceral Hypersensitivity”. Funded on 4/1/2008

- Dr. Jeffrey Kaiser: 5R01NS060674, Title: "Physiological Disturbances Associated with Neonatal Intraventricular Hemorrhage". Funded on 6/1/2008
- Dr. Edgar Garcia-Rill: R01 NS020246-22, Title: "Central modulation of rhythms". Funded on 12/1/2008
- Dr. Nancy Rusch: R01HL093526-01A1, Title: "Long-term Antihypertensive Therapy by Delivery of the BK Channel Gene to VSMCs". Funded on 5/5/2009

#### **At the Univ. of Tennessee:**

- Dr. Fu-Ming Zhou: R01 DA021194-01A2, Title: "Non-transporter cocaine mechanisms in dopamine system". Funded on 9/31/2007
- Dr. Hongwei Dong: R03 DC009049-01, Title: "Activity-Dependent Plasticity of Sensory Synapses in the Olfactory Bulb". Funded on 7/1/2007
- Dr. Matthew Ennis: R01DC003195-11, Title: "Metabotropic Glutamate Receptors in the Olfactory Bulb". Funded on 1/1/2007

#### **Requested reviewer for the following journals:**

- British Journal of Pharmacology
- Canadian Journal of Neurological Sciences
- Journal of Neurophysiology
- Journal of Neuroscience
- Journal of Neuroscience Methods
- Journal of Visualized Experiments
- Molecular and Cellular Neuroscience
- Nature Scientific Reports
- Neuroscience Letters
- Public Library of Science (plos.org)
- Science Advances
- PLOS one
- Physiology & Behavior

#### **Editorial board**

Advances in Neuroscience, Hindawi Publishing Corporation (since 2013)

#### **WEB DESIGN AND WEBMASTER EXPERIENCE**

- I advertise for my teaching, research and collaborations on a website that I personally design (<http://hayar.net>). I frequently update this website to demonstrate that, at UAMS, we have highly competitive teachers and scientists who lead the field of electrophysiological research in the brain. In addition, I constantly encourage my colleagues to advertise their research online, and help them in my role as webmaster responsible for maintaining and updating the websites for the Dept. of Neurobiology & Developmental Neurosciences, the Center of Translational Neurosciences (CTN), and the Arkansas Chapter of the Society for Neuroscience.

- Since July 2006, I am the webmaster and responsible for updating the following websites:

- 1- Dept. of Neurobiology & Developmental Sciences: <http://neurobiology.uams.edu>
- 2- Center of Translational Neurosciences: <http://www.uams.edu/ctn>
- 3- Arkansas Chapter of the Society for Neuroscience: <http://www.ar-neuro.org>

- Since August 2007, I am responsible for organizing and scheduling the Center of Translational Neurosciences and the Dept. of Neurobiology & Developmental Sciences seminars: <http://neurobiology.uams.edu/seminars>

- Since September 2010, I volunteered to become administrator of a SharePoint blog site for the “Neuroscience Magnet Group” established by the Dean of Medical School to enhance collaborative research:

<http://sharepoint.uams.edu/Divisions/neuromagnet>

- Since April 2011, I am responsible of administering the UAMS Academic Senate’s website:

<http://academicssenate.uams.edu>

- Since February 2015, I am responsible for updating the Institutional Animal Care and Use Committee’s website: <http://inside.uams.edu/iacuc>

-Neurobiology courses’ webpages:

1-Cellular & Developmental Neurobiology: <http://hayar.net/NBDS5114>,

2-Neuronal Signals: <http://hayar.net/NBDS5161>,

3-Basic Neuroscience: <http://hayar.net/NBDS5033>

## **EXPERIENCE IN COMPUTER HARDWARE AND SOFTWARE**

- Custom building high-end computers for research and troubleshooting PC hardware and software at the Center for Translational Neurosciences

- **Operating Systems:** MS-DOS, Windows, Macintosh

- **Application programs:** Microsoft Office, Canvas, Corel Draw, Photoshop, Adobe Acrobat, pClamp, Spike2, Origin, MiniAnalysis, Neuroplex, SAP, ARIA, Micromanager, ImageJ, Windows Movie Maker, Windows Media Encoder, Photoscape, Any Video Converter

- **Programming Languages:** Visual Basic, Visual C++, Origin C and Labtalk Script language, OriginLab, MatLab

- **Internet:** Webpage design (see my website <http://hayar.net>), Personal Web Server, FTP Server, Frontpage, Microsoft Expression Web, Wordpress.

- SAP user since 11/16/2006.

- Online grant submission (Grants.gov) and routing (ARIA, TRACKS)

## **PRESS RELEASE AND PUBLICITY**

UAMS News Bureau: Office of Communications & Marketing, 4301 W. Markham # 890, Little Rock, AR 72205

1- UAMS Faculty Member Receives Award for Smell Research. June 16, 2006.

<http://www.uamshealth.com/?id=1655&sid=1>

2- UAMS Researchers Identify Sleep-Wake Controls with Implications for Coma Patients and Those Under Anesthesia. July 20, 2007.

<http://www.uamshealth.com/?id=2849&sid=1>

3- Brain Mechanism Could Be Key to New Stimulants, Anesthetics. June 2, 2010

<http://www.uamshealth.com/News/Default.aspx?id=5349&sid=1&nid=8818>

4- Seeds of Science Award: Three Grants Presented to UAMS Cancer Researchers

<http://uamshealth.com/news/2016/01/29/three-grants-presented-to-uams-cancer-researchers-2/> January 29, 2016.

## **NATIONAL AWARD AND RECOGNITION**

I was awarded in 2006 the “AChemS Young Investigator Award for Research in Olfaction” by the Association for Chemoreception Sciences (AChemS), an international association that advances understanding

of the senses of taste and smell. The award is given annually to an outstanding junior scientist who is an emerging leader in the field of olfaction, and whose research record provides evidence of excellence and contributions that have had or are likely to have a major impact on research in the field of olfaction. I was given this award (\$2000) because I have played an important role in promoting chemosensory research by advancing our knowledge of olfactory bulb neurophysiology. My research project constitutes an essential step to our understanding of olfactory input processing at the level of the glomeruli and it helps us to unravel the fundamental network mechanisms responsible for encoding and processing sensory information. In 2010, I was a nominee for the “Secretary” position at the Association for Chemoreception Sciences (AChemS).

## **ESTABLISHING STATE-OF -THE-ART TECHNIQUES FOR EXPLORING THE BRAIN**

### ***1- Ultra fast imaging of neuronal activity***

Optical imaging techniques, nowadays, have become powerful tools for investigating cellular and network physiology. We have purchased a state-of-the art fast imaging system (NeuroCCD-SMQ, RedShirtImaging, CT) with a very high temporal resolution camera, capable of acquiring up to 5000 frames/sec. At this frame rate it is possible to image calcium and voltage signals at sub-ms temporal resolution. This acquisition rate will allow us to detect fast voltage or calcium signal transients in a single neuron or across a population of neurons. I have obtained interesting preliminary data and submitted them as part of new grant applications. Because this is a break-through technique and it is the first of its kind at UAMS, I have helped many colleagues to generate imaging data related to their project. For example, we have performed imaging experiments on the retina and the preliminary data has helped Dr. Z. Jimmy Zhou get funded by an NIH grant (R01 EY010894-11, entitled “Physiology of the vertebrate retina”). I have performed calcium imaging experiments on the intact dorsal root ganglion in collaboration with Dr. Elie Al-Chaer (Hayar et al., 2008). The purpose of the ongoing experiments is to elucidate the mechanisms of sensory hyper-excitability that lead to chronic pain and we are planning to submit soon an NIH grant on this project.

### ***2- Live confocal live imaging***

We have installed on top of an Olympus microscope a CSU-X1 spinning disk confocal (Yokogawa Electric Corp, Japan). This system has the world's fastest scanning speed (up to 2000 frames/s) and integrates well with our RedShirtImaging camera which is also capable of acquiring 2000 fps. It consists of a Nipkow spinning disk that rotates at 10,000 rpm and contains about 20,000 pinholes and a second spinning disk containing the same number of micro-lenses to focus excitation laser light into each corresponding pinhole. It can very rapidly raster scan the field of view with about 1,000 laser beams. Multi-beam scanning not only increases scanning speed, but also results in significantly lower photobleaching and phototoxicity. The addition of this relatively low-cost (\$150,000) confocal system is expected to enhance our fast live imaging technology by allowing us to image deeper in the tissue with much better signal-to-noise ratio and less light scattering.

### ***3- Ultraviolet laser technology to stimulate and image the brain***

We have purchased an ultraviolet laser uncaging system. This equipment generates a high energy ultraviolet laser beam which is linked to the microscope illuminator port via a 50  $\mu\text{m}$  diameter quartz optical fiber guide. Using this system, it is possible to perform spot illumination of areas as small as 5  $\mu\text{m}$  diameter to uncage compounds such as glutamate or calcium in a small region of a brain slice such as single dendrites. This technique can be combined with calcium-sensitive dye imaging. The ultraviolet laser light can also be used to evoke small brain lesions or to evoke a clot in a single capillary or blood vessel in the brain in vivo to mimic the effect of stroke and study the mechanism of local ischemia.

### ***4- Infrared laser technology to quantify local cerebral blood flow***

We have also purchased an infrared laser equipment (Advance Laser Blood Flowmeter ALF 21) for monitoring cerebral blood flow via Doppler effect. A semiconductor laser beam is stabilized and guided through

a quartz optical fiber with an open angle of approximately 28 degrees and then reflected by the organic tissues, get scattered, reflected, and so forth to diffuse. Light reflected by the moving blood changes its frequency by Doppler Shifts, in accordance with the speed of blood flow. The equipment can measure simultaneously blood flow velocity and mass. We are planning to use this equipment to measure the effect of hypoventilation and hypercapnia on blood flow in premature animals. This equipment will be used to generate preliminary results to apply for competitive multi-investigator NIH grants in collaboration with Dr. Jeffrey Kaiser, a neonatologist recently recruited at the Center of Translation Neurosciences.

**5- *Design an innovative method for long duration recording of electrocardiogram (ECG) and breathing activity*** in restrained mice and test the effects of fast-acting antidepressant drugs such as ketamine.

## **COLLABORATIONS**

In a highly competitive research environment, it is important to prevent the silo mentality and promote an environment of collegiality to facilitate sharing information and resources among faculty. I am a team player and I have been involved in several collaborative projects with researchers in my Department, at the University of Arkansas and with collaborators in other Universities especially members of the Association for Chemical Senses. I continuously seek to help members of my neuroscience community to initiate new research or to refine ongoing work. My working philosophy is that real success can only be achieved when your colleagues are also successful. I am an excellent team player because my colleagues can rely on me to troubleshoot and solve their scientific problems. I share openly and willingly any scientific information, knowledge and experience. I have an international background and I communicate constructively and listen actively to colleagues with different ideas and points of view and I treat them in a respectful and supportive manner.

