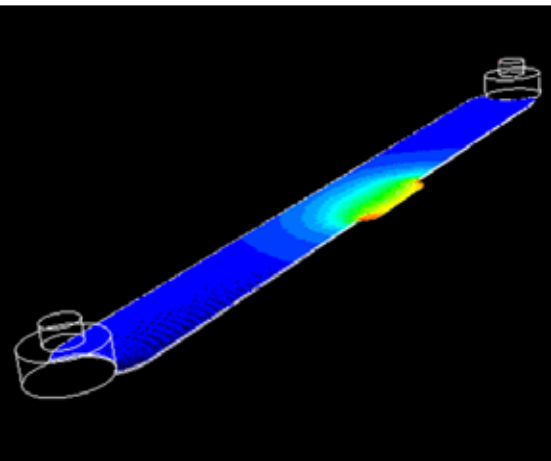
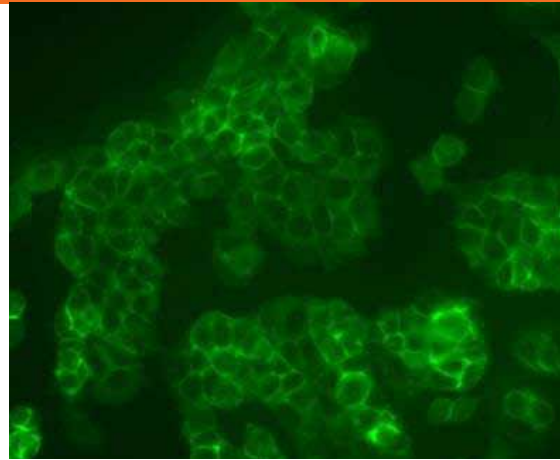
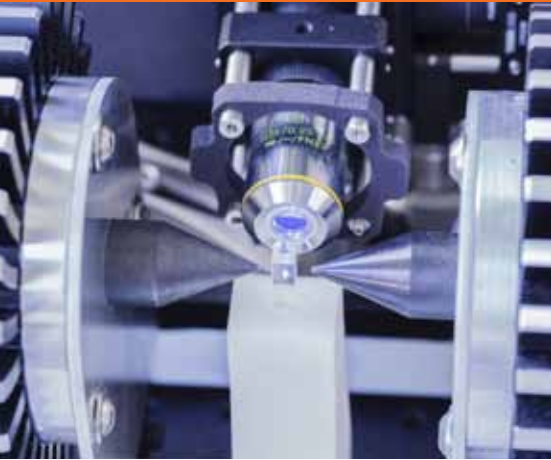


FRAUNHOFER INSTITUTE FOR
MANUFACTURING ENGINEERING AND AUTOMATION IPA

PROJECT GROUP FOR AUTOMATION IN MEDICINE AND BIOTECHNOLOGY
IN MANNHEIM

BIOPROCESS ENGINEERING



RESEARCH AND EXPERTISE IN MEDICINE AND BIOTECHNOLOGY

The Fraunhofer Project Group for Automation in Medicine and Biotechnology PAMB belongs to the Medical Faculty Mannheim of the Heidelberg University and was co-founded by the federal state of Baden-Württemberg and the Fraunhofer-Gesellschaft to exploit the potential for automation in medicine and biotechnology. It is the first institution known to focus on research in the area of automation for life sciences while offering development services in a clinical university setting.

Our interdisciplinary team of engineers and natural scientists works on innovative automation solutions in Bioprocess Engineering to support diagnosis and therapy: Our services include:

- Consultancy in Automation
- Bead Technologies
- Medical Sample Processing

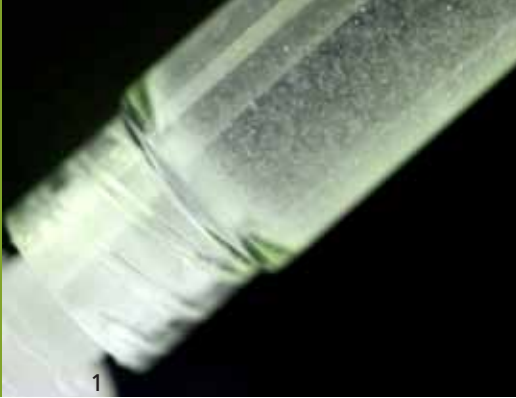
In all these areas, our products are recognized for their high functionality while maintaining ease of use. In addition, our products display a stage of development which enables companies to speed up time to market.

Through our services we help interested firms to enhance their marketability, thus generating added value for their company. The close interdisciplinary cooperation between engineers and scientists puts us in a position to develop application-specific and powerful solutions.

