Bio-analytic silicon chips for the detection of developmental-neurotoxic effects of chemicals and drugs in the context of the European REACH program

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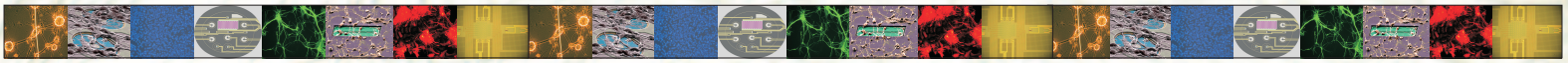


Abstract

Bio-analytic silicon chips can be used to investigate stem cell differentiation into neurons and for the *in vitro* on-line monitoring of cellular reactions induced by potential neurotoxic and developmental-neurotoxic substances. The chip systems allow for a parallel, label-free and non-invasive measurement of different parameters by CMOS silicon microsensors.

Sensor chip technology and system setup

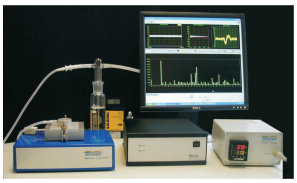
Analyzing systems

Metabolic cellular activity

BIONAS 2500 analyzing system

- non-invasive monitoring of cellular metabolism
- on-line measurement of different cellular parameters
- parallel measurement on six sensor chips
- simple handling in cell culture labs
- continuous measurement (hours up to to days)
- detection of recovery effects

Electrical cellular activity



Neurochip analyzing system

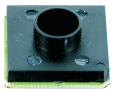
- non-invasive monitoring of cellular electrical activity
- on-line measurement of electrical activity and acidification
- simple handling in cell culture labs
- continuous measurement (hours up to days)
- automated fluid handling (optional)
- adressable stimulation (optional)

Sensor chips

-Silicon chips on a 68- pin ceramic carrier with plastic encapsulation and cell culture trough

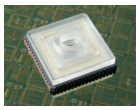
- Sterilizable

Bionas SC 1000 Metabolic Chip



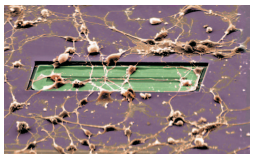
-Integrated pH, oxygen, adhesion and temperature sensors

Neurochip II
Electrophysiological Chip

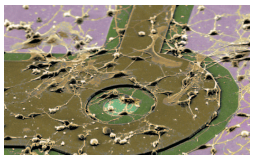


-Integrated Pd-MEA, pH and temperature sensors

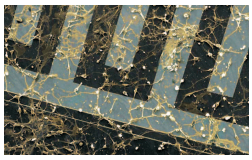
Integrated sensors



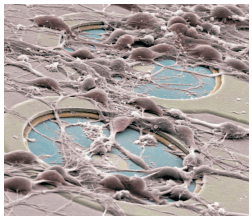
ISFET (ion-sensitive field effect transistor) for **acidification** measurement



Clark type electrode for **oxygen concentration** measurement

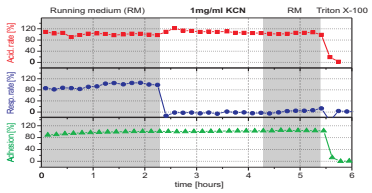


IDES (interdigitated electrode structure) for **cell adhesion** measurement

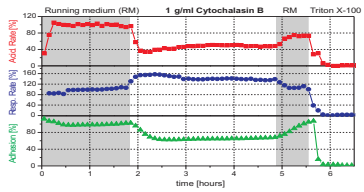


Pd-MEA for measurement of **electrical activity**

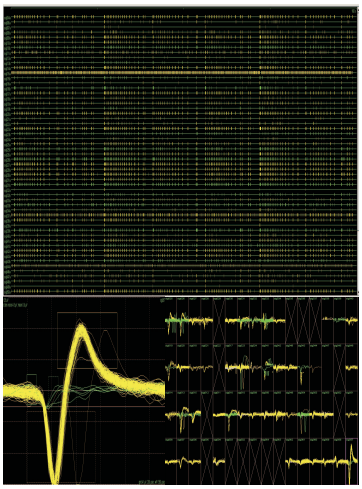
Measurement examples



Measurement with 1mg/ml KCN (CHO cells).
KCN-blocking of the cytochrome-C-oxidase results in the inhibition of the respiratory chain. The respiratory rate is rapidly reduced to 0% in CHO-cells while the acidification rate is slightly increased. The cellular adhesion (cell-layer impedance) is only slightly influenced.



Measurement with 1µg/ml Cytochalasin B (V79 cells)
Cytochalasin B on V79 cells inhibits glucose transports through the membrane as well as cellular proliferation by blocking actin polymerization. The acidification rate is reduced, while respiration is increased. However, adhesion (cell layer impedance) is reduced.



Electrically active neuronal networks from embryonic mouse spinal cord or brain are cultured directly on silicon-based MEAs with stable cell-electrode coupling for several months. This allows for the monitoring of histiotypic native or drug-modified electrical activity patterns.

Current projects, acknowledgements

MIBA – Microstructures and methods for Intracellular Bio-Analytics

Partners:
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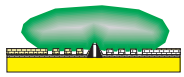
Chair of Biophysics, University of Rostock;
The Fraunhofer Institute of Mechanics and Materials, Halle



Schematic view of cell growing on a micro-structured needle.The needle is introduced into the cell by local electroporation.

Examples of micro-structured needles (left and center), cell- growth on a micro- structured needle (right).

DNT- developmental neurotoxicity

Partners:
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The more parameters we can study in parallel the better we will understand the effects of substances on the development of neural tissue *in vitro*

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