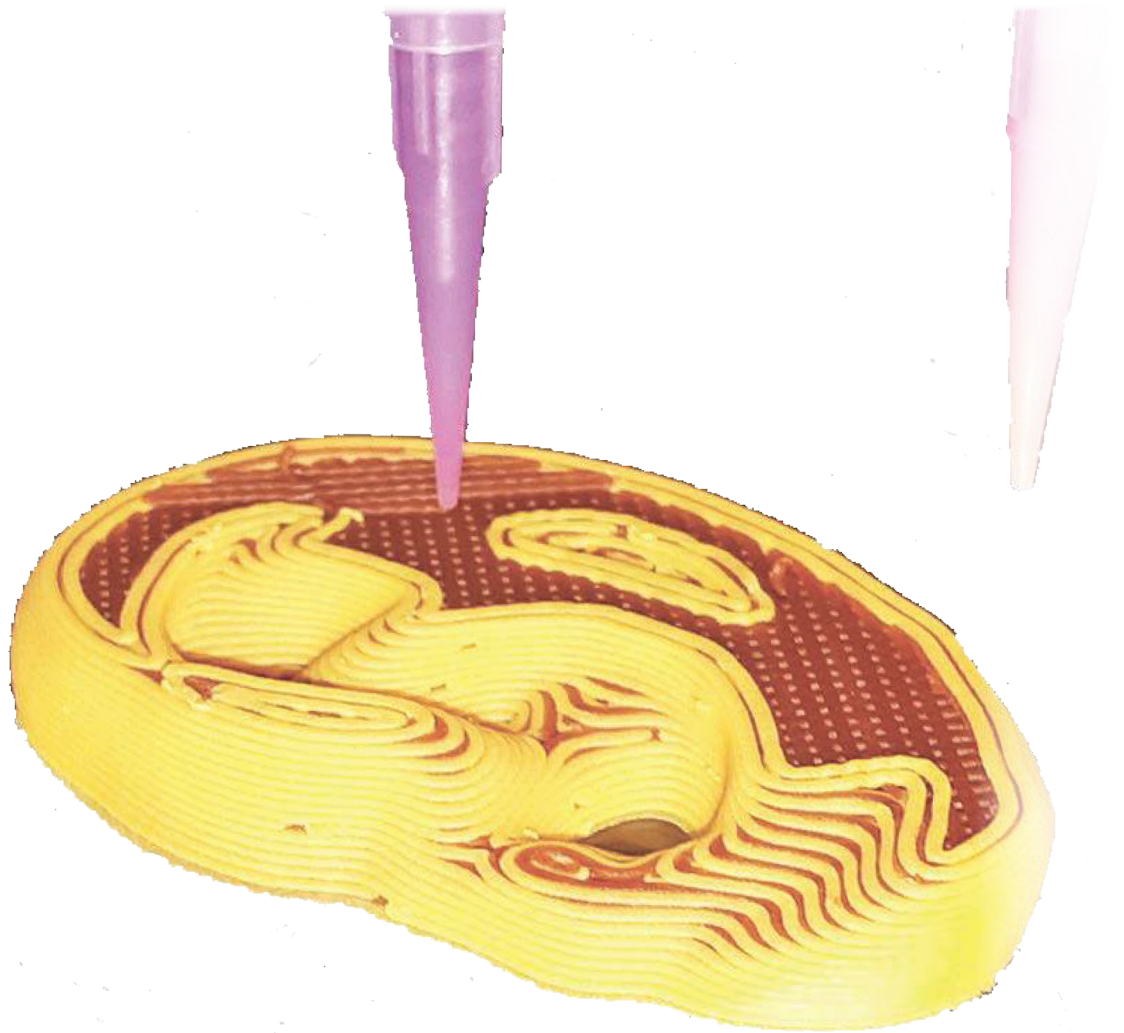


BioScaffolder 3.2/5.1

3D Prototyping, Cell Printing and More



GESIM

- Two different platforms with belts or linear drives for the small lab or the production scale
- Four independent Z-drives for maximum flexibility
- Compressed air-actuated printing at high *and* low temperatures
- And/or piston-based extrusion at room temperature or 250 °C
- Piezoelectric microdispensing, e.g. for cell suspensions, also in-flight droplet mixing
- Numerous add-ons (more to come): CAD import, fused deposition modelling, UV curing, melt electrospinning writing, glue dispensing, core/shell printing, polymer gradients, plasma treatment ...



