

Biomimicking Cell Culture Technologies



CEO Joose Kreutzer

Joose.kreutzer@biogenium.fi

Tel: +358 40 220 3434

www.biogenium.fi



Bio Genium MICROSYSTEMS

- Established 2018
 - Spin-off from Tampere university (Finland)
- Core knowhow
 - Designing of biological applications
 - Physiological oxygen / hypoxia
 - (Micro)fluidics and (Micro)fabrication
 - Organ-on-a-chip
 - Sensors and actuators
 - Manufacturing
 - Silicone (injection) moulding
 - Hardware and software
 - System thinking





Objective of Biogenium

BioGenium develops innovative
engineering systems and solutions
for life science applications
mimicking human physiology
With cells, tissues, organs or

other biological samples







- Own manufacturing and development
 - OxyGenie portable cell incubator
 - Novel approaches to mimic human physiology
- Engineering design services and contract manufacturing for biological applications

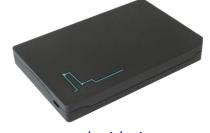
- Distributor of other products in FINLAND
 - Baker Company e.g. Hypoxia/anoxia workstations
 - <u>Lucid Scientific</u> Oxygen consumption rate



www.biogenium. fi



www.bakerco.com



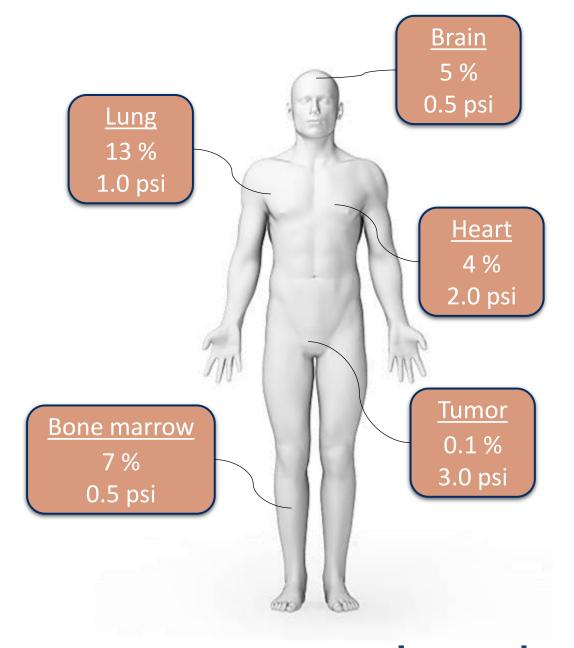
www.lucidsci.com



Core Problem

What does 21% O₂ and atmospheric pressure mimic in cell, tissue or organ experiments

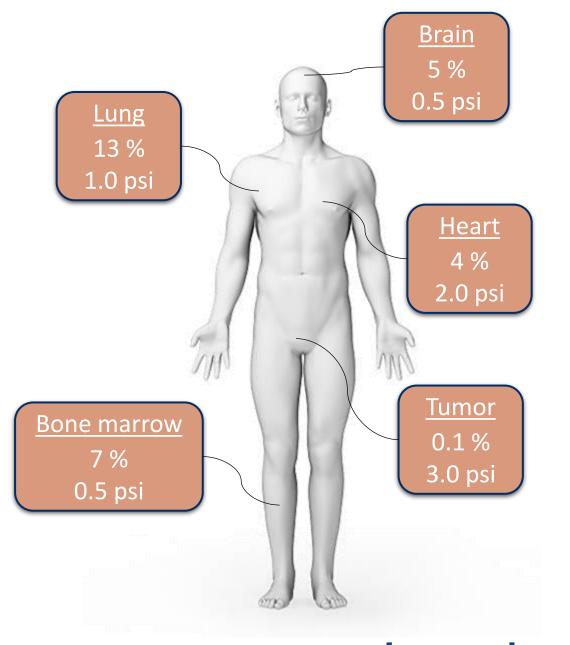






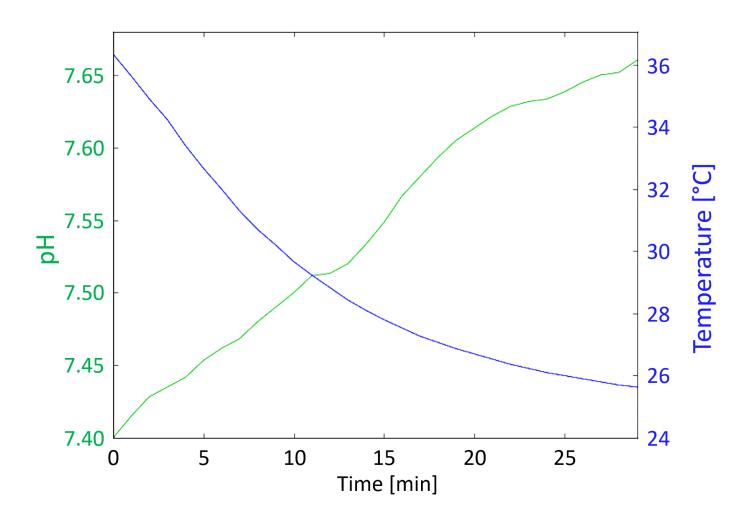
Vision of BioGenium

Relevant, stable and controlled culture environment for advanced biological research and drug development





