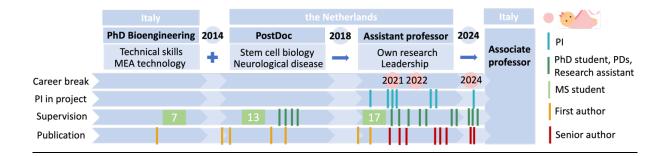# CURRICULUM VITAE

PERSONAL INFORMATION

Family name, First name: Monica Frega

Researcher unique identifier(s): https://orcid.org/0000-0002-9697-3282

Date of birth: 02/04/1985

Nationality: Italian
URL for web site: https://www.utwente.nl/en/tnw/cnph/people/scientific_staff/Frega-/

Date: 30/09/2024   Signature
Genova

EDUCATION

2014   PhD in Bioengineering (excellent)
                Dept. of Informatics, Bioengineering, Robotics and System Engineering (DIBRIS),
                University of Genova, Italy
                <u>Name of PhD Supervisor</u>: Prof. Sergio Martinoia

2010   Master in Bioengineering (summa cum laude)
                University of Genova, Genova, Italy

CURRENT POSITION(S)

2024   Associate professor
                Dept. of Informatics, Bioengineering, Robotics and System Engineering (DIBRIS),
                University of Genova, Italy

PREVIOUS POSITIONS

2018 – present Assistant professor (Universitair Docent 1, RTD-B equivalent)
                Dept. of Clinical neurophysiology (CNPH), Faculty of Science and Technology,
                University of Twente, Enschede, the Netherlands
2018 – present Second affiliation
                Dept. of Human Genetics, Radboud University Medical Centre, Nijmegen, the
                Netherlands
2014 – 2018   PostDoc
                Dept. of Human Genetics/Donder institute of brain, cognition and behavior, Radboud
                University Medical Centre, Nijmegen, the Netherlands
2014   PostDoc
                Dept. of Informatics, Bioengineering, Robotics and System Engineering (DIBRIS),
                University of Genova, Italy
2010   Research assistant
                Italian Institute of Technology, Genova, Italy

ABILITATIONS

2022   National Scientific qualification as associate in the Italian higher education system, in
                the call 2021/2023 (Ministerial Decree n. 553/2021 and 589/2021) for the disciplinary
                field of 09/G2 - Bioengineering.

MANDATORY LEAVES

2024   Maternity leave, child born on June 24th, 2024
2022   Maternity leave, child born on September 13th, 2022
2021   Maternity leave, child born on January 31st, 2021

TEACHING ACTIVITIES

2023 – 2024   Lecturer. Neuronal systems and research (theme Neurophysiology, 5 ECTS, 24 hours). Bachelor course for program of Technical Medicine, University of Twente, Enschede, the Netherlands.

2022 – 2023   Lecturer. Neuronal systems and research (theme Neurophysiology, 5 ECTS, 24 hours). Bachelor course for program of Technical Medicine, University of Twente, Enschede, the Netherlands.

2022 – 2023   Lecturer. Dynamic behaviour of neuronal networks (5 ECTS, 34 hours). Master course for programs of Biomedical Engineering, Electrical Engineering, Applied Mathematics and Technical Medicine, University of Twente, Enschede, the Netherlands.

2021 – 2022   Lecturer. Neuronal systems and research (theme Neurophysiology, 5 ECTS, 24 hours). Bachelor course for program of Technical Medicine, University of Twente, Enschede, the Netherlands.

2021 – 2022   Lecturer. Advances Techniques of signal processing (5 ECTS, 20 hours). Master course for programs of Biomedical Engineering, Electrical Engineering, Applied Mathematics and Technical Medicine, University of Twente, Enschede, the Netherlands.

2019 – 2020   Lecturer. Neuronal systems and research (theme Neurophysiology, 5 ECTS, 24 hours). Bachelor course for program of Technical Medicine, University of Twente, Enschede, the Netherlands.

