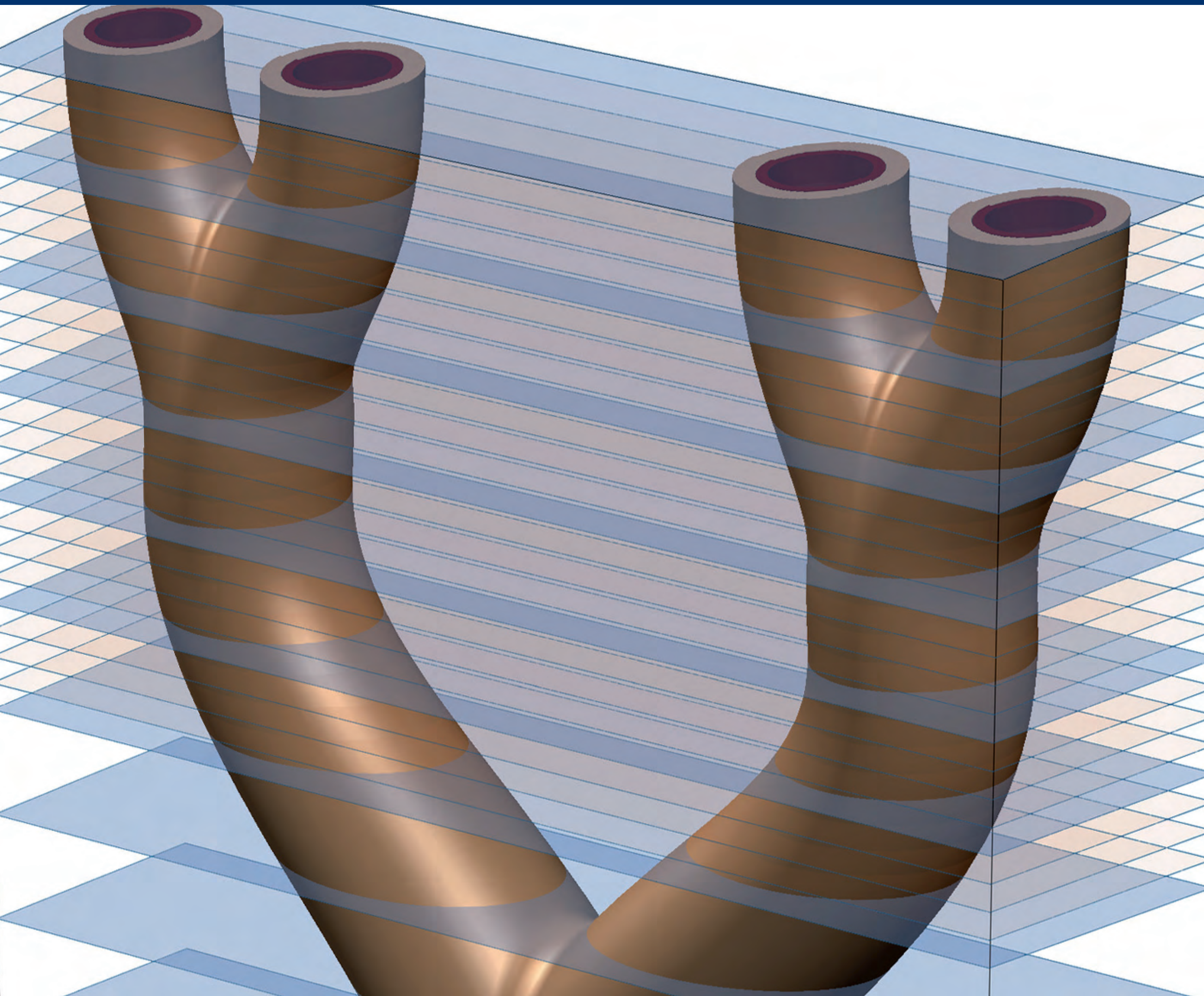
Fraunhofer

RAPID MANUFACTURING TECHNOLOGY FOR BIO-INSPIRED STRUCTURES

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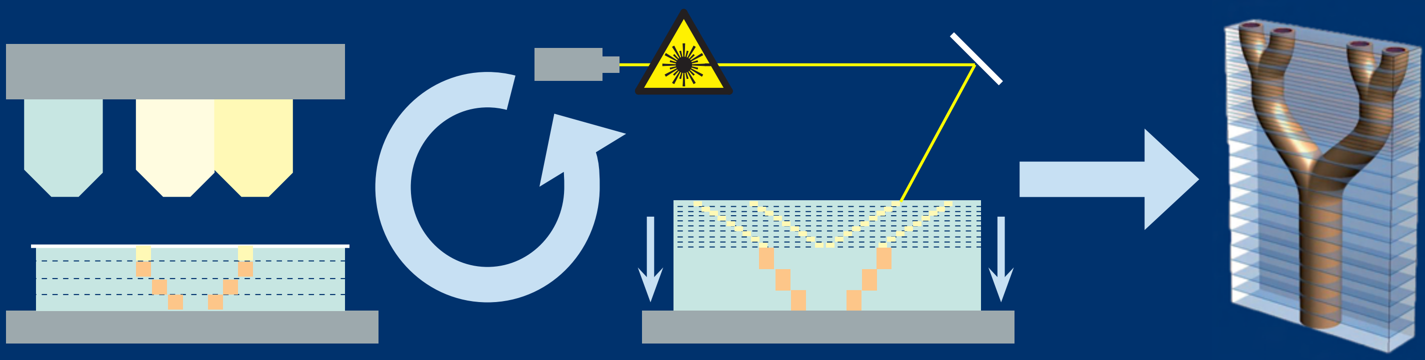

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MANUFACTURING OF BIO-INSPIRED STRUCTURES

WE HAVE GOOD REASONS TO LEARN FROM NATURE!

Nature continually optimizes materials and structures to fulfill complex and multiple functions. We want to develop artificial structures which perform as well as natural ones. In order to do so we need

- fabrication processes that do not set any limits to the generation of structures and shapes
- materials that allow for tailoring of their physical, chemical, and biological properties.

For example, tissue engineering aims to create functional tissues *in vitro* and to use them as transplants or as biomimetic test systems. A key challenge for engineering 3D tissue is to supply the cells with nutrients – as it is done in nature by the vascular system.

HOW CAN WE GENERATE BIO-INSPIRED STRUCTURES?

Fraunhofer introduces freeform fabrication in a new dimension for the manufacturing of flexible structures from the micrometer to the centimeter range. The technology uses new biocompatible materials and a manufacturing process combining 3D inkjet printing and a laser-based polymerization technique for cross-linking with utmost precision. This development is an important step towards future industrial processing of elastic biomaterials and the creation of biofunctional structures for tissue engineering and medical applications.