The small BS3.2 ...

BS3.2 with these head tools
(example): High-temperature piston
extruder, two 30 ml cartridge holders (without
heating), piezo dispenser (tubes not shown)

Are you looking for rapid prototyping or tissue printing for 3D cell culture and regenerative medicine? Look no further. The GeSiM BioScaffolder prints 3D scaffolds from cartridges and also seeds cells using the well-known GeSiM piezoelectric pipettes.

Scaffolds can act as mesh-like support on which cells grow in culture or even replace tissues. Or conductive material is printed onto elastic polymers to create sensors employed for surgery. Channels can be kept open by sugar paste that is washed away afterwards.

Possible applications are:

- Fabrication of 3D scaffolds as substrates for cell culture and organoids
- Pneumatically actuated paste printing at various temperatures with single-use (plas-

tic) and metal cartridges

- **Piezoelectric (ink-jet) microdispensing**, e.g. to coat scaffolds with matrix proteins or to spot cell suspensions
- Printing of live cells ("organ printing"), either embedded in scaffold material or seeded by piezo spotting
- Precise temperature control for printing of thermoplastics guaranteed by all-metal nozzles and cartridges
- Other dispensers: with solenoid valve, bulk/capillary and adhesive dispensers
- **UV curing** of printed photosensitive material
- **Melt electrospinning writing** (MEW) at high voltage to spin fine wires and arrange them to meshes as support for cells
- **Core/shell** dispenser for creating tubular structures, actuated by compressed air
- **High-temperature piston extruder** for printing plastic granules at up to 250 °C. It already works great in the BS3.2, but due to its weight is better suited for the BS5.1. A gradient mixer is available.

The four drives on the **multi-Z** tool head can handle different materials at various pressures and temperatures without exchanging cartridges. Many additional tools can be mounted. All extras are easily installed and configured.

Two platforms exist: a small one, **BS3.2**, with tooth belt drives for the research lab, and the **BS5.1** (formerly BS4.2), with fast linear motors for large-scale 24/7 scaffold production. The BS5.1 can be large or small. All platforms can handle the same tools (except for a few only for the BS5.1) and run the same software.

The BS3.2 fits in a biological safety cabinet (BSC); an extra large BSC can be purchased from GeSiM. Due to its fast movement and strong motors, the BS5.1 needs a special containment, either a cabinet built by GeSiM (see picture on the right) or an extra large BSC.

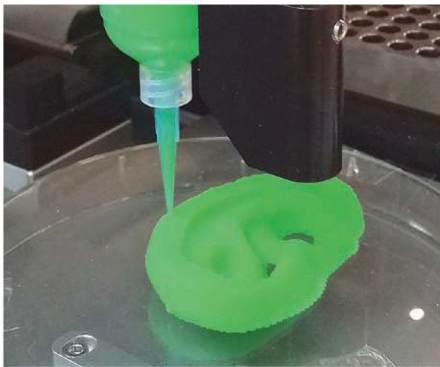


... and the BS5.1 (large or small)

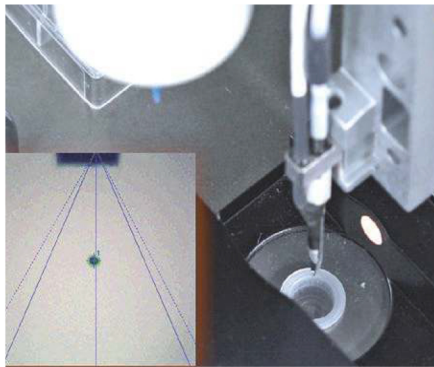


Large
BS5.1 with 50 ml syringe extruder (on front Z-axis) and a gradient mixer connected to two high-temperature piston extruders. The large size leaves ample and uncluttered space for the "service area" (tip cleaning/measurement, wash/dry, stroboscope etc.) on the right and two substrate holders on the left.

