

Curriculum Vitae

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Place of Birth: Milan, Italy

Education:

1994	BSc	Biology	University of Milan, Italy
1998	PhD	Human Physiology (Advisor: Dr. Mauro Mancina)	University of Milan, Italy

Postdoctoral Training:

1999-2000	Fellow	Neurophysiology (Advisor: Dr. Robert W. Greene)	Psychiatry Dept, Brockton VAMC; Harvard Medical School
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Faculty Academic Appointments:

2001	Instructor	Psychiatry Department	Brockton VAMC; Harvard Medical School
2001-2009	Instructor	Department of Neurology	BIDMC; Harvard Medical School
2009-2019	Assistant Professor	Department of Neurology	BIDMC; Harvard Medical School
2019-	Associate Professor	Department of Neurology	BIDMC; Harvard Medical School

Appointments at Hospitals/Affiliated Institutions:

2001-2009	Instructor	Department of Neurology	BIDMC
2009-2019	Assistant Professor	Department of Neurology	BIDMC
2019-	Associate Professor	Department of Neurology	BIDMC

Committee Service: Local

2012-	Institutional Animal Care and Use Committee, IACUC	BIDMC	Member
2021-	Harvard Catalyst Mentoring Program	Harvard	Mentor

National

2015-2018	SRS Scientific Review Committee	Sleep Research Society	Member
2016-2018	Sleep and Circadian Biology DataBlitz Organizing Committee	Sleep Research Society	Member
2020-2022	APSS Meeting Organizing Committee	Sleep Research Society	Member
2024-	APSS Meeting Organizing Committee	Sleep Research Society	Vice-Chair

Professional Societies:

1997-	Sleep Research Society (SRS)	Member
1999-2005	American Academy of Sleep Medicine (AASM)	Member
1999-2000	Italian Society for Sleep Research (SIRS)	Member
2001-	Society for Neuroscience (SFN)	Member

Grant Review Activities:

2014, 2017	NIH IFCN/DNDA Center for Scientific Review Neuroendocrinology, Neuroimmunology, Rhythms and Sleep Study Section	Temporary Member
2015, 2017	NIH IFCN/DNDA Center for Scientific Review Sensorimotor Integration Study Section	Temporary Member
2016-2018	Sleep Research Society SRSF Early Career Development Research Award	Member
2016	NIH IFCN/DNDA Center for Scientific Review Integrative Neuroscience	Temporary Member
2020	NIH BRAIN Initiative Targeted BRAIN Circuits Projects	Temporary Member
2021, 2024	NIH Fellowships Learning, Memory, Language, Communication, and Related Neuroscience	Temporary Member
2021	Fonds de la Recherche Scientifique – FNRS Incentive grant for scientific research	Temporary Member
2021-2024	Fonds de la Recherche Scientifique – FNRS The Excellence of Science	Temporary Member
2022	NIH IFNC/DNDA Center for Scientific Review Behavioral Neuroendocrinology, Neuroimmunology, Rhythms, and Sleep	Temporary Member
2023	Chan Zuckerberg Initiative, Collaborative Pairs Pilot Project Awards	Temporary Member
2023-2024	Swiss National Science Foundation	Temporary Member
2024	Natural Sciences and Engineering Research Council of Canada	Temporary Member

Editorial Activities:**Ad hoc Reviewer**

2009, 2014	Acta Physiologica Scandinavica
2013	American J. of Physiology Cell Biology
2017	Annals of Neurology
2016	AP Cell Physiology
2021	Behavioral Brain Research
2016, 2021	Brain Research
2018, 2024	Brain Research Bulletin
2015-2017	British Journal of Pharmacology

2023	Cell discovery
2021-2024	Current Biology
2011, 2007, 2018	Eur. J. of Neuroscience
2015, 2018	Frontiers in Neurology
2023	Fundamental & Clinical Pharmacology
2012	J. of Neuroscience
2019	Journal of Neurosurgical Anesthesiology
2008, 2015	J. Physiology
2015, 2019, 2024	J. of Sleep
2017	Molecular Neurobiology
2012, 2023	Neuron
2023	National Science Review
2018	Neuropharmacology
2009	Neuroscience
2006	Neurosci. Lett.
2024	Physiology & Behavior
2024	Progress in Pharmacology & Biological Psychiatry
2019, 2021, 2022	Science
2023	Scientific Report

Other Editorial Roles

Honors and Prizes:

1999 Young Investigator Award	American Academy of Sleep Medicine
2001 Young Investigator Award	Sleep Medicine Education & Research Foundation

Report of Funded and Unfunded Projects

Funding Information:

Past

2001-2003	<p>The Effects of Adenosine on the Membrane Properties of Basal Forebrain Cholinergic Neurons Sleep Medicine Education & Research Foundation Principal Investigator The goal of this project was to determine the presynaptic and postsynaptic mechanisms through which adenosine inhibits basal forebrain cholinergic neurons and promotes sleep.</p>
2003-2008	<p>Harvard Center on the Neurobiology of Sleep and Sleep Apnea: Electrophysiology Core (Core D) NIH/NHLBI (P50 HL60292) Core Director (PI: David P White MD) The goal of the Electrophysiology Core was to provide centralized services for <i>in vitro</i> electrophysiological studies, including patch-clamp recordings and extracellular recordings in brain slices.</p>
2005-2010	<p>Dopaminergic Control of Wakefulness NIH/NINDS 5RO1NS051609 Co-Investigator (PI: Jun Lu, MD) The goal of this project was to determine the role of dopamine in the regulation of wakefulness by identifying the afferents, and efferents of wake-active dopamine neurons in the ventral periaqueductal gray matter (vPAG), and to examine the effect of dopamine on target neurons of the vPAG.</p>

