Session: Biomaterials and 3D printing

Chair: Prof. Dr. Peter Loskill

Professor for Organ-on-Chip Research

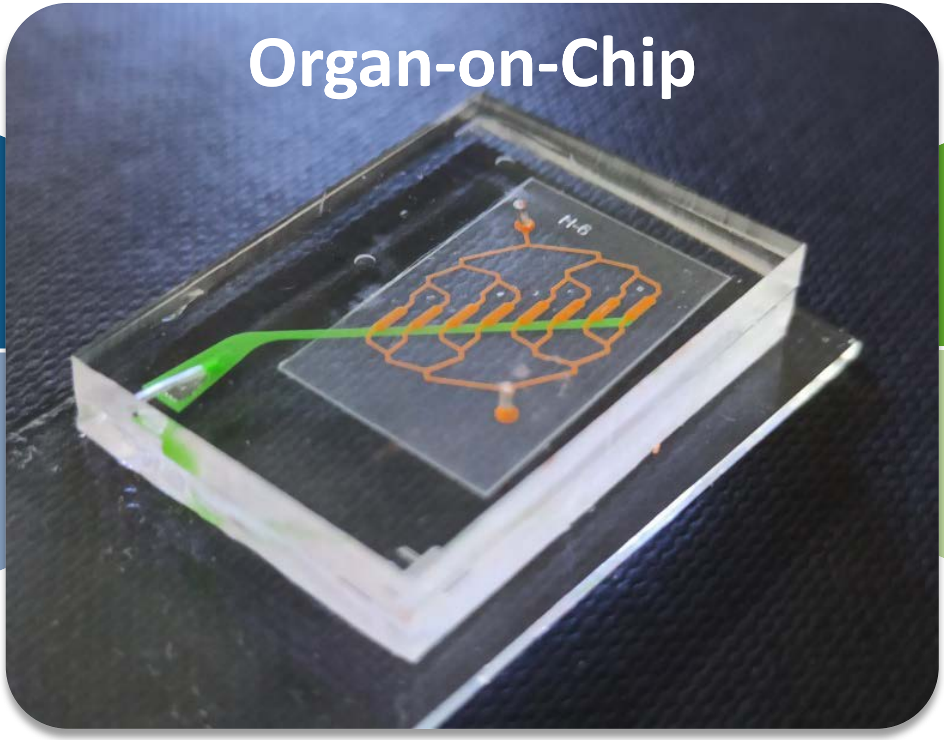
- µOrgano-Lab, Department of Biomedical Sciences, Faculty of Medicine, Eberhard Karls University Tübingen
- 3R-Center Tübingen for In Vitro Models and Alternatives to Animal Testing

PSIS workshop – Organ on Chip
April 29th, 2021

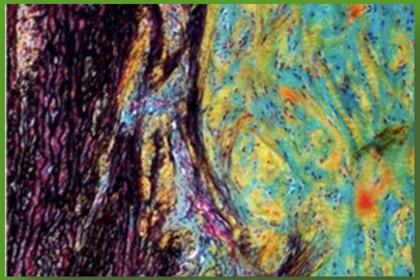
Biomaterials – Different types ⇋ different requirements

Chip material

- Seals microchannels and -chambers
- Provides housing for the tissues



ECM substitute



- Integral part of tissues and organs
- Provides 3D environment and anchor points for cells

Biomaterials – **Chip material**

- Key requirements
  - Long-term stability, sterilizable
  - No interference with the tissue/assay function (biocompatible, inert, low absorption)
  - Optical transparency
  - Applicable for rapid prototyping/microfabrication
  - (Economical) manufacturability

- Various types of materials in use, e.g.
  - Elastomers (e.g. PDMS)
  - Thermoplastics (PMMA, PS, PET, …)
  - Glass
  - Hybrid combinations

Campbell et al. *ACS Biomater. Sci. Eng.* (2021)

