The key technology for in 3-D vitro engineered tissues is the establishment of vascular scaffolds. Today it is not yet possible to generate vascular structures resembling the typical organisation of mature blood vessels in vivo. In the past, significant progress has been made mainly in the development of tissue-like engineered products that are not dependent on a significant level of vascular support, such as bioartificial cartilage and skin equivalents. The generation of adequate tissue substitutes of most other types of tissues require a functional vascular network for the supply of nutrients and the disposal of metabolites throughout a functional and growing tissue. Therefore, the generation of vascularised artificial tissues defines a challenging topic for future developments.

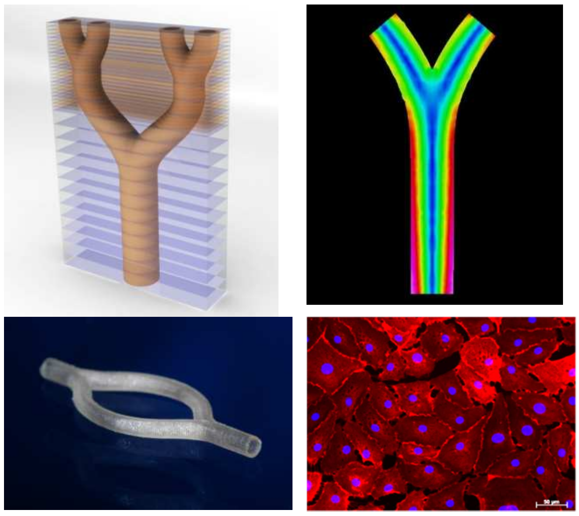

Fig. Schematic of layer by layer fabrication of bio-inspiered structures, fluid dynamic simulation of wall sheer stress in branched tube, artifical vessel, fabricated by laser-based stereolithography, endothelial cells growing on new flexible biomaterial.

Natural systems are able to execute complex functions because their forms and materials have been optimized in the course of evolution.
In order to develop artificial structures which perform as well as natural ones we need a) fabrication processes that do not set any limits to the generation of structures and shapes, b) materials that allow for tailoring of their physical, chemical, and biological properties.
A team of five Fraunhofer Institutes is currently developping materials and techniques to fabricate artificial blood vessel system that will be able to supply artificial tissue in future. We introduce freeform fabrication for the manufacturing of flexible structures from the micrometer to the centimeter range. The technology uses new biocompatible materials and a manufacturing process combining 3-D inkjet printing and laser-based polymerization techniques.
Based on the essential features of the natural vascular system software was developed to find the optimal branching of the artificial network tree, i.e. the length of individual branches, their branching points and branching angles. In order to characterize the artifical structures and to validate the model predictions, an experimental set-up was established for studying pulsatile flows and mechanical responses in artificial vascular systems.
Computational fluid dynamics calculations which take into account the complex blood rheology and the elasticity of the walls are used to find the optimal geometry of bifurcations.
Resins for 3-D rapid prototyping of biomaterials have been developed that fulfill a wide range of requirements: We have optimized photo cross-linkable blend systems with respect to viscosity, curing speed, flexibility, tensile strength and biocompatibility of the post-cured materials. The surfaces of the cross-linked materials provide reactive sites for (bio)-functionalization by chemical coupling of biomolecules.
In order to create biofunctional materials that promote the interaction between material and cells, the cross-linked synthetic materials are covalently coated with biologically active substances e.g. heparin.
After the synthetic material surfaces have been biofunctionalized, endothelial cells are seeded onto the biological coating at the inner vessel wall. The cells are cultured in a bioreactor system which provides a pulsatile flow of culture media mimicking the natural blood flow.
By combining 3-D inkjet printing and laser-based cross-linking processes such as two photon polymerization (TPP), we provide a technical platform which allows the freeform fabrication of structures ranging from the cm to the µm scale. Artificial vessels that provide a functional endothelial barrier represent promising components for in vitro test systems for new drugs or chemicals and therefore help to reduce animal experiments.

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