

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Froemke, Robert Crooks

eRA COMMONS USER NAME (credential, e.g., agency login): RFROEMKE

POSITION TITLE: Assistant Professor of Otolaryngology, Neuroscience & Physiology, Skirball Institute, NYU School of Medicine; Center for Neural Science, NYU

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Tufts University, Medford MA	B.A.	11/1998	Computer Science
University of California, Berkeley CA	Ph.D.	05/2004	Molecular & Cell Biology
University of California, San Francisco CA	Postdoctoral	04/2010	Neuroscience, Otolaryngology

**A. Personal Statement**

We study neuromodulation, cortical plasticity, and auditory perception in rats and mice. I have a broad background in systems neuroscience, performing my undergraduate work at Tufts on machine learning and building modeling tools for complex systems analysis. For my PhD work with Yang Dan at UC Berkeley, I examined spike-timing-dependent plasticity induced by natural spike trains in cortical networks. My postdoctoral research with Christoph Schreiner and Mike Merzenich at UCSF focused on synaptic plasticity in vivo as related to auditory perception and behavior. As PI or co-Investigator on several university- and NIH-funded grants (including a K99/R00 and an R01), I have performed studies on auditory perception and synaptic plasticity in rodents for 12+ years. I have successfully administered the projects, trained several students (graduating three PhDs and one MD/PhD), postdocs, and technicians, collaborated with many other researchers, and produced several peer-reviewed publications from each project. This includes several studies examining the relation between cortical modulation, synaptic plasticity, and auditory perception in rodents. Current work examines synaptic mechanisms of calibrating and controlling excitatory-inhibitory balance, cochlear implant function in deafened rats, cholinergic/noradrenergic/oxytocinergic modulation, and cortical plasticity in behaving mice.

1. Marlin BJ, Mitre M, D'amour JA, Chao MV, **Froemke RC**. Oxytocin enables maternal behaviour by balancing cortical inhibition. **Nature** 2015; 520:499-504. PMID: 25874674 PMC: 4409554
2. Martins ARO, **Froemke RC**. Coordinated forms of noradrenergic plasticity in the locus coeruleus and primary auditory cortex. **Nature Neuroscience** 2015; 18:1483-1492. PMID: 26301326 PMC: 4583810
3. D'amour JA, **Froemke RC**. Inhibitory and excitatory spike-timing-dependent plasticity in the auditory cortex. **Neuron** 2015; 86; 514-528. PMID: 25843405 PMC: 4409545
4. Kuchibhotla KV, Gill JV, Lindsay GW, Papadoyannis ES, Field RE, Hindmarsh Sten TA, Miller KD, **Froemke RC**. Parallel processing by cortical inhibition enables context-dependent behavior. **Nature Neuroscience** 2016; in press. PMID: 27798631 PMC: in process

## B. Positions and Honors

### Positions and Employment

2010- Assistant Professor, New York University School of Medicine, Skirball Institute Program in Molecular Neurobiology; Neuroscience Institute; Departments of Otolaryngology, Neuroscience & Physiology; Kimmel Center for Stem Cell Biology; Center for Neural Science.

### Other Experience and Professional Memberships

1996-1998 Senior research staff, Center for Connected Learning and Computer-Based Modeling  
2000 Neural Systems & Behavior Course, Marine Biological Laboratory, Woods Hole, MA  
2000- Member, American Association for the Advancement of Science  
2000- Member, Society for Neuroscience  
2004 Grass Fellow, Marine Biological Laboratory, Woods Hole, MA  
2005- Member, Association for Research in Otolaryngology  
2007 Okinawa Computational Neuroscience Course, Okinawa, Japan  
2008 Methods in Computational Neuroscience, Marine Biological Laboratory, Woods Hole, MA  
2009 Teaching Assistant, Biology of Memory Course, Cold Spring Harbor Laboratory, NY  
2010 Kavli Institute for Theoretical Physics, UC Santa Barbara  
2013 Co-Director, Biology & Disorders of Learning & Memory Course, Cold Spring Harbor Lab, NY  
2013-2015 Co-Chair, Cosyne Workshop Committee (2 year appointment)

### Honors

1998 Benjamin Brown Prize in Computer Science, Tufts University  
2001 Howard Hughes Medical Institute Predoctoral Fellowship  
2002 Outstanding Graduate Student Instructor, University of California, Berkeley  
2004 First place, General Scientific Meeting presentation, Marine Biological Laboratory  
2005 Jane Coffin Childs Postdoctoral Fellowship  
2006 Sandler Translational Research Postdoctoral Fellowship  
2008 K99/R00 Career Award, NIDCD  
2011 Whitehead Fellowship  
2012 Alfred P. Sloan Research Fellowship Award  
2012 Pew Scholar Award  
2012 Klingenstein Fellowship Award  
2013 NYU Grand Challenge Award  
2013 Hirsch/Weill-Caulier Career Award  
2014 McKnight Scholar Award  
2015 NYU Skirball Collaborative Paper Award (with Moses Chao)  
2015 NYU "Next Gen Stars" Inaugural Speaker  
2016 Kavli Fellow  
2016 HHMI Faculty Scholars Award