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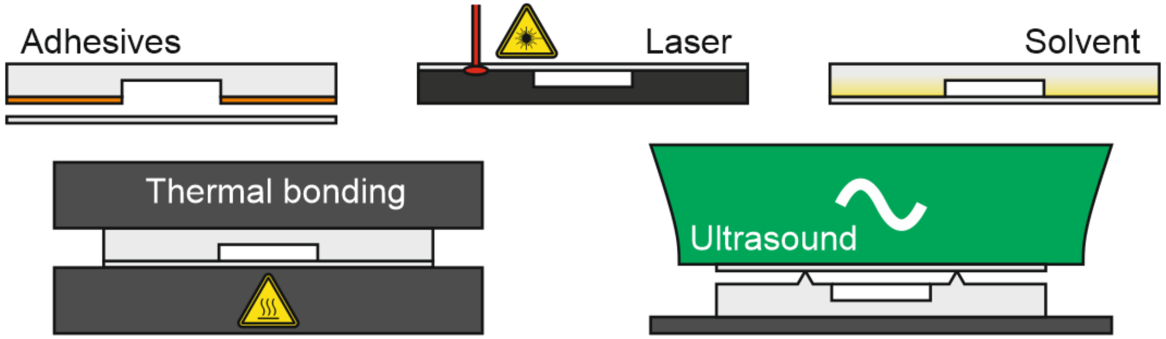
- Structured and bonded via different fabrication approaches (e.g. lithography, injection molding mechanical/laser structuring, hot embossing, 3D printing, thermal bonding …)



Schneider et al. *Lab Chip.* (2021)

➡ ***Large potential for standardization*** *(closely connected to the ”microfluidics” topic)*

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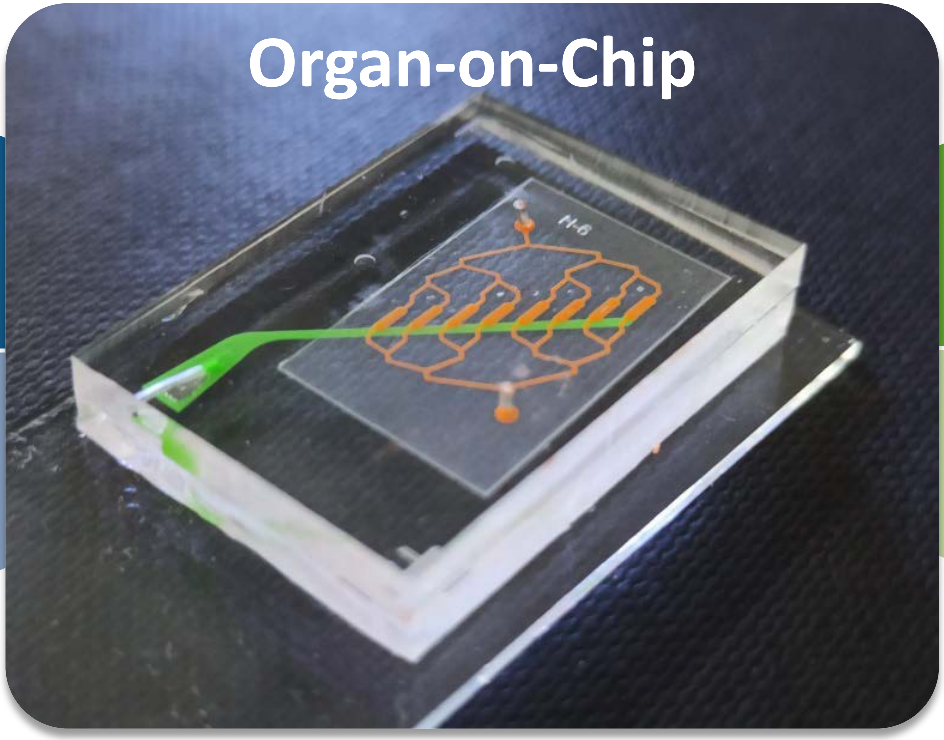
Organ-on-Chip



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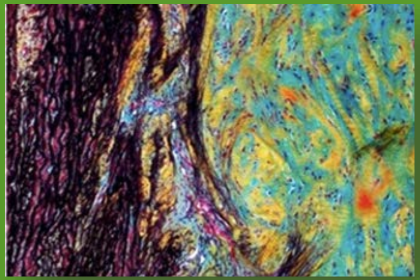

