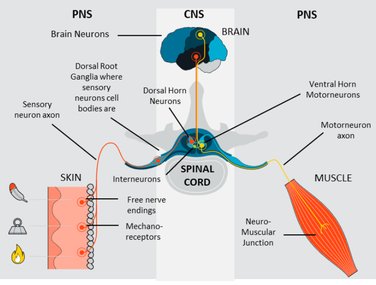
COMPARTIMENTALIZED MEA PAIN-ON-CHIP PLATFORM

Hélène O. B. GAUTIER[1], Aurélie Batut[1], Louise Dubuisson[1], Audrey Azema[1], Camille BAQUERRE[1], Jessica RONTARD[1], Benoît G. C. MAISONNEUVE[1], Thibault HONEGGER[1]
1 - NETRI, 69007, Lyon, France.

BACKGROUND



Pain can be nociceptive (tissue damage) or neuropathic (nervous system damage) which can severely impact the quality of life of patients. Pain signals are detected by sensory neurons, transmitted to the dorsal root ganglia, and processed in the spinal cord before reaching the brain. This pathway can be modeled using OoC technology, which replicates human neuroanatomy and enables realistic injury or treatment studies. We developed our pain platform coupled with multi-electrode arrays (MEA), allow us to study both the morphological and functional effects of different pain modalities.

RESULTS

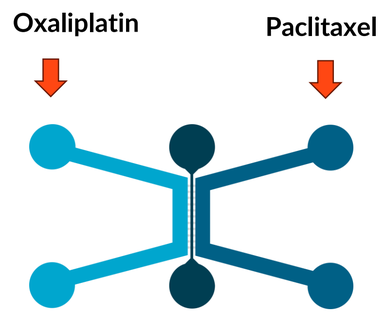
CIPN-ON-CHIP IMAGING PLATFORM

We initiated the development of our pain platform on our imaging devices: the NeuroFluidics line. We tested two molecules with mode of action on separate cell compartments.

CIPN-on-chip reproduce the hallmark of peripheral neuropathy

- Dose-dependant axonal degeneration (dying back)
- Target specifically neurons' soma or distal axons

A



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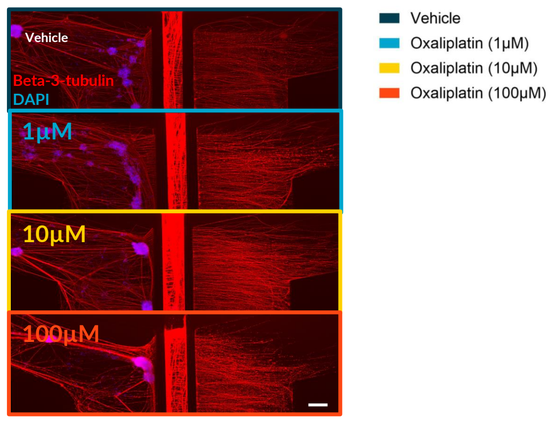

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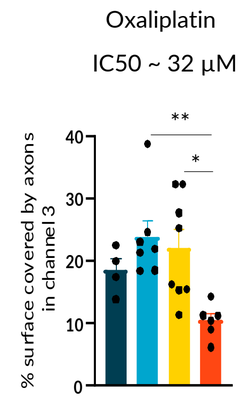


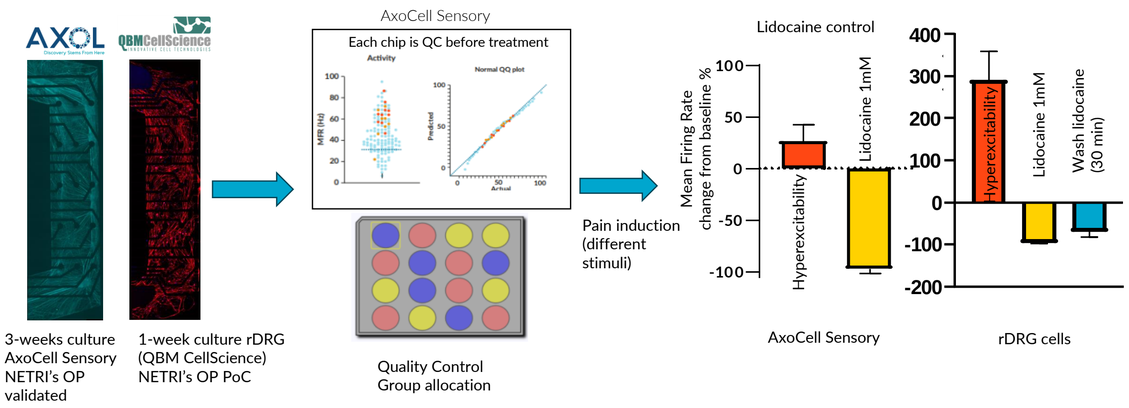
A: schematic of the DuaLink and drug application modality. B: Representative images of 72h oxaliplatin treatment. Scale bar = 100 µm. C: Highest dose of oxaliplatin reduces the surface covered by the axons.
For more details, see the App Note: Chemotherapy-Induced Peripheral Neuropathy-On-Chip Model: Utilizing the strength of compartmentalization. https://netri.com/resources/

