

Product survey: Lab-on-a-Chip products

Trickle becomes Mainstream

Developed in the early 90's of the last century from some vague ideas and concepts, microfluidic devices, though still in their "teens", may revolutionise many bioanalytical or molecular biological applications in the near future.

Space in the lab is usually very limited. Benches and racks are packed with benchtop devices, bottles, pipettes and all the stuff necessary for the daily lab work. Quite often, too many people have too little space, so everyone is staking a claim and constantly fighting for each and every extra square centimetre of bench space possible. However, that's no longer necessary. Labs suffering from crowded conditions may ease their pain by simply shrinking their routinely used devices, e.g. thermocyclers, to the size of a stamp. "That's only a pipe dream of someone totally fed-up and frustrated by the bad working conditions in a cramped lab", you may think. Not at all! Microfluidic devices, also known as Lab-on-a-Chip or micro total analysis systems (μ TAS), have enabled this dream to come true.

The basic idea of microfluidics stems from microchips used in computers and electronic circuits. Instead of switching binary data, as in computer chips, microfluidic chips direct minute amounts of liquid from the nanolitre to the attolitre scale, using channels with dimensions of tens to hundreds of micrometres, to miniscule wells, mixing and reaction chambers and detection channels. The microfluidic flow is controlled by miniaturised valves and pumps, which are integrated into the microfluidic chip channel system. In the early days of μ TAS, microfluidic chips were predominantly made of glass, quartz or silicon by applying techniques borrowed from the production of microelectronic chips. This picture has completely changed in the last couple of years. Today, most microfluidic chips, especially custom-made chips produced in small amounts by academic researchers, are made of the elastomeric plastic polydimethylsiloxane (PDMS).

Though there are numerous different fabrication procedures like laser abla-

tion and hot embossing, most microfluidic PDMS chips are microstructured by multilayer soft lithography (MSL) also referred to as casting. This technique, which was introduced by Stephen Quake's group at the California Institute of Technology (Caltech), Pasadena in 2000, has pretty much simplified the construction of microfluidic devices. A silicon wafer, patterned by classic lithographic techniques, is used as a mould into which a mixture of base elastomer and curing agent is poured. After curing, the PDMS sheet is simply peeled away from the master and bonded to a glass plate or another sheet of polymer. With this easy method, three-dimensional structures such as channels, pumps and valves can be built up layer by layer.

Necessity is the mother of invention

Multilayer soft lithography, however, still depends on the rather expensive and time-consuming production of a silicon master. Michelle Khine, assistant professor at the University of California, Merced, has neither money nor time, however, this young group leader obviously has a lot of fantasy and creative power. Very recently she came up with the idea of simply printing microfluidic channels onto Shrinky Dinks plastic using a laserjet printer. Shrinky Dinks is a children's toy made from thermoplastic polystyrene sheets onto which one can draw a picture and shrink it to 5/8ths of the original size by heating with an oven or a heat gun. Khine printed the microchannels she needed onto the Shrinky

Dinks sheets, heated them to 160°C and used the shrunken features as a rigid mould for soft lithography or directly as microfluidic chips. Sounds bizarre, however, the Shrinky Dinks chips really work. Khine's people use them for gradient generation in chemotaxis experiments or for generation

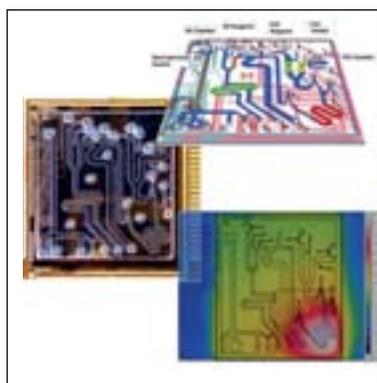
and cultivation of embryonic stem cell aggregates (embryoid bodies).

