3D Laser Lithography in Biotechnology and Medical Technology

High-Precision, Piezo-Based Nanopositioning Systems Advance Technology

Physik Instrumente (PI) GmbH & Co. KG_Auf der Roemerstrasse 1_76228 Karlsruhe, Germany
Tel. +49 721 4846-0, Fax +49 721 4846-1019 Email info@pi.ws, www.pi.ws

Laser technology makes it possible to create even very complex three-dimensional micro- and nanostructures in photosensitive materials. However, the high precision in three-dimensional "laser writing" required for such applications can only be realized when the materials to be processed are positioned in a correspondingly precise manner. Here, piezo-based nanopositioning systems can play out their strengths: they work with repeatability in the nanometer range with response times of less than a millisecond and thereby offer ideal prerequisites for a high reproducibility and precise path control. The application described in the following is proof of this.

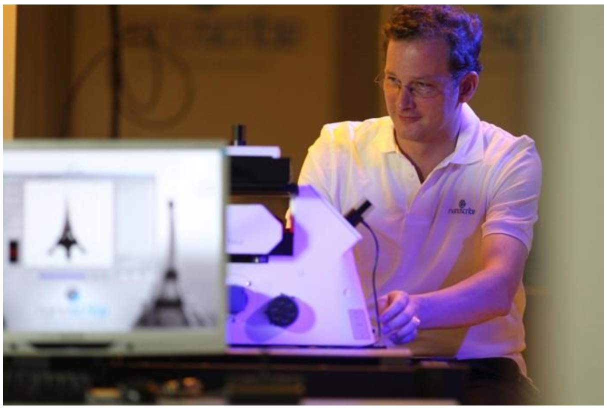

Fig. 1 Laser lithography system of Nanoscribe GmbH, which can be used to produce complex three-dimensional micro- and nanostructures in photosensitive materials. The structure data can be created with conventional CAD software (image: Nanoscribe GmbH)

Nanoscribe GmbH, located in Eggenstein-Leopoldshafen near Karlsruhe, Germany, sells laser lithography systems (Fig. 1) that can be used to realize complex three-dimensional micro- and nanoobjects in a fully automatic and reproducible way with a previously unavailable design flexibility and structure heights up to the millimeter range.

Today, this already benefits numerous applications, e.g. microstructures can be created via "laser writing" for small pumps and needles (Fig. 2) or surfaces can be equipped with particular biomimetic characteristics. Important keywords in this connection are gecko or lotus effect. A typical area of application for 3D laser lithography respectively 3D printing is also the creation of three-dimensional structures for cell biology.

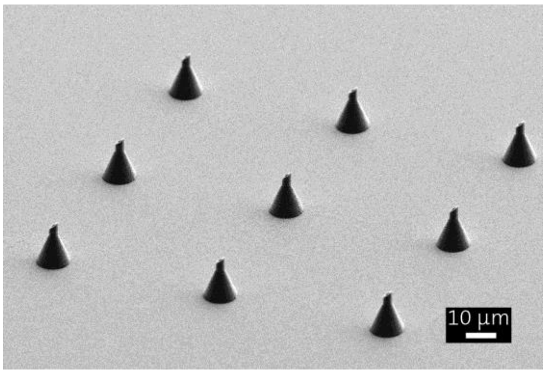

Fig. 2 Microinjection needles fabricated by 3D laser lithography (image: Nanoscribe GmbH)

Cell Cultivation in the Third Dimension

There are limits to classic cell cultivation in a flat Petri dish. This is because in natural tissue, cells in an organism are normally in an extracellular matrix, in other words in a three-dimensional and simultaneously flexible environment in a spatial network.

A Petri dish cannot simulate these real environmental conditions. As a result, its application possibilities are limited. A remedy is provided by the described method, which has been utilized by scientists at the Karlsruhe Institute of Technology (KIT). Using 3D laser lithography, flexible and freely designed structures can also be created. This means that cells can colonize a specially tailored spatial matrix, in other words a scaffold (Fig. 3).

