The HUMIMIC ActSense: a multifunctional device to incorporate electrical functionalities into microphysiological culture systems

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INTRODUCTION

The ability to simultaneously and continuously exploit different electrical sensing and actuation techniques during a single experimental run is of paramount importance in the context of multiphysiological systems. The long-term probing of cells' electrical activity and the assessment of the change in the impedance footprint over time provides fundamental information on dynamic tissue responses and organ-specific reactions.

In this work we introduce the HUMIMIC ActSense, a device that couples stimulation and sensing functionalities in a single multifunctional system.

Fig. 1 The HUMIMIC ActSense.

SUMMARY & CONCLUSION

In this work, we presented the HUMIMIC ActSense, a device that couples, on one hand, single frequency transepithelial electrical resistance (TEER) measurements with multi-frequency domain impedance spectroscopy and, on the other hand, electrical stimulation with multi-channel action potential recordings.

Together with HUMIMIC Chips featuring on-chip integrated transparent electrodes, the HUMIMIC ActSense equips researchers with a valuable tool to sense and control the electrical properties of the cultured tissues.

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HUMIMIC ACTSENSE FUNCTIONALITY

While simple TEER measurements have been successfully employed to assess the junction dynamics and barrier integrity of endothelial or epithelial models, the HUMIMIC ActSense additionally carries out electrical impedance spectroscopy techniques to probe the electrical footprint of a cultured tissue, allowing, e.g., the evaluation of the growth, spreading, and differentiation of different cell types at different maturation stages.

The simultaneous recording of the cells' electrical activity is implemented by 8 differential (16 single ended) sensing sites, which allows the sensing, e.g., of cardiac action potential, for a better understanding and assessment of heart tissue behavior and health. The multiple stimulation profiles can be used, e.g., to initially promote the maturation, and eventually pacing the contractions of mature cardiomyoces.

IMPEDANCE SPECTROSCOPY- TEER

- 1x ch. / 8x ch. through MUX.
- Single-frequency (TEER): 96-/24-well.
- Multi-Frequency measurements (impedance spectroscopy).
- Frequency Range: 10 Hz-100 kHz.
- Frequency Resolution: 0.1 Hz.

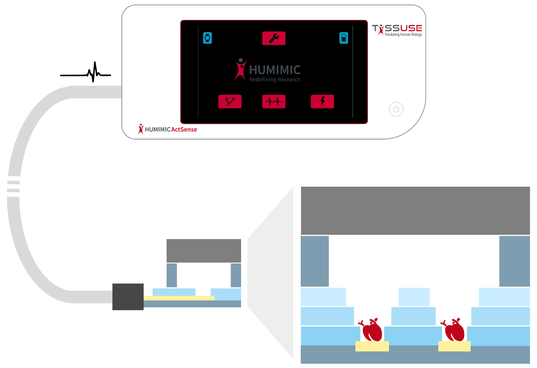
ECG- EMG -EEG

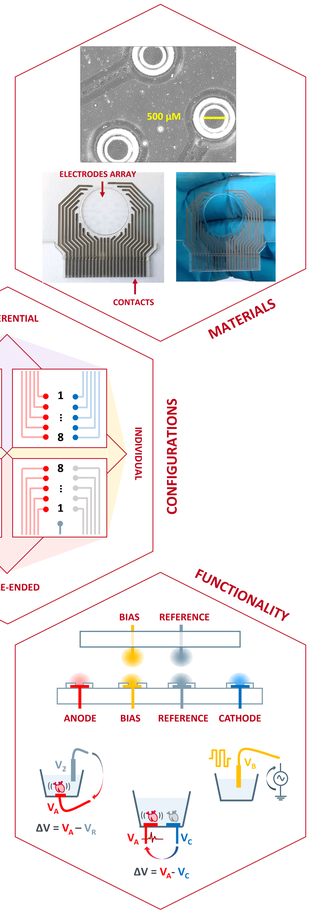
- Brain (EEG), muscle (EMG), and heart (ECG) activity recording.
- 8x differential ch. (16x single ended sensing sites).
- 24-Bit channel resolution: down to micro Volts.
- Gain: 1x, 2x, 4x, 6x, 8x, 12x, 24x.
- Data rates: up to 16 ksps.

STIMULATION

- 1x ch. / 8x ch. through multiplexing.
- Multiple voltage stimulation profiles (square, sine, train of impulses).
- Stimulation frequency: 0 Hz - 10 MHz.
- Cyclic stimulation possible.
- Gain: 1.5x, 2x, 2.5x, 5x.
- Attenuation: 1x, 10x, 100x, 1000x.

Fig. 2 Overview of the Humimic ActSense. **(Left)** Device functionality specifications: impedance spectroscopy measurement (top), electrical activity recording (center), and active stimulation (bottom). **(Right)** Electrodes integration: bright-field and phase contract optical microscopy pictures (top), electrode configuration (center), and electrode functionality (bottom).





ON-CHIP ELECTRODES

The HUMIMIC ActSense can be connected with HUMIMIC Chips featuring multi-electrode array (MEA)-like technology. The electrically conductive material of the integrated electrodes is poly (3,4-ethylenedioxythiophene): poly(sodium4-styrenesulfonate) (PEDOT:PSS), a transparent polymer that can be easily ink-jet printed on plastic materials at a very high throughput. The material is characterized by low thermal noise and superior charge injection when compared to standard metal electrodes, thus resulting in higher signal-to-noise recordings. Moreover, the transparency of the electrodes allow a simultaneous monitoring of the culture by means of standard microscopy techniques.

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