Microfluidic devices are dedicated to a lot of applications in molecular biology, ranging from analysing DNA to sequencing proteins. No wonder that some companies already offer Lab-on-a-Chip solutions. Among the first commercially available microfluidic devices are electrophoresis chips, using microfluidic channels instead of acrylamid or agarose gels to separate proteins or DNA fragments. Usually, a tiny capillary (sipper) integrated into the electrophoresis chip, resembling the bill of a humming bird, sips, e.g. a minute volume of a DNA probe, from a microtiter plate and aspirates it to a probe-well on the electrophoresis chip. A vacuum pulls the probe, together with fluorescent markers, into the separation channel, where the fragments are stained and electrophoretically separated before the bands are detected via laser-induced fluorescence.

PCR is another application that can be performed on a microfluidic chip. In 1998, Andreas Manz, then leading a group at the Imperial College in London, and his co-workers already published a science paper describing a microfluidic PCR device. The three steps of PCR, denaturation, annealing and extension, take place in different zones of the PCR chip that are heated up to the necessary temperatures of 95°C, 55°C and 72°C respectively. Speed is one of the major advantages of microfluidic PCR, also known as continuous-flow amplification. Instead of waiting 30 to 60 minutes for a conventional PCR to finish, the microfluidic PCR chip gets the job done in only five minutes.

Other Lab-on-a-Chip devices on the market are intended to analyse RNA or DNA fragments, to perform flow cytometrics on a chip or to size and quantitate proteins. Though the number of commercially available microfluidic devices is still low, it is a fair guess that it will increase dramatically in years to come. One question, nevertheless, remains: will it ever be possible to shrink a whole lab onto a few microfluidic chips?

HARALD ZÄHRINGER



Channel system of microfluidic chip used for electrophoresis and PCR.

Lab-on-a-chip products (microfluid devices)

