2D-3D Bioprinting for medical microdevices

Alive Strategic Axis

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What does bioprinting mean?

Integrating biological functions into microdevices

- Biomolecules
- Biomaterials
- Living cells
- «Vascular» structures
- Mechanics, topology

Biomarker Detection
Biomarker Analysis
Cell capture and sorting
Cell biology

Biosensors

Microphysiological systems
(Edington et al., Nature 2018)
> Microcontact printing (µCP)
Multiplexed and automated protein deposition on flat surfaces for bioassays

> Inkjet technology
Coupling inkjet with µCP to creating protein patterns for directed neuron growth

J. Foncy & A. Esteve et al, Plos One 2018
J. Fredonnet et al, Microarrays 2016
A. Esteve, MEE 2018
Integrating bioactivity in sensors

Tailoring sensor surface
Micro contact printing of antibodies on vibrating micro/nanocantilevers

Bioplume technology
Multiplexed DNA/protein deposition on surfaces and microdevices (optical fibers)

Silicon technologies
Micro contact printing of antibodies on vibrating micro/nanocantilevers

Salomon et al, Nanotechnology, 2012
Cellular capture and guidance

Controlling cell shape, position, growth

A) Surface patterning for cell culture

PDMS stamp inked by microfluidic

Antifouling treatment

Cell culture

B) Confocal Images

Microcontact printing and molding for cell capture and Neuron Guidance on 2D / 2.5D protein patterns

Foncy, Esteve et al, Plos One 2018

Biomaterial patterning

> Developping photosensitive biomaterials

Development of photosensitive silk protein based material for cell culture in controlled stiffness conditions

*Maziz et al. Submitted to Biofabrication, 2018*
Shaping biomaterials in 2D/3D

> Electrospinning

Fabrication of silk/PEG fibers or droplets with diameters ranging from 150 nm up to 4 µm

A. Maziz, C. Bergaud
A. Chalard et al, ACS Applied Materials and Interfaces, 2018

> Wet spinning (solvent exchange)

Fabrication of macromolecular Alkyl-galactonamides hydrogels fibers (100-500µm) for neuron cell culture.
3D Printing functional devices

- 3D printed microfluidic devices for biomarker analysis and cell sorting
  - Sorting of cells and particles (Deterministic lateral displacement)
  - Sorting CTC with 3D printed filters

High resolution (<1 µm)
Complex 3D structures

F. Mézières et al, JASA 2016
A. Accardo Add. Manufact. , 2018
A. Cerf, A. Esteve, K. Jimenez
3D model systems for cell biology

- Controlling the topology and mechanical properties of cell microenvironment
  - 3D scaffolds for neuron cell growth
  - 3D models for cell migration studies
  - Mechanical environment

Accardo et al, Materials Today, 2018
Accardo et al Small, 2017 / E. Desvignes
M. Delarue et al, Nature Physics, 2017

Controlling pressure, supply, confinement (yeasts)
Controlling cell microenvironment

> Controlling topological environment for cell culture

- Controlling stiffness, topology, material chemistry of the microenvironement
- Controlling cell position by printing?

F. Mézières et al, JASA 2016
J. Creff, A. Besson

Growth and differentiation of Mesenchymal Stem Cell on trabecular bone scaffolds

- 3D models for oncology / regenerative medicine
MultiFAB platform
(LAAS-CNRS / CIRIMAT)

Cutting edge technologies for 3D printing
- Selective Laser Sintering / Melting
  - Materials: Metals, alloys, ceramics, cermets
- Inkjet printing
- Two photon lithography
- Fused deposition modeling
  - Materials: ABS, PLA, Nylon
- Multi-material bio-printing
- Stereolithography
  - Materials: Photosensitive polymers, hydrogels, biomolecules

 joined Laboratories

Multiplexed microcontact printing
with reversible clamping

www.biosoftlab.com
https://www.laas.fr/projects/MultiFAB/
> **Novel opportunities for microdevices fabrication and integration**

> **An open field of research for cell biology**

   - *Fundamental studies in cell biology*
   - *Models systems for drug screening and diagnosis*
   - *Regenerative medicine*

> **Challenges:**

   - technological development
   - material development