- 2009 Pontine Control of REM Atonia
NIH/NINDS 1R01NS061863
Principal Investigator
The goal of this project was to define the physiology of the neuronal circuitry that controls the loss of muscle tone during rapid eye movement (REM) sleep to better understand how dysfunction of this circuitry causes REM sleep behavior disorder or cataplexy.
- 2009-2011 Pontine Control of REM Atonia (Administrative Supplement, Recovery Act Funds NOTOD-09-060)
NIH/NIHDS 3RO1NS061863-S1
Principal Investigator
The goal of these supplementary funds was to hire a summer student to help with the work on the parent grant 1R01NS061863
- 2009 Pontine Control of REM Atonia (Administrative Supplement, Recovery Act Funds: Funds for equipment)
IH/NIHDS 3RO1NS061863-S2
Principal Investigator
The goal of these supplementary funds was to purchase a new amplifier to update the one slice recording system.
- 2009-2011 Pontine Control of REM Atonia (Administrative Supplement, Recovery Act Funds NOTOD-09-056)
NIH/NINDS 1R01NS061863-S3
Principal Investigator
The goal of these supplementary funds is to hire a post-doctoral fellow for two years to work on the project of the parent grant 1R01NS061863
- 2010-2015 Mechanisms of State Switching in Sleep and Sleep Apnea: Electrophysiology Core
NIH/NHLBI 1P01HL095491
Core Director (PI: Clifford C. Saper MD PhD)
The goal of the Electrophysiology Core is to provide *in vitro* electrophysiological recordings brain slices to the individual projects of the program project grant.
- 2013-2015 Basal Forebrain Corticopetal GABAergic Neurons and Cortical Arousal
NIH/NINDS 1R21NS082854
Principal Investigator
Goal: To define the role of GABAergic basal forebrain neurons in the regulation of electrographic and behavioral wakefulness.
- 2015-2020 Mechanisms of Arousal in Sleep Apnea: Electrophysiology Core (Core C)
NIH/NHLBI 2P01L095491
Core Director (PI: Clifford C. Saper MD PhD)
Goal: to provide centralized services for electrophysiological studies, including patchclamp recordings, channelrhodopsin2 (ChR2)-assisted circuit mapping and associated data analysis for three projects within the program project grant.
- 2015-2020 Brainstem regulation of Sleep
NIH/NINDS 1R01 NS092652-01
Co-Investigator (PI: Patrick M. Fuller)

The goal of this project is to define the circuit basis by which parafacial GABAergic neurons produce sleep. The role of my lab is to determine the circuit interaction between parafacial GABAergic neurons and the wake-promoting parabrachial nucleus.

- 2017-2022 Mapping Brainstem Control of Bladder Filling and Voiding
NIH/NINDK 1R01 DK113030-02
Co-Investigator (PI: Mark Zeidel)
This project will use state of the art neural mapping methods, coupled with careful measurements of bladder function in awake and anesthetized mice, to define how the brain integrates signals from the bladder and the external environment to control bladder filling and voiding.
- 2017-2022 Dissection of a novel inhibitory hypothalamic arousal circuit
NIH/NINDS 1R01 NS103161-02
Co-Investigator (PI: Patrick M. Fuller)
Goal: The goal of this project is to define the cellular and synaptic bases by which LH^{VGAT} neurons produce wakefulness, with an emphasis on the circuit (synaptic) interaction between LH^{VGAT} neurons and neurons of the sleep-promoting VLPO, a major post-synaptic target of LH^{VGAT} neurons, as well as define the synaptic inputs to the LH^{VGAT}.

Current

- 2019-2024 Circuitry for circadian rhythms
NINDS 2R01 NS072337
Co-Investigator (PI: Clifford C. Saper MD PhD)
Goal: To determine the contributions and synaptic mechanisms of GABAergic and glutamatergic neurons in the dorsomedial hypothalamic nucleus, to the maintenance of circadian rhythms of corticosteroid secretion.
- 2020-2025 Mechanisms of sleep and sleep apnea: Electrophysiology Core (Core C)
NIH/NHLBI 1P01HL149630-01
Core Director (PI: Clifford C. Saper MD PhD)
Goal: to provide centralized services for electrophysiological studies, including patchclamp recordings, channelrhodopsin2 (ChR2)-assisted circuit mapping and associated data analysis for three projects within the program project grant.
- 2020-2025 Mechanisms of sleep and sleep apnea: Circuit and synaptic regulation of CO₂responsive parabrachial FoxP2 neurons
NIH/NHLBI 1P01HL149630-01
Project Leader, PI for Project 3 (P01 PI: Clifford C. Saper MD PhD)
Goal: to identify and map the inputs to the PBcl^{FoxP2} neurons. The activation of select forebrain inputs to PBcl^{FoxP2} neurons is expected to enhance the ventilatory response to hypoxia and hypercapnia without driving cortical arousals. The aim of this project is to identify and characterize these inputs, with the ultimate goal of selectively enhancing activity in the PBcl^{FoxP2} neurons to increase ventilatory responses, but not cortical arousals, in response to hypercapnia.
- 2021-2024 The effect of pitolisant on sleep-promoting neurons
Harmony Biosciences
Principal Investigator
Goal: The histamine H3 receptor inverse agonist pitolisant improves daytime sleepiness in narcolepsy and other hypersomnia disorders. The goal of this project is to determine the effects of pitolisant on sleep-promoting neurons of the ventrolateral preoptic area (VLPO) and to understand whether pitolisant operates in VLPO through local GABAergic neurons.

2021-2026 Regulation of arousal state by the suprachiasmatic clock
Co-Investigator (PI: Patrick M. Fuller)
NIHNINDS 1R01 NS118856

Goal: The proposal specifically seeks to define the cellular and synaptic bases by which the SCN clock produces and augments wake/arousal, with an emphasis on the synaptic interaction between SCN^{NMS} neurons and neurons of the sleep-promoting ventrolateral preoptic nucleus (VLPO).

