AxCellerate

De-risking development of medicines in neuroscience since inception

© AxCellerate – All rights reserved

Pre-clinical R&D model is evolving

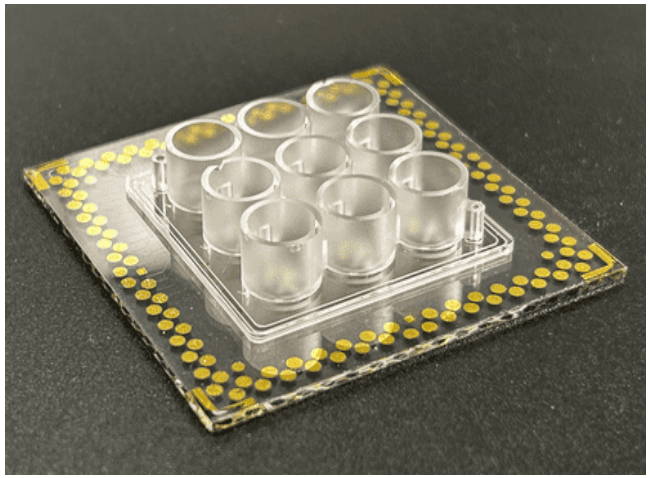
AI → hypothesis → automated experiment → **human-relevant model** → high-content data → AI → candidate selection

The next generation of AI-driven drug discovery
will depend on better human biological data.

Brain-on-chip/NAM platforms can **provide**
the human-relevant experimental data
that AI cannot generate by itself.

© AxCellerate – All rights reserved

NEURO-Chip: AxCellerate's innovative 3D non-invasive Brain-on-Chip validated and available



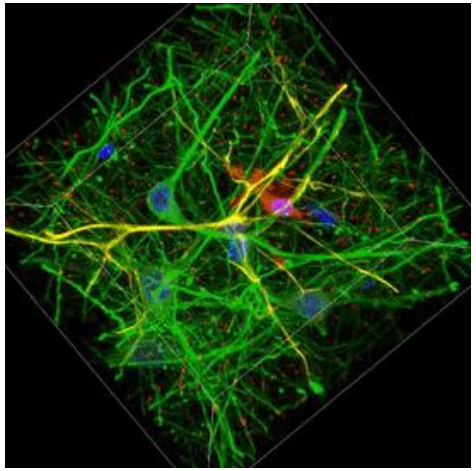
AxCellerate glass recording chip

The only **3D non-invasive Brain-on-Chip** purposely built:

- ❑ to measure accurate and reliable electrical activity.
- ❑ to anticipate **neuro-safety, neuro-toxicity** and **efficacy** of new medicines at **pre-clinical stage**.

NEURO-Chip

- ❑ **Enables high-fidelity, longitudinal electrophysiological** recordings from region-specific organoids.
- ❑ Guides axons into neurite-trapping microelectrodes, to **preserve cytoarchitecture.**
- ❑ Supports **accurate analysis** of network maturation and region-specific activity patterns.



Brain organoid cultured in AxCellerate device

© AxCellerate – All rights reserved

NEURO-Chip – Facilitates robust electrophysiological recording from 3D human neuronal models

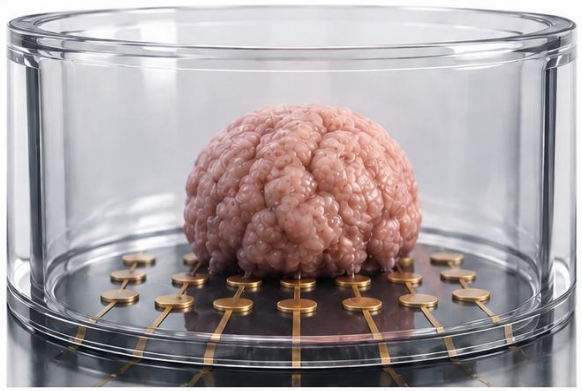
Conventional approach	NEURO-Chip
Organoid **sits on** electrodes	Organoid is **connected to** electrodes through axons
Electrode measures activity at the tissue/electrode interface	**Axons act as biological sensors** of tissue activity
Mainly 2D contact between cells and electrodes	**3D tissue architecture + functional innervation**
Measures whether neurons are active	Can interrogate **how activity is transmitted through the neural circuit**
Electrophysiology as endpoint	Electrophysiology as a **functional readout of 3D tissue physiology**
Strong on activity measurement	Strong potential for **activity + connectivity + pharmacology**

