INCDTIM
National Institute for Research and Development of Isotopic and Molecular Technologies

FROM SCIENCE TO TECHNOLOGY
SHAPING THE FUTURE

RESEARCH EXPERTISE IN INCDTIM

Technology Transfer Center of INCDTIM

SUMMARY

01.

STABLE ISOTOPE LABELED COMPOUNDS

STABLE ISOTOPE LABELED COMPOUNDS

Keywords: *labeled compounds, custom isotope labeling, ^{2}H, ^{13}C, ^{15}N, and ^{18}O*

DESCRIPTION

Isotopic labeling involves enriching a molecule with heavier isotopes like ^{2}H, ^{13}C, ^{15}N, or ^{18}O, allowing its path to be monitored in various biological and physico-chemical processes.

Isotopic labeling is carried out by three different methods:

- ***The chemical conversion of raw materials (obtained from isotope separation) into various precursors used in more complex labeling***. This step is carried out by classical syntheses, such as the conversion of nitric acid to ammonia with Dewarda alloy in a basic environment or by heterogeneous catalysis, such as the conversion of carbon monoxide to carbon dioxide or methane using metal catalysts deposited on a porous support
- ***Custom isotope labeling***, in which case, in the first step, the most suitable synthetic route to obtain the desired compound is identified, tested, and optimized with unlabeled reactants. In the second step, the synthesis with labeled substances is performed and validated, thus obtaining the personalized labeled compound
- ***Biosynthesis of labeled compounds***. Biological cultures are obtained that can incorporate ^{2}H, ^{13}C and ^{15}N isotopically labeled products into their metabolism. Ways to take advantage of the enzymatic (e.g. protein) background of these cultures can be determined, in particular in addressing certain medical conditions by shifting from non-specific to targeted treatment, e.g. by highlighting those molecular processes associated with metabolic pathologies.

APPLICATIONS

Areas of application:

Isotope technologies have multiple applications in nuclear medicine, energy industry, geology and dating, food and agriculture, environmental protection.

APPLICATIONS:

- ✓ Agriculture
- ✓ Biochemistry
- ✓ Biology
- ✓ Medicine
- ✓ Nutrition
- ✓ Nuclear Physics
- ✓ Environment

IsoPrime-100 mass spectrometer for determining isotope concentrations

INFRASTRUCTURE

^{13}C and ^{15}N isotope research and production facilities

These plants prove valuable in experimental research, refining and streamlining separation processes. Beyond this, they serve a productive purpose, yielding isotopically enriched $H^{15}NO_3$, ^{13}CO and $^{13}CO_2$. These outputs become crucial raw materials for synthesizing complex labeled compounds adapted to specific user needs.

Isotope labeling laboratory

The organic and inorganic synthesis laboratory has developed optimized technologies, paired with analytical control methods, to ensure processes meet specific user requirements. Our research team focuses on advancing specialized technologies for custom isotopic labeling services.

IsoPrime100 mass spectrometer

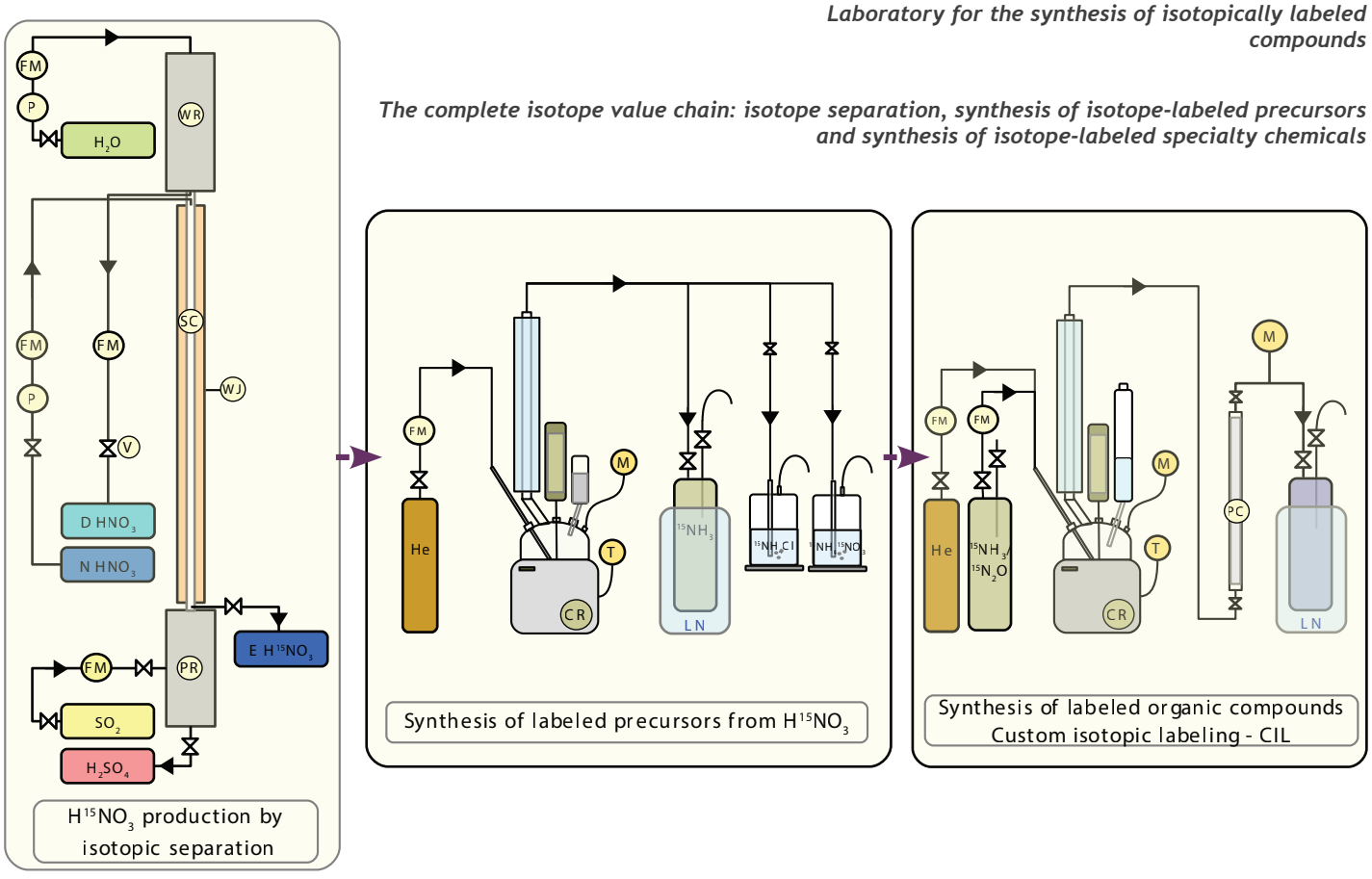
Determination of isotope concentration (up to 100%) in gaseous samples of CO, CO_2, N_2.

Liquid nitrogen production plant StirLIN-1

Allows the production of 120 l/day of liquid nitrogen, 99% purity, used in the synthesis of labeled compounds.

Laboratory for the synthesis of isotopically labeled compounds

The complete isotope value chain: isotope separation, synthesis of isotope-labeled precursors and synthesis of isotope-labeled specialty chemicals



TYPICAL APPLICATIONS - EXAMPLES:

Isotopes enable tracking of ^{15}N- and ^{13}C-labeled nutrient metabolism. Specifically, ^{15}N- and ^{13}C-labeled amino acids are utilizes in nitrogen and carbon metabolism studies, allowing researchers to measure the human body's protein synthesis rate.

Stable isotope-labeled compounds are used in medical studies, especially when radioisotopes are not suitable, such as in pregnant or breastfeeding women.

The stable isotopes ^{10}B, ^{7}Li, ^{15}N, ^{157}Gd and ^{91}Zr find applications in advanced nuclear reactors. Notably, ^{15}N (enriched to 99% atomic) is utilized in uranium nitride nuclear fuels, effectively minimizing the production of radioactive ^{14}C.

Understanding inorganic nitrogen dynamics across soil profiles is crucial for both agronomic practices and assesing water pollutants. To elucidate nitrogen dynamics, researchers have employed double-labeled ammonium nitrate ($^{15}NH_4{}^{15}NO_3$) in agricultural studies. This labeled fertilizer allows for precise tracking of nitrogen pathways within plants, enabling detection in roots, stems, and leaves. The resulting data provides selective and accurate insights for specialized research.

Nuclear Magnetic Resonance (NMR). ^{13}C and ^{15}N are among the most widely studied nuclei in nuclear magnetic resonance (NMR) spectroscopy of organic compounds. The insights gained from NMR spectra enable detailed characterization of local atomic scale structures and molecular dynamics.

ADVANTAGES

- In situations where conventional methods are limited or insufficient, isotopic techniques provide a powerful tool for obtaining valuable information.
- Compounds labeled with stable isotopes of biogenic elements are preferred over radioactive tracers due to the incompatibility of the radioactivity with complex biological systems.
- Our labeled inorganic compounds typically exhibit yields above 80%, and the methods we've developed are readily scalable.
- INCDTIM has a long-standing expertise in developing and implementing technologies for light stable isotope separation, and is currently the only European producer capable of enriching ^{13}C and ^{15}N isotopes to high levels (up to 85% for ^{13}C, and 99% for ^{15}N).

ESTIMATED COSTS

The production of ^{15}N isotope is economically viable only at yields of tens of kilograms per year.

The cost of stable isotope-labeled compounds is determined by several factors, including:

- Amount and concentration of isotopes used
- Raw materials required for synthesis
- Complexity of the synthesis procedure
- Time needed for customized synthesis specific to each user's needs.

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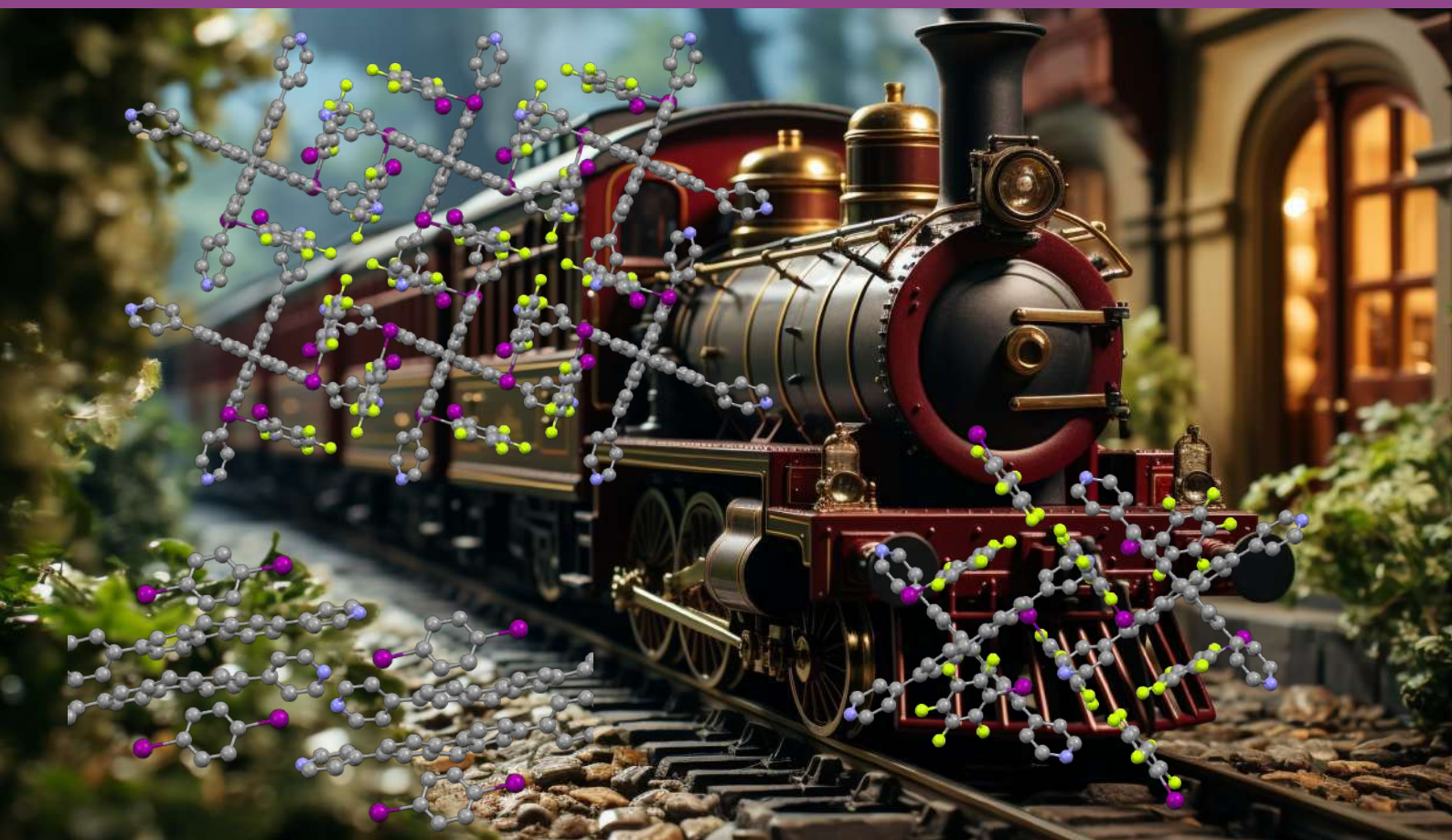
02.

COMPLEX SUPRAMOLECULAR SYSTEMS



COMPLEX SUPRAMOLECULAR SYSTEMS

Keywords: *supramolecular systems, inclusion compounds, bioactive substances*

DESCRIPTION

Supramolecular systems are new materials of interest for many industrial branches and have particular impact in pharmaceutical, food supplements, cosmetics, chemical (pesticides) industries.

The incorporation of substances of interest into various carrier matrices, resulting in the formation of supramolecular systems, aims to improve some of their physico-chemical properties, such as solubility, reduction or elimination of undesirable odors, increase physical and chemical stability by protecting against reactions induced by light, heat and moisture. They may also help to stabilize emulsions and suspensions.

In the case of bioactive substances, whether synthetic or natural, the goal is to improve bioavailability, controlled release and transportation to the target, with the aim of reducing adverse effects by lowering the dose required for effective therapy. By implication, significant cost savings can be achieved by identifying optimized formulations.

(Macro)molecules used as carrier matrices: cyclodextrins, dendrimers, metal-organic polymers, zeolites and many others.

Cyclodextrins are cyclic oligosaccharides consisting of 6, 7 or 8 glucose units (α-, β-, γ-cyclodextrin) with a hydrophilic outer surface and a hydrophobic central cavity. The hydrophilic exterior confers enhanced solubility in water and the hydrophobic cavity constitutes a micro-framework which can accommodate non-polar molecules or parts thereof, which have corresponding dimensions.

Dendrimers are single-centered nano-sized supramolecules containing three types of structural components: the central unit (core) surrounded repetitively inside by layers of identical and branched units, nodes, determining the generations (G-n, n>1) and peripheral functional groups, which play an important role in the (physico-)chemical properties of the dendrimer. Their particular properties allow a wide range of applications in combinatorial chemistry, medicine and nanoscience. One important application is the use of dendrimers as drug-delivery systems for the transport of biologically active substances to the site of action, due to the presence of multiple peripheral groups that allow functionalization and controlled release.

Biodegradable metal-organic polymers (BioMOFs) are organic-inorganic hybrid compounds obtained by coordinative assembly of metal ions and organic ligands. They are of increasing interest for their use as carriers of bioactive substances due to their specific properties: high loading capacity with active compounds, ability to incorporate bulky guest molecules, high stability and non-toxicity.

To obtain supramolecular systems with high yield, we use the following experimental techniques in our laboratory:

- ✓ dry or wet mechanical mixing
- ✓ magnetic stirring in solution/suspension
- ✓ co-evaporation
- ✓ co-precipitation
- ✓ lyophilization
- ✓ atomization

Crystallization and Polymorphism Laboratory

APPLICATIONS

Areas of application: R&D, nanomedicine, optimization of industrial processes, obtaining products with increased efficacy

Industries: health and medical sciences industry, pharmaceuticals, cosmetics, food supplements, chemicals (phytosanitary)

INFRASTRUCTURE

The preparation of supramolecular systems is carried out in the **Crystallization and Polymorphism Laboratory**, equipped with:

i. ***Zinsser Crissy Light XL small-scale parallel crystallization platform*** in *high-throughput* mode, capable of processing 24 experiments simultaneously under temperature controlled conditions. The platform offers the possibility of automatic addition of solvent/solvent mixtures, setting of various temperature regimes ranging from 2÷200°C and horizontal stirring of samples

ii. ***Eyela PPS-5511 large-scale crystallization platform*** with five synthesis reactors, allowing parallel experiments to be carried out under controlled temperature conditions for each individual reactor

iii. ***Retsch MM 400 ball mill MM 400*** offers the possibility to run two experiments in parallel, with or without added solvent, by setting the mixing frequency and mixing time

iv. ***Memmert HCP10 climatic chamber*** with temperature (up to 160°C) and humidity control for stability testing

v. ***System for in situ monitoring of the dissolution rate µDISS Profiler*** with which four experiments can be performed in parallel, equipped with a spectrometer, and experiments can be performed at a controlled temperature.

Eyela PPS-5511 large-scale crystallization platform

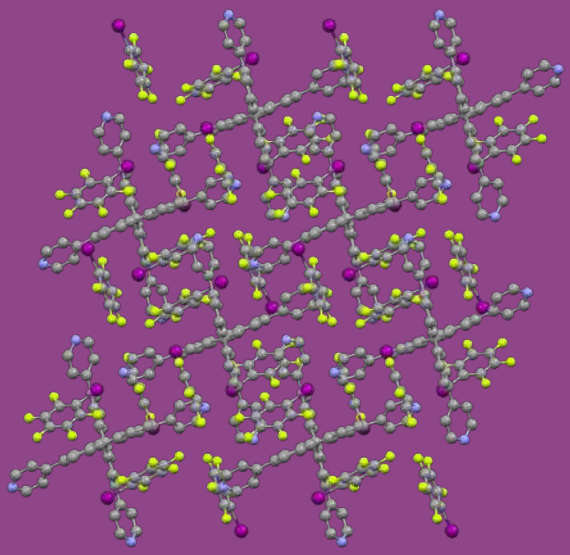
Retsch MM 400 ball mill MM 400 and Memmert HCP10 climatic chamber

System for in situ monitoring of the dissolution rate µDISS Profiler

Zinsser Crissy Light XL small-scale parallel crystallization platform

TYPICAL APPLICATIONS – EXAMPLES:

Pharmaceutical and food supplement industry. Encapsulation of pharmaceutically active substances in cyclodextrins, dendrimers or bioMOFs in order to increase solubility, bioavailability and stability, controlled release or to ensure transportation of the active substance to the target.



Cosmetics industry. Encapsulation of bioactive substances in cyclodextrins to increase solubility, bioavailability and stability, absorption, increase efficacy of cosmetics for skin care and make-up, increase release time of fragrances.

