# MicCell™

## Frequently Asked Questions

**Which components do you need to set up the MicCell™ system?**

- An inverted fluorescence microscope (not included in the shipment)
- A MicCell *Channel Plate* that contains the microchannel and that is located under the MicCell lid. The microchannel is capped by a coverslip from below. You can obtain either a ready-made channel plate from GeSiM (including lid) or mold it in our casting station.
- A mechanical support to hold the PDMS channel layer in place directly above the microscope objective
- An adapter ("working plate") that connects the support (with the flow cell/channel plate) with the microscope
- A module ("fluid processor") containing all active components of the *external* fluidic system (syringe pumps, distribution valves), plus reservoirs and tubes
- A Windows® control software for both the interactive and the programmable control of all active elements
- Optional: hydrogel microvalves for automated sample injection

Some customers do not use a computer-controlled external fluidic system, but manual syringes or their own syringe pumps. In this case, however, you will not have access to the flexibility and ease of use of the GeSiM fluidics and must develop your own peripheral system.

**Which type of microscope is recommended?**
We usually design our systems for the Axiovert 200M from Zeiss, but we can build adapters for virtually every microscope (Leica, Olympus, and others), with both inverted and standard optics.

**Is it possible to use the MicCell™ platform without an inverted microscope?**
Yes, but then you miss all the advantages of current high-performance microscopy, such as automatic image analysis, and so you must resort to other detection methods, e.g., a stereo microscope with CCD camera or electrochemical detection using microelectrodes (for the recording of electrically active cells, for instance). Design changes can be implemented to a certain degree; please inquire.

**Which type of external pumps and valves are used in the MicCell™ and what are their properties?**
Plug-in modules of syringe pumps and distribution valves from Tecan Systems are built into a special housing with a single RS-232 interface for all modules. The minimal addressable volume of the pump is 10 nanoliters and the pumps can address up to 24000 steps in a maximum period of 20 min. GeSiM can deliver a two-pump module for continuous fluid delivery. The available 4/1 or 6/1-port distribution valves (one channel in/four or six out, or vice versa) allow the automatic switching of liquids. Pump(s) + valves + hydrogel valve controller make up the *fluid processor*.

**Which materials get in contact with the sample?**
Glass, PTFE (Teflon), PEEK, and PDMS. PDMS is usually no problem, but if it is (e.g., for the activity of proteins), the PDMS layer must be rinsed with buffer for a prolonged period.

**When does the use of PDMS make sense or no sense?**
PDMS is an ideal material, as it is on the one hand chemically inert and on the other hand soft so that it can seal any channel efficiently. It is, however, permeable for small molecules such as alcohol or oxygen. So if oxygen must be kept away from your sample (e.g. to avoid oxidative photodamage), a tightly sealing flow cell (e.g. glass with polymer walls) or a permanently bonded cell should be used instead.

**The PDMS channel plate is the heart of the MicCell™. Can GeSiM fabricate it in large quantities?**
Yes, the production of hundreds of units per month is possible, if the user does not want to cast it himself/herself.

**How can the MicCell™ be adapted to a new application? How long does it take?**
In most cases, only the channel configuration will change, but not the support (the holder), the external fluidics, and the interface to the external tube system. So we usually only need to manufacture a new silicon master for molding the PDMS channel plate, which takes about six weeks. If we must redesign the coverslip or the support plate, add microelectrodes, or rewrite the control software (all of which can be done), such changes may require ten weeks.

**Can GeSiM deliver special coverslips, e.g., ones with metal electrodes?**
Yes, 150 µm to 1 mm thick, rectangular coverslips of almost any size can be shipped. GeSiM can pre-structure the coverslip surface, if needed. We can manufacture customized microelectrodes of almost any material, but recommend platinum, gold, or the transparent ITO (indium tin oxide). To insulate all parts except the electrode pads, plasma deposition of silicon oxide ($SiO_2$) or silicon nitride ($Si_3N_4$) is possible. The minimum size of a single electrode is 5 µm. GeSiM has found a way to contact the coverslip reversibly and can also fabricate systems in which both the top *and* the

bottom of the microchannel contain microelectrodes. In this case, however, the channel layer canot be made of PDMS, but consists also of a glass plate, with polymer channel walls.

**Is the MicCell™ restricted to coverslips of standard size (22x22 mm)?**
No, we offer a solution for a size of 22x50 mm whose default setup contains 10 fluid connections. Plus other setups, e.g. of slide size (25x75 mm).

**Is it possible to introduce tiny volumes (microliters) of sample with almost no dead volume into the channel system?**
Yes, the GeSiM hydrogel microinjector was designed to do exactly this. Here a standard fitting with a built-in hydrogel valve is directly attached to the MicCell. Hydrogels can also be directly integrated into the microsystem, if needed.

**Can a hydrogel valve open slowly or can the switching behavior be influenced by a slow temperature ramp?**
No, there is a single defined phase transition temperature. When it is reached, the microvalve switches instantaneously, without intermediate state.

**What other accessories can be built into the MicCell™?**
- Mixers,
- integrated flow and pressure sensors,
- temperature control: heating and cooling by integrated or external devices, with sensing,
- microelectrodes of all kind (multielectrode arrays, dielectrophoretic control, impedance sensor)

**Can one observe intransparent objects in the MicCell™ under an inverted microscope?**
Yes, we have designed a MicCell with integrated *sample carrier*, which is a movable holder that allows to move a 2.5x2.5 mm chip into the fluidic channel. As sample and sample carrier are opaque, the object must be illuminated from the objective side along the optical path. The specimen can be turned a full 360° around the optical axis of the microscope.

**Is the system expensive?**
It is at least much cheaper than an inverted microscope. The naked flow cell consisting of MicCell support, working plate (adapter), and flow channel will be around 1000 €. If you let us make the PDMS channel plate, it costs less than 100 € (including a recycled PMMA lid) and can be reused several times. Apart from this, you need only new coverslips, i.e. the total cost of ownership will be low. A complete external fluid processor for an automatic liquid handling, including control software, can be obtained from ca. 7500 €, a hydrogel valve costs around 600 €.

## Applications

Please regard this list as a first suggestion, without being exhaustive:

- Microreaction technology, e.g. hybridization or stopped-flow chamber, using fluorescence detection
- Immobilization of biomolecules such as protein or DNA (e.g. by microarraying) on the coverslips before bringing them into the microchannels
- Generation of concentration gradients perpendicular to the microchannel cross section by a "gradient mixer"
- Semi-automatic drug screening using adherent cells or tissue slices
- Viability tests and other cell-based physiological assays
- Measurement of the interaction of cells with immobilized proteins, DNA, RNA, oligo- or polysaccharides, lipids, and other ligands
- Handling and sorting of suspended cells and particles by dielectrophoresis: please contact Evotec Technologies GmbH (www.evotec-technologies.com)
- Cell handling and sorting using optical tweezers
- Identification of cancer or stem cells using an "optical stretcher" (patent University of Leipzig)
- Electroporation in the flow
- Testing of the uniformity of microbeads and other particles, potentially with sorting
- Manipulation of elongated macromolecules (e.g. DNA or motor proteins) in hydrodynamic flow fields for the bottom-up construction of nanostructures, force measurements, etc.
- Micro-capillary electrophoresis under the microscope
- Integration of, e.g., column or filtration material for micro-purifying with or without microscope control
- Liquid processing independent of a microscope (e.g. assays using electrochemical detection)
- Chemical synthesis on the nanoscale
- Observation of opaque objects in the MicCell using the pivotable sample carrier
- In general: rapid prototyping for the development of novel microfluidic systems

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