My ultimate goal is to understand the alterations in neuronal networks in pathological conditions, such as neurodegenerative diseases, functional pain, hypertension, and when the brain becomes addictive to alcohol and drugs of abuse. Since my recruitment at the Dept. of Neurobiology & Developmental Sciences on January 2006, I have built 6 patch-clamp electrophysiology setups: 3 in my lab and 3 others in my colleagues' labs (Dr. Elie Al-Chaer and Dr. Garcia-Rill at the Center for Translational Neurosciences). I have trained and co-mentored 6 graduate students, 8 research assistants, 3 postdoctoral fellows, 1 medical student, and 4 high-school students in several techniques such as patch-clamp recordings in different brain structures involved in olfaction, vision, sleep and pain.

### **List of ongoing and previous collaborations since recruitment at UAMS in 2006 (newest collaborations are listed first)**

1. Collaboration with newly-recruited faculty, Dr. Linda Larson-Prior and Dr. Ronald Salomon, at the Dept. of Psychiatry, UAMS, to write a proposal to investigate the mechanisms of action of antidepressants such as ketamine and fluoxetine on the properties of serotonergic raphe neurons.
2. Collaboration with Dr. Fen Xia, the new Chair of Department of Radiation Oncology at UAMS. The project consists of exploring the mechanisms by which chemotherapeutic drugs such as cisplatin can induce peripheral neuropathy. We will conduct this study using electrophysiology and imaging techniques from dorsal root ganglion neurons dissected from different animal models of cancer. This collaboration has the potential to generate new preliminary data to submit NIH grant and to promote the likelihood that UAMS will get the National Cancer Institute (NCI) designation.
3. Collaboration with Dr. Radwan Al Faouri (Nano Institute, Univ. of Arkansas at Fayetteville) to establish a lysenin channel-neuronal membrane model in order to investigate the properties and modulation of some of the potentially lethal pore-forming toxins. A proposal was submitted to the Arkansas Bioscience Institute on 5/27/2016. The goal of the proposal is to investigate the function of lysenin channels when they are transfected into the membrane of cerebellar Purkinje cells in brain slices. We will be testing the kinetic

properties and the voltage-dependency of these channels, and then we will investigate whether we can block them with selective drugs, therefore preventing them from creating excitotoxic damage to neurons.

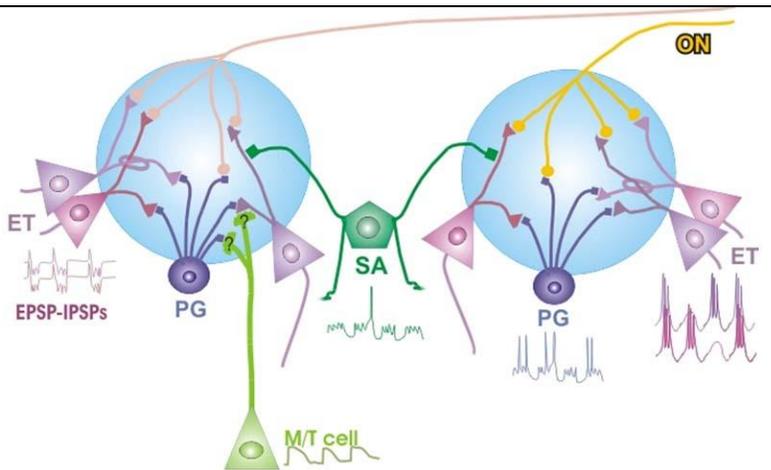
4. Collaboration with Dr. Peter Crooks (Dept. of Pharmaceutical Sciences, UAMS) to test an antagonist of the nicotinic receptors  $\alpha 9\alpha 10$  using electrophysiological and imaging techniques. Dr. Crooks is internationally recognized for his research in anticancer drug discovery and he is interested in developing new pain medication to treat acute and chronic pain.
5. Collaboration with Dr. Maxim Dobretsov (Dept. of Anesthesiology, UAMS) to investigate the role of the alpha3 isoform of neuronal sodium-potassium ATPase in controlling the activity of Purkinje cells. An R03 grant has been submitted on this research project on 10/15/2015 and a CTN pilot study grant has been submitted on 10/23/2015. This research project will provide insight into the fundamental mechanisms leading to dystonia and it will help us develop strategies to cure or more effectively treat people who are affected by this neurological disorder.
6. Collaboration with Dr. Antino Allen (Dept. of Pharmaceutical Sciences, UAMS) to prepare and submit a NASA grant in which I am co-I. The grant was discussed at a study section but was not ranked high enough to receive funding. I am also collaborating with Dr. Allen on a behavioral test (licking) to investigate motor functions in irradiated mice. I have also collaborated with him to perform electrophysiological experiments that consist of recording field potentials in hippocampal slices to investigate the effects of irradiation on synaptic plasticity in irradiated mice. This is a model of space radiation that astronauts encounter while traveling long journeys into space.
7. Collaboration with Dr. Edgar Garcia Rill (Dept. of Neurobiology and Developmental Sciences, UAMS) to investigate electrical coupling in the reticular activation system which is involved in the regulation of rapid eye movement sleep. We had a funded 5-year collaborative grant that started on 8/1/2009. We have published so far 10 articles and 8 abstracts in collaboration.
8. Collaboration with Dr. Elie Al-Chaer (Dept. of Pediatrics, UAMS) to investigate the effect of visceral hypersensitivity on the electrophysiological properties and calcium signaling in dorsal root ganglion neurons using the whole-cell patch clamp technique in the intact ganglion. We have published so far 1 article and 2 abstracts in collaboration. We have another manuscript in preparation on the effects of purinergic receptor activation in spinal cord slice.
9. Collaboration with Drs. Kim Light and Dwight Pierce (Dept. of Pharmaceutical Sciences) to investigate the alterations in cerebellar neuronal circuit interactions in a rat model of Fetal Alcohol Spectrum Disorders. We have published so far 4 articles and 4 abstracts in collaboration.
10. Collaboration with Dr. Sung Rhee (Dept. of Pharmacology and Toxicology) to investigate a novel scaffolding molecule in the muscle cells of small cerebral arteries that may ensure that potassium channels are expressed in adequate numbers and in the right location in the muscle cells of cerebral arteries to optimize blood flow to the brain. We had a funded 5-year collaborative grant that started on 4/1/2010.
11. Collaboration with Dr. Nancy Rusch (Dept. of Pharmacology and Toxicology, UAMS) to perform *in vivo* experiments using an infrared laser equipment (Advance Laser Blood Flowmeter ALF 21) for monitoring cerebral blood flow via Doppler effect. The goal of the collaboration was to bring together a team of researchers with various expertises in order to strengthen research in the cardiovascular field. Preliminary data were obtained and I provided a consultant letter that was used in a grant application on antihypertensive gene therapy, which was subsequently funded on 5/5/2009.
12. Collaboration with Dr. Kathryn Hamilton (Louisiana State University) to characterize the cell types of the olfactory bulb external plexiform layer and to understand the contributions of these cells in this layer to olfactory discrimination. We have published so far 8 papers and 7 abstracts in collaboration. We had a funded 3-year collaborative grant that started on 4/1/2009.

13. Collaboration with Dr. Mahmoud Kiaei (Dept. of Neurobiology and Developmental Sciences, UAMS) to investigate the licking pattern in a mouse model of amyotrophic lateral sclerosis (ALS). We generated interesting preliminary data showing that a disruption in motor behavior can be detected at early age before any ALS symptom becomes obvious and these data could be used to support future grant applications.
14. Collaboration with Dr. Jeffrey Kaiser (Dept. of pediatrics, UAMS) to develop an animal model of intraventricular hemorrhage and to test the effect of hypercapnia and hypertension on cerebral blood flow and other respiratory and cardiovascular parameters. New techniques haven developed in my lab to investigate brain hemorrhage by ultra-fast imaging of small blood vessels. A recent R03 grant on this topic has been submitted on 10/15/2015.
15. Collaboration with Dr. Jimmy Zhou (Dept. of Physiology and Biophysics, UAMS, and Yale Univ.) to investigate retinal waves using imaging of calcium and voltage-sensitive dyes. Dr. Zhou got funded by a second R01 grant application on the synaptic function and organization of the mammalian retina. Then, he moved to Yale Univ. where he became Vice Chairman and Director of Research at the Dept. of Ophthalmology and Visual Science.
16. Collaboration with Dr. Tammy Kielian (Dept. of Neurobiology and Developmental Sciences, UAMS) to investigate the effects of brain infection on electrical coupling in glial cells labeled by GFAP in transgenic mice. Dr. Kielian has moved her laboratory to the University of Nebraska Medical Center in Omaha, NE. One of my postdoctoral fellows, Dr. Nikolay Karpuk has moved with her to continue working on this project.
17. Collaboration with Dr. Naim Haddad (Dept. of Neurology, UAMS) to establish a method of EEG dipole source mapping in epilepsy and neurodegenerative diseases. We have applied for a “Pilot study Center for Translational Neuroscience Award” and setup EEG equipment to start this pilot study. Dr. Haddad moved subsequently to another position at Weill Cornell Medical College in Qatar.
18. Collaboration with Dr. Atom Sarkar (Dept. of Neurosurgery, UAMS) to help set up a Human Electrophysiology Core for recording from human brain tissue from surgeries performed in epileptic or cancer patients.
19. Collaboration with Dr. Roger Buchanan (Arkansas State University) to determine how repetitive transcranial magnetic stimulation (rTMS) alters the effects of chronic exposure to cigarette smoke on the rat P13 potential. We obtained a funded collaborative grant from the Arkansas Bioscience Institute.
20. Collaboration with Dr. Jason Chang (Dept. of Neurobiology and Developmental Sciences, UAMS) to investigate the mechanisms of neurotoxicity of methyl mercury in glial cells and neurons.
21. Collaboration with Dr. Xiong Liu (Mesolight, LLC) to develop a novel fluorescence contrast agent for near-infra-red deep tissue imaging based on up-converting nanoparticles (UCNPs). A collaborative grant was submitted on 08/05/2010.
22. Collaboration with Dr. Matthew Ennis (Univ. of Tennessee Health Science Center) on a research project to study metabotropic glutamate receptors (mGluR) in the olfactory bulb. I provided preliminary showing how mGluR activation enhances External Tufted cell rhythmic bursting and synchronize the glomerular network. Dr. Ennis’ grant renewal was approved for funding in 2007. I have subsequently published with Dr. Ennis 5 articles.