2019 – 2020   Lecturer. Advances Techniques of signal processing. Master course for programs of Biomedical Engineering, Electrical Engineering, Applied Mathematics and Technical Medicine, 5 ECTS, 20 hours. University of Twente, Enschede, the Netherlands.

2019 – 2020   Lecturer. Dynamic behaviour of neuronal networks (5 ECTS, 34 hours). Master course for programs of Biomedical Engineering, Electrical Engineering, Applied Mathematics and Technical Medicine, University of Twente, Enschede, the Netherlands.

2018 – 2019   Lecturer. Neuronal systems and research (theme Neurophysiology, 5 ECTS, 24 hours). Bachelor course for program of Technical Medicine, University of Twente, Enschede, the Netherlands.

2018 – 2019   Lecturer. Advances Techniques of signal processing (5 ECTS, 20 hours). Master course for programs of Biomedical Engineering, Electrical Engineering, Applied Mathematics and Technical Medicine, University of Twente, Enschede, the Netherlands.

2017 – 2018   Lecturer. Translational neuroscience (2 hours). Master course of Cognitive Neuroscience, Donders Institute, Radboud University Nijmegen, Nijmegen, the Netherlands.

2017 – 2018   Teaching assistant. MED-MIN16 Translational Neuroscience (20 hours). Bachelor course for program of Medicine and Biomedical Sciences, RadboudUmc, Nijmegen, the Netherlands.

2016 – 2017   Teaching assistant. MED-MIN16 Translational Neuroscience (20 hours). Bachelor course for program of Medicine and Biomedical Sciences, RadboudUmc, Nijmegen, the Netherlands.

2016 – 2017   Teaching assistant. NWI-MOL137 Cell Biophysics (16 hours). Bachelor course for program of Molecular Life Science, Radboud University Nijmegen, Nijmegen, the Netherlands.

2015 – 2016   Teaching assistant. MED-MIN16 Translational Neuroscience (20 hours). Bachelor course for program of Medicine and Biomedical Sciences, RadboudUmc, Nijmegen, the Netherlands.

2015 – 2016   Teaching assistant. NWI-MOL137 Cell Biophysics (16 hours). Bachelor course for program of Molecular Life Science, Radboud University Nijmegen, Nijmegen, the Netherlands.

EARLY ACHIEVEMENTS TRACK-RECORDS
My research activities fall into the field of applied bioengineering. During my PhD project in Bioengineering at the University of Genova, I focused on the development of a novel 3D *in vitro* model and for the first time I demonstrated the possibility to assess the activity of 3D neuronal networks on MEAs. The work was judged 'excellent' by the PhD committee and recognized as 'outstanding PhD research' from Springer. I also had the opportunity to work together with clinicians, helping patients recovering from stroke. This experience certainly changed me. From that point, I felt the need to use my bioengineering background for creating innovative models for scientific problems with medical impact. Between 2014 and 2018, I worked as a postdoctoral researcher in the group of prof. dr. Nael Nadif Kasri at RadboudUmc, where I applied my expertise in bioengineering to state-of-the-art stem cell biology to study neurodevelopmental disorders. I have developed a protocol to differentiate pluripotent stem cells (iPSCs) in neuronal networks on MEAs and I have used this technology to study patient-specific phenotypes, to dissect molecular abnormalities leading to the phenotype and to ameliorate the phenotype by using a targeting approach. While my academic path and PhD allowed me to develop engineering and technical capabilities, during the post-doc I acquired expertise in stem cell biology. Through this unique combination, I became a truly interdisciplinary researcher. Rapidly, with my knowledge and experience, I become a reference point for the entire Human Genetics department and for many groups in the Netherlands and Europe. Since 2018, I work as Assistant Professor at the University of Twente. I develop my research line by using a multi-level strategy that combines human *in vitro* models and patients' clinical redouts (i.e., EEG recordings) assisted by real-time data processing and computational models to study neurological disorders in a patient-specific manner.
I authored more than 20 peer-reviewed publications, 2 books published from Springer and I gave more than 30 scientific talks at International/National Conferences and Research Institutions. I have won several research grants, and I have also been invited to the final step for the ERC starting grant. Because of my recognized expertise in stem cell biology, MEAs technology and data analysis, I provide technological consulting to researchers in Europe regarding MEA technology combined with iPSCs.