Example: Oxygen, Temperature and pH variations

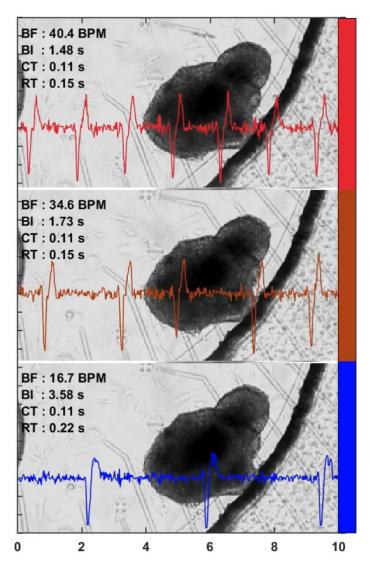


Petri dish taken out from an incubator to a laminar hood

- → Temperature drops rapidly
- → pH increases



Example: Oxygen, Temperature and pH variations



 $pO_2 = 10kPa$

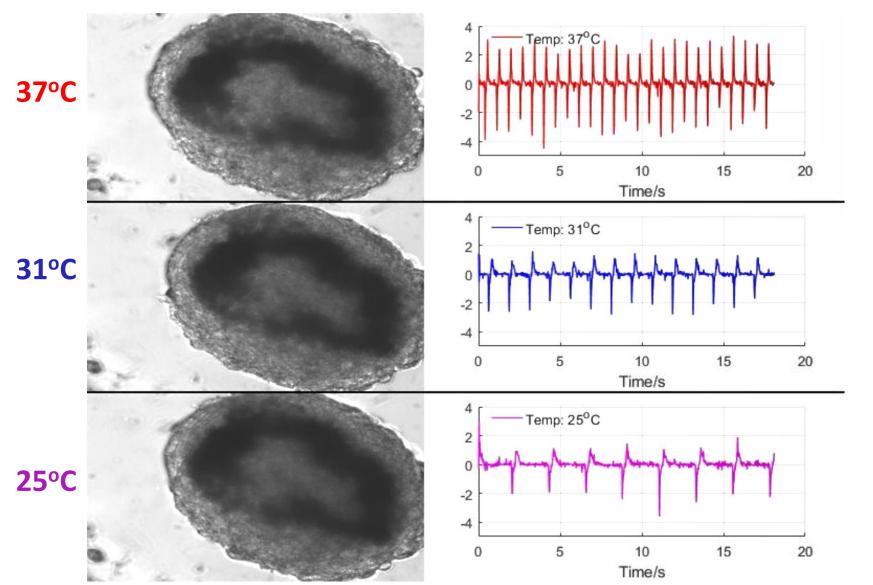
pO2 = 4.5kPa

pO2 = 1.1kPa

Decreased partial oxygen pressure affects to electrophysiological activity

(and other biological functions)

Example: Oxygen, Temperature and pH variations

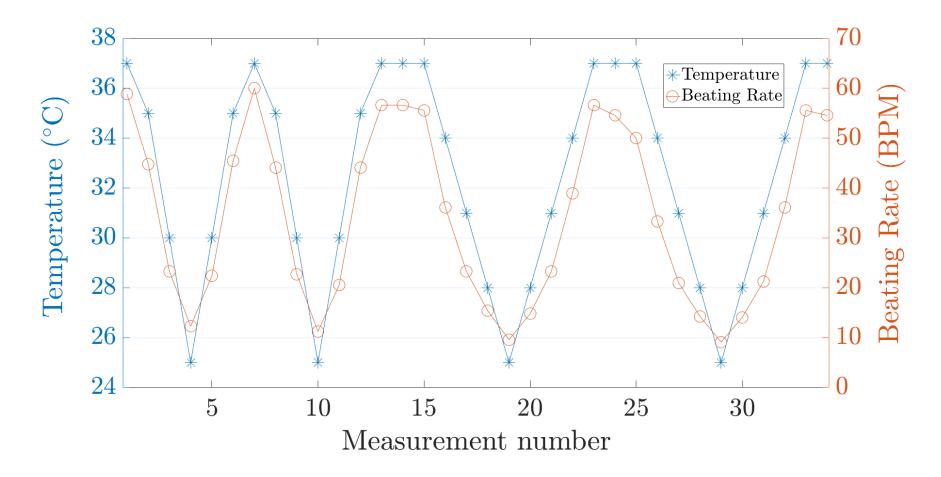


Decreased temperature affects to electrophysiological activity

(and other biological functions)