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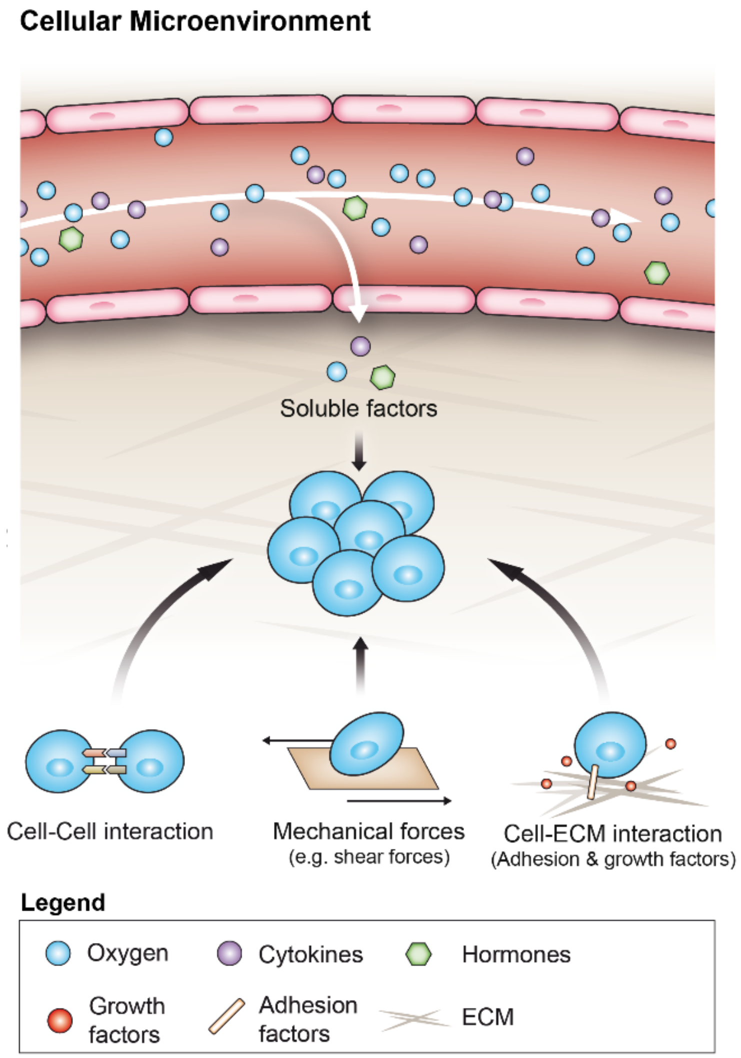
Biomaterials – ECM substitute

- Defines the cellular microenvironment and provides mechanical and biochemical cues

- Large diversity of materials with distinct advantages and limitations
  - Due to tissue-specificity and complexity of in vivo ECM



Biomaterials – ECM substitute

Natural biomaterials	Strengths	Weaknesses	OOC models
Collagen	• Biocompatible • Low antigenicity/immunogenicity • Degraded enzymatically • Contains cell adhesive domains • Can be formed into specific geometries • Major component of native ECM • Cells able to remodel and contract gel matrix • Culture media, proteins, and growth factors can be transported across collagen gel • Orientation of collagen fibers can be achieved • Cells can penetrate, remodel, and contract gel matrix	• Chemical crosslinking used for increased stability • Without mechanical support, collagen-based cell models remain intact for short time	• *Cardiac* • *Hepatic* • *Vascular* • *Skeletal muscle* • *Kidney* • *Neuronal networks* • *Tumor spheroids* • *Microvessels* • *Cancer cell migration*
Fibrin	• Biocompatible • Noninflammatory • Biodegradable • Gel formation at room temperature through enzymatic polymerization of fibrinogen by thrombin • Bioadhesive properties • Delivery of proteins and growth factors	• Weak mechanical properties	• *Skeletal muscle* • *Vascularized human tissue* • *Fibrin clot formation in lung model*
HA	• Biocompatible • Natural ECM component • Structural component of tissue and joints • Degradable with hyaluronidase • Tunable elastic modulus capability	• Weak mechanical properties	• *Cancer metastasis* • *Barrier tissue*
Chitosan	• Biocompatible • Biodegradable • Similar in structure to glycosaminoglycans • Flexible and porous • Minimal foreign-body response	• Mechanical weakness • Instability	• *Vascular*
Aginate	• Biocompatible • Degradable • Immediate gelation upon exposure to divalent cations • Use as sacrificial material and gel dissolves culture medium	• Uncontrollable degradation • Limited protein adsorption • Lack of cell binding	• *Cardiac* • *Tumor spheroids* • *Hepatocyte spheroids* • *Liver, tumor, marrow*
Gelatin	• Biocompatible • Biodegradable • Similar in composition to collagen • Contains cell adhesion sites • Less antigenic than collagen • Tunable and physiologically relevant elastic modulus	• Chemical crosslinking for stability	• *Cardiac, vascular* • *Muscle*
Synthetic biomaterials	• Tunable mechanical propertieS • Tunable degradation properties • Less batch-to-batch variability than natural biomaterials • Chemical modification to incorporate bioactive molecules • Polyesters degraded through hydrolysis • Moldable	• Lack of cell adhesion ligands prior to modification • Degradation products could have cytotoxic effects • Immune response must be evaluated	• *Cardiac* • *Hepatic*

