Microfluidic CMOS microelectrode array-based organ-on-chip systems:

A platform for personalized medicine

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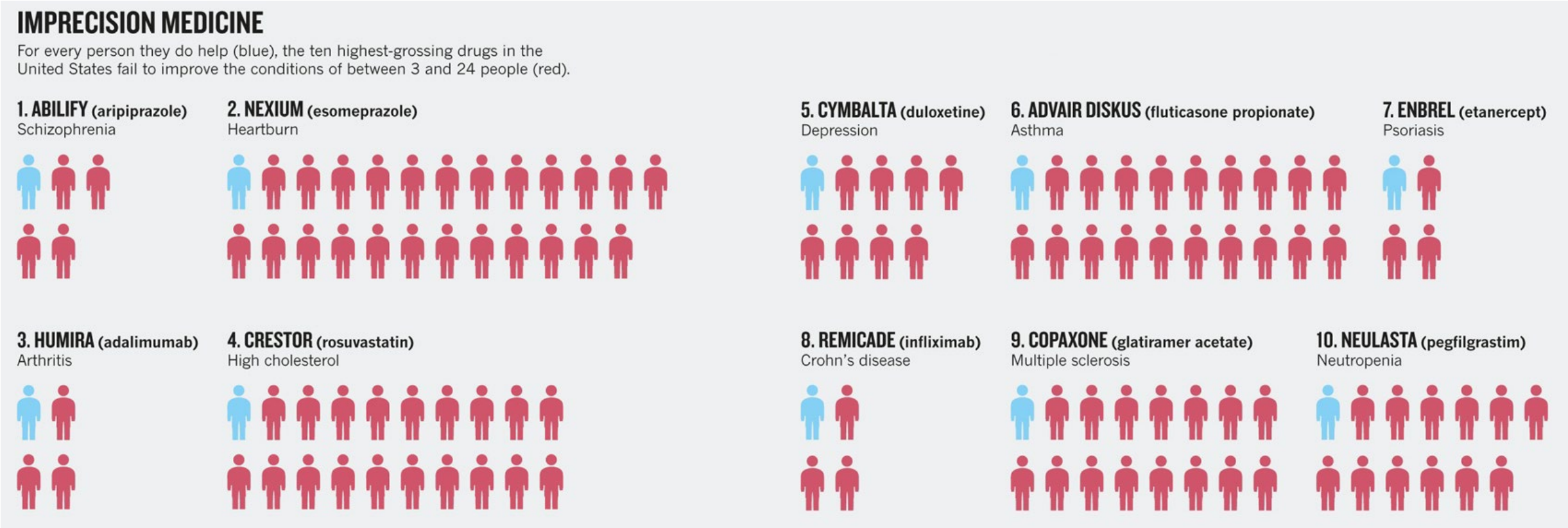
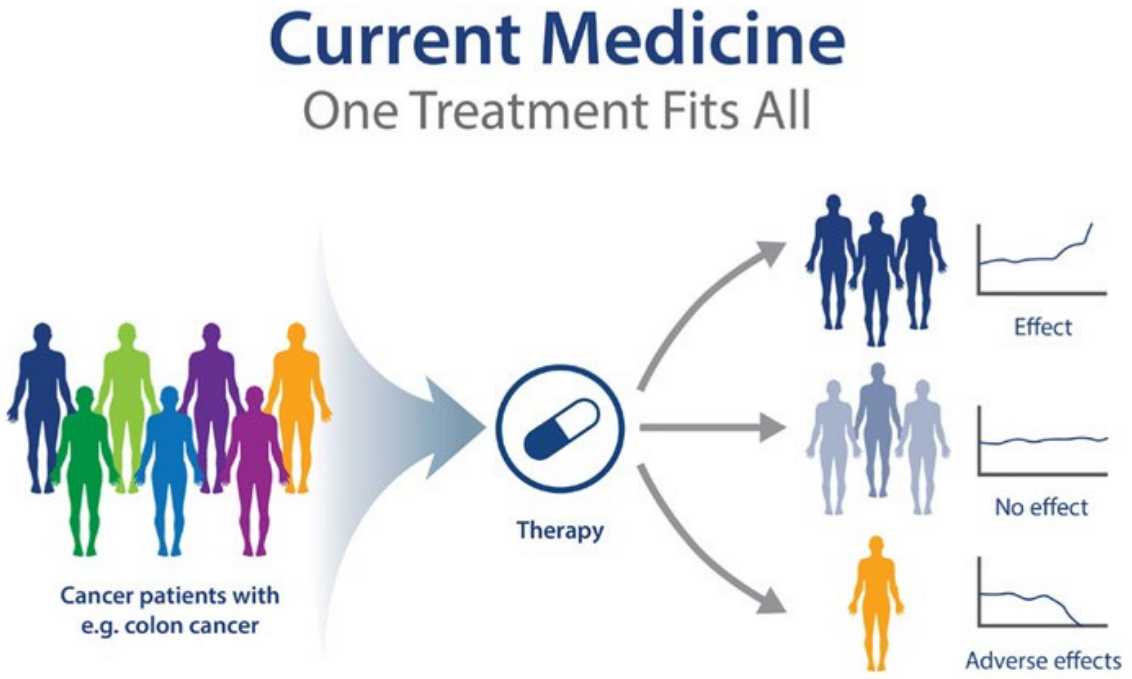
Current healthcare system is highly inefficient

