INSTITUTE OF SCIENTIFIC INSTRUMENTS
Academy of Sciences of the Czech Republic, v. v. i.

AKADEMIE VĚD
ČESKÉ REPUBLIKY

alisi Handbook of application capacities of the Institute of Scientific Instruments of the AS CR, v. v. i.

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Handbook
of application capacities
of the Institute
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of the AS CR, v. v. i.

ISI
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# Handbook of application capacities of the Institute of Scientific Instruments of the ASCR, v. v. i.


ISI ASCR Institute of Scientific Instruments AS CR, v. v. i.

alisi Aplication Laboratories of Microtechnology and Nanotechnology

## Handbook of application capacities of the Institute of Scientific Instruments of the ASCR, v. v. i.

The handbook you have just opened provides an overview of the application potential of the Institute of Scientific Instruments of the ASCR, v.v.i. (ISI). For more than 50 years research activities of the ISI have focused on searching for new physical methods and development of novel instrumental components and technologies for acquisition, imaging, and diagnostics applicable on various scales ranging from macro-world down to the nano-world. ISI has also successfully co-operated with industrial partners, resulting in a number of unique devices that were the first prototypes of their kind in the Czech Republic or even the world. Examples of these include electron microscopes and, later, an electron beam writer, lasers and interferometric systems for precise measurements, NMR spectrometers, and cryogenic systems. Over the past 20 years ISI has focused primarily on further exploration and improvement of physical methods in the established areas of ISI's interests. Our approach typically covers all the aspects of the problem, starting from the theoretical description to the implementation of unique instrumental elements or even complex devices.
Our R&D activities cover:

- the employment of electron beams for imaging, diagnostics, lithography, and welding;
- the design of new pulse sequences for magnetic resonance tomography and their utilization in the detection of chemical changes in living organisms, including humans;
- the measurement of thermal radiative properties of materials at low temperatures; designs of cryogenic systems;
- technologies of thin films deposition;
- acquisition and processing of biosignals in medicine;
- the utilization of laser beams for welding, spectroscopy, precise measurement of lengths and gas refractive index, manipulation with microobjects and nanoobjects.

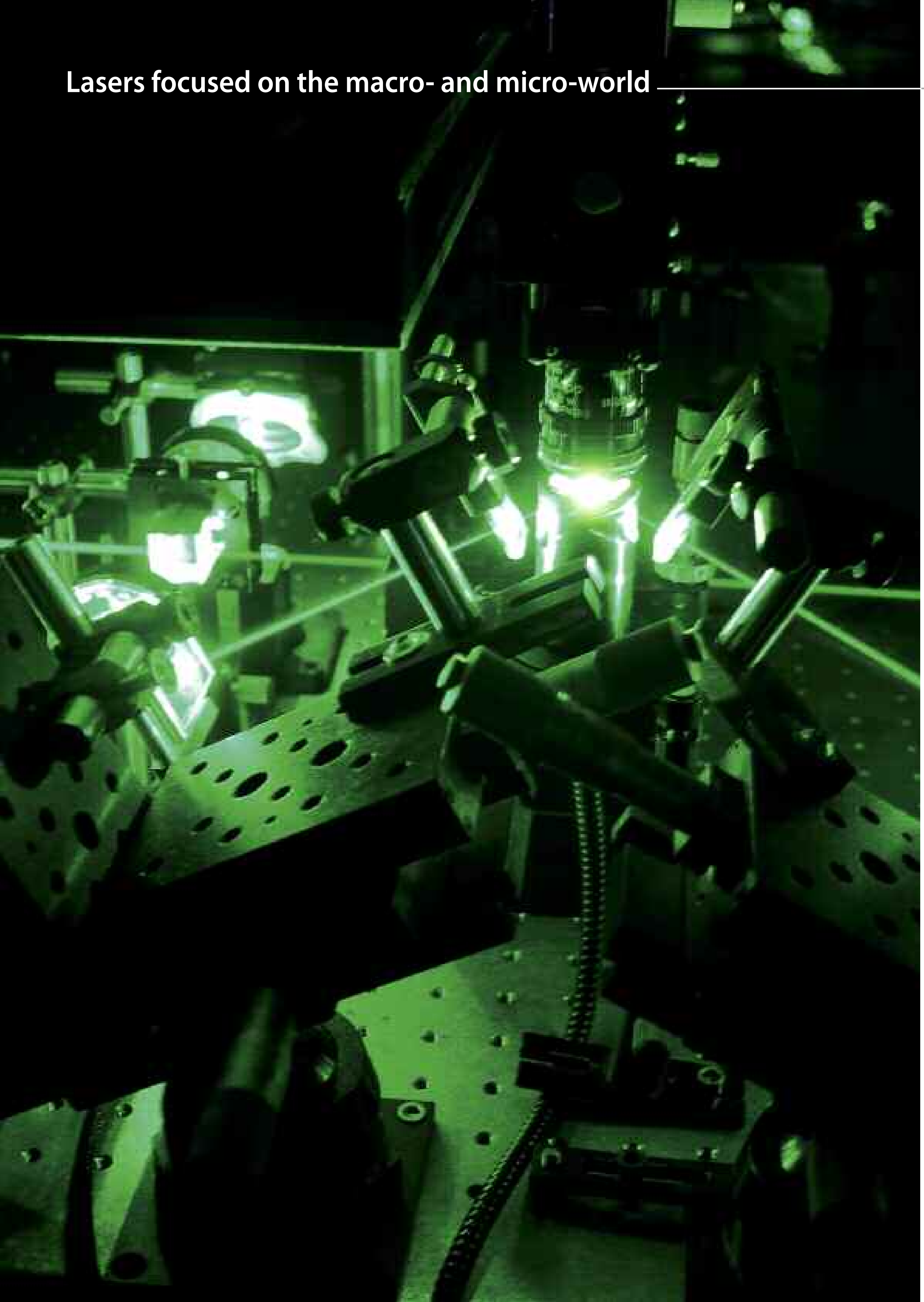
Thanks to its scientific results ISI has succeeded in a hard competition and in 2010 was granted CZK 432 mil. to realize the project of Application Laboratories of Advanced Microtechnologies and Nanotechnologies (ALISI), which will significantly broaden and modernize the ISI research basis. The following pages will provide you more detailed information about ISI's selected application activities.

Prof. Pavel Zemánek
Deputy Director of ISI

20 March 2010, Brno


# Obsah

# Lasers focused on the macro- and micro-world



*Set-up for optical sorting of microobjects (p. 8).*



Optical techniques have recently discovered many new applications, ranging from biology to the nuclear industry. These techniques provide information on the chemical composition of the targets with spatial resolution down to micrometers. The main advantages of optical techniques are **fast and non-contact measurements** provided **in real-time**, and relatively **low equipment costs**.

The group of *Optical micromanipulation techniques* offers the following expertise:

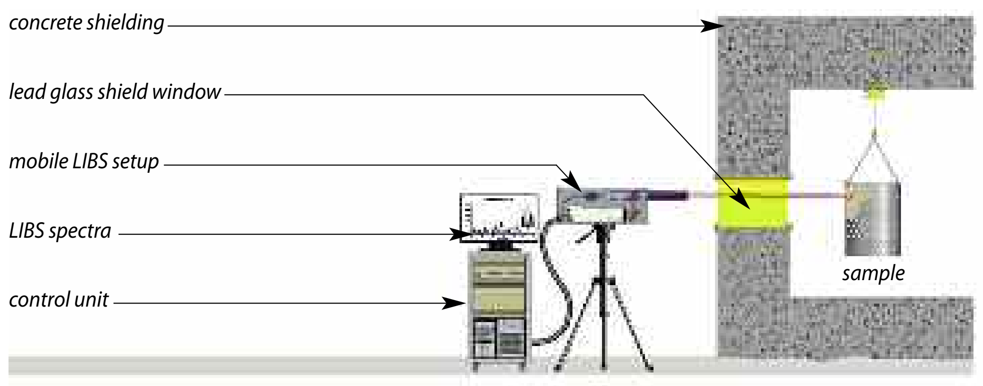
- Construction of unique instrumentation for diagnostics that employs laser-based spectroscopy techniques such as Laser Induced Breakdown Spectroscopy (LIBS) and Raman spectroscopy.
- Applications of focused laser beams in microworld for contactless manipulations and sorting of microobjects, production of microstructures using the technique of photopolymerization, and two- and three-dimensional modification of objects using laser ablation.
- Searching and development of new methods for identification of microorganisms, their separation or alternatively, destruction.

## Applications of laser-induced breakdown spectroscopy – LIBS

Recently, there has been increased interest and demand in nearly all scientific research areas for experimental techniques that enable fast and unambiguous interpretation of the acquired data. This interest follows industrial requirements for fast and accurate material identification and analyses without lengthy laboratory techniques.
The technique of LIBS involves formation of luminous plasma generated by focusing the radiation from a pulsed fixed-frequency laser (less then 1 J/pulse) onto the surface of the sample to be analysed. The light emitted by the hot plasma is dispersed by a spectrometer and the characteristic emission lines produced by the excited elements during the plasma cooling make it possible to determine the elemental composition of the sample within the focus area. Detection limits of LIBS range from a few ppm to hundreds of ppm (w/w).
The on-site capabilities of LIBS imply that a measurement can be carried out without target manipulation, and the result is obtained instantaneously (in real-time). A sample does not have to be prepared to utilize the analysis; for example, solvents and any surface contaminants can be ablated off the sample before carrying out a measurement. Thus, LIBS is an ideal technique for identifying problems where the target may be coated with industrial sludge or a thick oxide layer, or even submerged in liquids.

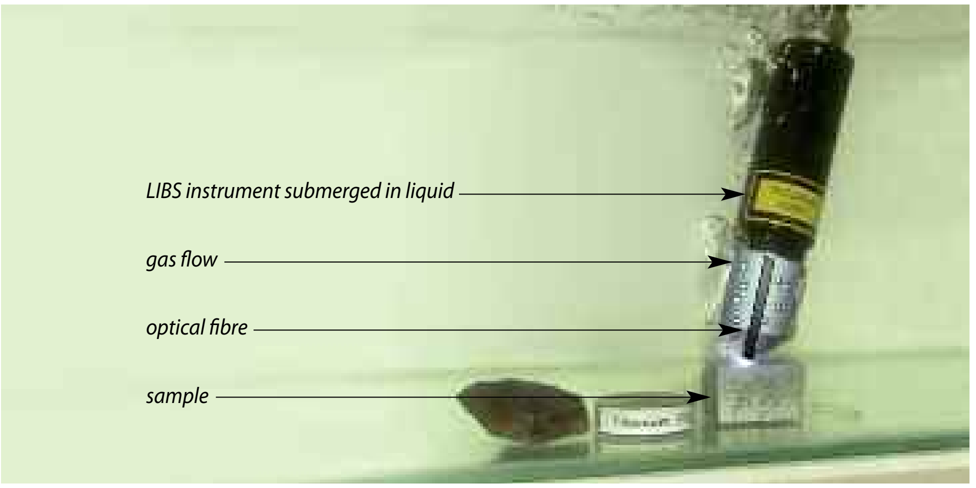
**The additional advantages and applications of LIBS:**

- With LIBS the entire interaction between the system and the target is **purely optical**. Thus, the analysis can be performed **remotely**, provided that an optical connection can be established between the instrument and the target, e.g. with the use of an optical fibre. For remote applications the target can be placed up to hundreds of meters away from the mobile LIBS instrument (sediments inside storage tanks, oil rigs, and rigid steel constructions).



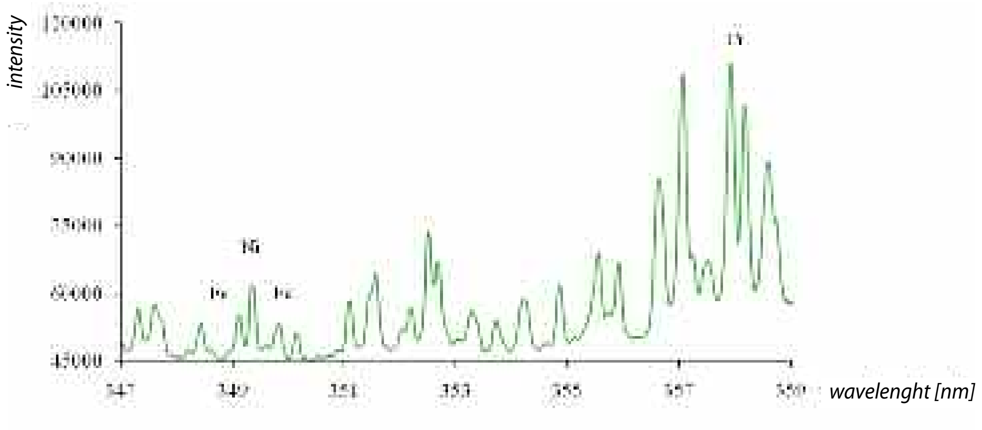

*Schematic drawing showing the application of a mobile LIBS instrument.*

LIBS setup for material identification of samples submerged in liquids (up to a few meters). Detail shows gas flow to clean the sample surface from liquid so that ablation takes place within gaseous environment.




- LIBS excels in instances where **on-site**, **real-time**, and **on-line** measurements in various production phases are required (e.g. for metal identification problems). Different types of steel (e.g. FV520, NAG, 17/4, and 18/13) can be identified simply by following some of the representative elements (e.g. Mo, Ni, and Ti).

Emission lines identified in the LIBS spectrum of a metal sample – Fe, Ni, and Cr.




- LIBS **can detect the following elements** – Be, U, I, Al, C, Ca, Mg, Cr, Pb, Si, Li, Hg, Sr, Rb, Ti, Fe, Ni, V, Mn, Mo, etc.
- The most appropriate applications of LIBS are those encountered **in the nuclear and chemical industry**, where quantitative or qualitative remote analysis, without any physical contact with the sample, is preferred. A mobile LIBS setup based on the optical fibre delivery system can be identified as a natural solution to some of the analytical problems where exposure of personnel to highly radioactive or toxic material is understandably undesirable.
- Various setups can be used for **environmental monitoring**. Specially engineered systems can be designed and assembled for each analytical problem, allowing fast decisions to be made concerning the identification of target materials which can then be **immediately sorted and labelled**.
- LIBS can be used for quantitative analysis with reasonable precision even for **small samples** provided a tightly focused beam is used for material ablation (this is limited by the focusing optics).

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## Laser Raman spectroscopy

**Laser Raman spectroscopy** is a powerful technique for the identification of a wide range of samples – solids, liquids, and gases. It is a straightforward, non-destructive technique requiring no sample preparation. Raman spectroscopy involves illuminating the sample with monochromatic light (laser) and using a spectrometer to examine light that is scattered by the sample. Spectral composition of the scattered light carries information about different molecular or crystal vibrational modes which can serve as a unique characteristic for different materials. This makes Raman spectroscopy a useful technique for fast material identification (usually a few minutes are required) and characterisation of the content of DNA, RNA, lipids, proteins, sugars, pigments, saccharides, and amides within the sample. Typical Raman spectrometers for material identification use a microscope to focus the laser beam on a small spot so that the information about chemical composition from femtolitre volumes can be obtained.

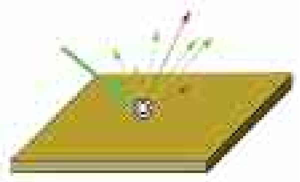
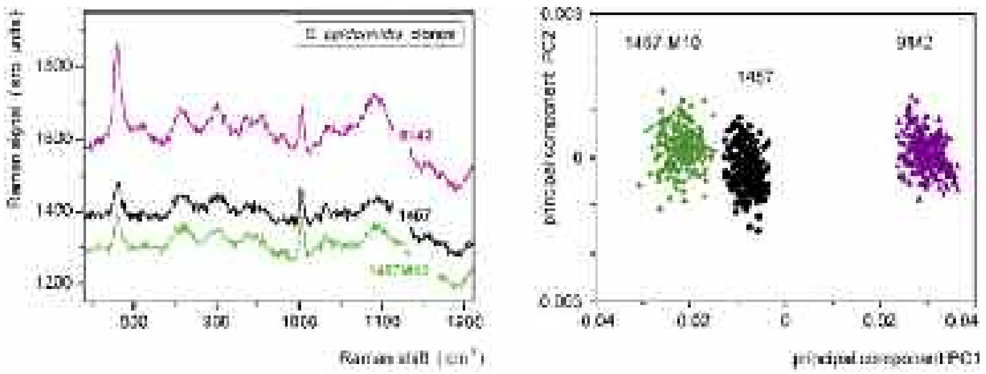



Diagram of principles behind Raman spectroscopy: Scattered light of the same wavelength as incoming laser; Raman shift from the incident laser energy gives a Raman spectrum. Different materials have characteristic Raman spectra.

Even though the principle of this method has been known for almost a hundred years, only recently has started to be utilized in many unique applications triggered especially by the development of sensitive detectors.

**The advantages and applications of Raman spectroscopy:**

- Raman spectroscopy is capable of **rapidly identifying biological samples**. For example, medically relevant bacterial strains can be detected (e.g. *Staphylococcus epidermidis*). Raman spectroscopy can **discriminate between biofilm-positive and biofilm-negative** bacterial strains in real-time. Thus, time and cost of patient treatment related to virulent infection can be reduced because an appropriate therapeutic strategy can be chosen.




Typical Raman spectra of the three bacterial strains of Staphylococcus epidermidis (identified by colour and strain number).

Plot of Principle Component relation for the three Staphylococcus epidermidis strains. 1457-M10 strain is biofilm-negative.

- Raman spectra can serve for identification of cells in **oncological applications** (e.g. diagnostics for early recognition of cancerous cells in-vivo and in-vitro) and identification of **cells invaded by viral infections**.
- **Non-destructive analysis** in the **pharmaceutical industry** (e.g. on-line characterization of tablets) and production of chemical maps of different surfaces or identification of nano-structures are possible.
- Raman spectroscopy can be combined with optical tweezers to form so-called Raman tweezers. This powerful combination can be used for **identification and sorting of microorganisms** freely moving in liquids.

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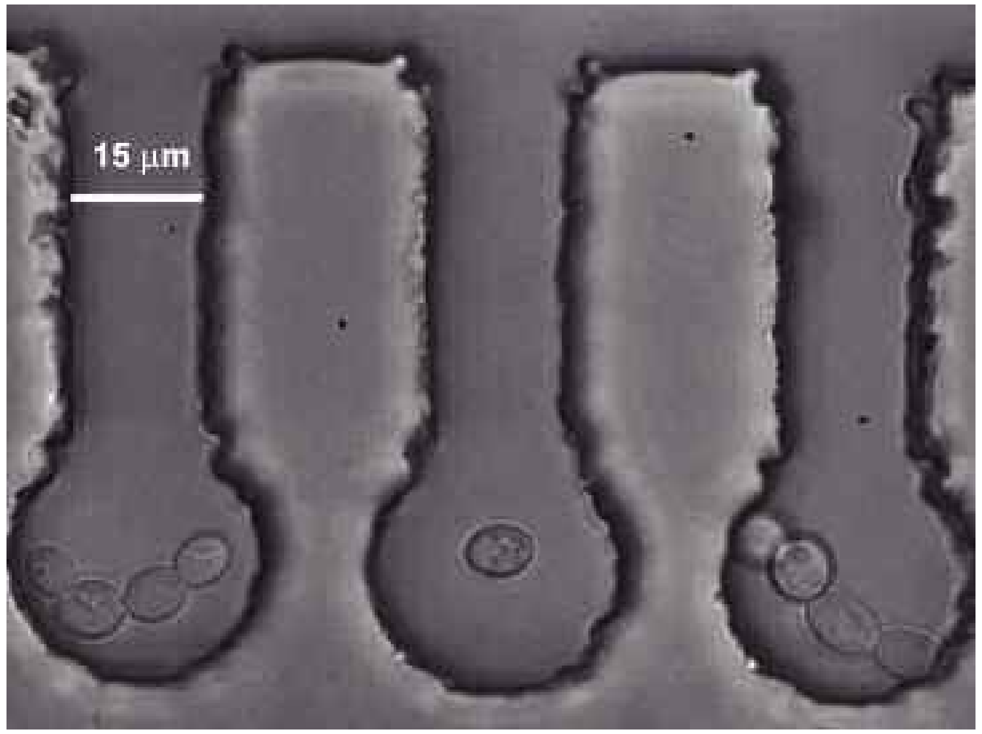
## Optical micromanipulation techniques

Optical micromanipulation techniques use the transfer of momentum from light to microobjects. Such a transfer occurs, for example, during light scattering from the microobjects, which is accompanied by a change of direction of the light propagation. Optical micromanipulations make it possible to influence the motion of objects of sizes from tens of nanometers to tens of micrometers just by illumination with a laser beam. Optical tweezers represent an optical analogy to the classical mechanical manipulation tool, using a single tightly focused laser beam to confine objects in a contactless way. Since the objects are trapped in the vicinity of the beam focus, repositioning of the focus also causes repositioning of the objects, i.e. their controlled spatial micromanipulation. Several laser beam foci can be placed simultaneously within the specimen in a controlled way, therefore enabling simultaneous confinement and controlled micromanipulation with multiple objects. This tool is mainly used for manipulation of objects suspended in a liquid medium (living microorganisms or cells in water or appropriate solution, microobjects placed behind transparent obstacles etc.). Since such small objects can only be observed using optical microscope, both techniques are often combined.

**Examples of optical micromanipulation application:**

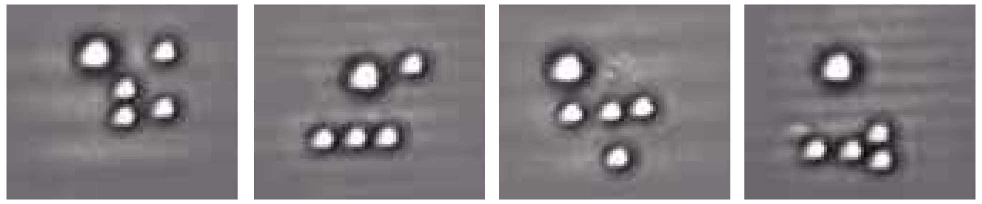
- **A compact version** of optical tweezers has been developed based on an adapter inserted between the microscope and lens and containing an integrated laser diode or optical fibre connector. Optical micromanipulation is therefore possible without disturbing the optical path of the microscope.
- Optical tweezers can be **combined with several optical spectroscopic techniques** (e.g. Raman microspectroscopy, fluorescent spectroscopy) to enable contactless and non-destructive characterization of the trapped microobjects.
- Highly promising is the combination of **optical micromanipulation** techniques with **microfluidic systems** (lab-on-a-chip) that can serve, for example, for the study of stress at the level of individual cells followed by cell sorting.

*Example of the microfluidic structure of cultivation microchambres with living yeast cells. The side chambers are occupied by non-stressed cells that divide, and a non-dividing stressed cell is placed in the middle chamber. The cells were positioned in the chambers with optical tweezers.*






- In addition to tightly focused beams there are also other configurations of laser beams for regular **microobject confinement and arrangement in the space or on the surface**.
- Illumination of moving microobjects influences their motion and can cause rectification of their stochastic motion leading to optical sorting of different suspension components (e.g. different types of cells).



*Example of optical sorting of microobject by size. Silica microspheres of sizes 2 and 3 micrometers move in opposite directions after the laser beam illumination.*

**Examples of applications of laser beams focused down to micrometer spots:**

- The significant increase of the laser beam intensity near its focus initiates photopolymerization – a chemical reaction that solidifies the liquid monomer into a solid polymer. Complex microstructures can be created by controlled positioning of the focused laser beam within the monomer solution.
- Focused pulsed laser beams of suitable wavelength offer many opportunities of employing their destructive effects (microablation) to volume or surface modifications of objects including, for example, intervention inside living cells.