Company	Product/Device	Chip Material Chip Size	Technology	Application(s)	Miscellaneous, Specialities, Generally	Price [EUR]
Agilent Technologies Sales and Service Waldbronn, Germany http://www.chem.agilent.com Contact: Phone: 0800-603 1000 CustomerCare_Germany@ agilent.com	Agilent 2100 Bioanalyzer	Fused quartz 1.8 X 1.8 CM	Voltage driven separation by gel-electro-phoresis with Laser induced Fluorescence detection. Pressure driven isolation and counting of differently stained cells detected by two separate fluorescent light sources.	Quantitative, high resolution DNA analysis; Normalized RNA integrity analysis and quantitation; Fast sizing and quantification of Proteins; Analysis of broad range of cell parameters.	<ul style="list-style-type: none"> - Supports the use of the RNA integrity number (RIN Number) for QA/QC of RNA - Very fast analysis time (<30 min for RNA, <45 min for Proteins) - New Assays for the analysis of small nucleic acids (miRNA, siRNA, oligonucleotides), in the size range of 6-150 nt - New high sensitivity Protein Assay reaching Silver stain sensitivity, quantitative up to 4 orders of magnitude, highly reproducible, providing digital data 	Approx. 18.000,- (depending on configuration)
	Agilent 1200 Series HPLC-Chip/MS/ System	Polymer Chip Surface	Nano HPLC-Chip/MS	Microfluidic chip-based separation technology for nanospray LC/MS	<ul style="list-style-type: none"> - Integrates columns, connection capillaries, and nanospray emitter on the polymer chip surface - Re-useable, integrated biocompatible HPLC-Chips - Easy to use operation with automatic chip loading, solvent and sample delivery - High pressure switching of flows & automated chip positioning in the MS source 	Upon request
BF-Biolabs Denzlingen, Germany www.bf-biolabs.com Contact: Phone: +49 (0)7666 880837 info@bf-biolabs.com	Custom-made Microarrays	Schott Nexterion Coated Slides (75 x 25 mm), CodeLink Activated Slides (75 x 25 mm), Custom	Contact Spotting	Gene-Expression, Gene ID, SNP	- Oligonucleotide (70mer)-, cDNA-, or Protein-Array	Please inquire
	Full Service: SNP- and Gene Expression-Assays, Data Management	Operon OpArrays, Schott Nexterion Coated Slides (75 x 25 mm), CodeLink activated Slides (75 x 25 mm)	RNA quality control, cDNA production, Assay execution, Readout, Data management	Gene-Expression, Gene ID, SNP	-	Please inquire
	Absolut Precision Printheads for Microarrayer	-	Contact Spotting	MicroGrid II, Genetix QArray2, Custom made	- Suitable for: BioRobotics-, Telechem-, Point-, or Genetix-Pins	Please inquire
BioCat Heidelberg, Germany www.biocat.de Contact: Elke Gamer Phone: +49-6221-7141516 gamer@biocat.de	Multiple Substrate Array MSA	Glass slide Size: 2 slides (2 x 10 arrays, 64 microspots per array)	To determine the interaction with ECM proteins, cells are seeded into wells containing one microarray each. After short-term incubation of cells on the array, unattached cells are washed away and remaining cells are analyzed either alive or after fixation and staining with dyes or immunolabeling reagents.	Microarray-based cell adhesion profiling. Profiling of differential cell adhesion (e.g. comparing cell populations: treated versus untreated, healthy versus diseased). Screening of ECM-induced cell phenotypes (e.g. morphology). Screening specificity of cell-matrix interactions.	<ul style="list-style-type: none"> - Parallel screening of interactions of cells with fourteen different extracellular matrix (ECM) proteins - 5000-20000 cells needed per microarray - Ten microarrays are placed on one microslide which allows analysis of ten cell suspensions per slide - Recommended use together with Pro-Plate Multiarray Slide System 	Please inquire
	RayBio Label-based Human, Mouse, and Rat High-Density Antibody Arrays	Glass slide	Biotinylated sample is added onto the antibody array and incubated at room temperature. After incubation with Alexa Fluor 555-Streptavidin, the signals can be visualized by fluorescence.	High-density expression screening of 507 human, 308 mouse, or 90 rat target proteins including cytokines, chemokines, adipokine, growth factors, angiogenic factors, proteases, soluble receptors, soluble adhesion molecules in cell culture supernatants or serum.	<ul style="list-style-type: none"> - High density, e.g. 507 human cytokines on a single array - Direct biotin labeling of proteins - High sensitivity: detection of as little as 5 pg/ml - Affordable, quick and simple to use 	770,- (RayBio Biotin Label Human Antibody Array) 665,- (RayBio Biotin Label Mouse Antibody Array) 870,- (RayBio Biotin Label Rat Antibody Array)
	RayBio Human, Mouse, and Rat Cytokine Antibody Arrays	Glass slide	Multiplex sandwich ELISA-based methodology.	Simultaneous detection of changes of the expression level of multiple cytokines caused e.g. by apoptosis, inflammation, angiogenesis, etc.	<ul style="list-style-type: none"> - Simultaneous detection of up to 174 cytokines - High sensitivity: detection at pg level - Only 10-50 ul of sample required - High-throughput compatible: up to 16 samples can be processed on one slide - Lower costs/sample 	Depending on number of antibodies per array, on number of arrays per slide, and on number of slides per package
	Quantibody Human, Mouse, and Rat Cytokine Antibody Arrays	Glass slide	Multiplex sandwich ELISA-based methodology.	Simultaneous quantitative measurement of the concentration of multiple cytokines in serum, plasma, CSF, cell lysate, conditioned media and other body fluids.	<ul style="list-style-type: none"> - Specific cytokine standards for quantification included - Similar or better detection sensitivity compared to ELISA - Up to 40 cytokines at once - Less than 50 µl of sample required - Cost effective 	See above

Lab-on-a-chip products (microfluid devices)