## C. Contribution to Science

1. We study the organization and plasticity of cortical synapses, and the relations between circuit dynamics and the control of social cognition, with a particular emphasis on oxytocin. It has historically been difficult to determine how modifications of specific synapses relate to changes in behavior. We have examined how neurons in the rodent hypothalamus affect synaptic transmission in the cortex and elsewhere to produce behavioral changes in adult rats and mice. This is some of the first work using cortical plasticity to persistently enhance sensory perception and cognition. Furthermore, we provided the first direct evidence that oxytocin transiently reduces synaptic inhibition in the cortex, increasing the salience of incoming sensory inputs. We have used optogenetics and pharmacological approaches to examine how oxytocin can enable newly-maternal mice to recognize the significance of infant vocalizations and distress calls. As part of our work on oxytocin, in collaboration with Moses Chao's lab we generated the first specific antibodies to the mouse oxytocin receptor, which we have shared with many international laboratories (including the Grinevich and Stoop labs). We have also worked to understand the functional anatomy and circuit logic by which oxytocin neurons and other hypothalamic cell types project to target areas.

- a. Marlin BJ, Mitre M, D'amour JA, Chao MV, **Froemke RC**. Oxytocin enables maternal behaviour by balancing cortical inhibition. **Nature** 2015; 520:499-504. PMID: 25874674 PMC: 4409554
  - b. Mitre M, Marlin BJ, Schiavo JK, Morina E, Norden S, Hackett TA, Aoki C, Chao MV, **Froemke RC**. A distributed network for social cognition enriched for oxytocin receptors. **Journal of Neuroscience** 2016; 36:2517-2535. PMID: 26911697 PMC: 4764667
  - c. Eliava M, Melchior M, Knobloch-Bollmann S, Wahis J, da Silva Gouveia M, Tang Y, Ciobanu AC, del Rio RT, Roth LC, Althammer F, Chavant V, Goumon Y, Gruber T, Petit-Demoulière M, Busnelli M, Chini B, Tan L, Mitre M, **Froemke RC**, Chao MV, Giese G, Sprengel R, Kuner R, Poisbeau P, Seeburg PH, Stoop R, Charlet A, Grinevich V. A new population of parvocellular oxytocin neurons controlling magnocellular neuron activity and inflammatory pain processing. **Neuron** 2016; 89:1291-1304. PMID: 26948889
  - d. Wong LC, Wang L, Yumita T, D'amour JA, Chen G, Chang B, Bernstein H, You X, Feng J, **Froemke RC**, Lin D. Effective modulation of male aggression through the lateral septum to medial hypothalamus projection. **Current Biology** 2016; 26:593-604. PMID: 26877081 PMC: 4783202
2. More generally, we examine how cortical modulation and plasticity can improve auditory perception and behavior, in the context of behavioral training and perceptual learning. We have a particular emphasis on conducting well-controlled and parametric studies of auditory psychophysics in rodents. We have conducted a series of studies examining how manipulations of modulatory systems- the cholinergic attentional system of the nucleus basalis and the noradrenergic arousal system of the locus coeruleus - lead to synaptic plasticity and produce behavioral changes in adult rats. We assessed baseline auditory abilities to determine which stimuli were difficult to perceive, and leveraged the cholinergic system to boost up the strengths of synapses at these thresholds. We found that auditory perception was improved for at least hours afterwards, indicating that direct cortical modifications can be useful for enhancing sensory perception and behavior. We have contrasted these changes with the action of noradrenalin and stimulation (electrical or optogenetic) of the rat locus coeruleus, identifying how cholinergic and noradrenergic modulation differentially affect plasticity and perception. This is some of the first work identifying inhibitory synapses and circuits as central targets of neuromodulators, and our findings that acetylcholine disinhibits auditory cortex has been replicated by several other labs, in rats and in mice, and other sensory systems. This is also some of the first work directly utilizing mechanisms of long-term synaptic plasticity to enduringly enhance sensory perception and cognition for hours to weeks after brief episodes of stimulation and pairing. We are also the first group to record synaptic excitation and inhibition in behaving rodents, and one of the first three groups to perform 2-photon imaging of neuromodulatory axon fibers projecting to cortex during behavior.
- a. **Froemke RC**, Carcea I, Barker AJ, Yuan K, Seybold B, Martins ARO, Zaika N, Bernstein H, Wachs M, Levis PA, Polley DB, Merzenich MM, Schreiner CE. Long-term modification of cortical synapses improves sensory perception. **Nature Neuroscience** 2013; 16:79-88. PMC: 3711827
  - b. Martins ARO, **Froemke RC**. Coordinated forms of noradrenergic plasticity in the locus coeruleus and primary auditory cortex. **Nature Neuroscience** 2015; 18:1483-1492. PMID:26301326 PMC: 4583810
  - c. Carcea I, Insanally M, **Froemke RC**. Dynamics of cortical activity during behavioral engagement and auditory perception. **Nature Communications** 2016; in press. PMID: in process PMC: in process
  - d. Kuchibhotla KV, Gill JV, Lindsay GW, Papadoyannis ES, Field RE, Hindmarsh Sten TA, Miller KD, **Froemke RC**. Parallel processing by cortical inhibition enables context-dependent behavior. **Nature Neuroscience** 2016; in press. PMID: 27798631 PMC: in process
3. Our work on cortical plasticity and auditory perception is very promising from a translational perspective, in terms of recovery of function and restoration of hearing after injury, aging, or disease. These studies are now being integrated together with a collaborative project involving Mario Svirsky and Tom Roland at NYU, Jon Viventi at Duke, and industry support from Cochlear Ltd.- we have developed the leading behaviorally-validated and physiologically-calibrated system for studies of multichannel cochlear implant use and training in rats, together with  $\mu$ -ECoG recording of neural activity over weeks to months in trained animals.
- a. Insanally M, Trumpis M, Wang C, Chiang CH, Woods V, Bossi S, **Froemke RC**, Viventi J. A low-cost, multiplexed  $\mu$ ECoG system for long-term, reliable high-density recordings in rodents. **Journal of Neural Engineering** 2016; 13:026030. PMID: in process PMC: in process
  - b. King J, Shehu I, Roland JT, Svirsky MA, **Froemke RC**. A physiological and behavioral system for hearing restoration with cochlear implants. **Journal of Neurophysiology** 2016; in press. PMID: in process PMC: in process