A Multitude of Functions



Pressure-driven paste printing from a 30 ml cartridge without heating



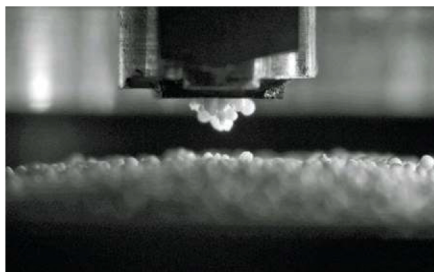
Piezo pipette dispensing test in a stroboscope. Inset: digital video image of the flying droplet



Twin-tip system with two piezo dispensers for in-flight/on target droplet mixing, with illumination (PTFE tubes not shown). Bottom picture: straight piezo dispensers for sample uptake.

Practically unlimited choices for tools on print head and work deck

The system is designed for maximum flexibility. This has resulted in an enormous number of tools that can deliver materials as diverse as hydrogel bioinks and high-melting plastic granules. (For a list of materials and tools used, see another document.) Here we show a few; also expect many more to come.



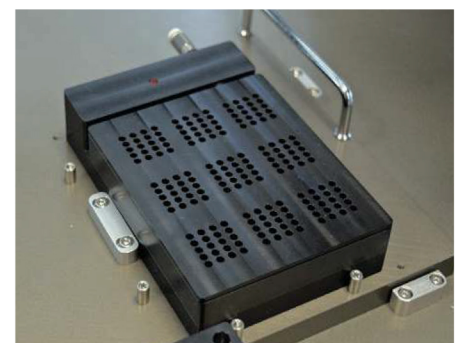
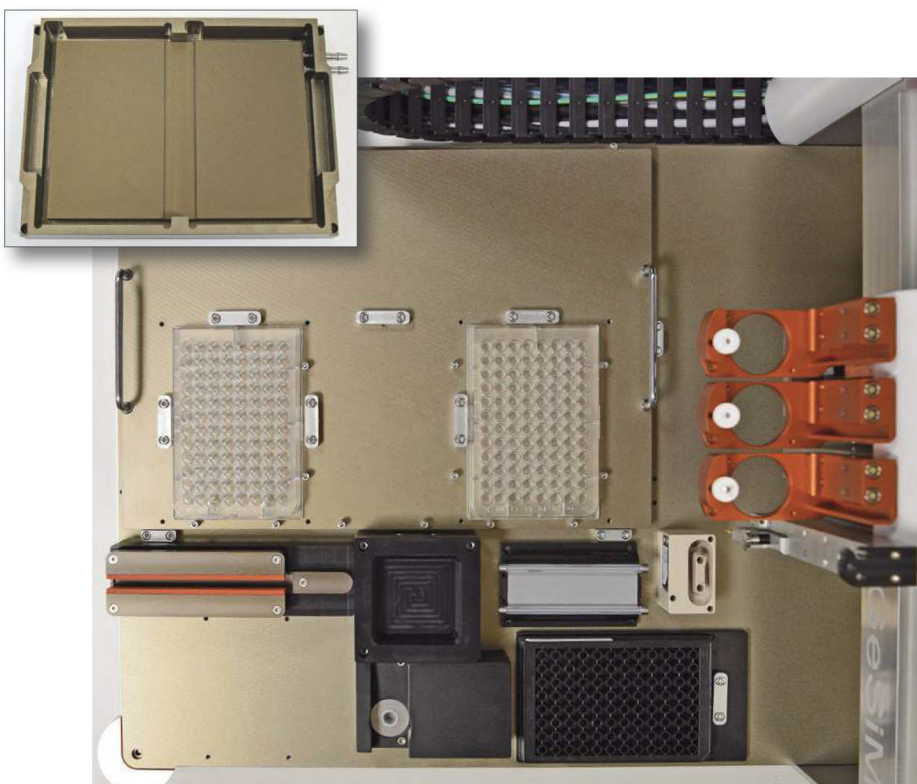
Our expertise in piezoelectric microdispensers made of silicon and glass has made it possible to use the same technology in the BioScaffold. Possible applications are the printing of cell suspensions and protein (e.g. cytokine) gradients. The "Twin Tip" setup allows the mixing of two drops on the surface to start chemical reactions. Further dispensers are e.g. our solenoid valve and micro-powder dis-

pensers or third-party tools such as adhesive dispensers with piezo and pneumatic valves..