Company	Product/Device	Chip Material Chip Size	Technology	Application(s)	Miscellaneous, Specialities, Generally	Price [EUR]
Bio-Rad Laboratories München, Germany www.bio-rad.com Contact: Phone: +49 89 31 884-177 TechSupport@bio-rad.com	Experion Automated Electrophoresis System	Glass chip, 16 wells to analyse up to 12 samples	The Experion automated electrophoresis system automatically performs all the steps of gel-based electrophoresis, providing a comprehensive platform for the analysis of nucleic acids and proteins in as little as 30 minutes.	Protein, RNA, DNA	<ul style="list-style-type: none"> - Accurate, single-step protein sizing from 10 to 260 kD - Protein sensitivity down to 2.5 ng/µl - RNA purity determination at nanogram and picogram levels - Single-step sizing and quantitation analysis of DNA fragments - Simple chip priming-automated method for reproducible, error-free results 	From 13.800,-
Caliper Life Sciences Rüsselsheim, Germany www.caliperls.com Contact: Claudia Dymaszewski Phone: +49(0)6142-8349311 germany@caliperls.com	EZ Reader Microfluidic Plate Reader	- 4 or 12 Sipper Chips	The Mobility Shift Assay provides for an integrated separation step on the chip, allowing the simultaneous detection and quantitation of both substrate and product. In addition, each reaction well may be sampled multiple times in real-time kinetic mode.	Profiling, Drug Screening, Assayentwicklung	<ul style="list-style-type: none"> - Mobility Shift Assay (Detection of Product and Substrate) - Automatic Analysis - Can be used with validated ProfilerPro plates - 4 Profiler Pro Panel Kits with 24 different kinases on one 384 wellplate with all necessary reagents - ProfilerPro Substrates und Protocols for follow up assays are also available 	-
Carl Zeiss MicroImaging Bernried, Germany www.zeiss.de/microdissection Contact: Phone: +49 81589971 0 palm-info@zeiss.de	AmpliGrid from Advantix in combination with PALM MicroBeam	AmpliGrid AG480F Standard size	Non-contact Laser Capture Microdissection (LCM)	Genetic typing of single cells, single cell sequencing (all fields of biomedical research, immunology, population genetics), stem cells	<ul style="list-style-type: none"> - Combines harvesting of ultrapure starting material from tissue preparation or cell cultures with On-Chip Cell Analysis in an extremely low volume reaction format - 48 discrete reaction sites for single cell analysis - No intermediate step 	Price on application, depending on configuration
Dolomite Microfluidics Royston, UK www.dolomite-microfluidics.com Contact: Gillian Davis Phone: + 44 (0)1763 242491 email: sales@dolomite-microfluidics.com	MITOS Edge Connector 4-way	4mm thick chips, 10mm-90mm length, 15mm wide. Wetted materials are PTFE & perfluoroelastometer	Microfluidic connector	Allows fast and reliable connection between Dolomite chips and 1.6 mm tubing	- Fast reliable fluidic connection	344,-
	MITOS T-junction chip with header	Chip size: 45 mm x 15 mm, 4mm thick. Glass. 2 inputs, 1 output	Glass microfluidic device	T-junction chip, a glass microfluidic device designed for mixing fluids, microreactions and droplet formation.	- Glass T-junction chip	329,-