ADVANTAGES

- The existing facilities allow the realization of services to obtain supramolecular systems
- Specialized staff is able to cover with the highest professionalism all stages of a contractual collaboration, from experimental design, performing experiments to correlation of results with other complementary information

Plant protection industry. Obtaining supramolecular systems of pesticides, fungicides or herbicides with cyclodextrins or dendrimers in order to optimize the efficiency of these products and to mask unpleasant odours.

ESTIMATED COSTS

The total cost of CDI services to obtain supramolecular systems results from:

- complexity and number of experiments performed, chemical reagents and solvents required, labor
- operating time of the equipment, consumables and their wear and tear.

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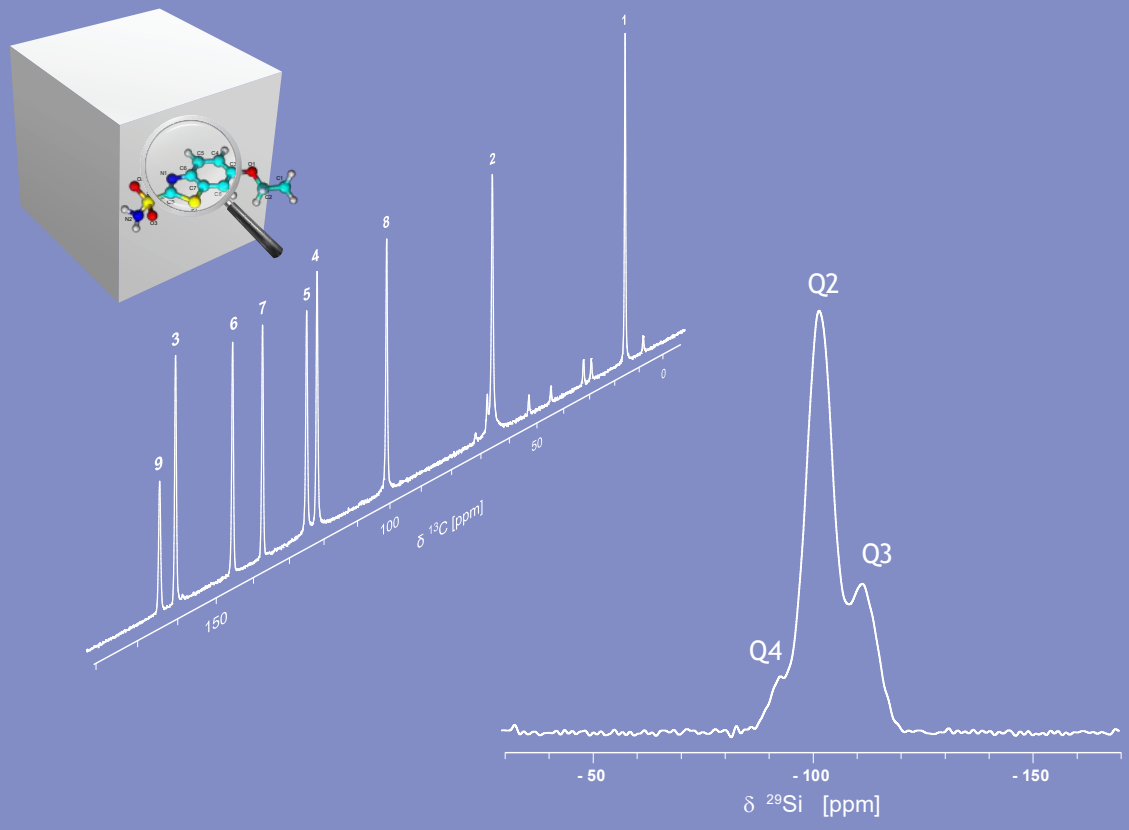
03.

SOLID STATE NMR SPECTROSCOPY*




HELIUM
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SOLID STATE NMR SPECTROSCOPY

Keywords: *nuclear magnetic resonance, NMR, solid states, structure*

DESCRIPTION

Solid State Nuclear Magnetic Resonance Spectroscopy (ss-NMR) is an analytical technique for characterization of organic or inorganic materials, the signal being generated by atomic species with non-zero nuclear magnetic moment.

The nuclei most frequently studied in the case of organic compounds are ^{13}C, ^{15}N, ^{1}H, ^{2}H, ^{31}P, and ^{17}O, and in the case of inorganic materials ^{29}Si, ^{27}Al, ^{31}P, and ^{119}Sn.

The information extracted from ss-NMR spectra is used for local structural characterization at the atomic-scale and for studying molecular dynamics over a time scale extending across more than ten orders of magnitude (between 10^{-10}–1 s).

An important advantage of ss-NMR spectroscopy is its versatility, as there are a very large number of different experimental conditions that can be applied in current practice to extract the desired information, namely:

- **Primary information** such as chemical structure/identification of structural groups is extracted from **simple 1D ss-NMR spectra** – these do not require special efforts to calibrate the pulse sequences used; depending on the complexity of the system being investigated, the interpretation of the results may be immediate or may require combining with molecular modeling
- To obtain more **complex information** such as the connectivities between structural units or local spatial parameters (such as interatomic distances, torsion angles, etc.) it is necessary to record **2D/3D correlation ss-NMR spectra between the nuclear species of interest**. For this purpose, a very wide variety of experimental methods (pulse sequences) have been developed, optimized to obtain the desired parameters with the highest possible selectivity and accuracy. With a few exceptions, recording correlation ss-NMR spectra requires isotopic labeling of the positions of interest.

NMR Spectroscopy Laboratory. NMR spectrometer Bruker Avance III 500 MHz dedicated to solid-state applications

APPLICATIONS

Areas of application: research and development, process/product optimization in industry, quality control (detection of impurities, stability under different environmental conditions, etc.).

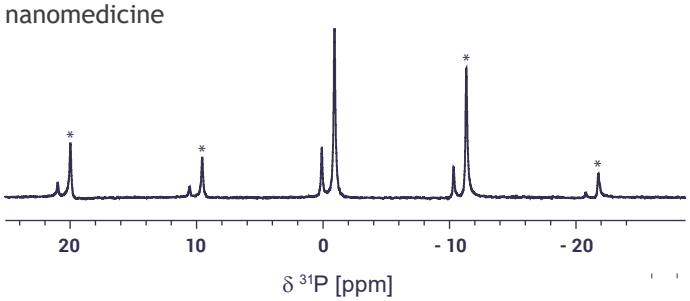
Systems:

i. ***organic and inorganic crystalline compounds*** (pharmaceutically active compounds, natural active compounds from extracts, (bio)molecular systems that can be crystallized, metal-organic structures, minerals)

ii. ***amorphous materials*** (polymers, biopolymers and polymer composites, glass, ceramics and their composites

iii. ***nanosystems*** (decorated and/or functionalized nanoparticles, nanostructured hybrid materials, etc.)

Industries: pharmaceuticals industry, dietary supplements industry, medical devices, chemical industry, environment/pollution control, agro-food industry, health, nanomedicine



^{31}P ss-NMR characteristic spectrum of an organic molecule

INFRASTRUCTURE

The NMR spectroscopy laboratory is equipped with a Bruker Avance III 500 MHz spectrometer, dedicated to solid-state applications. It features a *wide bore* cryo-magnet, three radio frequency channels and is equipped with three probe heads, covering almost the entire range of high resolution ss-NMR spectroscopy applications:

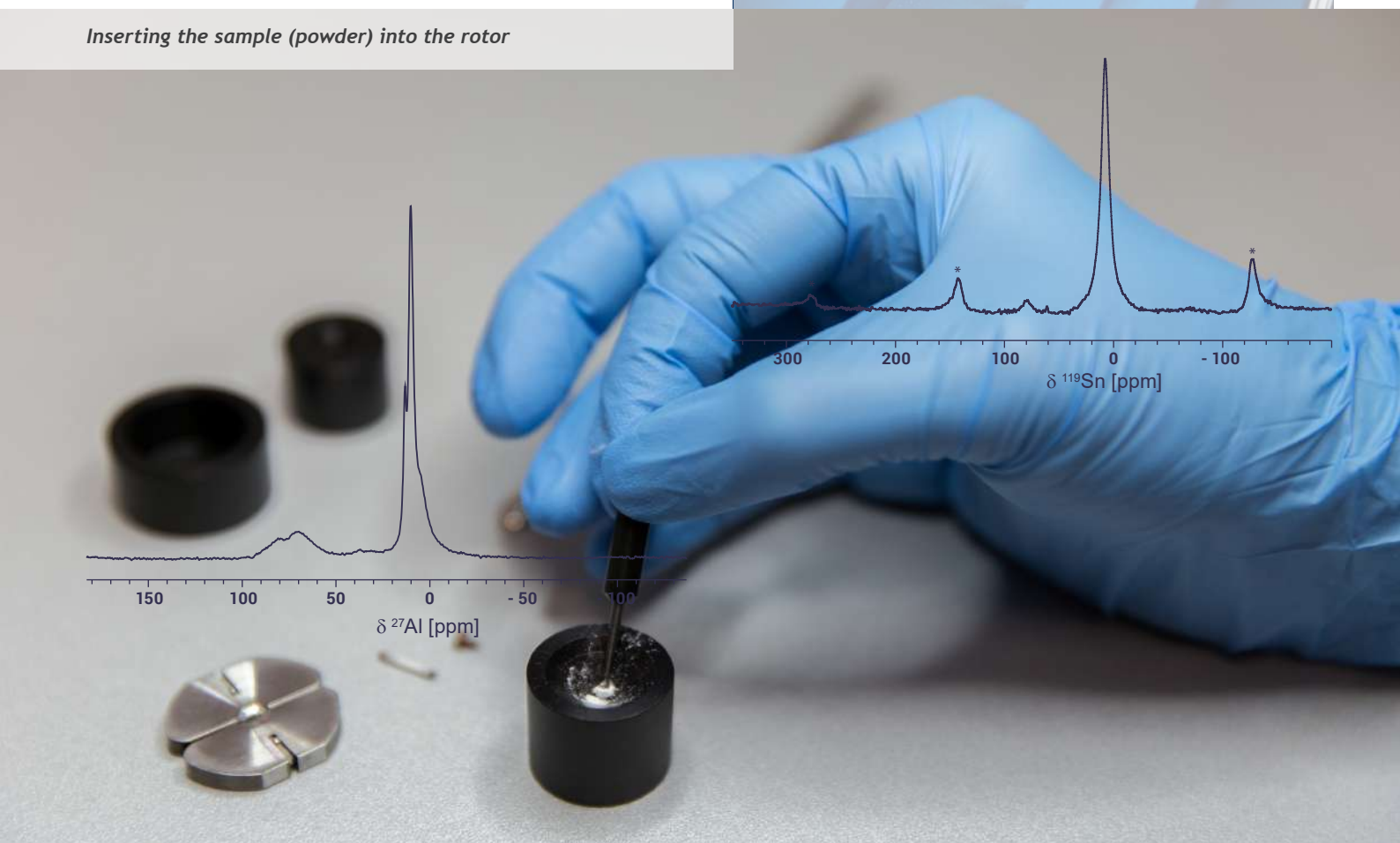
i. ***a CP-MAS probe with two channels***, a 4 mm rotor and maximum sample spinning frequency of 15 kHz

ii. ***a CP-MAS probe with three channels***, a 2.5 mm rotor and a maximum sample spinning frequency of 35 kHz

iii. ***an fast MAS probe with two channels***, a 1.3 mm rotor and a maximum sample spinning frequency of 65 kHz

Fast MAS solid-state NMR probe head

Inserting the sample (powder) into the rotor



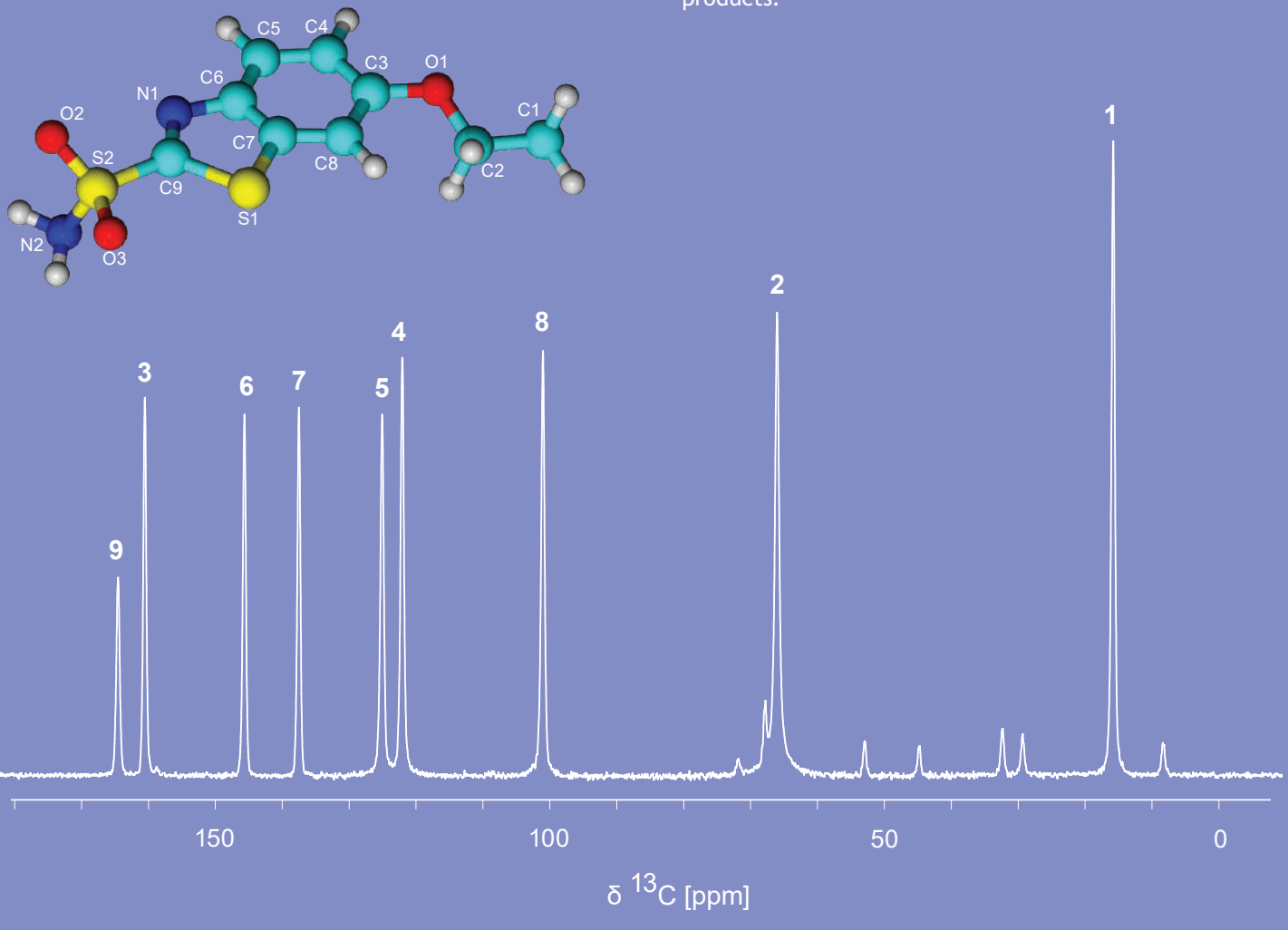
TYPICAL APPLICATIONS – EXAMPLES:

Purity determination of synthetic or natural bioactive pharmaceutical compounds. The presence of any type of impurities in the mass of the bioactive substance can be detected, e.g. chemical impurities present in the raw material, solvent residue left over from the production process, or unwanted crystalline forms formed during storage.

Crystal structure determination for synthetic or natural bioactive pharmaceutical compounds. It can be achieved by an NMR crystallography approach, in which experimental ss-NMR experimental data are used in combination with X-ray diffraction results on powder or single crystal and molecular modeling by quantum chemical calculations. The advantage of the method, compared to the determination of the crystal structure based solely on X-ray diffraction data, is given by the increased confidence and accuracy with which the final structural model is provided.

Stability studies for oral pharmaceutical products. They can be performed both on the finished product (tablet/capsule) and on the bioactive substance in the drug product. In essence, they consist in identifying structural changes that may occur as a result of interactions between the active substance and excipients, long-term storage (due to environmental factors), desolvation, etc. Unlike the usual techniques, X-ray and DSC, ss-NMR spectroscopy is more sensitive because it detects incipient changes that do not affect the whole substance mass.

Structural characterization of polymer-based materials/composites. A very wide range of materials can be covered, from classical to nanostructured systems. For each type of polymeric system, ss-NMR spectroscopy is a useful tool both in the new product/material development phase and for quality control of existing materials/products. The first type of applications concerns the acquisition of structural and molecular dynamics information useful in establishing structure-function relationships of materials. The second category of applications refers to the identification of a set of experimental ss-NMR parameters to characterize the quality of polymer-based products.



^{13}C ss-NMR characteristic spectrum of an organic molecule of pharmaceutical interest (ethoxzolamide)

ADVANTAGES

- INCDTIM offers R&D services based on ss-NMR spectroscopy, used either independently or in combination with other complementary analytical techniques, covering nearly the entire range of practical applications
- Before entering into a contractual relationship we provide consulting to define the client's/partner's needs and, if necessary, we perform preliminary tests free of charge
- Our existing equipment allow us to address most of the ss-NMR methods used in current practice, many of which are already implemented in our laboratory
- We have specialized staff trained at prestigious research centers abroad, capable of covering all stages of a contractual collaboration with the highest level of professionalism: defining the problem to be adressed, designing the experiment, collecting data, interpreting results and correlating them with other complementary information, if necessary
- Upon request, we also offer the possibility of isotopic labeling with ^{13}C, ^{15}N and ^{2}H.

ESTIMATED COSTS

The total cost of R&D services based on ss-NMR spectroscopy consists of two components:

- spectrometer usage time, which includes consumables and wear
- labor, which includes personnel and indirect costs associated with sample preparation operations, analysis and interpretation of results, preparation of the analysis/research report: negotiable, depending on the complexity of the study.