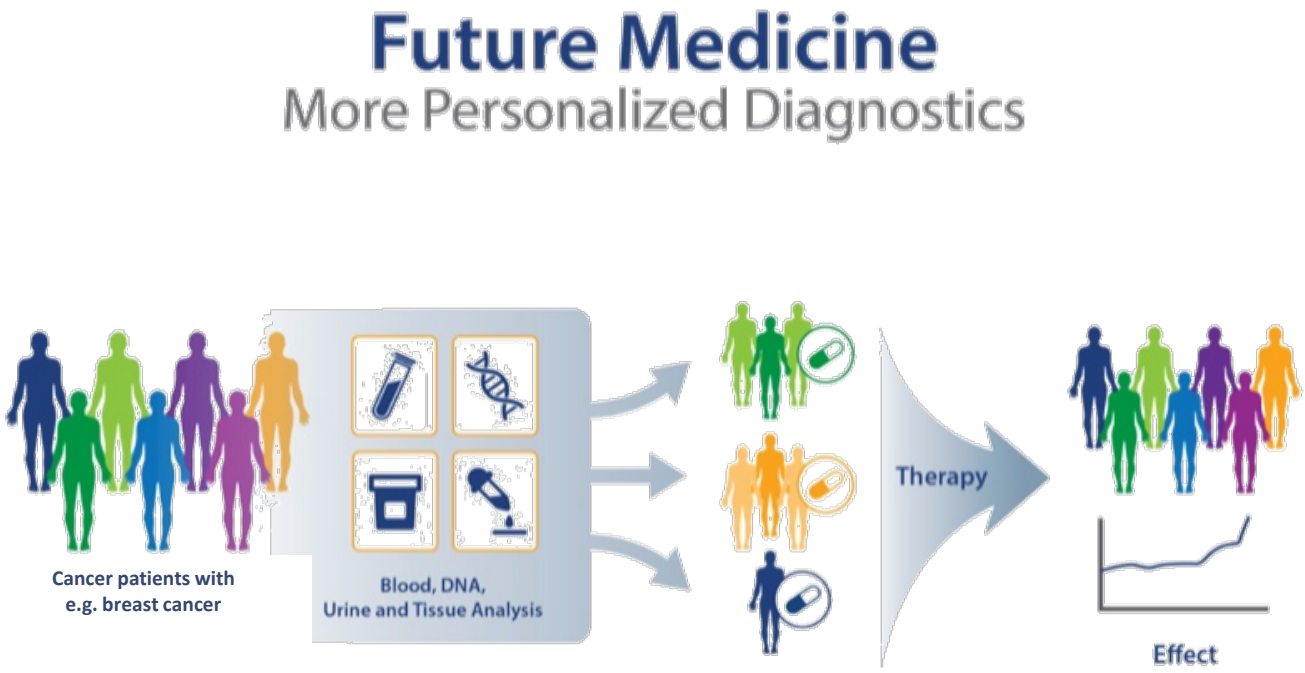


Nature 520, 609–611 (30 April 2015).

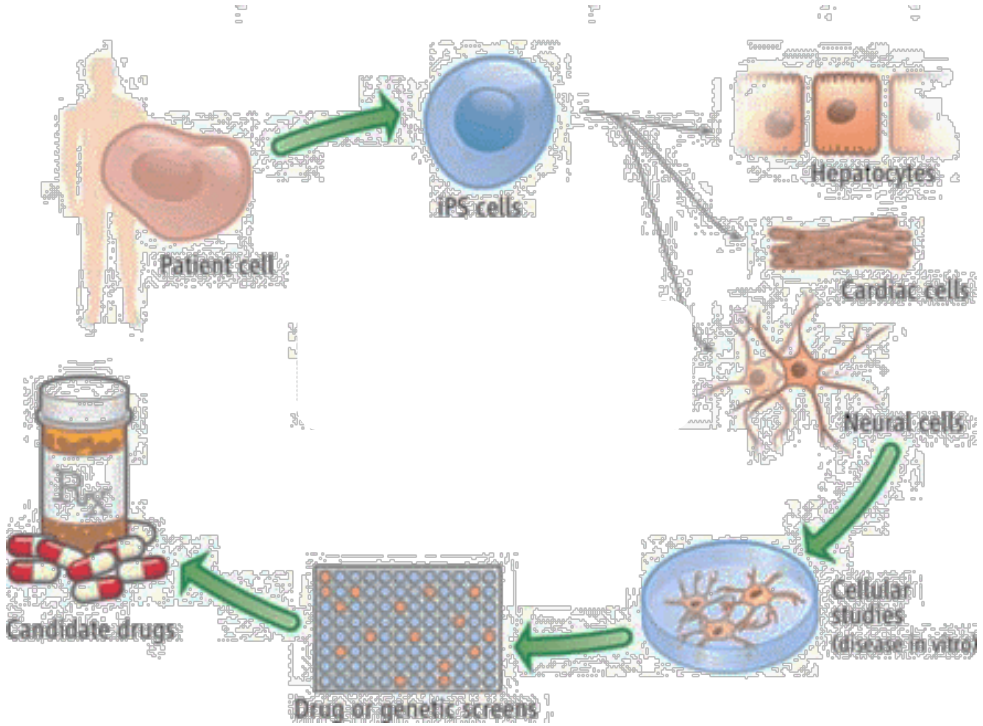
Tailoring treatment to patients with personalized medicine



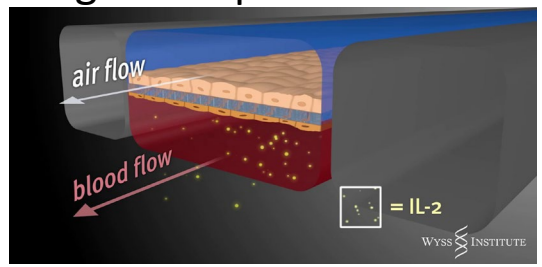
Jody Barbeau, 2018, CrownBio, accessed 29 October 2019, https://blog.crownbio.com/pdx-personalized-medicine#_



Modeling patients-on-chip for personalized medicine

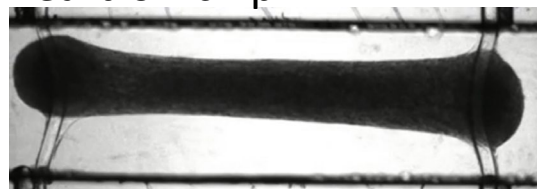


Lung-on-chip



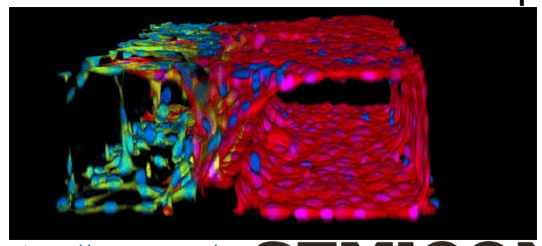
https://www.emulatebio.com/

Heart-on-chip



https://tarabiosystems.com/

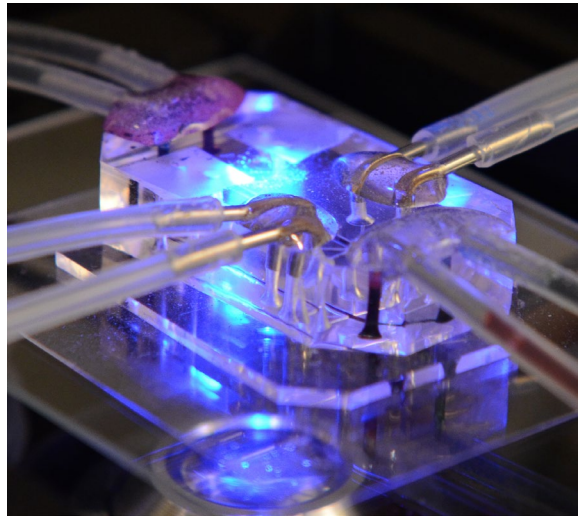
Blood-brain-barrier-on-chip



https://mimetas.com/

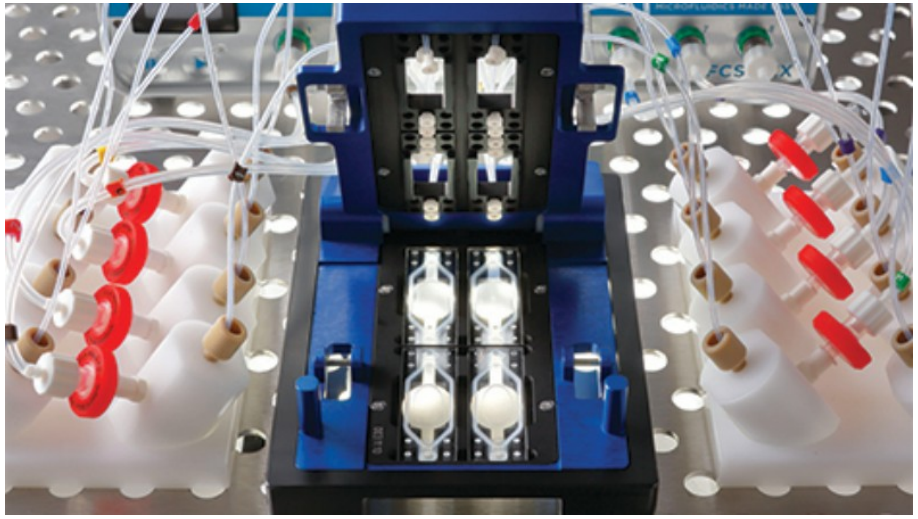
Challenges for current organ-on-chip systems