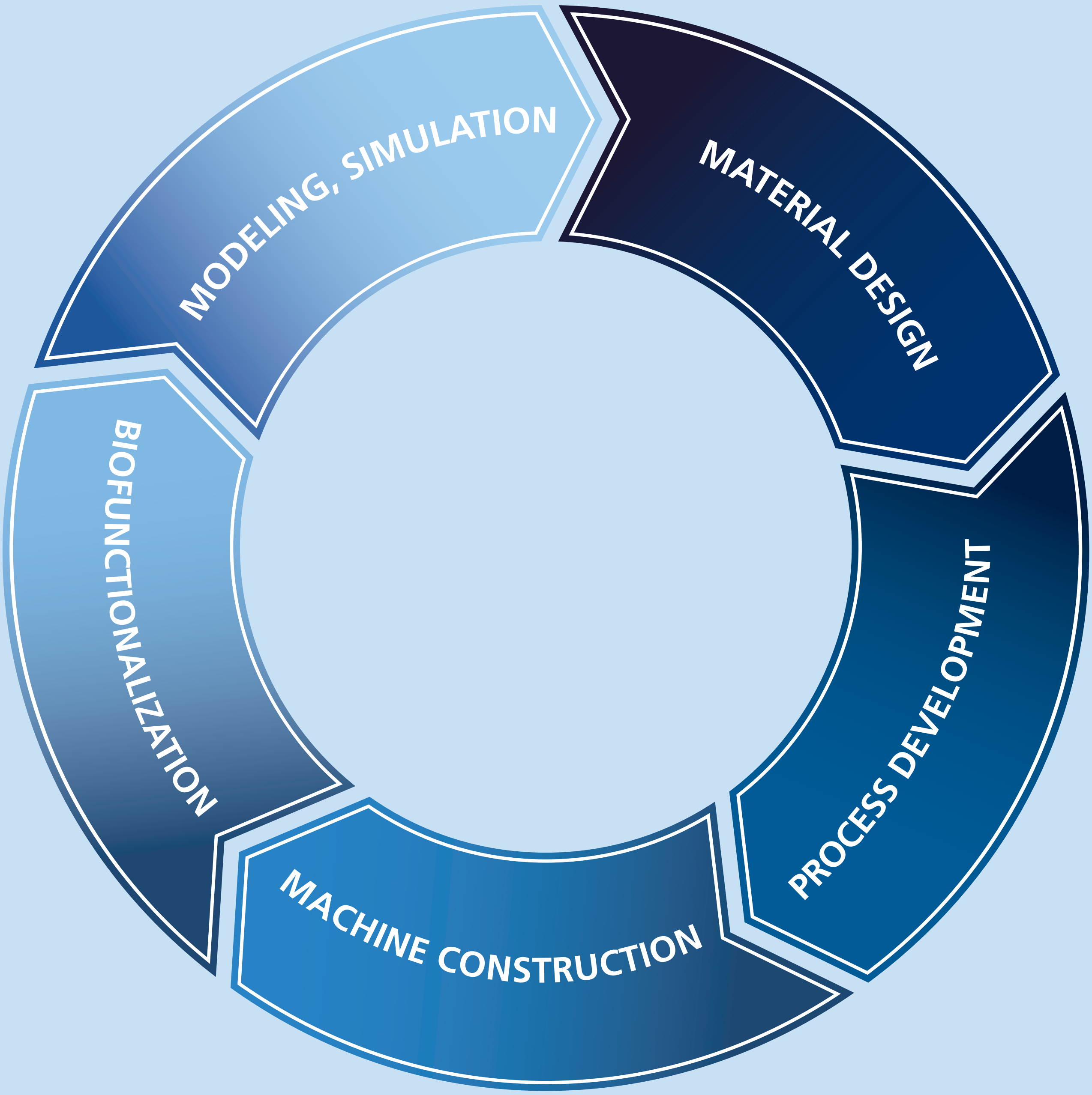
With the help of modeling and simulation, we are developing a bio-inspired technical realization of a vascular system which mimics the functionality of a natural blood vessel system.