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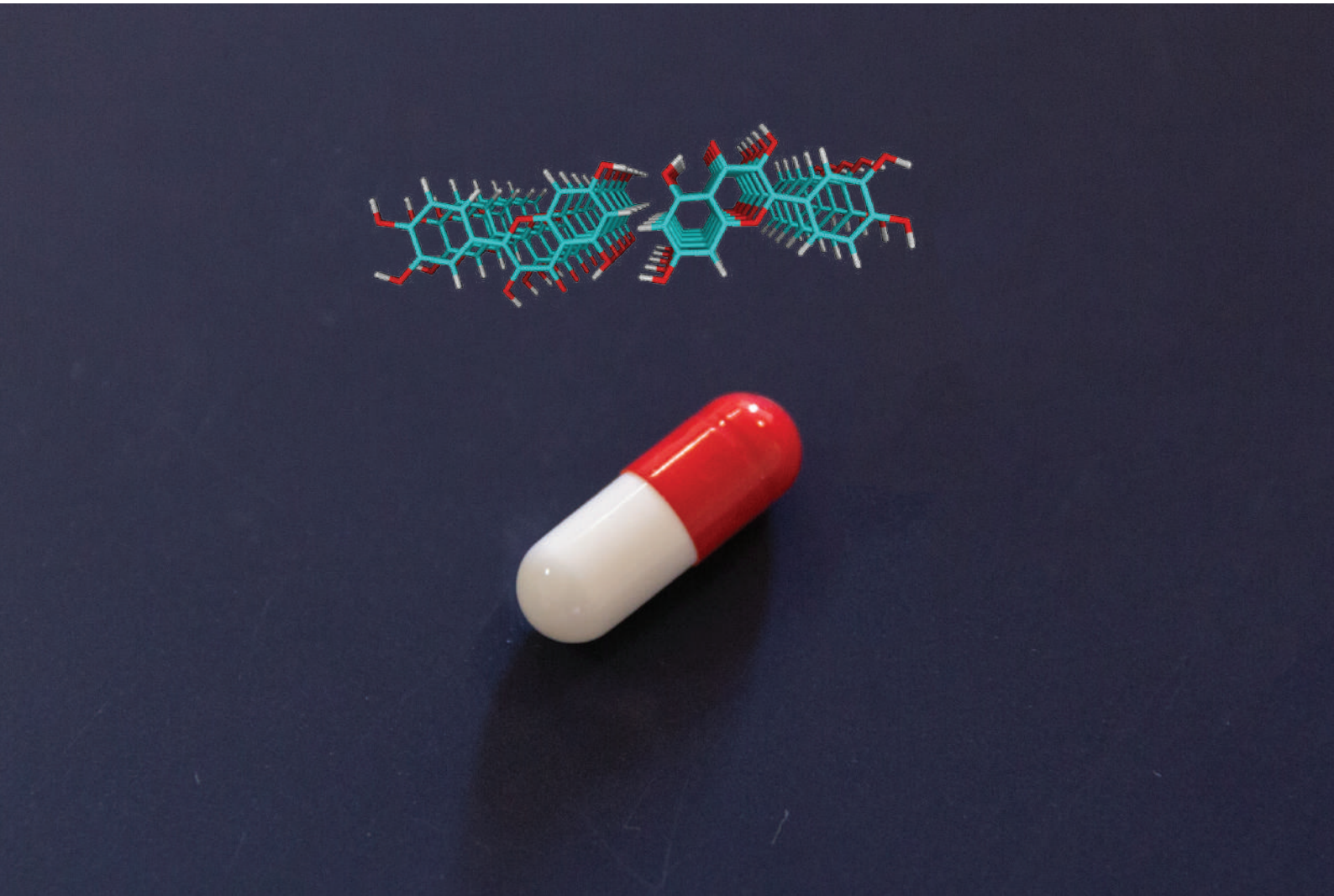
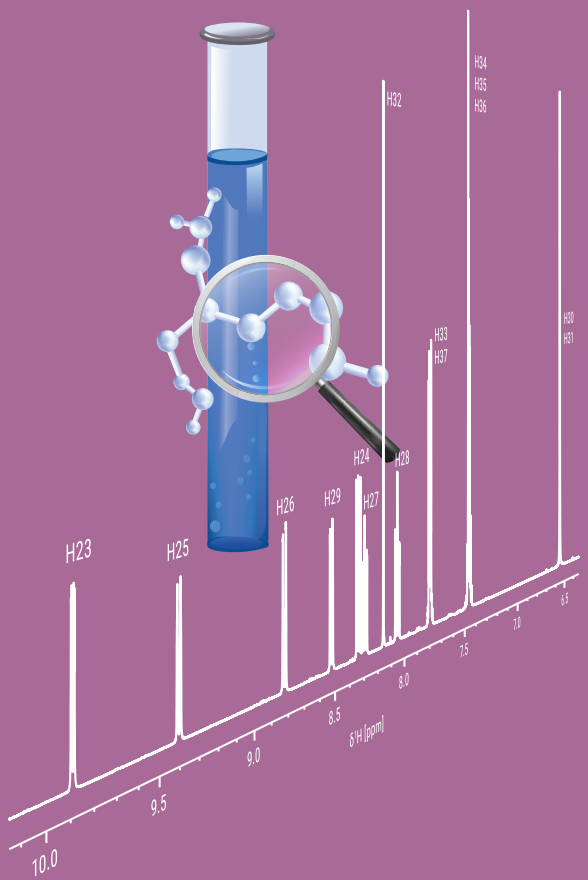


04.

LIQUID STATE NMR SPECTROSCOPY

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LIQUID STATE NMR SPECTROSCOPY

Keywords: *nuclear magnetic resonance, liquid state NMR, structure, intemolecular interactions*

DESCRIPTION

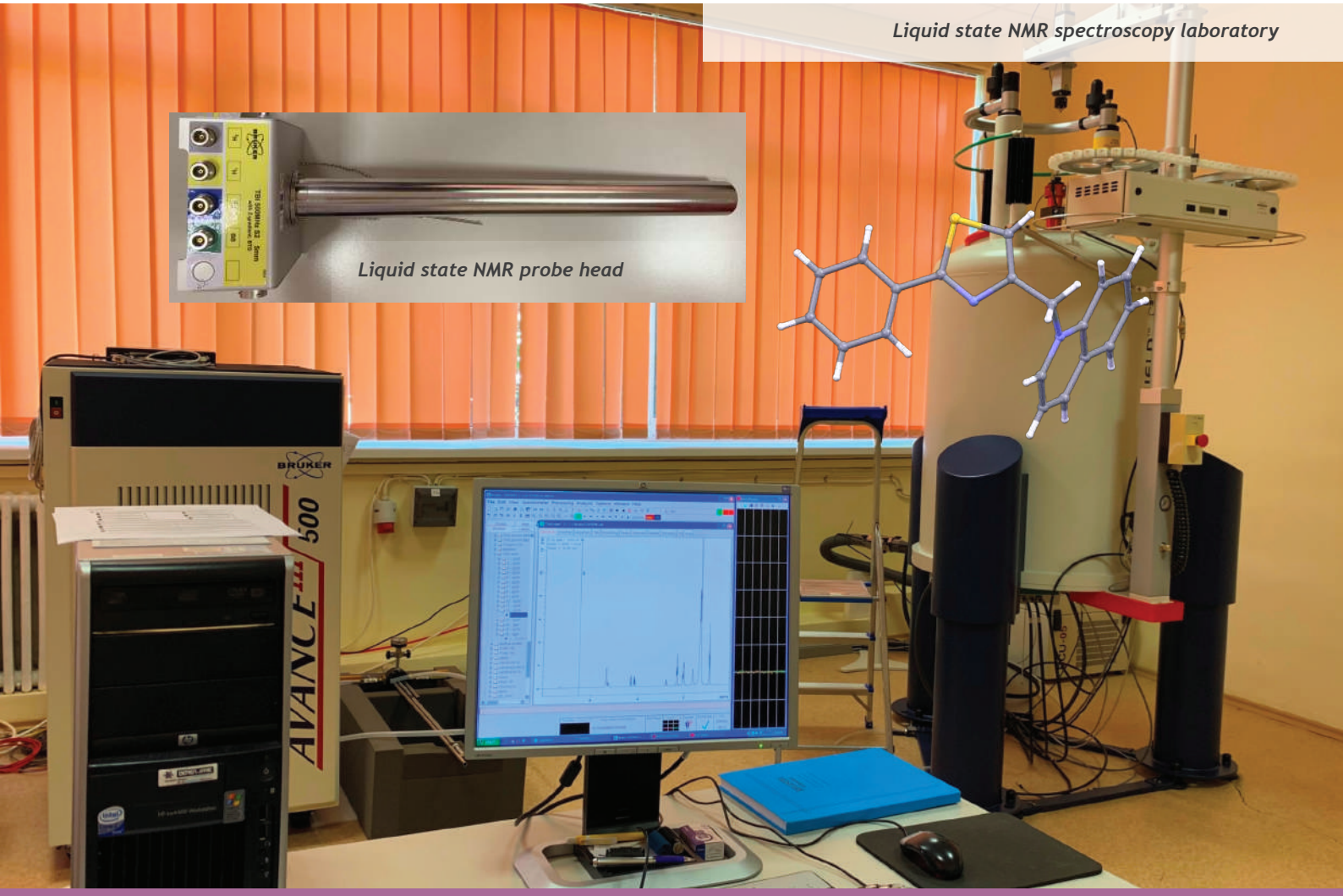
Nuclear Magnetic Resonance Spectroscopy on liquid samples is an analytical technique for the characterization of molecular and biomolecular systems with which information about structure, dynamics and intermolecular interactions is obtained.

NMR spectroscopy involves the quantum magnetic properties of atomic nuclei. These properties are influenced by the molecular neighborhood, and their measurement provides a map of interatomic bonds and a description of molecular dynamics.

The nuclei most often studied are ^{1}H, ^{13}C, ^{15}N, ^{2}H, ^{19}F, ^{31}P by 1D measurements. The most commonly used 2D measurements are: COSY, HETCOR, HSQC, HMBC, ROESY.

APPLICATIONS

Areas of application: research and development, optimization of industrial processes / products, quality control (authentication, adulteration, detection of impurities, stability under different environmental conditions, quantitative determinations, etc.)



Liquid state NMR spectroscopy laboratory

Liquid state NMR probe head

Systems:

- ∫ ***organic and inorganic compounds*** (pharmaceutically active compounds, natural active compounds from extracts, cosmetics)
- ∫ ***complex supramolecular systems*** (cyclodextrin inclusion complexes, protein-bioactive molecule molecular complexes)
- ∫ wines, spirits, food matrices
- ∫ organic matrices from underwater geological structures

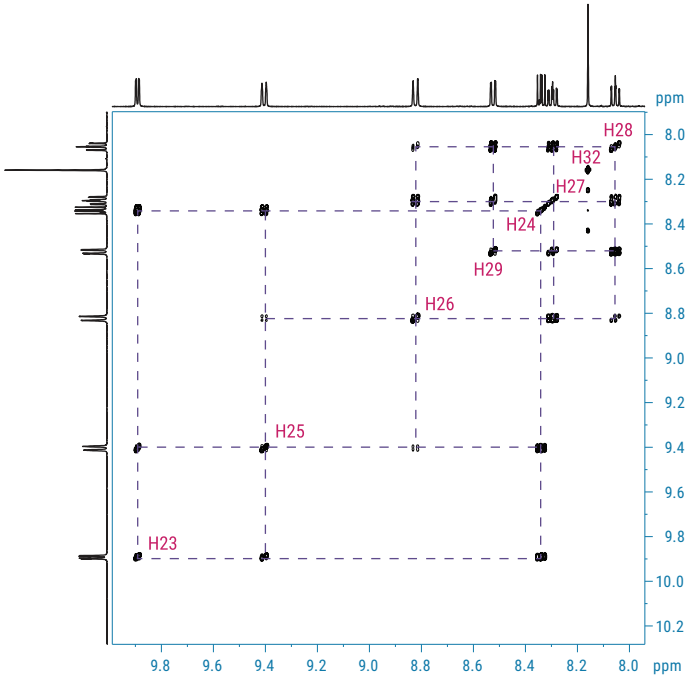
Industries: pharmaceutical industry, food supplements industry, chemical industry, environment / depollution, agro-food industry, health – nanomedicine

INFRASTRUCTURE

The NMR spectroscopy laboratory is equipped with a Bruker Avance III 500 MHz spectrometer dedicated to applications on liquid samples. It consists of a cryo-magnet with the magnetic field produced by the 11.7 Tesla superconducting coil, three radio-frequency channels and is equipped with four sample heads, which cover almost the full range of applications of high-resolution NMR spectroscopy on liquid samples:

i. ***two-channel BBO type sample head***

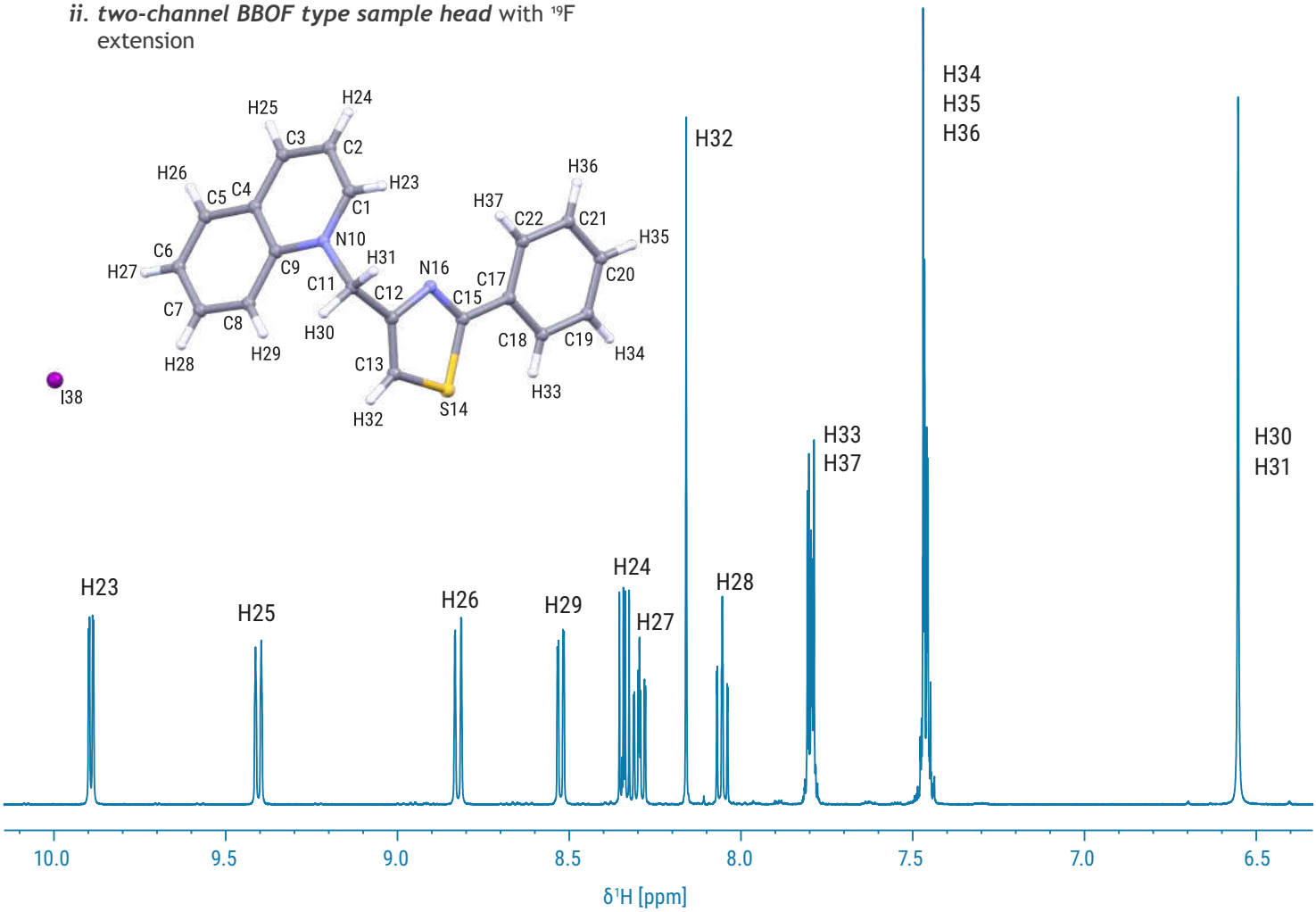
ii. ***two-channel BBOF type sample head*** with ^{19}F extension



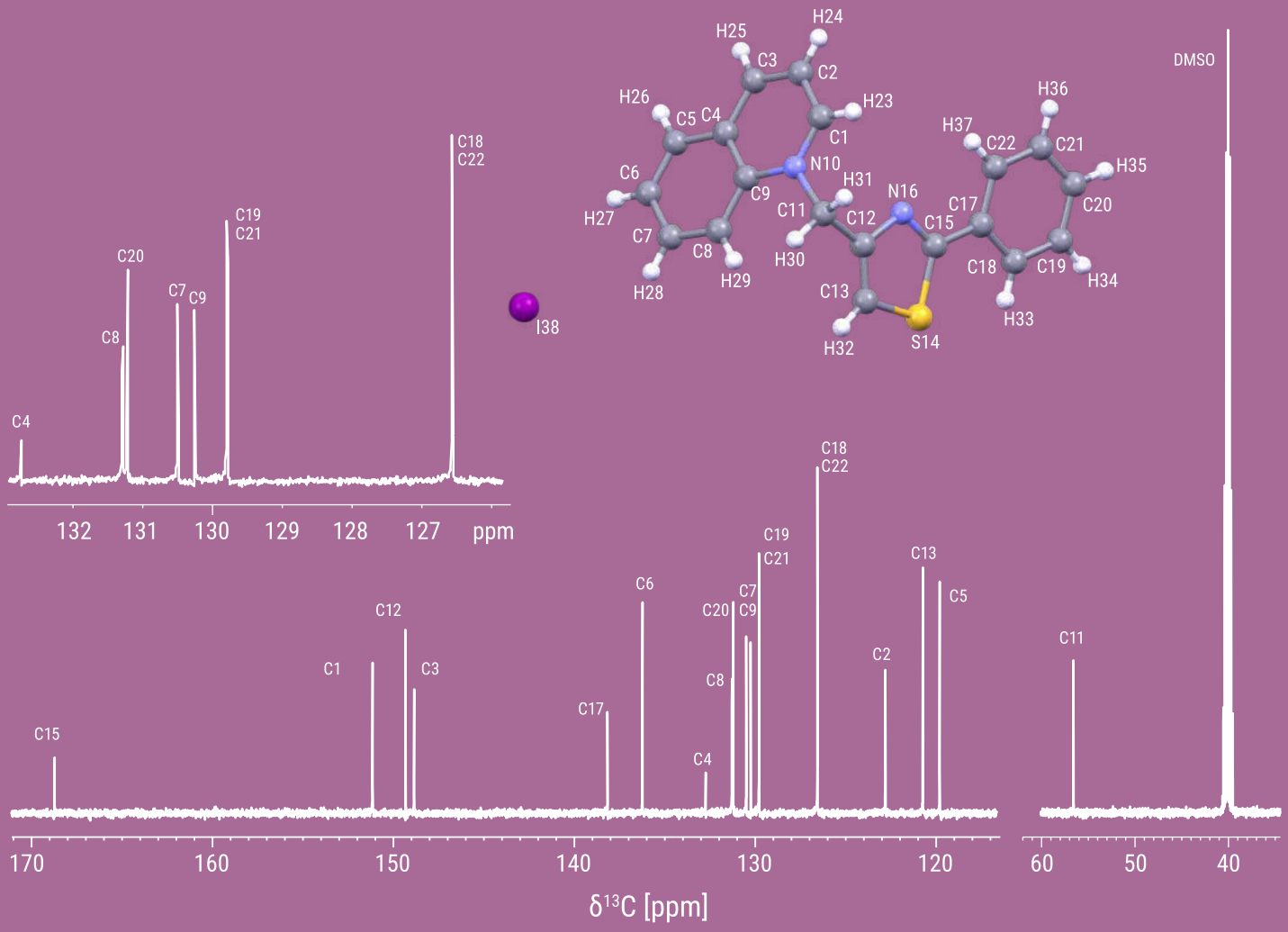
^{1}H-^{1}H COSY NMR spectrum (8-10 ppm) of 2PTMQI molecule

iii. ***three-channel TBI type probe head*** (triple resonance: ^{1}H, ^{13}C, ^{15}N)

iv. ***SEX type probe head*** for ^{2}H measurements at natural abundance, with magnetic field stabilization on ^{19}F



^{1}H NMR spectrum of an organic molecule with pharmaceutical applications, phenyl-thiazole-4-yl-methyl-quinolinium iodide - 2PTMQI



¹³C NMR spectrum of 2PTMQI molecule

TYPICAL APPLICATIONS – EXAMPLES:

Molecular inclusion complexes of cyclodextrins with pharmaceutical substances. Cyclodextrins are cyclic oligosaccharides composed of 6, 7 or 8 glucose units (α-, β-, respectively γ-cyclodextrin) having a hydrophilic outer surface and a hydrophobic central cavity. Cyclodextrins are used to improve the solubility, stability and bioavailability of bioactive substances, as drug carriers to optimize controlled release of drugs, to enhance their antioxidant effect, to mask unpleasant taste or odor. By means of high-resolution ^{1}H NMR spectroscopy, the association constant, stoichiometry and geometry of the inclusion complex can be determined.