Kattipparambil Rajan et al. **Video-Based Movement Analysis** *IEEE Access,* 2020

Example: Oxygen, Temperature and pH variations



2°C drop decrease beating rate of hiPSC-derived cardiomyocytes by ¼ from origin



OxyGenie™: Portable Cell Culture Device



The first in the world:

Culture, maintain, transfer and observe your cells under stable and controlled physiological conditions



OxyGenie™: Portable Cell Culture Device

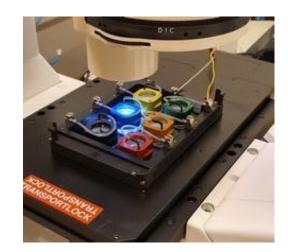


Instrument





Flow Divider



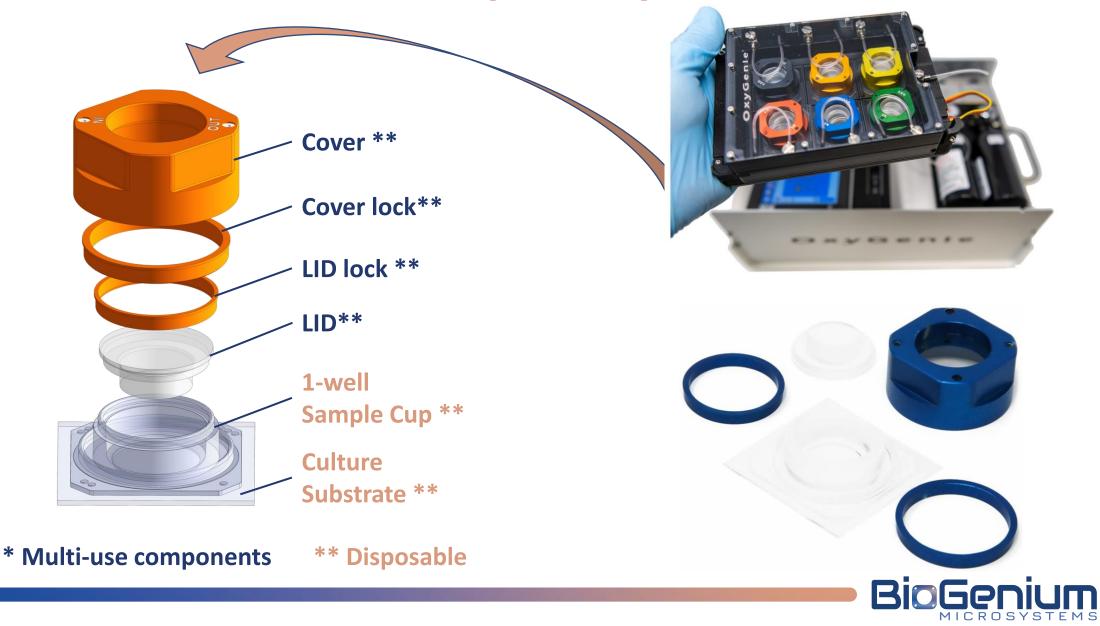
www.BioGenium.fi

Metsälä et al. Rad. Onc. 2018
Shah et al. Cells 2019
Häkli et al. Sci. Rep. 2021
Gaballah et al. Cells 2022
Aalto et al. FEBS 2022
Häkli et al. Stem Cell Int. 2022
Santiago et al. Front. Neurosci. 2023
Pelkonen et al. BioRxiv. 2025

Ha et al. *Radiother. Oncol.* 2022 Barghouth et al. *Radiother. Oncol.* 2023 Bragulat-Teixidor et al. *EMBO Rep.* 2024



OxyGenie™: 1-well Sample Cup



One Sample Cup -> Multiple Applications

- Chronic hypoxia (Standard glass LID)
- Acute hypoxia (Acute LID)
- O₂ Gradient (Gradient LID)
- Co-culture (Co-LID)
- Engineered Heart Tissue (EHT LID)
- Wound healing (Wound Inserts)
- Electrical Stimulation (Pace Plate)
- Physiological Pressure
- Transfer of biological samples

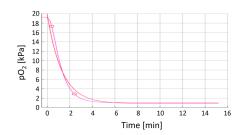


* Multi-use components

** Disposable

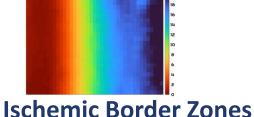


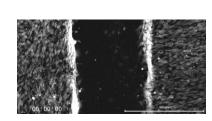
One Sample Cup Multiple Applications



Drug Development

- Engineered Heart Tissues









- Fast O2 Exchange

Ischemia

- Chronic Long-term Hypoxia



- Disposable Inserts

Co-Culture

- Membrane Separated Culture

Physiological Pressure

High Pressure Freezing

- Leica Live Cell CLEM Workflow

Stimulation

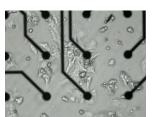
- Electrical Stimulation

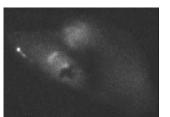
Measurements

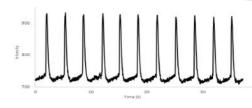
- Imaging under physiological conditions