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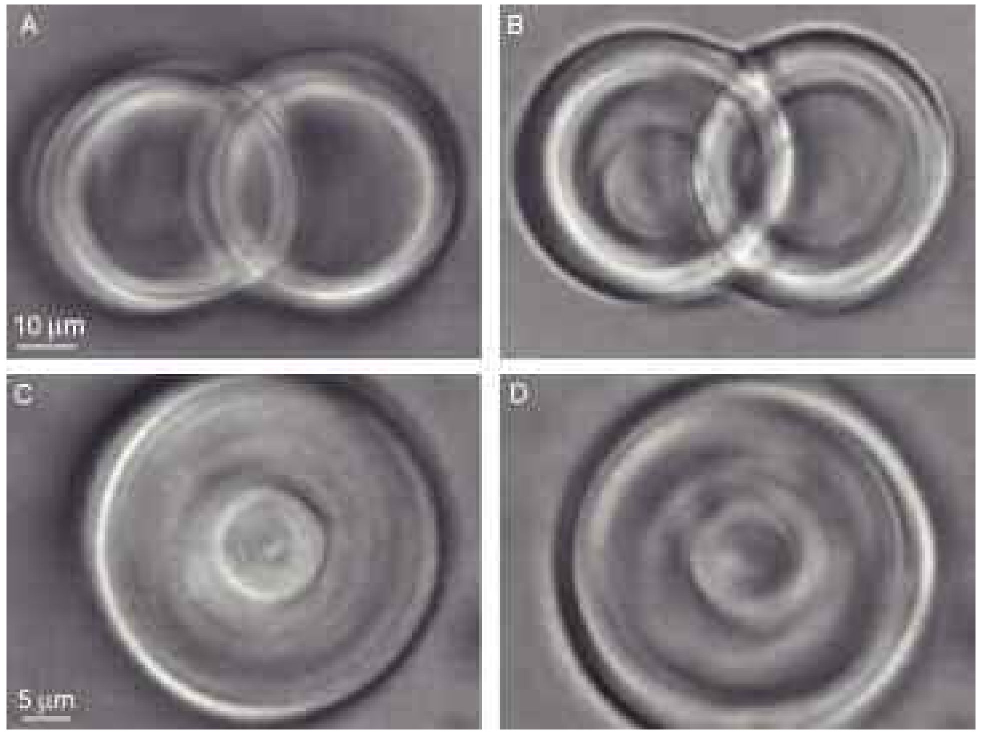


*Example of microstructures created by photopolymerization. Narrow hollow fibres have a wall width of 2 micrometers and their length reaches several centimetres. Figures A and B compare shapes and dimensions of opposite ends of the fibres separated by several centimetres.*

# Special Technologies



*The Special Technologies team* is engaged in:

- Research and development of technologies and constructions necessary e.g. for building electron microscopes working with high or ultrahigh vacuum. The most important of these technologies are **electron beam welding, vacuum brazing, the design and manufacture of vacuum feedthroughs**, etc.
- **Magnetron sputtering** of thin metal layers such as Al, Si, Mo, Ti, Ni, Ag, C, ITO, Nb, W, TiN, $Si_3N_4$, $SiO_2$, and their combinations. The team also managed the preparation of multi-layer systems for X-ray optics, consisting of nanometer double-layers with total thickness of tenths of a micrometer, with accuracy to tenths of a nanometer.
- **Vacuum deposition** by means of electron beam heating and spectro-photometric measurements of their spectral reflectivity and transparency.
- Deposition of **abrasion-resistant layers** like carbon, carbon-nitride, nano-structured multi-layers and carbon-based nano-composites.
- Testing of hard abrasion-resistant layers by a dynamic impact tester (we are one of only two facilities in the Czech Republic that possess this instrument).

*Electron beam welding of a stainless steel tube (p. 14).*

## Electron beam welding

Electron beam welding is a fusion joining method that applies an electron beam for local heating. At the point of impact, the kinetic energy of electrons, ranging from 30 to 200 keV, is transferred into heat which rapidly warms any material to its melting point. The process takes place in a high vacuum (pressure $10^{-2}$ to $10^{-3}$ Pa), most often **without additional material**. Thanks to very high power concentration, the focused beam penetrates rapidly into the metal, producing a **deep and narrow weld**. As a result of the clean, high vacuum atmosphere, even **highly reactive metals like titanium or zirconium can be welded**. Due to high vapor pressure at the melting temperature, some metals like Zn, Cd or Mg, cannot be welded in vacuum. Despite high acquisition costs, electron beam welders are widely used today, particularly in the **nuclear, cosmic, aviation and automobile industries**.

**The main advantages of electron beam welding include:**

- "Knife" form of the weld with a depth to width ratio of up to 25:1, resulting in minimal deformations and thermally affected zone.
- **Welding of refractory metals**.
- Very **deep** welds: with enough power in the beam, up to 300 mm in aluminum, or 100 mm deep welds in stainless steel can be realized.
- **High productivity.**
- Due to high vacuum working atmosphere, the re-melted zone can be **cleaner** than the basic material.

Three electron beam welders are installed at ISI Brno, all designed and manufactured in this institute. All three are equipped with cylindrical vacuum working chambers and welding manipulators for rotation and linear movement of the work-piece. The design of all three enables two positions of the electron gun on the working chamber: either **horizontal or vertical**. With the gun in the vertical position, the vacuum working chamber can be extended horizontally. Tubes (e.g. 5 meters long) can then be welded.
The technical parameters of these welders are:

- The oldest, but upgraded equipment ES-2 has a working chamber 600 mm in diameter and 490 mm in length. It is equipped with a 50 kV/1.5 kW electron gun.
- The "desk-top" EB welder SES-1 has a working chamber 235 mm in diameter and 165 mm in length. It is equipped with a 50 kV/1.5 kW electron gun. Five-meter zirconium tubes have been welded in the vacuum chamber when extended horizontally.

*Improved ES-2 e-beam welder, SES-1 desktop e-beam welder and MEBW-60/2-E experimental micro e-beam welder.*

- Experimental electron beam welder MEBW-60/2-E with a similar working chamber is equipped with a 60 kV/2 kW electron gun. The electronic equipment of this welder is completely digitalized and computer controlled. This enables, for example, automatic, pre-programmed welding that is perfectly reproducible.




*Examples of vacuum components welded by electron beam.*

The MEBW-60/2-E welder can also be operated in a mode similar to a scanning electron microscope. In this mode the objects in the vacuum chamber can be, at a magnification of up to about 30 times, displayed on the computer monitor, e.g. to inspect the weld before venting the working chamber. The welder in this mode can also be used for the precisely localized surface heating needed for hardening or annealing of thin surface layers.

**Applications of electron beam welders at ISI Brno:**

- **Welding** high and **ultra-high vacuum components** (fittings, valves, etc.).
- Components for **nuclear power engineering** (e.g. heat exchangers).
- **Joining of dissimilar materials** (e.g. aluminum to titanium and/or nickel, or silver, copper to stainless steel, titanium to steel, and many other combinations).
- **Welding of refractory metals** such as molybdenum or tungsten.
- **Welding of highly reactive metals** such as like titanium or zirconium.

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## Vacuum brazing and annealing

The Special Technologies team has great experience with **vacuum capillary brazing**. The most commonly used solders are silver- or nickel-based alloys, or copper. For soldering metals to brittle non-metal materials (e.g. quartz), so-called "active", soft solders are applied.

**For these technologies, our institute has at its disposal two vacuum furnaces:**

Vacuum furnace **PZ 810**, manufactured by Tesla Rožnov, with the following parameters:

- Maximum batch dimensions: diameter 350 mm, height 590 mm.
- Molybdenum heating and shielding elements, allowing long-term heating up to 1400 °C.
- Vacuum $5\times10^{-2}$ Pa up to 1 Pa, depending on the charge properties and working temperature.
- Maximum speed of temperature increase: **1500°C per hour**.
- Time of cooling in high vacuum: about 8 hours. If needed, the cooling period can be cut short by venting the furnace with **inert gas**.

*Renovated PZ 810 vacuum furnace.*

*Examples of vacuum soldering.*

Laboratory vacuum furnace built at ISI.

Vacuum furnace of our own design and manufacture suitable for **vacuum brazing and annealing** of small-sized components:

- Maximum batch dimensions: 150 mm in diameter, 200 mm in height.
- The vacuum space **can be extended upwards** (without heating) for welding objects in the hot zone, if the upper part does not exceed 18 mm (e.g. long tubes to flanges).
- Maximum working temperature: 1100°C.

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## Design and manufacture of feedthroughs

The team of Special technologies realizes research and manufacture of varies types of electric, vacuum-tight and high- or low- temperatures resistant feedthroughs. The technology is based on **glass-to-metal seals**, either with **kovar or other metals** (pressure-seals).The feedthroughs are usually welded to flanges or other construction components. To date we have developed the following types:

- One-pin coaxial feedthroughs for working temperatures from –196°C up to +400°C.
- Seven- or twelve-pin feedthroughs for temperatures from –196°C up to +400°C.
- High-current feedthroughs for temperatures from –60 to +300°C.
- High-pressure feedthroughs for the nuclear industry, with working temperatures from –60 up to +300°C.
- Individual, and custom feedthroughs.

*Vacuum feedthroughs examples.*

**Applications of feedthroughs**

- Special feedthroughs for various instruments such as electron microscopes, ultrahigh vacuum devices, etc.
- Nuclear power engineering.

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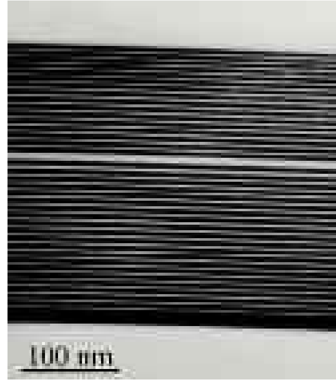
## Thin layers deposited by magnetron sputtering and their dynamic impact testing

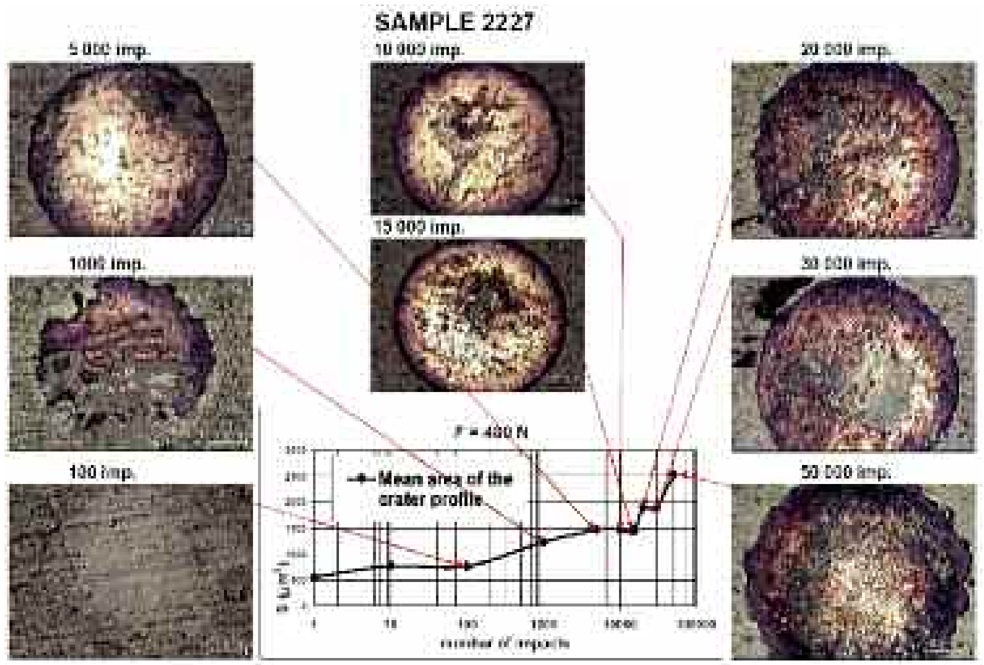
We can deposit thin layers by high-frequency magnetron sputtering in the commercial equipment LEYBOLD-HERAEUS Z 550, enabling the production of layers in small series or on single substrates of up to 100 mm in diameter and a thickness of 20 mm. The machine is equipped with three magnetrons, each with a Ø152 mm target. This makes it possible to deposit three different materials in one evacuation cycle. For special applications (for example ion etching) the substrate can be preheated and electrically charged.




*Multilayer coating for x-ray optics.*

**Applications of magnetron sputtering:**

- We can deposit **multi-layers for X-ray optics**, in combinations of double-layers such as molybdenum/silicon, nickel/carbon, scandium/silicon and others suitable for X-rays in the wavelength **range from 12 to 50 nm**. Maximum reflection at perpendicular impact is up to 70%.
- For very short wavelengths (less than 4 nm) multi-layer systems cannot be used because the roughness of the interface causes decreased reflectivity. Nevertheless, the periodical multi-layers are applicable for inclined rays, providing much higher reflexivity than much thicker mono-layer deposits.
- At present we are one of only two places in Czech Republic where **characteristic properties of hard abrasion-resistant nano-composite and multi-layer deposits can be evaluated** by a dynamic impact tester. During testing the sample surface is impacted periodically by a small wolfram-carbide ball, imitating a dynamic strain of layer/base system of stamping dies, cutting tools, parts of automobile motors, etc.




*Results of the thin layer dynamic impact test.*

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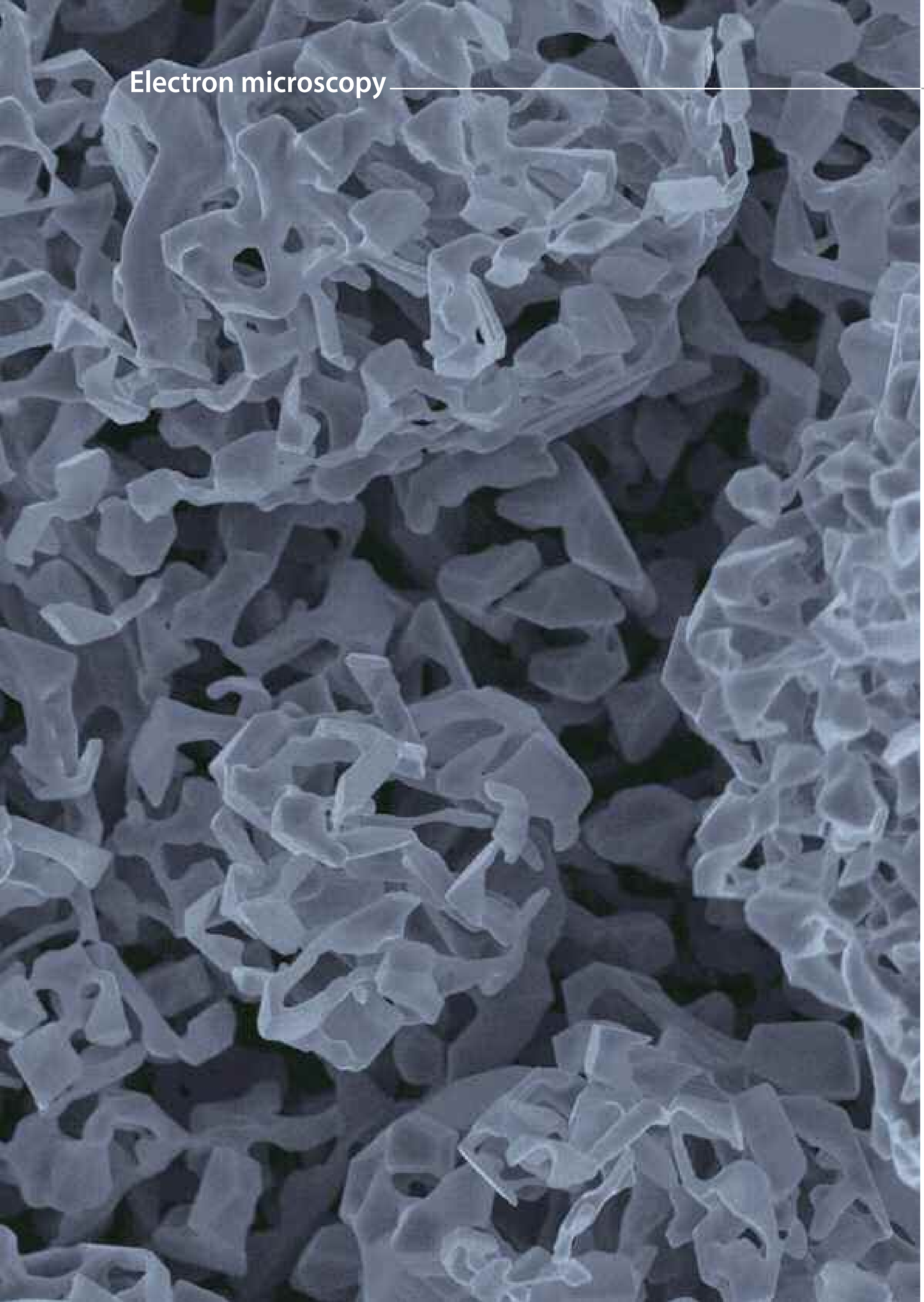
# Electron microscopy

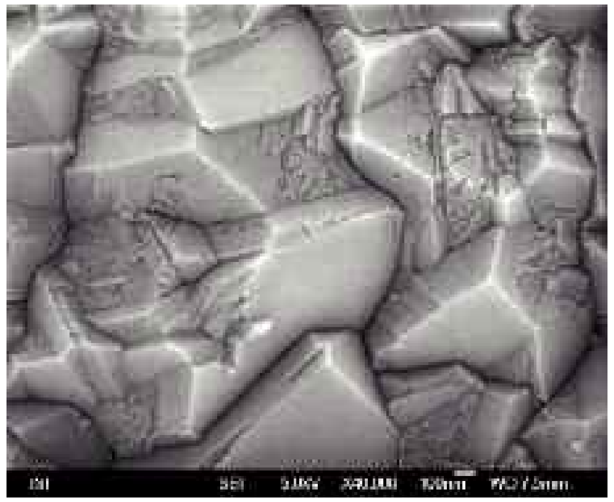




*Electron microscopy* is a globally used technique for the examination of matter with an extremely broad scope of applications in life, materials and even social sciences. The Laboratory of Electron Microscopy (LEM) has a great deal of experience in the development and use of instrumentation as well as in electron microscopy methodology; at present it offers several unique methods of imaging and analysis of solid surfaces at high spatial resolution.

*Nanostructure of a catalyzer (p. 20).*

- The ultimate spatial resolution is achievable by means of the cold field emission source of electrons available in the JEOL JSM 6700F scanning electron microscope with verified resolution of 1 nm at the electron energy of 15 keV. The microscope is equipped with the energy dispersive analyser of X-rays Oxford INCA Energy 350 for chemical microanalysis.
- Methodology for the very low energy scanning electron microscopy has been developed at ISI and the corresponding attachments are installed on several microscopes in LEM. The method enables the preservation of image resolution down to arbitrarily low energy, which is not possible in commercially available instruments. At very low energies plenty of novel contrast mechanisms reveal electronic and crystallinic structures of the sample.
- Environmental scanning electron microscopy (ESEM) enables the study of samples of living substances and materials under elevated pressure of surrounding gas up to 3000 Pa. In this environment charging of nonconductive samples is avoided and even wet matter can be protected against drying . The ESEM instruments also work under the standard high vacuum conditions.
- Electron microscopy under ultrahigh vacuum conditions of $10^{-8}$ Pa enables one to study atomically clean surfaces that can be cleaned in-situ with ion beam bombardment. The device offers excellent conditions for the low energy microscopy.
- LEM has available standard preparation techniques such as sputtering and evaporation of surface coatings, ion beam thinning, exact cutting. Complementary light optical imaging is possible with the confocal microscope Olympus LEXT 3100.

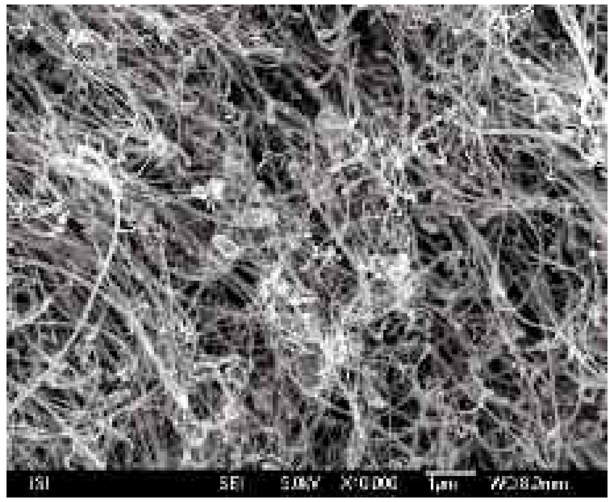


*Surface of a synthesized diamond coating.*

*Clusters of micrometer sized diamond grains.*

## High resolution scanning electron microscopy and X-ray microanalysis

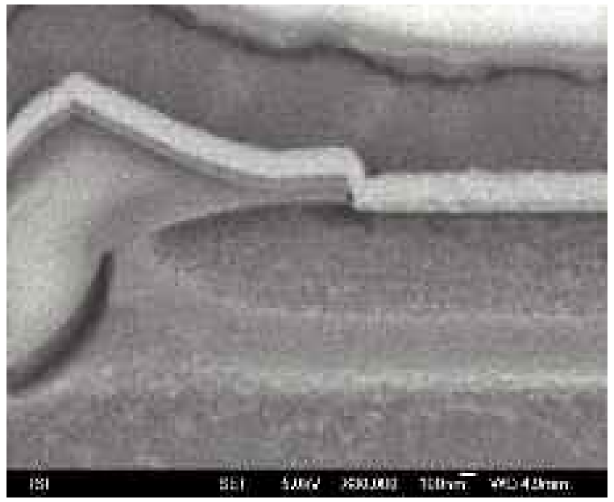
The high resolution scanning electron microscopy applications are met in nearly all scientific branches. In combination with the X-ray microanalysis it provides information about the surface topography of a sample together with its local quantitative composition as regards chemical elements.