Studies on drug binding to plasma proteins. The current concerns of our group are directed towards understanding and elucidating the mechanisms of interaction between bioligands and plasma proteins in the liquid state, using high-resolution ^{1}H NMR spectroscopy, relaxometry and NMR scatterometry, complementary to other experimental methods (ITC, UV-Vis, fluorescence), as well as ab initio computational methods and molecular dynamics simulations. From a biochemical and clinical point of view, the study of

drug-protein interactions is of paramount importance. Drug transport in the body occurs via the circulatory system. Plasma proteins have the ability to bind and transport a wide range of drugs, metabolites and organic compounds. When two ligands compete for one or more binding sites on the protein molecule, competitive binding occurs. There are situations in which the ligand may be replaced by another drug on its binding site, or a newly administered drug that binds to a different binding site and may alter the binding affinity of the first drug.

Wine authentication using ethanol (D/H) ratios. ^{2}H NMR analysis. The method refers to the quantitative determination of deuterium at natural abundance in ethanol extracted from wine, a method capable of characterizing the geographical origin and possible adulteration of wines. The distillation of wine to obtain ethanol is carried out using a Teflon rotary-belt distillation apparatus to avoid isotopic fractionation. This method is based on the determination of isotope ratios D/H from specific positions of the ethanol molecule.

Applications of ^{1}H NMR spectroscopy in wine authentication. At the European Union level, the development of new methods for wine authentication, allowing the differentiation of grape variety, year of production or geographical area is a priority. One of these methods, which is in the development phase, is related to the discrimination of wines by analyzing the minor constituents in wine using high-resolution ^{1}H-NMR spectroscopy and chemometric processing of experimental data. Their detection is sensitive, wine being a mixture of very many compounds at different concentrations. The major components are water and ethanol, and the minor components are glycerol, tartaric acid, sugars, glucose, malic acid, malic acid, succinic acid, acetic acid, proline, isoleucine, alanine, lactic acid, aliphatic and aromatic alcohols, amino acids, phenols, etc.

Statistical determination of the similarity of the organic composition of soil samples extracted from underwater geologic structures by high-resolution ^{1}H NMR spectroscopy. We developed a specific method for the preparation of soil samples extracted from underwater geologic structures drilled at different depths from different locations. Complex ^{1}H NMR measurements result in spectral data that are processed and compared by statistical methods using Linear Discriminant Analysis (LDA).

ADVANTAGES

- INCDTIM offers CDI services based on NMR spectroscopy, used on its own or in combination with other complementary analytical techniques, covering almost the full range of practical applications
- Prior to entering into a contractual relationship we provide consultancy to define the client/partner's needs as accurately as possible and, if required, we carry out preliminary tests free of charge
- Existing facilities allow us to address most of the MRI methods used in current practice, many of which are already implemented in our laboratory
- We have staff able to cover with the highest professionalism all the stages of a contractual collaboration: definition of the problem to be solved, experimental design, data collection, interpretation of the results and their correlation with other complementary information, if necessary.

ESTIMATED COSTS

The total cost of RD&I services based on NMR spectroscopy consists of two components:

- spectrometer usage time, which includes consumables and wear
- labor, which includes personnel and indirect costs associated with sample preparation operations, analysis and interpretation of results, preparation of the analysis/research report: negotiable, depending on the complexity of the study.

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05.

X-RAY DIFFRACTION

X-RAY DIFFRACTION

Keywords: structural analysis on solids, X-ray diffraction on powders and single crystals, crystalline structure

DESCRIPTION

X-ray diffraction is an analytical technique used for characterizing solid materials, whether organic or inorganic, with diffraction intensities generated as a result of the interactions between X-rays and the electrons of the atoms in the lattice.

Depending on the behavior of the compounds we want to investigate, we use either powder diffraction or single crystal diffraction. The information extracted by the two diffractometric techniques is used for the structural characterization of the crystal lattice.

An important advantage of X-ray diffraction is the rapidity of obtaining information, the method is non-destructive and requires a small amount of sample.

The information extracted from X-ray powder diffractograms includes:

- ***Qualitative analysis of crystalline phases:*** based on the fact that each crystalline phase has a specific diffractogram
- ***Quantitative phase analysis:*** If a sample contains multiple phases, the percentage of each identified phase in the examined sample can be determined based on the number and intensity of the diffraction lines
- ***Microstructural analysis:*** determination of crystallite sizes, lattice stresses and defect probabilities
- ***Determination of the degree of crystallinity:*** resulting from the ratio of the area of diffraction maxima to the total area which includes both diffraction maxima and the area of halos due to the amorphous phase
- ***Determination of crystalline structure from powders***

In the case of single-crystal X-ray diffraction the crystal structure of the compound under investigation is obtained.

X-Ray Diffraction Laboratory. Rigaku SmartLab Diffractometer

APPLICATIONS

Areas of application: research and development, optimization of industrial products, purity check and impurity detection, stability assessment under different environmental conditions, etc.

Systems:

i. organic and inorganic crystalline compounds: natural and synthetic bioactive compounds, (bio)molecular systems that can be crystallized, metal-organic structures, minerals

ii. amorphous materials: polymers, biopolymers and polymer composites, graphene and graphene-based composites, glass, ceramics and their composites

Industries: pharmaceutical industry, dietary supplement industry, medical devices, chemical industry, environment/ pollution control, health – nanomedicine

INFRASTRUCTURE

The X-ray diffraction laboratory is equipped with three diffractometers:

*i. **Bruker D8 Advance***: used for powder measurements; equipped with a Ge (111) monochromator placed in the incident beam and an ultrafast detector of the LYNXEYE type; the diffractogram collection is performed in Bragg-Brentano geometry in reflection mode

Selection and mounting of monocrystals

*ii. **Rigaku SmartLab***: equipped with a 9 kW rotating anode, high resolution theta-theta goniometer, allows recording measurements in reflection and transmission mode. In addition to powders, measurements of thin films can also be performed with this diffractometer

*iii. **Oxford SuperNova***: equipped with two microsources (Cu, Mo), a high performance CCD detector, with Cryojet allowing measurements in the temperature range 90÷490 K, it is used for single crystal measurements.

Oxford SuperNova X-Ray Diffractometer

TYPICAL APPLICATIONS – EXAMPLES:

Synthetic or natural bioactive compounds:

- ∫ Impurity detection (above 5%): chemical impurities present in the raw material or unwanted crystalline forms occurring during storage
- ∫ Determination of crystalline structure: by single-crystal X-ray diffraction or NMR crystallography – experimental X-ray powder diffraction data are used in combination with results obtained by solid-state magnetic resonance and molecular modeling by quantum chemical calculations
- ∫ Stability studies: can be performed for both the finished product (tablet/capsule) and the bioactive substance; stability studies consist in identifying structural changes that may occur during storage at different environmental conditions or following desolvation.

Dental materials:

Crystalline phase identifications and crystallite size calculations can be performed for changes in tooth structure following exposure to different dental materials (structural changes of hydroxyapatite or fluoroapatite in enamel composition).

Molar analyzed by X-ray for structural changes induced by the consumption of carbonated drinks

Structural characterization of thin films:

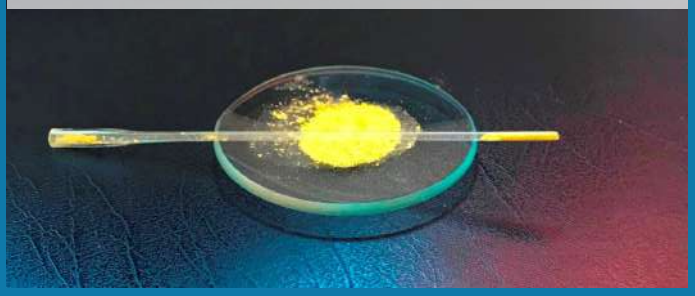
in the case of thin films, the following information can be extracted by performing reflectivity experiments, Rocking curves and mappings in reciprocal space, pole figures, diffraction at grazing incidence: composition, orientation/texture, lattice tension, thickness, roughness.

Solar cell samples analyzed by thin layer X-ray

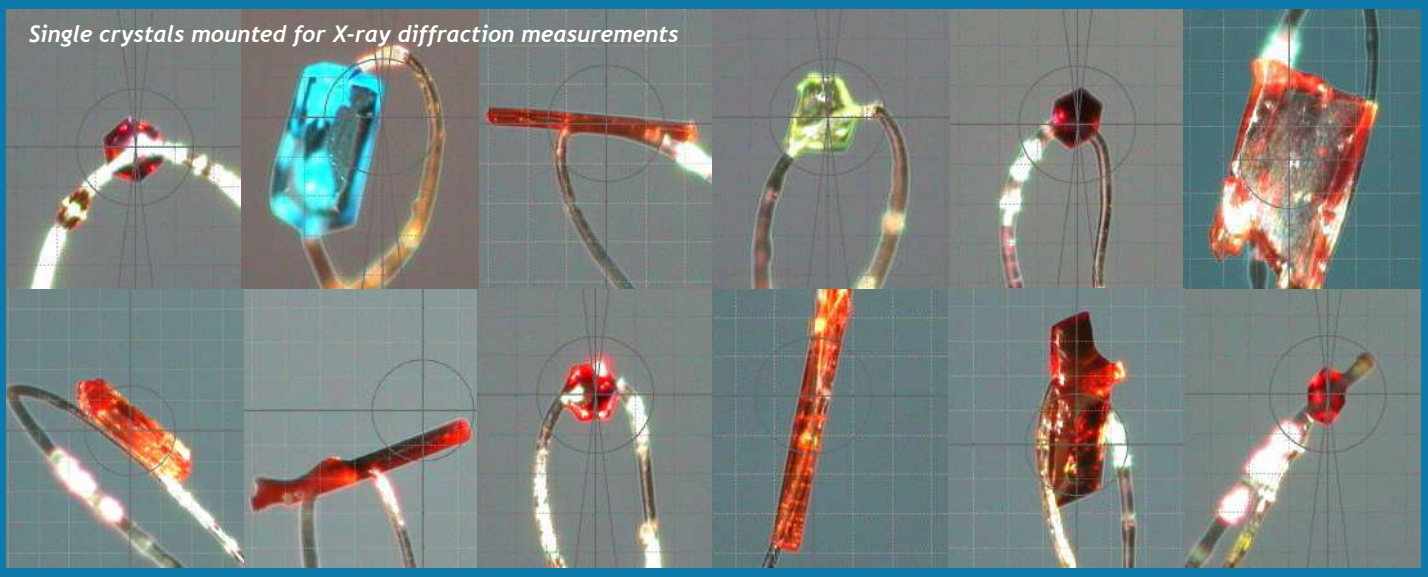
Structural characterization by Small Angle X-ray Scattering (SAXS).

This type of measurement can be performed on powder or suspension samples. By analyzing the data from SAXS measurements, information on particle size and particle size distribution can be obtained.

Sample preparation for SAXS measurements



Single crystals mounted for X-ray diffraction measurements



ADVANTAGES

- INCDTIM offers R&D services based on X-ray diffraction, used independently or in combination with other complementary analytical techniques, covering almost the whole range of practical applications
- Before entering into a contractual relationship, we provide consultancy to define the client/partner's needs as accurately as possible and, if required, we carry out preliminary tests free of charge
- The existing equipment (the three diffractometers) allows us to employ diffraction methods commonly used in practice, which are already implemented in our lab
- We have specialized personnel capable of covering all stages of a contractual collaboration: identifying the problem that needs to be solved, experimental design, data collection, interpretation of results and their correlation with other complementary information, if necessary.

ESTIMATED COSTS

The total cost of X-ray diffraction based R&D services consists of two components:

- diffractometer usage time, which includes consumables and wear and tear
- labor costs, which include personnel and indirect costs associated with sample preparation operations, analysis and interpretation of results, preparation of the analysis/research report: negotiable, depending on the complexity of the study.

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06.

EPR SPECTROSCOPY

EPR SPECTROSCOPY

Keywords: *Electron Paramagnetic Resonance Spectroscopy, EPR, paramagnetic species, transition metals, free radicals*

DESCRIPTION

Electron Paramagnetic Resonance Spectroscopy (EPR) or **Electron Spin Resonance (ESR)** is an analytical technique for analyzing organic or inorganic materials, the signal being generated by unpaired electronic species. The EPR spectrum is obtained by sweeping a magnetic field while the sample is subjected to a microwave field of given frequency.

The specific EPR parameters are:

- ∫ g-factor – characteristic of the type of paramagnetic ion in the sample
- ∫ line width – influenced by magnetic and crystalline interactions
- ∫ signal intensity – due to the concentration of spins in the sample
- ∫ hyperfine constant – determined by the molecular and local structure of the paramagnetic ion.

Typical systems that can be studied by EPR are:

- transition metal and rare earth ions
- free radicals
- point defects (localized crystal imperfections).

EPR spectra allow the **identification of paramagnetic**

EPR Spectroscopy Lab. Bruker ELEXSYS E 500 paramagnetic resonance spectrometer

species both **qualitatively** and **quantitatively**, provide information on **local structure** and **spin dynamics**.

Primary information, such as the identification of paramagnetic species, can be obtained by room temperature measurements in X-band.

Complex information related to the local structure and interactions in the system is obtained by measurements:

i. at varying temperatures (4÷500 K)

ii. in multi-frequency and

iii. by applying the magnetic field at different angles to the sample surface.

Depending on the complexity of the system, the interpretation of the results can be immediate or more laborious, requiring the combination of various computational techniques – fits, theoretical simulations of experimental spectra.

APPLICATIONS

Areas of application: R&D, optimization of industrial processes/products, biomedical and environmental

Systems:

i. nanomaterials, nanocomposites, glasses and ceramics, conducting and semiconducting materials, superconductors

ii. free radicals, organo-metallic compounds and zeolites, polymers

iii. spin markers, antioxidants and contrast agents, free radicals in tissues, oxygen and nitrogen radicals in biological systems; radicals generated in photochemical reactions

Industries: food industry, chemical industry, environment/cleaning, pharmaceutical industry, health-nanomedicine

INFRASTRUCTURE

The ESR spectroscopy laboratory is equipped with a **Bruker ELEXSYS E 500** spectrometer dedicated to both solid and liquid samples.

The spectrometer is equipped with two microwave bridges:

i. X-band (9 GHz) and Q-band (35 GHz)

ii. an electromagnet generating a maximum field strength of 1 T (X-band) and 1.5 T (Q-band) respectively

iii. goniometer which allows the sample to rotate in the magnetic field

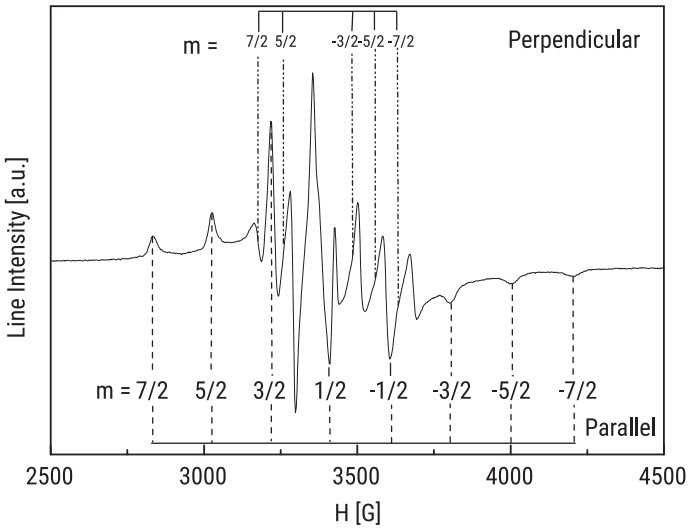
iv. two variable temperature units allowing measurements in the range 4÷300 K, and 77÷500 K respectively.

The following cavities required for different applications are available:

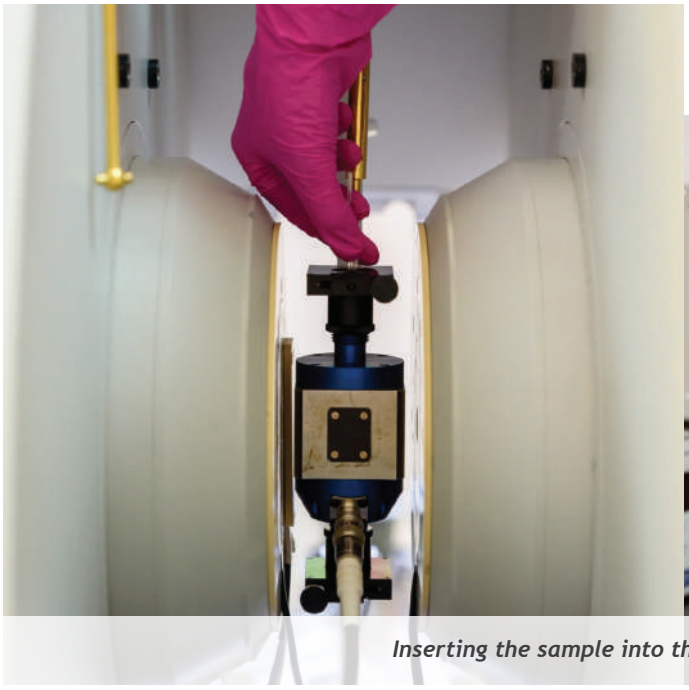
i. ***standard cavity*** operating in the temperature range 4÷500 K

ii. ***high sensitivity cavity*** for both solid and liquid samples

iii. ***dual-mode cavity***, dedicated to the investigation of forbidden transitions in transition metal and rare earth ions; biradicals and triplets.