2022-2027 Neuronal circuit controlling sleep-promoting ventrolateral preoptic neurons
NIH/NHNINDS 1R01 NS122589-01
Principal Investigator

Goal: The goal of this project is to define the long-range and local cellular and circuit bases by which arousal and sleep-promoting afferent inputs to the sleep-promoting neurons of the ventrolateral preoptic area (VLPO) contribute to behavioral and electrocortical sleep and arousal

2016-2027 Molecular-Genetic Dissection of Basal Forebrain Circuitry Regulating Arousal
NIH/NINDS 5R01 NS073613-11
Co-Investigator (PI: Patrick M. Fuller)

The goal of this project is to define the functional synaptic basis by which basal forebrain GABAergic neurons wake. The role of my lab is to identify the downstream targets through which basal forebrain GABAergic neurons drive and maintain wakefulness.

Report of Local Teaching and Training Teaching of Students in Courses:

2016	Applications of optogenetic and pharmacogenetic tools 6 classroom hours Graduate students	Harvard Medical School
2016-2020	Conduct of Science	Harvard Medical School 5 classroom hours per year Graduate students
2017	Anatomical, cellular and synaptic bases of REM sleep	BIDMC 2 classroom hours Neurology residents
2019	Basis of the Hypothalamic Functions and Techniques in Neuroscience	Department of Biology and Biotechnology; University of Pavia, Italy 12 classroom hours
2021-2024	Harvard Catalyst Education Program “Career Catalyst”	10 classroom hours per year Postdoctoral Fellows
2024	Basis of the Hypothalamic Functions and Techniques in Neuroscience	Department of Biology and Biotechnology; University of Pavia, Italy 12 classroom hours

Laboratory and Other Research Supervisory and Training Responsibilities:

2016- **Roberto De Luca, PhD**

Instructor of Neurology BIDMC
Supervision: 2 hours per week

2023- **Ida L. Boccalaro, PhD**
Postdoctoral Research Fellow
Supervision: 4 hours per week

2023- **Enrico Rillo**
Senior undergraduate student, (Boston University)
Supervision: 6 hours per week

2021- **Natalia Machado, PhD**
Instructor of Neurology BIDMC
Supervision: 2 hours per month

2021-2024 **PhD students from the Harvard Catalyst Mentoring Program** Supervision:
1 hours per month

2024- **Hannah Pridgeon**
Undergraduate student, (Simmons College)
Supervision: 1 hour per week

2024- **Caroline Vella**
BSc student in Cognitive Psychology and Biopsychology (University of Padova, Italy) Supervision:
3 hours per week

Other Mentored Trainees and Faculty:

2008-2009 **Joanna M. Hawryluk**
Senior undergraduate student (Simmons College)
Supervision: 8 hours per week as honors thesis advisor and laboratory mentor Subsequent
Role: Postdoctoral research fellow, UMass Worcester

2009-2010 **Fen-Jun (Eddie) Weng, PhD**
Postdoctoral Research Fellow
Supervision: 4-5 hours per week
Subsequent Role: Department of Brain and Cognitive Science, MIT, Dr. Yingxi Lin supervisor

2009-2010 **Loris L. Ferrari**
PhD Student (University of Milan)
Supervision: 8 hours per week as laboratory supervisor and mentor.
Subsequent Role: Research Associate, Department of Neurobiology, UMass Worcester.

2010-2011 **Sarah A. Keating**
Senior undergraduate student (Mount Holyoke College),
Supervision: 4 hours per week as honors thesis advisor and laboratory mentor. Subsequent
Role: Nursing School

2011-2012 **Rhiannan H. William, PhD**
Postdoctoral Research Fellow
Supervision: 4-5 hours per week
Subsequent Placement: Stanford Research Institute, Dr. Thomas Kilduff supervisor

2013-2017 **Daniel Park**
Senior undergraduate student, (UMass Boston)
Supervision: 5 hours per week as laboratory mentor.
Subsequent Placement: Industry

2015-2019 **Lin Zhu, PhD**
Postdoctoral Research Fellow
Supervision: 2 hours per week
Subsequent Placement: Industry

2018-2019 **Bianca Viberti**
Graduate Student (Neurosciences, University of Trieste, Italy)
Supervision: 4 hours per week
Subsequent Role: PhD. Program in Neuroscience; Bern University; Switzerland

2017-2019 **Somdeb Banerjee**
Research Assistant
Supervision: 4 hours per week
Subsequent Role: Medical Student, Tulane School of Medicine, New Orleans, LA

2018-2019 **Michela Cristofolini**
Graduate Student (Neurosciences, University of Pavia, Italy)
Supervision: 4 hours per week
Subsequent Role (November 2019): PhD. Program in Neuroscience; Trento University; Italy

2021-2022 **Oleksandra (Sasha) Fanari**
Graduate Student (Master Degree in Bioengineering, University of Pavia, Italy)
Supervision: 4 hours per week

2021-2022 **Andrea Pigozzi**
Graduate Student (Master Degree in Bioengineering, University of Pavia, Italy)
Supervision: 4 hours per week

2020-2023 **Francesca Raffin**
Graduate Student (Neurosciences, University of Pavia, Italy)
Member of her Ph.D. Thesis Committee, Dissertation scheduled for March 2024 Supervision:
4 hours per week

Local Invited Presentations:

No presentations below were sponsored by outside entities

Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.

2003 "Adenosine Inhibits Basal Forebrain Cholinergic and Noncholinergic Neurons *In Vitro*" Invited presentation, Sleep Ground Rounds/Division of Sleep Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston MA

2010 "Sleep in Brain Slices: Cellular Mechanisms of Sleep and Muscle Atonia", Invited presentation focusing on young investigators, Research Day 3/5/2010, BIDMC, Boston, MA

2011 "Pontine Control of REM Atonia – *In Vitro* Brain Slices" Invited presentation, Neurology Seminar Series, BIDMC, Boston, MA

2015 "From Wake to Sleep - *In Vitro* Studies of Neuronal Circuits and Neuromodulators"

Invited presentation, Neurology Department Seminar Series, BIDMC, Boston, MA

- 2017 “Functional Circuitry of CNS State”
Session Co-Chair, APSS Annual Meeting, Boston MA
- 2018 “Neuronal Circuits in Sleep and Wake Regulation”
Invited presentation, Neurology Department Seminar Series, Boston, MA
- 2023 “Hypothalamic Networks Supporting Arousal”
Invited presentation, Sleep Ground Rounds/Division of Sleep Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston MA

Report of Regional, National and International Invited Teaching and Presentations

No presentations below were sponsored by outside entities

Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.