febit biomed Heidelberg, Germany www.geniom.eu, www.febit.eu Contact: Philipp Habermeier Phone +49(0)6221-6510300 sales@febit.de	Geniom Arrays	8 independent arrays with individual fluid control. Three-dimensional disposable microchannel chip. Up to 15,624 features per array, resulting in up to 124,992 features per biochip. Enables parallel hybridization of 8 different samples.	Geniom RT Analyzer - microfluidic platform for the automated processing of microarray experiments Geniom One - microfluidic platform integrating DNA microarray synthesis and analysis	microRNA profiling, Gene expression profiling, Pathogen & virus typing, Epigenetic profiling, SNP typing & Genotyping, Enzyme-on-Chip, Custom arrays tailored to customer specifications.	<ul style="list-style-type: none"> - febit is able to provide you with virtually any DNA and RNA based assay in any species - Serves as a reaction chamber for Enzyme-on-chip Reactions. Enclosed cartridge for easy handling and auto-alignment to fluidics and optics 	Please inquire
GeSiM Grosserkmannsdorf, Germany www.gesim.de Contact: Steffen Howitz Phone: +49-351-2695-322 info@gesim.de	MicCell: versatile modular microfluidic perfusion system for the microscope	Diverse, normally PDMS 22 x 22 mm, 22 x 50 mm, 25 x 75 mm, other sizes on request	PDMS casting using a special molding station and Teflon-coated silicon masters, standardized connections for immediate use after gel casting, many accessories (microvalves!), customization	Diverse: e.g. cell perfusion (shear stress, microelectrode arrays etc.), cell adhesion tests, single-molecule handling using directed flow, laser tweezers, kinetic measurements, hybridization chamber, gradient formation, applications without microscope (e.g. SPR)	<ul style="list-style-type: none"> - Available for many inverted and upright microscopes - All control devices in one external "Fluid Processor" box - Many accessories: syringe pump(s), selector valve, 2/2 valve, hydrogel microvalve(s) to inject µl volumes, microelectrodes on chip, etc. - GUI-based software for interactive and programmed operation - Fully modular and customizable (e.g. version for slide scanner available) 	On request (depends on configuration)
Greiner Bio-One Frickenhausen, Germany www.gbo.com/bioscience Contact: Jörg Stappert, Björn Breth Phone: +49(0)7022 948-0 info@de.gbo.com	PapilloCheck	DNA-Chip for 12 analysis	PCR/microarray	For the early detection of cervical cancer Detection and genotyping of 24 different HPV types	<ul style="list-style-type: none"> - Type-specific identification of 24 HPV types (18 high risk and 6 low risk types) - IVD-CE Automated analysis with Check-Scanner and CheckReport Software 	On request
	CytoCheck	DNA-Chip for 2 or 12 analysis	PCR/microarray	Detection of 40 different mycoplasma species. In addition, a universal probe tests for the presence of mycoplasma species in general	<ul style="list-style-type: none"> - Validated under GMP-conditions according to Ph. Eur. - Ready-to-use kit - Rapid analysis within 4 hours - Comprehensive on-chip controls - Automatic evaluation using Check-Scanner and CheckReport Software 	On request