MAJOR COLLABORATIONS
Because of my interdisciplinary career, I have built a network of collaborators in different fields. Currently, my group at the University of Twente is composed by engineers and medical doctors, with whom I have a daily collaboration. In particular, **Prof. Dr. van Putten** and **Prof. Dr. Hofmeijer** are neurologists that combine their work at the hospital with research at the University. They visit patients with epilepsy and stroke on a daily basis and perform clinical trials in their hospitals. The strong collaboration I have with them ensures the feasibility of the proposed project. Furthermore, **Dr. le Feber**, appointed as assistant professor, is an expert in neuronal network activity characterization on MEAs. **Dr. Piastra** is an expert in EEG signals and models to reconstruct the brain signals.
During my Postdoc at the department of human genetics (RadboudUmc, the Netherlands) I had the opportunity to work with molecular biologists and clinicians. In particular, I have established a strong collaboration with **Dr. Kasri**, expert in neuronal differentiation from hiPSCs. I am still appointed as a

researcher in his group to support him and his PhD students in analysis of hiPSCs-derived neuronal network on MEAs.

Since my PhD I have maintained a collaboration with **Prof. Martinoia**, full professor at the University of Genova (Italy). We are promotors of PhD students that are developing human 3D neuronal networks. Together with him, I have established Erasmus plus programs between the University of Genova (Italy), RadboudUmc (the Netherlands) and University of Twente (the Netherlands).

FELLOWSHIPS AND AWARDS

2014   Price for the Best Young Researcher
              Italian Group of Bioengineering, Pavia, Italy
2016   Recognizing outstanding PhD research - Springer theses

SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS

- **PhD students**

From 06/2024 Promotor of a PhD student (Juliette Lévénez)
              Dept. of Clinical neurophysiology (CNPH), University of Twente, Enschede, the Netherlands.
2022 – present Promotor of a PhD student (Nina Doorn)
              Dept. of Clinical neurophysiology (CNPH), University of Twente, Enschede, the Netherlands.
2021 – present Promotor of a PhD student (Eva Voogd)
              Dept. of Clinical neurophysiology (CNPH), University of Twente, Enschede, the Netherlands.
2018 – present Supervisor of a PhD student (Eline van Hugde)
              Dept. of Human Genetics, Radboud University Medical Centre, Nijmegen, the Netherlands
2018 - 2022   Promotor of PhD student (Lorenzo Muzzi)
              Dept. of Informatics, Bioengineering, Robotics and System Engineering (DIBRIS), University of Genova, Italy
2016 – 2021   Supervisor of a PhD student (Britt Mossink)
              Dept. of Human Genetics, Radboud University Medical Centre, Nijmegen, the Netherlands
2016 - 2021   Supervisor of a PhD student (Katrin Linda)
              Dept. of Human Genetics, Radboud University Medical Centre, Nijmegen, the Netherlands
2015 – 2020   Supervisor of a PhD student (Teun Klein Gunnewiek)
              Dept. of Human Genetics, Radboud University Medical Centre, Nijmegen, the Netherlands

- **Research assistant**

From 01/2024 Supervisor of Research Assistant (Juliette Lévénez)
              Dept. of Clinical neurophysiology (CNPH), University of Twente, Enschede, the Netherlands.
2022   Supervisor of Research Assistant (Marta Cerina)
              Dept. of Clinical neurophysiology (CNPH), University of Twente, Enschede, the Netherlands.
2021   Supervisor of Research Assistant (Areti Sfakianou)
              Dept. of Clinical neurophysiology (CNPH), University of Twente, Enschede, the Netherlands.