MEA PAIN PLATFORM DEVELOPMENT

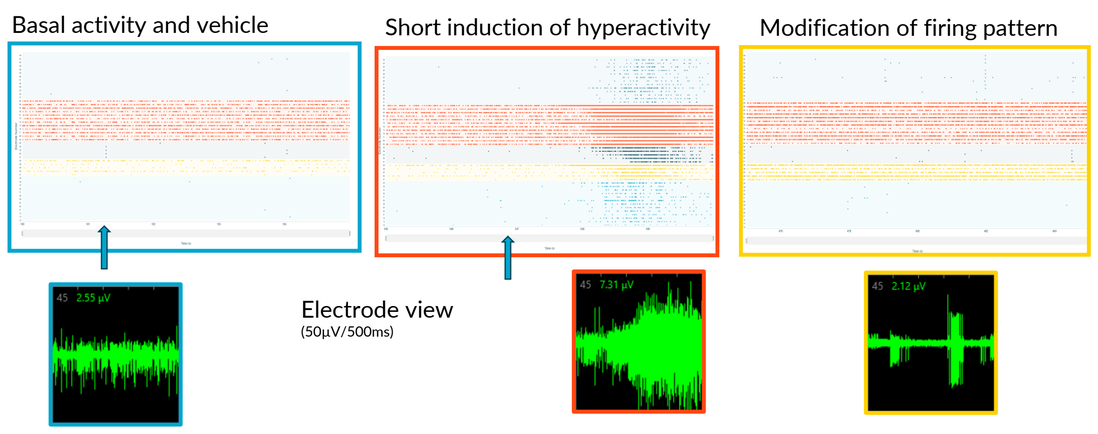
We adapted AxoCell Sensory culture to our MEA platform and developed the methodology to ensure quality control and group allocation before treatments (adapted from Negri et *al.*, 2020). We validated the platform using already described stimuli, agonists and antagonists (Atmaramani et *al.*, 2020; Black et *al.*, 2024).

Compartimentalized MEA Pain-on-chip platform

- Enhanced axonal signals
- Standardized quality control
- Thermal sensitivity
- Adapted protocols for short (seconds) and long (hours/days) effect detection



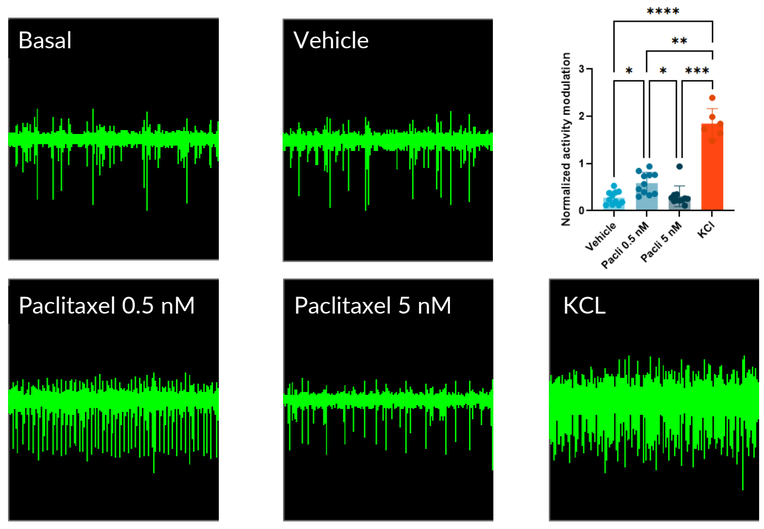
Methodology and processes in place to perform compartimentalized MEA recordings for pain applications



NETRI compartimentalized raster plots (Top) and électrodes view (Bottom, 50µV/500ms). Arrows indicate when vehicule/veratridine was applied