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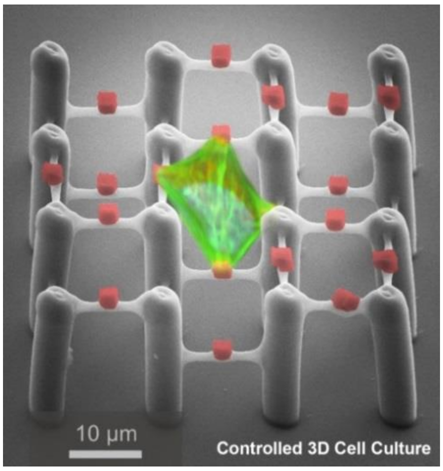

Fig. 3 Three-dimensional structure: Cells docking on the "handles" (image: courtesy of Prof. Dr. Martin Bastmeyer, Zoological Institute at KIT)

The displayed structure itself consists of 25 µm high posts that are connected with thin rungs at different heights. This basic structure consists of a protein-repellent polymer. In addition, "handholds" or "docking sites" for the cells are located in the middle of the rungs. The cells can selectively affix here because special adhesive proteins are attached at these positions. Such a matrix opens up numerous new possibilities (Fig. 4).

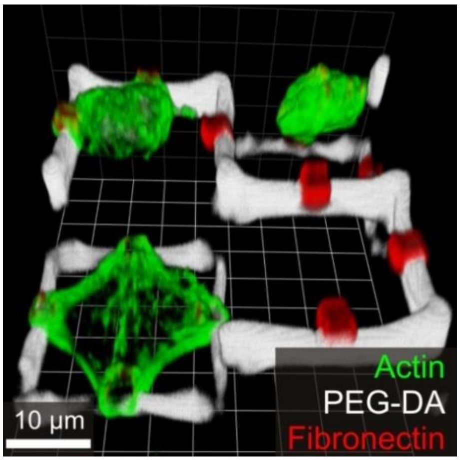

Fig. 4 The influence of the physical environment on stem cell differentiation or cell migration can be investigated with tailored cell scaffolds (image: courtesy of Prof. Dr. Martin Bastmeyer, Benjamin Richter, KIT)

In this way, the influence of the physical environment (stiffness and architecture) on stem cell differentiation or cell migration can be investigated. Forces can be measured and reactions to various stimuli can be observed and analyzed. The results include knowledge regarding tissue regeneration or the influence of active pharmaceutical ingredients on wound healing, for example.

"Writing" with a Laser Pen

How structures are fabricated is not trivial at all, however, the principle is easy to understand: as a result of strongly focusing ultrashort laser pulses into the photosensitive and biologically compatible polymer, the polymer is exposed to light in the focus through a nonlinear process.

Comparable to a pen that is guided in three dimensions, the laser beam writes into the material along any desired paths. Line widths from several micrometers down to 150 nm are achieved in this way.

However, a high precision with the 3D trajectory writing mode can only be realized when the positioning is correspondingly precise. During the writing process, the laser and focus remains fixed and the workpiece has to be moved according to the three-dimensional writing task.

The difficulty is compounded even more by the fact that it is not enough to move towards certain positions in a highly precise manner. The path is just as important as the target here, and the application therefore also requires a precise path control. During the travel, the laser intensity is then varied according to the track speed, in order to achieve the desired printing result.

The system used for sample positioning is thus a key component of the laser lithography device "Photonic Professional" of Nanoscribe GmbH.

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Precise Positioning of the Laser Focus

Here a positioning system was chosen from the product range of the PI (Physik Instrumente) company, located in Karlsruhe, Germany. PI offers the world's largest selection of high-dynamics and high-resolution piezo nanopositioning systems for scientific and industrial applications (Fig. 5, Fig. 6).

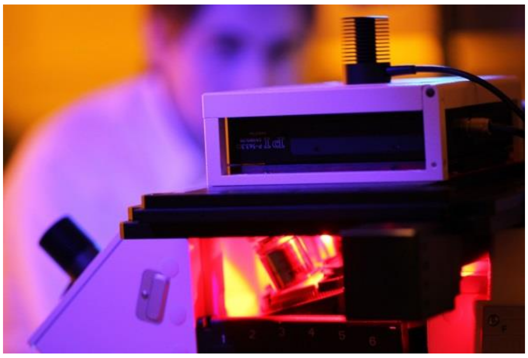

Fig. 5 The fine adjustment of the object or sample is performed by the piezo nanopositioning *system (image: Nanoscribe GmbH)*

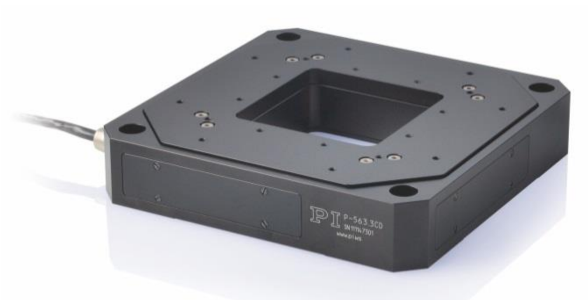

Fig. 6 The piezo nanopositioning system not only works with high precision but can also be integrated well in the device (image: PI)

The multi-axis stage P-563 is set on a usual microscope XY scanner stage, which allows a positioning range of the piezo writing volume on an area of up to 100 × 100 mm². The travel range of the piezo can cover a writing volume of up to 300 × 300 × 300 µm³, whereby the repeatability is in the nanometer range.