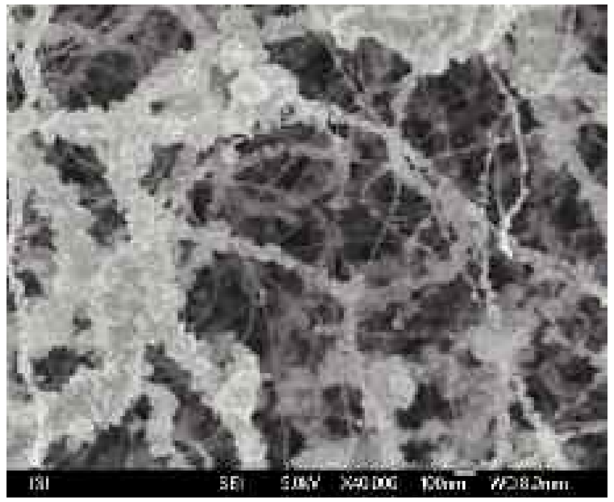
*Structure of randomly grown carbon nanotubes.*

*Magnified structure of the carbon nanotubes.*

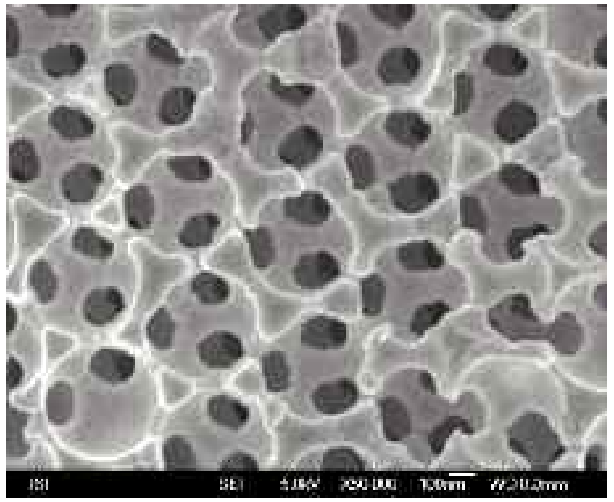
*Fractional surface of corundum ceramics.*



*Cross-section of a multilayered semiconductor structure.*

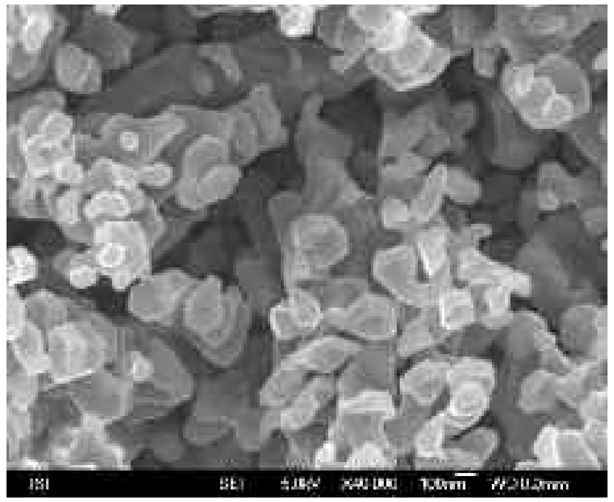


*Carbon based nanostructure with iron particles on a silicon substrate.*

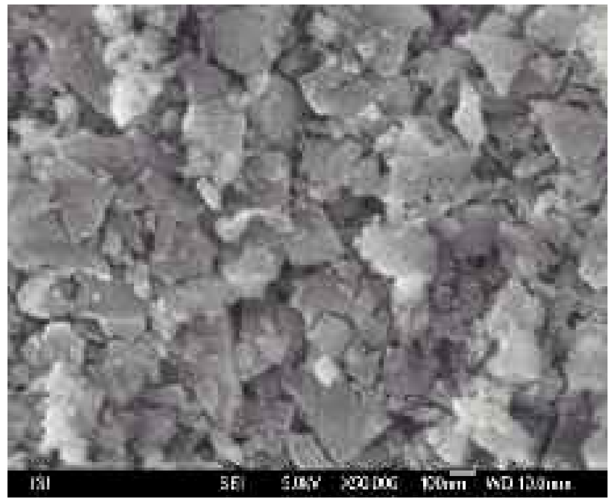


*Nanostructured golden electrodes of electrochemical sensors.*

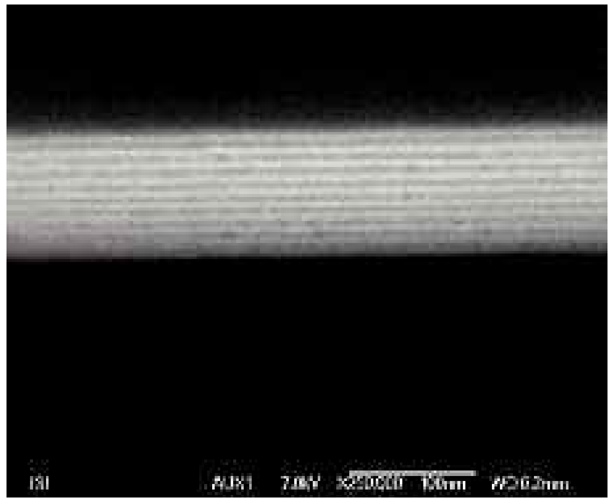




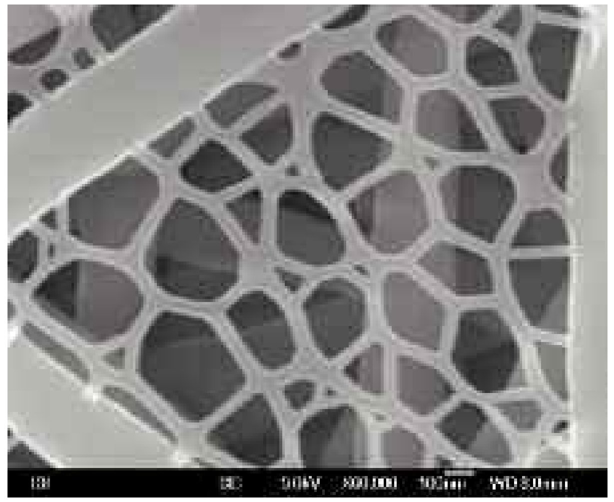
*Iron oxide deposited on the silicon surface.*



*Industrial diamond powder for machining of hard materials.*



*Cross-section of a Mo-Si multilayered nanostructure.*



*Textiles made of nanofibres.*

**Advantages and application examples:**

- Imaging with four different detectors provides **complex information** about the sample.
- Surface observation at very low energies down to about 20 eV at high resolution.
- **Secondary electrons** informing about the surface topography are detected with two complementary detectors.
- **Backscattered electrons** are also detected with two different detectors, with a possibility of acquiring the complete emission including **the high angle scattered electrons** not available in conventional instruments.
- **Resolution of 1 nm**, achieved without any aberration corrector. Filter of secondary electrons is used to suppress charging effect in the image.
- Quantitative chemical composition in combination with the high resolution imaging leaves very little unknown about any sample.
- Low magnification mode enables one to very comfortably seek out the area of interest.

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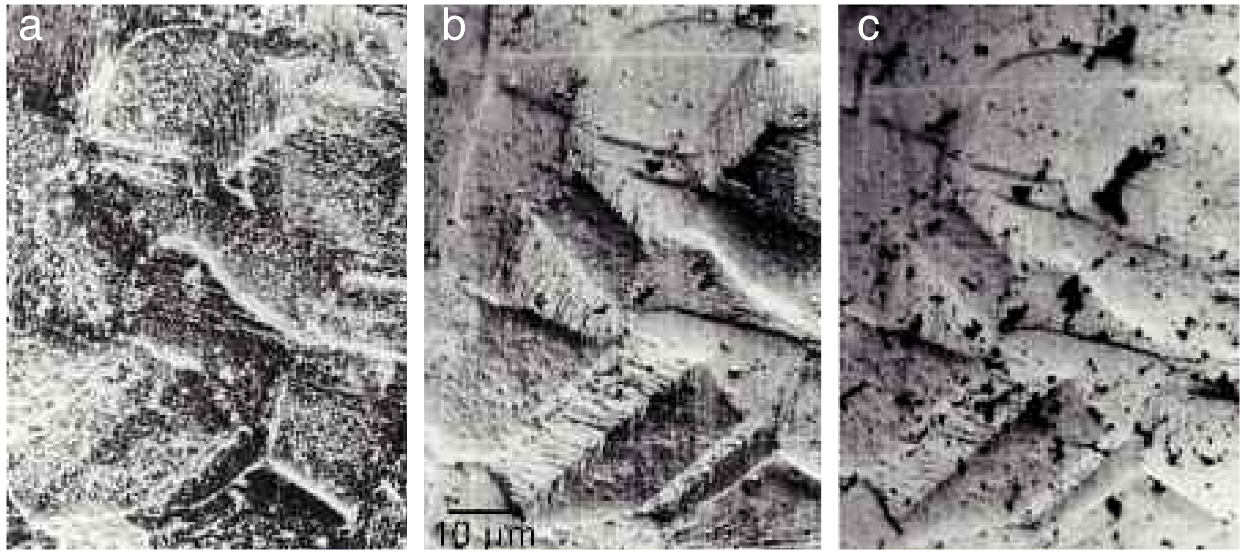
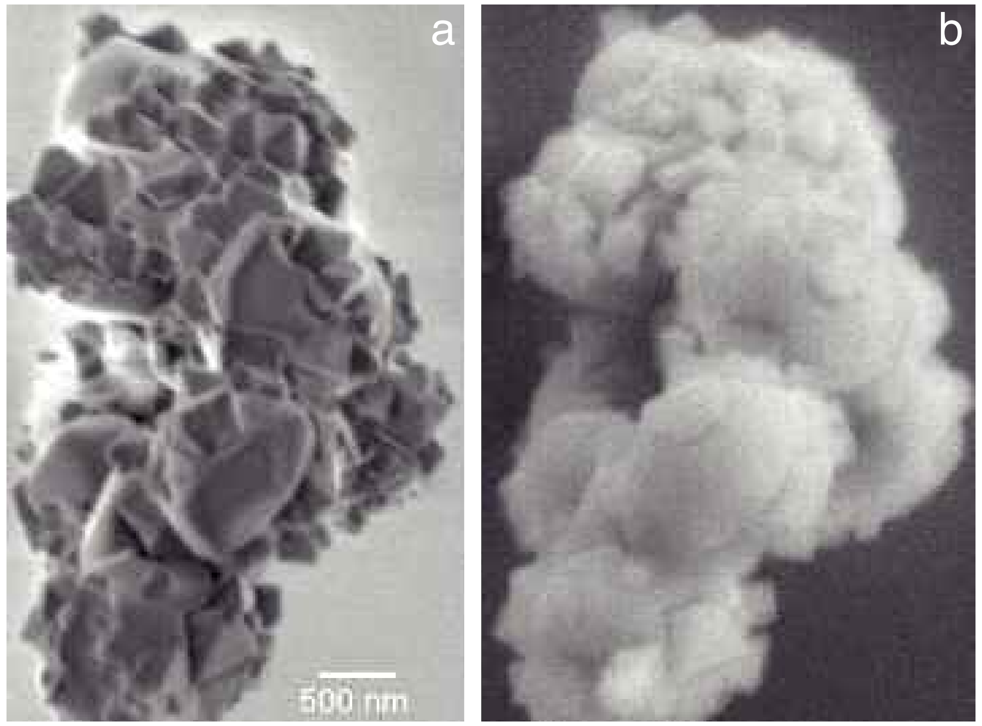


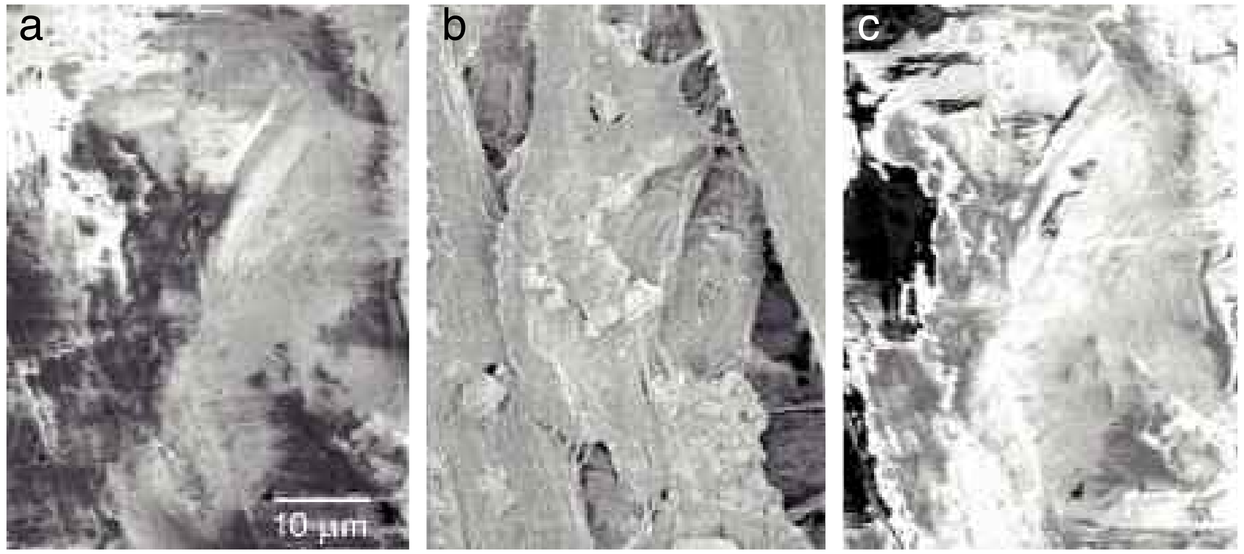

*Surface of the polycrystallinic copper sheet imaged at electron energies 5 keV (a), 200 eV (b) and 10 eV (c).*

## Scanning microscopy with slow electrons

Scanning microscopy with **slow electrons** utilizes the principle of so-called **cathode lens retarding of the electron beam** just in front of the sample surface. In this way the electron beam is formed and focused at high energy and so the illuminating spot governing the image resolution can be very small for all energies of electrons between 15 keV and 1 eV. The unique detector solution provides **very high efficiency** of signal collection and **high amplification** even at the lowest energies.

*Spinel crystals growing on the ceramic surface in the aluminum alloy based metal matrix composite: (a) 1 keV image with the complete emission of backscattered electrons acquired, (b) standard micrograph at 10 keV.*

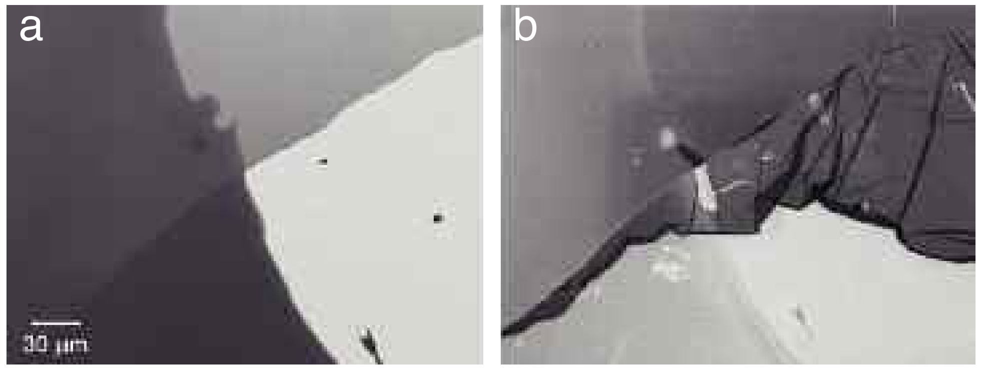


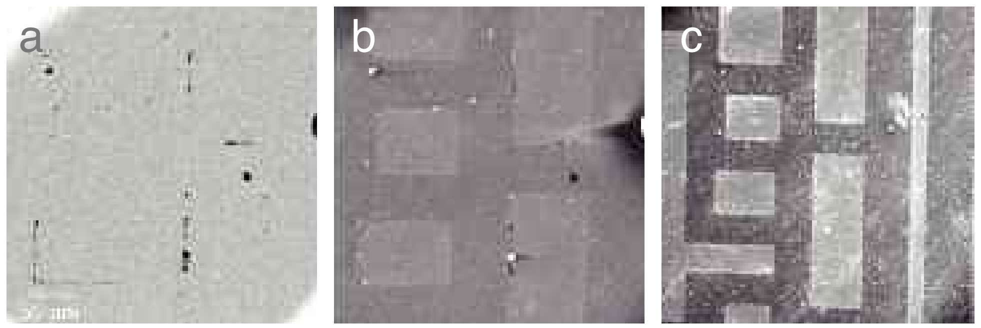

*Surface of writing paper in its original nonconductive status, imaged below (a), at (b) and above(c) the optimum electron energy for suppressed charging.*

**Advantages and application examples:**

- Diminished volume of the interaction of slow electrons inside the sample and thus **improved resolution** for real samples and **enhanced surface sensitivity**.
- Increased signal of secondary electrons **improving the signal-to-noise ratio** in the image signal.
- Imaging of **nonconductive samples** at optimum energy of electrons not causing local charges even under high vacuum.
- In depth analysis of samples via energy based **tomography**.
- Imaging of dopants in **semiconductors** and measurement of their density.

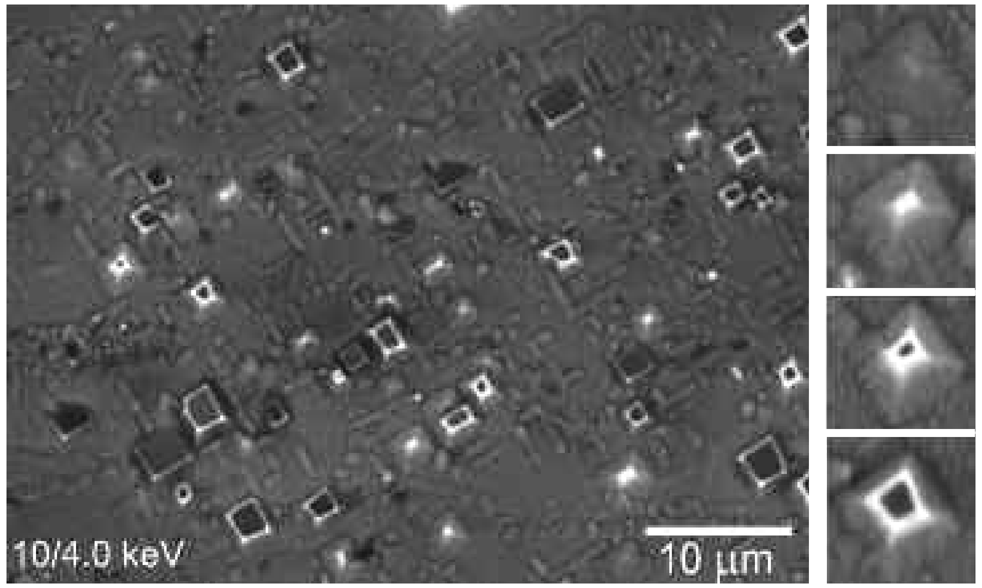



*A patterned multilayer structure imaged under different surface sensitivities controlled with energy of electrons; image at 9800 eV (a) and 850 eV (b).*

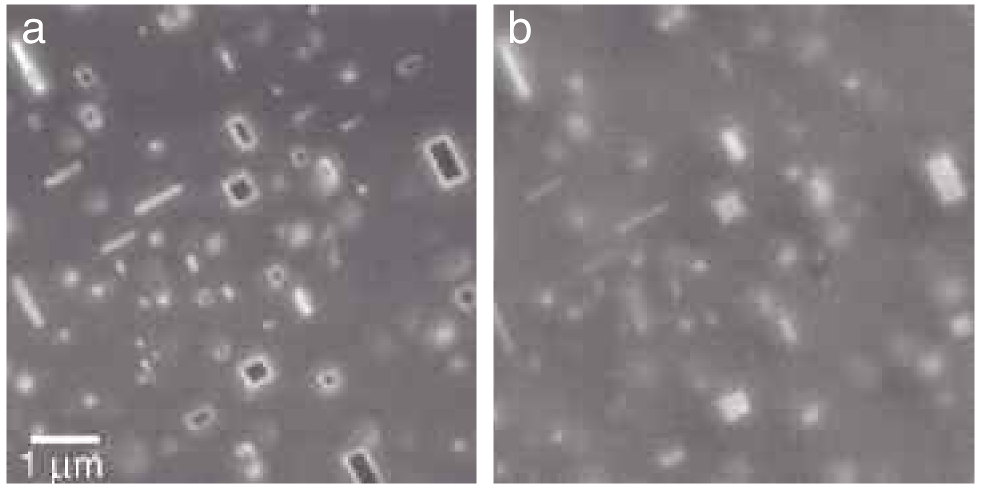



*P-type silicon patterns on the n-type silicon substrate imaged by means of conventional detectors (a, b) and using the cathode lens mode (c).*

Precipitates in the Al-Mg-Si-Ag alloy, imaged using the complete emission of backscattered electrons.




Precipitates in the Al-Mg-Si alloy shown at optimized energy of electrons (a) in comparison with the conventional image (b).




Internal strain inside grains in hot rolled ferritic steel.

- Tailoring the electron energy to maximum contrast **between different materials**.
- Acquisition of signal electrons backscattered under large angles from the optical axis, bearing enhanced **crystallinity contrast**.

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## Environmental scanning electron microscopy and detection systems

The environmental scanning electron microscopy (ESEM) is a modern solution for the observation of any type of nonconductive objects **without the necessity of coating with a metallic or carbon layer**. In addition, **wet samples of animate or inanimate origin can be preserved and observed** close to their natural status.

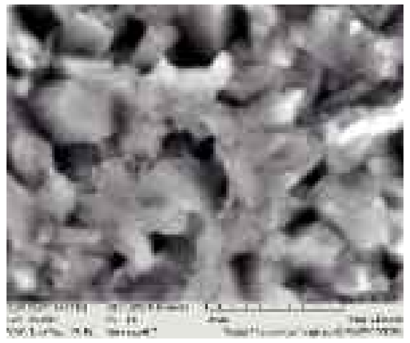
If the gas pressure in the specimen chamber of ESEM is higher than about 200 Pa, the primary and signal electrons collide with gas molecules in the vicinity of the sample and ions generated in this way compensate for the charging of the specimen by incident electrons. If the pressure of gas, or rather water vapours, in the specimen chamber is higher than 611 Pa (at 0°C), wet objects do not dry up and remain observable in their original non-collapsed shape.

**The ESEM can be used to study:**

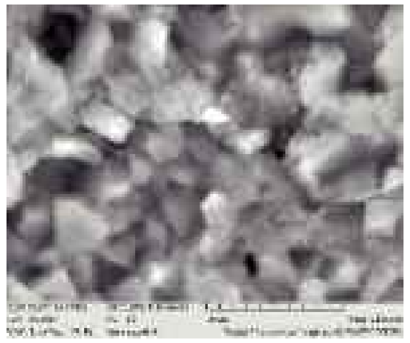
- the **surface structure** of conducting and non-conducting **natural animate and inanimate samples**;
- **wet samples** and samples near the phase transition (condensation, evaporation, melting, solidification, etc.);
- specimens in conditions of mechanical and thermal strain in the vacuum or in a gas of optional humidity;
- material, topographic or voltage contrast enabling one to observe electric charge accumulation and distribution e.g. on transistor gates;
- reactions of various chemical substances in the specimen chamber;
- aggressive chemical substances, e.g. battery mass;
- various types of specimens in conditions **close to atmospheric pressure**.

**Selected applications of ESEM and research results obtained in cooperation with industrial partners:**

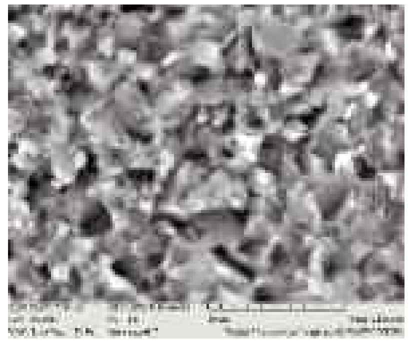
- Study of dozens of selected materials before and after corrosion by chemical substances, specification of the resistance and lifetime of examined materials and assessment of **the changes of their mechanical properties due to corrosion**.