- **Master students**

2018 – present 12 Mater students

2018 – 2021	Dept. of Clinical neurophysiology (CNPH), University of Twente, Enschede, the Netherlands 5 Mater students Dept. of Human Genetics, Radboud University Medical Centre, Nijmegen, the Netherlands
2014 – 2018	8 Master students Dept. of Human Genetics, Radboud University Medical Centre, Nijmegen, the Netherlands
2010 – 2014	7 Master students Dept. of Informatics, Bioengineering, Robotics and System Engineering (DIBRIS), University of Genova, Italy

GRANTS

Project Title	Funding source	Amount (Euros)	Period	Role
On-chip technology for spatiotemporal analysis of neuronal metabolofunction (NeurO2ChipH)	Dutch Research Council (NWO)	949'898	2024	**Direction of activities** Task leader. Promotor of a PhD student
BRAINMODEL: standardized, IPSC-based medicine for immediate application in monogenic neurodevelopmental disorders	Dutch Research Council (NWO)	5'636'000	2021-2026	**Direction of activities** Co-applicant. Work Package Leader. Local responsible. Promotor of a PhD student (Nina Doorn).
Model for the evaluation and development of new therapeutic approaches in duplication 15q disease	Nonsolo15 ODV	20'000	2023	**Direction of activities** Supervisor of a visiting PhD student (Verdiana Palladio).
Mechanisms of cerebral recovery after cardiac arrest and non-invasive brain stimulation	NIH R01	778'577	2023-2026	**Direction of activities** Work Package Leader. Promotor of a research assistant and a PhD student (Juliette Lévénez).
Modelling individual Stroke and Experimental Treatments	Institutional research grant	150'000	2021-2024	**Direction of activities** Co-applicant. Promotor of a PhD student (Eva Voogd).
Neuroprotective role of lactate release from astrocytes	Institutional research grant	50'000	2021	**Direction of activities** Co-applicant. Principal supervisor of a research assistant (Marta Cerina).
EEG in-a-dish: towards precision medicine for epilepsy	Twente University and RadboudUmc	80'000	2020	**Direction of activities** Co-applicant. Principal supervisor of a research assistant (Areti Sfakianou).

Towards personalized treatment of genetically classified refractory epilepsies using Human Induced Pluripotent Stem Cells (hiPSCs) as an ex-vivo tool.	Dutch Epilepsy Fund	190'000	2018-2021	**Participation in activities** Collaborator. Supervisor of a PhD student (Eline van Hugde) on activities related to the use of bioengineering techniques to study neuronal activity.
MELAS syndrome	Stichting Stofwisselingskracht		2015-2020	**Participation in activities** Collaborator. Supervisor of a PhD student (Teun Klein Gunnewiek) on activities related to the use of bioengineering techniques to study neuronal activity.
Preclinical investigation of epigenetic compounds in models for Kleefstra syndrome	GENESPARK/KIDS.I.Q		2016-2021	**Participation in activities** Collaborator. Supervisor of a PhD student (Britt Mossink) on activities related to the use of bioengineering techniques to study neuronal activity.
Electrophysiological characterization of hippocampal circuitry in models for Koolen-de-Vries syndrome (KdVS)	RadboudUmc, Donder Institute research grant		2016-2021	**Participation in activities** Collaborator. Supervisor of a PhD student (Katrin Linda) on activities related to the use of bioengineering techniques to study neuronal activity.

INSTITUTIONAL RESPONSIBILITIES

2024	Member of PhD thesis Committee Western University, Canada (Kartik Pradeepan)
2023	Member of PhD thesis Committee University of Tampere, Finland (Ropafadzo Mzezewa)
2023	Member of PhD thesis Committee University of Genoa, Italy (Marta Carè)
2023	Member of PhD thesis Committee International school of advanced studies, Italy (Elena Gjorgievska)
2020	Member of PhD thesis Committee University of Tampere, Finland (Tanja Hyvärinen)
2020	Member of PhD thesis Committee University of Antwerp, Belgium (Sebastiaan Van de Vijver)

EDITORIAL ACTIVITIES

2022 - present   Guest editor. *Frontiers in molecular neuroscience.*
2019   Editor of the book: In vitro neuronal networks. From culturing methods to neuro-technological applications. (2019) Chiappalone, Pasquale, <u>Frega</u> (eds). In vitro neuronal networks, advances in neurobiology, vol 22, Springer, Chan.