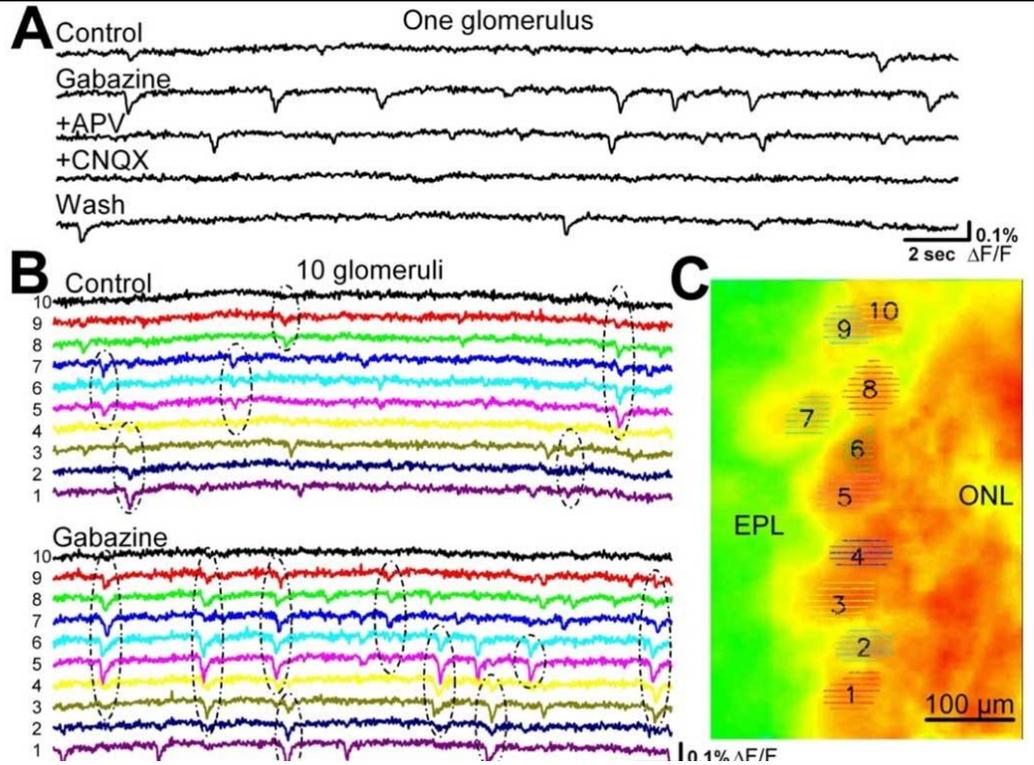
## Olfactory Research: External tufted cells coordinate olfactory bulb activity

An impairment of olfactory bulb function has been shown recently to be associated with Parkinson's and Alzheimer's diseases. This association prompts additional investigations of the anatomy and connectivity of the olfactory bulb in order to unravel the mechanisms of sensory processing by bulbar circuits and to understand the neuronal basis of olfactory dysfunction in neurodegenerative diseases. The olfactory bulb is characterized by an array of modules called glomeruli that are organized in a way such that odor information is represented spatiotemporally among glomeruli. Despite dramatic advances in chemosensory research, we still do not understand how sensory input is encoded in neural activity within and among glomeruli before being relayed to higher-order cortical structures. According to the combinatorial receptor and glomerular codes for odors, the fine tuning of the output level from each glomerulus is important for information processing in the olfactory system. We have made significant advances in understanding how synchronous bursting activity of external tufted cells (ET) is coordinated by both synaptic and gap junction coupling in addition to olfactory nerve input. Therefore, one important physiological function of the glomerular network might be to generate and propagate synchronous activity as an essential step in olfactory coding. However, the role of periglomerular cell (PG) GABAergic signaling in shaping glomerular input/output is still largely unknown. Immature PG cells migrate from the subventricular zone and integrate into the glomerulus to perform discrete network operations such as providing feedback inhibition to ET cells. Most PG cells are both GABAergic and dopaminergic and they may degenerate in the early stages of Parkinson's disease, thus causing disturbance in glomerular network interactions and olfactory dysfunction. In this renewal application, we investigate the functional role of PG cells using a combination of *in vitro* techniques such as electrophysiological and optical multicellular and population recordings at high temporal resolution. The main goal of this proposal is to study the impact of PG cell activity on the output of the glomerulus. We will test the following hypotheses: (1) PG cell population fire correlated bursts of action potentials and release GABA synchronously in a bursting fashion onto themselves and onto ET cells. (2) GABA released from PG cells activates GABA<sub>B</sub> receptors onto ET cells and modulates the release of glutamate from ET cell dendrites. (3) Center-surround GABAergic and glutamatergic interglomerular synapses shape the pattern of glomerular activity and coordinate spatiotemporal activity among neighboring glomeruli. This research will promote our understanding of interneuronal population coding in the olfactory system. In particular, it will provide insight into how interneurons shape the activity of output cells and modulate their synchronous firing. Therefore, delineating the interactions among interneurons and output neurons of the olfactory bulb would help us understand the normal function of the glomerular neuronal circuit and how it may be altered in neurodegenerative diseases that are associated with smell deficits.

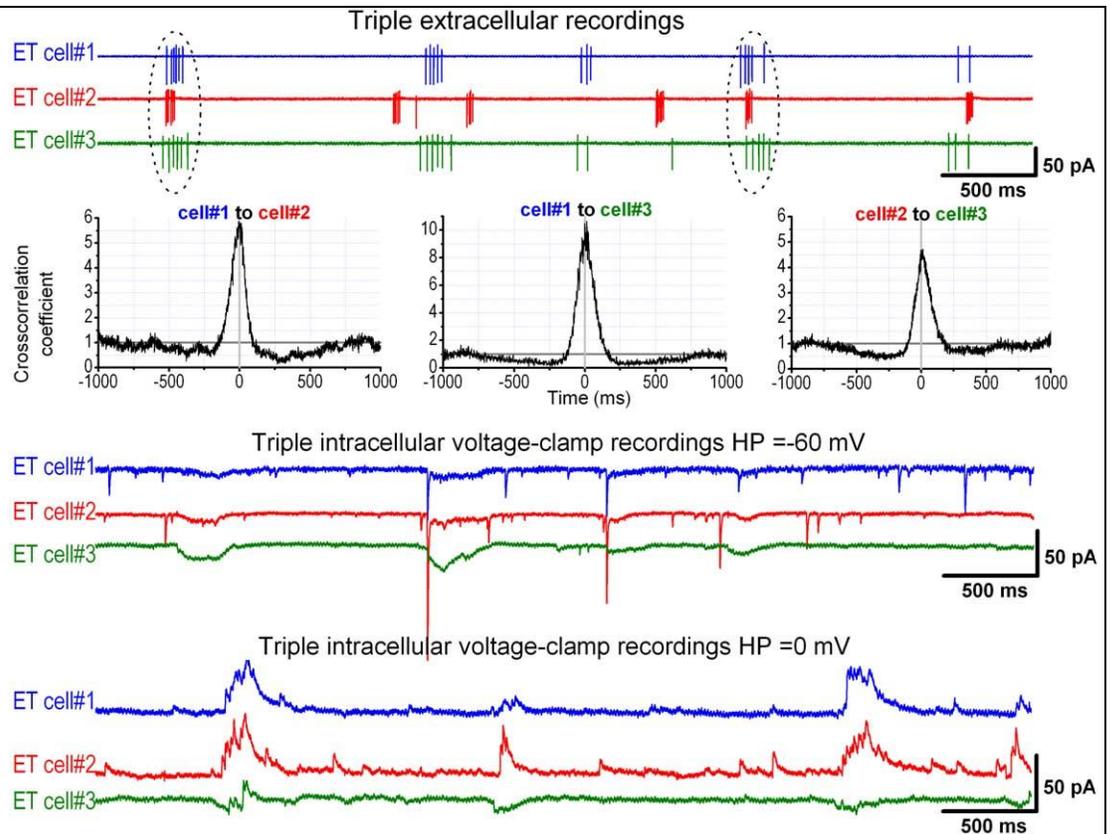
Schematic model of the intraglomerular circuitry. Glutamatergic ET cells have intrinsic, rhythmic burst firing and are contacted directly by olfactory nerve (ON) terminals. ET cells (right) exhibit synchronous spike bursting activity because they are connected by gap junctions (oval) (Hayar et al., 2004, 2005). ET cells (left) are synchronized further by synchronous EPSPs from the same olfactory nerve (ON) axons, and by correlated bursts of IPSPs from the same and different sets of periglomerular (PG) cells. The EPSPs and IPSPs occur in sequence and they respectively trigger and subsequently terminate the bursting. ET cells of the same glomerulus fire in synchrony and directly elicit bursts of EPSPs in other JG interneurons, the periglomerular (PG) and short axon cells (SA), most of which do not receive ON input. PG cell dendrites ramify in a restricted portion of a single glomerulus and thus might serve for local intra-glomerular inhibition via dendrodendritic interactions with ET or mitral cell (MC) dendrites. By contrast, SA cells have dendrites and axons extending throughout several glomeruli and thus might serve for inter-glomerular (i.e. lateral) inhibition. ET cells may represent a rhythm generator of the glomerular network. The synchronously bursting ET cell glomerular "ensemble" represents an oscillating neuronal circuit that monosynaptically synchronizes the activity of PG and SA neurons within the same glomerulus, and may possibly coordinate the activity of MC projection neurons via glutamate spillover.



Evidence for inter-glomerular interactions. An olfactory bulb slice was stained with the voltage-sensitive dye di-4-ANEPPDHQ (75  $\mu$ M). Optical recordings were obtained with an acquisition rate of 128 frames/sec and 80x80 pixels resolution using a 10X objective. A. Spontaneous optical signals were obtained from a single glomerulus (glomerulus#5 shown in panel C; a decrease in fluorescence intensity indicates depolarization) in different pharmacological conditions. Disinhibition by gabazine increased the amplitude and the frequency of the spontaneous events whereas APV reduced their duration. They were blocked by addition of CNQX indicating that they represent population excitatory postsynaptic responses. B. Optical signals from 10 regions of interest, each representing a single glomerulus. Note that the optical events (dashed ovals) were correlated among neighboring glomeruli. Gabazine increased the number of correlated events and widened their spatial distribution. C. Representative frame of the region where the spontaneous optical glomerular responses were recorded. ONL: olfactory nerve layer EPL: external plexiform layer.