Scalability of production



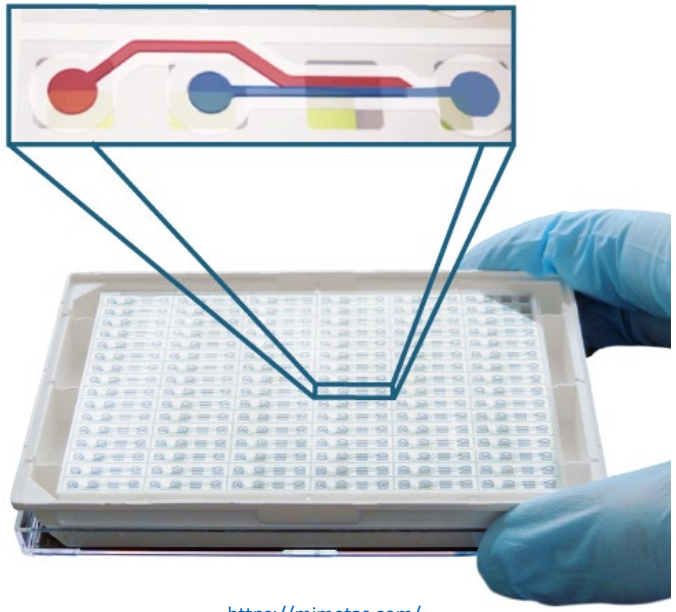
https://www.emulatebio.com/

Assay throughput



https://www.micronit.com/

Sensor integration



https://mimetas.com/

Microfluidic CMOS microelectrode array-based organ-on-chip systems

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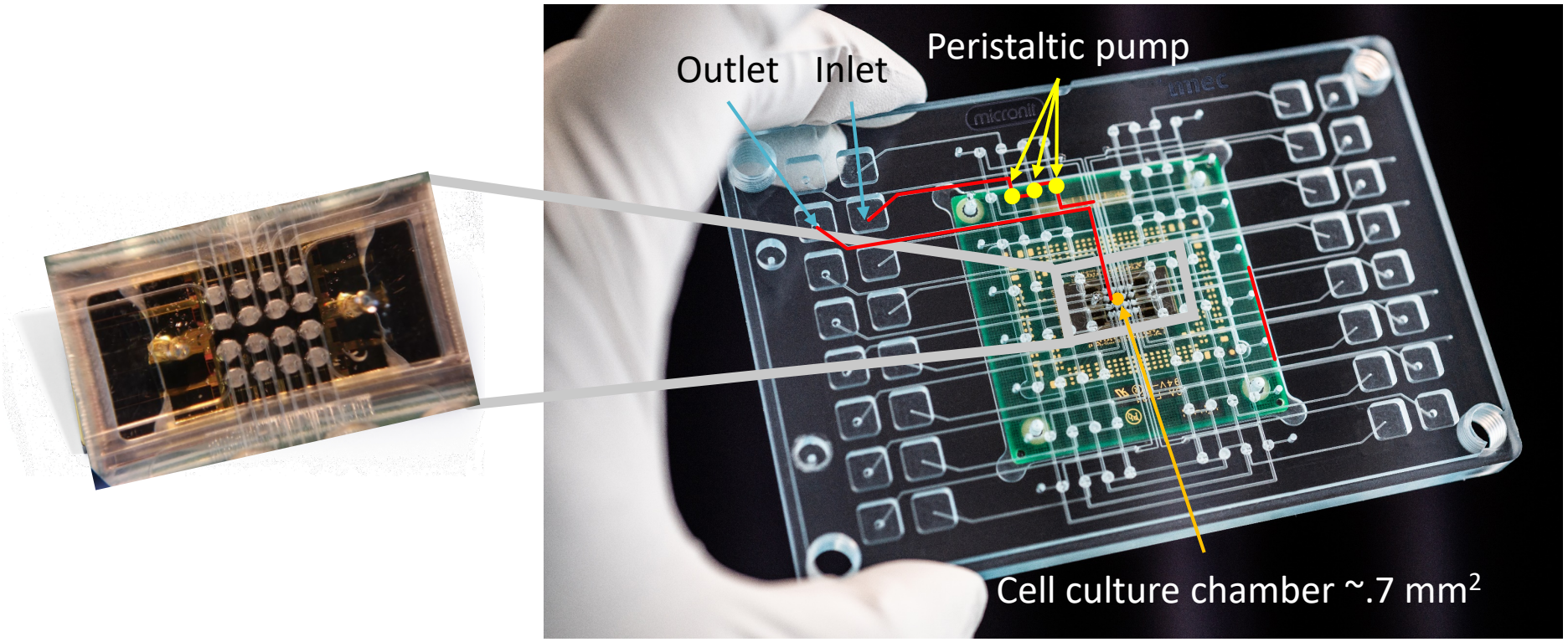
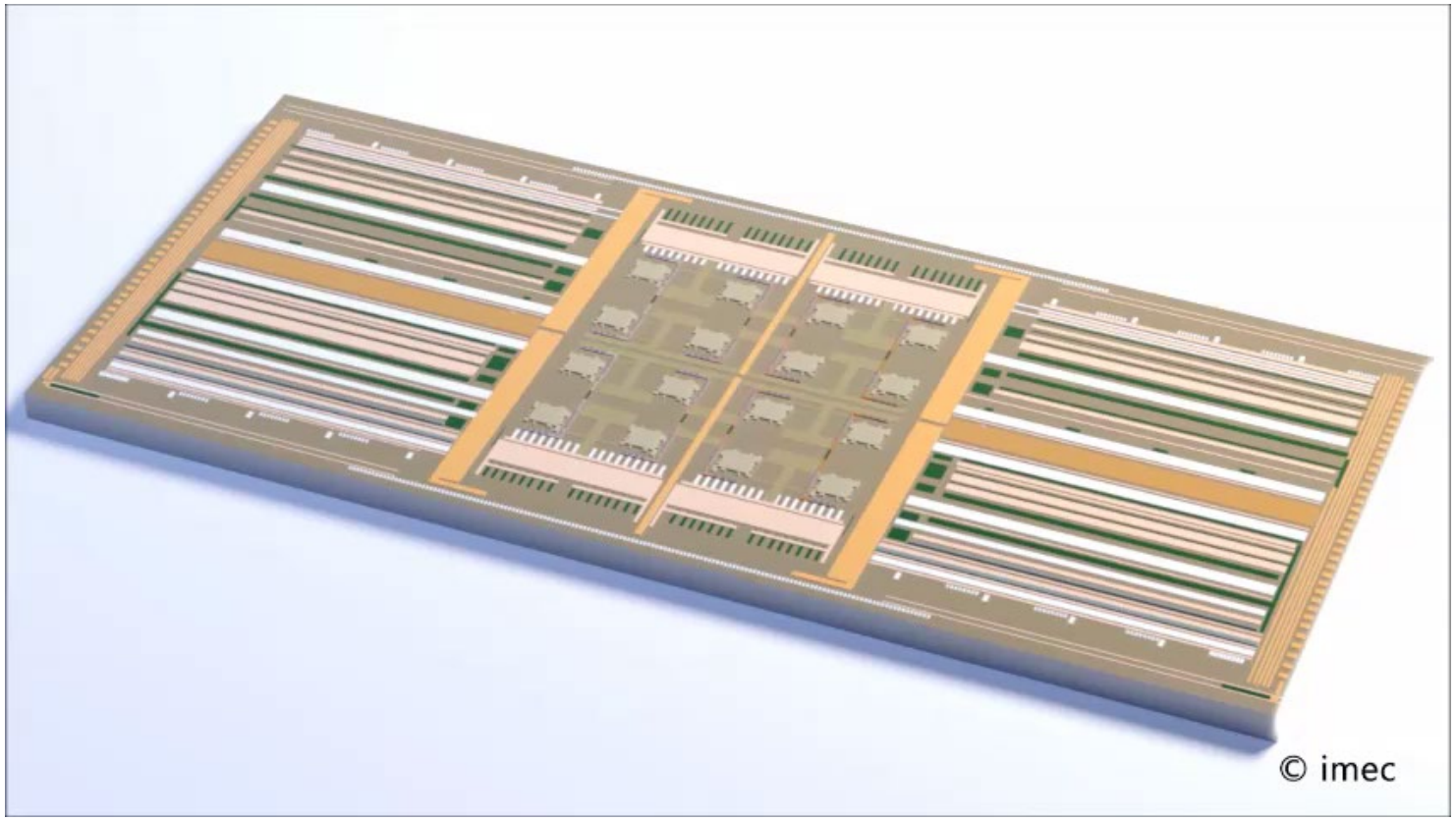
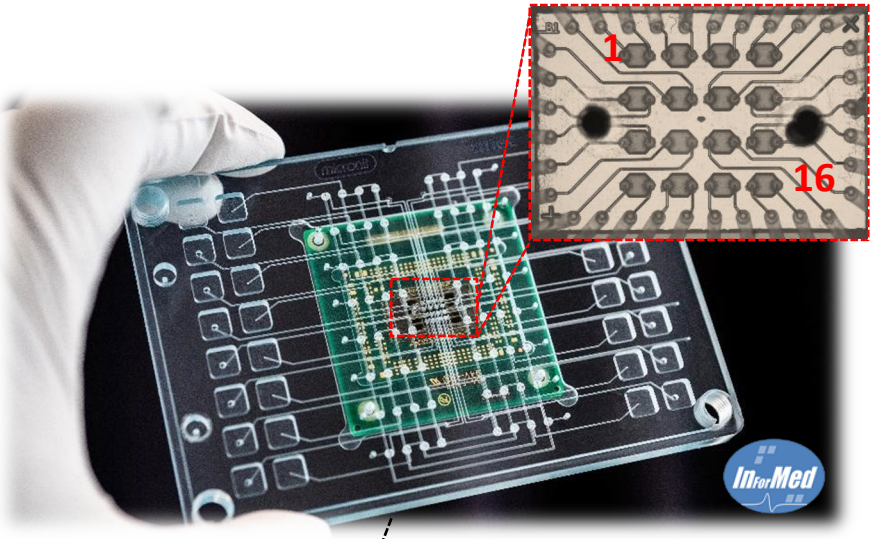
Microfluidic packaging strategy for higher throughput testing