From 2D Contact to 3D Innervation

Enhanced physiological relevance with 3D innervated organoid-on-chip

1) Organoid on Flat Surface

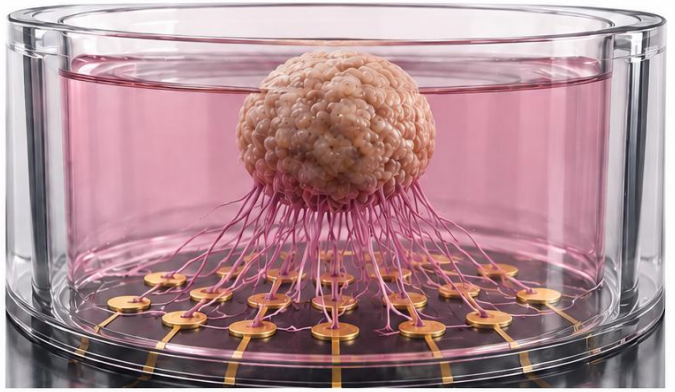
Organoid rests on a flat surface with microelectrodes at the bottom



- ⊖ Limited electrode-to-cell contact
- ⊖ Reduced physiological representation

2) Suspended Organoid with 3D Innervation

Organoid rests on a 3D hydrogel and contact microelectrodes via its axons



- ✓ Axons used as biosensors of organoid activity
- ✓ Higher sensitivity and physiological relevance

3D innervation enables more natural neuronal network activity and more predictive data.

© AxCellerate – All rights reserved

Publications about the technology developed by AxCellerate



IOP Publishing Biofabrication 14 (2022) 025004 https://doi.org/10.1088/1758-5090/ac63fb

Biofabrication

PAPER

A multimodal 3D neuro-microphysiological system with neurite-trapping microelectrodes

Beatriz Molina-Martínez[1,4,5], Laura-Victoria Jentsch[1,6], Fulya Ersoy[1], Matthijs van der Moolen[1], Stella Donato[1], Torbjorn V Ness[2], Peter Heutink[1,3], Peter D Jones[1] and Paolo Cesare[1,4]

[1] NMI Natural and Medical Sciences Institute at the University of Tübingen, 72770 Reutlingen, Germany
[2] German Center for Neurodegenerative Diseases (DZNE), & Hertie Institute for Clinical Brain Research, 72076 Tübingen, Germany
[3] Faculty of Science and Technology, Norwegian University of Life Sciences, 1432 Ås, Norway
[4] Equal contributions.
[5] Current address: Biobide Spain, Paseo Mikeletegi 56, Bajo, San Sebastian 20009, Spain.
[6] Author to whom any correspondence should be addressed.

E-mail: paolo.cesare@uni.de

Keywords: 3D engineered neural electrophysiology

Supplementary material for this

Abstract

Three-dimensional cell structural and function phenotypes in engineer especially functional m individual neurons with electrophysiological rec with other readout mod microfluidic microelect neuronal cultures. We d imaging and optogenet automated handling an neurons. This microphy the functional, morpho treatment by therapeuti

1. Introduction

Despite recent decades' in ing diseases of many orga remain mostly unsolved. F in clinical trials reflect t of the nervous system bu tially inadequate preclinic two-dimensional (2D) cul ably mimic certain aspect with high throughput [1 entirely predictive of cli three-dimensional (3D) mimic the structure of ne towards levelling the trans in vivo studies [2–4].

© 2022 The Author(s). Published b

IOP Publishing Biofabrication 16 (2024) 025013 https://doi.org/10.1088/1758-5090/ad218a

Biofabrication

PAPER

Cancer-mediated axonal guidance of sensory neurons in a microelectrode-based innervation MPS

Matthijs van der Moolen[1,2], Andrea Lovera[1], Fulya Ersoy[1,2], Sacha Mommo[3], Peter Loskill[1,2] and Paolo Cesare[1,2,4,*]

[1] NMI Natural and Medical Sciences Institute at the University of Tübingen, Markwiesenstr. 55, 72770 Reutlingen, Germany
[2] Department for Microphysiological Systems, Institute of Biomedical Engineering, Eberhard Karls University Tübingen, Österbergstr. 3, 72074 Tübingen, Germany
[3] PEMTOprint SA, Via Industria 3, 6933 Muzzano, Switzerland
[4] Current address: Euras Research, Institute for Biomedicine, via Volta 13A, 39100 Bolzano, Italy.
[*] Author to whom any correspondence should be addressed.

