BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Fellin, Tommaso	Senior Principal Investigator

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Padova, Italy	B.Sc.	07/1998	Physics
University of Padova, Italy	Ph.D.	03/2003	Biophysics
University of Padova, Italy	Postdoctoral	02/2005	Neuroscience
University of Pennsylvania, PA	Postdoctoral	03/2008	Neuroscience

A. Personal Statement

My laboratory aims to understand how specific spatial and temporal patterns of network dynamics are generated, transferred, and integrated within the cortical circuitry, as well as how these dynamics influence behavior. A necessary technical step to achieve this aim is to develop a technique that allows us to: *i)* monitor endogenous patterns of activation and thus map the activity of large numbers of neurons with high spatial (< 1 micron) and temporal (~1 ms) resolution within the intact brain; and *ii)* replicate or alter these endogenous patterns of activation by artificially manipulating the electrical activity of specific cells in space and time.

Over the past ten years, we have been working on a particular technique, patterned illumination using ‘wave-front engineering’ and we have been pioneering its application in living rodents to achieve our dual goal. We first designed and built a “patterned illumination module”, a compact, simple optical path that can be easily implemented with commercial two-photon scanheads to allow spatial shaping of laser light. We validated this approach for calcium imaging at high frame rates (up to 70 frames/s) from multiple cells simultaneously and demonstrated that this technique can be used for photo-uncaging MNI glutamate in arbitrary two dimensional patterns in cultured neurons. We reported the first application of this optical set-up for *in vivo* experimental conditions in living rodents, using wave-front modulation to provide inertia-free focus control, i.e., dynamically focusing in depth while keeping the objective in a fixed position. As a necessary step towards the development of an optical system that allows the generation of artificial patterns of network activation *in vivo*, we applied our patterned two-photon illumination microscope to map the activity of cortical cells with millisecond temporal resolution and subcellular spatial resolution in the scanless configuration. We also validated the scanless approach in GRIN lens-based endoscopes for fast imaging in deep brain regions. Moreover, we combined scanless imaging of GCaMP6 signals in population of neurons with wide-field single-photon optogenetic stimulation of the inhibitory opsin Archaerhodopsin. More recently, we combined two-photon holography to stimulate neurons expressing blue light-sensitive opsins (ChR2 and GtACR2) with two-photon imaging of the red-shifted indicator jRCaMP1a in the mouse neocortex *in vivo*. We demonstrated efficient bidirectional control of neural excitability across cells types and layers with holographic stimulation and improved spatial resolution by opsin somatic targeting. Moreover, we performed simultaneous two-photon imaging of jRCaMP1a and bidirectional two-photon manipulation of cellular activity with negligible effect of the imaging beam on opsin excitation (no crosstalk). We also conceived and validated a method to significantly increase the signal-to-noise ratio in population GCaMP6s imaging. The method was validated in anesthetized and awake mice and it led to more precise identification of functional neuronal ensembles.

In addition to the contribution to technology development described above, we have applied advanced optical approaches to dissect out the cellular circuits underlying spontaneous network oscillations and sensory-evoked circuit dynamics in the mouse cortex. We used optogenetics, which allows the remote control of cellular excitability with light, to investigate the role of excitatory and inhibitory neurons in the propagation of cortical network dynamics and the control of cortical state, using slow oscillations as an experimental model. For example, by combining selective expression of excitatory and inhibitory opsins in layer V and layer II/III pyramidal neurons with electrophysiological recordings *in vivo*, we showed that activation/inactivation of a subset of pyramidal neurons located in layer V, but not layer II/III, was sufficient and necessary to generate and attenuate slow oscillations, respectively. Based on patch-clamp recordings, we proposed that the differential role of layer V and II/III in the regulation of slow network activity is linked to the differential ability of these neurons to propagate prolonged depolarization within and across cortical layers. These results are of importance because they represent the first demonstration that the cortex is endowed with layer-specific excitatory circuits that have distinct roles in the coordination of ongoing cortical activity. More recently, we provided the first direct demonstration that, during somatosensation, layer V pyramidal neurons in the mouse primary somatosensory cortex not only relay sensory information to higher order brain areas as posited by the "canonical" model of cortical function, but they actively sculpt local cortical processing, leading to temporal sharpening of responses to sensory inputs.

