Microfluidic CMOS microelectrode array-based organ-on-chip systems: A platform for personalized medicine

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Current healthcare system is highly inefficient

**IMPRECISION MEDICINE**

For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

1. **ABLEIFY** (aripiprazole)  
Schizophrenia  
2. **NEXIUM** (esomeprazole)  
Heartburn

3. **HUMIRA** (adalimumab)  
Arthritis

4. **CRESTOR** (rosuvastatin)  
High cholesterol

5. **CYMBALTA** (duloxetine)  
Depression

6. **ADVAIL DISKUS** (fluticasone propionate)  
Asthma

7. **ENBREL** (etanercept)  
Psoriasis

8. **REMICADE** (infliximab)  
Crohn’s disease

9. **COPAXONE** (glatiramer acetate)  
Multiple sclerosis

10. **NEULASTA** (pegfilgrastim)  
Neutropenia

Tailoring treatment to patients with personalized medicine

Current Medicine
One Treatment Fits All

Future Medicine
More Personalized Diagnostics

Cancer patients with e.g. colon cancer

Therapy

Effect
No effect
Adverse effects


Cancer patients with e.g. breast cancer

Blood, DNA, Urine and Tissue Analysis

Effect

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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

Assay throughput

Sensor integration

https://www.emulatebio.com/

https://www.micronit.com/

https://mimetas.com/
Microfluidic CMOS microelectrode array-based organ-on-chip systems
Microfluidic packaging strategy for higher throughput testing
Multi-modal 16,384-electrode CMOS-based MEA
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- 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
Application: heart-on-a-chip
In vitro cell cultures are strikingly different from in vivo cells.
Nanogrooved surface induces cell alignment
High-quality, multiparametric recordings at single-cell level

Massively parallelized recordings

Quinidine

Blebbistain

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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.
Predicting a patient’s response to treatment

Doctor’s office → Skin biopsy or blood sample → Sample preparation → Clinical lab or outsourced → Cardiac Differentiation (Stem cell reprogramming) → Drug response (E-Phys Contractile) → Risk prediction

- Nanotopography
- MEA
- LFI

Patient Risk prediction

Doctor's office

Drug response E-Phys Contractile

Risk prediction

Sample preparation

Clinical lab or outsourced

Cardiac Differentiation Stem cell reprogramming

Upscaling
Outlook: expanding the platform to different organ models

- Brain-on-chip
- Heart-on-chip
- Liver
- Gut
- Microbiome
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