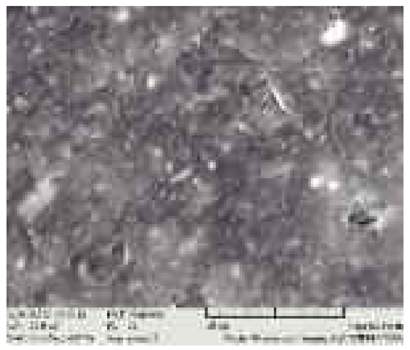
*Uncorroded surface of the alumina ceramic.*



*Ceramic surface corroded in $H_2SO_4$.*

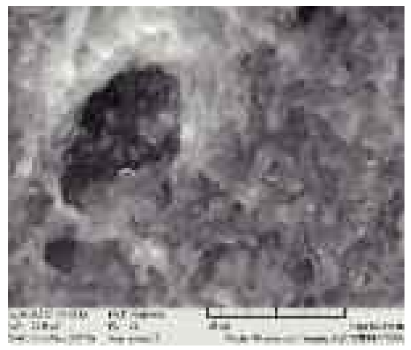


*Ceramic surface corroded in $H_3PO_4$.*



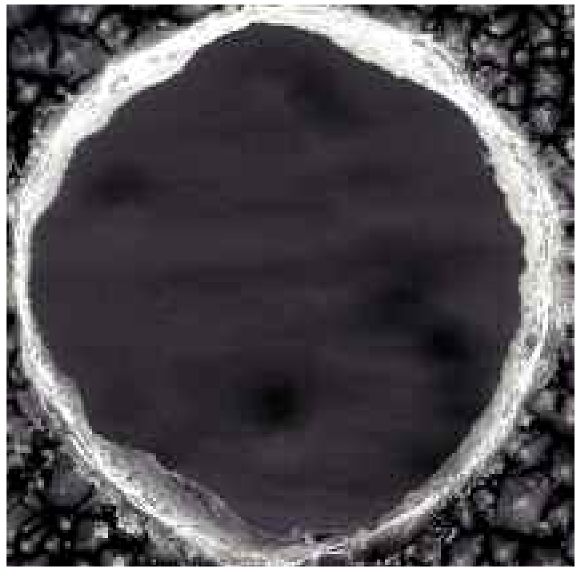
*Uncorroded surface of an O-ring sealing.*

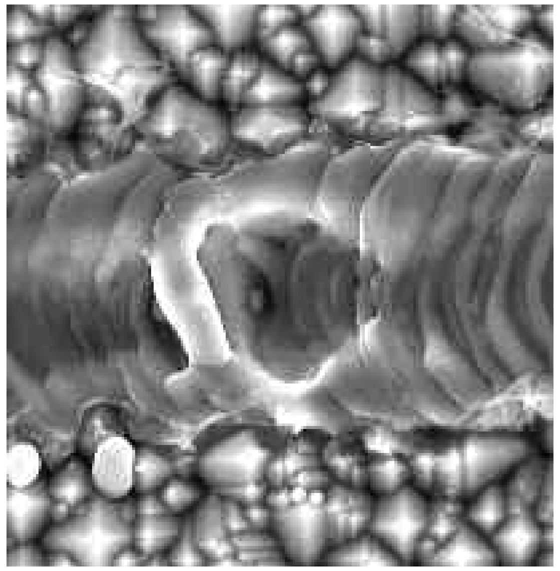
*Sealing ring surface corroded in $H_2SO_4$.*

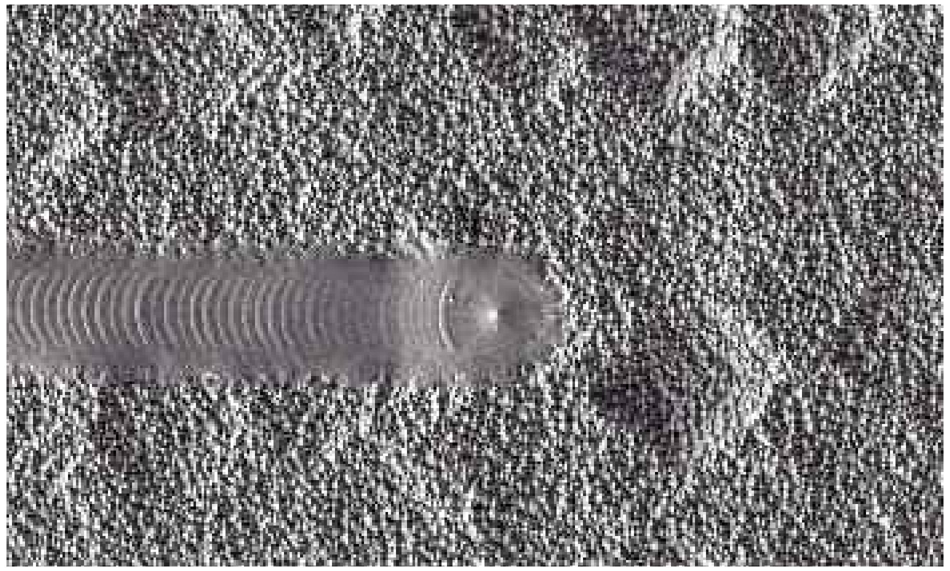


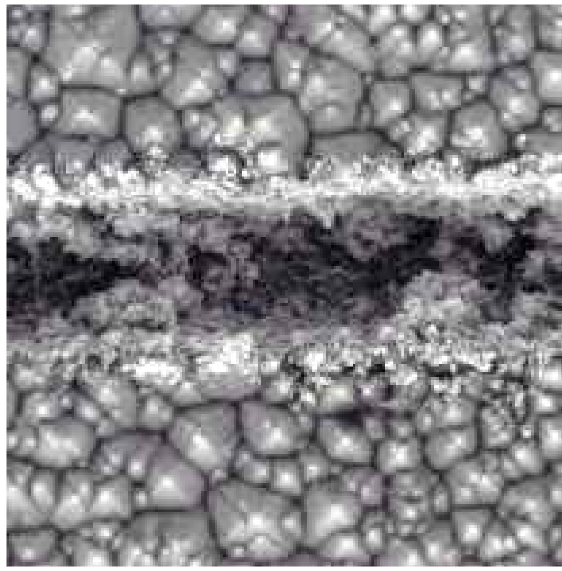
*Sealing ring surface corroded in $HNO_3$.*

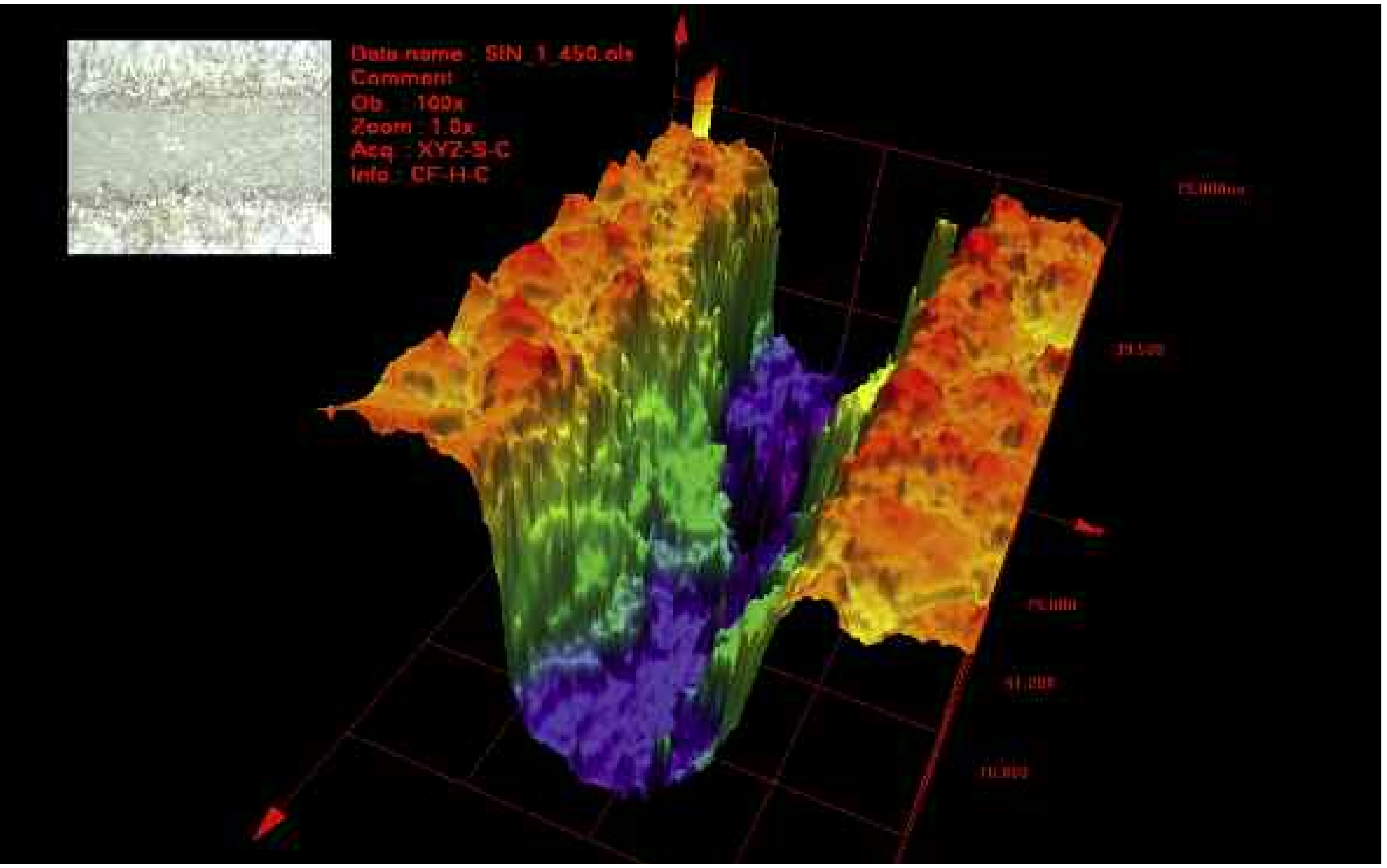
*Surface structure of solar cells machined with various laser systems.*












- Study of **inner surfaces** of several types of **vascular catheters** in order to assess the surface relief from the point of view of danger of the embolism.
- Study of the surface of working electrodes of **electrochemical sensors** oriented at mapping the **surface topography structure**, measurement of its real and geometric surface area and subsequent optimization of the production process and launching of a new type of electrochemical sensor.
- Study of the surface structure of **solar cells** to map the effects of laser beam machining on cell properties.
- In cooperation with a medical institution an extensive study has been performed on the effects of different techniques for the removal of **tartar from human teeth**.

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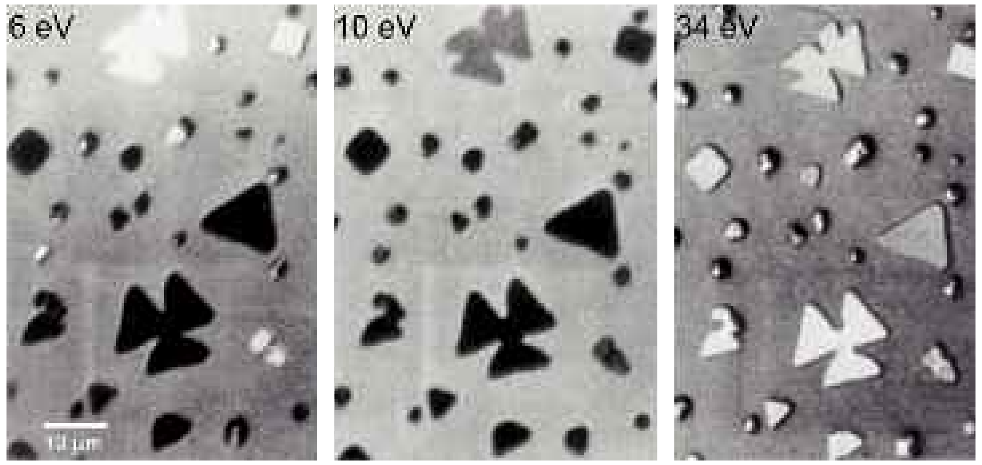
*Surface topography of human teeth on the boundary between the tartar and cleaned enamel.*

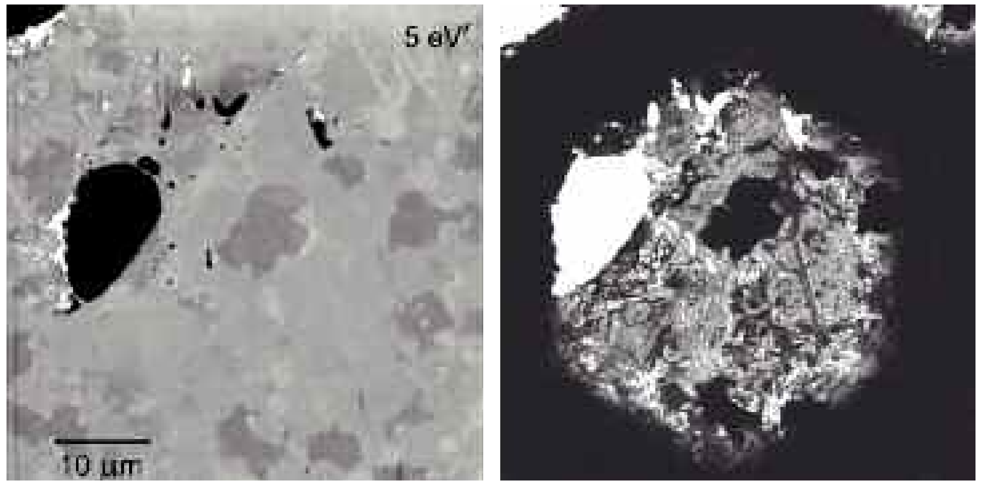
*Inner surface of vascular catheters in ESEM.*

## Electron microscopy under ultrahigh vacuum conditions

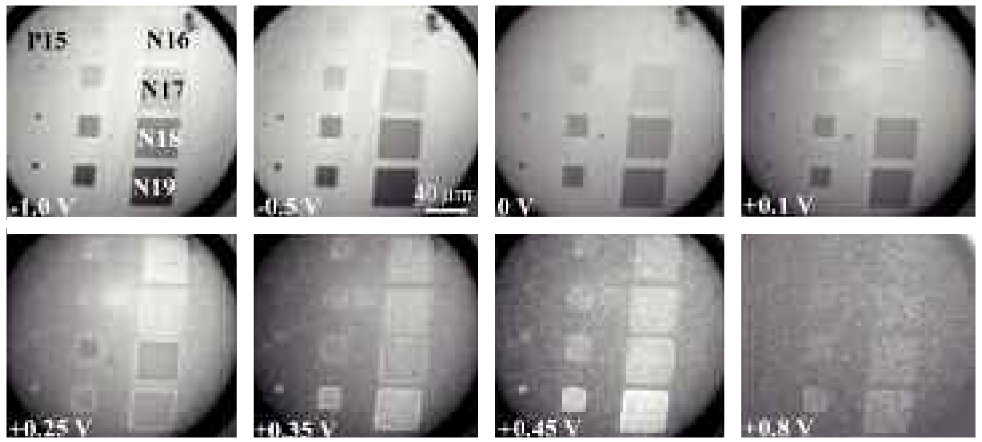
Microscopy and the analysis of **very clean surfaces under ultrahigh vacuum** conditions represent an irreplaceable tool for contemporary and, in particular, new nanotechnologies.
ISI has built its own version of the ultrahigh vacuum scanning electron microscope for examination of atomically clean and defined or even in-situ prepared surfaces of solids. The microscope has an operational vacuum of $10^{-8}$ Pa thanks to its complete bakeability, but samples are readily exchanged via vacuum airlock. The device is composed of three vacuum chambers: the observation chamber, preparation chamber and airlock. In the observation chamber the electron optical column enables one to work at all electron energies down to fractions of eV or even to acquire the mirror image of the sample. Detectors available include acquisition of the complete backscattered emission at all energies, secondary electron emission, transmitted electron emission and detection and analysis of gases released by electrons. The device will soon be equipped with an **energy analyzer of Auger electrons**. In the preparation chamber devices are available for ion beam cleaning and sputtering of the sample surface.




*Atomically flat two-dimensional crystals of lead on the silicon surface, imaged by means of the dark-field diffraction contrast.*




*Mutually overlapped graphene (single atom, thick, free-standing two-dimensional carbon films) with bright spots of a single graphene layer, imaged with backscattered electrons (left) and transmitted electrons (right), showing the atomic layers in extreme contrast.*




*N-type silicon areas of various dopant densities on a p-type silicon surface, imaged using the energy filtered photoemission electron microscope.*

ISI plans to purchase a **photoemission electron microscope** combined with a direct imaging **low energy electron microscope** for complex **examination of clean crystalline surfaces of all kinds**.

**Advantages and application examples:**

- The unique sample stage/detector assembly enables the adjustment of the device for perfect performance at arbitrarily low energies.
- The electric field above the sample collects the complete emission and hence provides full available information.
- A very high collection efficiency of signal detection increases the signal-to-noise ratio in images and **speeds up data acquisition**.
- At very low energies novel contrast mechanisms appear in micrographs, revealing the electronic and crystalline structure in addition to the conventional topographic and material contrast.
- Small interaction volume substantially improves the resolution of details **immersed below or protruding above the surface** and the surface sensitivity in general.
- Grains in polycrystals become visible in high contrast, including subgrains, twins, etc., with the possibility of identifying their orientation.
- **Internal stress in polycrystalline materials** is mapped in high contrast and resolution.
- The **doped areas in semiconductors** can be quantitatively examined and critical dimensions measured exactly.
- At very low energies the radiation damage of extremely sensitive samples ceases.
- Thanks to their longer wavelength very slow electrons produce **diffraction and interference phenomena**, providing novel tools for the examination of **nanostructures**.

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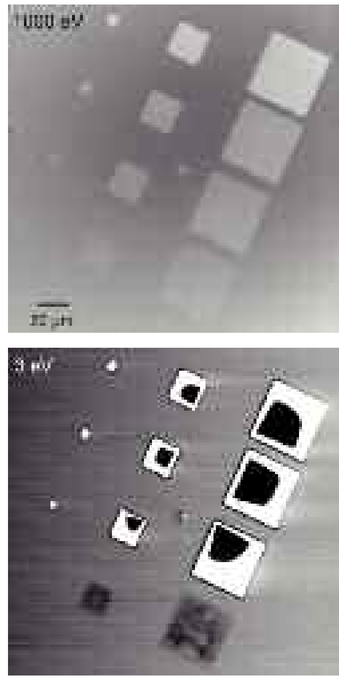
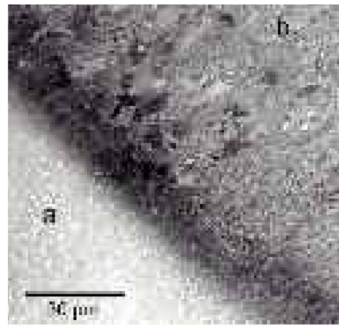
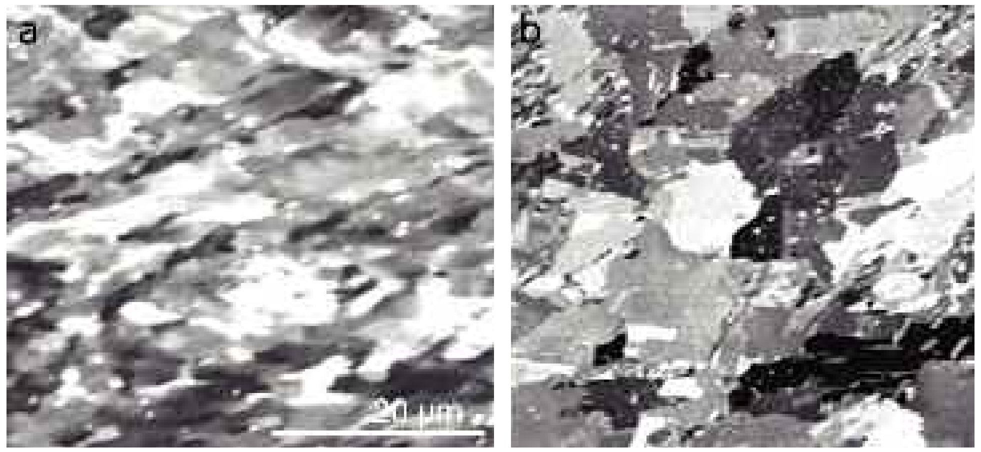



*Areas imaged at 1000 eV with the contrast proportional to the dopant density and at 3 eV with the dynamic contrast enabling critical dimensions to be measured.*




*Ultrafine grained copper sheet as inserted in the ultrahigh vacuum (a) and after ion beam cleaning that reveals the crystalline structure (b). Landing energy of electrons: 2 keV.*




*The ultrafine grained copper in the as-pressed, highly deformed status (a) (showing unsharp grain boundaries owing to clustering of dislocations) and after annealing (b). Landing energy of electrons: 10 eV.*

# Cryogenics and superconductivity


*Liquid helium containers (p. 32).*

*The Cryogenics and Superconductivity Group* started its activities in the research and development of **superconducting magnets** for **nuclear magnetic resonance** (NMR), including scientific and technical background for reaching and preserving of very low temperatures (down to 4.2 K, or −269°C). During its years of activities the group has taken into account additional fields of cryogenics, e.g. **vacuum technique, low temperature thermometry, material engineering**, etc. Presently the group deals with projects of basic and applied research. In both cases the group uses its comprehensive experimental background, in the Czech Republic entirely unique, for verifying and testing scientific and technical theories and knowledge. The group's own **helium liquefier** is a very important and supportive component.

*The Cryogenics and Superconductivity Group* offers its experience in the following fields:

- Low temperature thermometry.
- Design and realisation of **cryogenic systems.**
- Determination of thermal-radiation properties of materials.
- Vacuum technique.
- **Magnetic fields measurement** and **superconducting magnets design.**
- Consulting and training courses **in safety in cryogenics.**

## Low temperature thermometry

In this field we use devices designed in the institute; these allow:

- **Temperature sensor calibration** in the range of 1.4 K – 100 K, with an accuracy better than ± 16 mK by use of secondary temperature etalon.
- **Measurement of the thermal conductivity** of materials and components in the temperature range of 10 K–300 K. Samples up to 40 mm in diameter and up to 50 mm in length can be measured in the existing device. For larger samples it is possible to design and manufacture a new device according to the customer's needs.

*Apparatus for measurement of longitudinal heat flux in shaft of helium compressor.*

*Cryostat for superconducting magnet of NMR spectrometer.*

## Design and realisation of cryogenic systems

We have designed and manufactured many specialised cryogenic systems for a wide range of applications. We have projected both theoretical and experimental procedures (e.g. programs, tests, attribute verifying) leading up to the realisation of the specific system according to the customer's requirements.

We offer long term experience in these fields:

- **Numerical modelling of steady and non-steady thermal processes** in cryogenic systems by use of the KRYOM 3.3 program (developed at the institute).
- **Thermal cycling of materials** in the temperature range of 4.2 K–373 K.
- Determination of the low temperature mechanical properties of materials.
- **Cooling by liquefied gases.**
- Distribution of the **KRYOM 3.3** program licence. The program analyses and optimises cryogenic devices.

**Examples of devices developed at the institute:**

- Low loss cryostats for superconducting magnets.
- Cryogenic systems for physical experiments.
- Helium cryopump for ultra-clear pumping without vibration and electromagnetic fields.

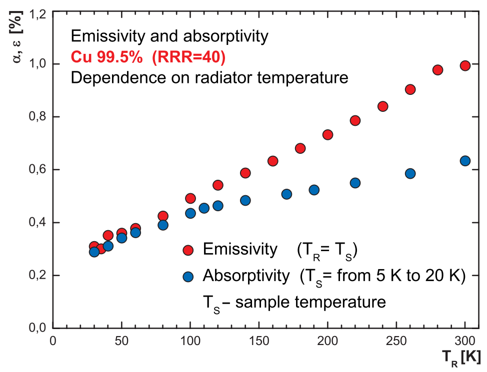
*Preparation of black surface absorptivity measurement.*

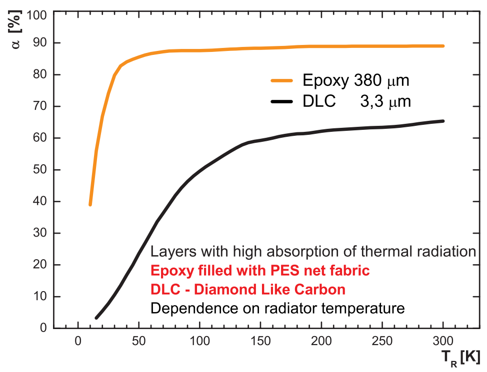
## Determination of thermal-radiation properties of materials

Radiation and absorption attributes of surfaces play a substantial role in cryogenics and significantly affect the efficiency and operational cost of cryogenic systems. In many cases, it is necessary to eliminate parasitic thermal flux from "warm" to cold surfaces.

**We perform:**

- The measurement of thermal dependences of material **emissivity and absorptivity** (samples of 40 mm in diameter) in the temperature range of 20 K–300 K.




*Thermal dependences of emissivity and absorptivity of copper and absorptivities of non-metallic surfaces with high absorptivity of thermal radiation ("black surfaces").*

*Helium bath cryopump for ultra-clean pumping of vacuum spaces without vibration and electrical power.*

## Vacuum technique

Long-term activities have given us practical knowledge in the following fields:

- Quantitative and qualitative **determination of residual gases** in vacuum systems up to nucleon number 100.
- **Ultra-clean pumping of vacuum** spaces using **a helium cryopump** designed at the institute. Pumping speed is 25 l /s for helium gas; ultimate pressure 10–7 Pa is achieved without vibration and without electric power.
- Measurement of pressure in the range of 100 Pa–0.6 MPa in non-aggressive environment with an accuracy of 0.1 %.
- **Seeking of leakage in vacuum systems** and in cold vacuum systems, seeking of leakage for superfluid helium (λ – leakage).

## Stationary magnetic fields

Long term research in the area of superconducting magnets for NMR spectroscopy has given us experience in the following fields:

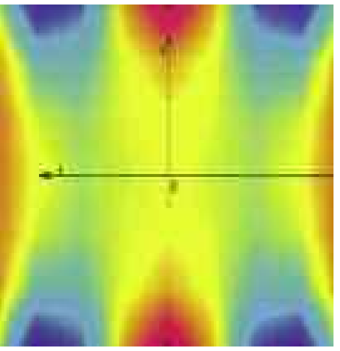
- **Mapping of stray magnetic fields** by Hall probes.
- Precise **measurement of homogeneous magnetic fields** in the range 0.7–13.7 T applying the method of nuclear magnetic resonance.
- Experimental assessment of the influence of stationary magnetic fields up to 4.7 T on developed technical systems.
- **Design and realisation of superconducting magnet systems** with rotational symmetry.

## Consulting and training courses in safety in cryogenics

Risks in cryogenics are significant but are not immediately discernible. Persons working in this area must be well informed and must complete the appropriate courses. There is danger of serious injury (e.g. low temperature burns, mechanical injuries, asphyxiation).
Almost all vessels for liquid gas storage are pressure vessels, which are subject to very strict regulations for manufacturing, handling and maintenance.

We offer **consulting and training** courses in these areas:

- Safety handling with cryoliquids.
- Safety storage and transport of cryoliquids.



