www.envisiontec.com

Biofabrication

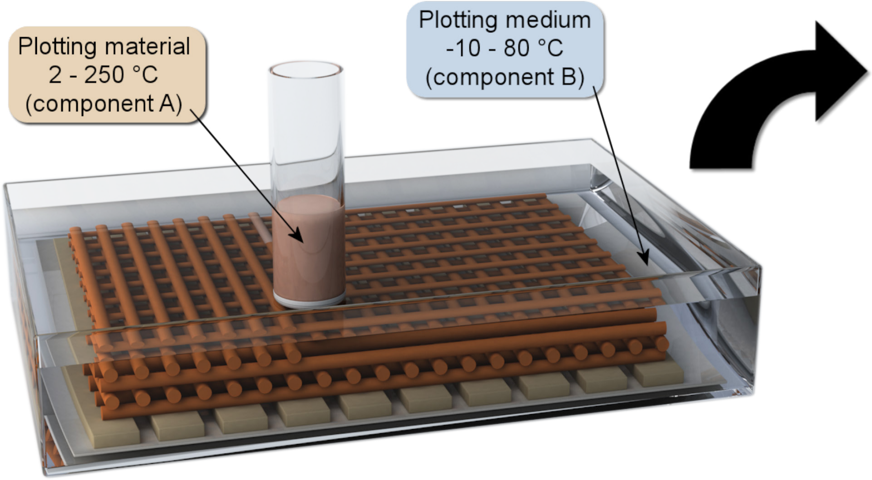
3D Bioprinting - The Future Is Now!

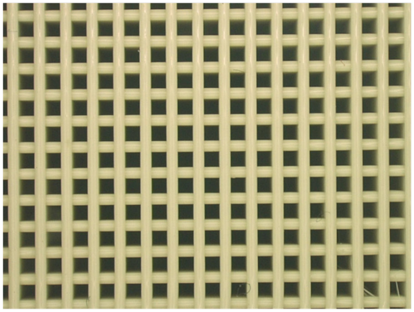
The EnvisionTEC 3D-Bioplotter® system has been used since 2000 for a variety of medical applications. Most research done to date using our machines has been in the pre-clinical setting, yielding many publications by pre-eminent scientists from the materials science, neuroimaging, and toxicology disciplines. In the clinical setting, patient CT or MRI scans are used to create STL files to print solid 3D models which can then be used as templates for implants.

Tissue Engineering and Controlled Drug Release require 3D scaffolds with well-defined external and internal structures. The 3D-Bioplotter® has the capacity of fabricating scaffolds using the widest range of materials of any singular Rapid Prototyping machine, from soft hydrogels over polymer melts up to hard ceramics and metals. Complex inner patterns can easily be designed using the 3D-Bioplotter® software to both control the mechanical properties, increase cell adhesion, as well as improve the flow of nutrient media throughout the interconnecting pores of the printed implants.

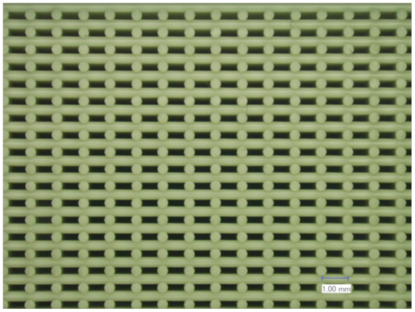
Al Siblani - CEO EnvisionTEC

The 3D-BIOPLOTTER® Process





3D non-woven with interconnecting pores



A simple process:

A liquid, melt, paste or gel is dispensed from a material cartridge through a needle tip from a 3-axis system to create a 3D object.

One single requirement:

The material to be used must, through a physical or chemical reaction, solidify.