Multi-modal 16,384-electrode CMOS-based MEA



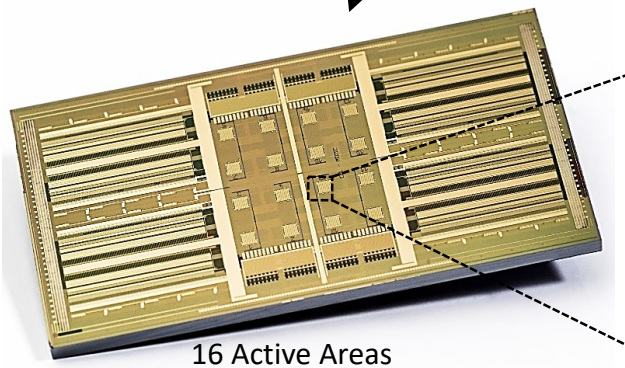
Multi-modal 16,384-electrode CMOS-based MEA



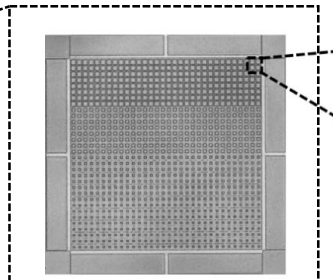
- 0.13 µm CMOS-Technology with dedicated BEOL processing
  - High density 16k electrodes with electrodes pitch 15 µm
  - Multi-modal
- Bio-assay with 16 active areas and single cell resolution
- Structured cellular growth

Six modalities to interact with cells:

1. Extracellular Recording
2. Intracellular Recording
3. Constant Voltage Stimulation
4. Constant Current Stimulation
5. Fast Impedance Monitoring
6. Impedance Spectroscopy

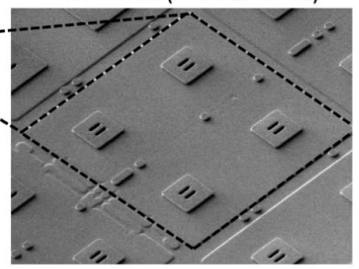


16 Active Areas
16 x1024 electrodes

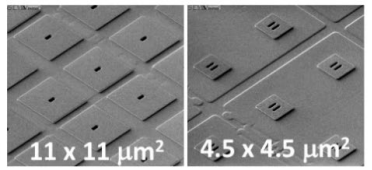


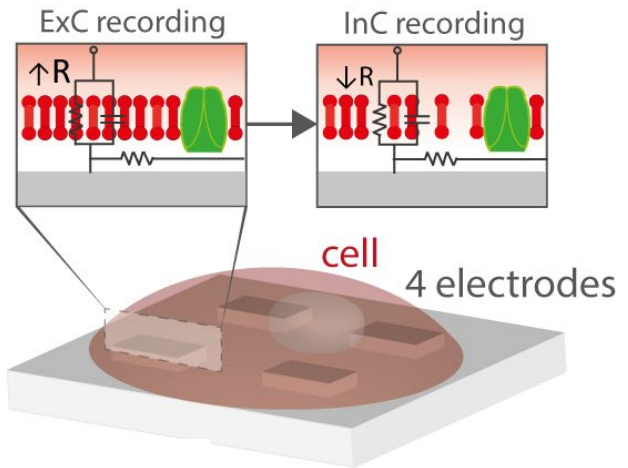
1 well
16 x 16 pixels

Pixel detail (4 electrodes)