Triple recordings from ET cells. Three ET cells were first recorded extracellularly using electrode containing ACSF for a period of about 10 min. Then we performed intracellular recordings from the same ET cells in voltage clamp, using patch pipettes containing QX-314 and cesium methylsulfonate. At holding potential of  $-60$  mV, the ET cells displayed relatively large amplitude synchronous fast EPSCs (downward deflections) followed sometimes by synchronous slow EPSCs. At the holding potential of  $0$  mV (near the reversal potential of excitatory ionotropic receptors), only synchronous bursts of IPSCs could be observed in all 3 cells (bottom 3 traces).

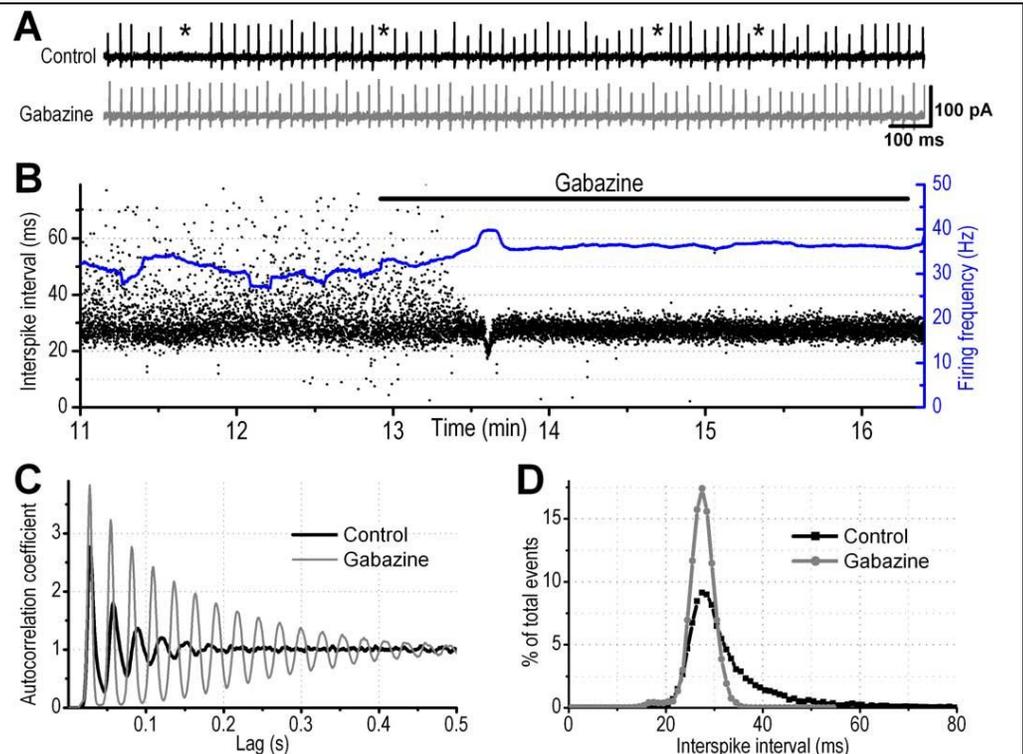


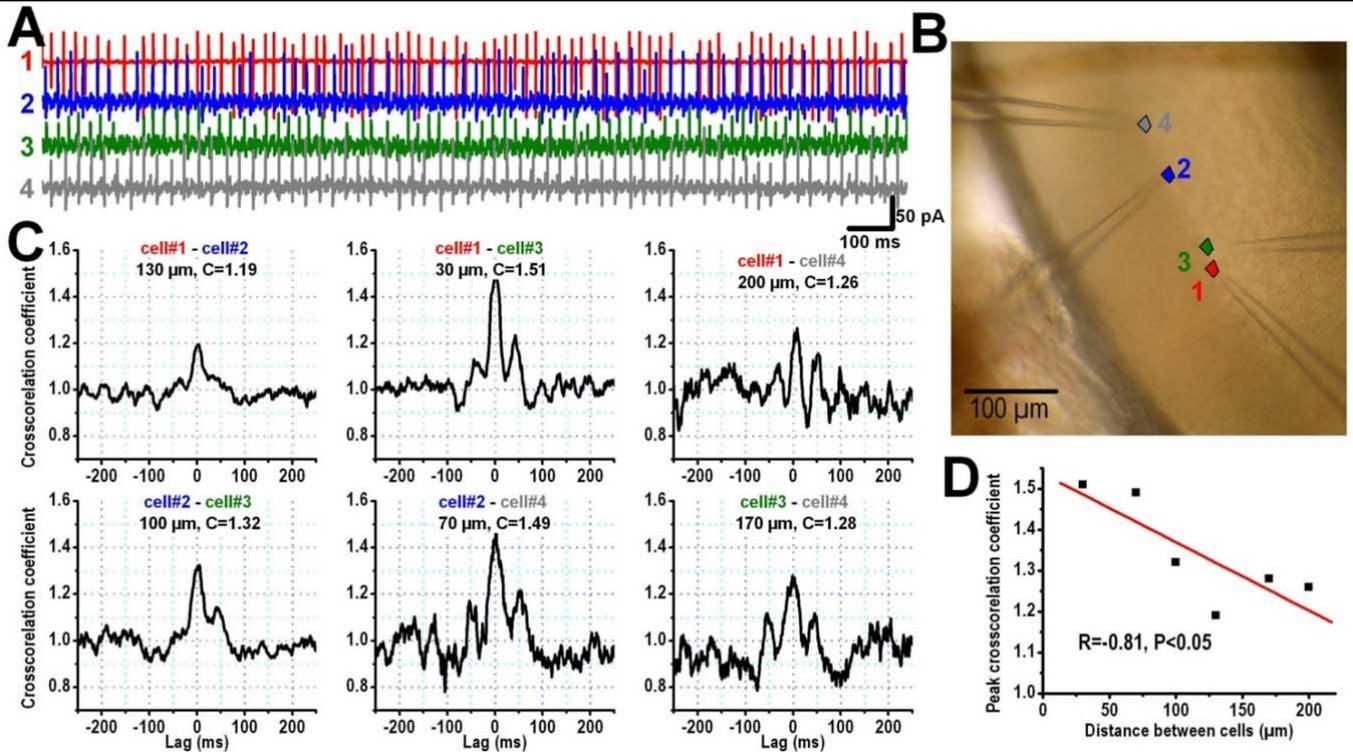
## Alcohol Research: Neuronal circuit interactions in a rat model of Fetal Alcohol Spectrum Disorder

Purkinje cells (PCs) in the cerebellum are particularly vulnerable to damage caused by alcohol exposure during early brain development. It is unknown how neuronal circuit interactions are altered during alcohol exposure and how neurons that survive the insult of alcohol manage to compensate for the loss of a significant number of PCs. In order to investigate the damage on cerebellar circuits caused by developmental alcohol exposure, we will use a rat model of fetal alcohol spectrum disorder (FASD), which mimics the deleterious effects on the fetus caused by alcohol ingested by a pregnant mother during the third trimester. Because PCs are the sole output of the cerebellar cortex, we hypothesize that a disruption in coordinated activity among PCs is the leading cause of cerebellar dysfunction in the FASD model. This hypothesis will be tested using a combination of sophisticated electrophysiological and imaging techniques where it is possible to record multiple neurons simultaneously and characterize the spatiotemporal propagation of their activity. Our main goal is to elucidate the impact of alcohol exposure on cerebellar network processing in the FASD model. We will test the hypothesis that the PC synchronized activity is impaired in the FASD model. In particular, we will test whether PCs which survive the alcohol treatment exhibit an altered synchronized activity caused by a change in GABAergic synaptic transmission and the delayed hyperpolarization-activated current (I<sub>h</sub>). These experiments will be performed using multiunit extracellular loose-patch and intracellular whole-cell patch clamp recordings. The mechanisms and degree of synchronized activity will be analyzed as a function of distance between PCs. We will also test whether the spatiotemporal population activity of PCs is altered in the FASD model by performing neuronal population recordings using ultrafast imaging of cerebellar slices that have been labeled with voltage- and calcium- sensitive dyes. Moreover, we will test the hypothesis that disruption in neuro-plasticity at the level of the synapses is altered in the FASD model. For these experiments, we will use another combination of techniques such as immunofluorescence, confocal microscopy and 3D-reconstruction for quantitative analysis in fixed tissues, as well as dynamic visualization of axons and spines in live cerebellar slices. The results of this study are expected to provide a break-through in our understanding of the functioning of homeostatic neuronal circuits altered by alcohol exposure. This knowledge is necessary to conceptualize and identify appropriate interventions to alleviate the brain damage induced by developmental alcohol exposure. This project is very important for public health because it will enhance our understanding of the fundamental mechanisms of developmental alcohol effects on cerebellar control of motor movement. It also raises the awareness of the general population about the detrimental effects of alcohol and drugs of addiction on brain networks.