Some devices (e.g. camera and UV) can be mounted together with others on the same Z-drive. Others (high-temperature extruder) require an additional supporting (passive) Z-axis to handle their weight. Piezo and similar dispensers need a fluidic system with mi-

crotitre plate(s), bottles and tubes. Sometimes vacuum is needed, e.g. for substrate holders.

The work deck reflects this flexibility, too. Holders, heated or cooled, are available for various substrates, of course for multi-well plates, but also slides, membranes, foils or custom objects.

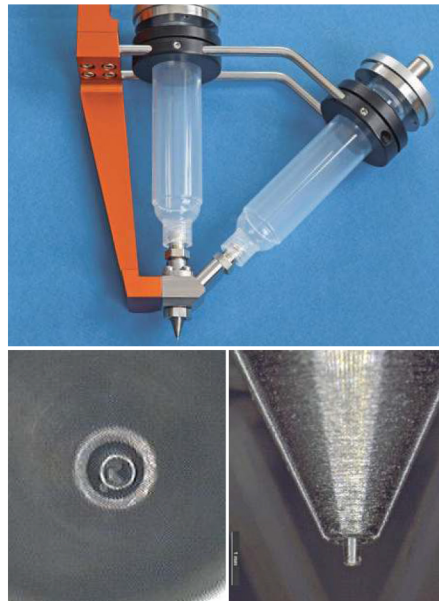


Heatable substrate holder, in place of an MTP on the substrate holder, with holes for vacuum fixation, ideal for slides

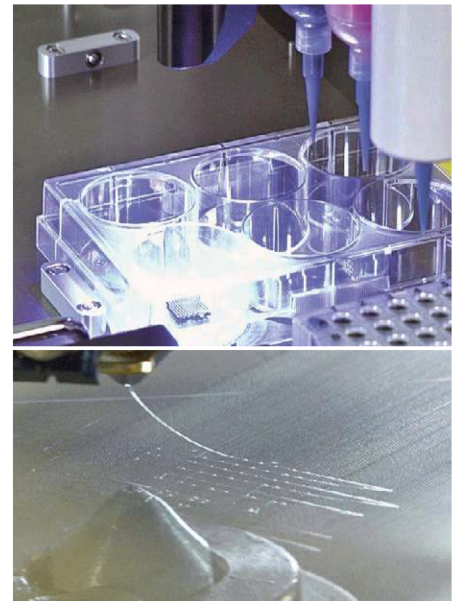
BS3.2 work deck. Top row (rear): substrate holder for three MTPs (portrait orientation). Middle row: tip cleaner, tip measurement groove, dry pad for tips, wash station. Bottom row (front): free space (e.g. for MTP), stroboscope and MTP holder (non-heatable). Small picture: coolable holder for two MTPs, mounted in place of two non-heated MTPs on the tray.



Peltier-cooled (left) and heatable cartridge holder, both actuated by compressed air. The right Z-axis holds a piezo pipette and a Z-sensor.



Core/shell dispenser. Top: core and shell cartridges (vertical/slant), assembled; bottom: enlarged views of the tip (Michael Gelinsky lab, TU Dresden).

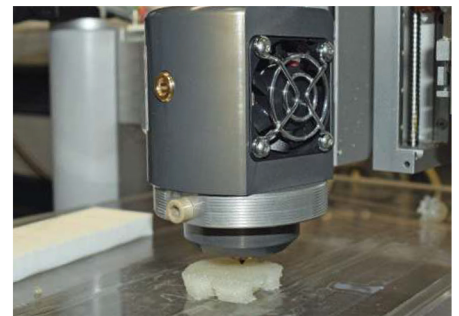


Cross-linking of a polymer by UV light transmitted through an optical fibre (top) and MEW of polycaprolactone (PCL, bottom)

All GeSiM systems (except the Nano-Plotter microarrayer, which will soon change) are based on the same mechanical and software platform. As tools are described by pre-defined, ready-to-use software templates developed by GeSiM, they can be easily added to a system and handled using a consistent user interface. It is therefore possible to use tools from the BioSynthesizer and the μ Contact-Printer, especially in the larger BS5.1.