REVIEWING ACTIVITIES

2014 – present Ad hoc reviewer (i.e. *Scientific reports, Cerebral cortex, Journal of neural engineering*).

TECHNOLOGICAL CONSULTING AND TRAINING
To researchers in Europe regarding MEA technology combined with iPSCs.
Nael Nadif Kasri (RadboudUmc, Nijmegen, the Netherlands)
Vivi Heine (VU University Medical Centre, Amsterdam, the Netherlands)
Ype Elgersma (Erasmus, Rotterdam, the Netherlands)
Michele Gabriele (Milano, Italy-Giuseppe Testa lab)
Sergio Martinoia (Genova, Italy)
Maria Schreiter (Leipzig, Germany - Barbara Treutlein lab)
Laurent Roybon (Lund, Sweden)

ORGANISATION OF SCIENTIFIC MEETINGS

2018 – present   Organizer of MEAs workshops. RadboudUmc and University of Twente, the Netherlands
2016   Organizer and chair of a session entitled "Human induced pluripotent stem cell-derived astrocyte models for neurological disorders" at the Dutch neuroscience meeting.
                 10th June 2016, Amsterdam (the Netherlands)
2012   Co-organizer of the 6th Summer School of Neuroengineering "Massimo Grattarola".
                 11th - 15th June 2012, Genova (Italy).

PRESENTATIONS

- **Presentations to national and international conferences**

2024   **Invited speaker.** XLIII annual school of Bioengineering, September 17th, Bressanone (Italia). *Human neuronal networks on micro-electrode arrays: a robust tool to study disease phenotype.*

2023   **Invited speaker.** 6th Annual Neuroscience R&D Conference, October 9th, London (United Kingdom). *Human neuronal networks on micro-electrode arrays are a robust tool to study disease phenotype in vitro.*

2023   **Invited speaker.** 3rd in vitro 2D and 3D neuronal network summit, May 16th, Zurich (Switzerland). *A human in vitro model of the ischemic penumbra.*

2021   **Invited speaker**. IEEE Women in Engineering, December 2nd Genova (Italy). *How I become a STEM scientist.*

2019   **Keynote speaker**. iPSC studies in neuronal health and disease, December 2nd, Rotterdam (the Netherlands).

2019   **Invited speaker.** Kleefstra syndrome Italian conference, October 19th, Verona (Italy). *Brain on a dish to study Kleefstra syndrome.*

2019   **Invited speaker**. 40th Meeting for Friendship Amongst Peoples, August 22nd, Rimini (Italy). *Simple models for complex brains.*

2019   **Invited speaker**. Brain on a chip meeting, January 10th, Delft (the Netherlands). *Human neurons on micro-electrode arrays: a model for neurological disorders.*

2018   **Selected speaker**. 11th International Meeting on Substrate-Integrated Microelectrode Arrays, July 6th, Reutlingen (Germany). *Neurons derived from induced pluripotent stem cells on microelectrode arrays: a human model for neurodevelopmental disorders.*

2018   **Invited speaker**. IEEE International symposium of circuit and systems, May 29th, Florence (Italy). *Brain on a chip technology for investigating neuronal disease: towards precision medicine.*

2018   **Invited speaker**. 20th annual international clinical symposium Kempenhaeghe, June 23th, Kempenhaeghe (the Netherlands). *Dilemmas in diagnostic. Knowledge gaps and future research.*

2017   **Invited speaker**. MaCSBio lecture series. July 14th, Maastricht (the Netherlands). *Exciting cells on-a-chip: relevance for neurodevelopmental disorders.*

2017   **Invited speaker**. Dutch Neurodevelopmental meeting. March 8th, Nijmegen (the Netherlands). *Human Induced Pluripotent Stem Cells models of neurodevelopmental disorders.*

2017   **Invited speaker**. Dutch Neuroscience Meeting. June 16th, Lunteren (the Netherlands). *Molecular mechanisms in human neurons.*

2016   **Invited speaker**. Dutch Neuroscience Meeting. June 10th, Lunteren (the Netherlands). *How astrocytes affect neuronal circuitry in neurodevelopmental disorders.*

