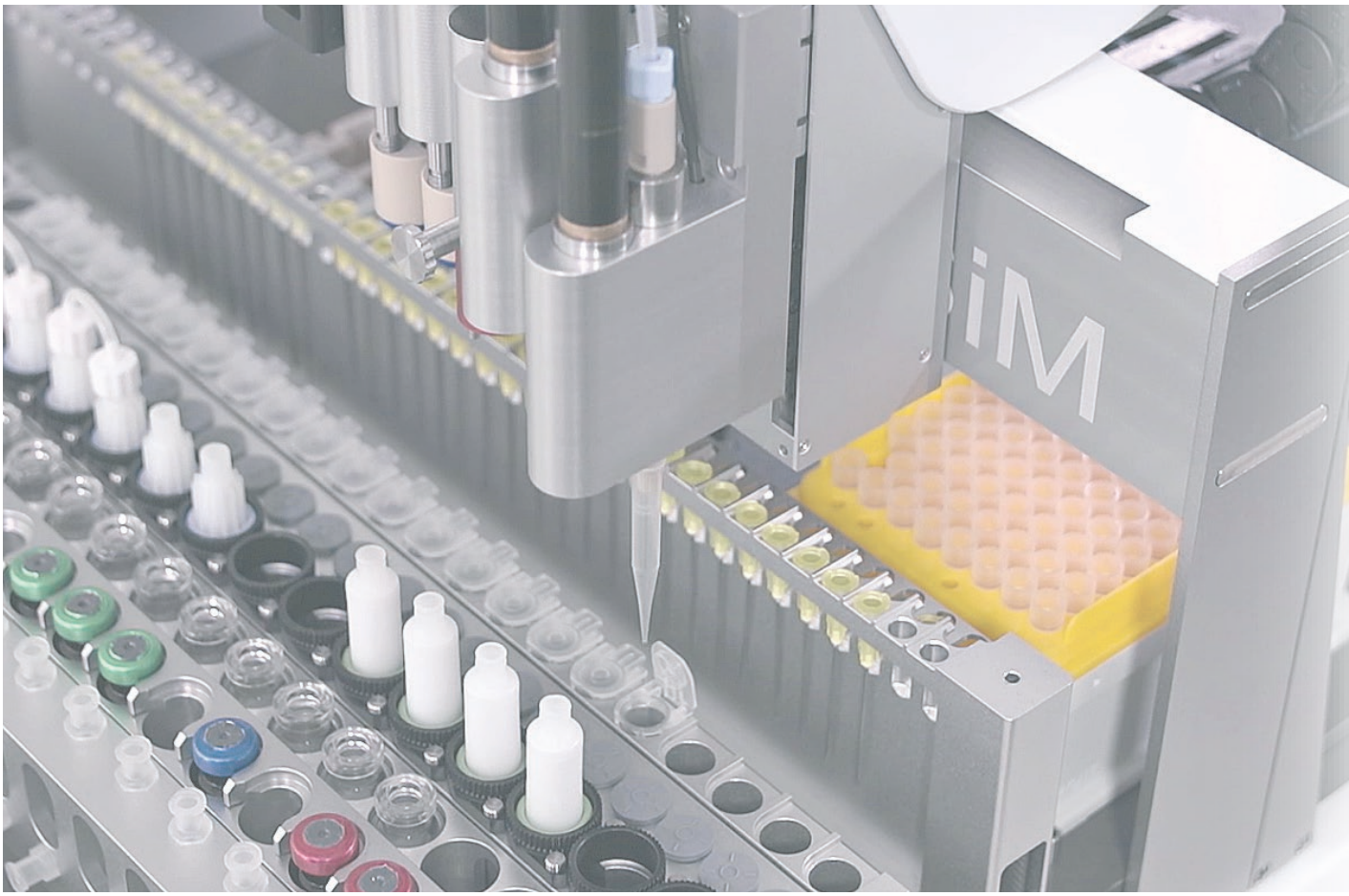
GESIM

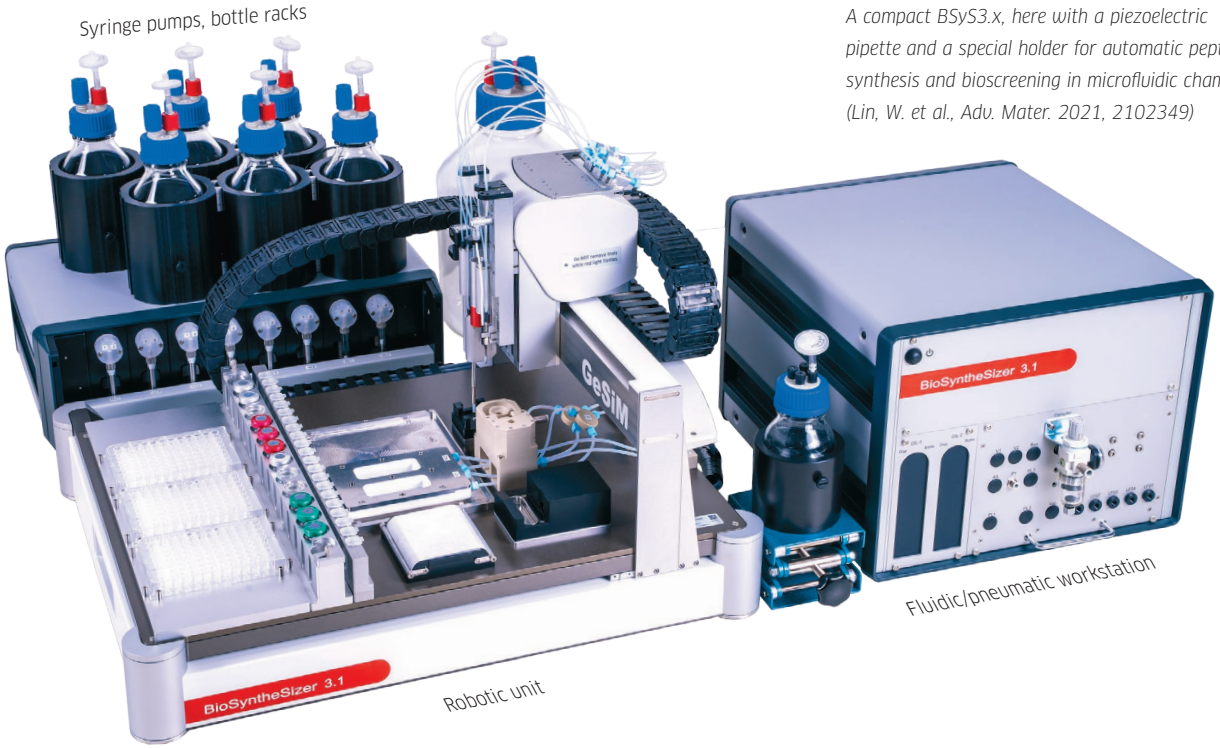
BioSyntheSizer

Multi-Synthesis Liquid Handling Robots



CHEMICAL SYNTHESIS

BSyS Platforms



A compact BSyS3.x, here with a piezoelectric pipette and a special holder for automatic peptide synthesis and bioscreening in microfluidic chambers (Lin, W. et al., Adv. Mater. 2021, 2102349)

BSyS platform

The BioSyntheSizer, or BSyS for short, stands for (bio)chemical synthesis using various protocols in a compact, modular instrument. To reach this goal, GeSiM invented a multi-Z head with up to seven Z-drives on which a multitude of tools can be mounted. The work deck holds stations for tip washing, wash stations for solvent and water, a heatable reactor and easy to mount racks for various containers (e.g. crimp vials, Eppendorf tubes), filter cartridges, purification columns, plates/slides, pipette tips, needles etc.

The heart of the BSyS is the reactor, a heatable chamber with quick temperature ramps for chemical reactions at elevated temperature and high pressure.

BSyS3.3, BSyS5.1, BSyS5.1/E, BSyS-2LL

The **BSyS3.3**, our small platform, is already prepared for almost all tools. Larger instruments with fast linear motors, i.e. the **BSyS5.3** or the extra-large **BSyS5.3/E**, are designed for higher throughput and more complex syntheses that require more space for tips, vials, microtitre plates (MTPs), microfluidic chips and other objects.

