BIOGRAPHICAL SKETCH

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NAME: Froemke, Robert Crooks

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

POSITION TITLE: Associate Professor of Otolaryngology, Neuroscience & Physiology, Skirball Institute, Neuroscience 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, plasticity, and behavior in rodents and humans. 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, R01s, and U/P grants), I have performed studies linking changes in neural activity to changes in perception and behavior in rodents for 14+ years. I have successfully administered the projects, trained several students (graduating three PhDs and two MD/PhD), postdocs (three now in faculty/group leader positions), and technicians, collaborated with many other researchers, and produced several peer-reviewed publications from each project. In general we study the synaptic mechanisms by which sounds acquire meaning. The three major lines of research in the lab focus on: 1) oxytocin and maternal care in mice, 2) mechanisms of synaptic plasticity for coordinating or 'balancing' excitation and inhibition in rodent cortex, and 3) cochlear implant use in rats and humans.

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** 2017; 20:62-71. PMID: 27798631 PMC: 5191967

B. Positions and Honors

Positions and Employment

2017-present Associate Professor with Tenure
2010-2017 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)
2015-2018 Member, Program Committee, Society for Neuroscience Annual Meeting (3 year appointment)
2017-2021 Standing Member, CDRC/NIDCD Fellowship Review Study Section (4 year appointment)
2019- Co-Director, Neural Systems & Behavior Course, Marine Biological Lab, Woods Hole MA

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 Hirschl/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 Howard Hughes Medical Institute Faculty Scholars Award

C. Contribution to Science (selected from 72 publications; 40 in last 5 years)

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 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. 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
d. Tirko NN, Eyring KW, Carcea I, Mitre M, Chao MV, **Froemke RC,** Tsien RW. Oxytocin transforms firing mode of CA2 hippocampal neurons. **Neuron** 2018; 100:593-609. PMID: 30293821

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 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** 2017; 8:14412. PMID: 28176787 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** 2017; 20:62-71. PMID: 27798631 PMC: 5191967

3. Our work on cortical plasticity and auditory perception is 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 Svirksy 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 μ-ECoG recording of neural activity over weeks to months in trained animals. As part of this work, we have developed a new scheme for decoding neural activity patterns without trial averaging or pre-selecting cell populations, essentially using every spike from all cells across each individual trial to understand how 'nominally non-responsive' cells without trial-averaged responses are important to behavior.
    a. 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; 116:844-858. PMID: 27281743 PMC: 4995281

b. Insanally M, Trumpis M, Wang C, Chiang CH, Woods V, Bossi S, **Froemke RC**, Viventi J. A low-cost, multiplexed μECoG system for long-term, reliable high-density recordings in rodents. **Journal of Neural Engineering** 2016; 13:026030. PMID: 26975462 PMC: 4894303
c. Cheung SW, Atencio CA, Levy ER, **Froemke RC**, Schreiner CE. Cortical anisomorphism in asymmetric sensorineural hearing loss. **J Neurophysiol** 2017; 118:932-948. PMID:28515283
d. Insanally MN, Carcea I, Field RE, Rodgers CC, DePasquale B, Rajan K, DeWeese MR, Albanna BF, **Froemke RC**. Spike-timing-dependent ensemble encoding by non-classically responsive cortical neurons. **eLife** 2019; e42409.

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 have related neuromodulation and plasticity of specific cortical circuit elements to behavioral performance using a large number of different tasks, across species, and united with a straightforward circuit model of perceptual learning.
    a. **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
    b. Dorrn 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
    c. 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
    d. Kuchibhotla KV, Hindmarsh Sten TA, Papadoyannis ES, Elnozahy S, Fogelson K, Kumar R, Boubenec Y, Holland PC, Ostojic S, **Froemke RC**. Dissociating task acquisition from expression during learning reveals latent knowledge. **Nature Communications** 2019; 10:2151.

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.
    a. **Froemke RC**, Dan Y. Spike-timing-dependent synaptic modification induced by natural spike trains. **Nature** 2002; 416:433-438. PMID: 11919633
    b. **Froemke RC**, Poo MM, Dan Y. Spike-timing-dependent plasticity depends on dendritic location. **Nature** 2005; 434:221-225. PMID: 15759002
    c. 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
    d. Field RE, D'amour JA, Tremblay R, Miehl C, Rudy B, Gjorgjieva J, **Froemke RC**. Heterosynaptic plasticity determines the set-point for cortical excitatory-inhibitory balance. **BioRxiv** 2019.

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

U19 NINDS NS107616 2018-2023
Oxytocin modulation of neural circuit function and behavior
The goal of this study is to build tools and determine general principles of oxytocin modulation of neural circuits for socio-spatial behavior. Role: Co-PI (with Dick Tsien, Gyuri Buzsaki, Dayu Lin, Moses Chao, Adam Mar)

P01 NINDS NS074972 2018-2023
Development & function of 5HT3aR-expressing cortical GABAergic interneurons
The goal of this proposal is to understand how 5HT3aR interneurons regulate cortical circuit function in development and adulthood. Role: Co-PI (with Bernardo Rudy and Gord Fishell)

R01 NINDS NS109885 2018-2023
The biophysics and potential cell-type selectivity of acoustic neuromodulation
The goal of this study is to determine how ultrasound modulation might affect neural activity in cortical circuits. Role: Co-PI (with Shy Shoham and Kimmel Eitan)

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)

DARPA TNT Award 2017-2021
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)

Pew Innovation Fund 2017-2019
Gut-brain connections: regulation of immune response and sickness behavior
The project aims to understand gut-brain signaling for sickness behavior. Role: Co-PI (with Dan Littman)

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

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

Completed Research Support (partial list)

K99/R00 NIDCD DC009635 2008-2015
Synaptic basis for perceptual learning in primary auditory cortex

Pew Scholarship 2012-2016
Neural basis of learned social behavior

Klingenstein Fellowship 2012-2015
Plasticity of excitatory-inhibitory balance in the auditory cortex

Alfred P. Sloan Research Fellowship 2012-2014
Synaptic plasticity in the cerebral cortex

McKnight Scholar Award 2014-2017
Neural circuitry and plasticity for control of mammalian social behavior