B. Positions and Honors

- Positions and Employment

1997-1998	Undergraduate student, Department of Physics and Department of Biochemistry, University of Padova, Padova, Italy.
1998-2003	Ph.D. student, Department of Experimental Biomedical Sciences, University of Padova, Padova, Italy.
2003-2004	Postdoctoral fellow, Department of Experimental Biomedical Sciences, University of Padova, Padova, Italy.
2003	Guest researcher, Istitute de Neurophysiologie INSERM, Paris, France.
2005-2008	Postdoctoral fellow, Department of Neuroscience, University of Pennsylvania School of Medicine, PA, USA.
2008-2013	Junior Team Leader, Department of Neuroscience and Brain Technologies, Italian Institute of Technology, Genova, Italy.
2013-	Senior Team Leader, Department of Neuroscience and Brain Technologies, Italian Institute of Technology, Genova, Italy.
2016-	Co-Founder and Chief Scientific Consultant, SmartMicroOptics s.r.l.
2017-	Senior Team Leader (tenured), Department of Neuroscience and Brain Technologies, Italian Institute of Technology, Genova, Italy.
2019-2023	Coordinator Neuroscience Area, Italian Institute of Technology, Genova, Italy.
2023-	Associate Director, Technologies for Life Sciences Research Domain, Italian Institute of Technology, Genova, Italy.

- Other Experience and Professional Memberships

2003-	Member, Society for Neuroscience (SfN)
2000-	Member, Italian Society of Pure and Applied Biophysics
2011-2016	Scientific Review Associate, The European Journal of Neuroscience
2013-2017	Editorial Board Member, The Journal of Neuroscience Methods
2013-	Member, Optical Society of America (OSA)
2015-	Member of the board of directors, Life Science area, Italian Institute of Technology
2016-	Review Editor and Editorial Board member, Frontiers in Neural Circuits
2016-	Review Editor and Editorial Board member, Frontiers in Synaptic Neuroscience
2016-	Member of Society of Photo-Optical Instrumentation Engineers (SPIE)
2021	Associate editor, Frontiers in Neural Circuits

2021 Editorial board member, Neurophotonics
2022 Review Editor and Editorial Board member, Frontiers in Integrative Neuroscience

- Honors

2002 Borsellino Award, XVI National Congress of the Italian Society for Pure and Applied Biophysics, Trento, Italy
2003 Young investigators grant (#CPDG031725), University of Padova, Italy
2006 Neuroscience award "Maurizio Mangrella"
2006 Post-doctoral Research Fellowship, Epilepsy Foundation
2015 Smart Cup 2015 award to SmartMicroOptics
2015 European research Council (ERC) Consolidator grant
2018 U19 NIH Brain Initiative grant

C. Selected Peer-reviewed Publications *(15 best peer-reviewed publications)*

1) Kagiampaki Z., Rohner V., Kiss C., Curreli S., Dieter A., Wilhelm M., Harada M., Duss S.N., Dernic J., Bhat M.A., Zhou X., Ravotto L., Ziebarth T, Wasielewski L.M., Sönmez L.6, Benke D., Weber B., Bohacek J., Reiner A., Wiegert S., Fellin T., Patriarchi T. "*Sensitive multicolor indicators for monitoring norepinephrine in vivo*" **Nature Methods**, (2023), ahead of print.

2) Aime M., Calcini N., Borsa M., Campelo T., Rusterholz T., Sattin A., Fellin T., Adamantidis A. "*Paradoxical somatodendritic decoupling supports cortical plasticity during REM sleep*" **Science**, (2022), 13: 724-730.

3) Sità L., Brondi M., Lagomarsino De Leon Roig P., Curreli S., Panniello M., Vecchia D., Fellin T. "*A deep-learning approach for online cell identification and trace extraction in functional two-photon calcium imaging*" **Nature Communications**, (2022), 13:1529.

