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In Vitro Neuronal Networks

From Culturing Methods to Neuro-Technological Applications

Springer

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This book is dedicated to our mentors

Preface

In vitro cultures of dissociated neurons coming from different brain areas retain important functional properties of the tissue of origin, thus representing a perfect trade-off between more realistic (but complex) experimental models and theoretical (but limited) modeling approaches. Moreover, the possibilities offered by the latest technologies allow the simultaneous monitoring of several units at high spatiotemporal resolution and for very long time periods, from hours to days and even months. These technological developments are giving new opportunities in terms of experimental design, but also posing new problems in terms of data management and interpretation.

In this book, the authors provide an overview of the incredible developments achieved in the study of in vitro neuronal networks to make the scientific community aware of the enormous potential of this experimental model but also of its limitations. We will start from culturing methodologies, including the use of innovative nanotechnologies and nanomaterials. The establishment of stem cell-derived neuronal cultures will be also discussed, as well as the description of in vitro experimental models exhibiting pathological behaviors. We will review the techniques used for measuring networks' activity from many channels, mostly focusing on planar microelectrode arrays. Then, we will present recent improvements in large-scale data analysis and interpretation. Finally, we will introduce a set of applications for novel experimental designs, including neurotoxicology, stem cell technology, closed-loop electrophysiology, and hybrid systems.

The book has four major parts:

Part I: In Vitro Neuronal Cultures: Experimental Models and Nanomaterials
Part II: Recording Techniques
Part III: Data Analysis Methods
Part IV: Applications

This book is designed for professionals from both academic and non-academic fields working, or starting to work, with cultures of neurons in vitro. Target specialists among academics could be professors, technicians, postdocs, and graduate and

undergraduate students. Outside academia, managers in business development/sales could be interested in knowing the latest state-of-the-art achievements. It is also designed for teaching undergraduate and graduate students and researchers.

Genova, Italy — Michela Chiappalone
Genova, Italy — Valentina Pasquale
Enschede, The Netherlands — Monica Frega

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I would like to thank my PhD advisors, Prof. Massimo Grattarola and Prof. Sergio Martinoia, for introducing me to the fantastic world of in vitro neuronal systems. I thank all my lab members for the great job they do every day. I would also like to thank my family, my husband Emanuele and my kids Nicolò, Filippo, and Elena, for their constant support in any step of my career in research.

Michela Chiappalone

I would like to thank Prof. Sergio Martinoia, Dr. Michela Chiappalone, and Dr. Paolo Massobrio, who taught me everything I know about in vitro neuronal systems and MEAs. They always encouraged me to pursue my career with passion and courage. This book is dedicated to them.

Valentina Pasquale

I express my gratitude to my PhD advisor, Prof. Sergio Martinoia, because his passion and his way of working inspired me and led me during my first steps into the research world. I would also like to thank my husband Mattia who is always present by my side. Both of them have always encouraged me to follow my passions, supporting my research path and helping me in any step of my career.

Monica Frega

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About the Editors

Michela Chiappalone's research interests are in the field of neuroengineering. She obtained a PhD in Electronic Engineering and Computer Science from the University of Genova (Italy) in 2003. In 2002, she has been visiting scholar in the Department of Physiology, Northwestern University (Chicago, IL, USA). After a postdoc at the University of Genova, in 2007, she joined the Neuroscience and Brain Technologies Department at the Istituto Italiano di Tecnologia (IIT) as a postdoc. In 2013, she got a group leader position ("researcher") in the same institution. In 2015, she has been visiting professor at KUMED (Kansas City, KS, USA), hosted by Prof. R.J. Nudo. From 2012 to 2015, M. Chiappalone has been coordinator of the FET Open European Project BrainBow, judged excellent. In 2017, M. Chiappalone joined the Rehab Technologies IIT-INAIL joint lab of IIT to lead a group aimed at interfacing robotic devices with the nervous system for applications in neuroprosthetics, neuromodulation, and neurorehabilitation. In 2018, she got the National Scientific Habilitation as Full Professor of Bioengineering. She authored 60 papers published in international journals, 50 peer-reviewed contributions to international conferences, and 8 book chapters, and she gave more than 60 scientific talks at international/national conferences and research institutions.

Valentina Pasquale got the PhD in "Humanoid Technologies" from the University of Genova and Istituto Italiano di Tecnologia in 2010. During her PhD, she focused on developing analysis tools to characterize the spontaneous and evoked activity of cortical and hippocampal networks cultured on microelectrode arrays, seen as a reduced biological model for the generation of coordinated neuronal activity. During postdoc, she was involved in neuro-robotics and neuro-prosthetics studies, aimed at understanding how to interface artificial devices (as a small robot or a simulated neural network) and neuronal systems, with the final goal of advancing the design of future brain-machine interfaces and brain prostheses. Currently, she has been working as senior postdoc in Dr. Tommaso Fellin's lab (Optical Approaches to Brain Function). Her interests include in vivo studies combining optogenetics and electrophysiology for a deeper understanding of inhibitory interneurons' contribution to the generation and control of sleep waves. She is also involved in the design and development of technological tools for patterned optical stimulation through light phase modulation.

Monica Frega received her PhD in Bioengineering from the University of Genova in 2014. During her PhD, she developed a novel 3D neuronal model, and she demonstrated the possibility of coupling cultured 3D networks to microelectrode array devices and functionally monitoring their electrophysiological activity. Her thesis "Neuronal network dynamics in 2D and 3D in vitro neuro-engineered systems," carried out under the supervision of Prof. Dr. Sergio Martinoia, was judged "excellent" by the PhD committee and recognized as "outstanding PhD research" from Springer. Between 2014 and 2018, she worked as a postdoctoral researcher in the group of Prof. Dr. Nael Nadif Kasri at Radboudumc (Nijmegen, the Netherlands), where she applied her expertise in bioengineering to state-of-the-art stem cell biology to study neurodevelopmental disorders. While her academic path and PhD allowed her to develop engineering and technical capabilities, during the postdoc, she acquired expertise in stem cell biology. Through

these working experiences, Monica Frega became a truly interdisciplinary researcher. In 2018, Monica Frega started her job at the University of Twente as assistant professor in the Clinical Neurophysiology group. Her research mainly focuses on neurological disorders, with the aim to bridge the gap between research and clinic. She makes use of human in vitro models (neuronal cells derived from human-induced pluripotent stem cell from healthy subject and patients grown on microelectrode arrays) in combination with EEG data recordings from patients to study basic physiological processes involved in neurological disorders.