Thanks to our close collaboration with the Medical Faculty Mannheim of the Heidelberg University we are able to conduct pretests for numerous developments to ensure maximum customer benefit while reducing the development risks.

PROCESS TECHNOLOGY FOR
MEDICINE AND BIOTECHNOLOGY





CONSULTANCY IN AUTOMATION

For many years, we have been working in the field of automation in medicine and biotechnology and have delivered several automation solutions for different applications. Our senior consultants are able to analyze your requirements and to set up concepts for automated production lines based on different technologies. Existing products or production lines can be analyzed and evaluated by our experts to gain maximum benefit.

Our consultancy services include a wide range of methods:

- Requirement and specification analysis
- Concept development
- Technology scouting
- Value analysis
- Efficiency analysis

The Bioprocess Engineering group has specific knowledge in process automation

in clinical and laboratory environments. By optimizing the cost structure of your processes, we can help you strengthen your position in the market. Our consultants will assist you in conducting workshops together with your in-house experts to develop new ideas and utilize existing knowledge for your products or processes. Analytical thinking is combined with creative methods such as morphological analysis by Zwicky.

1 *Embolization surgery: Automated production of multi-modal visible embolization particles exhibits quality-assured contrast properties during interventional surgery.*

2 *Assay on Beads: New assay technologies can help to increase process efficacy.*





BEAD TECHNOLOGIES

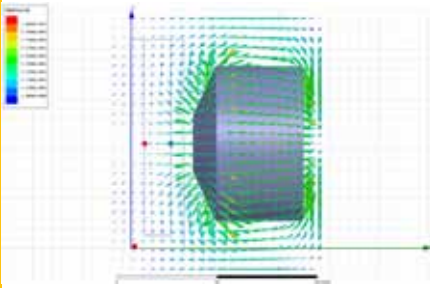
BeadTECH

In recent years, the use of magnetic beads for purifying biomolecules or cells has become much more common. Even in medical technology, magnetic beads are now increasingly used. They are easy to handle and can efficiently be applied, especially in conjunction with laboratory automation platforms. A distinction is made between systems which do not require amplification of the applied magnetic field (open gradient magnetic separation, OGMS) and systems with local field amplification (high gradient magnetic separation, HGMS). Functionalized magnetic beads make it possible to bind and separate almost any analyte that is known. The idea behind the systems developed by us is to open up ways to utilize magnetic beads not only for purifying biomolecules but also for simultaneous analysis with improved

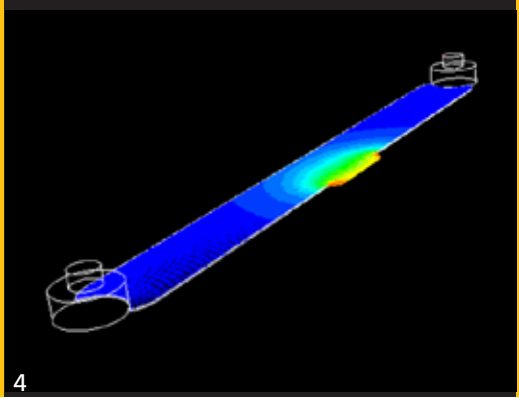
signal-to-background ratio. These improved signal characteristics are of particular advantage for multiplexing, enabling the detection of multiple analytes in very low concentrations.

1 *Oscillating electromagnets: Oscillating fields can focus magnetic beads in a laser spot to enhance signal-to-noise ratio.*

2 *Microscopic cell analyzer: Based on BeadSIM Technology, surface marker analysis can be performed by particle tracking under microscopes.*



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BeadSIM

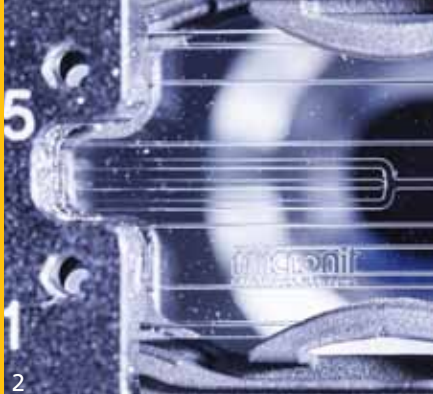
The simulation of magnetic systems and magnetic particle movements can help early on to find potential process errors and to increase yields. Our simulation experts assist in designing the optimal magnetic system for your individual separation requirements. Furthermore, electrical measurement systems for the detection of magnetic beads can be efficiently designed and operated. Then, our engineers build up your system based on the simulation results. Whether you want to integrate a micro-fluidic separation system for cells under a microscope or whether you want to use a microwell plate separator in a robotic platform with switchable magnetic fields, we can help you to find, design, and develop the appropriate solution.