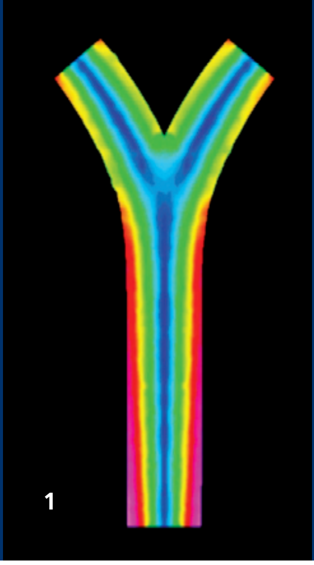
OUR VISION

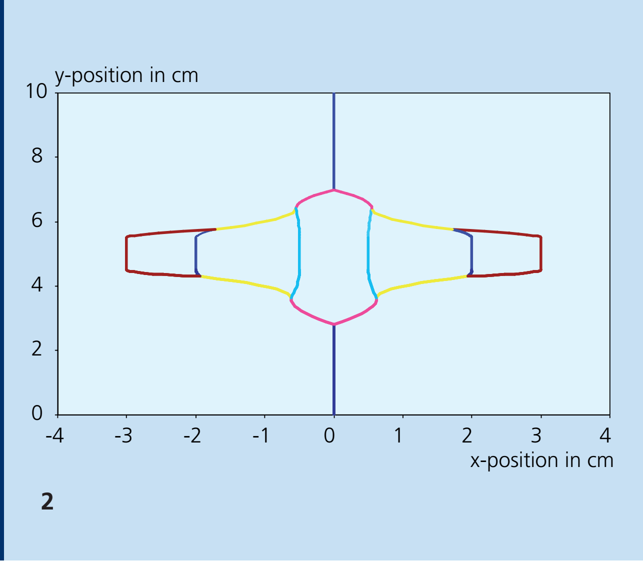
Creating artificial blood vessels with high resolution rapid prototyping and biofunctional materials.

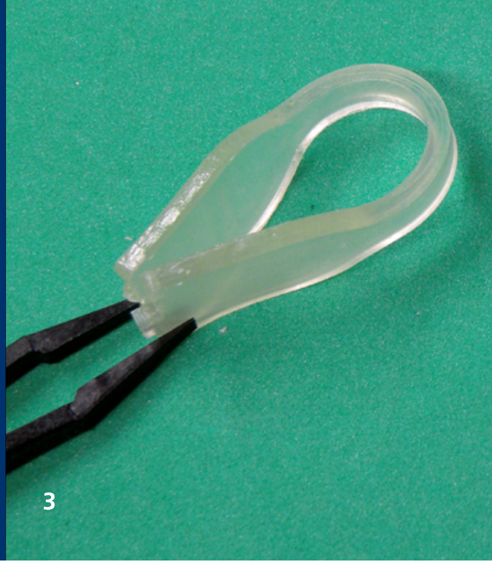
1 *Principle of additive manufacturing based on 3D inkjet printing and two-photon polymerization..*

Natural systems are able to execute complex functions because their forms and materials have been optimized in the course of evolution. A multi-disciplinary team of Fraunhofer-researchers cooperates in order to create a biomimetic technical implementation of a blood vessels system.









BIOMIMETIC DESIGN – THE IMPORTANCE OF MODELING AND SIMULATION

The vascular system consists of a branched network of vessels which conduct the blood from the heart to numerous capillaries, thus supplying the body's tissue with nutrients. The basic features of the natural vascular system can be used to design an artificial blood vessel network. 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). The calculations are based on the optimization principles which underlie the geometry of natural vascular systems. In addition, the local geometry of the artificial network is optimized in order to achieve good flow conditions: the shear stresses at the vascular walls have to lie within a suitable range in order to stimulate endothelial cells, and dead flow zones have to be avoided in order to prevent a stenosis (clogging) of the blood vessel or thrombus formation. Computational fluid dynamics calculations which take into account the complex blood rheology and the elasticity of the walls are used to find the optimal local vessel structure.

In order to characterize the additive manufactured structures and to validate the model predictions, an experimental set-up is available for studying pulsatile flows and mechanical responses in artificial vascular systems.

1 *Simulation of the shear stress in a bifurcation.*

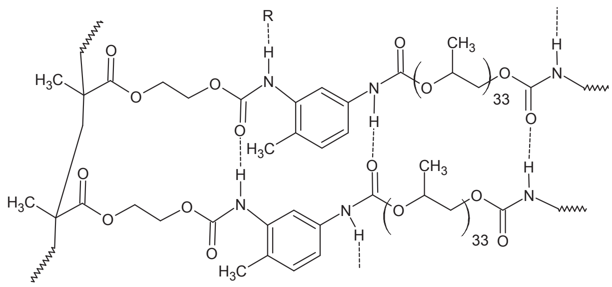
2 *Biomimetic geometrical model of the blood vessel network.*