E-mail: paolo.cesare@uni.de and paolo.cesare@eurac.edu

Keywords: microphysiological system, microelectrode array, dorsal root ganglia, pain, cancer

Supplementary material for this article is available online

Abstract

Despite recent advances in the field of microphysiological systems (MPSs), availability of models capable of mimicking the interactions between the nervous system and innervated tissues is still limited. This represents a significant challenge in identifying the underlying processes of various pathological conditions, including neuropathic, cardiovascular and metabolic disorders. In this novel study, we introduce a compartmentalized three-dimensional (3D) coculture system that enables physiologically relevant tissue innervation while recording neuronal excitability. By integrating custom microelectrode arrays into tailored glass chips microfabricated via selective laser-etching, we developed an entirely novel class of innervation MPSs (INV-MPS). This INV-MPS allows for manipulation, visualization, and electrophysiological analysis of individual axons innervating complex 3D tissues. Here, we focused on sensory innervation of 3D tumor tissue as a model case study since cancer-induced pain represents a major unmet medical need. The system was compared with existing nociception models and successfully replicated axonal chemoattraction mediated by nerve growth factor (NGF). Remarkably, in the absence of NGF, 3D cancer spheroids cocultured in the adjacent compartment induced sensory neurons to consistently cross the separating barrier and establish fine innervation. Moreover, we observed that crossing sensory fibers could be chemically excited by distal application of known pain-inducing agonists only when cocultured with cancer cells. To our knowledge, this is the first system showcasing morphological and electrophysiological analysis of 3D-innervated tumor tissue *in vitro*, paving the way for a plethora of studies into innervation-related diseases and improving our understanding of underlying pathophysiology.

1. Introduction

Microphysiological systems (MPSs) technology has made significant strides in enabling the investigation of complex biological interactions in accurately represented organs and tissues. However, the importance of innervation for proper tissue function has been largely overlooked [1]. Peripheral innervation plays an essential role in mediating the response of skin, bone, muscles and visceral organs to environmental changes and maintaining tissue homeostasis [2–4]. Additionally, in diseases such as cancer, aberrant innervation patterns can have significant effects on pain, highlighting the critical role of innervation in pathological conditions. Therefore, incorporating nerves in three-dimensional (3D) *in vitro* models is urgently required. Although previous approaches have used micropatterned structures to manipulate axons by injury and/or growth factor cocktails, these are limited to two-dimensional (2D) space and not appropriate for innervation of complex 3D structures such as organoids and spheroids [5–9]. To

© 2024 The Author(s). Published by IOP Publishing Ltd

Beatriz Molina-Martínez et al 2022 - Biofabrication

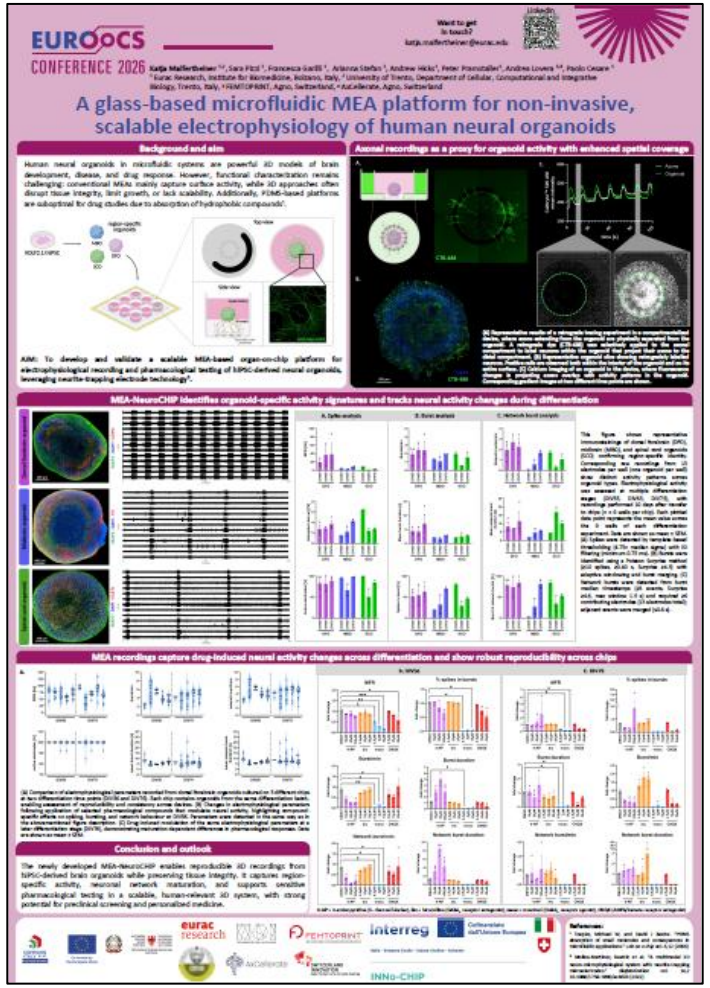
"This micro physiological platform opens up new avenues for high-throughput studies on the functional, morphological and molecular details of neurological diseases and their potential treatment by therapeutic compounds."