4. Excitatory-inhibitory balance is an important property of mature neural circuits, ensuring that excitability is carefully controlled for information processing without seizure generation or propagation failure. How are inhibitory inputs calibrated during development and adjusted throughout life, to ensure that inhibition balances excitation? Inhibitory maturation is believed to determine critical periods for cortical development, and changes to excitatory synapses related to learning must be matched by coordinated changes in co-tuned inhibitory inputs. Our lab specializes in examining combined forms of excitatory and inhibitory long-term synaptic plasticity with whole-cell recordings and 2-photon imaging in vivo, monitoring the dynamics by which excitation and inhibition are adjusted after changes in patterns of electrical activity or sensory experience. We have shown how these processes occur during a critical period for frequency tuning in the rodent auditory cortex. We are also the first and perhaps only group to show how, after transplantation, inhibitory progenitor cells integrate into the existing network to open a new critical period in adult visual cortex, using paired recordings from host and transplanted cells to show that these new neurons make and receive synaptic connections in the local circuit.
- Froemke RC**, Merzenich MM, Schreiner, CE. A synaptic memory trace for cortical receptive field plasticity. **Nature** 2007; 450:425-429. PMID: 18004384 PMC in process
  - Dornn A, Yuan K, Barker AJ, Schreiner CE, **Froemke RC**. Developmental sensory experience balances cortical excitation and inhibition. **Nature** 2010; 465:932-936. PMID:20559387 PMC2888507
  - Southwell D, **Froemke RC**, Alvarez-Buylla A, Stryker MP, Gandhi SP. Cortical plasticity induced by inhibitory neuron transplantation. **Science** 2010; 327:1145-1148. PMID: 20185728 PMC3164148
  - Cohen S, Ma H, Kuchibhotla K, Watson BO, Buzsáki G, **Froemke RC**, Tsien RW. Excitation-transcription coupling in parvalbumin-positive interneurons employs a novel CaM Kinase-dependent pathway distinct from excitatory neurons. **Neuron** 2016; 90:292-307. PMID: 27041500 PMC:4866871
5. Neural activity can be complex. We have examined spike-timing-dependent plasticity (STDP), focusing on synaptic modifications induced by naturalistic patterns of pre- and postsynaptic spikes recorded in vivo. From hundreds of experiments we could predict the sign and magnitude of long-term synaptic plasticity induced by complex spike trains, and continue to work with computational neuroscientists to understand how STDP might enable neural networks to store and recall information. Some experiments examine how synaptic integration and dendritic properties affect NMDA receptor activation to control induction of synaptic plasticity. More recently, we are examining how multiple synapses are co-modified, and we were the first group to show that excitatory and inhibitory STDP can be coordinated and induced together. We found that spike pairing can normalize the strength of inhibition relative to the strength of co-activated excitation, providing a natural mechanism by which excitatory-inhibitory balance can be established and maintained.
- Froemke RC**, Dan Y. Spike-timing-dependent synaptic modification induced by natural spike trains. **Nature** 2002; 416:433-438. PMID: 11919633
  - Froemke RC**, Poo MM, Dan Y. Spike-timing-dependent plasticity depends on dendritic location. **Nature** 2005; 434:221-225. PMID: 15759002
  - Ponte Costa R, **Froemke RC**, Sjöström PJ, van Rossum MC. Unified pre- and postsynaptic long-term plasticity enables reliable and flexible learning. **eLife** 2015; 4. PMID: 26308579 PMC:4584257
  - D'amour JA, **Froemke RC**. Inhibitory and excitatory spike-timing-dependent plasticity in the auditory cortex. **Neuron** 2015; 86; 514-528. PMID: 25843405 PMC: 4409545