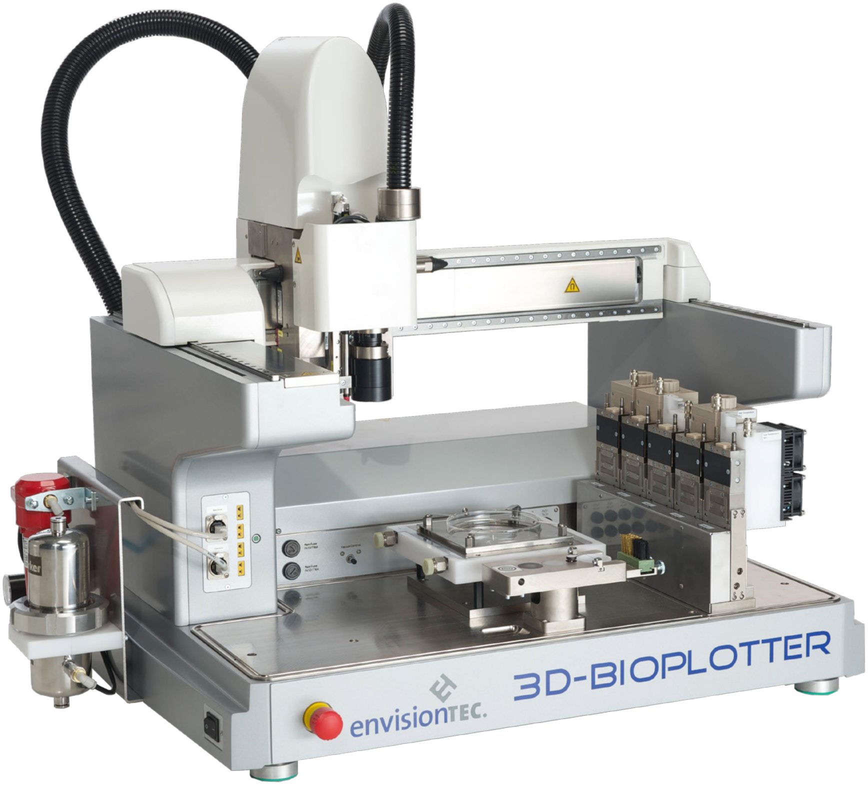
A world of possibilities:

The widest range of materials of any 3D printing technology can be processed.

Unique to the 3D-BIOPLOTTER® Process

- Uses raw materials (powder, pellets, etc.) without requiring a preprocessed filament.
- Medical-grade materials can be used.
- Designed for use in a sterile biosafety cabinet with built-in sterile and particle filters for the input compressed air.
- Materials are kept in sterilizable cartridges, thus avoiding touching the machine: easier to clean and sterilize.
- Each customer can create their own processing parameters.
- Not locked to any proprietary materials, customers can choose their prefered vendors, as well as required medical grades, mixture compositions and concentrations, additives, etc..

4th Generation 3D-BIOPLOTTER® MANUFACTURER SERIES



- Designed both as a tool for advanced Tissue Engineering research, as well as for use in a production environment.

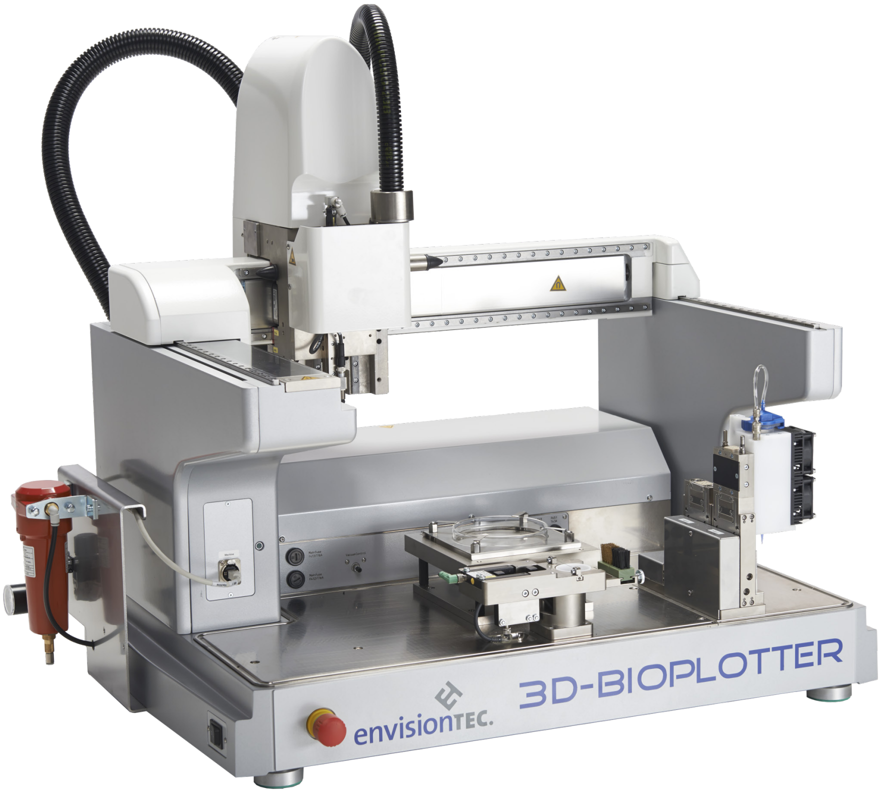
- Capable of using all hardware and software options of the 3D-Bioplotter Series.