2016   **Selected speaker**. 10th International Meeting on Substrate-Integrated Microelectrode Arrays. July 1st, Reutlingen (Germany). *Neuronal networks coupled to Microelectrode Arrays: network maturation impairments in neurodevelopmental disorders.*

2015   **Invited speaker**. Donders session. October 15th, Nijmegen (the Netherlands). *Neuronal network development and synaptic plasticity in the context of neurodevelopmental disorders.*

2015   **Selected speaker**. Master class. October 9th, Amsterdam (the Netherlands). *Harnessing the potential of Micro-Electrode Arrays and Induced Pluripotent Stem Cells for cognitive disorders.*

2014   **Selected speaker**. 4th congress - National Group of Bioengineering (GNB). June 26th, Pavia (Italy). *3D neural networks coupled to Micro Electrode Arrays: a new experimental model for neuro-electronic interfaces.*

- **Presentations to national and international seminars**

2022   **Invited speaker**. Radboud Research Round technology edition, February 21st Nijmegen (the Netherlands). *A human in vitro model of the ischemic penumbra.*

2019   **Invited speaker**. TechMed meeting, April 23rd, Enschede (the Netherlands). *Human neurons on micro-electrode arrays for personalized medicine.*

2018   **Invited speaker**. University of Antwerp, Antwerp, Belgium, May, 2nd.

2016   **Invited speaker**. Optogenetics meeting. February 25th, Nijmegen (the Netherlands). *Human neurons on chips: a model to study neurodevelopmental disorders.*

2016   **Selected speaker**. Maastricht Nijmegen science day. February 25th, Nijmegen (the Netherlands). *Modeling brain disease in a dish: reality or science fiction?*

2014   **Invited speaker**. TNU seminar. June 4th, Nijmegen (the Netherlands). *Neuronal network dynamics in 2D and 3D in vitro neuroengineered systems.*

- **Presentation for dissemination meetings**

2020   **Invited speaker**. Olympics of neuroscience, February 27th Genova (Italy).

2020   **Invited speaker**. Neuroscience: the adventure of scientific research, February 27th Genova (Italy).

2018   **Invited speaker**. Learning from beauty foundation. April 6th, Leiden (the Netherlands). *The beauty of scientific research.*

2016   **Invited speaker**. Maranatha cultural evening. May 26th, Tilburg (the Netherlands). *Neuroscience: the adventure of research.*

MEMBERSHIPS OF SCIENTIFIC SOCIETIES

2018 – present Member, "Brain on chip consortium", the Netherlands
2018 – present Member, Society for Neuroscience