#### **Complete List of Published Work in MyBibliography:**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/robert.froemke.1/bibliography/44917017/public/?sort=date&direction=ascending>

#### **D. Research Support**

##### **Ongoing Research Support**

R01 NICHD HD088411

2017-2022

Neural circuitry and plasticity for maternal behavior

The goal of this study is to determine when, where, and how oxytocin affects auditory cortical neurons for maternal responses to infant vocalizations. Role: Co-PI (with Regina Sullivan)

HHMI Faculty Scholars Award

2016-2021

Cortical plasticity and control of social behavior

This career award supports research on oxytocin and cortical plasticity for learned maternal behavior. Role: PI

DARPA TNT Award	2016-2020
An adaptable non-invasive neuromodulation platform for targeted augmentation of multi-domain learning This project grant examines the capacity of peripheral nerve stimulation to enhance auditory training and perceptual learning. Role: Co-PI (with Kip Ludwig, Justin Williams, David McCormick, and Matt McGinley)	
NYU CTSI Collaborative Translational Pilot Project Program	2016-2017
Optimizing cochlear implant use with neural recordings The goal of this study is to understand the neural basis of cochlear implant use in trained, deafened rats. Role: Co-PI (with Mario Svirsky, NYU)	
NYU Global Seed Grant for Collaborative Research	2016-2018
Neuromodulatory influences on economic preferences The goal of this study is to examine impulsivity behaviors in rats. Role: Co-PI (with Jeff Erlich, NYU Shanghai)	
Simons Foundation Explorer Grant	2016-2017
Synthetic infrared nanosensors for real-time monitoring of oxytocin release The goal of this study is to screen carbon nanotube-based sensors for specific detection of oxytocin in real time. Role: Co-PI (with Markita Landry, UC Berkeley)	
McKnight Scholar Award	2014-2017
Neural circuitry and plasticity for control of mammalian social behavior The goal of this study is to determine the 'social receptive field' of oxytocin neurons in the hypothalamus, and relate activation of the oxytocin system and cortical plasticity to learned maternal behavior. Role: PI	
Hirschl/Weill-Caulier Career Award	2014-2018
Neural basis of long-term memory formation The goal of this study is to examine how neuromodulatory circuits of the locus coeruleus are modified by sensory experience and neural activity. Role: PI	
R01 NIDCD DC012557	2012-2022
Synaptic basis for perceptual learning in primary auditory cortex The goal of this study is to directly examine the relation between adult cortical synaptic plasticity and perceptual learning via the noradrenergic modulatory system. Role: PI	
<b><u>Completed Research Support</u></b>	
K99/R00 NIDCD DC009635	2008-2015
Synaptic basis for perceptual learning in primary auditory cortex The goal of this study was to directly examine the relation between adult cortical synaptic plasticity and perceptual learning via the cholinergic modulatory system. Role: PI	
Pew Scholarship	2012-2016
Neural basis of learned social behavior The goal of this study was to determine how oxytocin affects vocalization responses in auditory cortex. Role: PI	
Klingenstein Fellowship	2012-2015
Plasticity of excitatory-inhibitory balance in the auditory cortex The goal of this study was to determine mechanisms that balance cortical excitation and inhibition. Role: PI	
Alfred P. Sloan Research Fellowship	2012-2014
Synaptic plasticity in the cerebral cortex This career award supported our research on synaptic plasticity. Role: PI	
NYU Provost's Grand Challenge Grant	2013-2015
Smart neuroprosthetics: brain-machine interfaces for the 21st century The goal of this study was to generate brain-machine interface devices for improving behavioral performance in rodents and primates. Role: Co-PI (with Bijan Pesaran, Dan Sanes, and Jonathan Viventi, NYU)	