3 *Permanent magnet design: Optimal geometric design of your magnetic separator helps to increase yields and to reduce cost per separation.*

4 *Microfluidic cell separation: Accumulation of cells in a certain region of a microfluidic channel can be pre-checked by simulation.*



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BeadTRAP

The BeadTRAP technology aims to trap magnetic beads in an applied magnetic field and to systematically manipulate them. Similar to optical tweezers, the local concentration of magnetic beads is greatly increased to improve the sensitivity of the chosen measurement method. In the future, it will be possible to simultaneously detect multiple analytes by combining the BeadTRAP technology with multiplexing techniques.

A modified version of this approach allows for a dedicated cell analysis. Appropriate microfluidic structures and targeted manipulation are used to determine the number of surface receptors located on the cell depending on the number of magnetic beads bound to a cell.

Assay on Beads

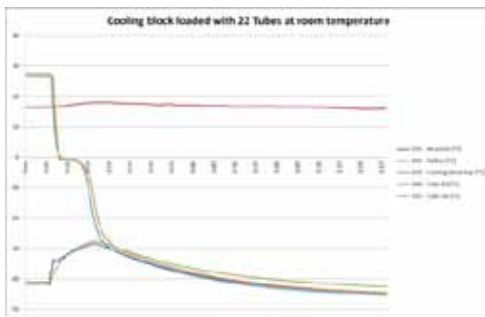
With our laboratory infrastructure we can help you to design and operate the best possible magnetic assay system.

The simulation tool ANSYS enables the simulation of magnetic fields and resulting bead movements in fluids, thus ensuring an optimal separation and analysis process. In our institute, we have several magnetic separation technologies which help to check whether a conventional system fits your needs or if an innovative custom-built system such as separation with Halbach-Arrays would be favorable. Our large library of magnetic beads is supplemented by the beads developed in-house. Currently, we are working on molecular imprinted beads mimicking the structure of biological molecules such as biotin, streptavidin, antibodies, or even DNA/RNA fragments.

1 *BeadTRAP signal: The dynamic signal allows for the analysis of low concentrations of biomolecules.*

2 *Particle production: Our microfluidic particle production system realizes particles in narrow size distributions and several functions, e.g. visibility in medical imaging systems like CT and MRI.*





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2

MEDICAL SAMPLE PROCESSING

Samples from the OR

In biomedicine, laboratory analyses have always formed the basis for diagnosis, treatment decisions, and disease monitoring. By refining these methods and increasing the knowledge of the pathological and biochemical background of diseases, the range of new biomarkers and parameters has been continuously expanded. However, significant changes can occur very fast between the time of sampling and analysis due to different transport times, temperatures, and transport routes. In Medical Sample Processing, we are dealing with new technologies for taking samples and for safely transporting samples under controlled conditions to create reproducible analyses. This topic is under development and currently comprises the following technologies.

BiopsyPROCESSOR

The BiopsyProcessor is used to dissociate tissue biopsies and to generate single cell suspensions for the further diagnosis of molecular substances. At present, the BiopsyProcessor operates on the basis of Miltenyi Biotec M-tubes or C-tubes. At controlled temperatures, it enables mechanical and enzymatic dissociation. The technology is currently used within the DiagnoSYS system, which enables automated chemosensitivity tests for breast and ovarian cancer. A second generation of the processing unit is currently refined by the EU project MITIGATE to enable the combination of sample collection and processing in the intervention room.



SampleCOLLECTOR

The SampleCOLLECTOR system enables the cooling of liquid samples such as blood to the desired transport temperature as soon as they are taken and to maintain temperature while they are transported to the central laboratory. The small, mobile system uses Peltier elements to cool the samples to -50°C . This technology is to be further developed as part of the research campus M²OLIE (Mannheim Molecular Intervention Environment) to ensure that samples collected and processed in the operation room for further analysis are transported under controlled conditions.

Services

Based on our current technologies and your specific requirements, we can design methods for disrupting cells or tissues and for isolating single cells from samples for an optimal analysis. In this context, we

can also test the viability and yield of your dissociation reagents. Furthermore, we can design solutions for sample cryo storage and transportation tailored to your tasks. We are looking forward to hearing from you.

1 *Temperature control: Storage temperature of processed tubes in mobile cooling systems.*

2 *Isolation of single cells: Device to isolate single cells from biopsy specimens.*

3 *Magnetic separation: The magnetic field of this separator can be switched on and off to allow for all process steps without plate movement. Integration in a thermo-shaker enables hot-elution separations.*

4 *DiagnoSYS: Automated platform for personalized chemosensitivity testing with integrated Biopsy Processor and magnetic cell separation.*



CONTACT

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