MICRO-FABRICATION METHOD OF POLYMER STRUCTURES FOR SCAFFOLDING FOR TISSUE REGENERATION AND BIOSENSOR DEVELOPMENT

INVENTORS: Gianluca Ciardelli
Paolo Giusti
Ilaria Morelli
Giovanni Vozzi

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Invention

The patented invention relates to the **micro-fabrication of imprinted polymeric structures with well-defined geometry for the fabrication of bioactive scaffolds**. The scaffolds can be used both as **substrates** for the study and fabrication of functional tissue substitutes and as **biosensors**.

Molecular Imprinting is a methodology , strongly developped in recent decades: it enables the fabrication of **cavities with synthetic polymeric structures with recognition properties**, **predetermined selectivity and high affinity**. This technique is based on the system used by enzymes for substrate recognition, through the so-called **"key-lock" model**.

The patented technology enables the fabrication of bioactive structures through the integration of soft-lithography and molecular imprinting of an adhesion protein, as a new microfabrication technique.

After a careful review of the literature, no methodology appears to be present to merge the principles of microfabrication with the method of molecular imprinting. Above all, there is no work in the literature involving the fabrication of polymeric microstructures with imprinted cells.

Drawings & pictures

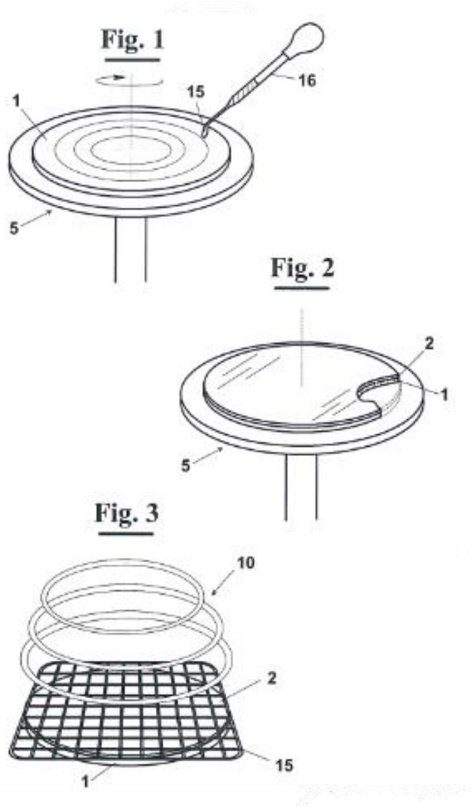

Fig. 1 - Silicon wafer on spin coater to undergo photolithography step for making a substrate with a mold function; **Fig.2** - Terminal stage of spin coating; **Fig. 3** - Overlay of the wafer in Fig. 2 coated with a transparency that reproduces a drawing of a cellular arrangement topology in a plane.

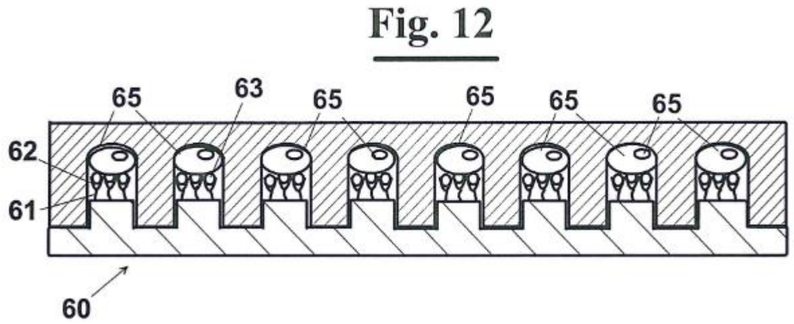

Fig. 12 - Polymer poured onto the mold (60) functionalized and moistened molecules and cells of interest