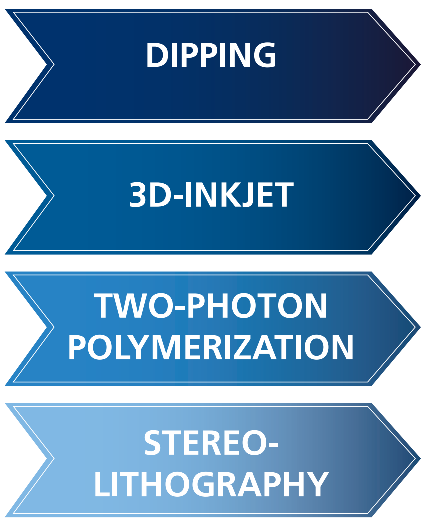
3 *Biocompatible elastomeric material.*

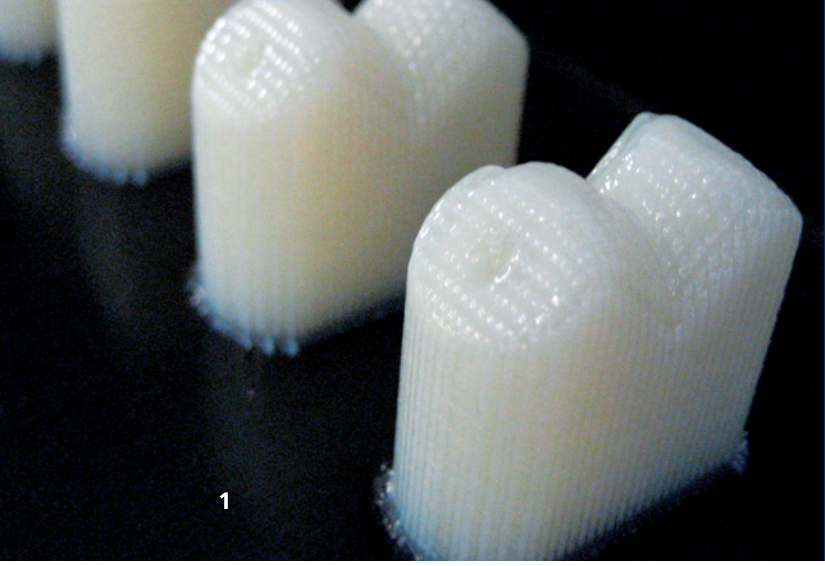
PRINTABLE RESINS: FLEXIBLE POLYMER MATERIALS – MULTIPLE MATERIAL DEMANDS

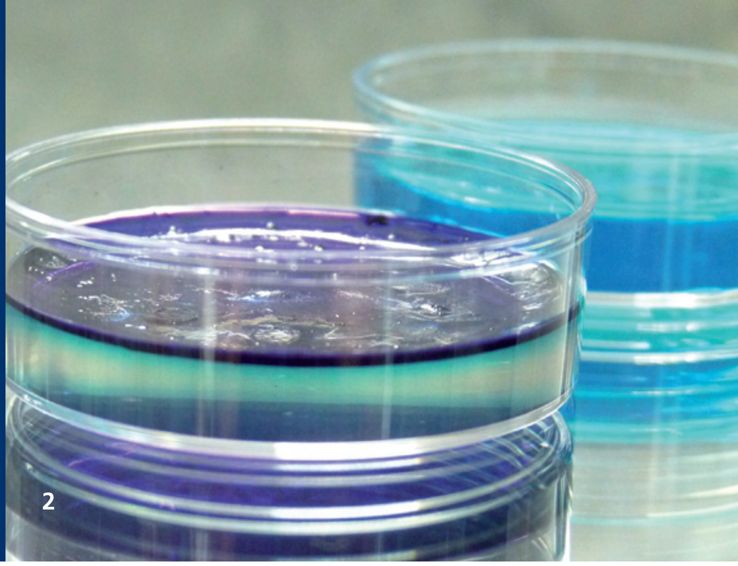
Resins for 3D rapid prototyping of biomaterials need to fulfill a wide range of requirements. They have to be suitable for the chosen process such as printing, two-photon polymerization, stereolithography or casting. The processed material has to be biocompatible and possess the required material properties.

We have optimized photo cross-linkable blend systems with respect to viscosity, curing speed, and wavelength of the photo initiation and flexibility, tensile strength and hydrophobicity of the post-cured materials. The surfaces of the cross-linked materials provide reactive sites for (bio)-functionalization by chemical coupling of biomolecules.