- Includes heated platform and sterile filter, recommended for Cell Printing / Organ Printing.

Machine Specification
Manufacturer Series

Axis Resolution (XYZ)	0.001 mm (0.00004”)
Speed	0.1 - 150 mm/s (0.004” - 5.91”/s)
Pressure	0.1-9.0 bar (1.45 - 130 psi)
Build Volume (XYZ)	150 x 150 x 140 mm (5.91” x 5.91” x 5.51”)
Needle Position Control	Z-Sensor + High Resolution Camera
Camera Resolution (XY)	0.009 mm (0.00035”) per Pixel
Needle Sensor Resolution (Z)	0.001 mm (0.00004”)
Minimum Strand Diameter	0.100 mm (0.004”) - Material Dependent
Number of Materials per Scaffold	Maximum 5 Materials Using 5 Print Heads
Print Heads Included	1x Low and 1x High Temperature Head
Filters Included	Particle and Sterile Filters
Platform Temperature Control	Heating and cooling capable (-10°C to 80°C)
Platform Height Control	Automatic z-height controlling system
Material Calibration	Semi-Automatic Material Calibration
Additional Features	Automated nozzle cleaning process
	4 external temperature sensor ports
	Layer by Layer Photographic Log

4th Generation 3D-BIOPLOTTER®
DEVELOPER SERIES



- Designed for research groups new to the field of Tissue Engineering, as well as for specialized use, where the limited capability may still meet requirements.
- Consisting of the same basic hardware and software as the Manufacturer Series, but with reduced functionality regarding camera, build platform and park positions.
- Not upgradable to the same capability of the Manufacturer Series.

Machine Specification
Developer Series

Axis Resolution (XYZ)	0.001 mm (0.00004”)
Speed	0.1 - 150 mm/s (0.004” - 5.91”/s)
Pressure	0.1 - 9.0 bar (1.45 - 130 psi)
Build Volume (XYZ)	150 x 150 x 140 mm (5.91” x 5.91” x 5.51”)
Needle Position Control	Photo Sensor
Camera Resolution (XY)	-
Needle Sensor Resolution (Z)	0.001 mm (0.00004”)
Minimum Strand Diameter	0.100 mm (0.004”) - Material Dependent
Number of Materials per Scaffold	Maximum 2 Materials Using 2 Print Heads
Print Heads Included	1x Low Temperature Head
Filters Included	Particle Filter
Platform Temperature Control	-
Platform Height Control	Automatic z-height controlling system
Material Calibration	Semi-Automatic Material Calibration
Additional Features	Automated nozzle cleaning process
	-
	-

Key Features 3D-BIOPLOTTER®

Input of outer shapes through STL files.

Multi-part and multi-material capable through the use of an automatic tool changer and multiple print heads.

Database of inner patterns (user-editable) in the controlling software, avoiding requiring patterns in the STL files.

Database of materials (user-editable) with all process parameters.

Individual temperature control of each printing head, both in the parking positions, as well as during printing.

2D Dot-Printing (Biopatterning) capability.

Complete control of all printing parameters (temperature, pressure, speed, etc) through the software.

Temperature curves with up to 5 set points and waiting times.

Low Temperature Print Head (0°C to 70°C) with disposable PE cartridges.

High Temperature Print Head (30°C to 250°C) with reusable stainless steel cartridges.

Automatic Platform Height Control for Petri Dishes, Well Plates, as well as other printing surfaces.

UV Curing Head (365 nm).

Needle cleaning station, with automatic cleaning before and during the print project available.

Luer Lock needle tips, 0.1mm to 1.0mm inner diameter available.

LOG file creation after project completion with all relevant data.

Footprint (L x W x H): 976 x 623 x 773 mm (38.4" x 24.5" x 30.4")
Weight: 130 kg (286.6 lb)
Electrical Requirements: 100-240 V AC, 50/60 Hz
Compressed Air Requirements: 6 - 10 bar (85 - 145 psi)

Application: Bone Regeneration

Ceramic/Metal Pastes	Thermoplasts
Hydroxyapatite	PCL
Titanium	PLLA
Tricalcium Phosphate	PLGA
Sintering	Phase Transition

Sample Papers:

- Li, J. P., et al. „**The effect of scaffold architecture on properties of direct 3D fiber deposition of porous Ti6Al4V for orthopedic implants.**" Journal of Biomedical Materials Research Part A 92.1 (2010): 33-42.
- Haberstroh, Kathrin, et al. „**Bone repair by cell-seeded 3D-bioplotted composite scaffolds made of collagen treated tricalciumphosphate or tricalciumphosphate-chitosan-collagen hydrogel or PLGA in ovine critical-sized calvarial defects.**" Journal of Biomedical Materials Research Part B: Applied Biomaterials 93.2 (2010): 520-530.
- Kim, Yoo Suk, et al. „**The Application of Three-Dimensional Printing in Animal Model of Augmentation Rhinoplasty.**" Annals of Biomedical Engineering (2015): 1-10
- Lindhorst, Daniel, et al. "**Effects of VEGF loading on scaffold-confined vascularization.**" Journal of Biomedical Materials Research Part A 95.3 (2010): 783-792.

Application: Drug Release

Thermoplasts

PCL

PLLA

PLGA

Phase Transition

Sample Papers:

- Kammerer, M., et al. „**Valproate release from polycaprolactone implants prepared by 3D- bioplotting.**" Die Pharmazie-An International Journal of Pharmaceutical Sciences 66.7 (2011): 511-516.
- Yilgor, P., et al. „**An in vivo study on the effect of scaffold geometry and growth factor release on the healing of bone defects.**" Journal of tissue engineering and regenerative medicine 7.9 (2013): 687-696.
- Yuan, Jing, et al. „**The preliminary performance study of the 3D printing of a tricalcium phosphate scaffold for the loading of sustained release anti-tuberculosis drugs.**" Journal of Materials Science 50.5 (2015): 2138-2147.
- Min Zhu, Kun Li, Yufang Zhu, Jianhua Zhang, Xiaojian Ye. „**3D-printed hierarchical scaffold for localized isoniazid/rifampin drug delivery and osteoarticular tuberculosis therapy**". Acta Biomaterialia, Volume 16, 1 April 2015, Pages 145-155.

Application: Soft Tissue Fabrication
Cell Printing & Organ Printing

<table>
<tr><th colspan="4">Hydrogels</th></tr>
<tr><td>Agar</td><td>Soy</td><td>Alginate</td><td>Chitosan</td></tr>
<tr><td>Gelatin</td><td>Hyaluronic Acid</td><td>Fibrin</td><td>Collagen</td></tr>
<tr><td colspan="2">Phase Transition</td><td>2 Component System</td><td>Precipitation</td></tr>
</table>

Sample Papers:

- Maher, Paul S., et al. „**Thermal imaging analysis of 3D biological agarose matrices.**“ International Journal of Medical Engineering and Informatics 3.2 (2011): 167-179.
- Billiet, Thomas, et al. „**The 3D printing of gelatin methacrylamide cell-laden tissue-engineered constructs with high cell viability.**“ Biomaterials 35.1 (2014): 49-62.
- Chien, Karen B., et al. „**In vivo acute and humoral response to three-dimensional porous soy protein scaffolds.**“ Acta Biomaterialia 9.11 (2013): 8983-8990.
- Chung, Eun Ji, Adam E. Jakus, and Ramille N. Shah. “**In situ forming collagen–hyaluronic acid membrane structures: mechanism of self-assembly and applications in regenerative medicine.**” Acta Biomaterialia 9.2 (2013): 5153-5161.
- Wang, Min-Dan, et al. “**Novel crosslinked alginate/hyaluronic acid hydrogels for nerve tissue engineering.**” Frontiers of Materials Science 7.3 (2013): 269-284.

Other Applications

Other Materials			
Polyurethane	Silicone	Acrylates	Graphene
Phase Transition	RTV 1	UV Curing	Evaporation

Sample Papers:

- Kiziltay, Aysel, et al. „**Poly (ester-urethane) scaffolds: effect of structure on properties and osteogenic activity of stem cells.**" Journal of tissue engineering and regenerative medicine (2013).
- Bakarich, Shannon E. "**Three-Dimensional Printing Fiber Reinforced Hydrogel Composites.**" ACS Appl. Mater. Interfaces 6.18 (2014): 15998-16006.
- Nathan-Walleser, Teressa, et al. „**3D Micro-Extrusion of Graphene-based Active Electrodes: Towards High-Rate AC Line Filtering Performance Electrochemical Capacitors.**" Advanced Functional Materials 24.29 (2014): 4706-4716.
- Tölle, Folke Johannes, Martin Fabritius, and Rolf Mülhaupt. "**Emulsifier-Free Graphene Dispersions with High Graphene Content for Printed Electronics and Freestanding Graphene Films.**" Advanced Functional Materials 22.6 (2012): 1136-1144.

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