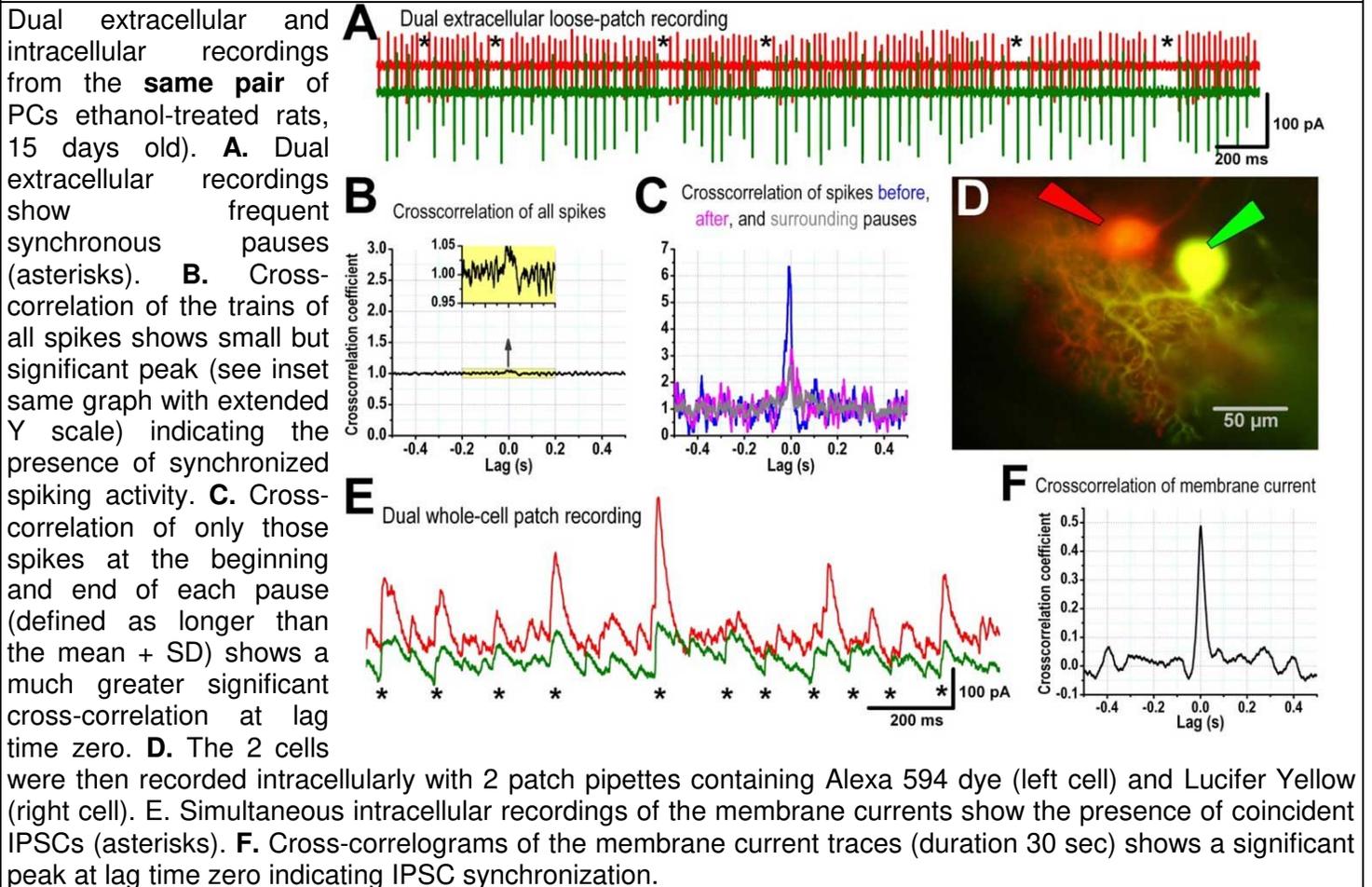
Effect of blocking inhibition on the firing pattern of a control PC.

**A.** Extracellular recording from a PC showing that the GABA-A receptor blocker, gabazine (10  $\mu$ M) eliminated the pauses in the firing (asterisks). **B.** Scatter plot of the interspike intervals showing that gabazine reduced the variability of the interspike intervals and slightly increased the firing frequency. **C.** Autocorrelograms of the spike trains show that gabazine increase the amplitude and the number of ripples. **D.** Histograms of the interspike intervals (bin = 1 ms) showing that gabazine changed the skewed distribution into a Gaussian distribution.





Simultaneous recordings of 4 adjacent PCs from control rat. **A**. Traces of spike trains from the 4 cells. **B**. Photo of the cerebellar slice (lobule 1) showing the position of the 4 extracellular electrodes in the PC layer. **C**. Cross-correlograms of the spike trains (during 6 min of recording) of the 6 different pairs of cells. Scatter plot of the peak cross-correlation coefficient as a function of distance between cells. **D**. The linear fit (red trace) indicates that this coefficient decreases as distance between cells increases.

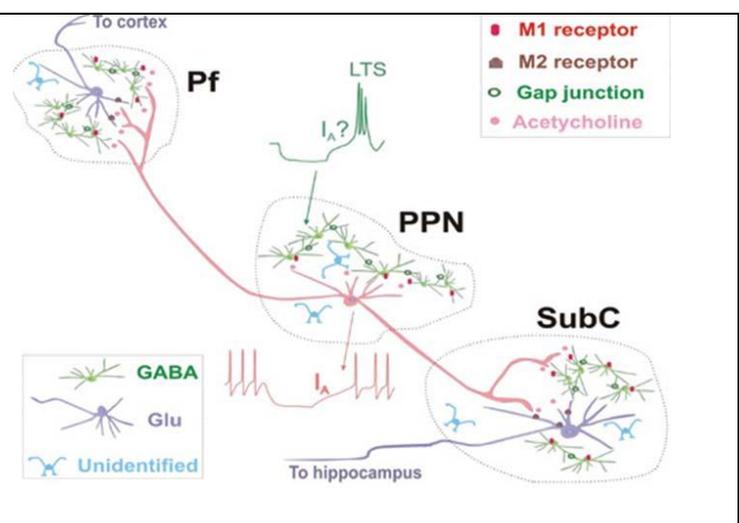


Dual extracellular and intracellular recordings from the **same pair** of PCs ethanol-treated rats, 15 days old). **A**. Dual extracellular recordings show frequent synchronous pauses (asterisks). **B**. Cross-correlation of the trains of all spikes shows small but significant peak (see inset same graph with extended Y scale) indicating the presence of synchronized spiking activity. **C**. Cross-correlation of only those spikes at the beginning and end of each pause (defined as longer than the mean + SD) shows a much greater significant cross-correlation at lag time zero. **D**. The 2 cells were then recorded intracellularly with 2 patch pipettes containing Alexa 594 dye (left cell) and Lucifer Yellow (right cell). **E**. Simultaneous intracellular recordings of the membrane currents show the presence of coincident IPSCs (asterisks). **F**. Cross-correlograms of the membrane current traces (duration 30 sec) shows a significant peak at lag time zero indicating IPSC synchronization.

## Sleep Research: Central Modulation of Rhythms

The pedunculopontine nucleus (PPN) helps control sleep-wake rhythms and modulates posture and locomotion. The proposed research will address three functional aspects (ascending, local and descending) of the PPN, the cholinergic arm of the Reticular Activating System (RAS). From 10-30 days postnatally there is a dramatic decrease in the percent of REM sleep in the rat. A hypothesis was proposed suggesting that disturbances in the developmental decrease in REM sleep, a return to a neonatal state of REM sleep drive, could lead to a number of disorders characterized by increased REM sleep drive. We tracked changes in ascending and descending projections from the PPN, along with developmental changes in neurochemical systems modulating the PPN. We found that certain neurotransmitters could be responsible for modulating the developmental decrease in REM sleep, reported new interactions between identified cell types, and proposed a push-pull model for PPN modulation of posture and locomotion. We also discovered the presence of electrical coupling in the PPN as well as in an ascending and a descending target of the PPN. Preliminary evidence suggests that changes in electrical coupling parallel the developmental decrease in REM sleep. This newly discovered mechanism will be explored using a) whole-cell patch clamp and intracellular sharp electrode recordings, b) pharmacological manipulation to induce and block electrical coupling, and c) measures of connexin-36 mRNA expression and protein levels before and during the developmental decrease in REM sleep (7-30 days), in 1) the parafascicular nucleus (Pf), an ascending target of the PPN, 2) the PPN itself, and 3) the SubCoeruleus (SubC) nucleus, a descending target of the PPN implicated in the generation of REM sleep. The discovery of electrical coupling in these RAS nuclei is critical given that recent findings suggest that the stimulant modafinil exercises its effects by increasing electrical coupling. Conversely, a number of anesthetics are known to decrease electrical coupling. The mechanistic characterization proposed represents a new paradigm for sleep-wake control and may revolutionize how we think about sleep-wake control, reveal how electrical coupling interacts with known transmitter inputs in the RAS to modulate sleep-wake states, and how we may develop new therapeutic strategies for the treatment of a number of devastating disorders that have as a common symptom the manifestation of increased REM sleep drive. In fact, by ignoring the role of electrical coupling we will fail to understand this system. We discovered the presence of electrical coupling, by which nerve cells can communicate directly through pores called gap junctions, in the part of the brain that controls sleep-wake cycles, the reticular activating system (RAS). We demonstrated the presence of electrical coupling using recordings from pairs of neurons. This finding helps explain the actions of some anesthetics, which are known to block gap junctions, and of a new stimulant, modafinil, which is now known to increase electrical coupling. This novel mechanism may promote ensemble activity in large numbers of neurons to promote rhythms during waking, and the absence of such activity may lead to sleep. We propose a series of detailed studies to investigate the organization (which cells are coupled, which are not), the control (which transmitter systems activate, which inhibit), and the modulation (which agents can increase vs. decrease coupling) of this mechanism. The mechanistic characterization proposed represents a new paradigm for sleep-wake control and may revolutionize how we think about sleep-wake control, reveal how electrical coupling interacts with known transmitter inputs in the RAS to modulate sleep-wake states, and how we may develop new therapeutic strategies for the treatment of a number of devastating disorders that have as a common symptom the manifestation of increased REM sleep drive. In fact, by ignoring the role of electrical coupling we will fail to understand this system.