EPR spectrum of SnO_2 nanoparticles doped with V ions

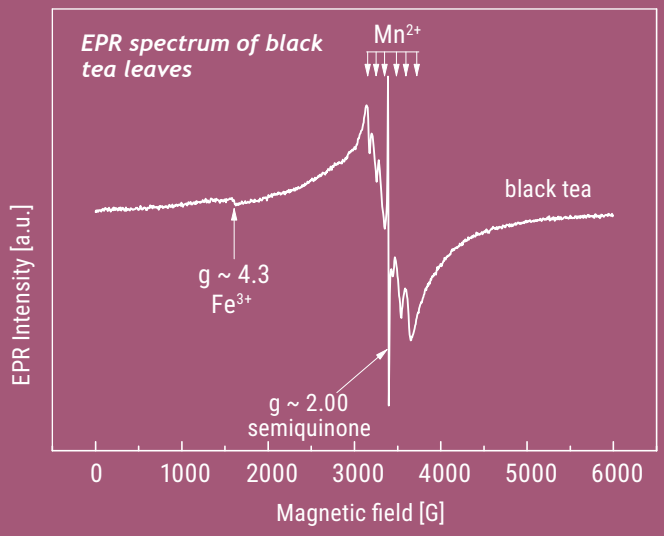


Inserting the sample into the EPR spectrometer cavity

TYPICAL APPLICATIONS – EXAMPLES:

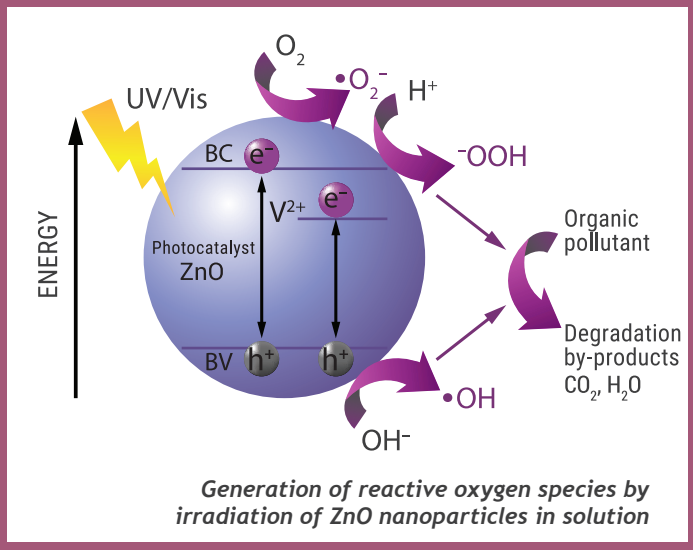
Structural characterization of solid materials containing paramagnetic species. Different types of materials with amorphous or crystalline structure can be analyzed. It is possible to determine, both qualitatively and quantitatively, the paramagnetic species, their oxidation state, local structure, interactions in the system under analysis, magnetic susceptibility.

Evaluation of antioxidant activity. Antioxidants play an important role in neutralizing dangerous free radicals generated during biological processes. With EPR it is possible to follow the kinetics of these reactions and to evaluate the antioxidant capacity.

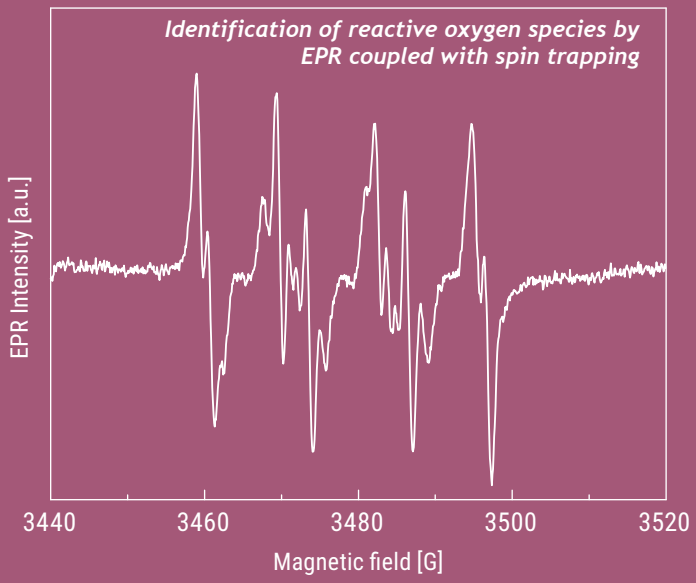


EPR spectroscopy allows evaluation of the antioxidants efficiency in the neutralization of free radicals generated by biological processes

Free radical identification by spin trapping method. The EPR technique coupled with spin traps allows the identification of reactive oxygen and nitrogen species with very short lifetimes. The identification of these species is vital in the biomedical field (detection of cellular lesions) and environmental protection (water purification by photocatalysis processes).

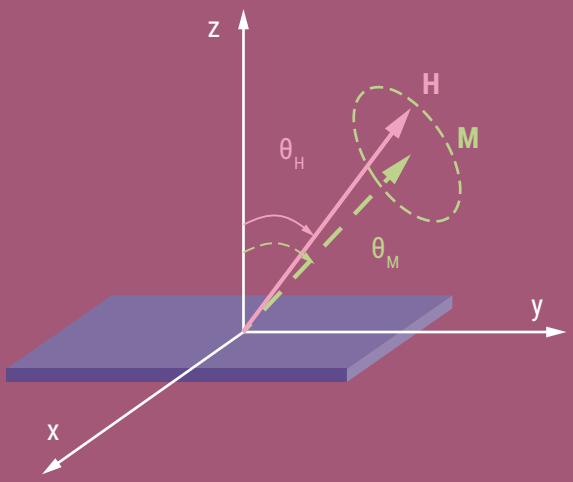


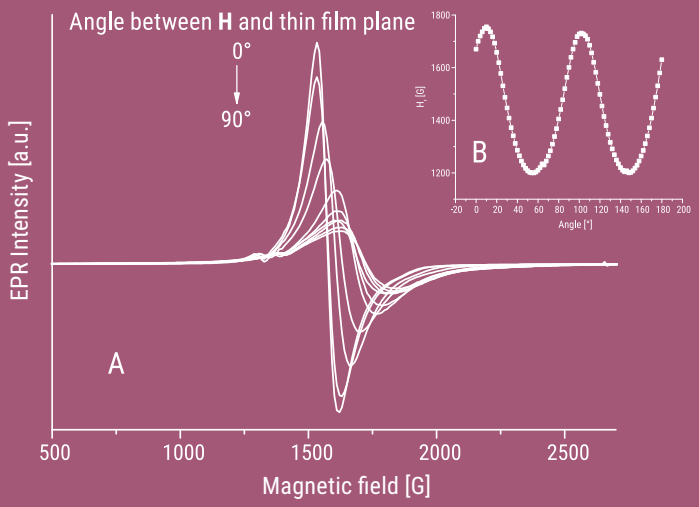
Generation of reactive oxygen species by irradiation of ZnO nanoparticles in solution



EPR applications in depollution. EPR allows identification of short-living reactive oxygen and nitrogen species

Determination of the magnetocrystalline anisotropy constant in thin films. In the case of thin films, the magnetocrystalline anisotropy can be obtained by applying the magnetic field at various angles to the sample. This gives information about the type of magnetic material (soft/hard).





(Left) Thin magnetic film. (Right) A. Electron paramagnetic resonance spectra obtained at different angles between the plane of the sample and the applied magnetic field. B. Angular dependence of the resonance magnetic field H_r.

ADVANTAGES

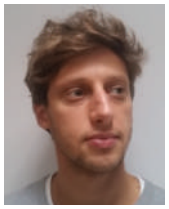
- INCDTIM offers R&D services based on EPR spectroscopy, used on its own or in combination with other complementary analytical techniques, covering almost the whole range of practical applications.
- Before entering into a contractual relationship, we offer consultancy to define the customer/partner's needs as accurately as possible and, if necessary, we carry out preliminary tests free of charge.
- Our existing facilities allow us to address most of the EPR methods used in current practice, many of which are already implemented in our laboratory.
- We have specialized staff, able to cover with the highest professionalism all stages of a contractual collaboration: definition of the problem to be solved, experimental design, data collection, interpretation of results and correlation with other complementary information if necessary.

ESTIMATED COSTS

The total cost of R&D services based on EPR spectroscopy consists of two components:

- ✓ spectrometer usage time, which includes consumables and wear. For one measurement at room temperature
- ✓ labor, which includes personnel and indirect costs associated with sample preparation operations, analysis and interpretation of results, preparation of the analysis/research report: negotiable, depending on the complexity of the study.

CONTACT



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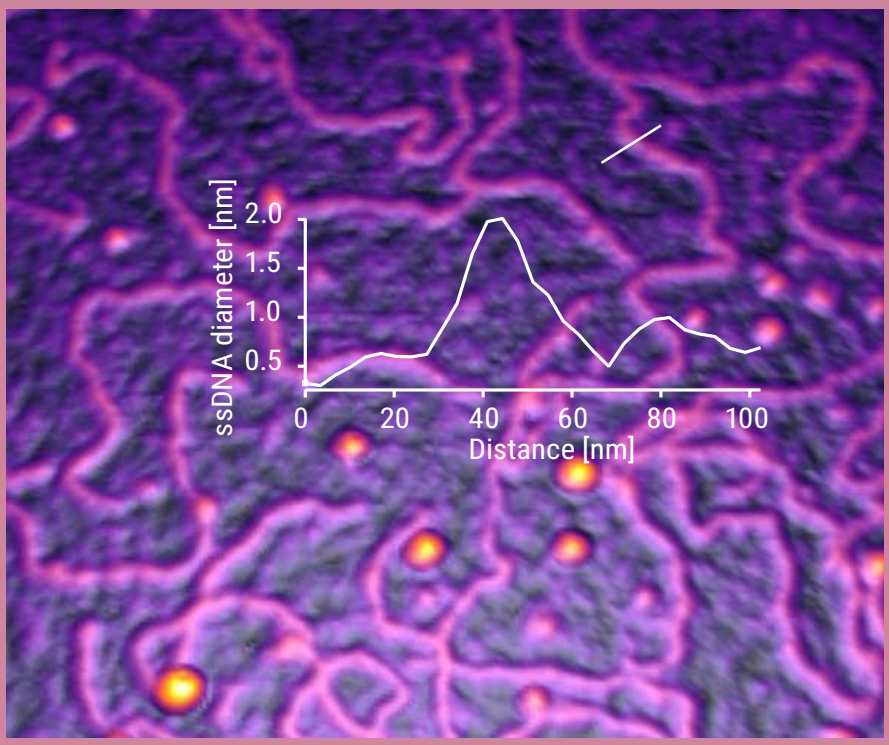
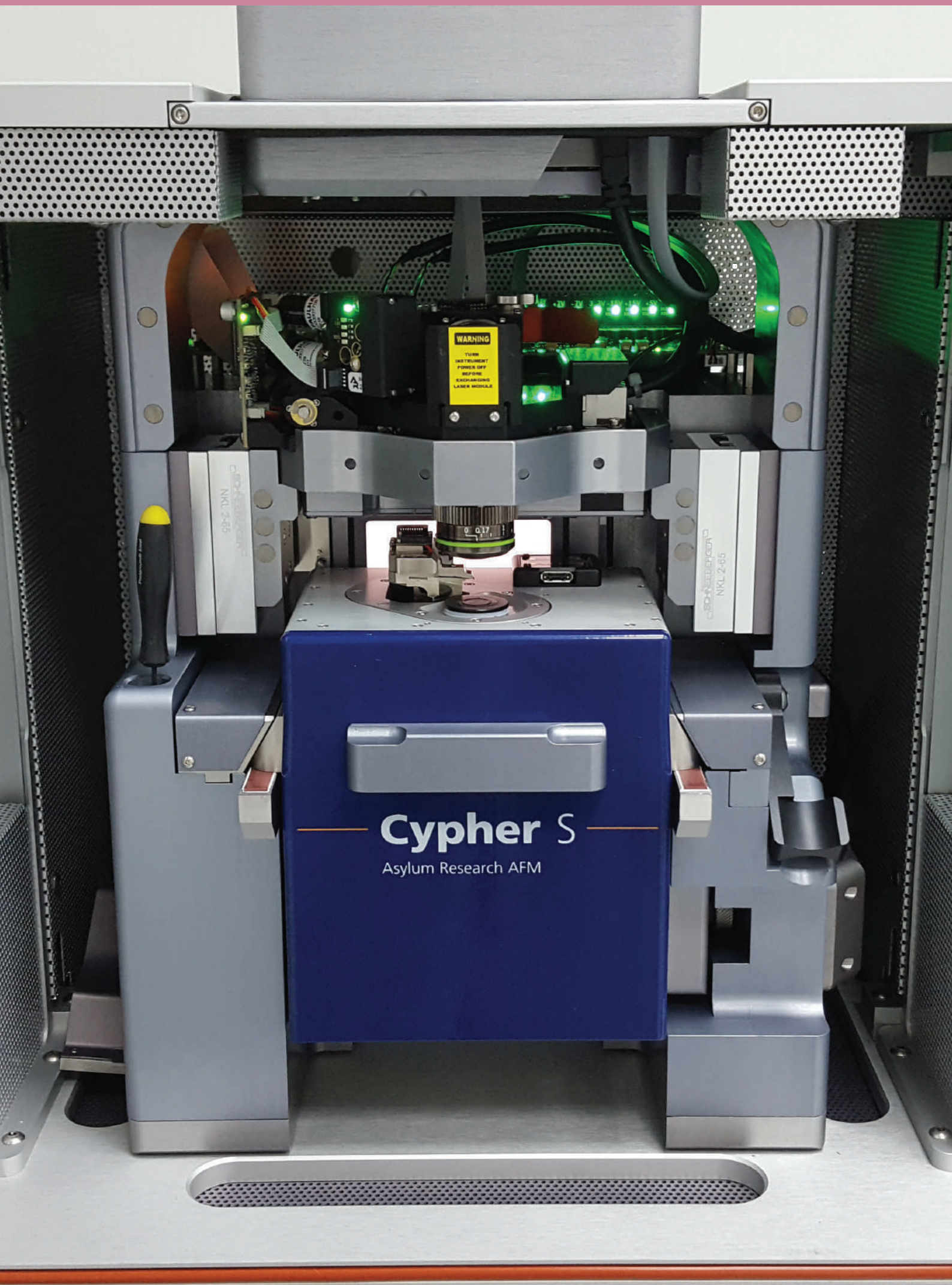
07.

ATOMIC FORCE MICROSCOPY




WARNING
TURN INSTRUMENT POWER OFF BEFORE EXCHANGING LASER MODULE
Cypher S
Asylum Research AFM

ATOMIC FORCE MICROSCOPY

Keywords: *atomic force microscopy, AFM, surface characterization, nanomaterials, nanoparticles, thin films, polymers, electrochemical sensors*

DESCRIPTION

Atomic Force Microscopy (AFM) is part of the Scanning Probe Microscopy (SPM) family of techniques for the investigation of surfaces by scanning with a very sharp tip.

The AFM image is obtained by monitoring the position of a probe (scanning probe) attached to a microcantilever as it scans the sample surface.

The AFM topography has nanometer resolution in the xy-plane and sub-nanometer resolution in the z-direction and can be obtained in two common modes: contact and intermittent contact/tapping. A 3D image of the surface is obtained by recording the height at each scanning point. In tapping mode, the microcantilever oscillates at a frequency close to its resonant frequency and the amplitude of the oscillation is monitored. During scanning, the cantilever vibrates so that the AFM tip periodically touches the sample surface, the friction between the tip and the surface, present in the contact mode, being avoided, preventing damage of the sample.

APPLICATIONS

Areas of application: As an investigation technique, AFM microscopy is suitable for all types of surfaces. The applications are practically unlimited, AFM microscopy being used in all fields:

- **research:** nanotechnology, life sciences, nanoparticles, polymers
- **industry:** manufacturing process control, corrosion analysis, morphology of coatings, glass, ceramics, metals
- **medicine and dentistry:** implants, filling materials, endodontic sealants

Systems: nanomaterials, biomaterials, nanoparticles, polymers and polymer blends, electrochemical sensors, metals, life science samples (cells, bacteria), medical devices (implants).

AFM Laboratory

Industries:

- ***Automotive industry:*** development of new materials, quality control of surfaces nanoscale analysis and measurement. The automotive industry is continuously developing advanced materials to keep pace with the challenges it faces in making cars more efficient. The use of nanotechnology can bring much needed advances in materials used in many automotive components, from metals to polymers
- ***Industrial process control:*** surface evaluation of samples for process development and/or manufacturing process control
- ***Photonics: 3D measurement of structures***. AFM images are independent of optical properties and do not require conductive coating of samples, provide excellent contrast for optically smooth samples, glass surfaces, diffraction gratings, etc.
- ***Medicine, biology:*** nanoscale imaging of biomaterials, cell surfaces, implants, etc.

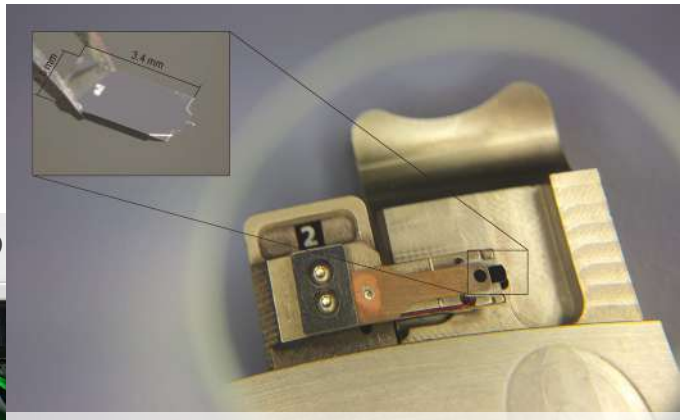
Microscopul AFM Ntegra Spectra (NT-MDT)

INFRASTRUCTURE

INCDTIM Cluj-Napoca provides the infrastructure for the study of surfaces by AFM:

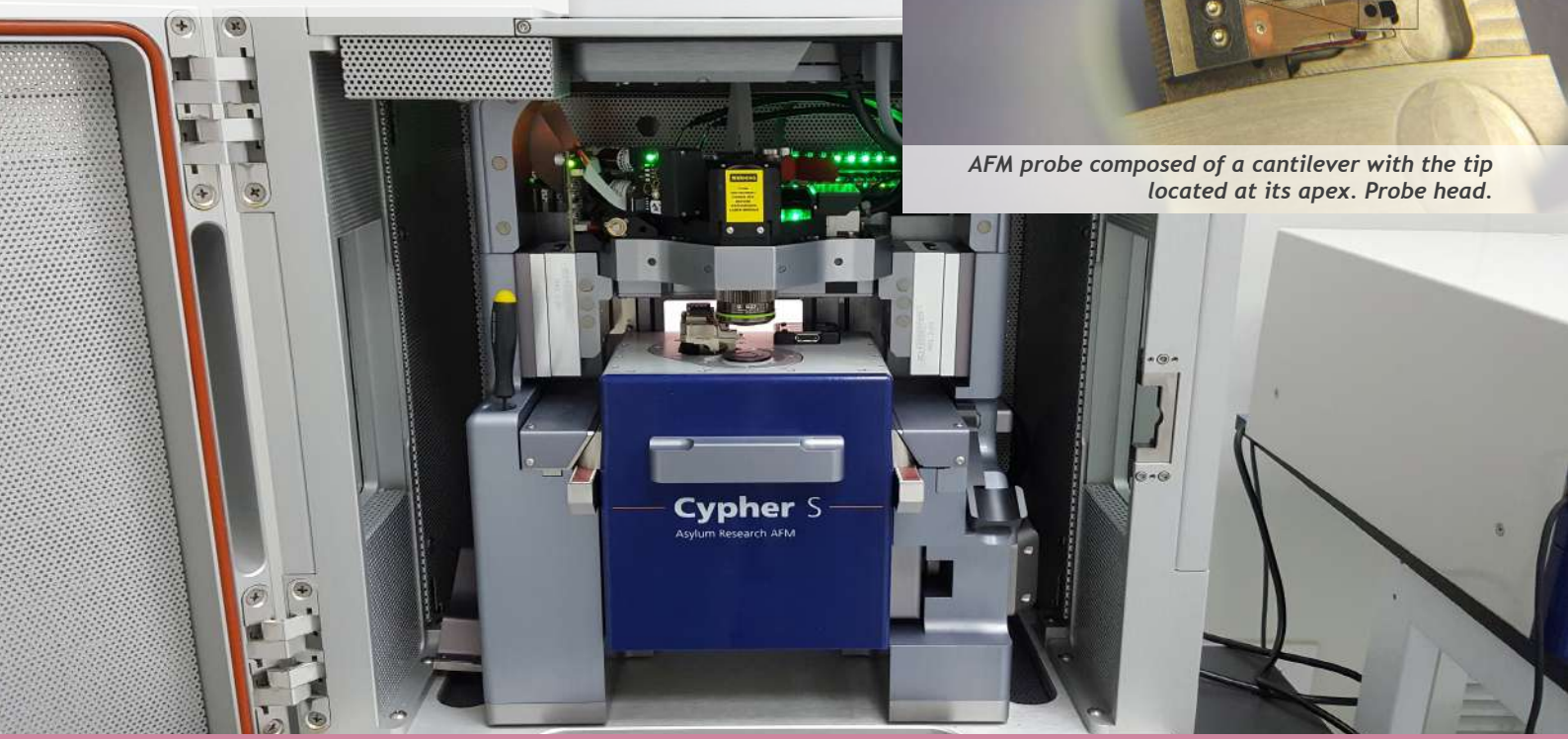
1. **Ntegra Spectra AFM platform (NT-MDT).** Maximum scanning area: 100 μm × 100 μm, z_{max} 10 μm, equipped with Olympus IX71 microscope, configurations: direct, 100X objective (NA 0.7), inverted 100X objective with oil immersion (NA 1.3), optimized for samples on transparent substrate. Most AFM modes are available. Data acquisition and image processing: Nova software.