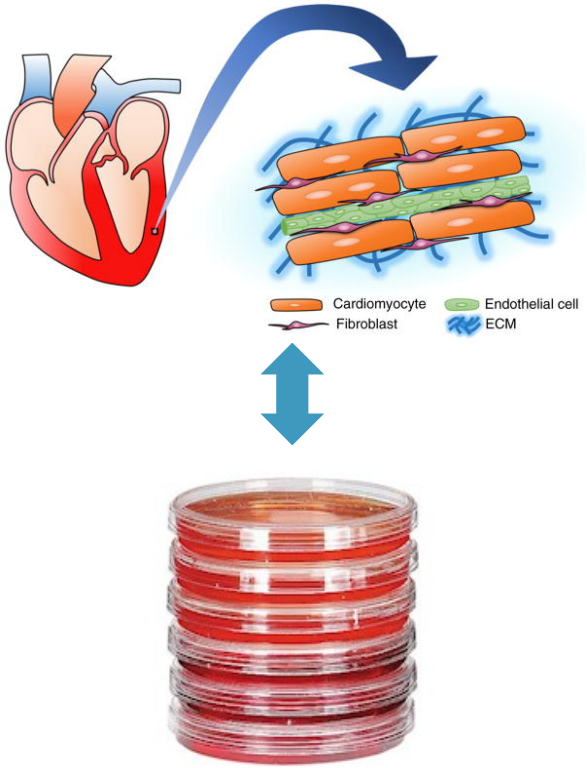
Different electrode sizes



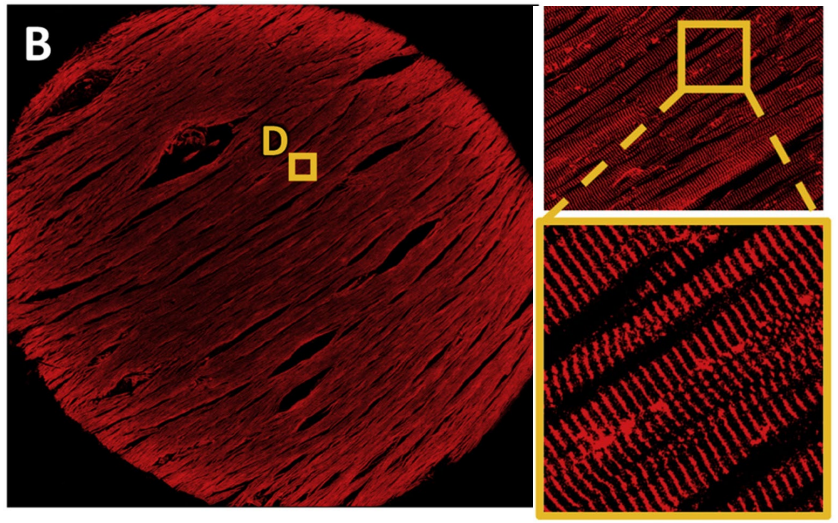


Application: heart-on-a-chip

In vitro cell cultures are strikingly different from in vivo cells

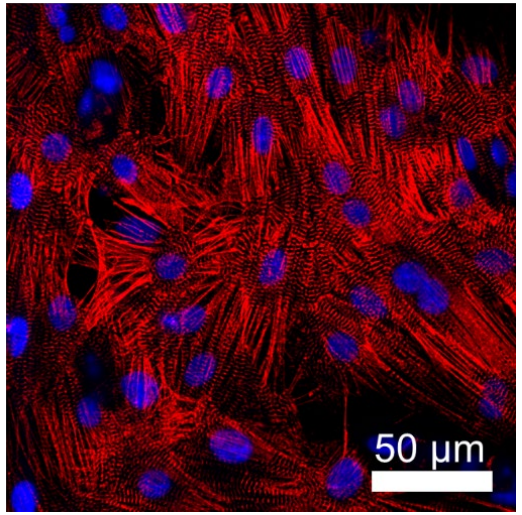


In vivo cardiac tissue

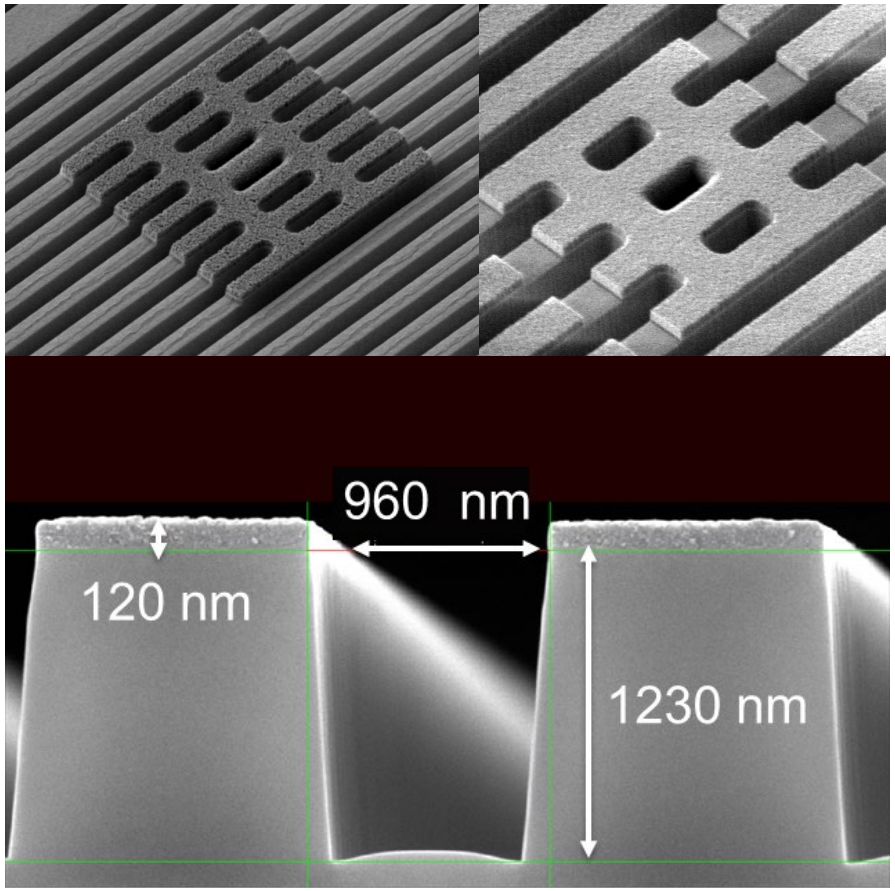


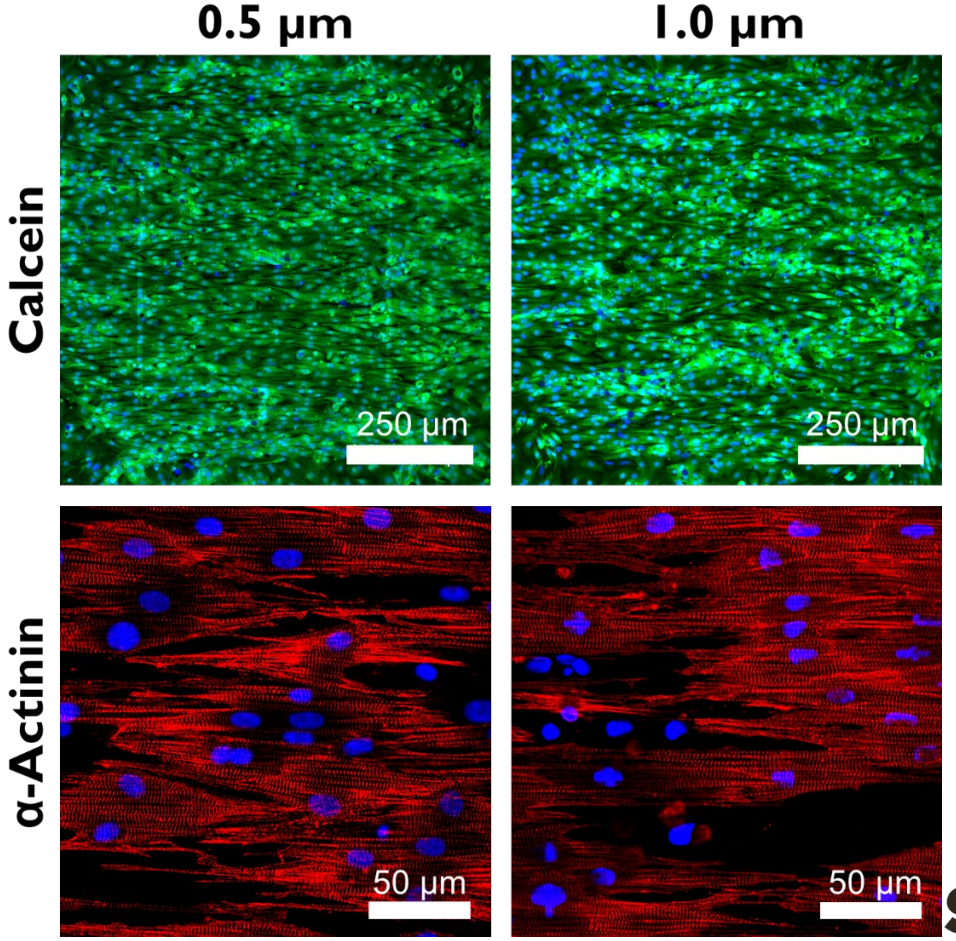