- Electrophysiological measurements

Analysis



















Irradiation of HeLa cells under physiological oxygen

Irradiation of HeLa cells

0 *Gy*

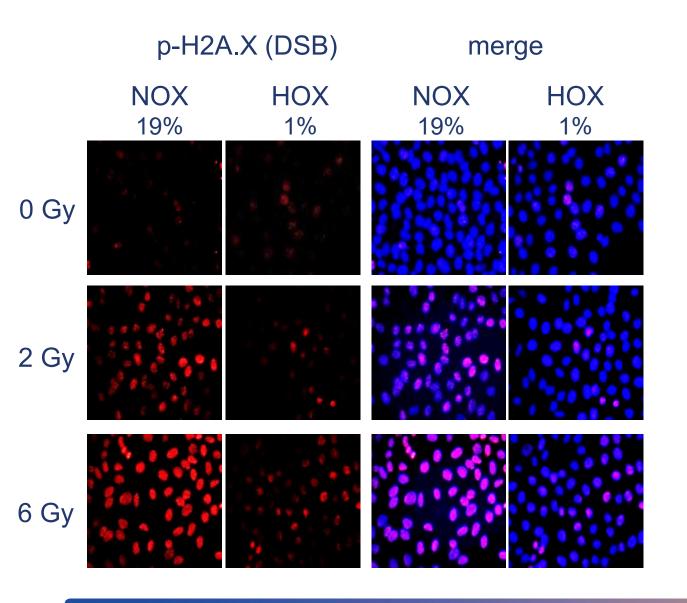
2 *Gy*

6 *Gy*





Irradiation of HeLa cells under physiological oxygen



p-H2A.x used as a marker of double strand breaks, indicative of irradiation response

- → Presence of O₂ breaks more DNA
- → High O₂ do not correlate to conditions *in vivo*

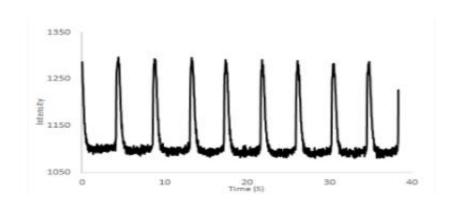
Similar effect e.g. with photoactivated molecules used for drug development



hiPSC derived Cardiomyocytes: Calcium imaging

Response to Hypoxia – drug development

Control

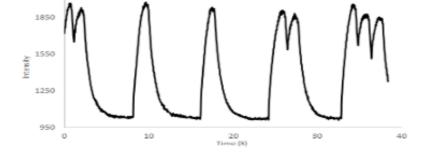


No visible abnormalities in the Ca²⁺ data



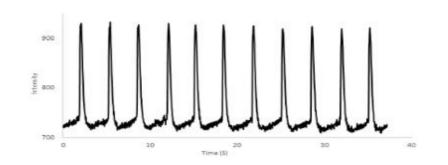
Ca²⁺ imaging

Нурохіа



Hypoxia reveals the hidden disease

Hypoxia & drugs



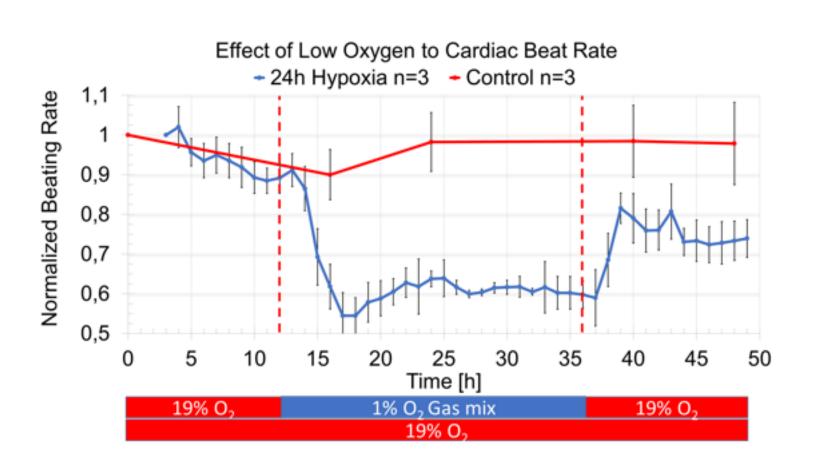
"Patient" healed with the commercial heart drug (Levonsimendan) Cover lock
Lid
Lid lock
1-well Chamber
Cover slip #1,5