FREEFORM FABRICATION AT HIGH RESOLUTION – TAILORED MANUFACTURING TECHNIQUES

Additive manufacturing methods permit the production of objects with complex shape. By combining 3D 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 centimeter to the micrometer scale.

Photosensitive materials are deposited by 3D inkjet printing and cross-linked by UV-irradiation to build up structures layer-by-layer. In order to generate micro-scale features, TPP is used to polymerize high resolution structures such as capillaries and pores within the layer of resin deposited by the inkjet process (see graphic on page 3).

BIOFUNCTIONAL MATERIALS – FROM BIOCOMPATIBILITY TO BIOFUNCTION

Once the specific mechanical properties have been adjusted by tailoring the chemical material composition, then the biological properties can be customized. Cytotoxicity tests are performed in order to evaluate the cytocompatibility of novel materials, and appropriate rinsing processes are developed in order to remove soluble toxic components. In order to create biofunctional materials that promote the interaction between material and cells, the cross-linked synthetic materials are coated with biologically active substances. Alternatively, materials can be made biofunctional by modifying biomolecules in such a way so that they can be blended directly into the synthetic resins or inks before cross-linking.

CELL BIOLOGY – TOWARDS LIVING SYSTEMS

Creating vascular systems from synthetic polymers is challenging because many of the materials which are used are potentially thrombogenic. The surface of the artificial vessel walls is covered with a confluent layer of endothelial cells. In this way the vessel walls more closely resemble natural vessels and will be less prone to thrombus formation. After the synthetic material surfaces have been biofunctionalized, the 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.

Artificial vessels that provide a functional endothelial barrier represent promising components for *in vitro* test systems for new drugs or chemicals. Moreover, the ability to supply pre-seeded artificial vessels might be one step on the way towards producing functional artificial vessel substitutes with small diameters for coronary artery bypass grafting.

1 *Branched tube structures during additive manufacturing process.*

2 *Stained biomolcule coating covering a synthetic hydrogel.*

THE FRAUNHOFER-GESELLSCHAFT

Research of practical utility lies at the heart of all activities pursued by the Fraunhofer-Gesellschaft. Founded in 1949, the research organization undertakes applied research that drives economic development and serves the wider benefit of society. Its services are solicited by customers and contractual partners in industry, the service sector and public administration.

At present, the Fraunhofer-Gesellschaft maintains more than 80 research units in Germany, including 60 Fraunhofer Institutes. The majority of the more than 18,000 staff are qualified scientists and engineers, who work with an annual research budget of €1.65 billion. Of this sum, more than €1.40 billion is generated through contract research. More than 70 percent of the Fraunhofer-Gesellschaft's contract research revenue is derived from contracts with industry and from publicly financed research projects. Almost 30 percent is contributed by the German federal and Länder governments in the form of base funding, enabling the institutes to work ahead on solutions to problems that will not become acutely relevant to industry and society until five or ten years from now.

Affiliated international research centers and representative offices provide contact with the regions of greatest importance to present and future scientific progress and economic development.

With its clearly defined mission of application-oriented research and its focus on key technologies of relevance to the future, the Fraunhofer-Gesellschaft plays a prominent role in the German and European innovation process. Applied research has a knock-on effect that extends beyond the direct benefits perceived by the customer: Through their research and development work, the Fraunhofer Institutes help to reinforce the competitive strength of the economy in their local region, and throughout Germany and Europe. They do so by promoting innovation, strengthening the technological base, improving the acceptance of new technologies, and helping to train the urgently needed future generation of scientists and engineers.

As an employer, the Fraunhofer-Gesellschaft offers its staff the opportunity to develop the professional and personal skills that will allow them to take up positions of responsibility within their institute, at universities, in industry and in society. Students who choose to work on projects at the Fraunhofer Institutes have excellent prospects of starting and developing a career in industry by virtue of the practical training and experience they have acquired.

The Fraunhofer-Gesellschaft is a recognized non-profit organization that takes its name from Joseph von Fraunhofer (1787–1826), the illustrious Munich researcher, inventor and entrepreneur.

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