Prog Biophys Mol Biol. 2017 Nov;130(Pt B):302-314.

In vitro cardiac models

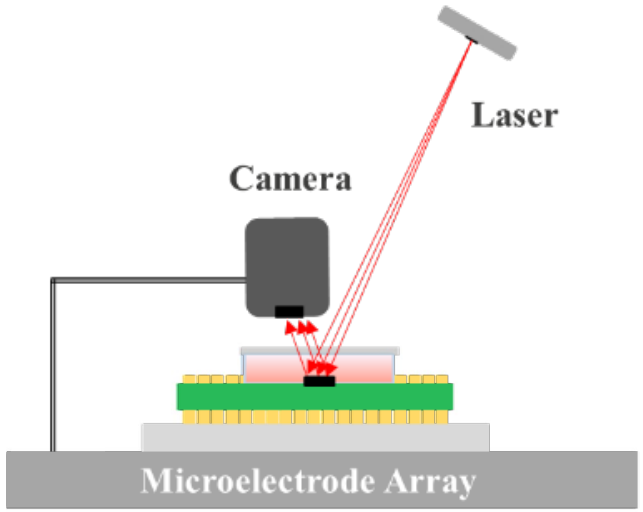


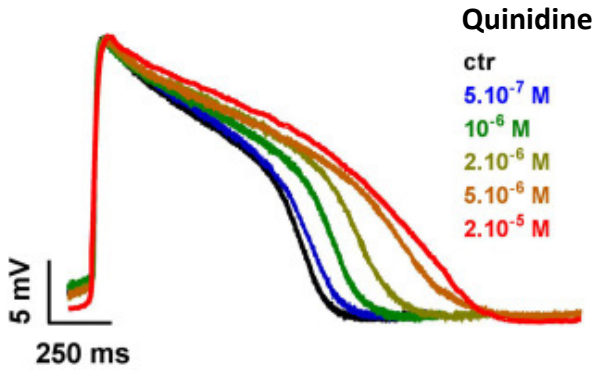
Nanogrooved surface induces cell alignment





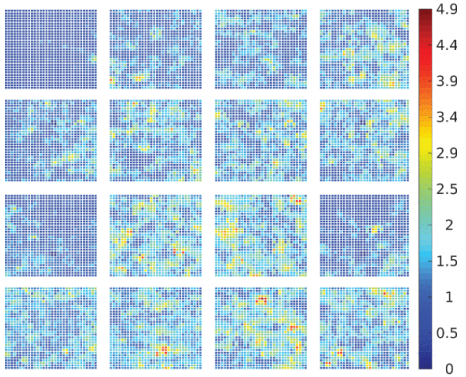
High-quality, multiparametric recordings at single-cell level





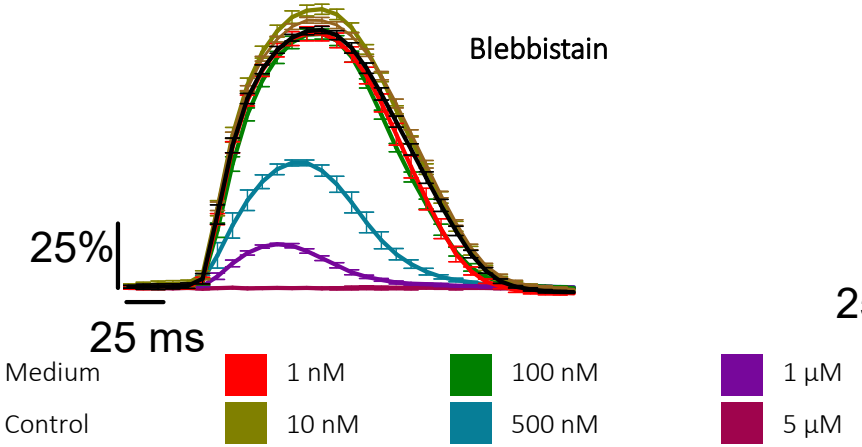
J Pharmacol Toxicol Methods. 2017 Sep;87:48-52.