1-well Assembly

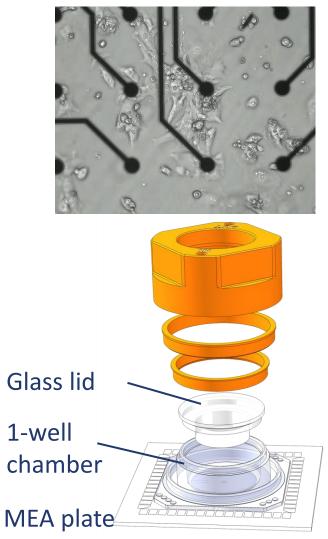
Gaballah et al. *Cells*, 11(6) (2022)

hiPSC derived Cardiomyocytes: MEA recordings

Response to Hypoxia



Multielectrode Array (MEA) recordings

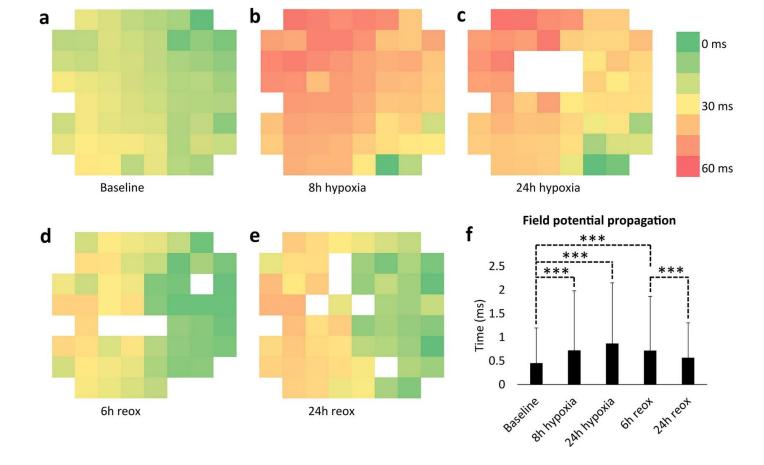


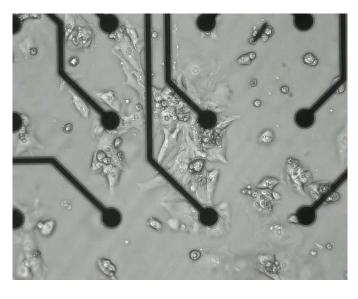


hiPSC derived Cardiomyocytes: MEA recordings

Response to Hypoxia

Field potential propagation reduced under hypoxia





Multielectrode Array (MEA) recordings

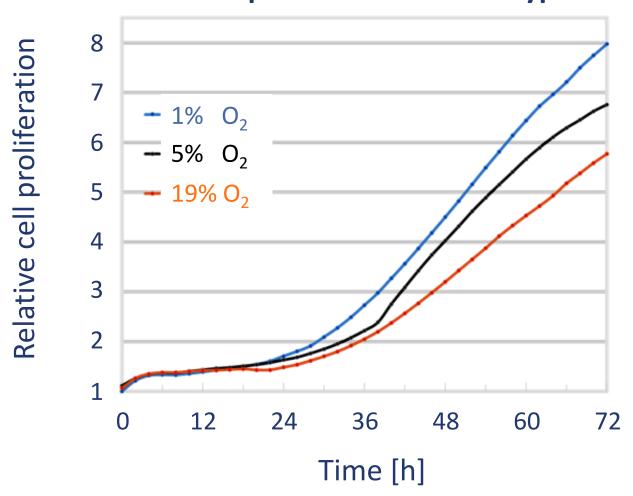


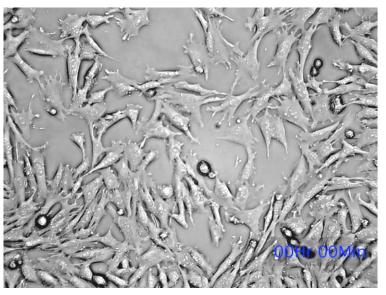


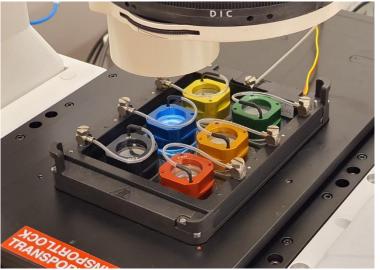
Fibroblasts: Phase-Contrast Time Lapse Imaging