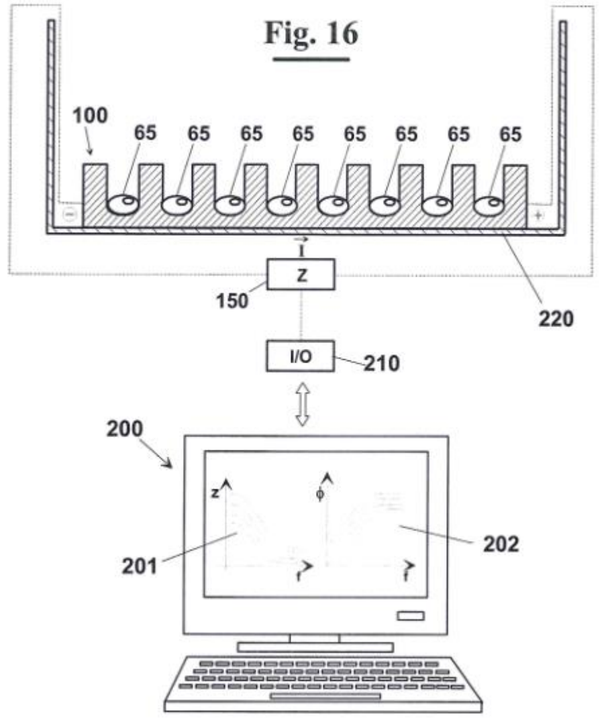

Fig. 16 - Possibility offered by the invention to monitor cell growth over time using an impedance meter.

Industrial applications

The present invention relates to the field of **bioengineering** and more specifically relates to a method for the **micro-fabrication of polymeric structures** with well-defined geometry for the fabrication of **scaffolds for tissue regeneration**, for the creation of **cellular models** for biological tissues, or for the **development of biosensors**.

The methodology described here finds application in several areas:

- **Tissue engineering** for the fabrication of microfabricated polymer scaffolds for tissue regeneration;
- **Pharmaceutical companies** for drug testing: the cells, once adhered, proliferated and having activated their cellular processes, represent valid cellular models of biological tissue;
- **Sensor and biosensor companies**: such systems can be used to recognize the presence of imprinted molecules in unknown solutions and assess their binding;
- **Biomedical companies** for the fabrication of polymeric structures to be implanted or integrated into medical devices; these medical device can release drugs in a controlled manner or perform clinical in-loco analyses by introducing the microfabricated polymeric system into the examination site and analyzing the presence of a particular biomolecule, with which it has been imprinted, by analyzing the change in its impedance.

Possible developments

The methodology developed is based on making a **silicone mold with a well-defined topology** by casting on a master obtained by photolithographic technique and presenting the negative of the geometry to be made. The obtained silicone mold, given its hydrophobic nature, is subjected to physical and chemical treatments in order to make it **hydrophilic**. In order to anchor proteins or molecules to be imprinted in the polymer to this modified surface, two consecutive chemical reactions were performed: a) a derivatization with polyfunctional silanes in toluene and b) an activation of the reaction between carboxyl and nucleophilic groups. The microfabricated and surface-modified mold is active in order to be able to bind the molecules to be imprintable.

Imprinting proteins or portions thereof, as well as whole cells, could ensure scaffolds with better biological interaction properties than those commonly produced and used. Moreover, the presence of the imprints could favor the binding of the chosen molecules to the supporting structures, even under conditions of chemical-physical incompatibility of the materials involved, as in the case of contact between a hydrophobic surface and an aqueous solution.

Polymers obtained by the patented method have been used in numerous applications, from materials for separations to substitutes for antibodies and enzymes, from recognition elements in biosensors to systems for controlled drug delivery.

The research team has extensive experience in the design and development of polymer microstructures and is studying similar and increasingly cutting-edge technologies, with the goal of increasing the technological readiness levels of the inventions and adapting microstructures to various needs.

The team is interested in collaborating with industrial partners and considering possible licensing or transfer of the invention for commercialization by interested companies.

For more information:

Tech Transfer Office of University of Pisa

Headquarters: Lungarno Pacinotti 43/44, Pisa (PI) 56126

Web site: www.unipi.it/index.php/trasferimento

E-mail: valorizzazionericerca@unipi.it

For more information:

Ufficio Regionale di Trasferimento Tecnologico

Sede: Via Luigi Carlo Farini, 8 50121 Firenze (FI)

E-mail: urtt@regione.toscana.it

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