National

- 1999 “GABAergic and Glutamatergic Transmissions in the Laterodorsal Tegmentum are Modulated Presynaptically by Adenosine”
Invited talk, APSS Annual Meeting, Orlando FL
- 2000 “Endogenous Adenosine Inhibits the Excitatory Synaptic Transmission in the Laterodorsal Tegmentum”
Invited talk, APSS Annual Meeting, Las Vegas NV
- 2001 “Pharmacologically Distinct NMDA Channel Distribution in the Same Pyramidal Neuron” Invited presentation, Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas, TX.
- 2001 “An Absence of Adenosine Effects in Laterodorsal Tegmental Neurons of A1R Knockout Mice Associated with Increased Wakefulness”
Invited talk, APSS Annual Meeting Chicago IL
- 2003 “The Effects of Adenosine on the Membrane Properties of Basal Forebrain Cholinergic Neurons”
Invited talk, APSS Annual Meeting, Chicago IL
- 2003 “Dopamine Induces Excitation of the Basal Forebrain Cholinergic Neurons”
Invited talk, APSS Annual Meeting, Chicago IL
- 2005 “Long Term Synaptic Plasticity is Impaired in Animals with Lesions of the Ventrolateral Preoptic Nucleus”
Invited talk (“DataBlitz”), Society for Neuroscience Annual Meeting, Washington DC
- 2007 “Carbachol Excites Spinal Cord Projecting Neurons of the Sublaterodorsal Nucleus Whole-cell Recording in In Vitro Slices”
Invited talk, APSS Annual Meeting, Minneapolis, MN
- 2012 “Pharmacologic- and Opto-genetic Tools to Dissect Sleep-Related Pathways in Brain Slices”
Minisymposium: Dissection of CNS Circuitry Regulating Sleep and Arousal - Conditional Transgenic and Genetically Engineered Receptor-Channel Systems.
Invited talk, Society for Neuroscience Annual Meeting, New Orleans LA
- 2013 “Sleep Neurobiology: From Rats and Mice to Flies and Worms”
Session Chair, APSS Annual Meeting, Baltimore, MD
- 2014 “Optogenetic Release of Histamine Reveals Distal and Autoregulatory Mechanisms for Controlling Arousal”
Invited presentation for the Symposium: Dissection of Neural Circuitry Regulating Sleep-Wake Using Genetically Engineered Systems. APSS Annual Meeting, Minneapolis MN.

- 2018 “Regulation of Lateral Hypothalamic Orexin Neuron Activity by Local GABAergic Neurons”
Invited talk, 7th International Narcolepsy Symposium, Beverly, MA
- 2018 Noradrenaline and Dopamine: Evolving Roles in Sleep/Wake Regulation, Synaptic Plasticity and Memory”
Discussion Leader, Sleep Regulation and Function. Gordon Research Conference, Galveston, TX.
- 2020 “The circuit and synaptic basis of arousal and sleep”
Invited talk, Department of Neurobiology, University of Massachusetts Medical School, Worcester, MA.
- 2021 “Hypothalamic Networks Supporting Wakefulness”
Invited presentation, Advances in Sleep and Circadian Science Series, Sleep Research Society, Virtual.
- 2023 “Long-Range and Local Networks that Regulate Sleep-Promoting Ventrolateral Preoptic Neurons”. Invited presentation for the Symposium: New Insights Into The Waking, Sleeping, And Dreaming Brain. APSS Annual Meeting, Indianapolis IN
- 2023 “Hypothalamic Networks Supporting Wakefulness”
Invited presentation, Systems Neuroscience, Department of Neurological Surgery UC Davis School of Medicine, Davis, CA
- 2024 “A Hypothalamic Circuit for Circadian Regulation of Corticosterone Secretion”
Invited presentation, Systems Neuroscience, Department of Neurological Surgery UC Davis School of Medicine, Davis, CA
- 2024 “Inhibiting Sleep to Promote Arousal”
Invited presentation, Neuroscience Seminar, UCSF, San Francisco, CA
- 2024 “Inhibiting Sleep to Promote Arousal”
Invited presentation, Sleep Wake and Cognition Impact Symposia. Session One: Fundamental mechanisms of sleep-wake cycle and disorders of consciousness. Department of Neurological Surgery and Department of Neurology, UC Davis School of Medicine, Davis, CA
- 2024 “What We Know About Sleep: How It Is Generated and How Certain We Are Across Species and Ages”. Chan Zuckerberg Initiative Sleep Discussion Group; virtual meeting

International

- 2000 “Adenosine inhibits mesopontine cholinergic neurons: pre and postsynaptic effects”
Invited presentation, Riunione della Società Italiana di Ricerca sul Sonno (SIRS). Isola d’Elba; Italy.
- 2008 “The Wake-Promoting Role of Orexin in the Basal Forebrain”.
Invited Presentation, Acta Physiologica International Symposium – 10 Years of Hypocretins/Orexins Physiology and Pathophysiology. University of Oulu, Oulu, Finland.
Invited contribution to the symposium sponsored by the Scandinavian Physiological Society/Acta Physiologica Scandinavica Jubileumsfond & Federation of the Finnish Learned Societies
- 2019 “Neuronal Circuits for Sleep and Wake Regulation”
Invited lecture, Department of Biology and Biotechnology; University of Pavia, Italy
- 2019 “Sleep and Wakefulness, regulation and function”
Lecture Series; Master's degree in Neurobiology; University of Pavia, Italy
- 2020 “Basal Forebrain-Hypothalamic Networks Supporting Wakefulness”
Invited talk, Department of Cell and Systems Biology; University of Toronto, Canada.