Response to Hypoxia

Increased proliferation under hypoxia









LID Variants: Acute Ischemia on Chip

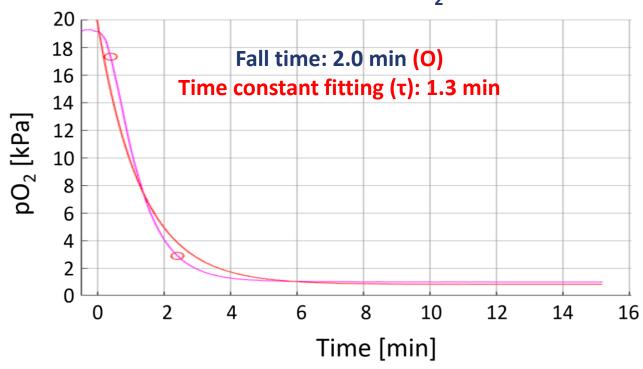
Ischemia =

restriction in blood supply to tissues, causing a shortage of oxygen

Effective in minute(s) in nature

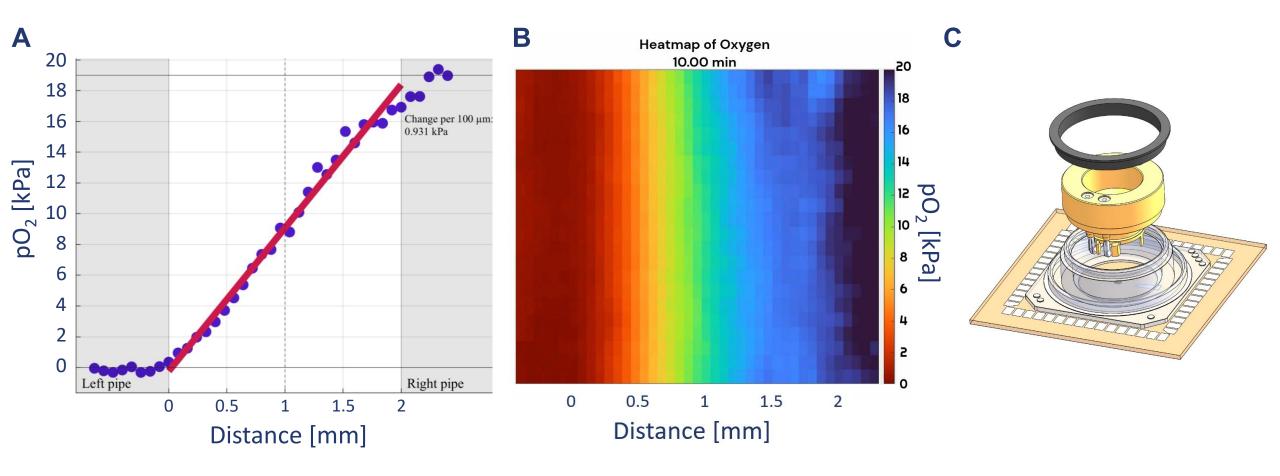


Example:
Oxygen Dynamics with Acute LID for step response from 19% to 1% O₂





LID Variants: O₂ Gradient on Chip



- (A) Linear oxygen gradient between "the walls" forming the gradient (2mm gap; gap distance can be varied)
- (B) 2D oxygen distribution between "the walls" (Oxygen measurements in Tampere University)
- (C) 1-well Chamber on top of the multielectrode array with gradient LID



LID Variants: Co-culture with "Co-LID"

Different membranes attached to the LID

! Use your own membrane!

e.g. Dialysis and microporous membranes

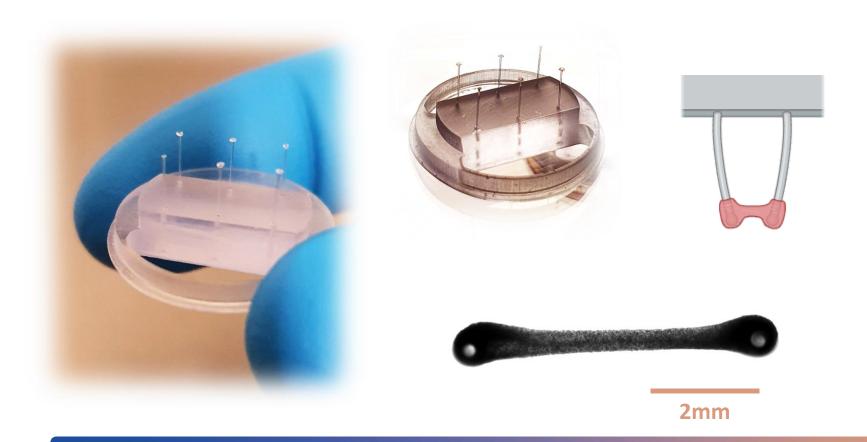






LID Variants: Engineered Heart Tissue "EHT LID"