Two-level lab (2LL) instruments exist for special applications, e.g. automatic cell culture in the GeSiM 'Microfluidic Workstation'. A possible configuration is (1) liquid handling + cell culture chips + condenser on the upper level and (2) a very compact fluorescence or phase contrast microscope on the lower level. More details are found on our website.

Print head tools

The tool head has almost unlimited functionality – optical devices, nozzles/ejectors for standard pipette tips or Luer needles, dispensers for non-contact transfer of small volumes (GeSiM piezoelectric and solenoid valve dispensers, third-party dispensers). Bulk liquid handling is performed with a syringe pump.

A GeSiM specialty is the **twin dispenser** whose two tips are automatically swivelled after sample uptake so that two drops can be mixed at the surface, e.g. to initiate a rapid chemical reaction. The **3-lumen pipette** performs azeotropic drying of solutes, with or without heating, by flushing a vial with solvent and gas while using vacuum to remove the azeotrope of solvent and water. The vacuum function is also used for gripping vials.

Another special you'll hardly find anywhere else is the **powder dispenser** for really small amounts of solids. It aspirates a few beads and transfers them into a vial. Depending on the size of the cavity, powder dispensers can operate down to a single bead (!). The **pH titration** pipette, containing a glass electrode and three capillaries (acid/base/mixing) is utilised for automatic pH adjustment in liquids.