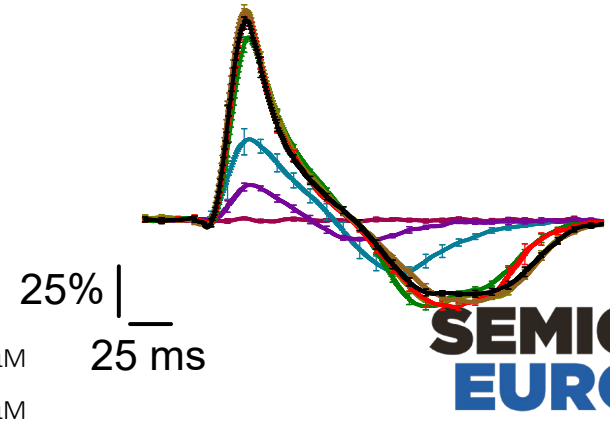
Massively parallelized recordings



IEEE J. Solid-State Circuits. 2018 Nov;53: 3076-3086.

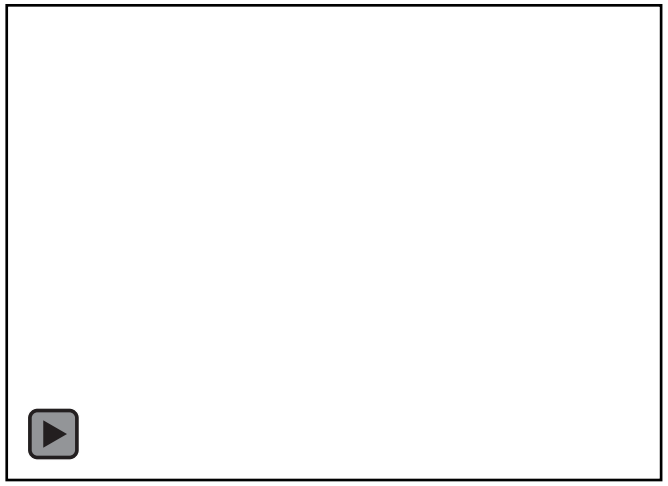
Biomedical Optics Express, 2018, 9, 4, 1827-1841.



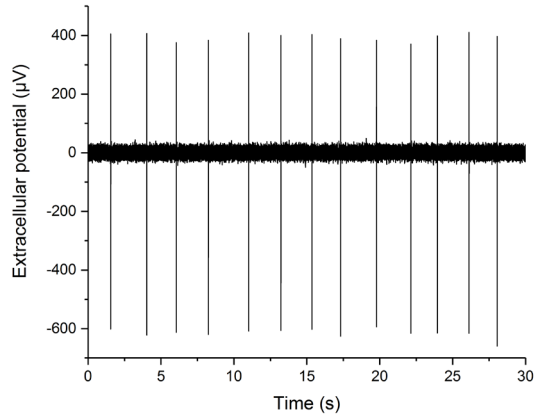


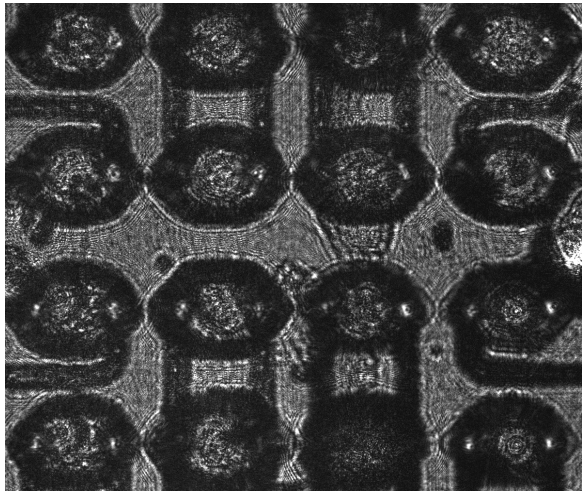
Cardiac cells cultured in microfluidic chambers

Calcium imaging

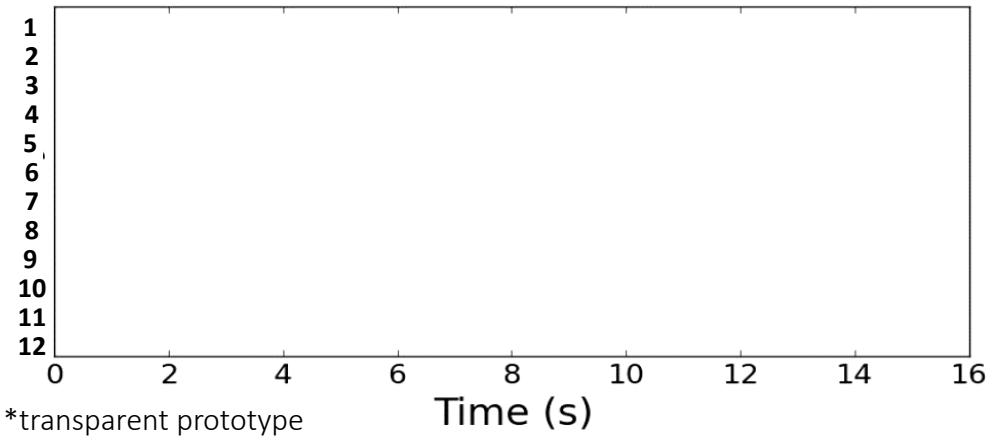


Electrophysiology





Contractile motion (Pixel-intensity variation)