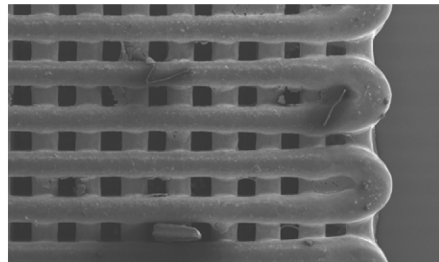
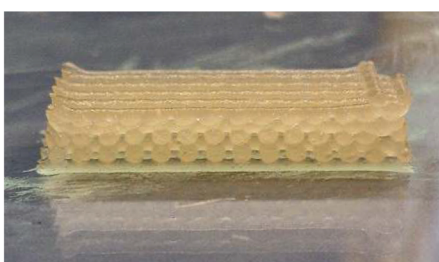
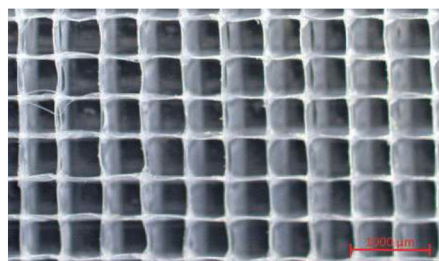
Heatable piezo valve dispenser (VERMES) printing thermoplastic



Commercial FDM extruder for plastic filaments in the BS3.2

Examples of additive manufacturing

from our test lab and others:



Top row: cylinders of polycaprolactone (PCL), MEW (100 PCL layers printed at 5 mm/s, 85 °C and 10 kV, no tear-off; strand thickness 15 μ m) and a microfluidic channel printed on a slide. Bottom row: alginate scaffold and scanning electron micrograph of a bone cement scaffold after setting (material: InnoTERE, Radebeul).

Piston-Based Extruders and Gradient Mixer

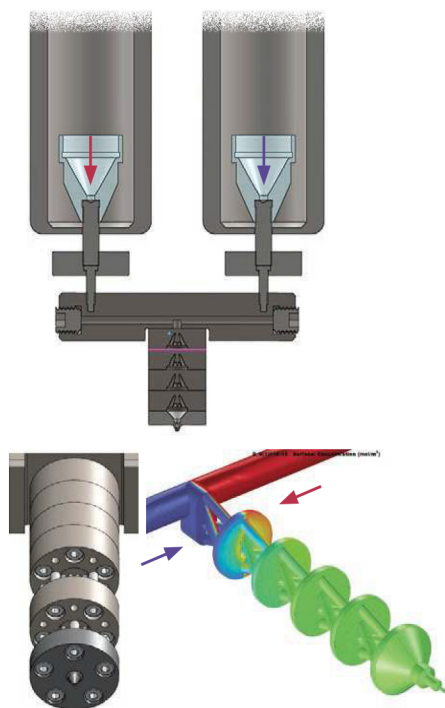
High-temperature piston extruder

High-melting plastic granules can be printed with the GeSiM high-temperature (HT) piston extruder. It is not a screw extruder! Not only can it print at the high temperatures needed to melt many thermoplastics (using an all-metal cartridge and a two-zone heater to up to 250 °C), it can also exert much higher pressure than possible with the air-based extruders.

It accepts commercial polymers as well as home-made granules and thus can print materials not suitable for filament printers. Works both in the BS3.2 and the BS5.1.

Melt blending printing head (HT mixer/extruder)

Melt compounding of plastics with additives/fillers or printing a gradient of two materials in a scaffold require mixing of two materials. Such a mixer has been developed in the EU project "FAST" aiming at functionally graded additive manufacturing of implants whose properties in the interior and on the surface differ. Two units of the HT extruder are coupled to a static mixer that is usually heated to higher temperatures.



