A modular flow-chamber bioreactor concept as a tool for continuous 3D-culture

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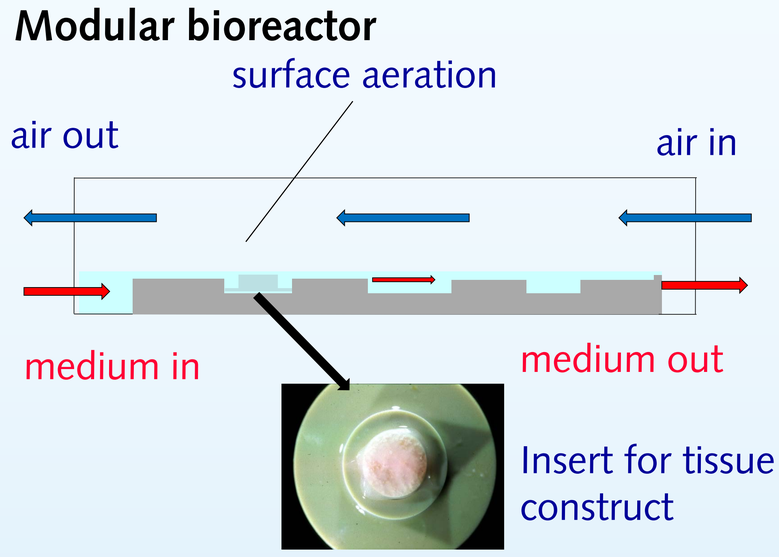
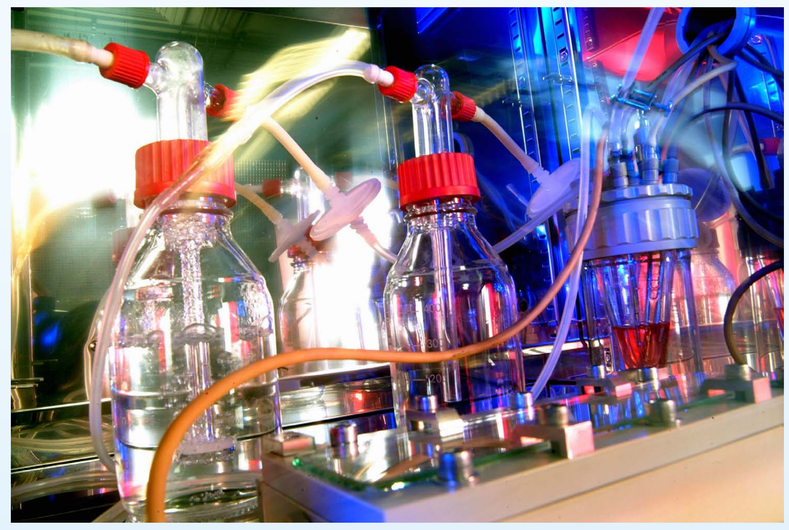
Concept

New challenges in drug development and drug testing arise from regulatory requirements. Animal trials have to be replaced by cell culture assays, preferably by test systems with human material. Standard 2 D monolayer cultures are often unsatisfatory and therefore tissue-like 3 D cultures are suggested as an alternative.

Here a multi-well flow chamber bioreactor (MWFB) as a tool for continuous 3D-culture is presented. Advantages of this reactor concepts can be seen in constant culture and flow conditions, removal of toxic reaction products, higher cell densities, and improved metabolism.

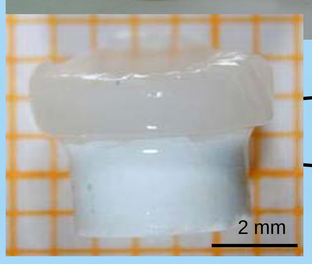
Modular bioreactor





- Simultaneous cultivation of tissue constructs in special inserts which are adapted to the dimensions of a 24-well plate to enable reference cultures.
- Oxygen is supplied via surface aeration directly in the chamber.
- By a small barrier at the end of the flow channel, a uniform and thin medium layer is created to minimize the diffusion barrier from the gas phase to the tissue constructs.
- Medium is supplied from a reservoir bottle in a circulation loop.
- The whole system can be placed in an incubator.