- 2020 “Hypothalamic Networks Supporting Wakefulness”
Invited lecture, Colloquium Series; Carleton University, Canada.
- 2021 “Imaging of Neuronal Activity from Calcium Imaging to Voltage Sensitive Dyes and GRAB Sensors”
Invited lecture, Department of Biology and Biotechnology; University of Pavia, Italy
- 2022 “Long-range and local networks that regulate sleep-promoting ventrolateral preoptic neurons”
Invited talk, World Sleep 2022, Rome, Italy
- 2023 “Inhibiting Sleep to Promote Arousal - long-range and local networks that regulate sleep-promoting ventrolateral preoptic neurons”
Invited talk, Annual Meeting of Japanese Society of Sleep Research, Yokohama, Japan.
- 2023 “Inhibiting Sleep to Promote Arousal”
Invited lecture, 184th WPI-IIIIS Symposium Series, International Institute for Integrative Sleep, University of Stukuba, Japan.
- 2024 “Inhibiting Sleep to Promote Arousal”
Invited lecture, Department of Biology and Biotechnology; University of Pavia, Italy
- 2024 “Inhibiting Sleep to Promote Arousal”
Invited lecture, 55th Systems Biology Seminar, Graduate School of Pharmaceutical Sciences Kyoto University
- 2024 “Long-range and local networks that regulate sleep-promoting ventrolateral preoptic neurons”
Invited lecture, Biological Sciences Seminar Series, Department of Biological Sciences; Graduate School of Science, University of Tokyo.
- 2024 “Inhibiting Sleep in Order to Stay Awake” Invited lecture, 209th WPI-IIIIS Symposium Series, International Institute for Integrative Sleep, University of Stukuba, Japan.

Report of Scholarship

Peer-Reviewed Scholarship in print or other media:

Research Investigations

1. Formenti A., **Arrigoni E.**, Sansone V., Arrigoni-Martelli E. and Mancina M. (1992). “Effects of acetyl-L-carnitine on the survival of adult rat sensory neurons in primary cultures”. *Int. J. Dev. Neurosci.* 10:207-214.
2. Formenti A., **Arrigoni E.** and Mancina M. (1993). “Two distinct modulatory effects on calcium channels in adult rat sensory neurons”. *Biophys. J.* 64:1029-1037.
3. Formenti A., **Arrigoni E.** and Mancina M. (1993). “Low-voltage activated calcium channels are differently affected by nimodipine”. *NeuroRep.* 5:145-147.
4. Formenti A., **Arrigoni E.**, Martina M., Taverna S., Avanzini G. and Mancina M. (1995). “Calcium influx in rat thalamic relay neurons through voltage-dependent calcium channels is inhibited by enkephalin”. *Neurosci. Lett.* 201:21-24.
5. **Arrigoni E.**, Rainnie D. G., McCarley R. W. and Greene R. W. (2001). “Adenosine mediated presynaptic modulation of glutamatergic transmission in the laterodorsal tegmentum”. *J. Neurosci.* 21(3):1076-1085.
6. Formenti A., De Simoni A., **Arrigoni E.** and Martina M. (2001). “Changes in extracellular Ca²⁺ can affect the pattern of discharge in rat thalamic neurons”. *J Physiol.* 535(1):33-45.
7. Basheer R., **Arrigoni E.**, Thatte H., Greene R. W., Ambudkar I.S. and McCarley R.W. (2002). “Adenosine induces IP3 receptor-mediated mobilization of intracellular calcium stores in basal forebrain cholinergic neurons”. *J. Neurosci.* 22(1):7680-7686.