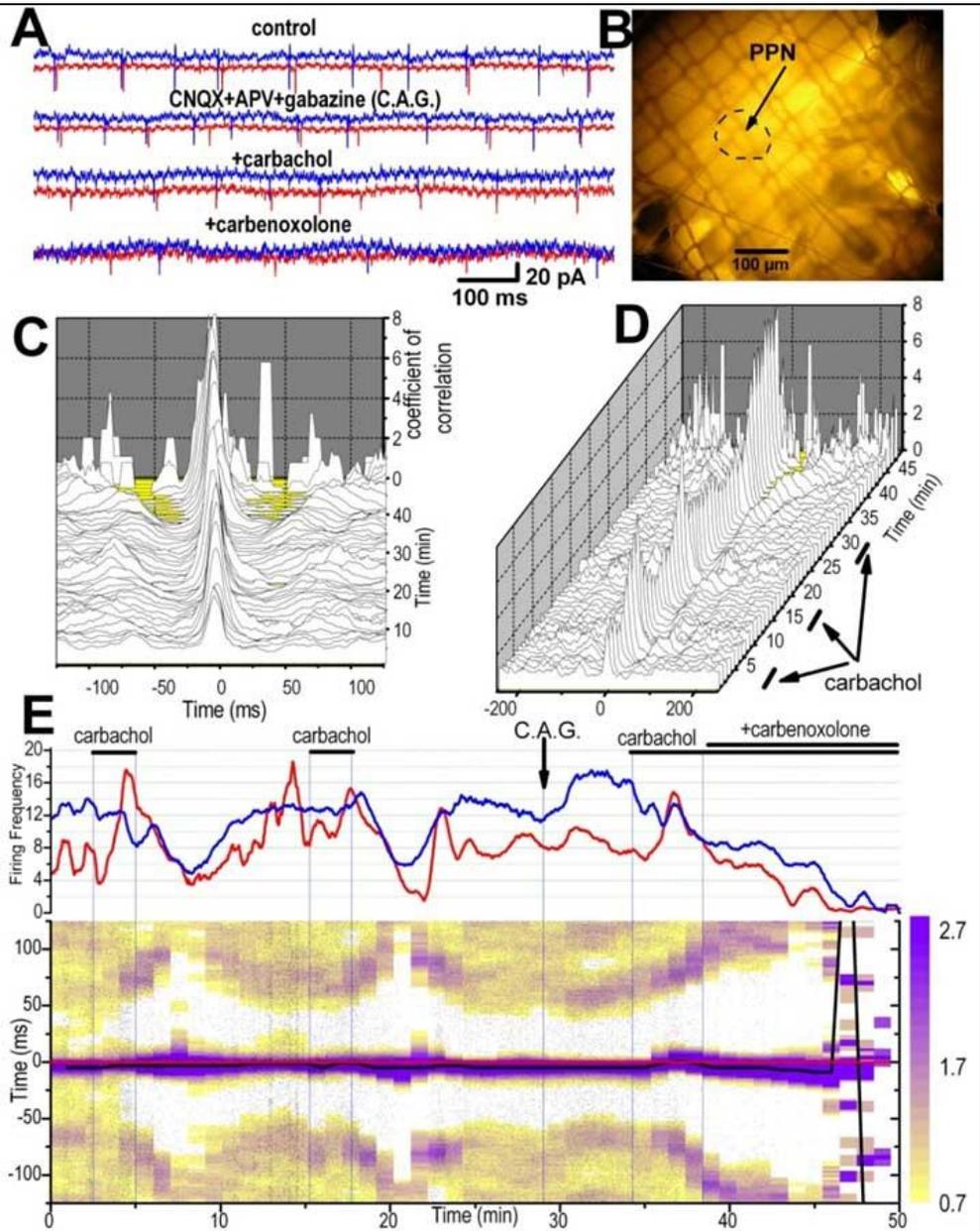
System Schematic. Pf, PPN and SubC are organized similarly to the specific relay and reticular nuclei of the thalamus. Thalamic relay neurons (TRNs) project to the cortex and send collaterals to inhibitory GABAergic interneurons (which are electrically coupled) in the reticular nucleus that in turn inhibits TRNs and local circuit neurons. Cortical projections return to the TRNs, local circuit cells, and to inhibitory GABAergic interneurons. Ascending cholinergic input from the PPN excites TRNs and inhibits reticular cells. These interactions lay the groundwork for the exploration of a novel mechanism for sleep-wake control based not only on known transmitter interactions, but also on superimposed ensemble activation provided by electrical coupling.



Synchronous activity in pedunculo pontine nucleus (PPN) and its modulation by carbachol. All data in this figure were obtained from the same paired recording. A. Simultaneous extracellular recordings (1 sec samples are shown) were made from 2 cells (red and blue traces) located in the PPN in different experimental conditions. Note that the occurrence of spikes coincided most of the time in both cells even in the presence of blockers of fast excitatory and inhibitory synaptic transmission (CNQX, 10  $\mu$ M + APV, 50  $\mu$ M + gabazine, 10  $\mu$ M). Carbenoxolone (300  $\mu$ M) reduced spike frequency and desynchronized the cells.

B. Photograph of the slice using 2X objective showing the anatomical location of PPN where the dual recording was performed. C. Sliding 3-dimensional crosscorrelograms of spikes indicate significant synchronous activity throughout 50 minutes of recording. Note that the crosscorrelation coefficient peak was near zero time lag and the significant correlation window was around 25 ms (i.e. the occurrence of spikes in both cells tended to coincide within 25 ms interval). Each crosscorrelogram was obtained using 2 minutes of sampling data and there was one minute interval between consecutive crosscorrelograms. D. Same sliding crosscorrelogram as in (D) but the 3-D graph was tilted in order to view the effect of carbachol on the peak of coefficient of correlation. The first 2 applications of carbachol were made in control aCSF and the third application was made in the presence of CNQX+APV+gabazine as in (E).

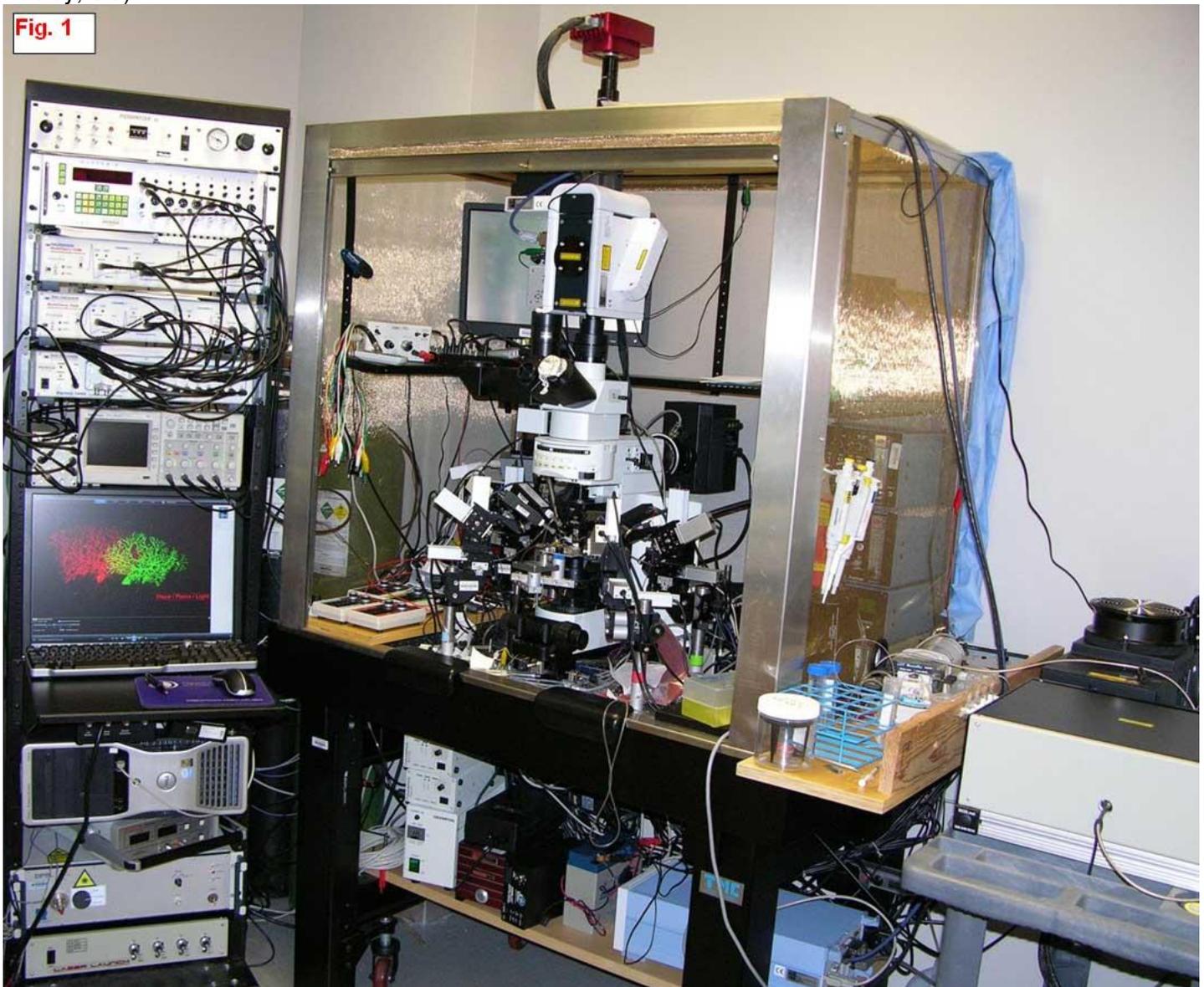
E. Upper panel represents a frequency histogram of both cells (red and blue traces) throughout 50 min of experiment. Carbachol produced multiphasic responses on the first cell (red) whereas it produced mainly inhibition on the second cell (blue). Lower panel is a scatter crosscorrelation. Each dot represents the interval between a spike occurrence in cell #2 and a given spike in cell #1 in a time window of  $\pm 125$  ms. The color-coded superimposed matrix represents the density of dots and is equivalent to a sliding crosscorrelation. Note that the crosscorrelation peak increased in magnitude after each application of carbachol (Dark blue indicates higher coefficient of correlation according to the right color-coded scale). Note also that the peak of correlation (black horizontal line) remains close to center (horizontal red line) except after application of carbenoxolone which gradually reduced the activity the cells and desynchronized them (between 47 -50 min). The persistence of a significance crosscorrelation coefficient in the presence of synaptic blockers and its reduction by carbenoxolone suggest that the 2 cells are coupled by gap junctions.