4) Curreli, S., Bonato J., Romanzi S., Panzeri S., Fellin T. "*Complementary encoding of spatial information in hippocampal astrocytes*" **PLOS Biology**, (2022), 20:e3001530.

5) Duffet L., Kosar S., Panniello M., Viberti B., Bracey E., Zych A.D., Radoux-Mergault A., Zhou X., Dernic J., Ravotto L., Tsai J.C., Tjagarajan S.K., Weber B., Stoeber M., Gogolla N., Schmidt M.H., Adamantidis A.R., Fellin T., Burdakov D., Patriarchi T. "*A genetically encoded sensor for ultrasensitive in vivo imaging of orexin neuropeptides*" **Nature Methods**, (2022), 19:231-241.

6) Forli A., Pisoni, M. Prints Y., Yizhar O., Fellin T. "*Optogenetic strategies for high-efficiency all-optical interrogation using blue light-sensitive opsins*" **eLife** (2021), 25;10:e63359.

7) Antonini A., Sattin A., Moroni M., Bovetti S., Moretti C., Succol F., Forli A., Vecchia D., Rajamanickam V.P., Bertoncini A., Panzeri S., Liberale C., Fellin T. "*Extended field-of-view ultrathin microendoscopes for high-resolution two-photon imaging with minimal invasiveness*" **eLife** (2020), 13;9:e58882.

8) Mariotti L., Losi G., Lia A., Melone M., Chiavegato A., Gomez-Gonzalo M., Sessolo M., Bovetti S., Forli A., Zonta M., Requie L.M., Marcon I., Pugliese A., Viollet C., Bettler B., Fellin T., Conti F., Carmignoto G. *"Interneuron-specific signalling evokes distinctive somatostatin-mediated responses in adult cortical astrocytes"* **Nature Communications** (2018) 9: 82.

9) Zucca S., D'Urso G., Pasquale V., Vecchia D., Pica G., Bovetti S., Moretti C., Varani S., Molano-Mazón M., Chiappalone M., Panzeri S., Fellin T. "*An inhibitory gate for state transition in cortex"* **eLife** (2017) 6: e26177.

10) Panzeri S., Harvey C.D., Piasini E., Latham P.E., Fellin T. *"Cracking the neural code for sensory perception by combining statistics, intervention and behavior"* **Neuron** (2017) 93:491-507.

11) Beltramo R., D'Urso G., Dal Maschio M., Farisello P., Bovetti S., Clovis Y., Lassi G., Tucci V., De Pietri Tonelli D., Fellin T. "*Layer-specific excitatory circuits differentially control recurrent network dynamics in the neocortex*" **Nature Neuroscience** (2013) 16(2):227-34.

12) Fellin T., Halassa M., Terunuma M., Succol F., Takano H., Frank M.G., Moss S.J., Haydon P.G. "*Endogenous non neuronal modulators of synaptic transmission control cortical slow oscillations in vivo*" **PNAS** (2009) 106:15037-42.

13) Halassa M., Florian C., Fellin T., Munoz J.R., Lee S.Y., Abel T., Haydon P.G., Frank M. "*Astrocytic adenosine controls sleep homeostasis and cognitive consequences of sleep loss*" **Neuron** (2009) 61:213-219.

14) Fellin T., Pascual O., Gobbo S., Pozzan T., Haydon P.G., Carmignoto G. *" Neuronal synchrony mediated by astrocytic glutamate through activation of extrasynaptic NMDA receptors"*. **Neuron** (2004), 43: 729-743.

15) A. Tottene*, T.Fellin*****, S. Pagnutti, S. Luvisetto, J. Striessnig, C. Fletcher, D. Pietrobon; *"Familial Hemiplegic Migraine Mutations increase Ca^{2+} influx through single human $Ca_V2.1$ channels and decrease maximal current density in neurons"*. **Proc. Natl. Acad. Sci.** (2002), 99(20):13284-13289.