8. Chamberlin N. L., **Arrigoni E.**, Chou T., Scammell T. E., Greene R. W. and Saper C. B. (2003). "Effects of adenosine on GABAergic synaptic inputs to identified ventrolateral preoptic neurons". *Neuroscience* 119:913-918.
9. Scammell T. E., **Arrigoni E.**, Thompson M. A., Ronan P. J., Saper C. B. and Greene R. W. (2003). "Focal deletion of the adenosine A₁ receptor in adult mice using an adeno-associated viral vector". *J. Neurosci.* 23(13): 5762-5770.
10. **Arrigoni E.** and Greene R. W. (2004). "Schaffer collateral and perforant path inputs activate different subtypes of NMDA receptors on the same CA1 pyramidal cell". *Br. J. Pharmacol.* 142:317322.
11. **Arrigoni E.**, Crocker A. J., Saper C. B., Greene R. W. and Scammell T. E. (2005). "Deletion of presynaptic adenosine A₁ receptors impairs the recovery of synaptic transmission after hypoxia". *Neuroscience* 132:575-580.
12. **Arrigoni E.**, Chamberlin N. L., Saper C. B., McCarley R. W. (2006). "Adenosine inhibits basal forebrain cholinergic and noncholinergic neurons in vitro". *Neuroscience* 140:403-413.
13. Tartar J. L., Ward C. P., McKenna J. T., Thakkar, M., **Arrigoni E.**, McCarley R. W., Brown R. E., Strecker R. E. (2006). "Hippocampal synaptic plasticity and spatial learning are impaired in rat model of sleep fragmentation". *Eur. J. Neurosci.* 23:2739-2748.
14. **Arrigoni E.**, Rosenberg P. A. (2006). "Nitric oxide-induced adenosine inhibition of the hippocampal synaptic transmission depends on adenosine kinase inhibition and is cyclic GMP independent". *Eur. J. Neurosci.* 24(9): 2471-2480.
15. **Arrigoni E.**, Lu J., Vetrivelan R., Saper C. B. (2009). "Long term synaptic plasticity is impaired in rats with lesions of the ventrolateral preoptic nucleus". *Eur. J. Neurosci.* 30(11):2112-2120.
16. **Arrigoni E.**, Mochizuki T., Scammell T. E. (2010). "Activation of the basal forebrain by the orexin/hypocretin neurons". *Acta Physiologica* 198(3):223-235.
17. Mochizuki T., **Arrigoni E.**, Clark E. L., Marcus J. N., Lowell B. B., Elmquist J. K., Scammell T. E. (2011) "Orexin receptor 2 expression in the posterior hypothalamus rescues sleepiness in narcoleptic mice". *Proc. Natl. Acad. Sci. USA.* 108(11):4471-4476.
18. Hawryluk J. M., Ferrari L. L. Keating S. A., **Arrigoni E.** (2012) "Adenosine inhibits glutamatergic input to basal forebrain cholinergic neurons". *Journal of Neurophysiology.* 107:2769-2781.
19. Oishi Y, Williams R. H., Agostinelli, L., **Arrigoni, E.**, Fuller P. M., Mochizuki T., Saper C. B., Scammell T. E. (2013). "Role of the medial prefrontal cortex in cataplexy". *J Neurosci.* 33(23):9743-9751.
20. Weng F. J., Williams R. H., Hawryluk, J. M., Lu J., Scammell, T. E., Saper C. B., **Arrigoni E.** (2014). "Carbachol excites sublaterodorsal nucleus neurons projecting to the spinal cord". *J Physiol.* 592(7):1601-1617.
21. Williams R. W., Chee M. J. S., Kroeger D., Ferrari L. L., Maratos-Flier E., Scammell T. E., **Arrigoni E.** (2014). "Optogenetic mediated release of histamine reveals distal and autoregulatory mechanisms for controlling arousal". *J. Neurosci.* 34(17): 6023-6029.
22. **Arrigoni E.**, Saper C. B. (2014). "What optogenetic stimulation is telling us (and failing to tell us) about fast neurotransmitters and neuromodulators in brain circuits for wake-sleep regulation". *Curr. Opin. Neurobiol.* 29C:165-171.
23. Anaclet C., Ferrari, L. L., **Arrigoni, E.**, Bass, C. E., Saper, C. B., Lu, J., Fuller, P. M. (2014). "The GABAergic parafacial zone is a medullary slow wave sleep-promoting center". *Nat. Neurosci.* 17(9): 1217-24.
24. Chen M. C., Ferrari L. L., Sacchet M. D., Foland-Ross, L. C., Qiu M., Gotlib I. H., Fuller P. M., **Arrigoni E.**, Lu J. (2015). "Identification of a direct GABAergic pallidocortical pathway in rodents". *Eur. J. Neurosci.* 41(6): 748-59.

25. Chee M. J. S., **Arrigoni E.**, Maratos-Flier E. (2015). "Melanin-concentrating hormone neurons release glutamate for feed-forward inhibition of the lateral septum". *J. Neurosci.* 35(8):3644-3651.
26. Anaclet C., Pederson N. P., Ferrari, L. L., Venner A., Bass, C., **Arrigoni, E.**, Fuller, P. M. (2015). "Basal forebrain control of wakefulness and cortical rhythms". *Nat. Commun.* 6:8744-8758.
27. Ferrari L. L., Agostinelli L. J., Krashes M. J., Lowell B. B., Scammell T. E., **Arrigoni E.** (2016). "Dynorphin inhibits basal forebrain cholinergic neurons by pre- and post-synaptic mechanisms". *J. Physiol.* 594(4): 1069-1085.
28. **Arrigoni E.**, Chen M. C., Fuller P. M. (2016). "The anatomic, cellular, and synaptic basis of motor atonia during rapid eye movement sleep". *J. Physiol.* 594(19):5391-5414.
29. Vetrivelan R., Kong D., Ferrari L. L., **Arrigoni E.**, Madara J. C., Bandaru S. S., Lowell B. B., Lu J., Saper C. B. (2016). "Melanin-concentrating hormone neurons specifically promote rapid eye movement sleep in mice". *Neuroscience.* 336:102-113.
30. Kroeger D., Ferrari L. L., Petit G., Mahoney C. E., Fuller P.M., **Arrigoni E.**, Scammell T. E. (2017). "Cholinergic, Glutamatergic, and GABAergic Neurons of the Pedunculopontine Tegmental Nucleus Have Distinct Effects on Sleep/Wake Behavior in Mice". *J. Neurosci.* 37(5):1352-1366.
31. Agostinelli L. J. Ferrari L. L., Mahoney C., Mochizuki T., Lowell B. B., **Arrigoni E***, Scammell T. E*. (2017). "Descending Projections from the Basal Forebrain to the Orexin Neurons". *J. Comp. Neurol.* 525(7):1668-1684.
32. Scammell T. E., **Arrigoni E.**, Lipton J. O. "Neural Circuitry of Wakefulness and Sleep". (2017). *Neuron.* 93(4):747-765.
33. Kaur S., Wang J. L., Ferrari L. L., Thankachan S., Kroeger D., Venner A., Lazarus M., Wellman A., **Arrigoni E.**, Fuller P. M., Saper C. B. (2017). "A Genetically Defined Circuit for Arousal from Sleep during Hypercapnia". *Neuron.* 96(5):1153-1167.
34. Pedersen N. P., Ferrari L., Venner A., Wang J. L., Abbott S. B. G., Vujovic N., **Arrigoni E.**, Saper C. B., Fuller P. M. (2017). "Supramammillary glutamate neurons are a key node of the arousal system". *Nat. Commun.* 8(1):1405-1421.
35. Ferrari L. L., Park D., Zhu L., Palmer M. R., Broadhurst R. Y., **Arrigoni E.** (2018). "Regulation of lateral hypothalamic orexin activity by local GABAergic neurons". *J. Neurosci.* 38(6):1588-1599.
36. Anaclet C., De Luca R., Venner A., Malyshevskaya O., Lazarus M., **Arrigoni E***, Fuller P. M*. (2018). "Genetic Activation, Inactivation, and Deletion Reveal a Limited and Nuanced Role for Somatostatin-Containing Basal Forebrain Neurons in Behavioral State Control". *J. Neurosci.* 38(22):5168-5181.
37. Machado N. L. S., Abbott S. B. G., Resch J., Zhu, L., **Arrigoni E.**, Lowell B., Fuller P. Fontes M. A. P., Saper C. B. (2018). "A glutamatergic hypothalamomedullary circuit mediates thermogenesis but not heat conservation during stress-induced hyperthermia". *Curr. Biol.* 28(14):2291-2301.
38. **Arrigoni E.**, Chee M. J. S., Fuller P. M. (2019). "To eat or to sleep: That is a lateral hypothalamic question". *Neuropharmacology* 154:34-49.
39. Kroeger D., Absi G., Gagliardi C., Bandaru S. S., Madara J. C., Ferrari L. L., **Arrigoni E.**, Munzberg H., Scammell T. E., Saper C. B., Vetrivelan R. (2018). "Galanin neurons in the ventrolateral preoptic area promote sleep and heat loss in mice". *Nat. Commun.* 9:4129.
40. Versteegen A. M. J., Klymko N., Zhu L., Mathai J. C., Kobayashi R., Venner A., Ross R. A., VanderHorst V. G., **Arrigoni E.**, Geerling J. C., Zeidel M. L. (2019). "Non-Crh Glutamatergic Neurons in Barrington's Nucleus Control Micturition via Glutamatergic Afferents from the Midbrain and Hypothalamus". *Curr. Biol.* 29(17):2775-2789.
41. Zhu L., Chamberlin N. L., **Arrigoni E.** (2019). "Muscarinic Inhibition of Hypoglossal Motoneurons: Possible Implications for Upper Airway Muscle Hypotonia during REM Sleep". *J. Neurosci.* 39(40):7910-7919.