Schematic drawing of the ISG cascading mixer ("interfacial surface generator", top), enlarged view of the mixer (bottom left) and finite element simulation of the mixing process (bottom right). Complete mixing requires a stack of four to five modules.



Mixing extruder (left) and piston extruder for 50 ml cartridges (right) in a BioScaffolder BS5.1. Note the two HT extruders on the gradient mixing chamber.

The piston speeds (ca. 10 to 200 $\mu\text{l}/\text{min}$) and hence the mixing ratio can be changed during printing. Due to its weight, this device can only be used in the BS5.1.



Concentric rings of coloured PEOT/PBT printed as a step gradient on a BS5.1

Piston extruder for plastic syringes (50 ml or other sizes)

Using the same extrusion principle as in the HT extruder, we have developed a piston extruder for 50 ml syringes. As it is not heated, it is intended for hydrogels ("bioinks", with or without cells) that must not or need not be heated.

Standard 50 ml syringes with Luer-Lock nozzle easily snap into the holder and their piston is moved downward for extrusion.

Other than for extrusion triggered by compressed air, this new system allows that the content of the syringe is sterilized in advance and stays sterile throughout printing. The high volume of the syringe makes this system also suitable for the production of bulky structures.

With little refurbishing, syringes of other sizes or double syringes can be mounted that e.g. mix cells into bioinks during manufacturing.

Atmospheric plasma module

Please visit our homepage frequently for new information on the plasma pen that has been integrated into the BioScaffolder in the FAST project. Currently this is an experimental set-up for the plasma treatment of scaffolds, e.g. for sterilization during printing.

The plasma pen does not simply generate a spark discharge. Instead it uses a cold argon plasma to which various gases can be added for selective chemical modification (e.g. carboxyl, amino, epoxy) or coatings.



Argon plasma pen from Nadir s.r.l., Italy

GeSiM Robotics software and a PLC drive the GeSiM BioScaffolders

The GeSiM Robotics software with its sleek graphical design handles all necessary operations:

- The system is configured using pre-defined templates containing basic data (e.g. positions, dimensions), allowed parent/child objects, permissible actions and parameters. You can define your own objects. A tree view shows the hierarchy of tools and their coordinate systems.
- Manual operation such as head movement (e.g. to determine the positions of points), Z-measurement or position adjustment of a microtitre plate
- Scaffold generator: easy to use definition of simple forms (polygons/circles, also with holes) or import of CAD data for scaffold printing. Patterns (within layers and layer-by-layer) can include piezo printing and UV exposure. Angles between layers, strand/layer distances, extrusion speed and connection/tear-off of strands can all be freely set. Patterns of outlines embedding the scaffold (more than one strand!) and support structures can be defined. Print height and pressures can be adjusted during printing.
- Sequence and Run: definition and unsupervised processing of a list of events, e.g.

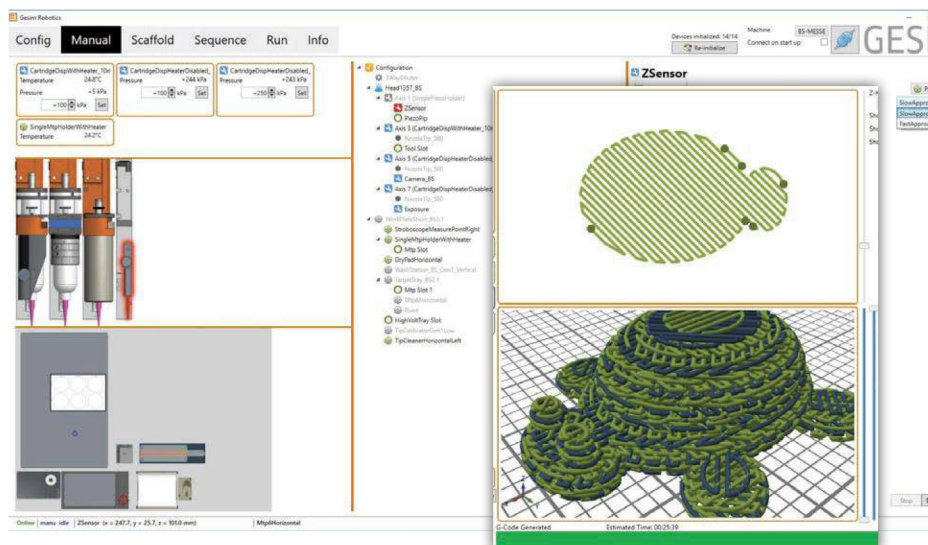
sample aspiration or printing of more than one scaffold. Steps can depend on other actions (e.g. waiting for a temperature); sequences can be nested.