2. **AFM Cypher S microscope (Asylum Research – Oxford Instruments).** Maximum scanning area: 30 μm × 30 μm, z_{max} 5 μm. The microscope is equipped with integrated videomicroscope with software-controlled optical zoom, optical resolution < 1 μm; NA 0.45; 3 Mpx color CMOS camera, field of view 650 μm × 900 μm. Deflection sensing optical system noise < 7 pm (cantilever not in contact with sample); < 15 pm (cantilever on surface); Z sensor noise < 50 pm; XY (closed-loop) sensor noise < 60 pm. Data acquisition and software AR processing with Igor Pro SPM modules. Sample dimensions: $Ø_{max}$ = 2 cm, h = 0.7 cm.



AFM probe composed of a cantilever with the tip located at its apex. Probe head.

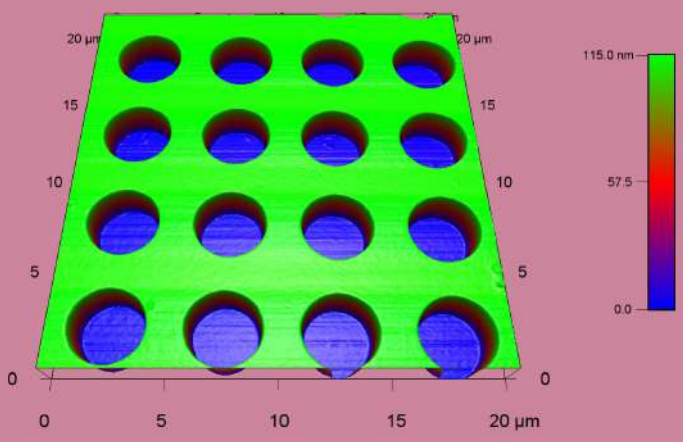
Atomic Force Microscope Cypher S (Asylum Research – Oxford Instruments)



TYPICAL APPLICATIONS – EXAMPLES:

AFM microscopy is used to measure the topography of hard or soft materials, conductive or insulating surfaces.

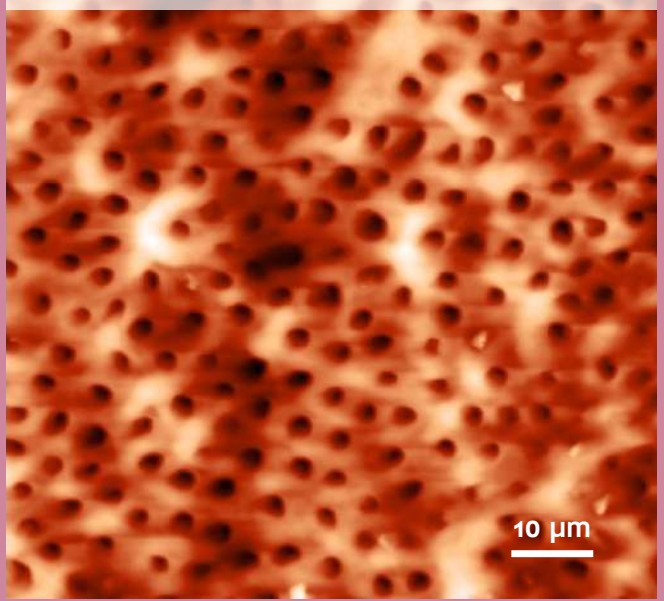
Nanotechnology (nanomaterials). Atomic force microscopes are essential tools for nanotechnology in the control of nanofabrication processes involving high-resolution visualization and measurement of nanostructures: nanoparticles, nanotubes, patterned surfaces, (meta)materials, composites, polymers, thin films, DNA, etc.



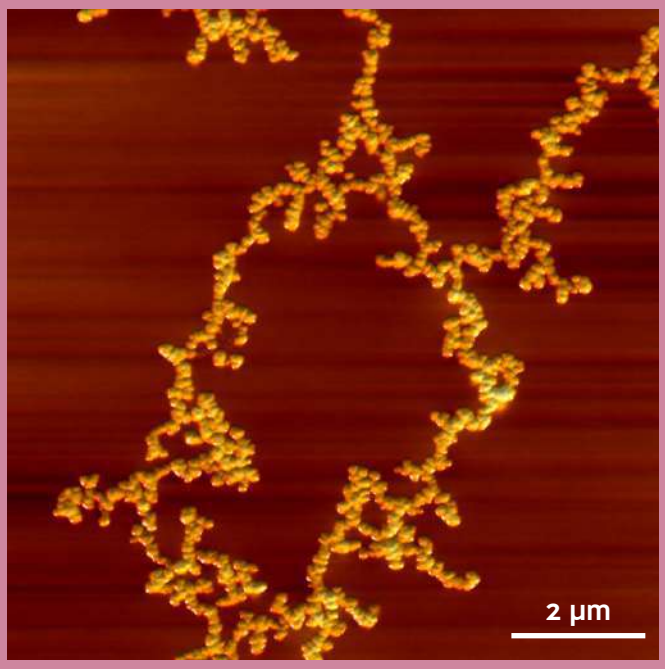
Micropatterned silicon substrate

Synthetic biomaterials. Synthetic materials in contact with living tissues, filling materials, endodontic sealants, implants and medical devices have a surface in direct contact with tissues in the body. The surface roughness of dental filling materials influences their adhesion to tooth walls and their porosity may influence their coloration and solubility in tissue fluids. On the other hand, the acceptance and regeneration of the tissue in which an implant is placed is influenced by surface characteristics. AFM allows evaluation of implant surfaces and control of processes at the interface with biological fluids or tissues.

AFM topography image of a dental filling material

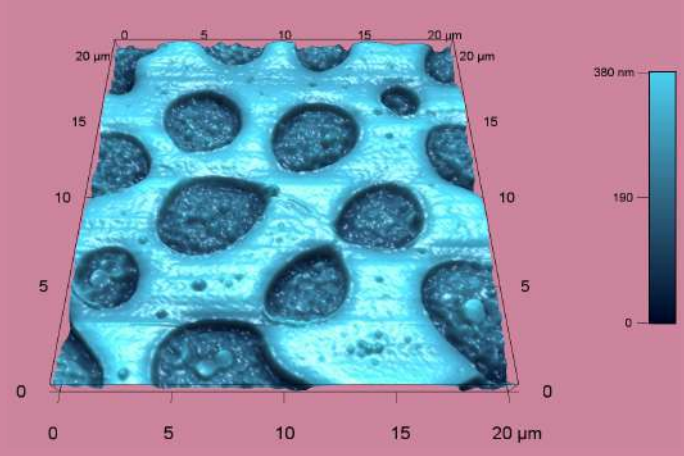


Nanoparticles. The dimensional characterization of nanoparticles by AFM has some advantages compared to other techniques (optical microscopy, electron microscopy, DLS), it provides statistical data of the distribution and numerical evaluation of the nanoparticle size. Variable nanoparticle geometries (nanospheres, polygonal shapes, fractals, clusters) can be identified and characterized. The values calculated directly from the AFM topography data allow to evaluate the percentage increase in surface area by the presence of nanoparticles on the substrate.



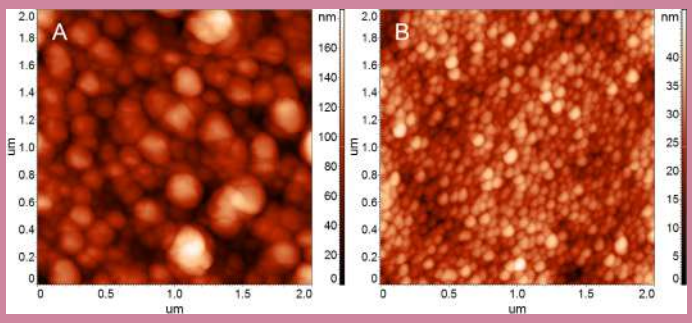
Gold nanoparticles (AuNPs) with Cystine

Polymers. Polymer composite materials can manifest nanoscale domains (block copolymers) that influence the mechanical properties of the bulk material. In some cases, certain materials are added to polymers precisely to modify their mechanical properties (to increase or decrease their elasticity). By AFM, possible heterogeneities in a polymer material and the areas where they are present in different parts of the investigated sample can be revealed.



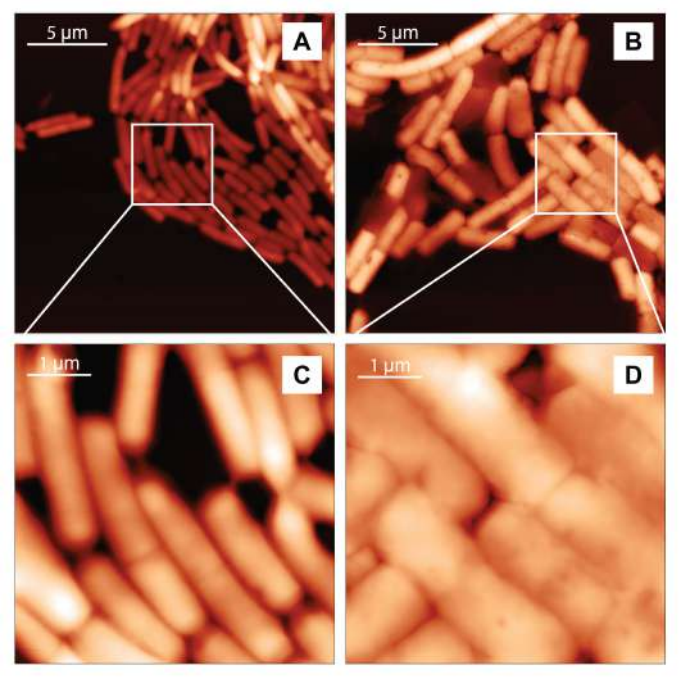
AFM topographic image of a polycarbonate-polycaprolactone (PC-PCL) blend

Electrochemical sensors. AFM microscopy is applied for the surface characterization of different electrochemical sensors or in the characterization of aptasensors with applications in early-stage cancer detection. AFM microscopy allows morphological and topographic characterization of the nanostructured electrode surface before and after each modification step. The increased sensitivity of modified sensors compared to that of the unmodified ones is influenced by increasing the surface area by nanoparticle deposition.



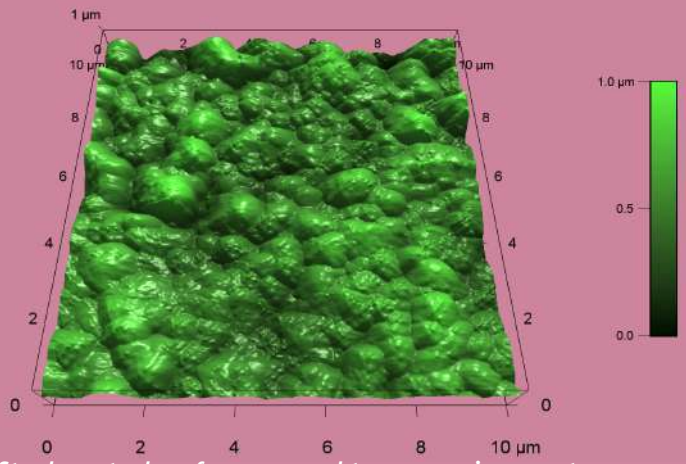
AFM topographic images of an electrochemical sensor modified with PPyNPs (left) and AuNPs@PPy (right) sucessfully tested for serum real samples

Cells, bacteria. AFM microscopy is commonly applied to examine bacterial cell surfaces. In contrast to electron microscopy which gives a general idea of cell morphology through a two-dimensional projection and allows the assessment of bacterial populations, AFM is less fast and less efficient in the quantitative assessment of populations, but allows much more detailed investigation of the morphology of soft cell surfaces (cells, bacteria) at the nanoscale. In addition, the effects of agglomeration and/or adhesion of bacteria to surfaces can be analyzed.



Bacteria. AFM images of Lactobacillus casei (left) and Listeria monocytogenes (right)

Corrosion. AFM can be used to investigate changes of the samples surface exposed to corrosive agents and to assess the efficiency of different corrosion protection agents. Surface roughness changes are provided as roughness parameters values.



Stanless steel surface exposed to a corrosive agent

ADVANTAGES

- Any type of material can be analyzed, the only requirements are related to the size of the sample (sample $Ø_{max}$ 2 cm, h_{max} = 0.7 cm) and the difference between the lowest and the highest point of the sample surface (h_{max} 5 µm) (with the naked eye, the sample appears smooth).
- Complementary to other imaging techniques which provides 2D images, AFM microscopy provides a 3D topographic image of investigated surfaces.

ESTIMATED COSTS

The total cost of AFM characterization involves machine operating time, labor and consumables, sample preparation operations, data processing, image analysis and preparation of the report:

- ✓ preliminary tests
- ✓ complex analysis
- ✓ outputs: topographic images for maximum areas of 30 × 30 µm², surface morphology down to nanometer scale, roughness evaluation, cross-section profiles, comparative analysis for samples subjected to different processes, thin coating layers, etc.

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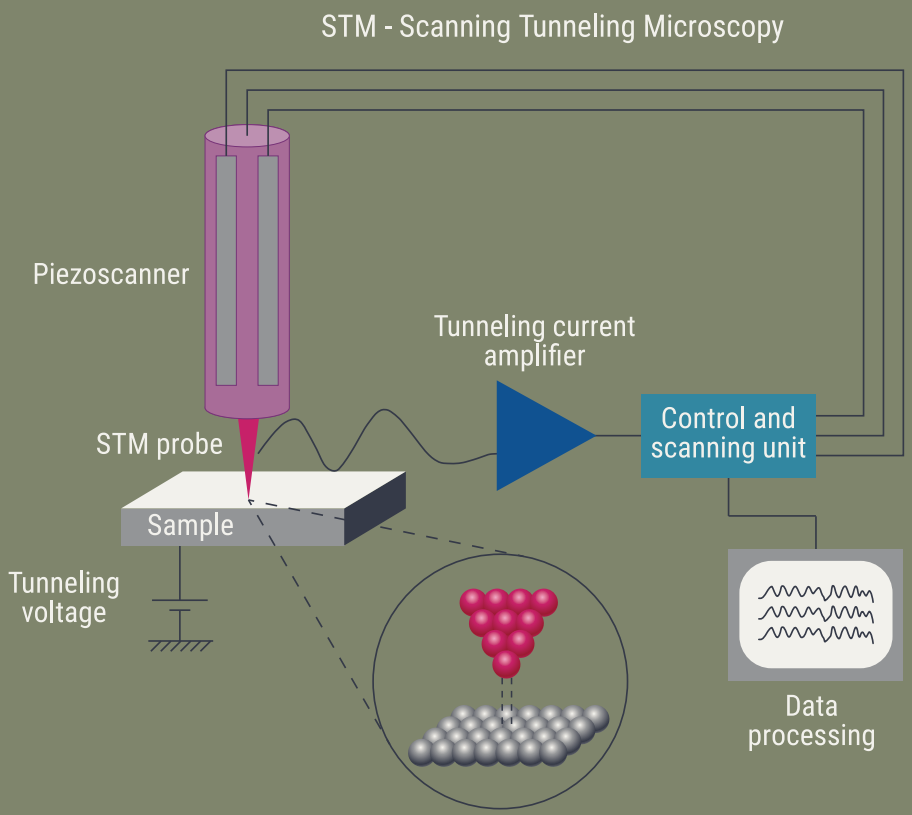
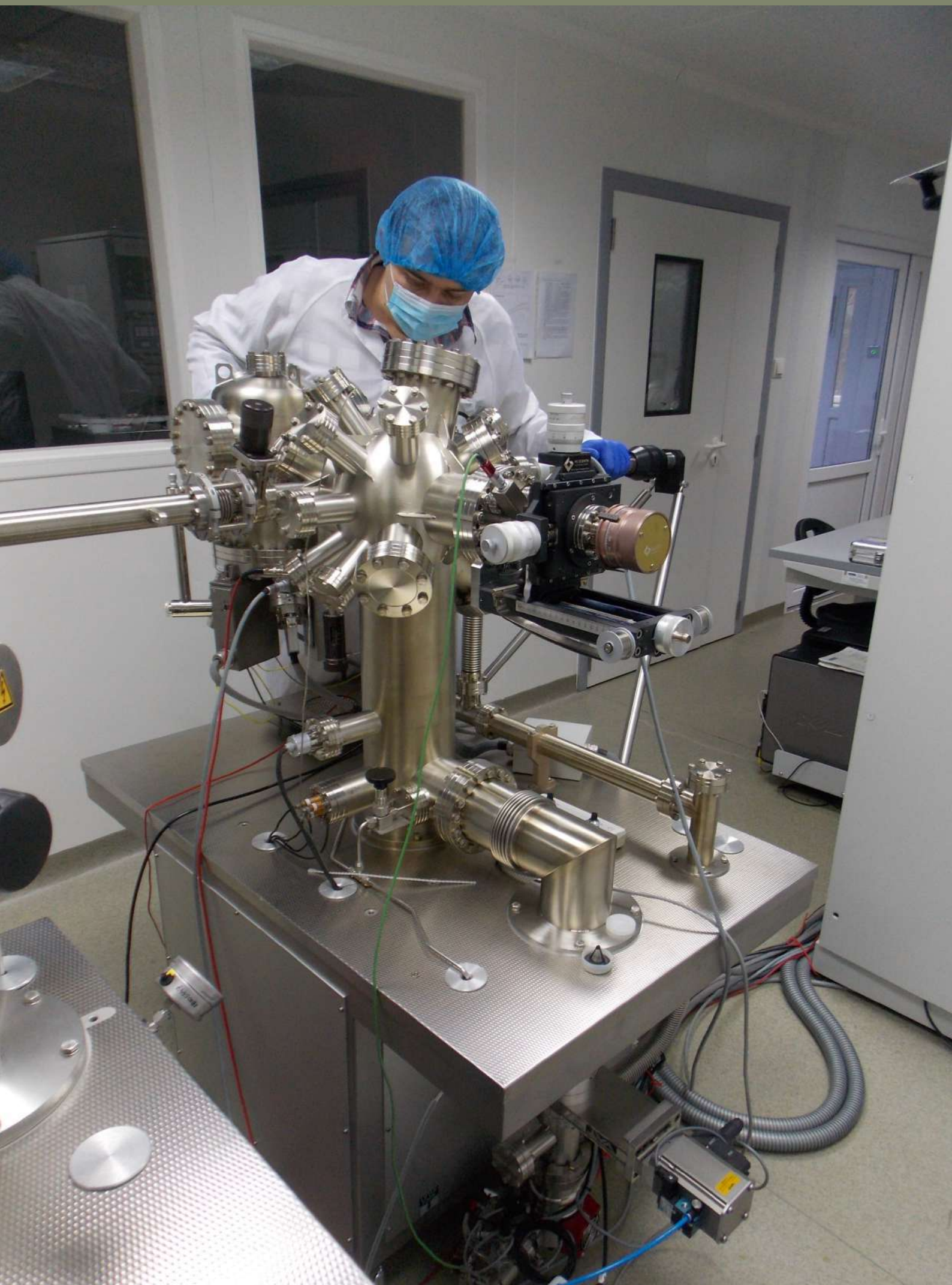
08.