Piezo actuators are the driving force behind this nanopositioning system. These piezo actuators convert electrical energy directly into mechanical energy and vice versa. At the same time, travel ranges of up to around one millimeter can be achieved with resolutions down to the nanometer range and high dynamics with frequencies of up to several kilohertz.

The very high motion resolution is only possible because the motion is based on crystalline effects and there are no classic mechanical components that have friction or mechanical play. Piezo actuators can furthermore move heavy loads and have a compact design.

Capacitive Sensors and Parallel Kinematics

Highly linear capacitive sensors integrated in the positioning system provide the precise actual value acquisition that is necessary to move the sample precisely and repeatably in relation to the laser focus. These sensors directly detect the motion and thereby allow a higher phase reliability and bandwidth than indirect systems.

The construction of the stage as a parallel kinematics multi-axis system also contributes to the high positioning accuracy. The piezo actuators are integrated in a frictionless parallel kinematics guide system with solid joints. All piezo actuators act on a central platform. This makes it possible to achieve an identical dynamic behavior for all motion axes.

This is especially advantageous in 3D lithography since the objects can have any type of structure. A "slower" axis, as is used e.g. during a line scan, would have an adverse effect here.

In addition, the sensors detect all controlled degrees of freedom simultaneously. This parallel metrology makes it possible to actively prevent axis crosstalk and lateral runout. This benefits path accuracy and reproducibility.

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A digital controller provides the necessary path control. The controller as well as the nanopositioning system come from the PI program. It is specially matched to the multi-axis, parallel-kinematics, piezo nanopositioning systems. This also fulfills the very high requirements for path control with 3D lithography devices.

The high-precision piezo nanopositioning systems thereby significantly contribute to bringing lithography technology a decisive step forward. This not only benefits users in medical technology and biotechnology but in other sectors as well.

Areas of application for three-dimensional "laser writing" are also found e.g. in the manufacturing of micro-optic components, photonic crystals and metamaterials as well as in the rapid prototyping of micro- and nanostructures, for example in micro-fluidic channels.

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Authors

Steffen Arnold, Head of “Marketing and Products” at Physik Instrumente (PI) GmbH & Co. KG

Martin Hermatschweiler, Managing Director of Nanoscribe GmbH

About Nanoscribe

Nanoscribe GmbH, the first spin-off of Karlsruhe Institute of Technology (KIT) introduced the 3D laser lithography system PhotonicProfessional on the market in early 2008.

Over the last five years, the company has established itself as market and technology leader in the area of 3D laser lithography. The multitude of systems sold to leading research institutes and universities across the world demonstrates the triumph of this innovative technology.

The portfolio of the company additionally comprises in-house developed resists tailored to the different needs of customers. The portfolio is completed by consultation on reproducing these three-dimensional polymer structures in metals or semiconductors.

About PI (Physik Instrumente)

In the past four decades, PI (Physik Instrumente) with headquarters in Karlsruhe, Germany has become the leading manufacturer of nanopositioning systems with accuracies in the nanometer range.

With four company sites in Germany and ten sales and service offices abroad, the privately managed company operates globally. Over 700 highly qualified employees around the world enable the PI Group to meet almost any requirement in the field of innovative precision positioning technology. All key technologies are developed in-house. This allows the company to control every step of the process, from design right down to shipment: precision mechanics and electronics as well as position sensors.

The required piezoceramic elements are manufactured by our subsidiary PI Ceramic in Lederhose, Germany, one of the global leaders for piezo actuator and sensor products. PI miCos GmbH in Eschbach near Freiburg, Germany, is a specialist for positioning systems for ultrahigh vacuum applications as well as parallel-kinematic positioning systems with six degrees of freedom and custom-made designs.

PI headquarters in Karlsruhe, Germany: More than 350 employees work on high-resolution drive systems and positioning systems