Pairs of pillars on the LID to hold the EHT cluster

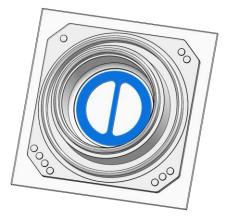


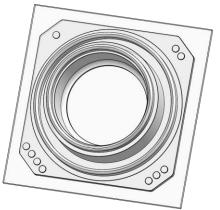




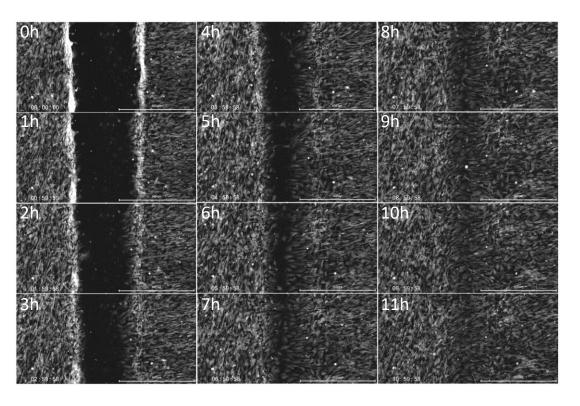
Wound healing assays with inserts

Insert to create straight and repeatable scratch for wound healing applications



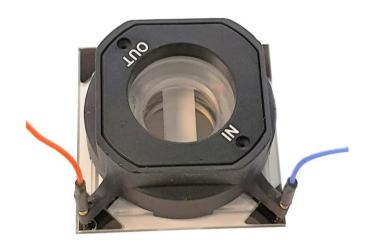




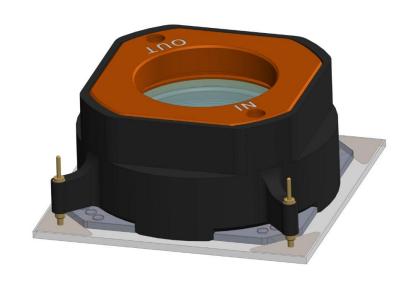




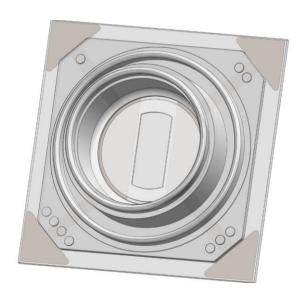
Electrical Stimulation with planar electrodes







- Planar stimulation plate
- 1-well culture chamber
- Acute LID
- LID lock and Cover locks
- Chamber cover
- Connecting adapter with spring loaded contacts



- Planar stimulation plate
- 1-well culture chamber

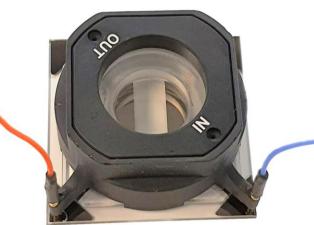
+

- Removable cell plating insert

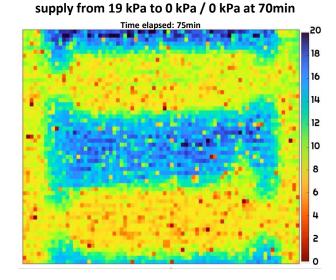


Electrical Stimulation with planar electrodes

Engineered Heart Tissues (EHTs) under hypoxia, perfusion, and electrical stimulation



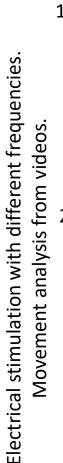


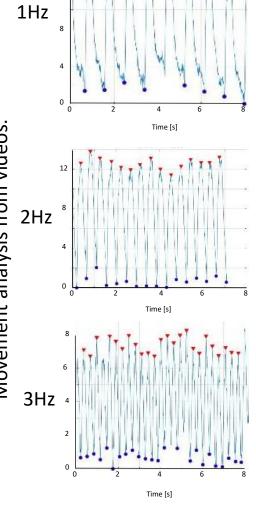


Oxygen measurements, perfusion and gas



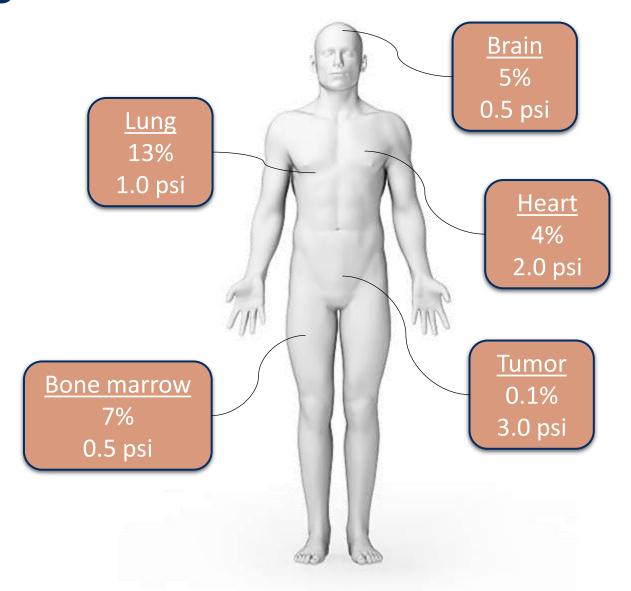
μEHT made with hiPSC-CMs and cardiac Fibroblasts Video by Cofiño-Fabres, C., et al. Adv. Healthcare Mat. (2024)