D. Research Support

- Ongoing Research Support

NIH (U19 NS107464) Fellin (PI) 10/1/2018-7/31/2024
Readout and Control of Spatiotemporal Neuronal Codes for Behavior
The goal of this project is to investigate the neural code underlying sensory perception and to develop highly efficient technologies for large-scale patterned optogenetic manipulation
Role: PI

Marie Skłodowska-Curie (MoWS) Fellin (PI) 11/1/2020-10/31/2022
Modelling of Whole-brain Slow oscillatory dynamics in physiology and pathology
The goal of this project is to develop a whole-brain model that recapitulates large-scale slow oscillatory dynamics
Role: co-PI

Marie Skłodowska-Curie (MoWS) Fellin (PI) 11/1/2020-10/31/2022
Modelling of Whole-brain Slow oscillatory dynamics in physiology and pathology
The goal of this project is to develop a whole-brain model that recapitulates large-scale slow oscillatory dynamics
Role: co-PI

H2020 Research and Innovation Framework Programme, Fellin (PI) 2021-2025.
Role: PI

Chan Zuckerberg Initiative Advancing Imaging Through Collaborative Projects, Fellin (PI) 2023-2024.
Role: co-PI

- Completed Research Support

Compagnia di San Paolo Fellin (PI) 31/07/2009-31/01/2014

New players in visual cortical plasticity in vivo: role of interneurons and astrocytes.
Role: Co-investigator

Telethon Foundation GGP10138 Fellin (PI) 01/01/2011-02/28/2014
Interneuronal dysfunction in genetic epilepsies: insights from a mouse model of severe myoclonic epilepsy of infancy
Role: PI

IIT interdisciplinary project Fellin (PI) 03/15/2013-03/14/2015
Microfabricated endoscopes for the optical probing of deep brain microcircuits with structured light.
Role: PI

IIT interdisciplinary project Fellin (PI) 03/15/2014-03/14/2016
Super-resolution deep functional brain imaging of cortical layers in vivo.
Role: PI

FP7-HEALTH (DESIRE) Fellin (PI) 11/01/2013-10/31/2017
Development and Epilepsy - Strategies for Innovative Research to improve diagnosis, prevention and treatment in children with difficult to treat Epilepsy
The goal of this project is to identify the mechanisms of brain development, maturation, and plasticity relevant in disease onset and progression
Role: PI

NIH (U01 NS090576) Maunsell (PI) 10/01/2014-09/30/2017
The role of patterned activity in neuronal codes for behavior
The goal of this project is to determine the neural code underlying visual perception in mouse V1
Role: co-PI

Marie Skłodowska-Curie (ETIC) Panzeri (PI) 07/01/2015-06/30/2017
Encoding and Transmission of Information in the Mouse Somatosensory Cortex
The goal of this project is to develop a novel theoretical framework to investigate how the mammalian cortex encodes sensory information
Role: co-PI

Flag-Era, Human Brain Project (SLOW-DYN) Sanchez-Vives (PI) 12/01/2015-11/30/2017
Slow Wave Dynamics: from experiments, analysis and models to rhythm restoration
The goal of this project is to develop a data-constrained model of the generation of slow oscillations
Role: co-PI

ERC (NEURO-PATTERNS) Fellin (PI) 10/01/2015-09/30/2020
How neuronal activity patterns drive behavior: novel all-optical control and monitoring of brain neuronal networks with high spatiotemporal resolution
The goal of this project is to develop technologies to perform fast scanless imaging and patterned optogenetic manipulation of neuronal circuits
Role: PI

Marie Skłodowska-Curie (ESNECO) Panzeri (PI) 7/1/2020-6/30/2022
Estimation of Neural Code from the Electroencephalogram (EEG)
The goal of this project is to develop mathematical methods to interpret how the EEG is generated by specific neural features
Role: co-PI

Marie Skłodowska-Curie (MoWS) Panzeri (PI) 11/1/2020-10/31/2022
Modelling of Whole-brain Slow oscillatory dynamics in physiology and pathology
The goal of this project is to develop a whole-brain model that recapitulates large-scale slow oscillatory dynamics
Role: co-PI