*Map of magnetic field with rotational symmetry.*

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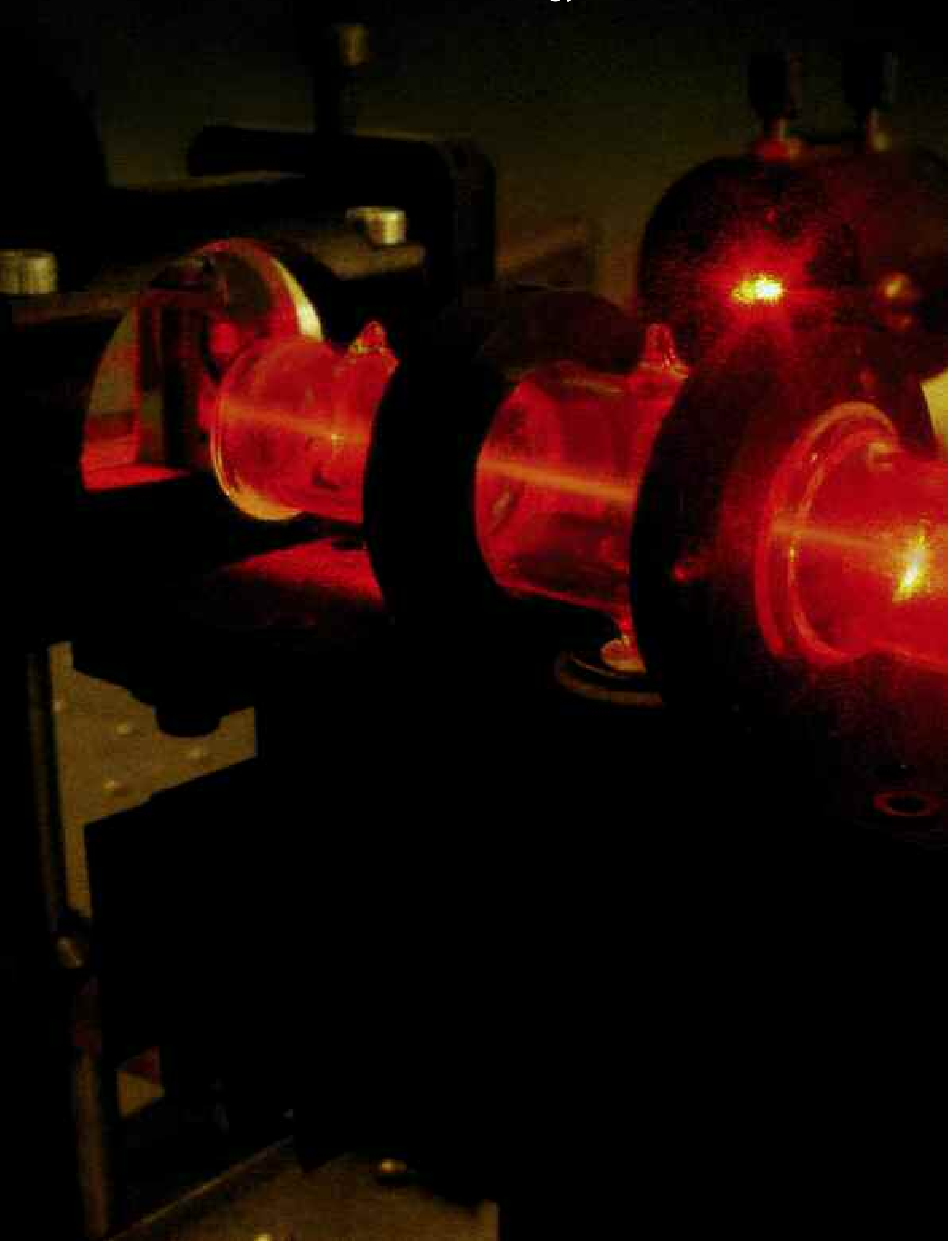
*Superconducting magnet 4.7 T for NMR spectrometer.*

# Lasers for measurement and metrology



*Experiment with absorption cell.* *(p. 38).*



In 2010 the laser celebrates its 50th birthday. From the curiosity that emerged from a scientific laboratory the laser has found its way into nearly all households. Among thousands of various applications laser dimensional measurement is one of the best known. In the laboratories of ISI the first Czech He-Ne laser was built only three years after its world premiere and its design has been gradually developed for the needs of Czech metrology.

This long history has produced our offered experience in the following fields:

- **Spectral modification** (narrowing) **of the emitted wavelengths** of gas and semiconductor lasers.
- The design of **lasers for metrological applications** with **extreme stability** of the emission optical frequency.
- Manufacturing of **cells filled with hyperpure gasses for absorption spectroscopy**.
- The design and realization of **interferometric measuring systems**.
- The design and **deposition of optical interference coatings**.
- The design and realization of **special electronics for control of experiments**.

## Lasers with high coherence for measuring purposes

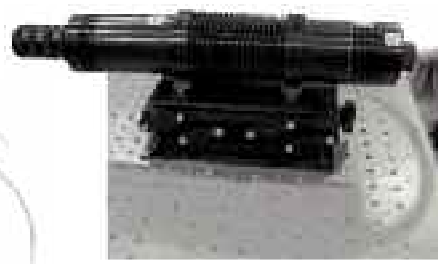
Lasers designed at ISI are unique due to their high coherence and are suitable for:

- **precision length measurements** on the basis of laser interferometry;
- **analysis of gases** and other transparent media through laser spectroscopy.

ISI is equipped with laser sources with high coherence operating at the following wavelengths: **502 nm, 532 nm, 543 nm, 633 nm, 760 nm, 780 nm, 1064 nm, 1315 nm, 1540 nm**. If required this set may be broadened to include additional wavelengths.

**Examples of realized designs:**

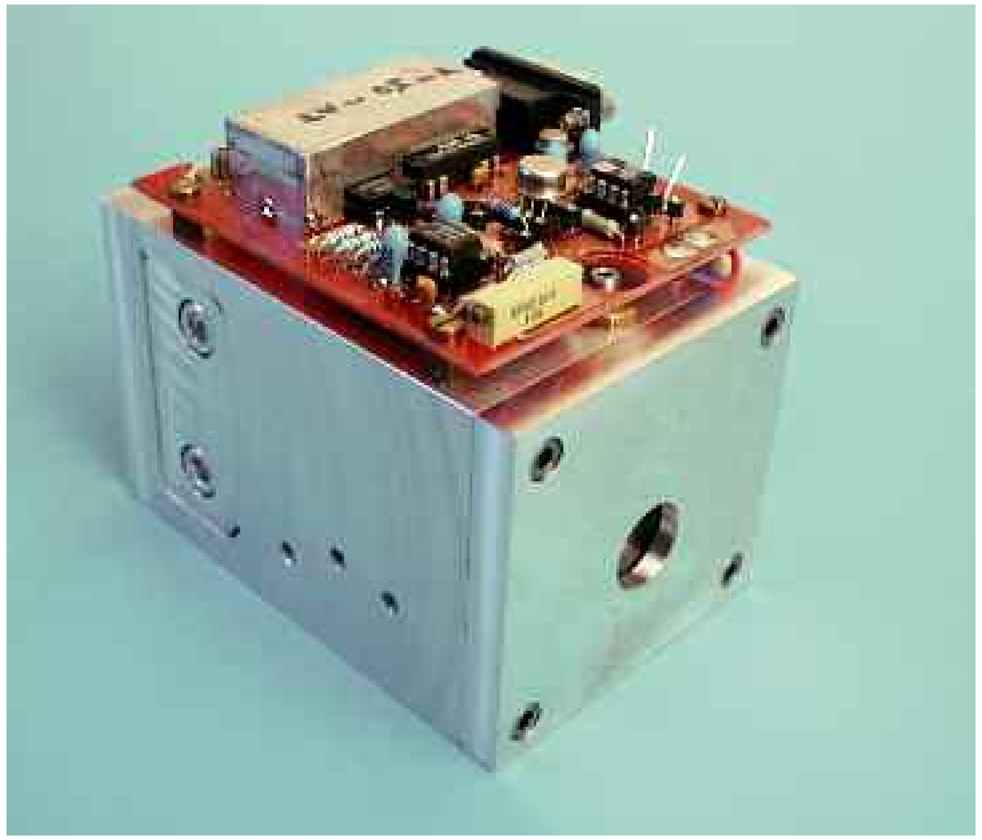
- **He-Ne lasers and discharge tubes for the construction of He-Ne lasers.** We designed technology for manufacturing and filling of the gas He-Ne lasers that dominate in the field of precise length measurements. These lasers are thermally stable and are suitable for operation as laser sources for measuring systems based on laser interferometry. Compared with commercial lasers our design offers fast wavelength tuning via an integrated piezoelectric transducer.



*Complete He-Ne laser (above) and its core component the discharge tube made of quartz glass (left).*

- **ECL lasers for measurement and spectroscopy.** Traditional He-Ne lasers operating in the visible spectral range are only tunable within a very narrow range. Laser diodes perform much broader tuning range but do not operate in a single-frequency regime and are thus not suitable for demanding applications like interferometry and spectroscopy – for example, for gas analysis. We designed semiconductor laser technology with an extended cavity, which effectively reduces the laser emission spectral profile and keeps the laser's broad spectrum of available wavelengths accessible through tuning. We achieved a compact tunable laser source suitable for spectroscopic applications with an operating wavelength given by the laser diode of choice.

*ECL laser operating at 633 nm wavelength with continuous tuning range of 0.1 nm. This laser is designed to replace the He-Ne.*



- **Laser systems with laser diodes VCSEL, DFB and DBR**. We designed specialized electronics for controlling the wavelength of commercial laser diodes operating with a narrow emission spectral range. These are the diodes with vertical cavity VCSEL (Vertical Cavity Surface Emitting Laser), distributed optical feedback DFB (Distributed FeedBack) and wavelength selective mirrors DBR (Distributed Bragg Reflector). The emission wavelengths of these diodes are controlled by the injection current of the semiconductor and also through the operating temperature. The control electronics are equipped with a set of signal processors controlling the operating point of the laser diode.

*Example of the control electronics of highly coherent laser diodes.*

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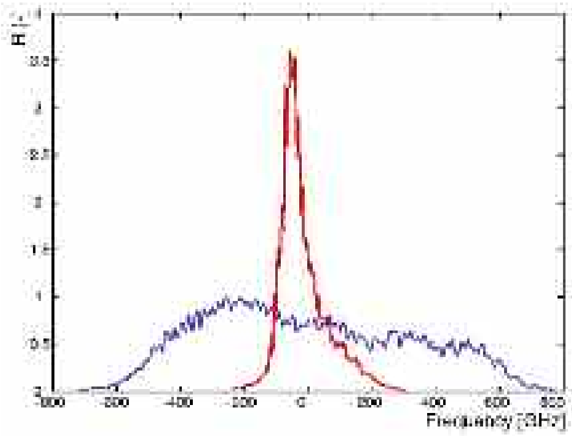
## High-power ECL lasers

High power ECL lasers are based on a similar technology of linewidth narrowing as the highly coherent ECL lasers for spectroscopy. They include an extended cavity with a wavelength selective mirror – an optical grating. Further linewidth narrowing was achieved through external "injection locking" using a Ti:Sa laser.

**We designed:**

- a power semiconductor laser with ECL configuration featuring 1.5 W of output power for laser polarization of the Xenon nuclei through spin exchange with Rubidium atoms. The polarized Xe is used as a contrast medium for magnetic resonance tomography. Similar power lasers are utilized as atmospheric communication transmitters for long-range free-space optical communications.

*Our design of a high-power laser with ECL configuration which uses a broad-stripe power laser diode (left) and the line-narrowing effect of this setup (right).*

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## Laser etalons of optical frequencies

Etalons of optical frequencies (wavelengths) are highly coherent lasers generating an output light with precise optical frequency (wavelength). The frequencies are in the order of hundreds of THz, which corresponds to the wavelength range of 500–1500 nm. These lasers operate as primary sources for the realization of the international definition of the unit of length – they are used by metrological institutions as sources of light for measuring laser interferometers. Regular **calibration of mechanical length etalons** by a system with direct traceability to the fundamental etalon of length is a key to any **industrial metrology**. Precision and stability of these laser etalons influences the whole chain of metrology, from the fundamental down to the industrial level. ISI is traditionally engaged in this technology and a set of the fundamental etalons of (wave)lengths has been developed here.

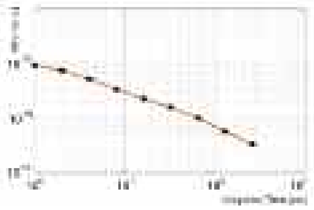
**Examples of realized systems:**

- **Stabilized He-Ne laser at the 633 nm** wavelength. The He-Ne laser with stabilization of its optical frequency developed at ISI is one of the fundamental etalons of wavelength and at present is used as a national etalon of length. The optical frequency of the He-Ne laser is stabilized through saturated absorption in the iodine vapor by the technique of derivative spectroscopy. This is a final product of the ISI – a compact system equipped with electronics

*The latest version of the Iodine-stabilized He-Ne laser designed at ISI with control electronics and software for operation in metrology centers.*

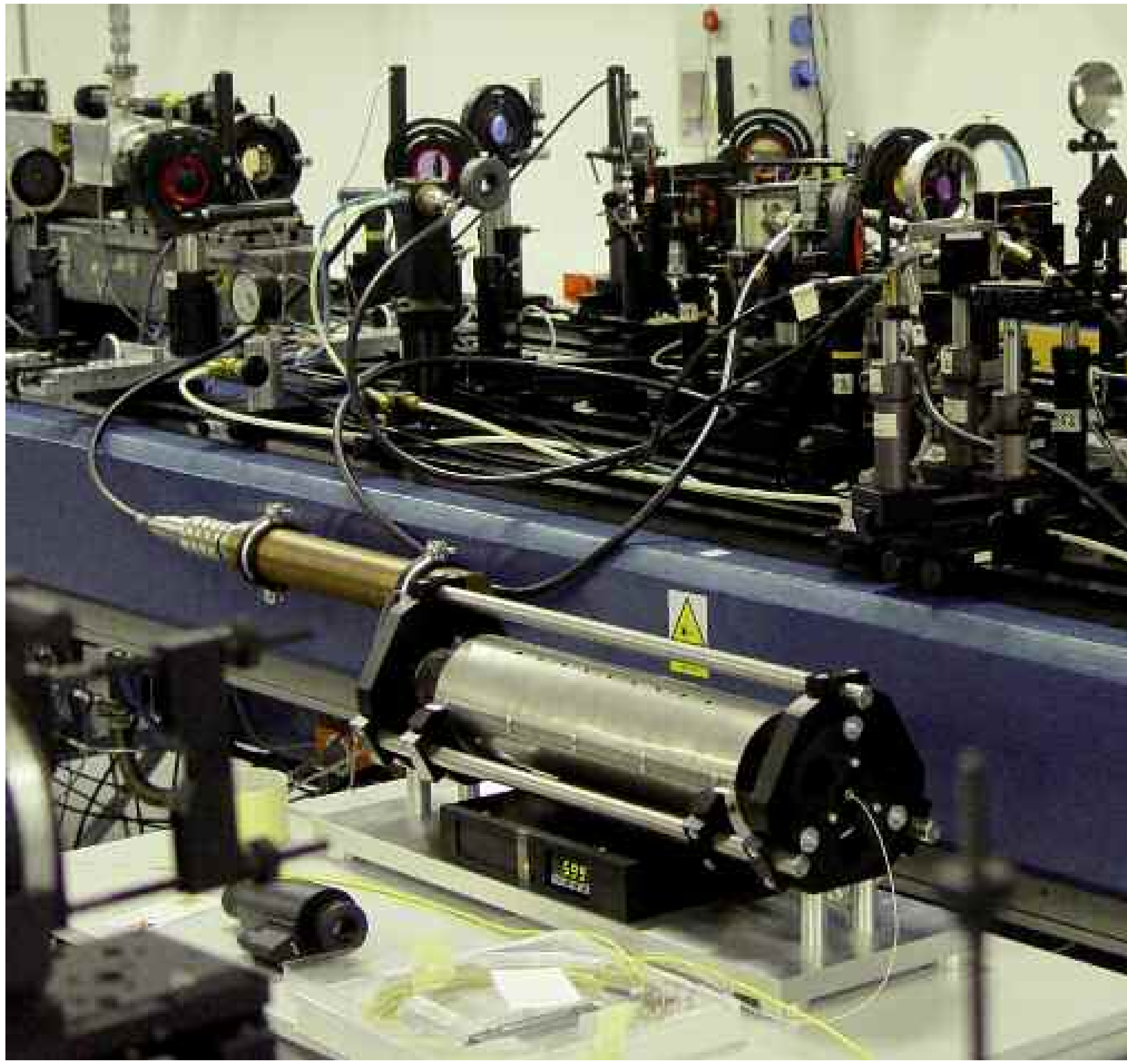
including computer control. Relative stability of the laser is on the $10^{-11}$ level for 1 s integration time. It is used for the calibration of He-Ne laser sources for interferometric systems.

- **Nd:YAG stabilized laser at the 532 nm and 1064 nm** wavelengths with **absorption in Iodine.** Vapor of molecular Iodine is the most common absorption medium for the stabilization of lasers in the visible spectral range. This offers a dense set of narrow hyperfine transitions with the best signal-to-noise ratio close to the 500 nm wavelength. Iodine stabilized Nd:YAG lasers (Nd:YAG–$I_2$) can reach stabilities close to the $10^{-14}$ level. ISI operates an experimental system based on the Nd:YAG laser generating stable optical frequencies at wavelengths of 532 and 1064 nm



*The complete setup of the etalon of optical frequency based on the Nd:YAG-$I_2$ laser (left), recording of the Allan variances of comparison of two such systems showing the high relative stability of their optical frequencies.*

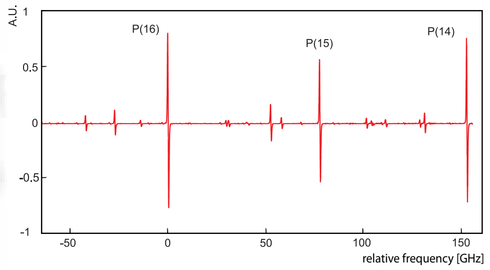
- **Stabilized system at the 1315 nm** wavelength. This system was designed according to the specifications and needs of the "Prague Asterix Laser System" (PALS) research center. We designed a system based on a narrow-linewidth DBR laser diode operating as a "master oscillator" at the front end of a cascade of optical amplifiers. This is a laser with fiber optic output with a frequency stabilized through linear absorption in vapor of dissociated Iodine.



*The final version of the "Master oscillator" for the laser center PALS.*

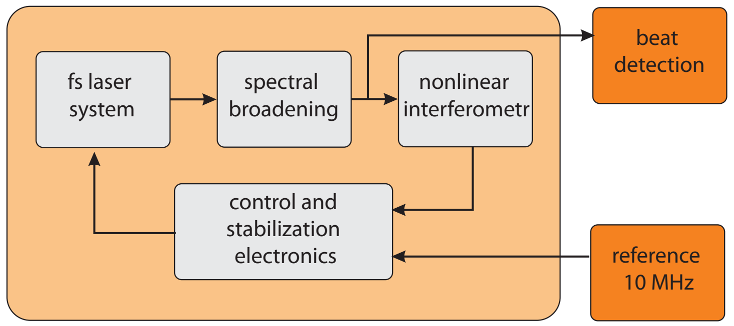
Detection and control is fully automatic and the instrument is controlled by several signal processors. The laser operates at the 1315 nm wavelength, in the telecommunication spectral range. It can also serve as an etalon for optical telecommunications.

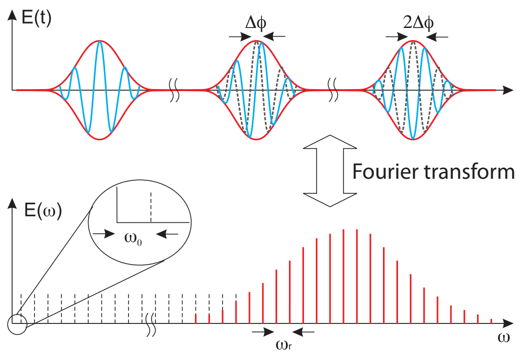
- **Etalon DFB laser at the 1540 nm** wavelength for optical communications. According to the needs of Czech Telecom (today Telefonica) we designed a stabilized laser operating as an etalon of optical frequency in the near infrared spectral range 1540 nm. The core of the system is a DFB laser diode with high coherence. The system operates with the stabilization of frequency through spectroscopy of the $^{13}C_2H_2$ acetylene and offers tuning over one of the spectral components of acetylene within the tuning range of up to 200 GHz. The system can be used for the calibration of wavemeters and spectral analyzers and for the adjustment of laser transmitters in optical telecommunication systems with a wavelength multiplex, so-called DWDM (Dense Wavelength Division Multiplexing).




*Spectroscopic part of the telecommunication etalon at the 1540 nm wavelength (left). Part of the recorded Acetylene spectrum, which is used as a reference for the stabilization of wavelength of the telecommunication etalon (right)*

- **Femtosecond synthesizer of optical frequencies.** In the laboratories of ISI we operate two systems for the synthesis of optical frequencies based on femtosecond pulsed lasers operating in the visible and infrared spectral range. The optical synthesizer allows the direct transfer of relative stability of frequencies between radiofrequency and optical spectral ranges, and they serve as references (etalons) of optical frequencies for metrology, interferometry and spectroscopy. Both systems will soon be linked to the reference of $H_2$ maser with relative stability at the $10^{-15}$ level.




*Block diagram of the optical synthesizer (left) and time and spectral expression of the pulsed light output, the optical comb (right).*

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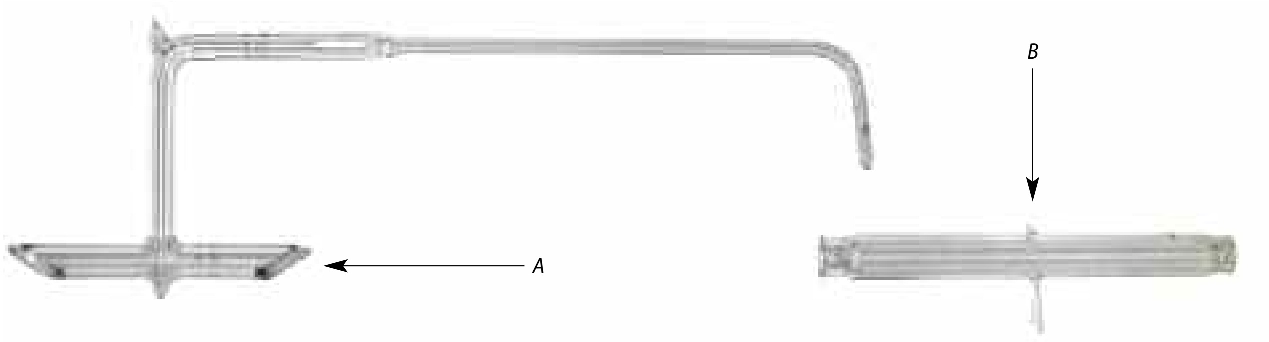
## Absorption cells for spectroscopy and etalons of optical frequencies

Absorption cells are made primarily for **laser spectroscopy of gasses** and to be used as references for laser **frequency stabilization** onto selected spectral components. The production technology of absorption cells in ISI is realized in a specialized glassmaking workshop, and the cells are custom designed mostly for national metrological institutions such as PTB in Germany, NIST in the USA and BIPM in France.

**Examples and parameters of manufactured cells:**

- Cells made of quartz glass with wedged windows with antireflection coated inner and outer window surfaces or with windows under the Brewster angle.






*Iodine cell with Brewster angle windows designed for a He-Ne laser etalon of optical frequency at 633 nm wavelength (A) and iodine cell with wedged windows (B).*

- Cells filled with superpure gasses (acetylene $^{13}C_2H_2$, Methane, Xenon, Krypton) or saturated vapor of Iodine, Cesium, Rubidium, etc. Cells filled with iodine serve as s reference for the primary etalons of (wave)length. The frequency shifts of iodine cells made at ISI are the smallest in the world (below 1 kHz of the optical frequency). The technology of the ISI allows the preparation of cells filled with various media based on application requirements.

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## Laser interferometric measuring systems

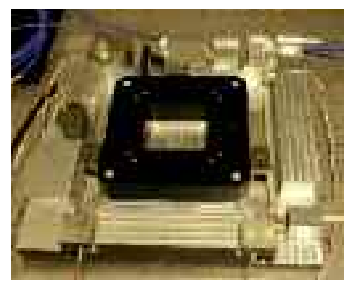
Laser interferometric measuring systems are based on the interference of two or more laser beams and represent a tool for the measurement of distances and other geometrical quantities. The scale of their potential application is very broad, and they may be used for the measurement of short distances in the range of millimeters or over meters or tens of meters. However, the primary resolution is in the range of tens of nanometer.