PUBLICATIONS
1. Doorn, N., Voogd, J.H.F., Levers, M.R., van Putten, M.J.A.M., Frega, M. Breaking the Burst: Unveiling Mechanisms Behind Fragmented Network Bursts in Patient-derived Neurons. *Stem cell reports,* in press.
2. Heuvelmans, A.M., Proietti Onori, M., Frega, M., de Hoogen, J.D., Nel, E., Elgersma, Y., van Woerden G.M. (2024). Modeling mTORopathy-related epilepsy in cultured murine hippocampal neurons using the multi-electrode array. *Experimental Neurology*, 379: 114874. IF: 4.6.
3. Cerina., M., Levers, M., Keller, J., **Frega, M**. (2024). Neuroprotective role of lactate in a human in vitro model of the ischemic penumbra. *Scientific reports, 14(1):7973.* IF: 4.6.
4. Voogd, E., Doorn, N., Levers, M., Hoffmeijer, J., **Frega, M**. (2023). Degree of differentiation influences neurobiological signatures and resistance to hypoxia of SH-SY5Y cells. *Journal of Neural Engineering,* doi: 10.1088/1741-2552/ad17f3. IF: 4.
2. Yuan, X., Puvogel, S., van Rhijn, J., Ciptasari, U., Esteve-Codina, A., Meijer, M., Rouschop, S., van Hugte, E.J.H., Oudakker, A., Schoenmaker, C., **Frega, M**., Schubert, D., Franke, B., Nadif Kasri, N. (2023). A human in vitro neuronal model for studying homeostatic plasticity at the network level. *Stem cell reports*, 18(11):2222-2239. IF: 5.9.
3. van Hugte, E.J.H., Lewerissa, E.I., Wu, K., Scheefhals, N., Parodi, G., van Voorst, T.W., Puvogel, S., Kogo, N., Keller, J.M., **Frega, M**., Schubert, D., Schelhaas, H.J., Verhoeven, J., Majoie, M., van Bokhoven, H., Nadif Kasri, N. (2023). SCN1A-deficient excitatory neuronal networks display mutation-specific phenotypes. *Brain*, 10.1093/brain/awad245. IF: 14.5.
4. Voogd, E., **Frega, M**., Hoffmejer, J. (2023). Neuronal responses to ischemia: scoping review of insight from human-derived in vitro models. *Cellular and molecular neurobiology,* 43, 3137–3160. IF: 4.
5. Doorn, N., van Hugte, E.J.H., Ciptasari, U.H., Mordelt, A., Meijer, H.G.E., **Frega, M**., Nadif Kasri, N.*, van Putten, M.* (2023). An in silico and in vitro human neuronal network model reveal cellular mechanisms beyond NaV1.1 underlying Dravet Syndrome. *Stem cell reports*, 18:1686-1700. IF: 4.9. * Shared last author.
6. Cerina, M., Piastra, M.C., **Frega, M**. (2023). The potential of in vitro neuronal networks cultured on micro electrode arrays for biomedical research. *Progress in Biomedical Engineering*, 5: 032002. IF: 4.7.
7. Muzzi, L., Di Lisa, D., Falappa, M., Pepe, S., Maccione, A., Pastorino, L., Martinoia, S., **Frega, M**. (2023). Human-derived cortical neurospheroids coupled to passive, high-density and 3D MEAs: a valid platform for functional tests. *Bioengineering*, 10(4), 449. IF: 4.6.
8. Andolfi, A., Arnaldi, P., Lisa, D. D., Pepe, S., **Frega, M**., Fassio, A., Lagazzo, A., Martinoia, S., Pastorino, L. (2023). A micropatterned thermoplasmonic substrate for neuromodulation of in vitro neuronal networks. *Acta Biomaterialia*, 158:281-291. IF: 9.7. Cit.: 2.
9. Di Lisa, D., Muzzi, L., Pepe, S., Dellacasa, E., **Frega, M**., Fassio, A., Martinoia, S., Pastorino, L. (2022). On the way back from 3D to 2D: Chitosan promotes adhesion and development of neuronal networks onto culture supports. *Carbohydrate Polymers*, 2971:120049. IF: 11.2. Cit.: 2.
10. Hu, M., **Frega, M.**, Tolner, E.A., van den Maagdenberg, A.M.J.M., Frimat, J.P., le Feber, J. (2022). MEA-ToolBox: an Open Source Toolbox for Standardized Analysis of Multi-Electrode Array Data. *Neuroinformatics*, 20(4): 1077–1092. IF: 3. Cit.: 5.
11. Taxis Di Bordonia e Valnigra, D., Hassink, G.C., Levers, M.R., **Frega, M**., Hofmeijer, J., van Putten, M.J.A.M., Le Feber, J. (2022). The Association between Hypoxia-Induced Low Activity and Apoptosis Strongly Resembles That between TTX-Induced Silencing and Apoptosis. *International Journal of Molecular Sciences,* 23(5):2754. IF: 5.6. Cit.: 2.
12. van Rhijn, J., Shi, Y., Bormann, M., Mossink, B., **Frega, M**., Recaioglu, H., Hakobjan, M., Klein Gunnewiek, T., Schoenmaker, C., Palmer, E., Faivre, L.,Kittel-Schneider, S., Schubert, D., Brunner, H., Franke, B., Nadif Kasri, N. (2022). Brunner syndrome associated MAOA mutations result in

NMDAR hyperfunction and increased network activity in human dopaminergic neurons. *Neurobiology of Disease*, 163:105587. IF: 6.1. Cit.: 5.