PACLITAXEL HYPERACTIVITY

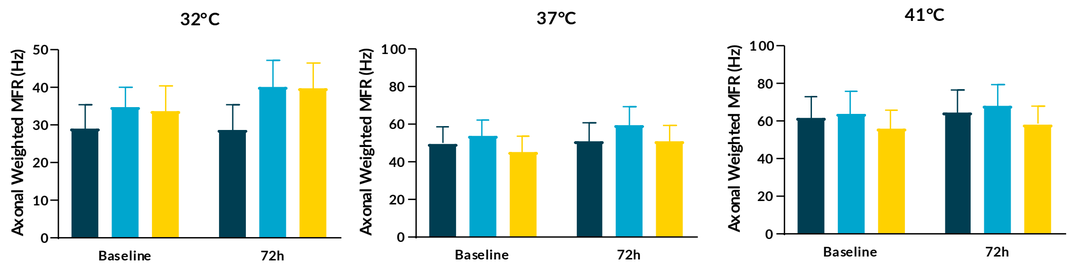
Paclitaxel increases electrophysiological activity in AxoCells sensory neurons.
Paclitaxel was added sequentially at 0.5nM first, then at 5nM. This enabled us to show a desensitization effect of the second exposure to paclitaxel.
This approach enables to detect acute effects on sensory neurons, without inducing cellular degeneration.



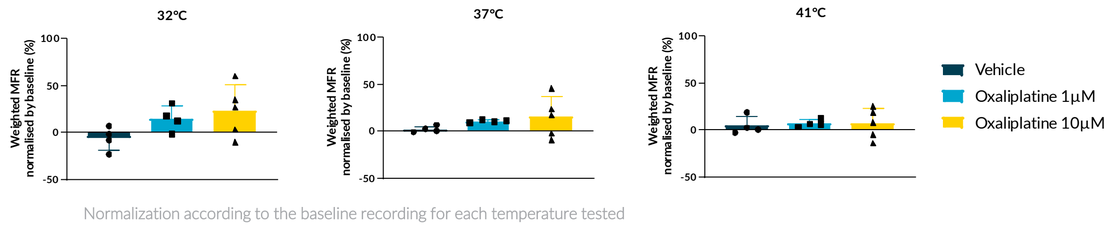
Electrode view (50µV, 500ms) before (baseline) and for each compound application. Graph shows the maximum local MFR changes for each compound normalized to the baseline. Mixed-effect statistical analysis.

OXALIPLATIN COLD SENSITIVITY

AxoCell sensory treated with oxaliplatin seems to react more to low temperature changes when compared to vehicle. More data is still needed to confirm this result.



Vehicle and oxaliplatin were applied in channel 1. AxoCells were recorded at 32°C, 37°C, and 42°C before and 72h after treatment.

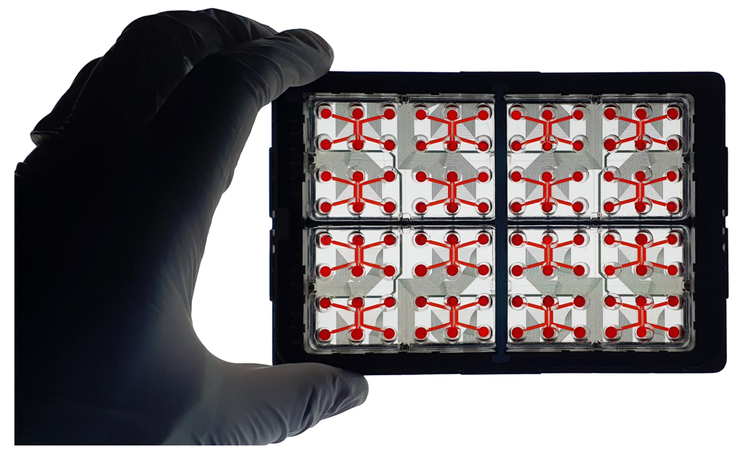


Normalization according to the baseline recording for each temperature tested

CONCLUSION & PERSPECTIVES

By integrating NETRI's engineering, biological, and digital expertise, we have developed a robust **compartimentalized MEA platform** with protocols suitable for Pain indications.
We demonstrated that our **CIPN-on-chip platform, coupled with MEA**, can effectively **recreate two types of chemotherapy-induced neuropathies: those induced by oxaliplatin and paclitaxel.**
NETRI's Pain-on-chip platforms provide pharmaceutical companies and researchers with a **novel translational tool**, for studying the **efficacy and mechanisms of new therapeutic interventions.**

This methodology **paves the way for modeling various types of pain, including diabetic neuropathy and inflammatory pain.** By utilizing the **electrophysiological digital signature of pain** with NETRI's NeuroFluidics™ MEA Line, we can explore both **the adverse effects and therapeutic potential of pain medications.**



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CONTACT
www.netri.com
Phone: +33 4 78 23 08 66
Email: contact@netri.com