Systems designed at ISI are used for:

- the measurement of the position of three-axis positioning stages;
- the calibration of scales of a broad range of various position sensors;
- measurements of the refractive index of air.

**Examples of applications:**

- **Interferometry for nanometrology.** Nanometrology is based on the imaging of samples using techniques of local probe microscopy, primarily Atomic Force Microscopy (AFM). When the scale of the objects in the nanoworld has to be measured the positioning of the AFM probe must be measured through interferometry with a direct link to the primary etalon of length (stabilized laser). The setup for measuring the probe is derived from a nanopositioning stage and a system of interferometers monitoring the sample position in three or even all six degrees of freedom. The local probe microscope is placed over the sample. The limits of uncertainty of the measurements are given by the mechanical stiffness of the whole setup and by the fluctuations of the refractive index of air. The resolution is below 1 nm.
- **Precise positioning systems and comparators.** Interferometric systems designed at ISI can offer resolution at the 0.1 nm level, i.e. the resolution of interatomic distances. Practical applications of these positioning and measuring systems are in the field of scale calibration of various position sensors used in industrial measurements.

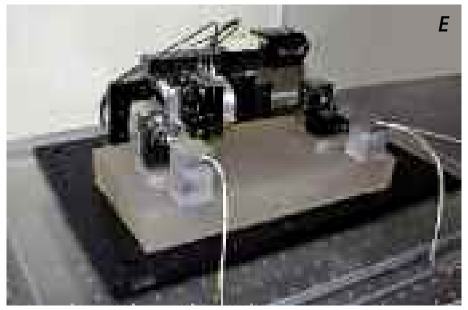


*Example of the multiaxis interferometer for the 3D positioning of the sample for AFM microscopy.*

*Laser comparators for calibration of position sensors. System for horizontal calibration (left, picture A) and vertical (right,figure B).*








*System for measuring of the refractive index of air with He-Ne lasers (left, figure C).*

*System for measuring the refractive index of air with femtosecond synthesizer of optical frequencies (right, figure D).*

*Example of experimental laser interferometer for displacement measurements with compensation of the variations of the refractive index of air (figure E).*

- **Measuring of the refractive index of air of gaseous media.** At the ISI laboratories we are also involved in the development of measurement techniques for the refractive index of gasses. We operate two systems for evaluation of the refractive index of air that can be used to measure any other transparent media, liquids and solid materials.
- **Interferometry with compensation of the refractive index of air.** An arrangement with differential measurement allows compensating the influence of variations of the refractive index of air. The basis of the configuration is a mechanical reference with very small thermal expansion, and the wavelength of the laser source is locked to its length through the sum value of the two counter measuring interferometers.

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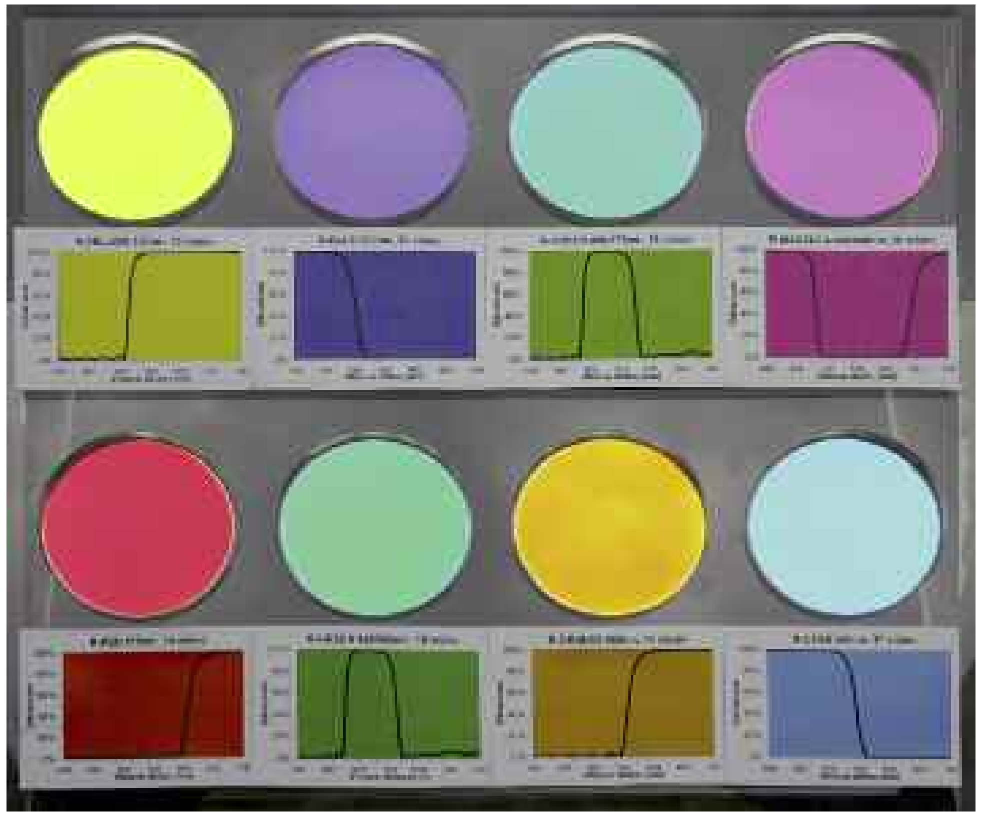
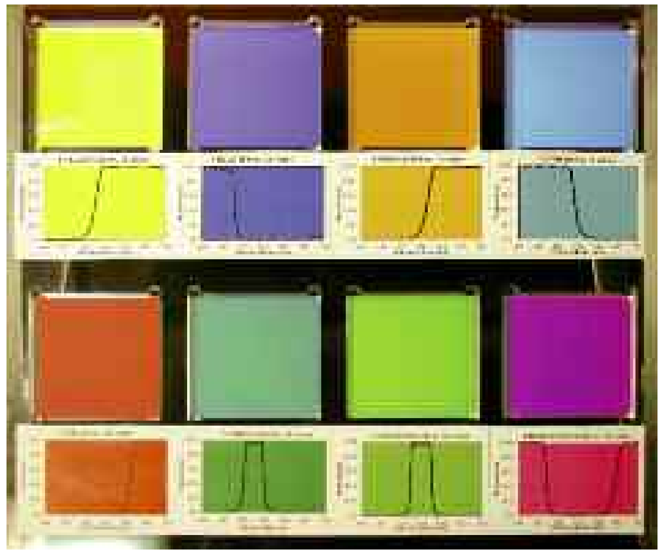
## Deposition of interference coatings by electron beam evaporation and spectrophotometric measurement of spectral reflectance and transmittance

Thin layer coatings are prepared by means of electron beam evaporation using a Balzers BAK550 coater equipped with two electron guns. Substrates can be preheated. Our coater is capable of small batch production of circular substrates with the largest diameter of 180 mm or rectangles up to 170 mm x 120 mm. The following materials can be deposited: $TiO_2$, $SiO_2$, $Ta_2O_5$, $ZrO_2$, $CeO_2$, $HfO_2$, $Y_2O_3$, MgO, $Al_2O_3$, $MgF_2$ and $Na_3AlF_6$.



*Dichronic filters – reflection color.*

*Various coated optical elements.*



*Dichronic filters – transmission color.*

**Application:**
Interference filters for **visible**, **near UV** and **near IR** part of the spectrum. For example:

- anti-reflection coatings;
- low-loss mirrors;
- cold mirrors;
- heat mirrors;
- dichroic filters;
- bandpass and edge filters;
- beamsplitters;
- polarizers;
- nonpolarizing beamsplitters;
- monochromatic filters.

Spectral reflectance and transmittance measurements are performed using a Varian Cary 5E spectrophotometer.

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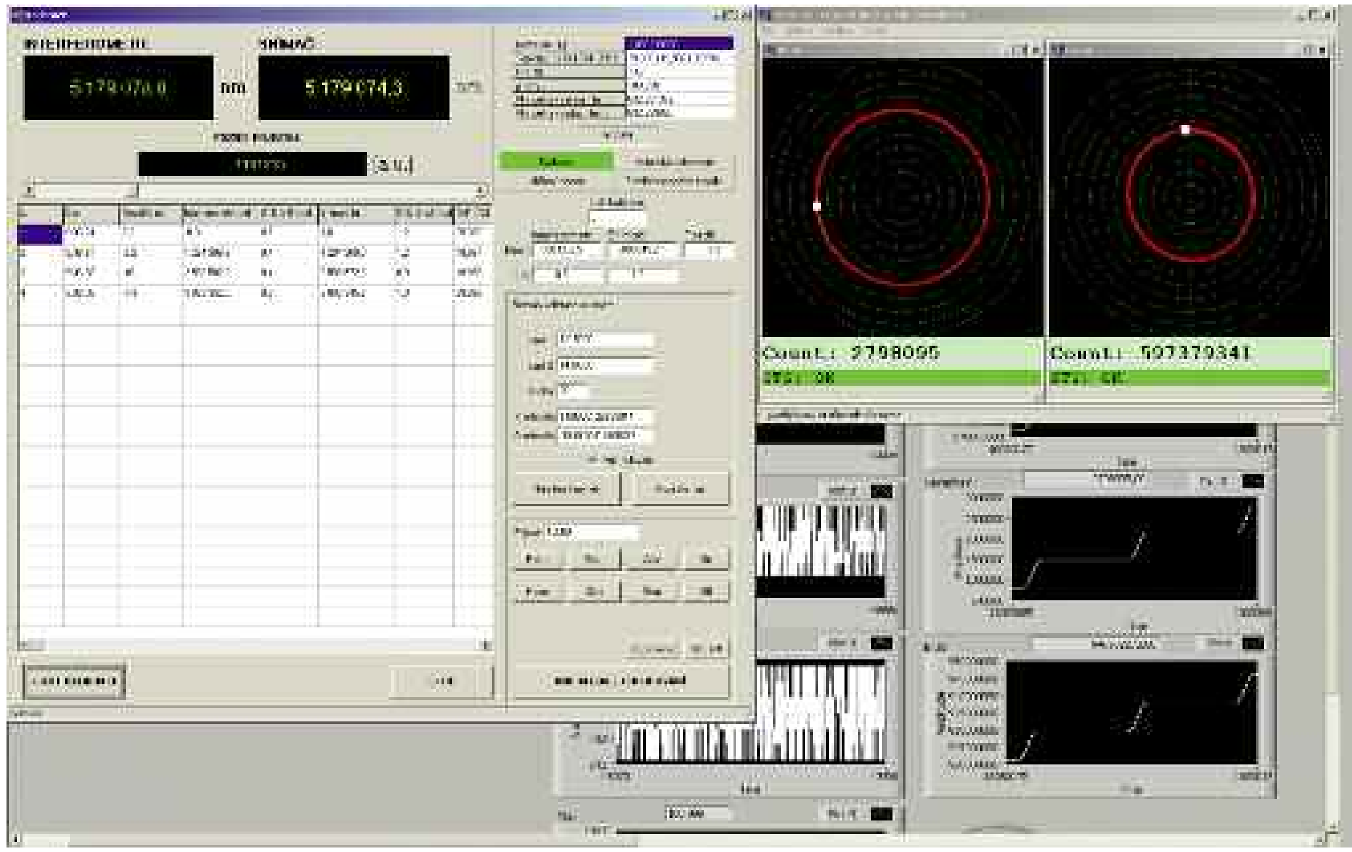
*Substrate carrier example.*



*Example of software for control of the calibration comparators of the ISI.*

## Special electronics and software

**The design of special electronics** for the control of experiments and data processing including software represent an important part of the research activities of our group.

This includes:

- low noise current controllers for laser diodes;
- precise temperature controllers for laser diodes and absorption cells;
- digital systems for phase sensitive detection;
- cards for signal digitization with A/D and D/A converters;
- high-voltage amplifiers for piezoelectric transducers;
- complete detection chains for derivative and frequency-modulation spectroscopy;
- communication interfaces for TCP/IP, USB and CAN busses and networks;
- power supplies and photodetectors.

**Software** developed at ISI includes:

- an original algorithm for linearization of the laser interferometer scale;
- a communication server for processing and data transfer through TCP/IP in real time;
- drivers for the LabView environment;
- control software for the CAN bus.

*Electronics for stabilization of optical frequency of laser diodes.*

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# Electron beam lithography



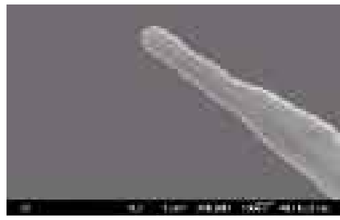
*The Electron Beam Lithography (EBL) Laboratory* of the ISI focuses on technological principles and the **preparation of submicron-sized structures** prepared in different solid-states materials. The results of the laboratory are used by both scientific and university labs and in some cases by industrial partners as well.

Our work in recent years has focused on:

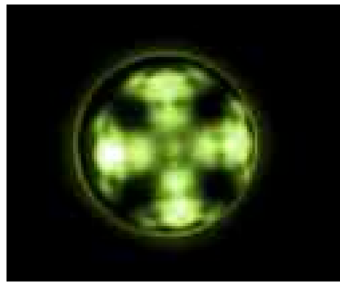
- e-beam lithography technology;
- phase diffractive optical elements (phase DOE's) and computer generated holograms (CGH).

Prior to these and other applications a necessary upgrade of the patterning tool (the e-beam writer) was performed. The upgrade included intensive hardware and software improvements of this complex system, while the physics part (original design developed by the ISI in the late 1970s) has remained practically unchanged.

*Laser beam shaping on the holographic (CGH) structure (p. 50).*



*Cathode – tip detail from SEM.*



*Cathode – angular emission pattern.*

## E-beam pattern generator

An e-beam writer (pattern generator) with a rectangular-shaped electron beam (Tesla BS 600+) allows for the fast exposure of high-resolution image information into a thin layer of electron resist spun on Silicon (or glass) substrates.

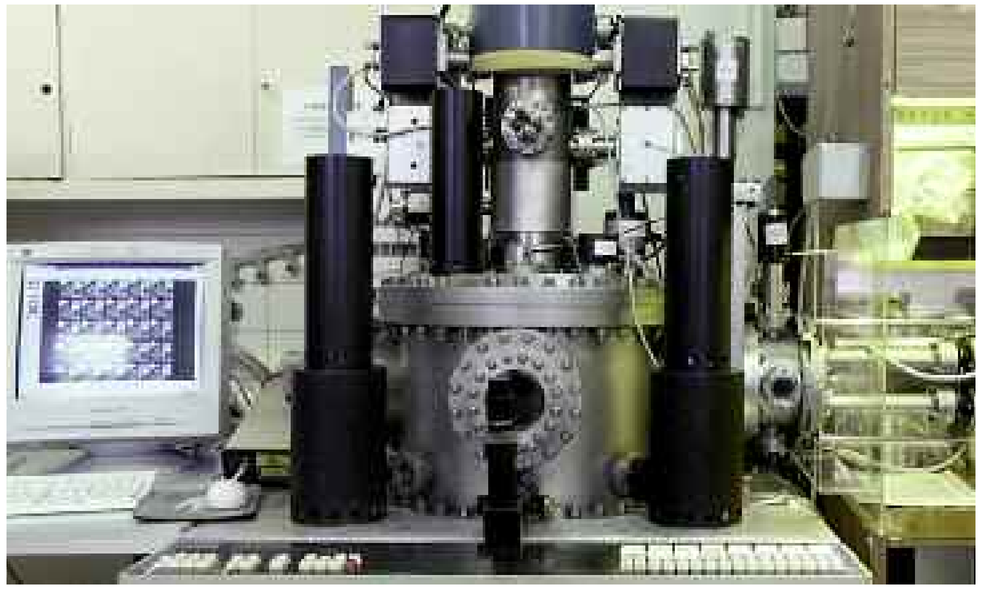
**The basic step** of the writing system is **50 nm**; the maximum grating density is about **2 000 lines per mm**.

**Pattern generator topics:**

- The thermal field effect ZrO/W Schottky cathode technology and activation process, general-purpose tip-forming process.
- Application SW add-ons.

**Selected R&D result used by industrial partners:**

- Two e-beam pattern generators (Tesla BS 601+) were upgraded and delivered to an industrial partner.



*E–beam pattern generator.*

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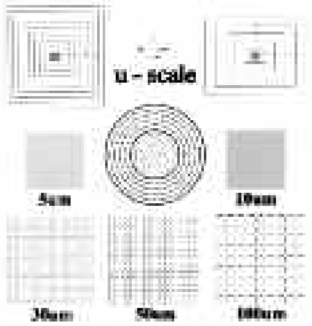
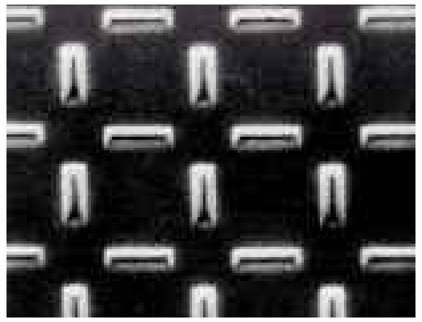
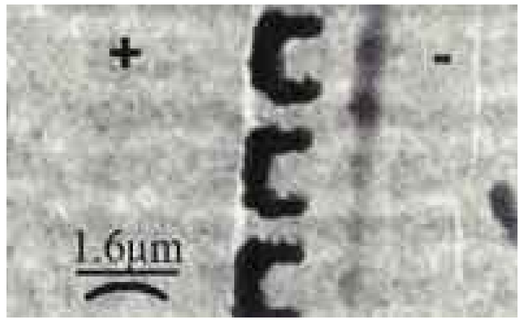


Dimension standard structure size 3x3 mm (layout overview).



Dimension standard structure (detail), grating period 5 μm (SEM).




Self-switching diode device (AFM).

## E-beam lithography technology

A required image is enregistered into **the thin polymer layer** (positive or negative electron resist) by the beam of electrons. The resist-layer mask is created by the development of the exposed patterns. The substrate surface (or the working layer previously deposited on the substrate – either a metallic or a dielectric one) is modified through the resist openings.

**EBL originated samples and applications:**

- Dimension standard structure
- Masters for nano-imprint lithography (NIL)
- Glass masks for optical and UV lithography
- Direct write lithography
- Micro- and nano-relief characterization by atomic force microscopy (AFM)

**Selected R&D result used by industrial partners:**

- A few samples of metrology dimension standards for both optical and e-beam microscopy were delivered to several customers. The precision of the samples is derived from the laser-interferometer calibrated exposure field of the e-beam pattern generator. The samples are basically composed of the scale, rectangular gratings with different periods and a set of geometrical shapes with a description.

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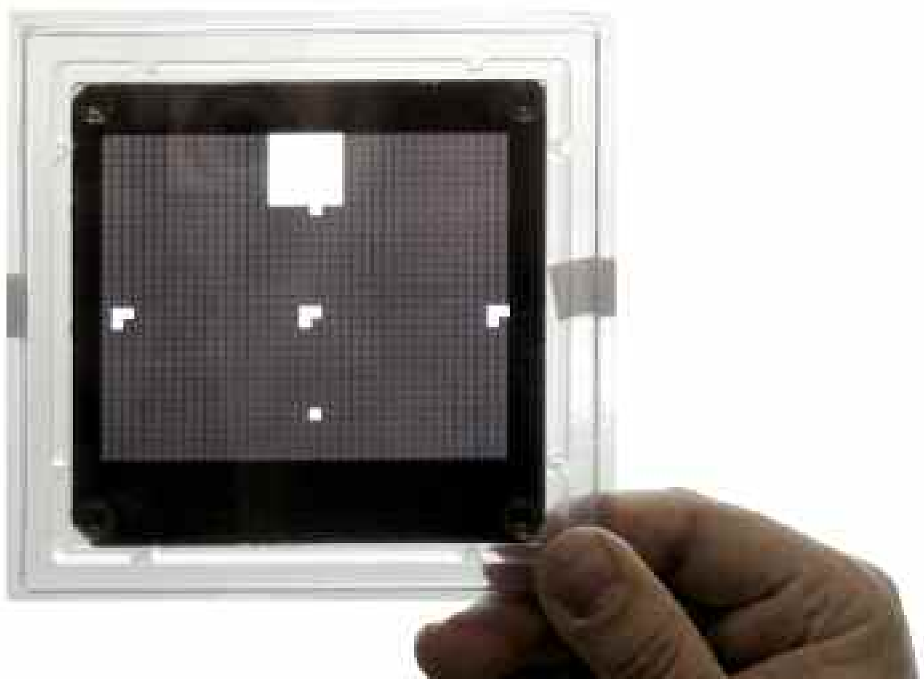


Lithography mask – Chromium on 4" glass.



## Optical diffractive structures

The resolution of the e-beam writer allows for the delineating of gratings with a period below 1 micron which si close to the visible light range (400–700 nm). With a relatively high writing speed, optical diffractive structures of several cm² can be prepared.

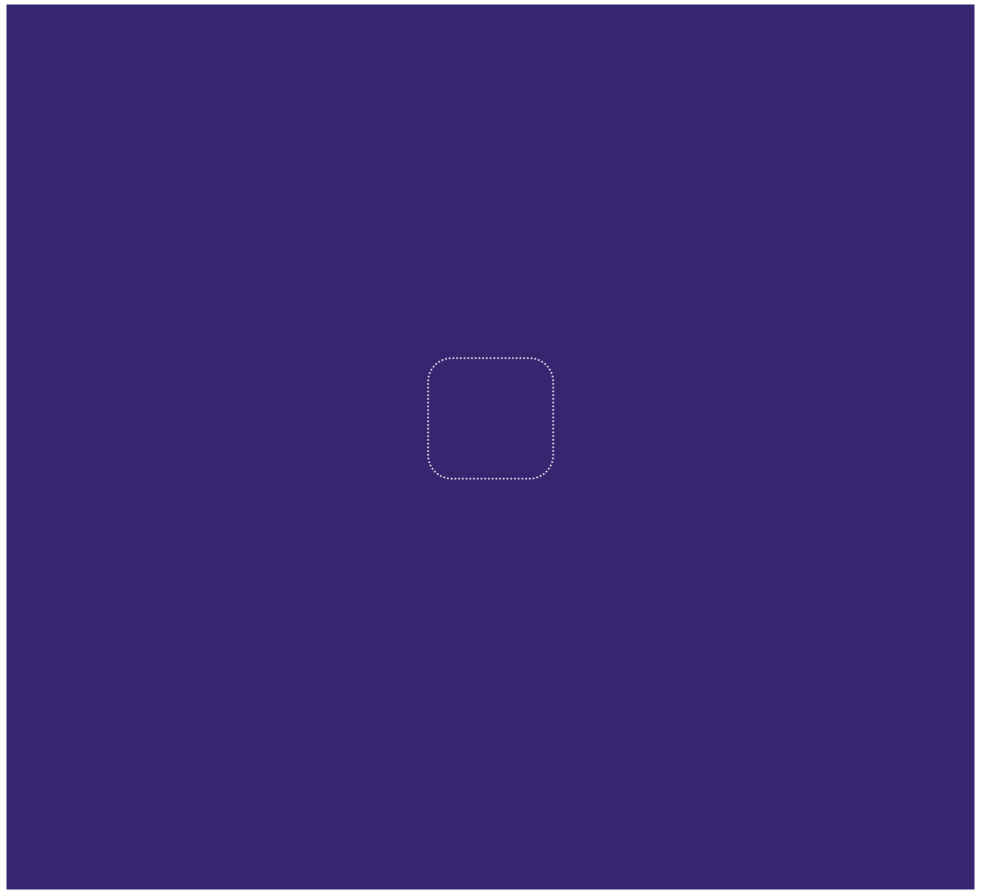
Due to the flexibility of the technology a varible set of diffraction gratings as well as their combination within one sample is possible e.g. reflection or transmission gratings, phase or amplitude gratings, regular (lines, crosses, circles) and irregular structures (Fourier, Fresnel), binary and multilevel profile and so on.

**EBL applications**

- **Phase diffractive optical elements** (phase DOE's) – methodology and technology of structure preparation.
- Industrial applications of EBL in the field of **computer generated holograms** (CGH), i.e. **synthetic holograms** patterned by the direct e-beam writing process (groove by groove) as opposed to the laser interference method.
- Optical diffractive **Fresnel lenses.**

**Selected R&D result used by industrial partner**

- A few dozen samples with **large-area holographic structures** (prepared in the polymer electron resist layer) were delivered according to the customer's technical specifications.