13. Linda, K., Lewerissa, E.I., Verboven, A.H.A., Gabriele, M., **Frega, M**., Klein Gunnewiek, T.M., Devilee, L., Ulferts, E., Hommersom, M., Oudakker, A., Schoenmaker, C., van Bokhoven, H., Schubert, D., Testa, G., Koolen, D.A., de Vries, B.B.A., Nadif Kasri, N. (2022). Imbalanced autophagy causes synaptic deficits in a human model for neurodevelopmental disorders. *Autophagy*, 18(2): 423-442. IF: 13.3. Cit.: 27.

14. Mossink, B., van Rhijn, J., Wang, S., Linda, K., Vitale, M.R., Zöller, J.E.M., van Hugte, E.J.H., Bak, J., Verboven, A.H.A., Selten, M., Negwer, M., Latour, Brooke L., van der Werf, I., Keller, J.M., Klein Gunnewiek, T.M., Schoenmaker, C., Oudakker, A., Anania, A., Jansen, S., Lesch, K., **Frega, M.**, van Bokhoven, H., Schubert, D., Nadif Kasri, N. (2022). Cadherin-13 is a critical regulator of GABAergic modulation in human stem-cell-derived neuronal networks. *Molecular psychiatry*, 27(10), doi:10.1038/s41380-021-01117-x. IF: 11. Cit.: 26.

15. Muzzi, L., Di Lisa, D., Arnaldi P., Aprile D., Pastorino L., Martinoia S., **Frega M**. (2021). Rapid generation of functional engineered 3D human neuronal assemblies: Network dynamics evaluated by micro-electrodes arrays. *Journal of Neural Engineering*, 18(6):066030. IF: 4. Cit.: 6.

16. Pires Monteiro, S., Voogd, E., Muzzi, L., De Vecchis, G., Mossink, B., Levers, M., Hassink, G., van Putten, M.J.A.M., le Feber, J., Hofmeijer, J., **Frega, M**. (2021). Neuroprotective effect of hypoxic preconditioning and neuronal activation in a human model of the ischemic penumbra. *Journal of Neural Engineering*, 18(3):036016. IF: 4. Cit.: 15.

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RESEARCH MONOGRAPHS

1. Frega, M. (2016). Neuronal Network Dynamics in 2D and 3D in vitro Neuroengineered Systems. ***Springer Theses***.

FUTURE RESEARCH ACTIVITIES

I aim to combine all expertise I have acquired in different fields to bridge the gap between research and clinical practice. In particular, I aspire to improve diagnosis and treatment choices in neurological disorders, thus ultimately to help patients. During the past years, the close collaboration with clinicians helped me realizing big challenges occurring when dealing with the majority of neurological disorders. Usually there is a striking clinical variability, it is difficult to predict how a patient will respond to medication, neuronal network phenotypes are understudied and molecular abnormalities leading to aberrant neuronal communication are mostly unknown. In addition, there is a big gap between clinical practice and research since clinicians diagnose and treat disorders based on clinical redouts while investigations on pathological neuronal communication, insight into molecular dysfunctions and drug testing are performed in *in vitro* models. Thus, in my research I aim at developing new approaches from bench to bedside for personalized treatment strategies to improve treatment in neurological disorders. To achieve this, I am using a multi-level strategy in which clinical phenotype, clinical redouts, neuronal network phenotype and single cell abnormalities can be studied for individual patients. This approach allows to investigate abnormal cellular functions in material (i.e., hiPSCs-derived neuronal networks) from patients with brain disorders and to link these to clinical outcome measures and patient-relevant symptom scales to find the best possible treatment for individual patients. I make use of computational models to link the different levels, to ultimately find biomarkers for treatment. I believe that this research line will have an impact in the field of basic neuroscience and translational medicine, since the identification of comparable biomarkers in humans and *in vitro* models is a fundamental step needed for a reliable translation of *in vitro* findings to patients and for improve personalized treatment decision.