Ahadian et al. *Adv. Healthcare Mater. 7: 1700506* (2018)

Biomaterials – ECM substitute

- Defines the cellular microenvironment and provides mechanical and biochemical cues

- Large diversity of materials with distinct advantages and limitations
  - Due to tissue-specificity and complexity of in vivo ECM

- Natural (e.g. animal- or plant-derived) or synthetic biomaterials

- Different processing approaches to generate various types scaffolds
  - Hydrogels (bulk injection, in-chip patterning, bioprinting)
  - (Freeze-)Dried membranes
  - Decellularized scaffolds
  - Electrospun scaffolds

➥ ***How to bring together in vivo diversity/complexity and standardization?***

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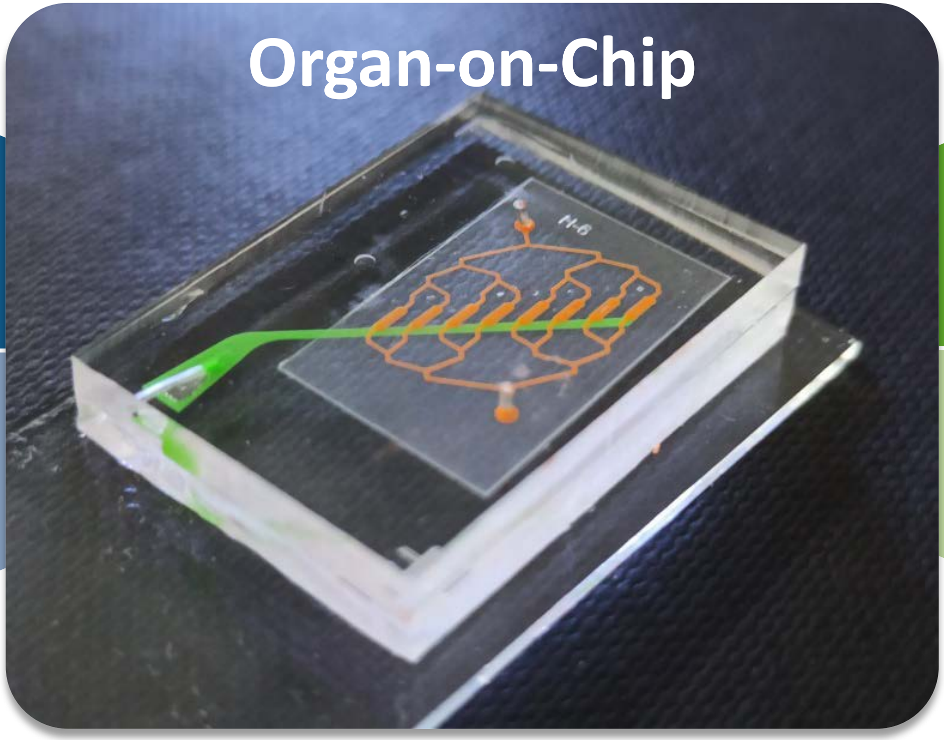

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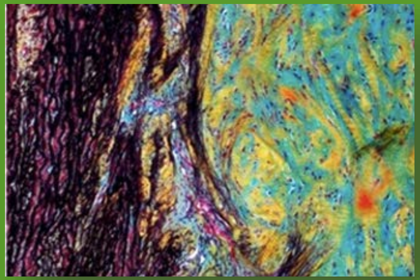

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