## **Innovative Methodologies: Combining multi-patch clamp electrophysiology with ultra-fast confocal imaging**

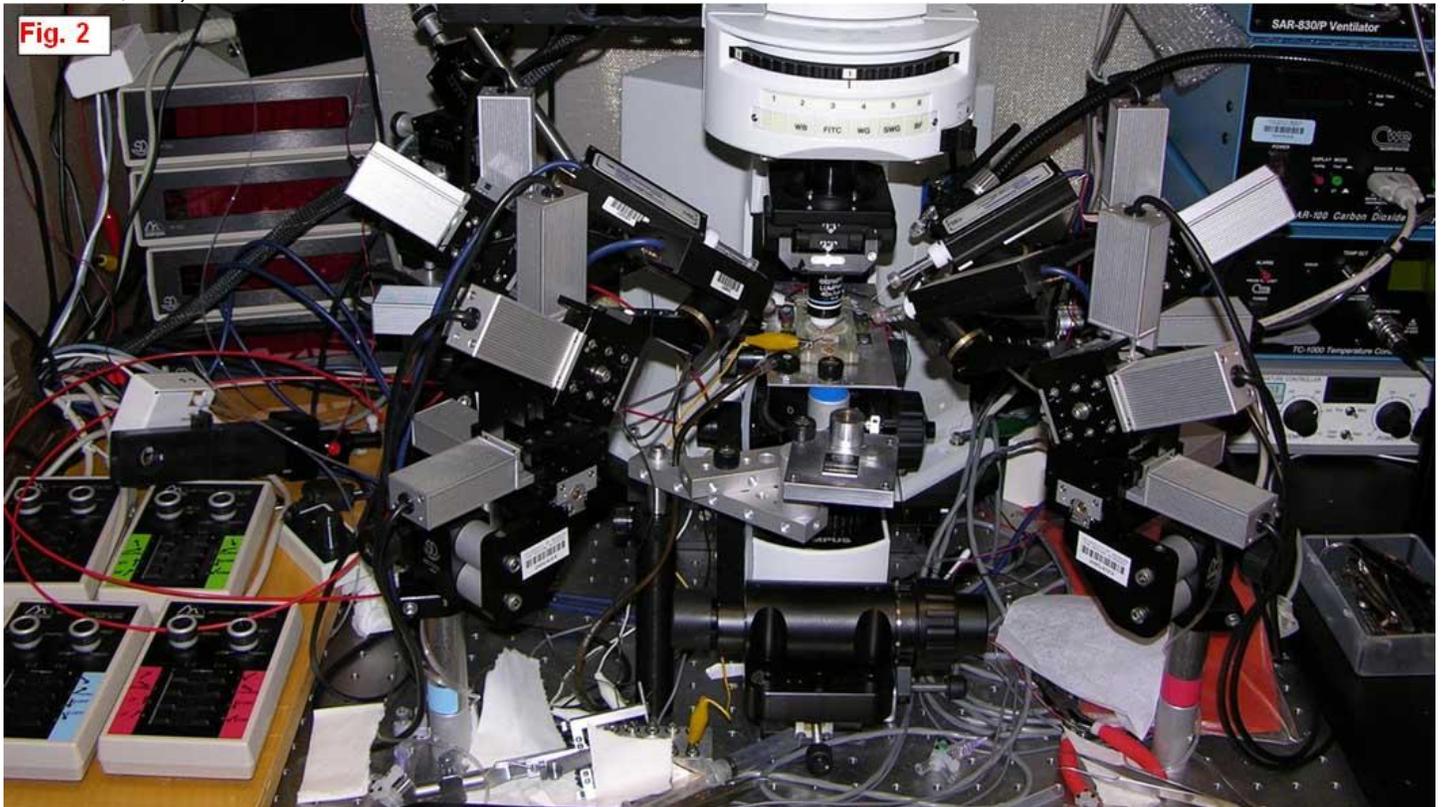
The laboratory where the PI works is fully equipped with an *in vitro* electrophysiological setup for patch clamp recordings in brain slices (see **Fig. 1**, below). This setup includes an anti-vibration table (TMC, Peabody, MA), an Olympus BX51WI microscope equipped with infrared DIC and epifluorescence, 4 fine motorized micromanipulators (model# MX7500, Siskiyou Corp., Grants Pass, OR, 4 axes each, see Figure, below) and 2 manual coarse micromanipulators (model# MX110L Siskiyou, and model# M-3333, Narishige, Japan) installed around a custom made patch-clamp recording chamber heated to 30 °C using a 12 V DC battery with temperature controlled by Bipolar Temperature Controller (TC2BIP, Cell MicroControls, Norfolk, VA). The motorized micromanipulators hold 4 headstages from 2 dual patch clamp amplifiers (Multiclamp 700B, Molecular Devices, Sunnyvale, CA; see **Fig. 2**, below). The 2 coarse micromanipulators are used to place stimulating electrodes controlled by a Master-8cp stimulator (AMPI Inst. Ltd, Jerusalem, Israel) or electrodes containing drugs for pressure application using a Picospritzer III, Parker Hannifin Corp., Fairfield NJ). The setup is also equipped with one Tektronix oscilloscope and an analog-to-digital acquisition system (Digidata 1440A) and pClamp analysis software. Photos of fluorescent cells are taken using a digital camera (Nikon, Coolpix 8700) connected to the microscope eyepiece via an adapter (MM99-5700, Martin Microscope Co., Easley, SC).

**Fig. 1**



The setup (**Fig. 1**) has a NeuroCCD-SMQ Imaging System (RedShirtImaging, Fairfield, CT) based on a Pixel Vision FastOne camera (80 x 80 pixels; back-illuminated, cooled CCD characterized by 2 kHz full-frame rate, 14 bit A-to-D resolution, well depth of 300,000 electrons/ms). To prevent photodynamic damage, the

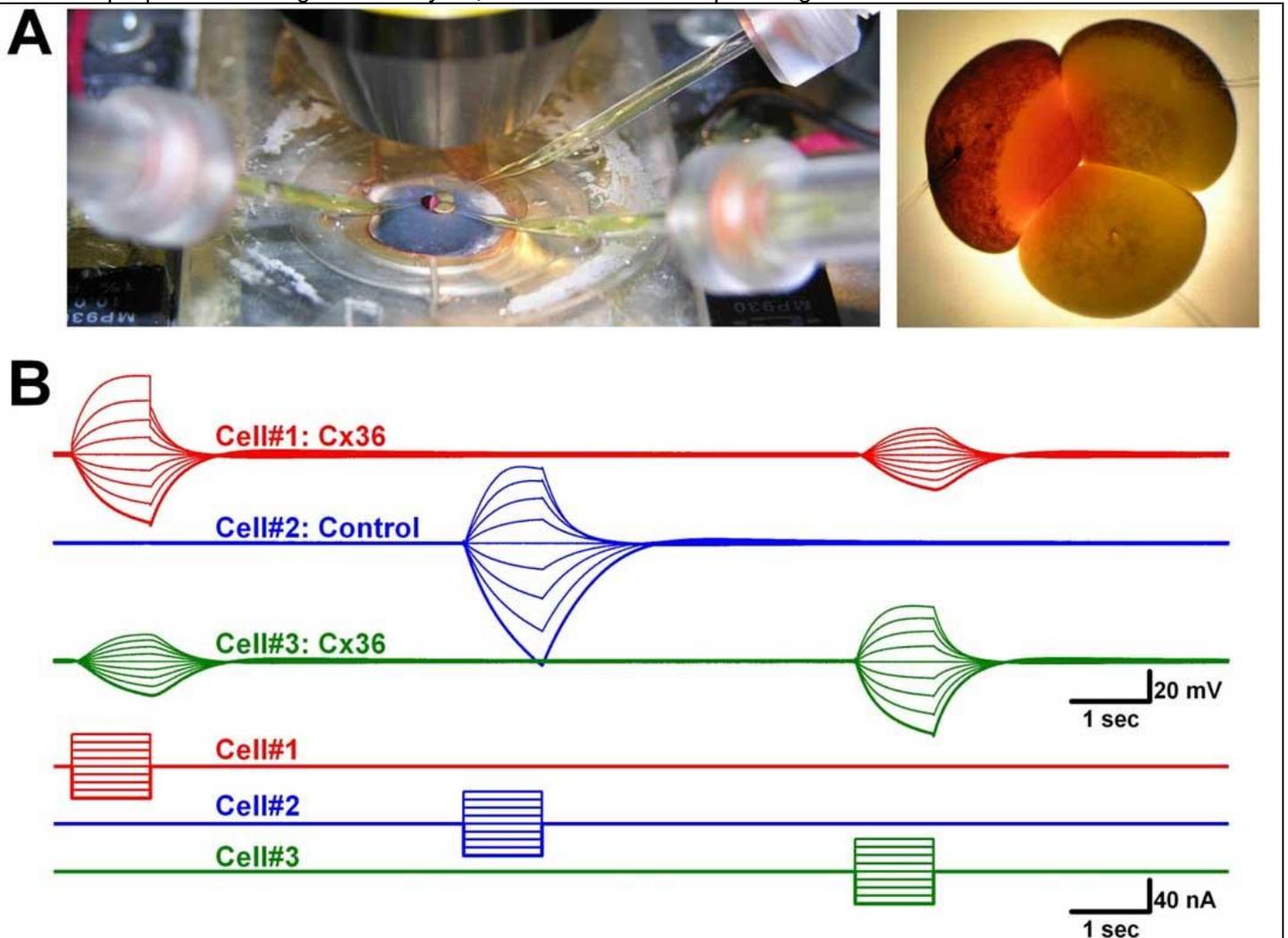
illumination time is kept to a minimum using a computer-controlled mechanical shutter (Vincent Associates, Model# VS25S2ZM1R3, 25 mm aperture, time to fully open or close is ~3 ms). The analysis and display of data are made using the NeuroPlex program (RedShirtImaging) written in IDL (Interactive Data Language, Research Systems, Boulder, CO) running on a PC computer. The laboratory is also equipped with a Vibratome (Ted Pella, Redding, CA) for dissecting brain slices, a micropipette puller (Sutter P-97), stereotaxic equipment (Model SR-6R, Narishige Japan), and an osmometer (Model 3320, Advanced Instruments, Inc., Norwood, MA).



For **live confocal live imaging**, we have installed on top of the Olympus microscope a CSU-X1 spinning disk confocal (Yokogawa Electric Corp, Japan). This system has the world's fastest scanning speed (up to **2000 frames/s**) and integrates well with our RedShirtImaging camera which is also capable of acquiring 2000 fps. It consists of a Nipkow spinning disk that rotates at 10,000 rpm and contains about 20,000 pinholes and a second spinning disk containing the same number of microlens to focus excitation laser light into each corresponding pinhole. It can very rapidly raster scan the field of view with about 1,000 laser beams. Multi-beam scanning not only increases scanning speed, but also results in significantly lower photobleaching and phototoxicity. The addition of this confocal system is expected to enhance our fast live imaging technology by allowing us to image deeper in the tissue with much better signal-to-noise ratio and less light scattering. An ultraviolet laser uncaging system (DSP355/30, 355 nm, 30 mW, Rapp OptoElectronic GmbH, Wedel, Germany) will be used for photo-stimulation.