Pipetting head (example) with (1) camera, (2+3) gripper/3-lumen pipette, (4) FlipTube opener, (5) piezo tip+Z-sensor, (6+7) nozzles for needles and tips

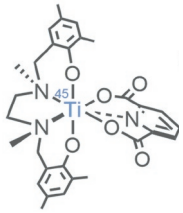
Easy to use control software

The clear and consistent graphical user interface is identical for all *GeSiM Robotics* instruments. Its tabs (Configuration, Manual, Sequence, Run, Info) give you full control of the instrument, manually or automatic, while providing utmost flexibility and expandability.

The BSyS is not just another liquid handler! It will become your companion for small-scale synthesis projects. And before we sell an instrument, we will optimise your application and find the best configuration for you. **Customization is our business.**

Titanium-containing antineoplastic agents

Research groups from Roskilde and Copenhagen, Denmark, have used the BSyS to develop, among others, Ti-containing cytotoxic compounds without cisplatin cross-resistance. To monitor their biodistribution, the radioactive ^{45}Ti nuclide was used for synthesis and the animals analysed by PET imaging. The small BSyS neatly fits in a standard 'hot chamber'.

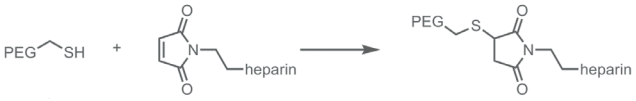


Synthesis of biocompatible hydrogels via in-situ cross-linking

The C. Werner research group at the Leibniz Institute for Polymer Research Dresden synthesizes hydrogels by coupling of polymer precursors via maleimide chemistry. Various hydrogel networks are possible, e.g. by functionalization of 4-star molecules of polyethylene glycol (PEG) with cysteine-containing peptides, followed by linking this branched polymer with heparin containing multiple maleimide groups:

This results in a cell-friendly hydrogel, and peptides in these polymers can induce specific cellular functions. High-resolution patterns of such peptides are obtained by in situ cross-linking that requires **on-chip droplet mixing** using a twin-tip piezo dispenser.

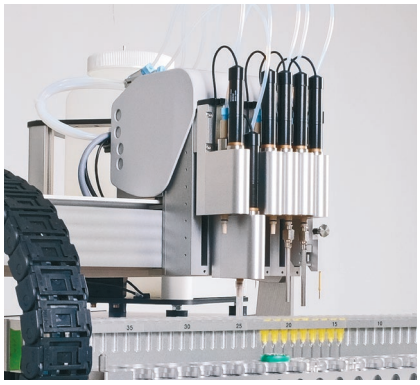
Ref.: Tsurkan, M.V. et al., Adv. Mater. 25, 2013, 2606–2610



Sol-gel conversion of a hydrogel for 3D bioprinting

The group of S.N. Nazhat at McGill University, Montréal, has found that dissolved collagen fibres can be aligned using an aspiration-dispensing cycle through fine needles, thus creating a gel suitable for additive manufacturing, i.e. 3D bioprinting of collagen hydrogel 'bricks'. For this project, GeSiM has designed a customized BioSyntheSizer with seven Z-drives that can handle disposable tips as well as steel needles with different gauge size.

Ref.: Kamranpour, N.O. et al., Biofabrication 8, 2016, 015018
Griffanti, G. et al., Adv. Funct. Mater., 2019, 1903874



BSyS print head with nozzles for plastic tips and capillary dispensers for the production of collagen gel plugs

Organs on chip (OOCs)

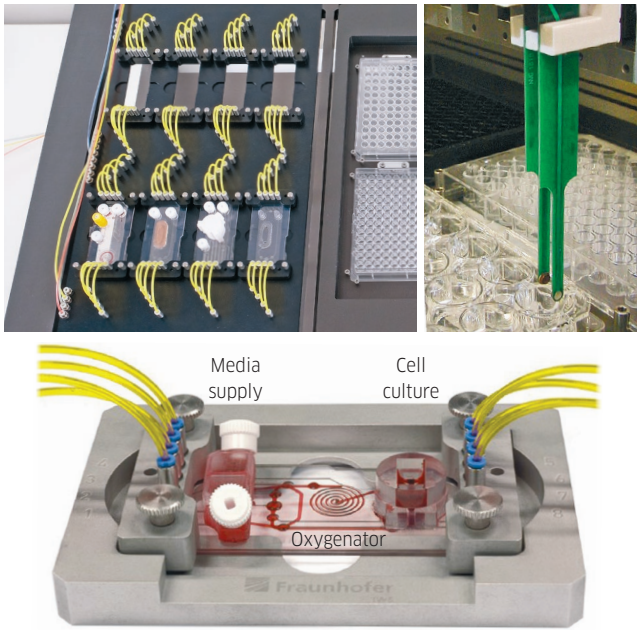
Our two-level 'Microfluidic Workstation', based on a BSyS5.1/E, includes bulk liquid handling and microfluidic chips at the top level and a ultra-compact fluorescence microscope at the bottom level to automate cell cultures in microsystems under microscope control, e.g. for toxicity/hypoxia tests, drug screening using 3D cell cultures and study of 'mini-organisms'.