ULTRA-HIGH VACUUM SCANNING PROBE MICROSCOPY





UHV SCANNING PROBE MICROSCOPY

Keywords: *scanning probe microscopy, STM, contact AFM, non-contact AFM, ultra-high vacuum, UHV*

DESCRIPTION

Scanning Probe Microscopy (SPM) is a technique for mapping at the nanoscale the physico-chemical surface properties of a material, such as relief, electrical conductivity, elastic modulus, magnetization, chemical composition, thus obtaining a picture of how these properties are distributed on the surface of the sample under study.

Depending on the physical or chemical properties being mapped, scanning probe microscopy can be of several types. Two important scanning microscopy techniques are Scanning Tunneling Microscopy (STM) and Atomic Force Microscopy (AFM). Each has different versions of functionality, and there is even a scanning technique that combines STM and AFM called Qplus.

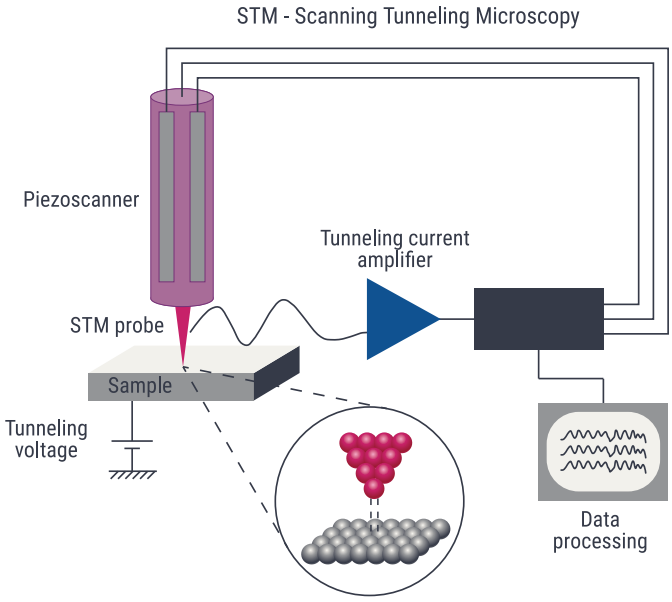
AFM scanning microscopy offers sub-nanometer resolution and, depending on the specific version used, can either record the surface topography of the sample to be studied or map certain mechanical properties of the surface (elasticity, hardness, coefficient of friction).

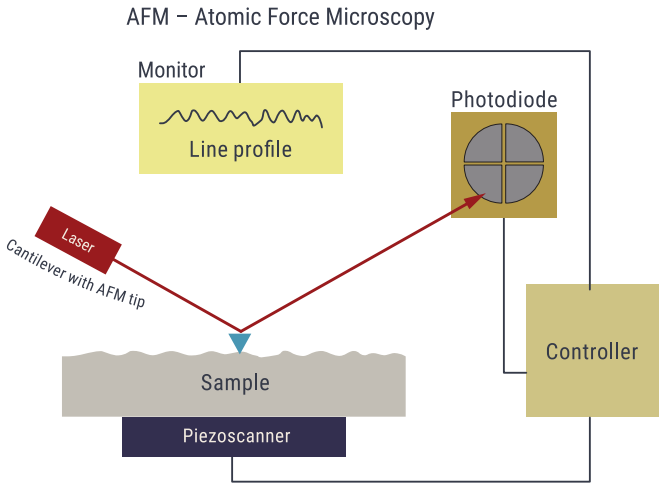
The operating principle of the AFM technique is based on the physical, mechanical interaction between a very sharp AFM tip, made of silicon or silicon nitride, and the surface of the sample to be studied, the tip having a radius of curvature of several nanometers. The AFM tip is attached to the end of a cantilever. There are three main versions of the AFM technique: AFM contact, AFM noncontact, AFM tapping mode.

In contact AFM mode, the cantilever presses the AFM tip against the surface to be studied. As the AFM tip scans the sample surface, the sample will also be moved vertically to keep the position of the laser beam spot reflecting off the cantilever tip constant. This means that the AFM tip's pressing force on the surface will be constant, thus the topography of the sample will be recorded as a multitude of linear profiles forming a three-dimensional image.

In noncontact AFM mode, the cantilever is placed in a vibrating state in the immediate vicinity of its resonant frequency. The AFM tip, as it is brought into the vicinity of the surface to be scanned, will sense an interaction with the sample surface, which will cause the cantilever's resonant frequency to change. Thus a difference will occur between the excitation frequency of the cantilever and the resonant frequency of the cantilever, and if this difference is kept constant during the scan, the interaction between the tip and the surface is constant, which means that the AFM tip will faithfully scan the surface relief.

The multitude of linear scan profiles thus recorded will form a three-dimensional image of the topography under investigation. The noncontact AFM mode is used when there is an adhesion force between the AFM tip and the





surface to be studied, which would make it difficult to scan in contact AFM mode due to the high friction forces between the tip and the sample.

The oscillation amplitude of the AFM tip in the noncontact mode is typically a few nanometers (< 10 nm) and can go down to a few picometers, with the resolution provided being better the smaller the oscillation amplitude.

The tapping AFM mode is similar to the noncontact AFM mode but the oscillation amplitude of the AFM peak is substantially higher, about 200 nm. Also, the AFM tip will make contact with the scanned surface at each oscillation at the position of minimum negative elongation. This AFM technique is suitable for those samples which cannot be scanned by the contact AFM method and which exhibit a topography with large vertical variations at a high inclination slope.

The principle of operation of STM is based on the quantum phenomenon in which the wave properties of electrons allow them to tunnel beyond the surface of a solid into regions of space that are forbidden to them according to the rules of classical physics. The sharp tip of a tungsten needle is positioned a few Ångstroms from the surface of the sample, and a small voltage applied between the tip and the surface causes the electrons to tunnel. As the tungsten tip scans the surface, it records variations in the tunneling current, and this information can be processed to provide a topographic image of the surface. The topographic images of the surface are collected in one of two modes: in constant height mode, where changes in the tunneling current are mapped directly, while in constant current mode the voltage controlling the height of the tip is recorded and the tunneling current is maintained at a preset level.

APPLICATIONS

Areas of application: R&D in electronics, biology, medicine, materials science

Systems:

Ultra-high vacuum scanning probe microscopy is mainly used for samples that have been fabricated under such conditions, avoiding taking them out into the ambient atmosphere to avoid contamination. There may also be situations where the sample of interest has been manufactured in ambient atmosphere and, for microscopy measurements, needs to be introduced into the ultra-high vacuum facility to benefit from a preliminary surface decontamination process by thermal degassing.

Industries:

STM and AFM microscopy allows the confirmation of the required surface quality, in terms of topography correlated with physico-chemical properties, for devices finding applications in the microelectronics and optoelectronics industry.

INFRASTRUCTURE

Isotopic and Molecular Technologies Department has a modern STM and AFM scanning microscopy facility (Omicron, Germany).

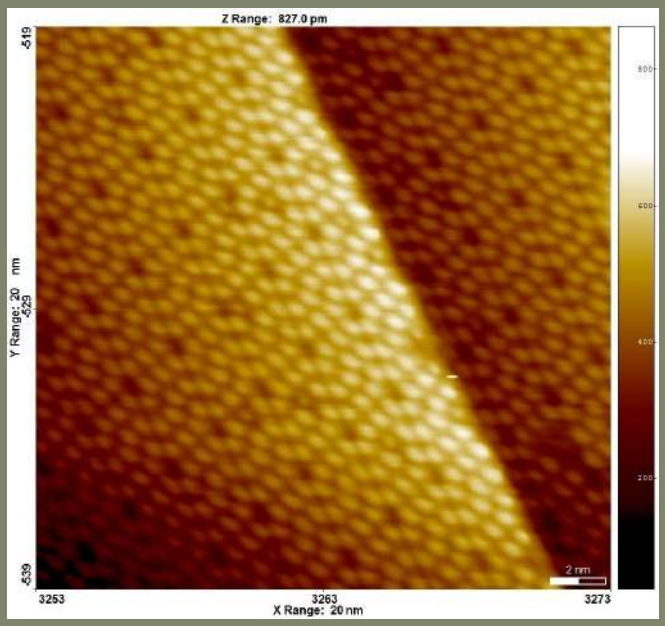
The facility has an ultra-high vacuum enclosure at a level of 10^{-10} mbar, provided by a pump system including a turbo-molecular pump, an ion pump and a titanium sublimation pump.

SPM equipment operates in ultra-high vacuum and at low temperatures

TYPICAL APPLICATIONS – EXAMPLES:

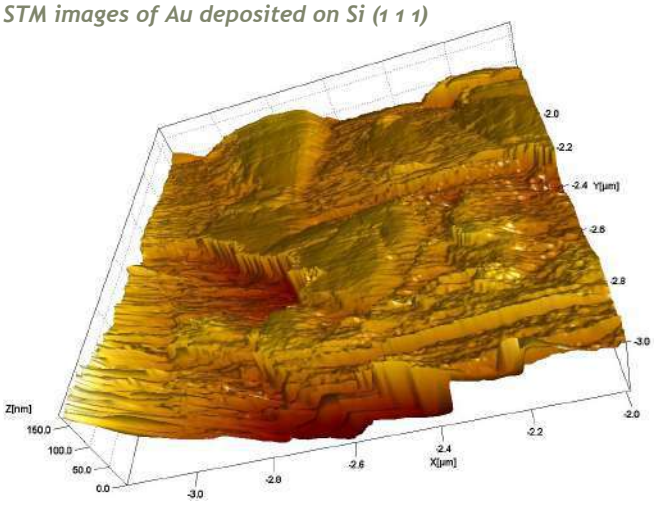
Nanoscience and nanotechnology. SPM microscopy is a visual imaging technique and is an essential method for the characterization of materials, in particular nanostructured materials such as thin films deposited by advanced, state-of-the-art techniques. Nanofabrication processes can be optimized by topographic characterization at the atomic level by both STM and AFM. Thus, STM microscopy is used to characterize and visualize conducting or semiconducting surfaces.

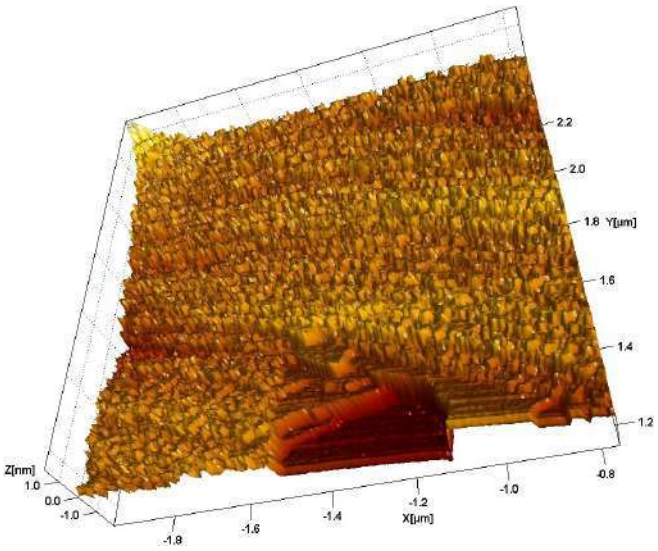
Ultra-flat metal surfaces. STM microscopy has been successfully applied at INCDTIM in the 2D and 3D characterization of ultra-flat metal surfaces fabricated by ultra-high purity deposition techniques. For gold films deposited on Si (1 1 1) substrate, the fabrication parameters could be optimized by topographic characterization of the nanostructured film surfaces with the variation of the substrate temperature during deposition. Furthermore, the technique allows to identify and characterize the growth modes of gold films – island or layer-by-layer growth – on the substrate.

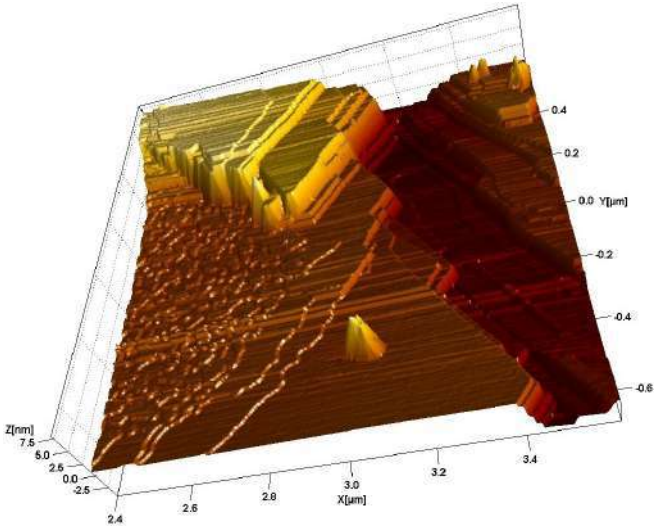


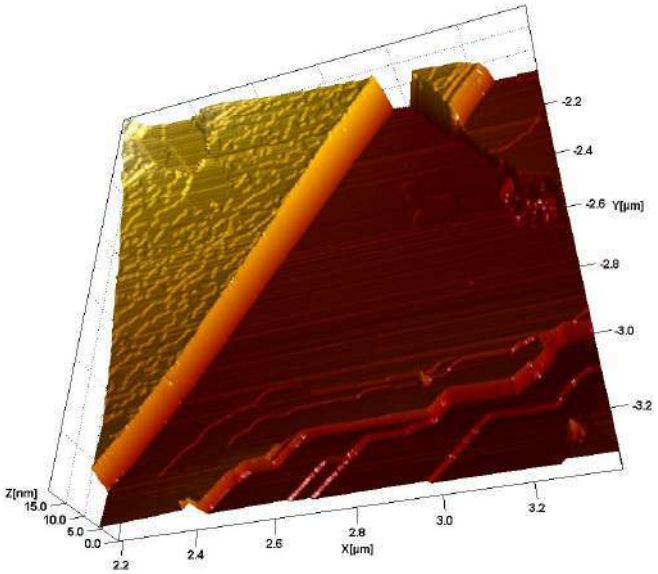
STM image of Si (1 1 1) 7 × 7

STM images of Au deposited on Si (1 1 1)



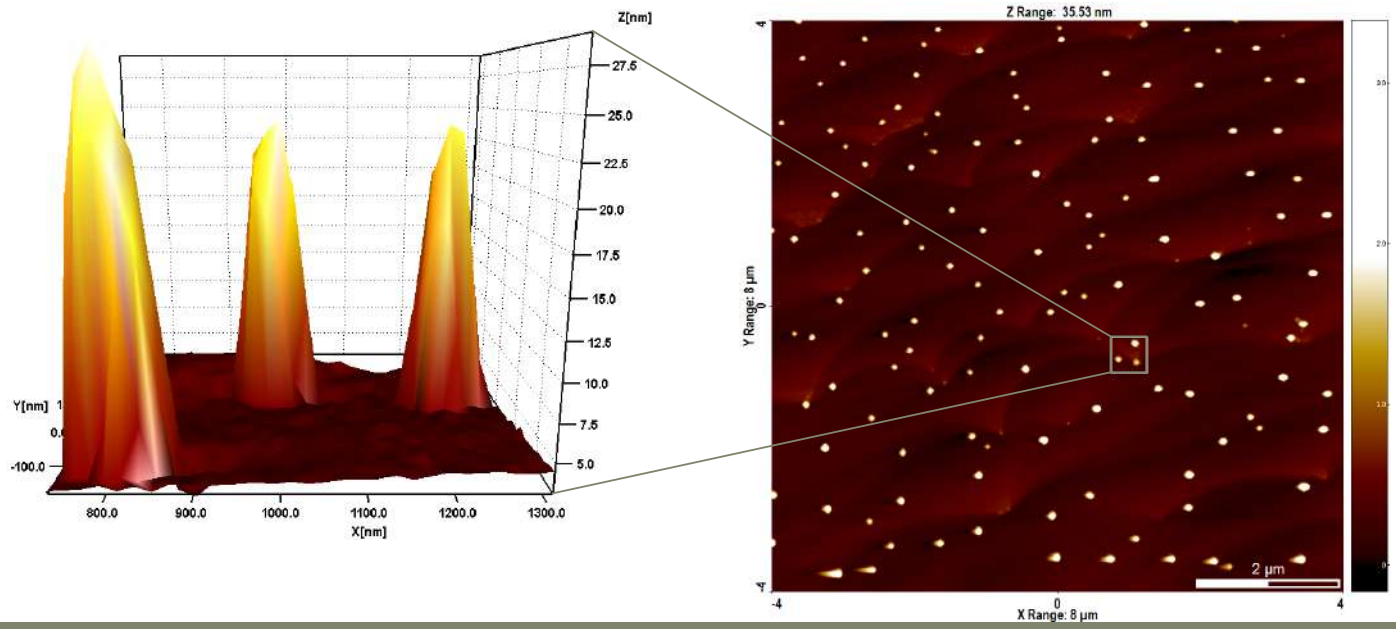






Nanoobjects on semiconductor surfaces. STM microscopy is frequently applied to examine nanoobjects grown on various metal and semiconductor surfaces. Our research group has experience in the realization and characterization of the topographic properties of Si nanocones deposited on 7 × 7 reconstructed Si (1 1 1) substrates by epitaxial molecular jet deposition. Depending on the envisaged application, the morphology of the fabricated Si nanocones can be tuned for optimal detection of very weak signals in the development of molecular and biological sensors and *lab-on-a-chip* devices.