## Oocyte triplet pairing for electrophysiological investigation of gap junctional coupling

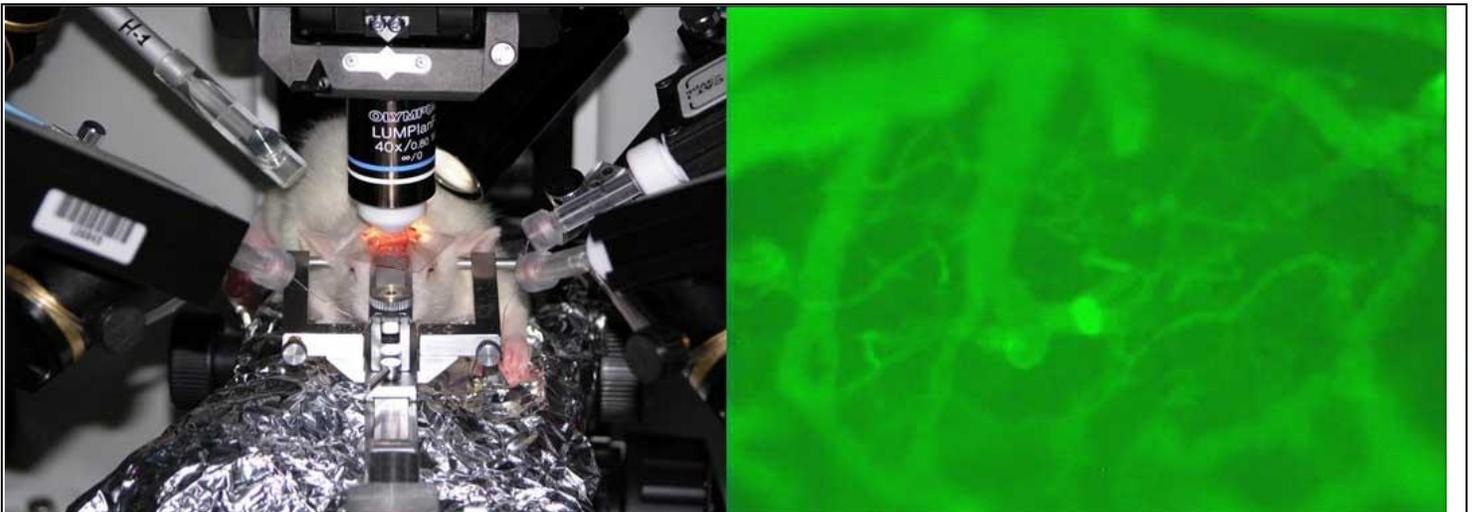
Gap junctions formed by expressing connexin subunits in *Xenopus* oocytes provide a valuable tool for revealing the gating properties of intercellular gap junctions in electrically coupled cells. We describe a new method that consists of simultaneous triple recordings from 3 apposed oocytes expressing exogenous connexins. The advantages of this method is that in one single experiment, one oocyte serves as control while a pair of oocytes, which have been manipulated differently, may be tested for different gap junctional properties. Moreover, we can study simultaneously the gap junctional coupling of 3 different pairs of oocytes in the same preparation. If the experiment consists of testing the effect of a single drug, this approach will reduce the time required, as background coupling in control pairs of oocytes does not need to be measured separately as with the conventional 2 oocyte pairing. The triplet approach also increases confidence that any changes seen in junctional communication are due to the experimental treatment and not variation in the preparation of oocytes or execution of the experiment. In this study, we show the example of testing the gap junctional properties among three oocytes, two of which are expressing rat connexin36.



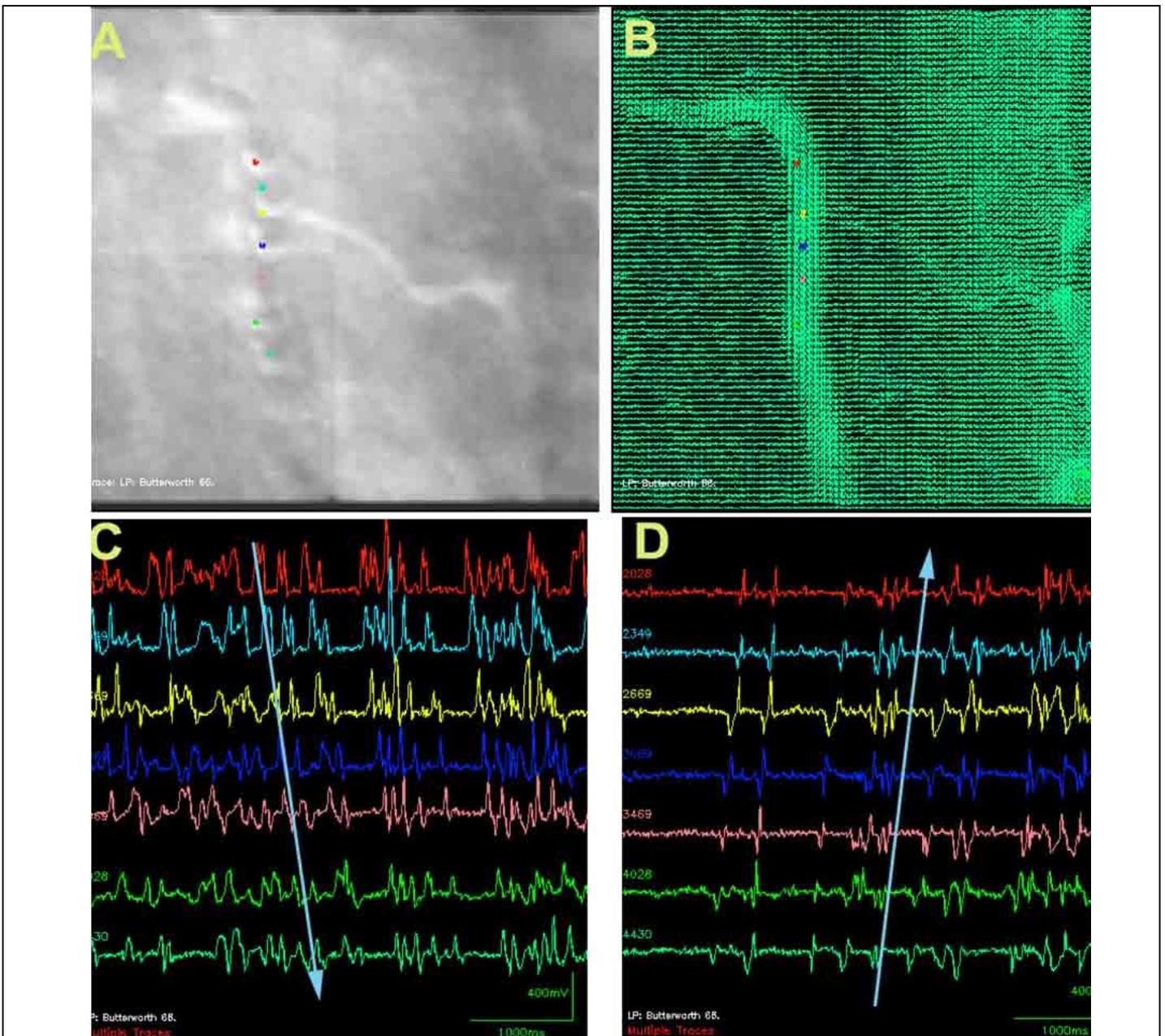
Simultaneous recordings from an oocyte triplet. A. Left panel: Photo of the impalement of the 3 oocytes which were placed in an agar well in a recording chamber superfused with an MMR solution and viewed with a 2X objective. Right panel: Photo of the oocyte triplet taken via the ocular piece. Note that the control oocyte is labeled by a red dye in order to be able to distinguish it from the 2 other oocytes that express connexin 36. B: Representative simultaneous intracellular triple recordings in current clamp mode showing the voltage responses to current pulses of 1 sec duration and incremental amplitude (from -40 nA to 40 nA, using 10 nA increment) injected at different time intervals in each oocyte. Note that injection of current in the transfected oocytes (red and green traces) produced voltage responses in the same cells as well as the other transfected oocytes. In contrast, injecting current pulses in the control oocyte (blue traces) produced no effect in any of the other 2 oocytes.

## **An ultra-fast imaging method for monitoring blood flow in the cerebral microcirculation**

The etiology of brain hemorrhage is multifactorial and can be induced by extreme alterations in many physiological parameters that influence cerebral blood flow (CBF) and the capacity for cerebral autoregulation, such as blood gases, arterial blood pressure, body temperature, the autonomic nervous system, and neuronal activity. Using animal research, this exploratory project aims at a better understanding of the physiological factors that influence CBF and cerebral autoregulation and the different factors leading to cerebral hemorrhage. The main goal of this project is to better understand the mechanisms that would favor or trigger cerebral hemorrhage. We hypothesize that small capillaries are the most structurally vulnerable part of the cerebral circulation and may rupture in extreme physiological conditions leading to cerebral hemorrhage. We think that investigating CBF at the level of single capillaries using an ultra-fast imaging method would provide new insight into how small microvessels react in response to different physiological stressors such as hypercapnia, high blood pressure and excessive neuronal excitability. Optical imaging techniques, nowadays, have become powerful tools for investigating CBF. Our novel method consists of imaging and quantifying cerebral microcirculation in rat olfactory bulb capillaries at 250-2000 frames/sec. Unlike laser line-scanning microscopy which is relatively slow to acquire full frame images, our method will allow to perform live imaging of red blood cell traffic at very high frame rate. We will test whether weakening the wall of blood vessels with ultraviolet laser irradiation in addition to inducing extreme physiological changes can deleteriously alter the microcirculation and result in cerebral hemorrhage. This project also aims at finding the optimal neuroprotective conditions that may prevent the rupture of vulnerable microvessels during extreme physiological conditions. By seeking a better understanding of the mechanisms leading to brain hemorrhage, the results of this research project will allow us to develop new strategies in the prevention and treatment of cerebral hemorrhage.



Left panel: Imaging setup. Blood vessels are visualized using an epifluorescent microscope (Olympus BX51WI) and 2 camera ports: a 3-CCD color camera (Hitachi HV-D30) for standard video microscopy, and a high speed imaging camera (NeuroCCD-SMQ, RedShirtImaging). Right panel: Imaging blood vessels using standard video microscopy (30 frames/sec, 720 x 480 pixels). Image of blood vessels of olfactory bulb glomeruli in rat in which we injected intravenously a solution of 2 MDa fluorescein-conjugated dextran in physiological saline (X10 objective, scale 402 x 301  $\mu\text{m}$ ).



Ultra fast imaging of RBC flow in capillaries. A capillary was visualized using 40X objective (N.A. 0.8) and an optical coupler (0.38 X). Optical recordings of RBC movement were obtained using a RedShirtImaging camera, NeuroCCD-SMQ (chip size 1.92 x 1.92 mm), with an acquisition rate of 250 frames/sec and 80 x 80 pixels spatial resolution. Each frame has a width of 124 x 124  $\mu\text{m}$  and a spatial resolution of about 1.5  $\mu\text{m}/\text{pixel}$ . An 80 sec data file (250 Mbytes) was acquired at the rate of 250 frames/sec. A. One typical frame is shown after contrast enhancement and depixelation. Note the presence of few RBCs visualized using oblique epi-illumination which renders them brighter at their front edge compared to their center. B. Matrix of 80 x 80 traces of the light intensity at each of 6400 pixels of the frame as a function of time. Note that large changes in light intensity (larger noise) occurred when RBCs move inside capillaries. C and D. Representative traces (indicated by the pixel#) of light intensity from 7 locations corresponding to the pixels shown in different colors in panel (A). Each event in the trace indicates light intensity changes corresponding to the crossing of one RBC. The slight shift in the event occurrence at different locations indicates movement of the RBC from top to bottom in (C) and bottom to top in (D). This indicates that RBCs can flow in both directions in the same capillary at different times.