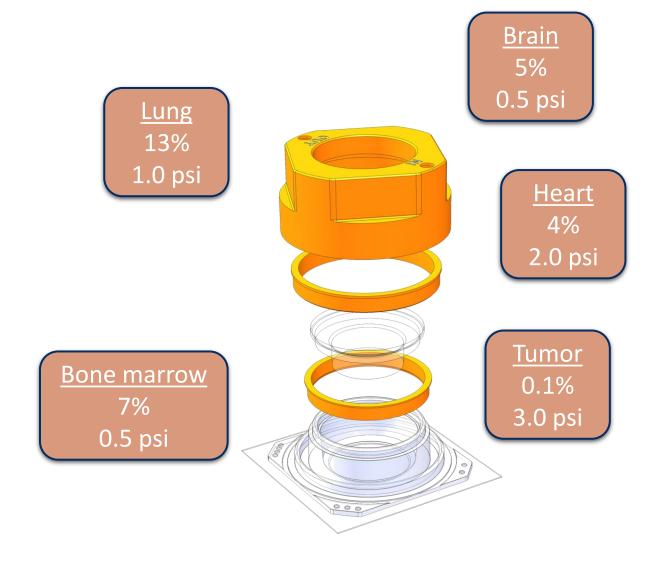


Physiological Pressure





Physiological Pressure



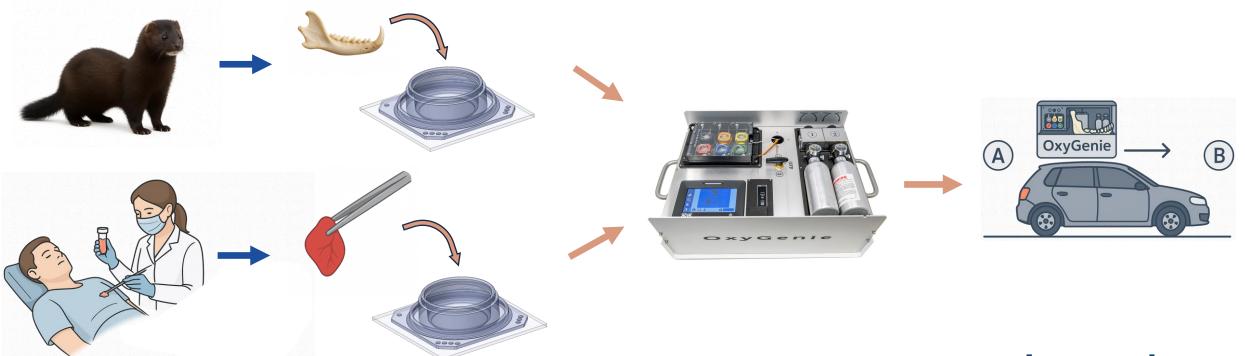
Physiological pressure possible to maintain inside the culture chamber

- Ask more about the details



Transfer of Biological Samples: e.g Mink's jaws

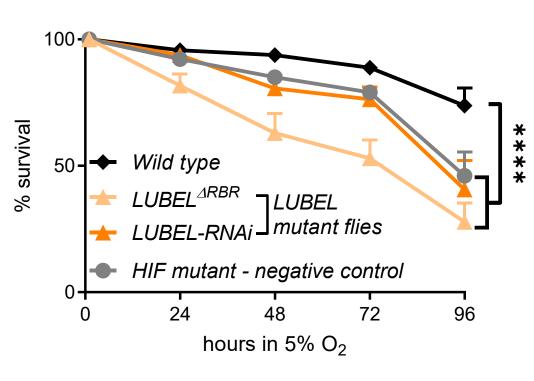
- Maintains physiological integrity during transport
- Ensures reproducibility and reliability of research
- Extends viability for advanced analyses
- Human-derived biopsies supported (OxyGenie is currently intended for research use only)



Small animals: Drosophila melanogaster

- Gene mutated drosophila melanogaster in hypoxia
- No liquid, no heating
- LUBEL is required for survival during hypoxia







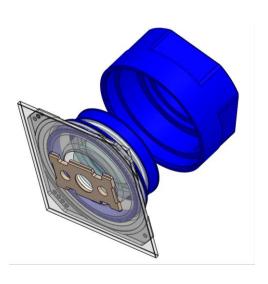
Leica Microsystems: High Pressure Freezing

www.leica-microsystems.com

- Live Cell CLEM Workflow *Coral Life*
- High resolution imaging + high pressure freezing of cells
- SampLink chambers
- How to Keep Your Samples Under Physiological Conditions











Multi Channel Systems GmbH

www.multichannelsystems.com

- OxyGenie Flow Divider for holding 4 MEA plates
- Electrophysiological experiments under hypoxia on MEA
 - Shah et al. Cells 2019
 - Häkli et al. Sci. Rep. 2021
 - Häkli et al. Stem Cell Int. 2022
 - Santiago et al. Front. Neurosci. 2023









Ask Details

Joose Kreutzer, CEO

joose.kreutzer@biogenium.fi

+358 40 220 3434

www.BioGenium.fi