Cultivation of cartilage-carrier-constructs

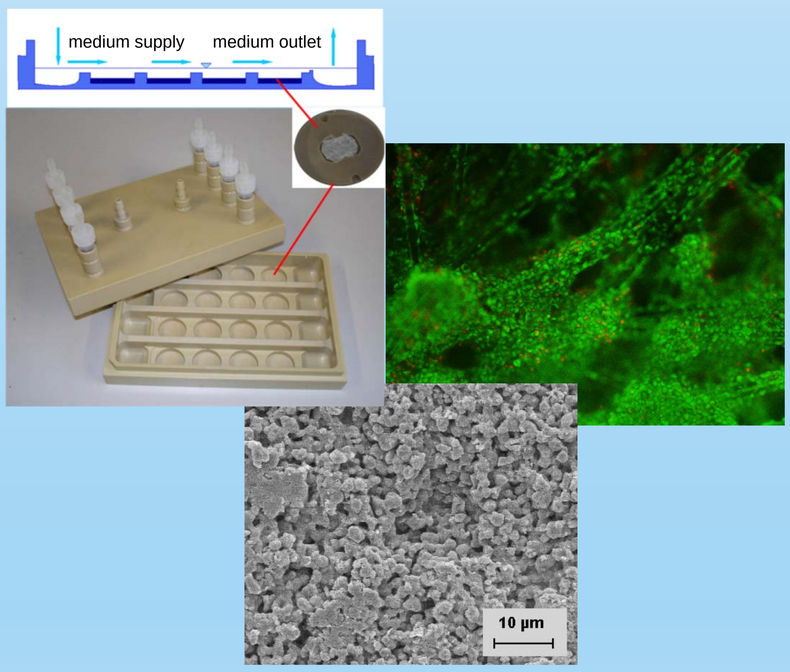


In vitro cultivated cartilage

Ceramic bone substitute

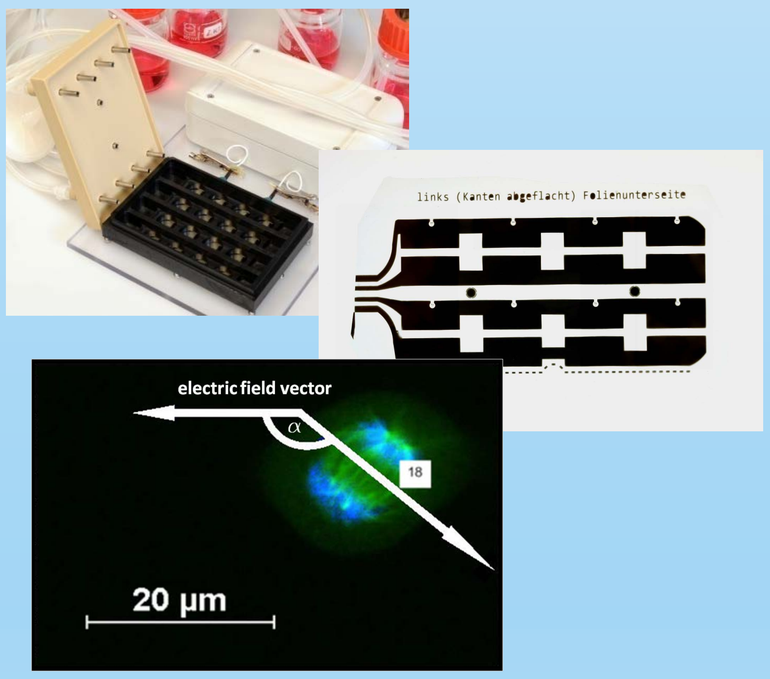
- Here the chamber can support 6 cartilage-carrier constructs cultivated in parallel**.
- Continuous medium supply.
- Sampling during long term cultivation
- Retention of paracrine factors
- Supplementation with vitamins and growth factors
- Application: Improved biochemical parameters of cultivated cartilage

3D culture of HepG2 on macro-porous matrix for drug testing



- Here the chamber can support 4x4 cell constructs cultivated in parallel**.
- The flow through the four channels can be adjusted independently.
- The carrier constructs can be separated from each other for measurements in static operation to conduct assays similar to the multi-well plate.
- Application: EROD-Assay for liver-specific activity in 3D

Electrical stimulation of cells



- Here 16 wells were equipped with foil electrodes at their bottom
- direct and unipolar pulsed voltage.
- The frequency can be varied between 16 Hz and 2 kHz, the voltage between 0 up to 600 mV and stimulation pulse to pause ratios between 1:1, 1:10 and 1:100
- Application: orientation of cell cleavage plane and cell migration due to electrical stimulation

Application for resorption of magnesium implants is currently investigated by Prof. Willumeit, Dr. Feyerabend, HZ Geesthacht

** supplier: medorex e.k., Germany

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