The organ-on-chips have integrated:

- Peristaltic micro-pumps for closed-loop operation and physiological fluid flow (heartbeat)
- Valves, oxygenators, dialyzers, electrodes
- Reservoirs and cell culture modules (e.g. 3D-printed)
- Membrane filters and sensors
- Coupling of organs (multi-organ chip) and single-cell handling

Measured data (selection): O_2, TEER (electrical resistance), impedance/microelectrode arrays etc.

Ref.: Busek, M. et al., CDBME 2, 2016, 71–75
Busek, M. et al., CDBME 5, 2019, 269–272



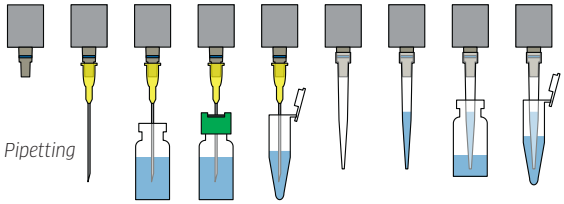
Top left: OOC deck (detail); top right: TEER sensor. Bottom: example of a closed-loop OOC chip (Fraunhofer IWS, Dresden).

Functions (Overview)

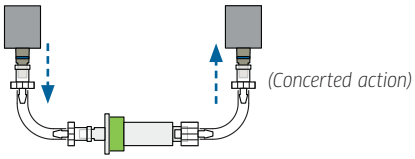
2022

Nozzles for disposable tips + needles, holders

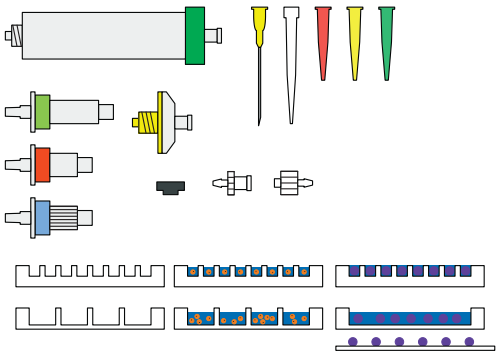
Single channel action



Double channel action

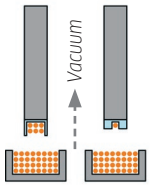


Columns and MTPs

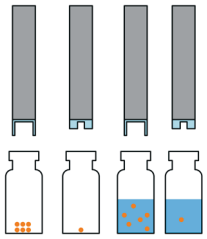


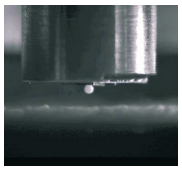
Powder microdispenser

Aspirate



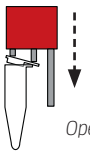
Release/dispense



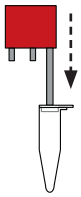


Powder dispenser: transfer of one (!) bead

FlipTube opener



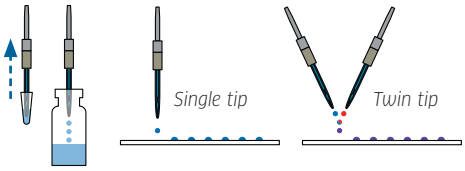
Open tube



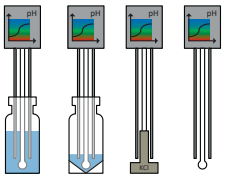
Close tube

Piezo dispenser

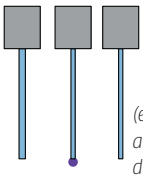
Sample uptake + release



pH titration pipette

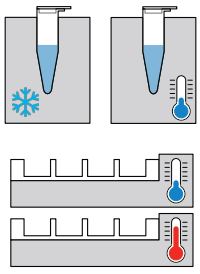


Capillary dispenser



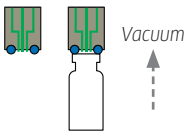
(e.g. to align and print hydrogel fibres)

Heating/cooling blocks



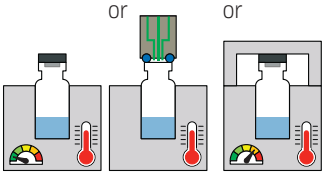
Freezing/cooling/heating

Gripper / 3-lumen pipette



Three capillaries for solvent/N_2/vacuum, e.g. for azeotropic drying of solutes

Heatable reactor



Low pressure | *Azeotropic drying with solvent/N_2/ vacuum* | *High temp. generates pressure*

Azeotropic drying in reactor

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