Lab-on-a-chip products (microfluid devices)

Company	Product/Device	Chip Material Chip Size	Technology	Application(s)	Miscellaneous, Specialities, Generally	Price [EUR]
Greiner Bio-One Contact see page 55	ParoCheck	DNA-Chip for 2 or 12 analysis	PCR/microarray	Detection of 10 or 20 Bacteria associated with periodontitis in human subgingival plaque samples	- IVD-CE - Ready-to-use kit - Rapid analysis within 4 hours - Comprehensive on-chip controls - Automatic evaluation using Check-Scanner und CheckReport Software	On request
	CarnoCheck	DNA-Chip for 12 analysis	PCR/microarray	Detection of 8 animal species (pig, cow, chicken, turkey, sheep, goat, donkey, horse) in food and complex-composition products	- Low LOD (up to 0.05%) - Ready-to-use kit - Rapid analysis within 3 hours - Comprehensive on-chip controls - Automatic evaluation using Check-Scanner and CheckReport Software	On request
	HairLoopCF	DNA-Chip for 2 or 10 analysis	PCR/microarray	Detection and genotyping of cystic fibrosis; simultaneous detection of 49 most common mutations in the CFTR gene.	- Best pan-ethnic coverage available, relevant to European population - IVD-CE - Ready-to-use kit - Rapid Analysis within 4 hours - Comprehensive on-chip controls - Automatic evaluation using Check-Scanner and CheckReport Software	On request
HSG-IMIT Freiburg, Germany www.hsg-imit.de Contact: Felix von Stetten Phone: +49(0)761/203-7393 felix.von.stetten@hsg-imit.de	Lab-on-a-Chip Foundry Service: Custom specific lab-on-a-chip implementation platforms: Transfer of biological assay to microfluidic lab-on-a-chip system	Materials: COP, COC, PMMA, PC, PDMS, PS, others upon request. Size: up to 14 cm x 14 cm	Microfluidic design and simulation, Milling, Laserablation, Soft-Embossing, Thermoforming, Surface modification and functionalization, Lamination, Molecular biological safety laboratory	Sample preparation, PCR, Immunoassay, custom specific applications	- Centrifugal microfluidicsBio-Disk Platform - Pressure Driven Systems - Rapid prototyping of plastic chips, fluidic and biological validation, system integration	Individual offer according to requested specification
ibidi Martinsried, Germany www.ibidi.de Contact: Ulf Rädler Phone: +49 89 520461731 uraedler@ibidi.de	ECIS carriers	Carrier from plastic material with gold electrodes	Impedance measurement system	Wound healing assays, Cell migration assays, Cell growth, Brain blood barrier simulation, Toxicological screenings	- Real time measurements - Non invasive Toxicological screenings - Drug uptake studies - Cultivation under flow possible - Various designs of the chambers also in 96 well format	40,- (8 well plates) 95,- (for 96 well plates)
	ibidi μ -Slides	Plastic material Standard glass Slides	Optical measurement via inverted microscopes	Cell imaging Immunofluorescence, Chemotaxis, Angiogenesis, Flow assays, Wound healing	- Small volumes (down to 25 μ l) - Multiple samples on a slide - Cost effective - Ideal near cell surrounding - Multiple handling steps integrated via design features as channels or membranes	Ranging from 2,- to 20,- (depending on coatings and design)
microfluidic ChipShop Jena, Germany www.microfluidic-chipshop.com Contact: Claudia Gärtner Phone: +49 3641 34 70 510	ChipGenie edition T: Continuous Flow PCR chip & Instrument	Polymer (PC) 25.5 mm x 75.5 mm x 1.5 mm	Microfluidics	PCR	- Continuous flow PCR - Ultrafast PCR	6.450,- (Instrument) 25,20/chip (>100 chips) 12,-/chip (>1.000 chips)
	ChipGenie edition E: Capillary electrophoresis system with contactless conductivity detection, chip & Instrument	Different polymers with electrodes Chip size: 16 mm x 95 mm	Microfluidics	Capillary electrophoresis, contactless conductivity detection	- Chip electrophoresis - on-chip detection - Electrodes on chip - Integrated electrodes - Conductivity detection	85,- /chip (>10 chips) 32,50 /chip (> 100 chips)
	lab-on-a-chip catalogue Chips & microfluidic support	Different polymers	Microfluidics	Microscopy, cell biology, electrophoresis, extraction etc.	- lab-on-a-chip catalogue - off-the-shelf microfluidic products	Prizing depends on chip type and quantity
Micronit Microfluidics Enschede, The Netherlands www.micronit.com Contact: Ms. M. Pelle Phone: +31 53 850 6 850 marketing@micronit.com	Microfluidic Chips	Glass	Powderblasting, HF etching, DRIE etching, Metal deposition, Surface Modification, Direct Bonding	Proteomics, Genomics, Cellomics, POC Diagnostics, Therapeutics, Agriculture, Food, Water / Air, High-Throughput Screening, Pharmaceutical Synthesis	- User-friendly microfluidic connections	-
Schott Jenaer Glas Jena, Germany www.schott.com/nexterion Contact: Alistair Rees Phone +49/3641 681-91967 Alistair.rees@schott.com	Microscope slides and other formats	Borosilicat Glass, Fused Silica, Optical Glass, Custom sized	-	Microarraying Microfluidics	- Primary manufacturer of technical glasses	On request