42. Venner A., Mochizuki T., De Luca R., Anaclet C., Scammell T. E., Saper C. B., **Arrigoni E.**, Fuller P. M. (2019). "Reassessing the Role of Histaminergic Tuberomammillary Neurons in Arousal Control". *J. Neurosci.* 39(45):8929-8939.
43. Venner A., De Luca R., Sohn L. T., Bandaru S. S., Verstegen A. M. J., **Arrigoni E.**, Fuller P. M. (2019). "An Inhibitory Lateral Hypothalamic-Preoptic Circuit Mediates Rapid Arousals from Sleep". *Curr. Biol.* 29(24):4155-4168.
44. Kaur S., De Luca R., Khanday M. A., Bandaru S. S., Thomas R. C., Broadhurst R. Y., Venner A., Todd W. D., Fuller P. M., **Arrigoni E.**, Saper C. B. (2020) "Role of serotonergic dorsal raphe neurons in hypercapnia-induced arousals". *Nat. Commun.* 11:2769.
45. Todd W. D., Venner A., Anaclet C., Broadhurst R. Y., De Luca R., Bandaru S. S., Issokson L., Hablitz L. M., Cravetchi O., **Arrigoni E.**, Campbell J. N., Allen C. N., Olson D. P., Fuller P. M. (2020). "Suprachiasmatic VIP neurons are required for normal circadian rhythmicity and comprised of molecularly distinct subpopulations". *Nat. Commun.* 11:4410.
46. **Arrigoni E.**, Fuller P. M. (2021). "The Role of the Central Histaminergic System in Behavioral State Control". *Curr. Top. Behav. Neurosci.* [Epub ahead of print] PMID: 34595740.
47. **Arrigoni E.**, Fuller P. M. "The sleep-promoting ventrolateral preoptic nucleus: what have we learned over the past 25 years?". *Int. J. Mol. Sci.* 23:2905.
48. **Arrigoni E.**, Fuller P. M. "Addicted to Dreaming?". *Perspective for Science. Science* 375:972–973.
49. De Luca R., Nardone S., Grace K. P., Venner A., Cristofolini M., Bandaru S. S., Sohn L. T., Kong D., Mochizuki T., Viberti B., Zhu L., Zito A., Scammell T. E., Saper C. B., Lowell B. B., Fuller P. M., **Arrigoni E***. (2022). "Orexin neurons inhibit sleep to promote arousal". *Nat. Commun.* 3(1):4163
50. Kroeger D., Thundercliffe J., Phung A., De Luca R., Geraci C., Bragg S., McCafferty K. J., Bandaru S. S., **Arrigoni E.**, Scammell T. E. (2022). "Glutamatergic pedunculopontine tegmental neurons control wakefulness and locomotion via distinct axonal projections". *Sleep.* 45(12).
51. Nardone S., De Luca R., Zito A., Klymko N., Nicoloutsopoulos D., Amsalem O., Brannigan C., Resch J. M., Jacobs C. L., Pant D., Veregge M., Srinivasan H., Grippo R. M., Yang Z., Zeidel M. L., Andermann M. L., Harris K. D., Tsai L. T., **Arrigoni E.**, Verstegen A. M. J., Saper C. B., Lowell B. B. (2024). "A spatially-resolved transcriptional atlas of the murine dorsal pons at single-cell resolution". *Nat. Commun.* 15(1):1966.
52. Ramirez-Plascencia O. D., De Luca R., Machado N. L. S., Eghlidi D., Khanday M. A., Bandaru S. S., Raffin F., Vujovic N., **Arrigoni E***, Saper C. B*. (2024). "A hypothalamic circuit for circadian regulation of corticosterone secretion". *Res Sq* [Preprint]. rs.3.rs-4718850.
53. Korkutata M., De Luca R., Fitzgerald B., **Arrigoni E.**, Scammell T. E. (2024). "Afferent projections to the Calca /CGRP-expressing parabrachial neurons in mice". *bioRxiv* [Preprint]. 8:2024.05.07.593004. doi: 10.1101/2024.05.07.593004.