- Info: software version, list of short-cuts, data export/import

Except for the Scaffold tab, the GeSiM Robotics software and hence the look and feel is the same on most GeSiM systems. It is the graphical front end for a programmable logic

controller (PLC) in the F-Box. Remote servicing is possible.

CAD data are imported with a proprietary slicer for **STL** and **3MF** files. Automatic centring is possible. Using 3MF data allows to print “colours”, i.e. different materials or patterns. Generation of a G-code file will calculate the required time and material.



Control software showing the configuration of print head and work deck. Tool properties are pre-configured and so the configuration can be easily changed. The Scaffold tab lets you define simple forms or import CAD files (STL and 3MF) and generate G-code for printing, as shown in the inset.

Features

- GUI-based Windows app, pre-configured
- Intuitive “scaffold generator” for the easy generation of simple forms and comfortable slicing of **CAD data** (STL and 3MF)
- Uses G-code with own extensions
- Three independent Z-drives (spindle) for cartridges, plus one for a liquid dispenser (piezo or other) and a Z-sensor
- Paste printing actuated by compressed air
- Choice of cartridge holders: for ambient temperature, heatable to up to 190 °C or **Peltier-cooled** (to 4 °C; also heatable)
- **Tip cleaner** for wiping off excess material
- **Tip measurement tool** for easy tip alignment
- **Z-sensor** to measure substrate heights, so no tedious adjustment necessary
- Piezoelectric GeSiM pipette (also heatable, various sub-nanolitre volumes), can aspirate samples from a (heatable) microtitre plate
- The **piezo dispenser** includes bottles, tubing, syringe pump, wash/dry stations, and

stroboscope for a functional test

- Also available as **twin piezo pipette** for mixing two droplets in flight!
- **Piston-based extruders** for either high temperature (250 °C) or room temperature (for plastic syringes), also gradient mixer
- Options: bulk dispenser, **solenoid** or other dispensers for adhesives, **core-shell** dispenser (controlled by two different pressures), filament extruder
- External electronic control unit with embedded computer (“F-Box”), connects to sensor cables, compressed air and system liquid (ultra-pure water)
- Adjustable dosage pressure: up to about 600 kPa (6 bar); slight vacuum optional
- Step width: 1 µm in X/Y (belt-driven), 10 µm in Z, encoder-controlled
- Substrate holders for three microtitre plates, also coolable
- **Heat plate** for up to 110 °C, with vacuum fixation
- Option: insulated collector plate (with

optimized materials!) and grounded metal tip for **melt electrospinning writing** of thin strands (> 5 µm), including DC power supply for ±30 kV (both polarities) and grounding kit

- Further options: object camera, triggered **UV** lamp + optical fibre for UV cross-linking, plasma pen (also for surface coating), powder dispenser, more to come
- Requirements: filtered and dried compressed air, (0.7 – 1 MPa; ask for our oil-free compressor), 115 – 240 V AC, Windows computer (pre-configured), enclosure or biological safety cabinet. See extra document.

Printable materials include bioinks (collagen, alginate, etc.) and other hydrogels, bone cement paste, Bioglass, biocompatible silicones, thermoplastic polymers (polycaprolactone, polylactic acid, ABS etc.), composites such as alginate/methyl cellulose, and many more. Please read also our BioScaffolder catalogue.

GESIM



Specifications subject to
change without notice



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