Van der Moolen et al 2024 - Biofabrication

"To our knowledge, this is the first system showcasing morphological and electrophysiological analysis of 3D-innervated tumor tissue in vitro, paving the way for a plethora of studies into innervation-related diseases and improving our understanding of underlying pathophysiology."

© AxCellerate – All rights reserved

Validation data presented at EUROoCS annual meeting Braga, 24 June 2026

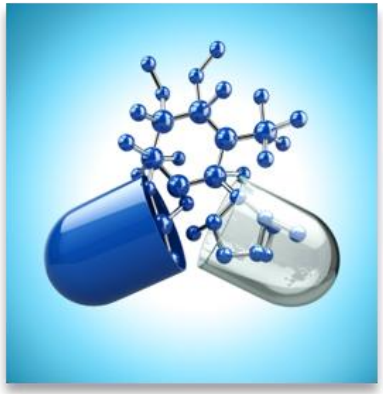


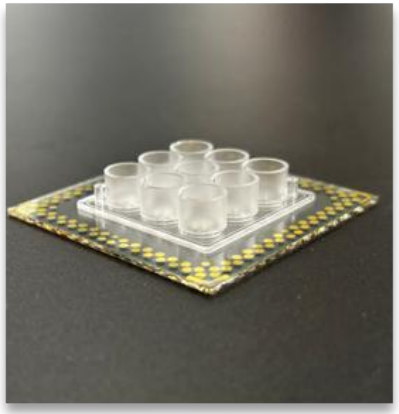
The data illustrate the **current strength of the AxCellerate platform**:

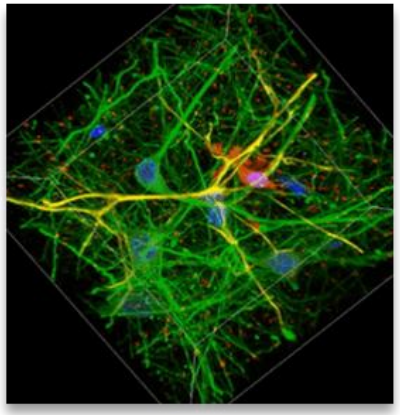
- **technical and biological reproducibility**,
- **pharmacological responses** in spikes, bursts, and network bursts that are aligned with the expected effects of reference excitatory and inhibitory compounds.

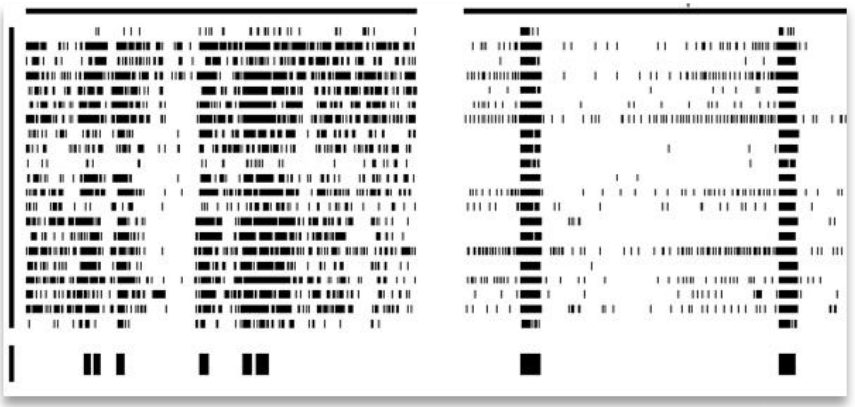
© AxCellerate – All rights reserved

What will be the objective of a co-joint project? Generate data for quantitative assay validation and feed AI models









New molecule / Partner should provide guidance on their needs → NEURO-Chip → Cultured brain organoid → Read out & REPORT

NEURO-Chip **connects living 3D human brain tissue to microelectrodes** through functional **axonal innervation**, transforming the organoid itself into a **biological biosensor for drug-induced changes** in neural function.

© AxCellerate – All rights reserved

AxCellerate

Don't replace your existing assays.

Add a new, differentiated functional layer to your neuroscience portfolio

© AxCellerate – All rights reserved