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Books and Chapters

- Arrigoni E.**, Fuller P. M. (2011). "An Overview of Sleep: Physiology and Neuroanatomy". Book title: *Therapy in Sleep Medicine*. Editors: Barkoukis, T. Matheson, J. Ferber, R. Doghramji, K. Publisher: Elsevier. Pages:43-71.
- Arrigoni E.**, Fuller P. M. (2019). "The circuit, cellular and synaptic bases of sleep-wake regulation". Book title: *Handbook of Sleep Research*. Editor: Dringenberg, H. C. Publisher: Elsevier. Pages:6588.
- Arrigoni E.**, Fuller P. M. (2024). "Highlights of Sleep Neuroscience". Book title: *Review of Sleep Medicine 5th ed*. Publisher: Elsevier. (in press)

Arrigoni E., Fuller P. M. (2024). “Neurobiology of Sleep”. Book title: Sleep Medicine. Publisher: Oxford University Press. (in press)

Arrigoni E., Fuller P. M. (2024). “Circuits and Neurotransmitter Systems Controlling Sleep and Wake” Section 2, Chapter 6. Book title “Fundamentals of Sleep and Circadian Science”. Oxford University Press. (in press)

Thesis:

1. **Arrigoni E.** “Patch-Clamp Study of Calcium Channel Modulation in Sensory Neurons *in vitro.*” [B.Sc. dissertation]. Milan, Italy: University of Milan; 1994.
2. **Arrigoni E.** “Cellular Mechanisms of Cortical Synchronization in Behavioral State Control” [Ph.D dissertation]. Milan, Italy: University of Milan; 1998.

Narrative Report

Starting from with my postdoctoral research and continuing to the present, which spans over twenty years, I've studied the neurobiology of sleep. I've specifically investigated the effects of neuromodulators and sleep factors on neurons and neuronal circuitry involved in maintaining sleep and wakefulness.

With support from my first R01 grant, I studied a group of neurons in the pons that have been implicated in controlling muscle atonia during REM sleep, and how dysfunction of this circuitry can lead to an inappropriate absence of atonia during REM sleep. Hence this work has high clinical relevance. For example, in REM sleep behavior disorder (RBD), which is not only itself a devastating disease, but also a prodromal feature of several neurodegenerative diseases such as Parkinson's disease, the absence of REM atonia permits the appearance of dream reenactment. I have therefore sought to characterize the underlying synaptic mechanisms that regulate these pontine REM-atonia neurons, with a particular emphasis on the roles of acetylcholine, monoamines and orexin in controlling their activity. Over the past eight years I have enhanced and extended my experimental approach by incorporating optogenetic-based, Channelrhodopsin2 (ChR2)-assisted circuit mapping (CRACM). This has proven to be a particularly valuable way to test, in a precise manner, the functional synaptic connectivity between neurons including in circuits spanning multiple synaptically coupled nodes. For example, using these optogenetic methods, my team and I have recently demonstrated synaptic release of histamine from axons and terminals of the tuberomammillary nucleus onto neurons of the ventrolateral preoptic area (VLPO) – a key sleep-promoting cell group. We also have expertise in combining CRACM whole-cell recordings with selective labelling of the postsynaptic neurons (AAV-based) or molecular profiling of the recorded neurons by single cell RT-PCR, allowing us to identify the phenotype of the neurons that respond (and do not respond) with opto-evoked synaptic events following photostimulation of selective afferent pathways.

With support from my R21 grant, I studied the role of basal forebrain circuitry in cortical activation. The focus of this project was on the role of cortically-projecting GABAergic basal forebrain neurons in the regulation of cortical EEG and behavioral arousal. In addition to optogenetic methods, I have manipulated GABA release in the cortex by activating or inhibiting presynaptic terminals using DREADDs (designer receptors exclusively activated by designer drugs).

With support of my second R01 grant, I studied the cellular and synaptic bases by which basal forebrain GABAergic neurons produce wakefulness. I am specifically interested in the synaptic interaction(s) between basal forebrain GABAergic neurons and downstream preoptic and hypothalamic nodes and how this circuit responds to changes in homeostatic sleep pressure.

I am currently engaged in two major research projects. In the first project, funded by my third R01 grant I am testing the hypothesis that arousal signals from the forebrain and brainstem inhibit sleep-active neurons of the ventrolateral preoptic area (VLPO) directly and indirectly through local GABAergic neurons. I propose that a significant portion of the input to this hypothalamic sleep-promoting center

operates through a local GABAergic circuit and that these GABAergic interneurons serve as a common node through which wake-promoting signals inhibit VLPO sleep-active neurons to produce arousal. Elaborating the functional role of this local GABAergic circuit will form the basis of future investigations and may inform the development of new drugs for treating a wide range of sleep and wake disorders. In the second project, which is part of an NHLBI P01 grant, I am studying the forebrain inputs to a group of neurons in the parabrachial nucleus that are responsive to hypercapnia and drive respiratory responses. The ultimate goal of this study is to selectively enhance activity in these neurons to increase ventilatory responses but not cortical arousals in response to hypercapnia.

In addition to my research, since joining BIDMC in 2001, I have mentored six postdoctoral fellows and ten undergraduate or graduate students and have contributed to the knowledge and education of a large number of trainees through seminars and laboratory interactions. I have also been a standing member of the BIDMC Institutional Animal Care and Use Committee (IACUC) since 2012. This is a major service commitment which has involved hundreds of hours reviewing animal protocols and participating in laboratory inspections for the Beth Israel Deaconess Medical Center research community. Nationally and internationally, I am an active member of the sleep research community. I am also a frequent reviewer for major journals, I have served as a grant reviewer for several NIH study sections, I was a member of the Scientific Review Committee for the Sleep Research Society and I was part of the APSS Meeting Organizing Committee for two years. In 2024, I returned to the APSS Meeting Organizing Committee as the committee's vice chair.