Embossed DOE sample: courtesy of Optaglio s. r. o.

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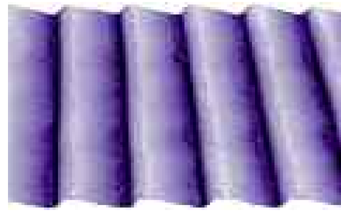
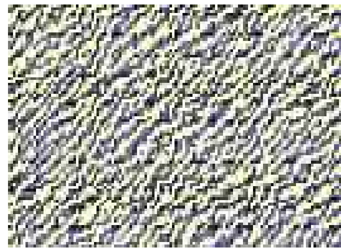
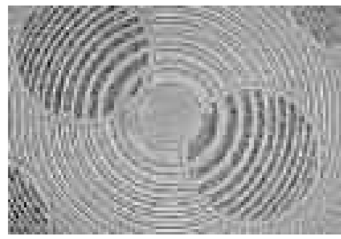
Detail of a general diffractive multilevel structure (optical microscope, 200x).



Relief of a regular asymmetric diffractive grating pitch 4 um, deepness 0.5 μm (AFM).

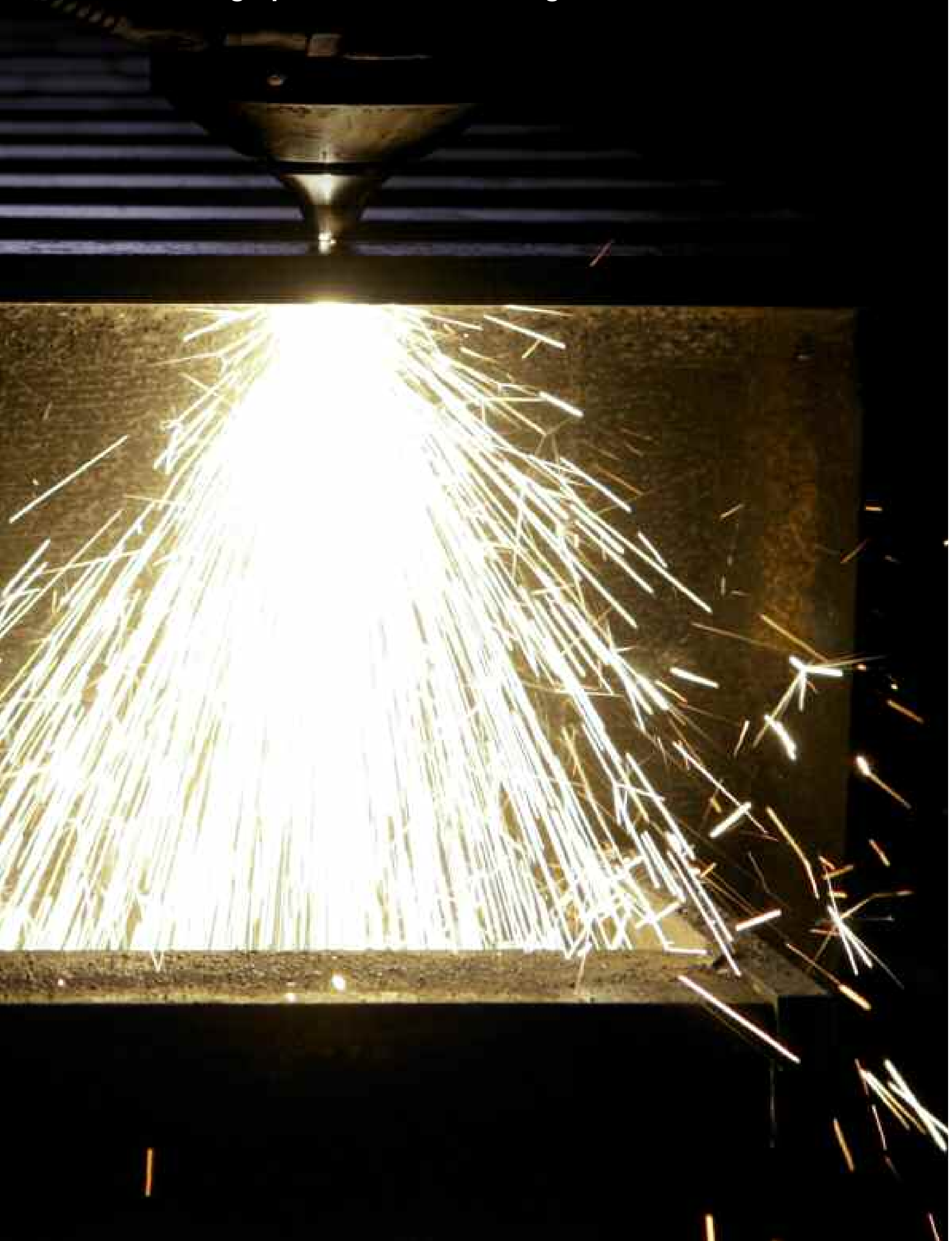


CGH structure (layout simulation).



Zonal structure with a diffuser (optical microscope.

# Advanced high power laser technologies





*Cutting laser in operation (p.54).*

Technologies that use a **laser beam for welding, drilling, cutting or hardening** are among the progressive and promising methods that allow manufacturers to increase the value of their products or create new products that cannot be made by different methods. Technological demands make it difficult for small and middle-sized companies to buy such machinery. It's economical benefits are not immediate as it is necessary to improve the process and, especially in case of **laser welding**, to perform a number of technological tests. These are some of the reasons we are creating a facility at ISI that will also offer state-of-the-art laser technologies in the form of a service.

## Advanced high power laser technologies

The principle of laser welding takes advantage of high energy density (approx. $10^7$ W/cm$^2$) in the area illuminated by the beam, which results in an immediate evaporation of the material with a minimum heat dissipation into the surrounding area. This process creates a cylindrical hole filled with evaporated metal at a pressure which prevents the liquid metal from closing the hole. If the beam is then moved at an appropriate speed the hole follows the beam and a **very narrow** but **very deep weld** can be created. This process does not need to take place in a vacuum – a protective atmosphere is applied to the welded spot to suppress oxidation. If a higher pressure process gas is applied along with the beam, the melted material is blown away, which results in cutting instead of welding. Compared to other welding or cutting methods **the use of a laser minimizes the heat impact on the material**, therefore **minimizing deformation**.

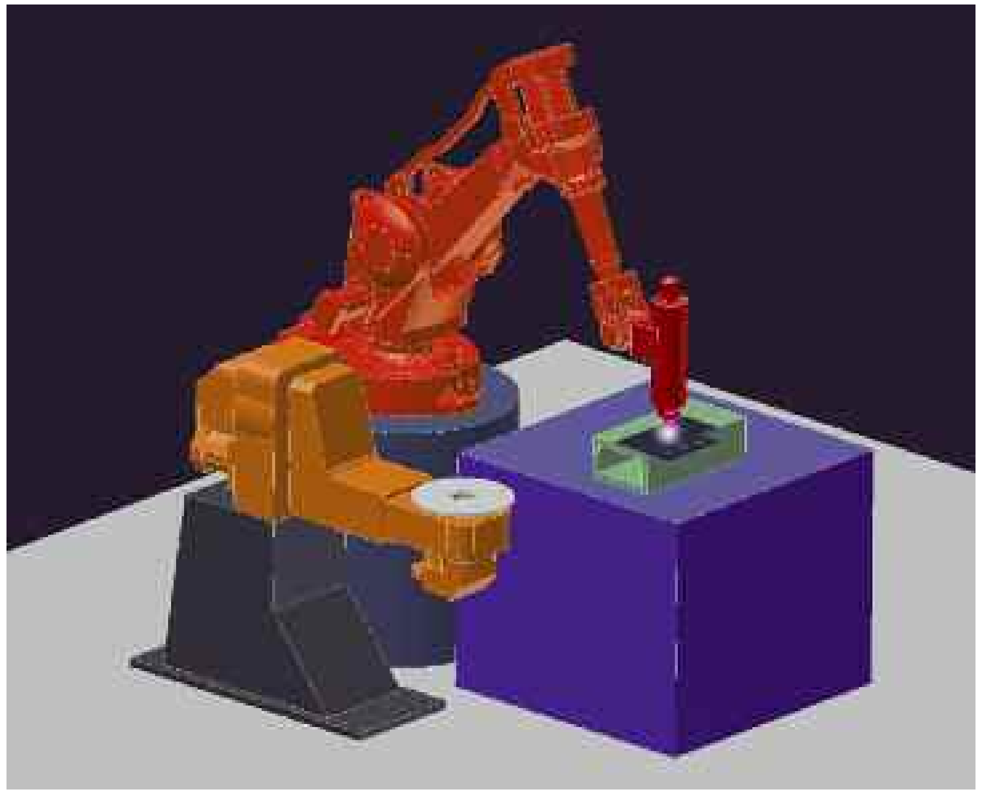
A fibre laser is used at ISI. The laser is connected to two application heads for **cutting and welding**. The cutting head is connected to a robotic arm through its own independent linear axis. This axis uses an integrated feedback system to keep the cutting head at a constant distance from the material, which is one of the most critical requirements in the cutting process. The welding head is equipped with a coaxial camera that allows a direct view of the welding process. The application heads are positioned by a six-axis robotic arm. Additional positioning of the processed part is realized by a two-axis positioning system connected to the robotic arm's control system. The highest possible flexibility is achieved in this manner.

**Laser parameters:**

- laser output: 2 kW;
- robotic arm reach: 1.6 m;
- positioning system load capacity: 250 kg;
- maximum weld depth: approx. 5 mm;
- maximum cut width: approx. 5 mm;
- process speed: up to 10 m/min.

*Large scale image of the laser weld cross cut.*

*The work place with the robotic arm and the positioning system.*

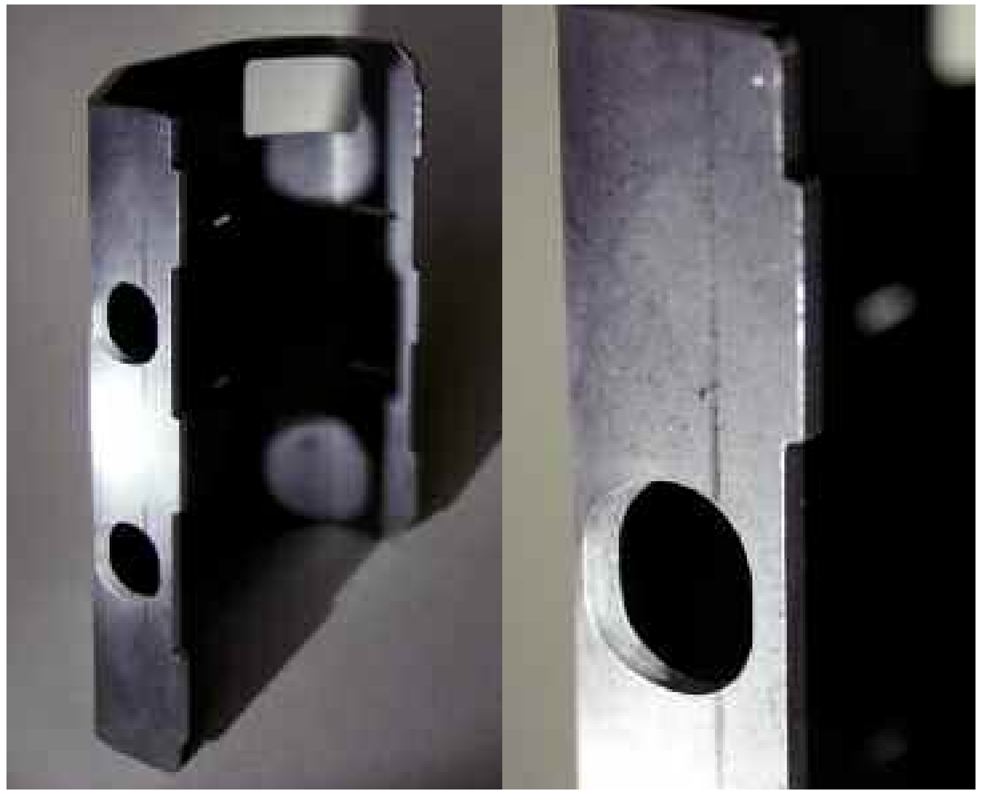


**Examples of high power laser use:**

- **Laser beam lap joint welding** of two or more sheets up to a total thickness of 5mm, square butt joint welding up to a total thickness of 5 mm, welding of metal sheets, mouldings, profiles and pipes, carbon and stainless steel, titanium and other metals and alloys, welding of materials coated with another metal (usually Zn, Al).

*A laser weld example.*

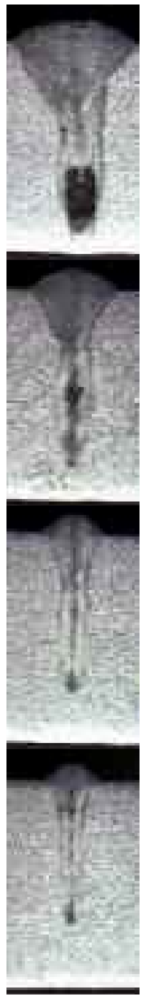




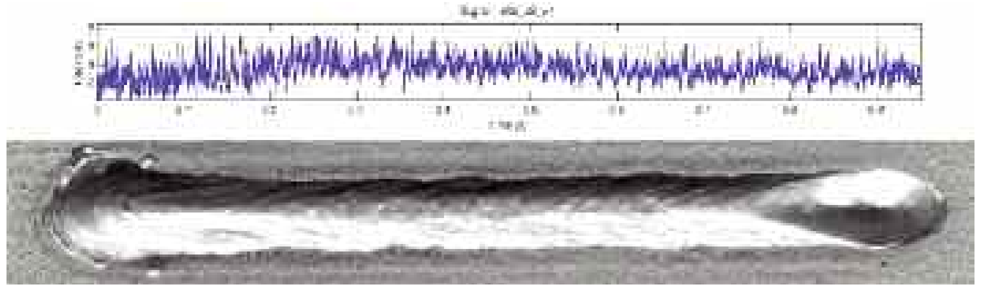
*Examples of laser cut parts (whole part and in detail).*

*A record of plasma radiation intensity during laser welding (lower left).*

*Dependence of weld shape on laser beam parameters (below).*



- **Laser cutting** of metal sheets, mouldings, profiles and pipes up to approx. 5mm thick, carbon and stainless steel, titanium and other metals and alloys, materials coated with another metal (usually Zn, Al) or with a protective foil.
- **Laser drilling** of metallic and ceramic materials shows a high width/depth ratio (up to 1:30) when the laser is operated in a pulsed regime.
- **Very small area hardening** of materials capable of producing martensitic structure up to approx. 1 mm in depth.
- **Technological and prototype testing.**
- **Welding process research** aiming at diagnostics and active control of the process and also the study of the weldability of materials.



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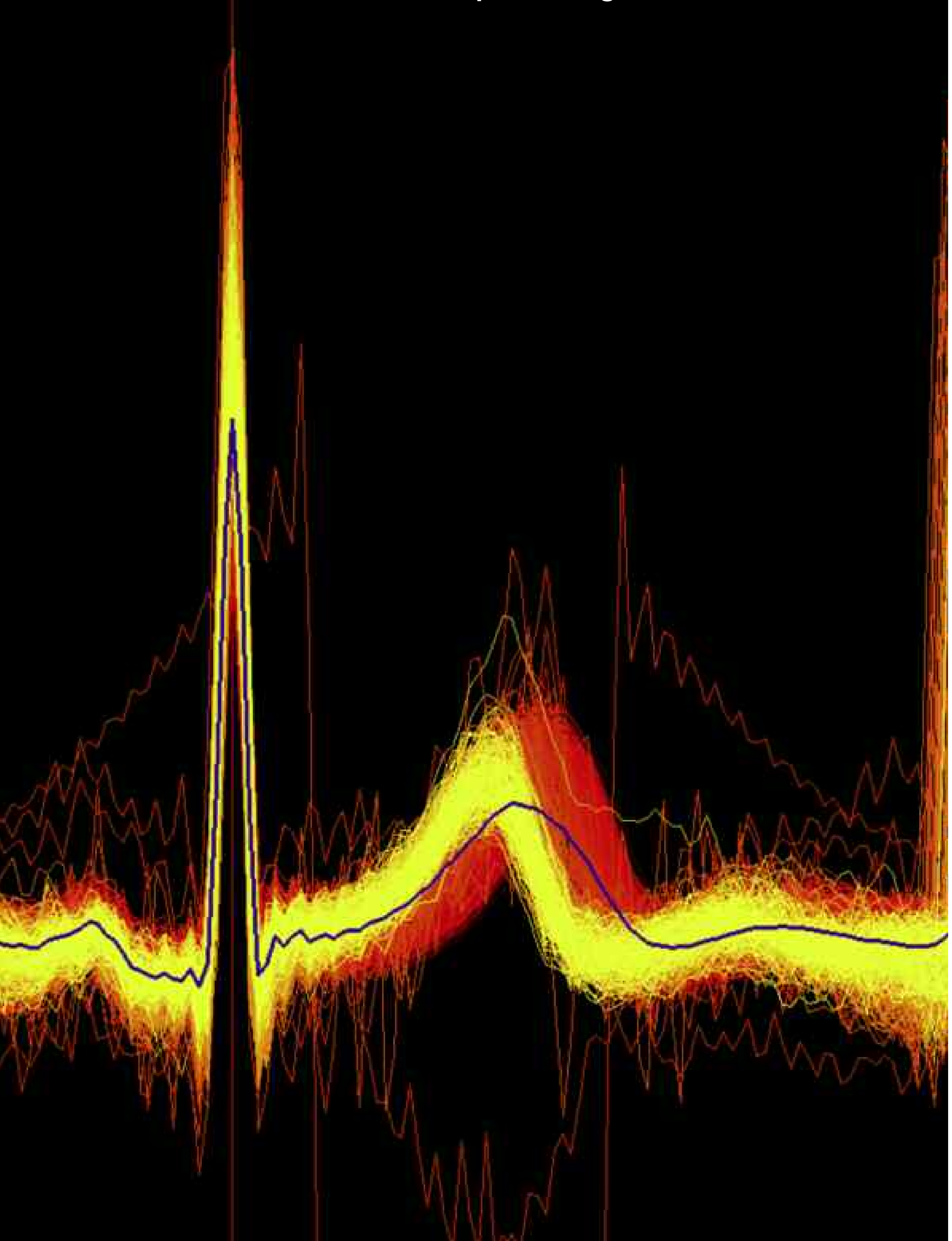
# Measurement and data processing in medicine

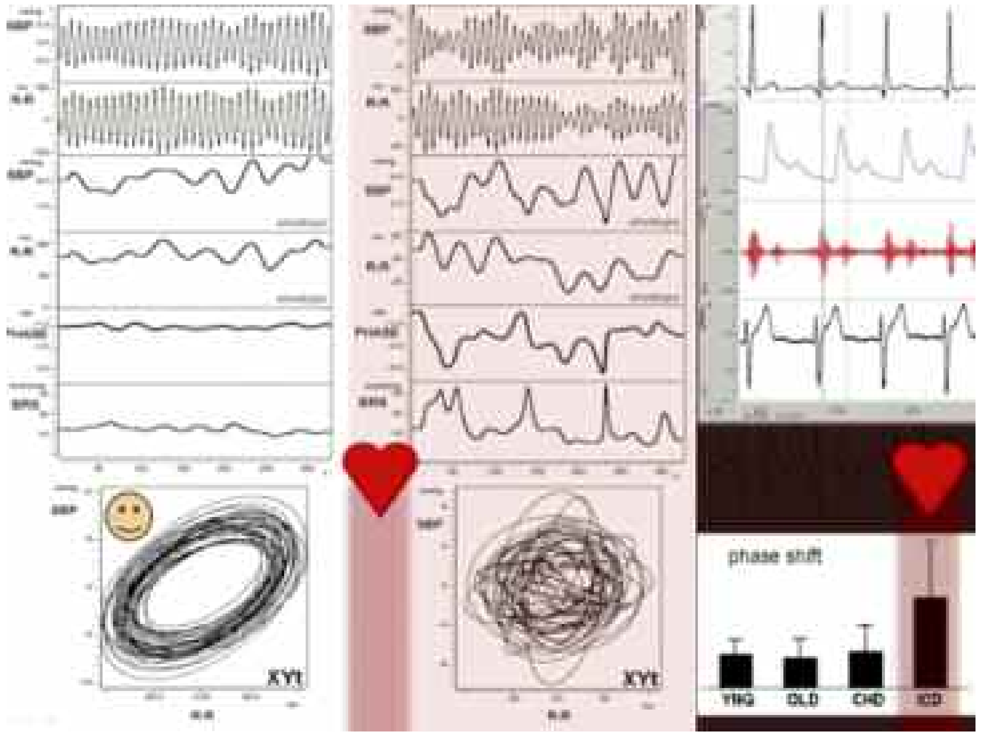


EKG signal (p.58).

The MediSIG team of the ISI provides a complete solution for **neurology**, **cardiology** and **medical signal analysis** and other applications.
The activities of the team include the development of **new non-invasive diagnostic procedures** in cardiology and neurology, **measurement and signal processing in medicine** and the design and construction of **experimental medical devices** and acquisition systems. The MediSIG team cooperates with domestic and foreign hospitals and physicians. Cooperation includes the implementation of measurement and diagnostics protocols, design of recording parameters and physiological signals, data digitizing and archiving, processing and detection of physiological parameters and statistical analysis and evaluation of results. The outcomes of interdisciplinary cooperation also include joint patents and original experimental equipment and methodology.

**MediSIG Cardiology – non-invasive diagnostics of cardiovascular disease**
Diagnostics is focused on determining the level of risk of coronary heart disease, sudden cardiac death, arrhythmia, heart attack and heart failure, as well as ischemic disease, high blood pressure risks and heart transplant innervations. It is based on the evaluation of multi-lead ECG signal, blood pressure, impedance cardiography, heart sounds and respiration. Results include the determination of complete hemodynamic parameters, blood vessel stiffness and control properties of blood circulation.

**MediSIG Neurology – EEG signal processing, epilepsy, Parkinson's disease**
MediSIG provides complete processing, analysis and statistical evaluation of EEG recordings from deep brain structures. Epilepsy that cannot be pharmacologically controlled can be treated only with surgery. Intracerebral or subdural electrodes are implanted to localize epileptic sources. Unique EEG recordings from depth electrodes allow the development of new techniques for analyzing evoked processes, synchronization and desynchronization, and signal propagation directions and connectivity between different brain structures during various mental activities.




*Sudden cardiac death risk stratification. In cooperation with St. Anne's University Hospital and Medical Faculty of Masaryk University, Brno, Czech Republic, Mayo Clinic, Rochester, MN, USA.*

## Software – methodology & processing

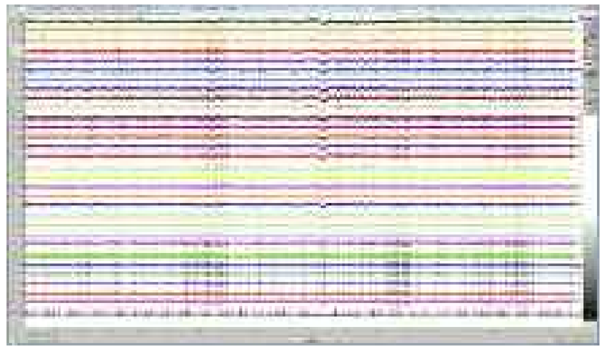
**ScopeWin – system for measurement and data processing in medicine**

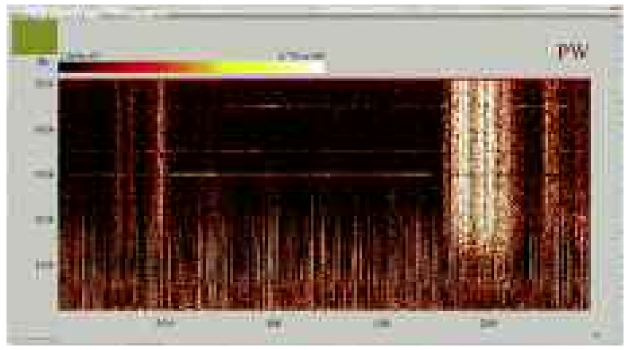
Basic features:

- **Data acquisition** – ScopeWin communicates with the NIDAQMx library, which covers the complete series of National Instruments hardware.
- **Visualization** – ScopeWin includes a graphic editor that allows comfortable data inspection, signal comparison, manipulation, cursor operation etc. Data can be converted to conventional formats.
- Post-acquisition **processing** includes the following features: frequency analysis, digital filtering, functions for mathematical signal processing (splines, derivation, integration, digital quadrature detection and demodulation, regression, 50 Hz signal detection, processing and elimination), two-dimensional analysis (time-frequency analysis – amplitude, phase and power), segmentation and averaging according to established criteria and several more. Most measurement, visualization and processing functions can be implemented as commands in the program and carried out sequentially without operator intervention.