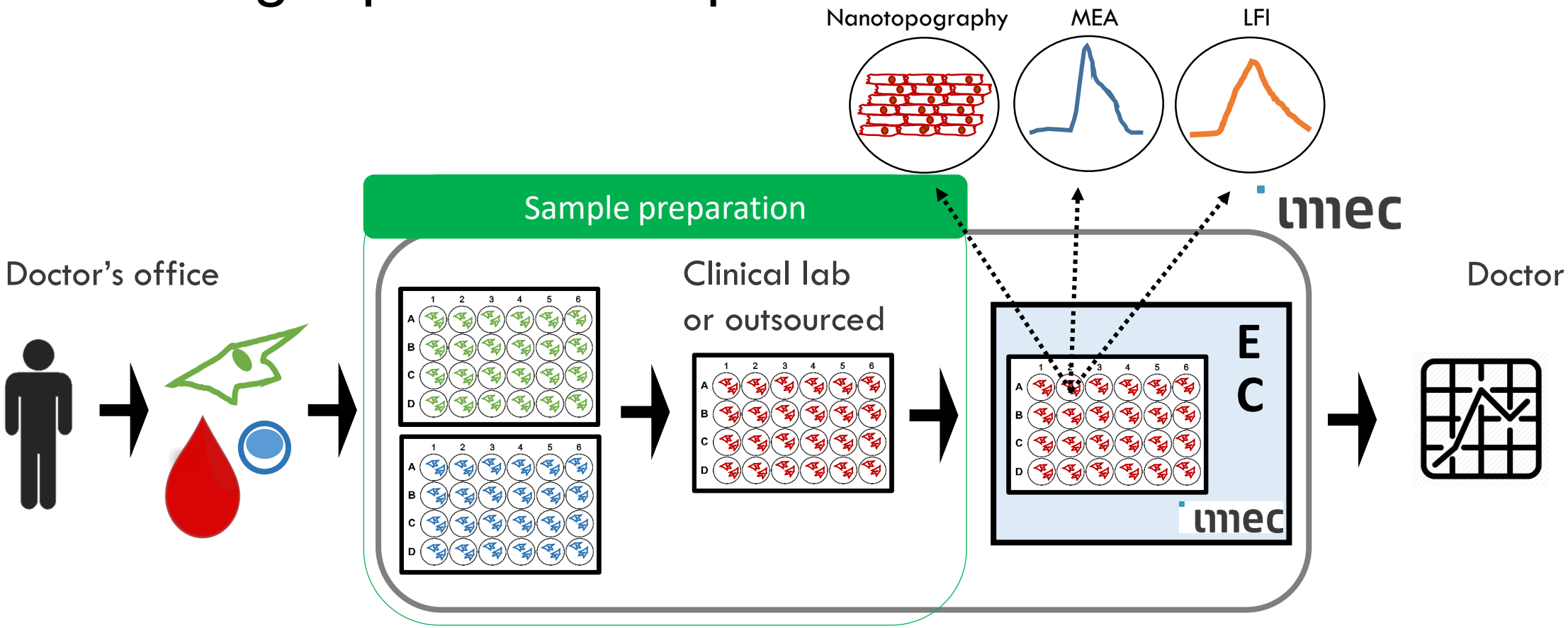
*transparent prototype

Conclusions

- CMOS-based MEA sensors for organ-on-chip offer high-quality recordings over thousands of cells;
- Microfluidic packaging increases assay throughput while maintaining conventional well-plate interface;
- Microfabricated surfaces influence cell growth to achieve more tissue-like morphology.

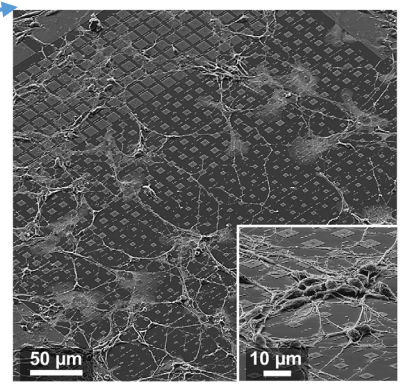
Outlook

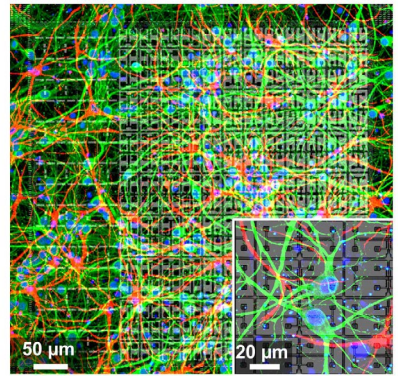
Predicting a patient's response to treatment



Outlook: expanding the platform to different organ models

Brain-on-chip

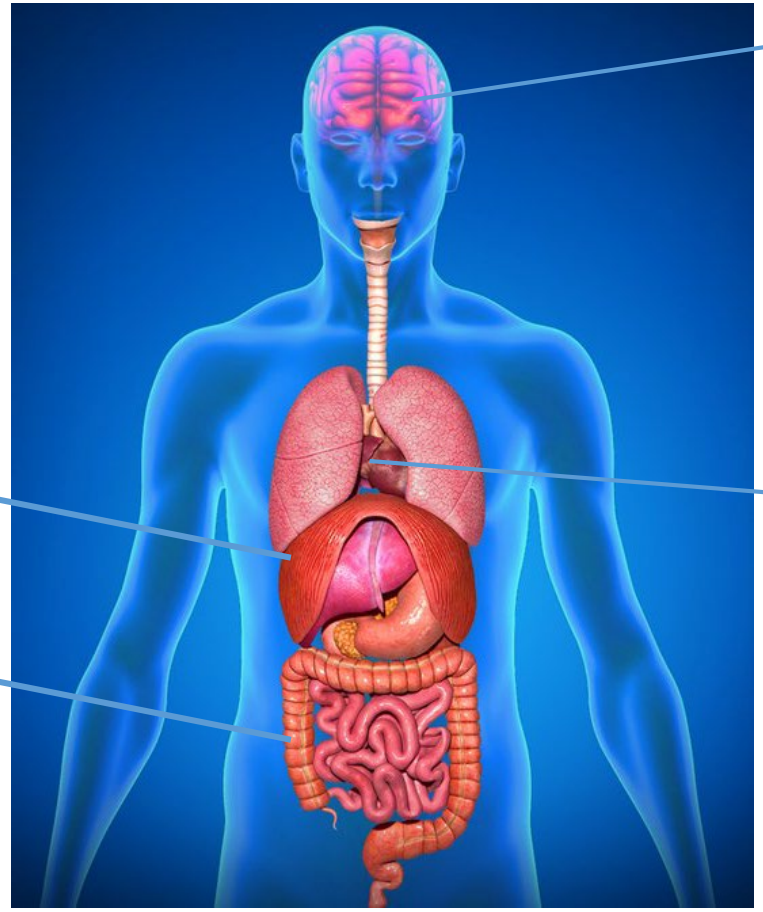




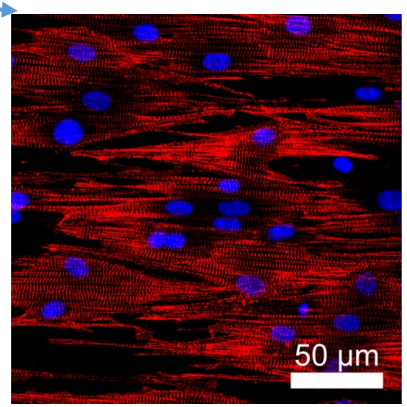
Front Neurosci. 2019 Jun 25;13:641

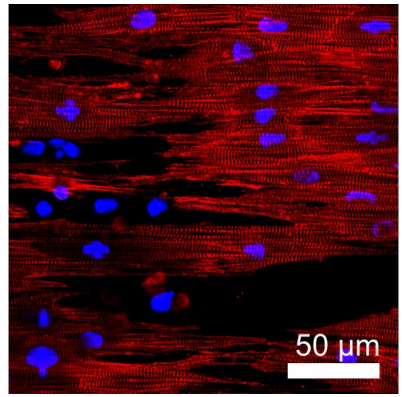
Liver

Gut Microbiome



Heart-on-chip





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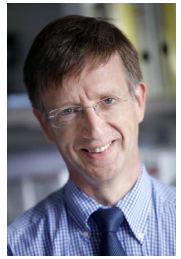
Acknowledgements

Prof. L. Lagae



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