ScopeWin signal processing in cardiology includes the following functions: ECG signal parameters detection (R wave, QT interval, heart rate, QT dispersion, T wave alternans), continuous blood pressure recordings analysis (systolic, diastolic, mean pressure, blood pressure variability, baroreflex), heart sounds (S1, S2), impedance cardiography (stroke volume and cardiac output, elasticity of blood vessels, pulse pressure wave) and respiration (breathing frequency and depth). ScopeWin provides procedures for complete evaluation of hemodynamic parameters. It also allows the implementation of new procedures and methods.

ScopeWin signal processing in neurology includes the following features: visualization of large datasets of intracranial EEG recordings, time-frequency analysis, segmentation, automatic removal of artificial segments and channels, averaging and evoked potential calculation, envelope analysis, etc.






*Analysis of EEG from depth electrodes. In cooperation with Brno Epilepsy Center, Departments of Neurology and Neurosurgery, St. Anne's University Hospital and Medical Faculty of Masaryk University, Brno, Czech Republic.*

**EEG signal analysis**

MediSIG provides professional advice with the realization of EEG measurement and complex data analysis. We use our own software (ScopeWin, ScopeMAT) equipped with advanced methods of analysis. The software is intended for **off-line data processing**, especially for **EEG**, **EKG**, **EMG** and **EOG** signals analysis.

Processed data are obtained from clinical and experimental intracerebral or scalp EEG recordings. Today they are recorded from up to 128 recording points with a sampling frequency of 1 kHz.

Data analysis includes:

- analysis of non-repeated signals (data recorded without subject stimulation);
- analysis of repeated events (data recorded during subject stimulation: visual/sound/tactile/etc.);
- impact of Deep Brain Stimulation (DBS) on EEG development.

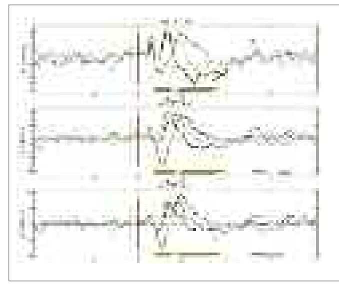


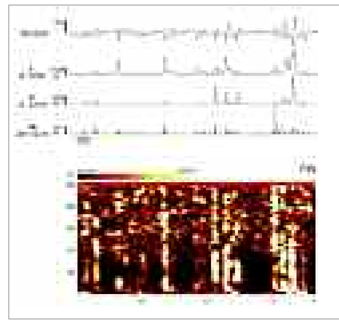
Developed software packages cover complex off-line methods suitable especially for neurological data analysis. Our software products allow:

- data blocks manipulation, data preprocessing, data analysis based on FFT, visual data representation and basic statistical data parameterization;
- statistical evaluation and automation of data processes (ScopeMAT);
- analysis of connections between brain structures based on EEG data from intracerebral electrodes;
- visualization of results on a stereotactic brain model;
- complex software for analysis and visualization – EEGVisual.

ScopeMAT software allows parametric batch data processing covering: FFT filtration, power analysis, time-frequency analysis, statistical evaluation of repeated events (Wilkoxon test, t-test, bootstrap test), automatic detection of power increase and decrease, automatic detection of statistically significant components in time or frequent domain, statistical tests for determination of repeated evoked signal differences recorded during different external conditions (subject stimulation of type A/B/etc., test for two modalities, Schoffe test for more than two modalities). Groups of subjects can also be evaluated using ScopeMAT software. We can compute "GrandAverages" and present significant results for different contact groups transparently.

The ScopeMAT software is proposed for the MATLAB environment. This solution allows quick algorithm implementation depending on application demand. The ScopeMAT software provides numerical and graphical outputs to many format types, including MS Word and MS Excel.





*Intracranial EEG signal analysis. In cooperation with St. Anne's University Hospital, Brno.*

## Data acquisition systems

In addition to software and experimental devices MediSIG also produces complete acquisition systems. It can simultaneously record up to 128 channels, sampling up to 5 MHz per channel with 16-bit resolution and higher. The hardware is built on top of National Instruments PCI / PCMCIA / USB devices. For experiment control and data recording the ScopeWin program is used.

Realization examples:

- ISI Brno acquisition systems.
- M&I – ISI high speed EEG recorder and analyzer (up to 200 channels, 40 kHz sampling each),
- ANNALab – acquisition system for neurology and cardiology, St. Anne's University Hospital Brno, Mayo Clinic, USA

## Experimental devices for measurement of biomedical signals

The MediSIG team mainly designs and constructs experimental devices for the measuring and data processing of biological signals. We concentrate on devices which are not available or do not yet have the desired parameters on the commercial market.

Examples of devices:

**The Detector of Vagus Nerve Stimulation.**

The device for detection of activity of vagus nerve stimulation is intended for independent monitoring of implanted vagus nerve stimulation. It measures the electrical potential from the patient's neck, processes it and detects activity of the stimulator.

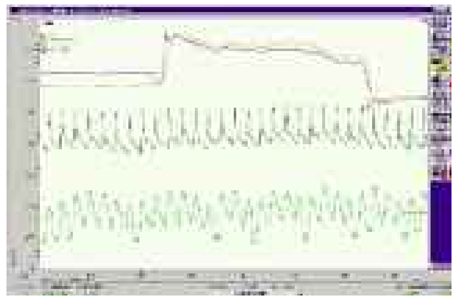
*The Detector of Vagus Nerve Stimulation.*

RECO – device for respiration control.

**RECO – device for respiration control.** LEDs bargraph for pacing of breathing. It is used for controlled excitation of the cardiovascular system. It enables setting of pacing frequency 1–39 min$^{-1}$, various modulations – ramp and sinus with depth of 25–100%.

**The Strain Gauge Plethysmograph.** The strain gauge plethysmograph, which can be used for several measurement techniques in medicine, essentially measures the changes in human limb volume directly. However, it can be also used in indirect measurement for evaluating limb blood flow, blood pressure, digital volume pulses, for measuring circumferential changes of exposed arteries and breathing. Our device can measure up to 10 channels simultaneously.

*The Strain Gauge Plethysmograph.*



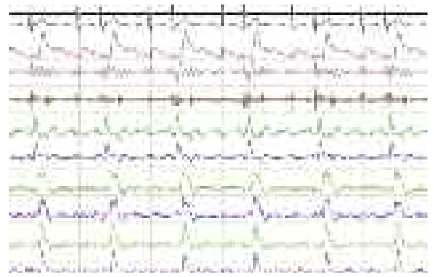
*The Strain Gauge Plethysmograph.*

**Experimental Syringe Mixing Pump For Ultrasound Contrast Agents.** The pump enables continual infusion and bolus while mixing the contents of the syringe. The control of the pump is ensured by microcontrollers and is fully programmable by the user. The device is battery operated and has a robust mechanical construction. Technical parameters: syringe 10 ml and 20 ml type, infusion flow rate 0.3..4.0 ml/min, bolus flow rate 0.3..4.0 ml/min, bolus time max. 60 seconds, mixing rate 30 cycles/min ±180°, minimum continuous working time 4.5 hours per one full battery charge.

**Multi-Channel Impedance Cardiography.** Impedance cardiography is a method based on measuring changes of thorax electrical impedance. From the changes of thorax electrical impedance it is possible to calculate important parameters of the cardiovascular system, like stroke volume or cardiac

*Experimental Syringe Mixing Pump For Ultrasound Contrast Agents.*





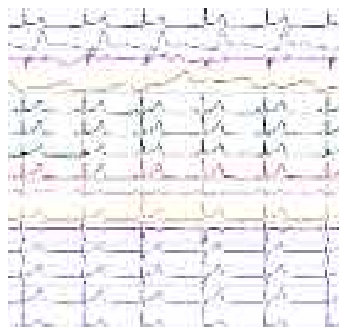
*Multi-Channel Impedance Cardiography, ECG, blood pressure, heart sounds.*

output. The monitor makes it possible to measure small changes of impedance on separate parts of the human body and to evaluate blood flow, particularly the propagation of pulse waves in the whole body. It also makes it possible to analyze vessel compliance. Commercial devices are equipped with one or two channels and the simultaneous survey of blood flow in many parts of the body is not possible. The main advantages of the monitor are the high quality of the impedance signal, coherent impedance detection in all channels, measurement of impedance phase changes and the option of stand-alone measurement without computer and supply voltage.

- The multi-channel device consists of two-channel units. Each unit is comprised of two current generators and two voltage detectors. The device makes it possible to interconnect up to 9 units with clock and synchronization signals and to build an 18-channel device. The unit stores the impedance signal on a SD/SDHC memory card, transfers it in real-time to the PC through the USB port, and possibly represents it on analogue output.
- The parameters of the unit are:
  – measurement frequency 30 to 70 kHz or 1 kHz to 1 MHz (optional)
  – measurement current 1 mA, adjustable
  – clock frequency of direct digital synthesis, AD converter and synchronous detector 60 MHz
  – overall dynamic range of 127 dBc/√Hz
  – phase resolution better than 0.001 degree
  – output data format 16-bit complex envelope at 10 kHz sampling
  – operating time 3 hours

**Device for microneurography.** The dedicated preamplifier and amplifier with signal filtering and detection are used for monitoring the electrical activity in the nerves. The amplifies and processed signals obtained by means of microelectrodes (special insulated needle with conductive tip) directly from the desired part of nerves.

**ECG 12.** Experimental 12 lead electrocardiograph amplifier with broad pass band up to 500 Hz. This device is intended to be used for special ECG measurements that cannot be performed with a standard commercial device. The amplifier is battery operated and is equipped with the 12 analog outputs, 1 monitor output and USB data acquisition unit.



*12 lead ECG monitor.*

MediSIG has also designed and constructed a wide range of various devices for measuring biological signals like electrical amplifiers and filters, pressure measurement devices for the monitoring of breathing, pressure monitoring in lungs and esophagus, devices for phonocardiography – special microphones with dedicated amplifiers, spirometers, etc. The majority of these devices are battery operated to enable use during measurements of weak biological signals, where using AC mains operated devices cause unacceptable artifacts in the measured signal.

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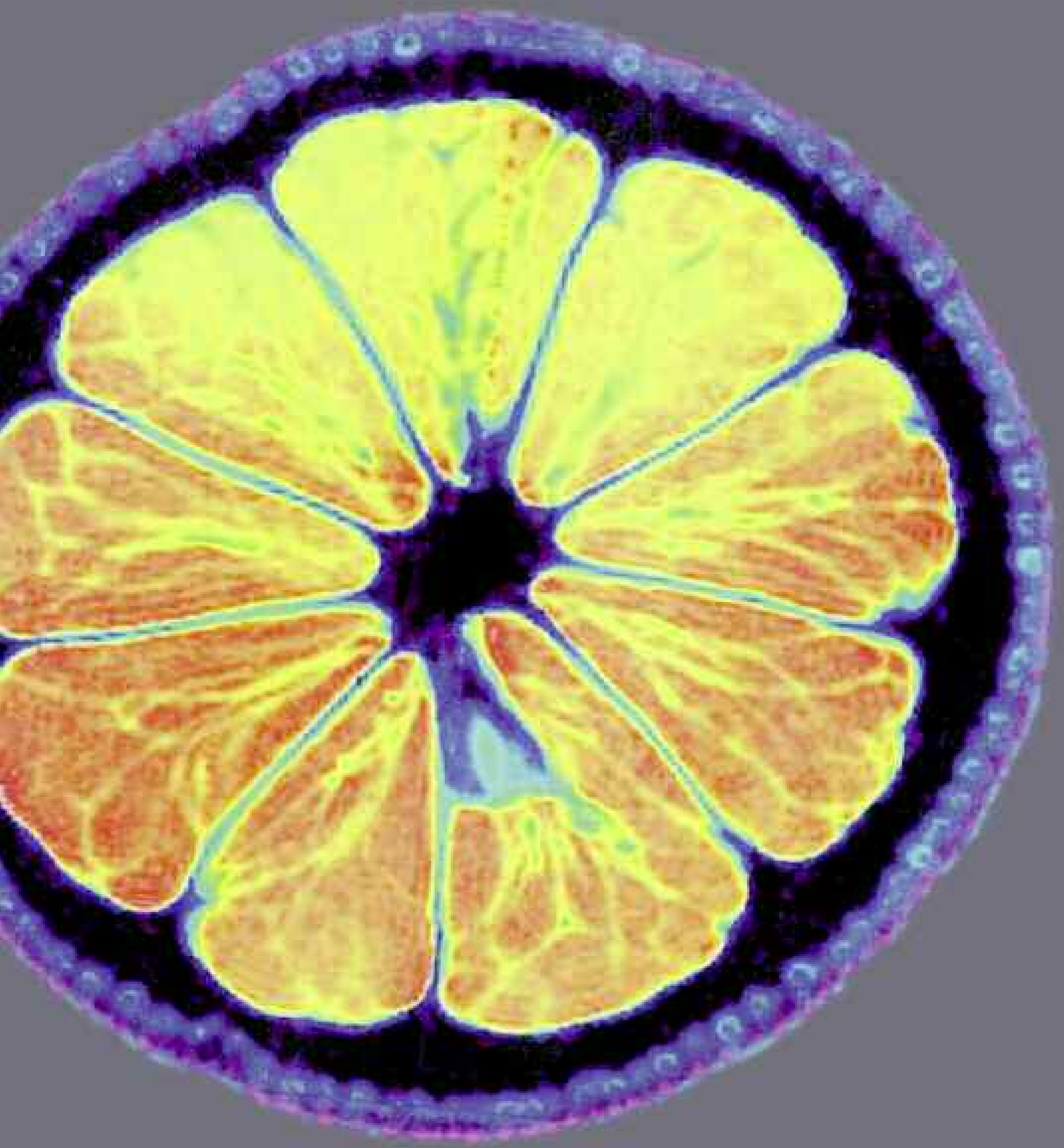
# Nuclear magnetic resonance





*Intact lemon cross-section (p.64).*

The research of the **N**uclear **M**agnetic **R**esonance group is oriented primarily towards methodology of localized **in-vivo MR spectroscopy, spectroscopic imaging**, and quantitative imaging such as **diffusometry** and **relaxometry**.
These nondestructive, noninvasive and non-ionising measurements are based on the nuclide-selective interaction between magnetic fields produced by the NMR scanner with the atomic nuclei located in the sample volume. The highest sensitivity is achieved with $^{1}H$ nuclei (protons) and, therefore, the prominent targets are water molecules, which are abundant in biological samples and many materials. In these measurements, the nuclei observed may not only describe the anatomy of the sample interior, but they also act as atomic probes reporting on their nearest environment and processes occurring on the time scale of picoseconds to hours.
Besides the ability to identify certain molecules, the acquired data can provide a statistical representation of the fast and random atomic and molecular interactions (manifested by relaxation times, diffusion coefficients, chemical exchange rates and seen as intensity modifications) as well as temporally and/or spatially resolved information on much slower processes (concentration changes, perfusion, flow or motion seen in consecutive images). Quantitative images mapping the spatial distribution of certain well-defined physical properties (relaxation times, diffusion coefficients and directions, flow velocity, temperature etc.) may be obtained, the presence of paramagnetic or superparamagnetic nanoparticles can be detected.

**Equipment:**
With the MR scanner(s) available in ALISI, virtually all kinds of measurements known from clinical MR scanners can be performed. Thanks to the increased sensitivity resulting from the high magnetic field and small coils, the achievable spatial resolution is much more adequate to the study of small samples. The application sphere is not limited to biomedical imaging; techniques targeting specific problems may be developed.

- MR scanner **4.7T/210mm** (proton resonance frequency **200 MHz**), optimum sample diameter **40 mm**, maximum diameter **100 mm**, maximum length about **300 mm**; measurable nuclei: $^{1}H$, $^{13}C$, $^{19}F$, $^{31}P$, $^{23}Na$, $^{129}Xe$ (immediately), other nuclei negotiable (depending on the availability of RF coils and filters).
- MR scanner **9.4T/210mm** (proton resonance frequency 400 MHz, as of mid 2011).
- **Physiological functions monitor** and isoflurane gas anesthesia unit for small animals (as of 2011).
- RF laboratory.

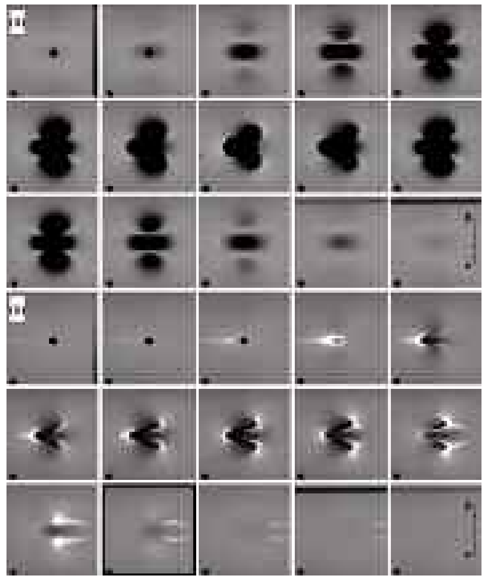
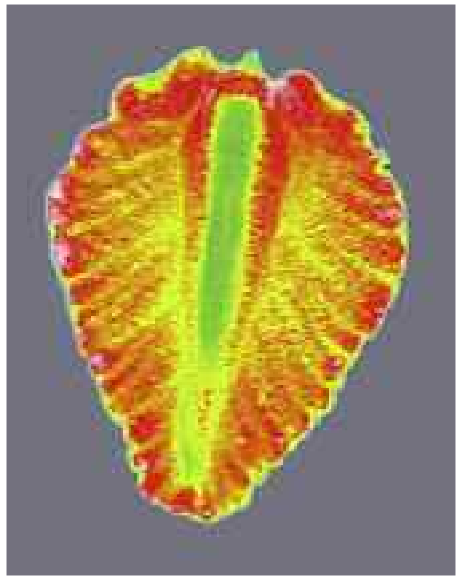
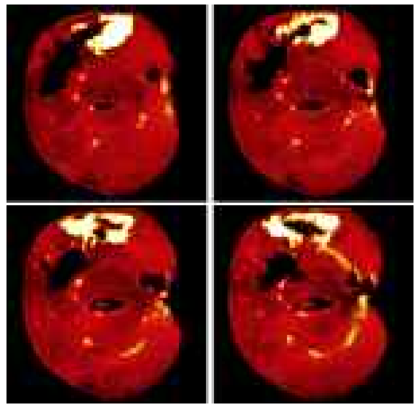


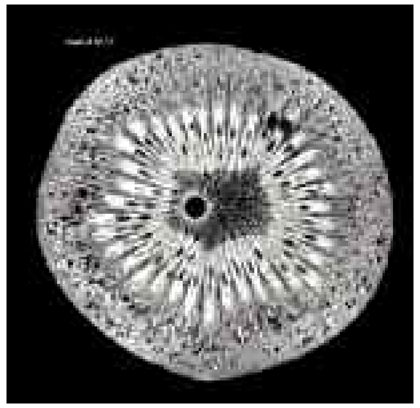
*Image artefacts produced in gradient echo (a) and spin echo (b) 2D MR images around a sample made of a paramagnetic dental material.*



*Strawberry cross-section.*

*The 4.7 T magnet.*





*Four adjacent slices of a decomposing worm-eaten apple. The hyperintense area results from faster relaxation of the smaller molecules of the decomposed tissue.*

*The bright seed indicates the presence of oil.*

*The anatomy of a kiwi fruit, measured at 4.7 T.*

## Imaging and data analysis

ALISI is prepared to optimize the measurement and data processing protocols for answering specific questions and to carry out the necessary measurements. Due to the complexity of the technology and the enormous flexibility of NMR measurements, collaborative work may be the most suitable way to maximizing the synergy between the core competence of the client and the NMR competence of the ALISI teams.

**MR imaging, localized spectroscopy and spectroscopic imaging**

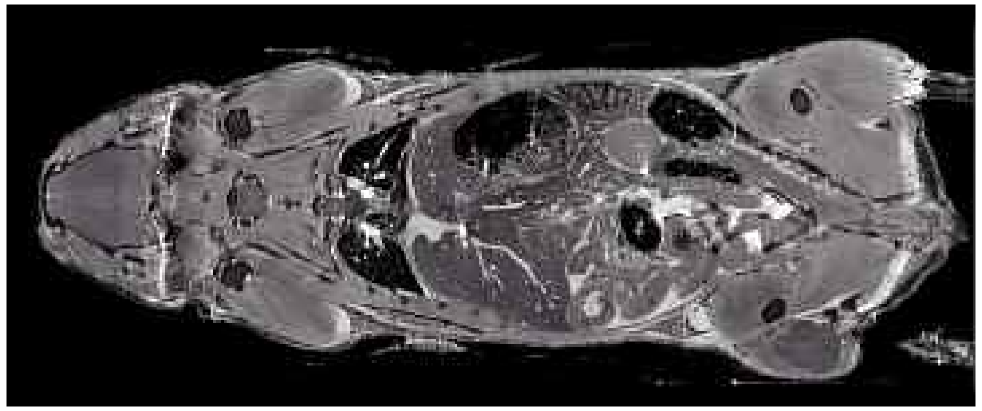
- Spatial mapping of 2D slices or 3D volumes, spatial resolution down to about 0.1 x 0.1 x 1 mm$^3$ (10 nL) now, 0.05 x 0.05 x 1 mm$^3$ (2.5 nL) as of 2011.
- Images weighted by spin density, $T_1$, $T_2$, $T_2^*$, diffusion, magnetic susceptibility.
- Molecule-specific images (water, fat, specific small molecules).
- Quantitative imaging of relaxation, diffusion, perfusion, flow, temperature changes, magnetic susceptibility.
- Mapping of the 3D spatial distribution of selected small molecules, particularly for in vivo studies of cell cultures, plants, extracted tissues, small animals (mouse, rat – as of 2011).
- Quantization of **metabolite** ratios **in vivo**.

**MR data analysis**

- **MR imaging and spectroscopic imaging**: own software Marevisi (developed in cooperation with National Research Council Canada – Institute for Biodiagnostics) – processing and visualization of multidimensional MR data sets.

*The 4.7 T magnet.*





*Mouse, imaged in a 9.4 T MR scanner.*

- MR spectroscopic imaging: quantum-mechanics based simulations and data processing, software jMRUI (developed in collaboration by a consortium of European research institutions).
- Customized MR data analysis solutions.
- Evaluation of perfusion studies.

**Education and training**

- Customized courses, demonstrations and system-operation training available to pre- or post-graduate university programs or research-oriented professionals.

## Application fields

**Biomedical research**

Numerous applications of the **small-bore high-field MR scanner** measurements are possible in the fast growing areas of **nanomedicine**, in the development and testing of

- stem cell based therapies for cardiology, neurology, orthopedics, diabetes treatment;
- targeted drugs for **oncology, cardiology, neurology, psychiatry**;
- contrast agents based on **superparamagnetic nanoparticles**.

High spatial resolution measurements of cell cultures, soft tissues, cartilage, excised organs, or in-vivo in mice or rats may be the bridge translating the molecular and cellular techniques to human medicine. It is an advantage that the same NMR techniques can be applied in models and in humans. Therefore, collaboration in human-oriented MR-based research is also possible, particularly in areas matching the team's research orientation. Biomedical molecular imaging, combining NMR with optical modalities (fluorescence, bioluminiscence, and/or Raman spectroscopy) is promising for the future.

The NMR expertise may be further applied in other areas related to the biomedical sector, such as

- design and construction of **NMR phantoms** and coils for special purposes;
- **testing of MR compatibility of materials and implants**;
- study of plant physiology.

**Industrial technology**

NMR imaging and/or spectroscopy may be applied in various areas of **the chemical, food, building, energy-producing industries**, such as

- characterization of porous materials and gels by relaxometric and diffusometric methods;
- measurement of magnetic susceptibility of materials;
- development of biotechnologies.

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