SERS substrates based on structured gold films. Viewing the morphological details of gold films having an insular pattern is particularly important when studying the applications of these films as SERS substrates.
This is so because it is the granularity of this insular pattern which makes these films efficient as SERS substrates.



STM images of Si nanocons deposited on Si (1 1 1)

ADVANTAGES

- **Particularly good resolution:** the image obtained can have a resolution about 1000 times better than that characteristic of optical microscopy, where light diffraction limits the resolution to a value comparable with the wavelength of the optical radiation used.
- **Nanolithography method:** AFM and STM microscopy can be used to create small structures on the sample surface, either by indentation of the surface (contact AFM) or by local melting (STM).
- **Preserves sample purity:** ultra-high vacuum scanning probe microscopy protects the surface under study from potential contaminants in the ambient atmosphere.
- **Easy access to auxiliary manufacturing equipment:** the ultra-high vacuum scanning probe microscopy facility is coupled to an Molecular Beam Epitaxy thin films deposition facility with argon ion beam sample treatment facilities and facilities for coating the sample with a thin protective layer of a suitable material of choice.

ESTIMATED COSTS

The price for the measurement of a sample by ultra-high vacuum scanning probe microscopy depends on the specific characteristics of the required measurement.

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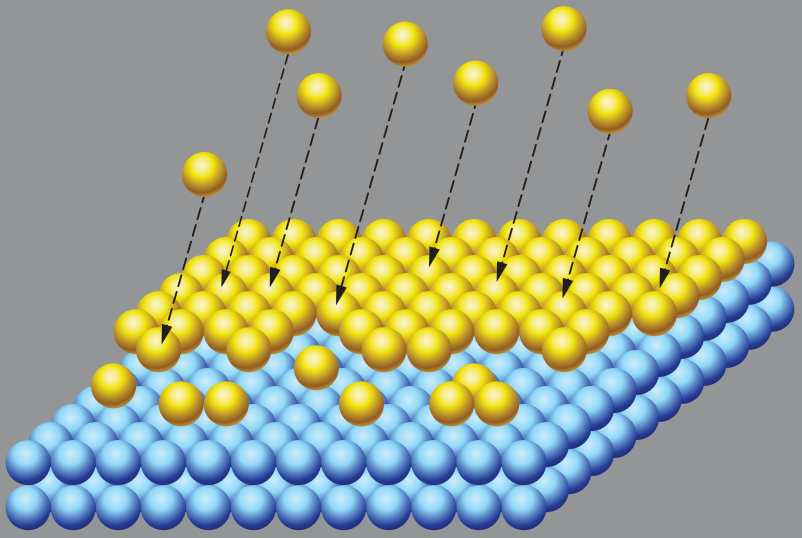
09.

EPITAXIAL FILM DEPOSITION BY MBE



View of the MBE system from the opposite side of the SPM

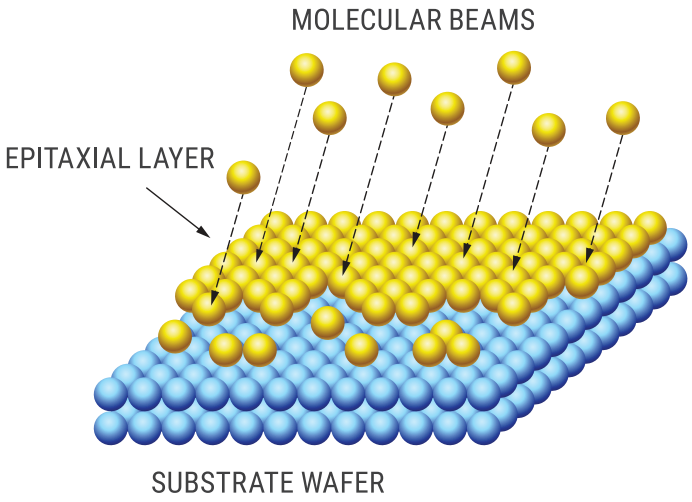
EPITAXIAL FILM DEPOSITION IN ULTRA-HIGH VACUUM BY MBE

Keywords: *ultra-high vacuum evaporation, thin film deposition, crystalline films, molecular epitaxy*

DESCRIPTION

Ultra-high vacuum (UHV) epitaxial film deposition by **Molecular Beam Epitaxy (MBE)** technique is a fabrication technology by which a film, from a material of interest, can be grown on a deposition substrate. The substrate is chosen both to favor the single crystal structure of the film and to provide the necessary adhesion.

The deposition of the film is achieved by sending a beam of atoms/molecules onto the substrate. This beam is obtained by thermal evaporation of the material of interest in an electrically heated crucible, thus ensuring a well-defined directionality of the beam on the deposition substrate. The deposition process takes place under ultra-high vacuum conditions at pressures of the order of 10^{-10} mbar in order to achieve a high purity of the material in the deposited film.



Epitaxial deposition process at atomic level in the MBE system

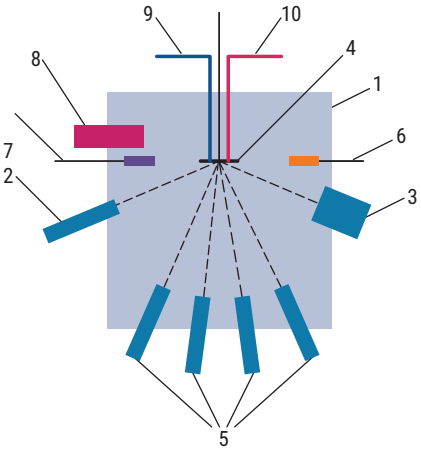
MBE system coupled wit SPM (close plan) via transfer arm

APPLICATIONS

Areas of application: R&D, electronics, optoelectronics, nanotechnologies

Systems: the materials that can be deposited by this technique are metals, semiconductors, and any other inorganic and organic materials in solid state that have a sufficiently high evaporation rate up to the maximum heating temperature of about 1450°C.

Industries: semiconductor devices, telecommunications, sensors, lasers



1 - MBE growth chamber
2 - RHEED electron gun
3 - RHEED fluorescent screen
4 - sample holder
5 - effusion cells
6 - beam flux monitor
7 - quartz microbalance
8- Argon ion gun
9 - liquid Nitrogen in
10 - liquid Nitrogen out

Schematic of principal elements of MBE

INFRASTRUCTURE

The Institute's Department of Molecular and Biomolecular Physics has a state-of-the-art molecular epitaxy facility (Omicron, Germany). The main technical features of the facility are as follows:

1. Ultra-high vacuum enclosure at a level of 10^{-10} mbar, provided by a pump system including a turbomolecular pump, an ion pump and a titanium sublimation pump
2. The installation is equipped with four evaporation cells from which different materials can be evaporated, simultaneously or sequentially, by heating up to temperatures of 1450°C
3. Electron gun for real time monitoring of the crystallinity of the deposited film
4. Atomic/molecular beam pressure monitor to control the deposition rate of the material on the substrate
5. Quartz balance for monitoring the thickness of film deposited on the substrate
6. Controlled temperature for the deposition substrate support between liquid nitrogen temperature, -196°C, and 827°C
7. Argon ion gun for cleaning the substrate prior to deposition or for treatment of the deposited film

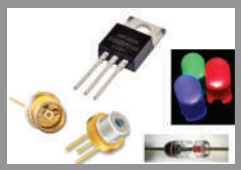
MBE system

TYPICAL APPLICATIONS – EXAMPLES:

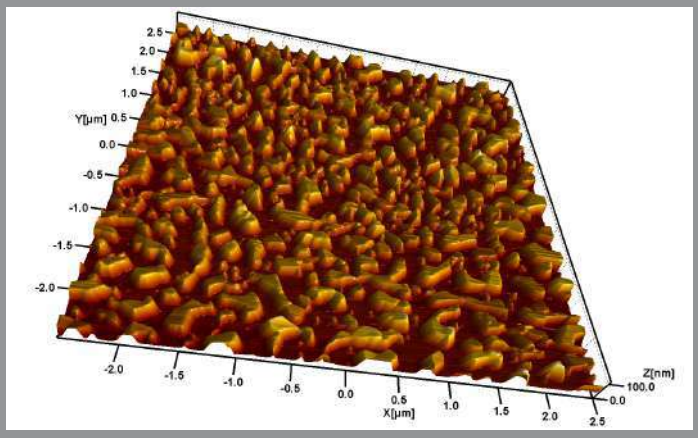
Deposition of crystalline metallic films with island structure for plasmonic devices. Such metal films can be realized for use as SERS (Surface Enhanced Raman Spectroscopy) substrates. This is a modern alternative to Raman spectroscopy that offers increased sensitivity compared to the classical Raman technique. It is therefore particularly useful both for detecting the presence of chemicals, even at very low concentrations, and for detecting micro-organisms.

Our research group has experience in the realization of SERS substrates by MBE. A recent realization is a crystalline gold film with an island structure, shown in the figures below. It has proven its usefulness as a SERS detection substrate, offering a 30% higher efficiency compared to a commercial sample, relative to the Crystal Violet Raman analyte.

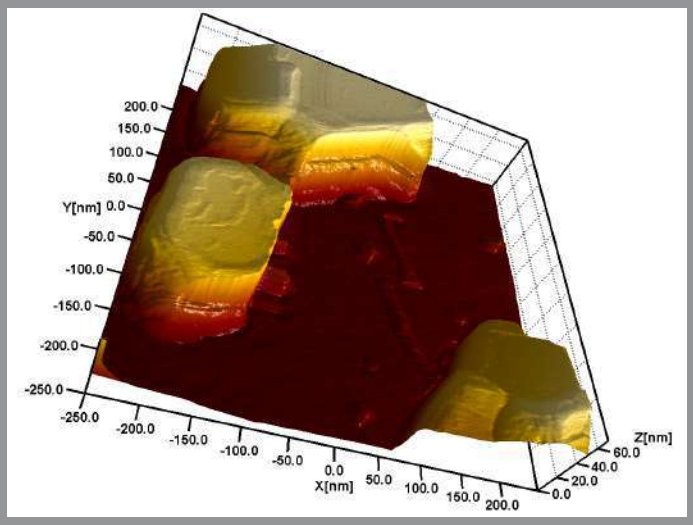
Conductive and semiconductor thin films for electronic and optoelectronic components and devices. Such conductive and semiconducting thin film structures are used to realize the new generation of electronic and optoelectronic components and devices, such as microprocessors, integrated circuits, diodes, transistors, laser diodes, LEDs. A wide range of such products are marketed worldwide by well-known companies such as INTEL, AMD, IPG Photonics, Hamamatsu and others.



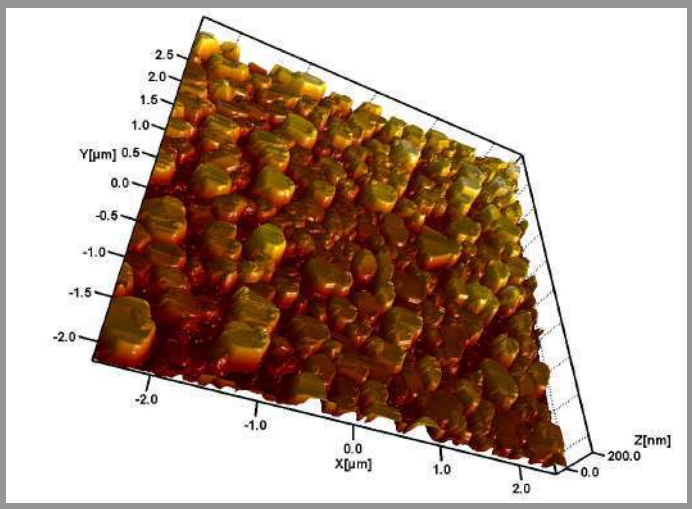
Electronic and optoelectronic components and devices



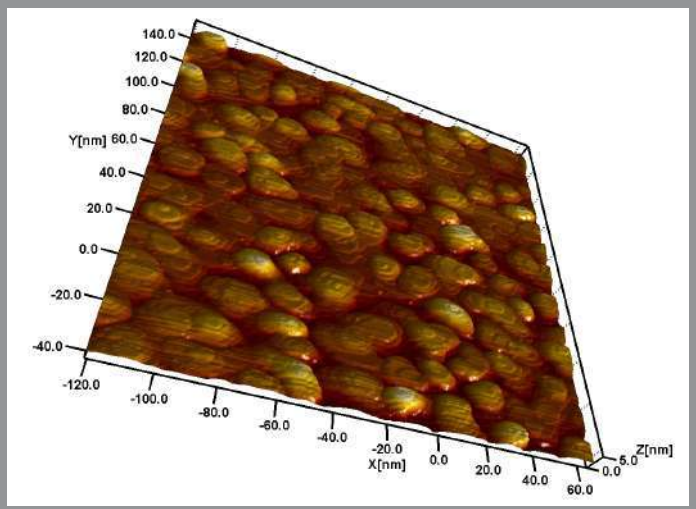
Contact-mode AFM image of crystalline gold film with island structure (2.5 µm x 2.5 µm)



Contact-mode AFM image of crystalline gold film with island structure (detail, 200 nm x 200 nm)



Contact mode AFM image of Au layer deposited in MBE on mica; the substrate has previously undergone an Ar ion-jet treatment for decontamination purposes



STM image of Au@Si. Silicon substrate is maintained at cryogenic temperature during deposition (T_{liqN2})

ADVANTAGES

- **Diagnosis at every stage of manufacturing.** The molecular epitaxy facility is coupled to another UHV facility which has AFM and STM scanning microscopy facilities. This allows both the characterization of the substrate topography and the topography of the deposited films immediately after their fabrication, without the sample leaving the UHV environment
- **Substrate temperature control.** This makes it possible to ensure the required substrate temperature during deposition, and to perform thermal treatments on the sample. These thermal treatments can be performed both prior to deposition, for degassing and pyrolytic cleaning of the substrate, and after deposition, for example to achieve desired micro-/nanostructuring effects of the deposited films
- **Argon ion treatment.** Equipping the molecular epitaxy installation with the Ar ion gun allows more aggressive cleaning of the deposition substrate. This is necessary when there are contaminants that are strongly bound to the deposition substrate and could not be removed by the traditional method of sonication in various chemical solvents,

ESTIMATED COSTS

The price for the realization of an epitaxial thin film deposition depends on the complexity of the desired manufacturing process. Factors influencing the price of an epitaxial thin film deposition process are as follows:

1. Cost of the material(s) of interest
2. The complexity of the cleaning and treatment process of the deposition substrate, which takes place prior to the deposition of the film of interest, if this is required
3. Number and thickness of layers to be deposited
4. The temperature at which the deposition substrate is maintained during deposition – a cryogenic temperature incurs additional costs
5. Post-deposition thermal treatments
6. Imaging the topography of the deposited layer(s) by atomic force microscopy or tunneling microscopy
7. Labor, including personnel and indirect costs associated with sample preparation and imaging operations.

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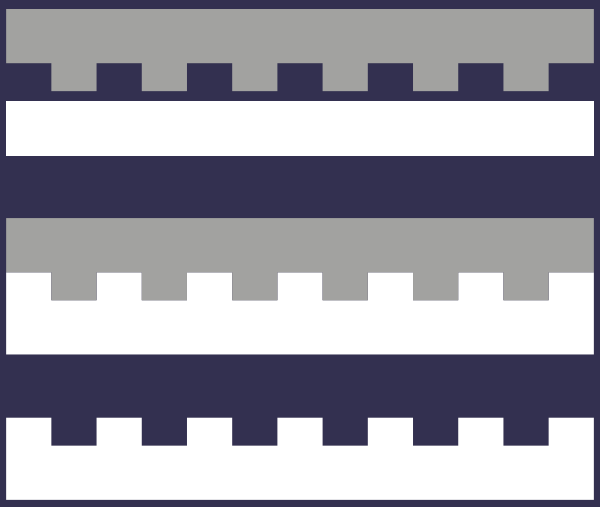
10.

NANOIMPRINT LITHOGRAPHY




Eitre® 3

NANOIMPRINT LITHOGRAPHY

Keywords: *nanoimprint lithography, micro-/ nanostructured surfaces, micro-/nanoelectronics, micro-/nanocounterfeiting elements*

DESCRIPTION

Nanoimprint Lithography (NIL) is a modern, high-resolution technique with high-throughput for the fabrication of high quality and ordered micro/nanostructured surfaces down to 10 nm in size.

To fabricate various micro/nanostructured patterns on the surfaces, customized molds are used, which have to be designed in advance and usually are made out of rigid materials (e.g. silicon or chromium).

The micro/nanopatterns fabricated by NIL can be imprinted on rigid substrates (silicon, glass) or flexible substrates (such as plexiglas, PMMA or polycarbonate).

The micro/nanostructures imprinting process can be done by a thermal process or by irradiation with ultraviolet (UV) light depending on the photosensitivity of the working substrate.

NIL Eitre®3 system

APPLICATIONS

Areas of application

Systems:

i. ***Solar cells*** for photoactive layer fabrication, polarization control, color and information storage on hard disks

ii. ***Biological applications*** including sensing, nanofluidic devices for DNA stretching or tissue engineering

iii. ***Advanced electronic circuits*** integrated in smart devices with low power consumption thanks to the possibility of micro/nanoimprinting of sub 10 nm patterns on large areas

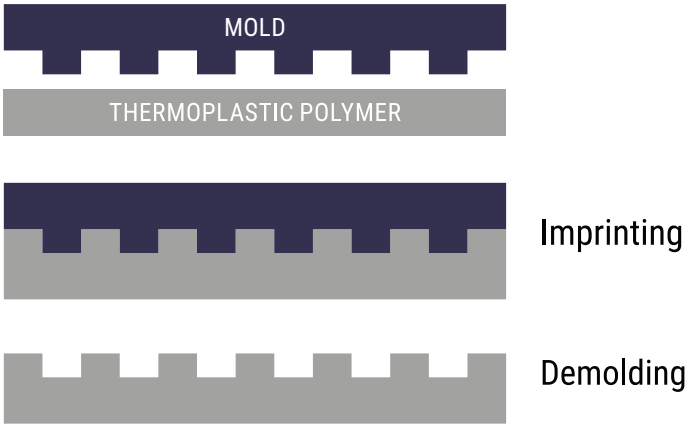
iv. ***Anticounterfeiting elements for the safety, authenticity and traceability of original products*** such as pharmaceuticals, automotive components/parts, food etc.

Industries: electronic circuit industry, semiconductor systems industry, energy industry, pharmaceutical and medical industry

INFRASTRUCTURE

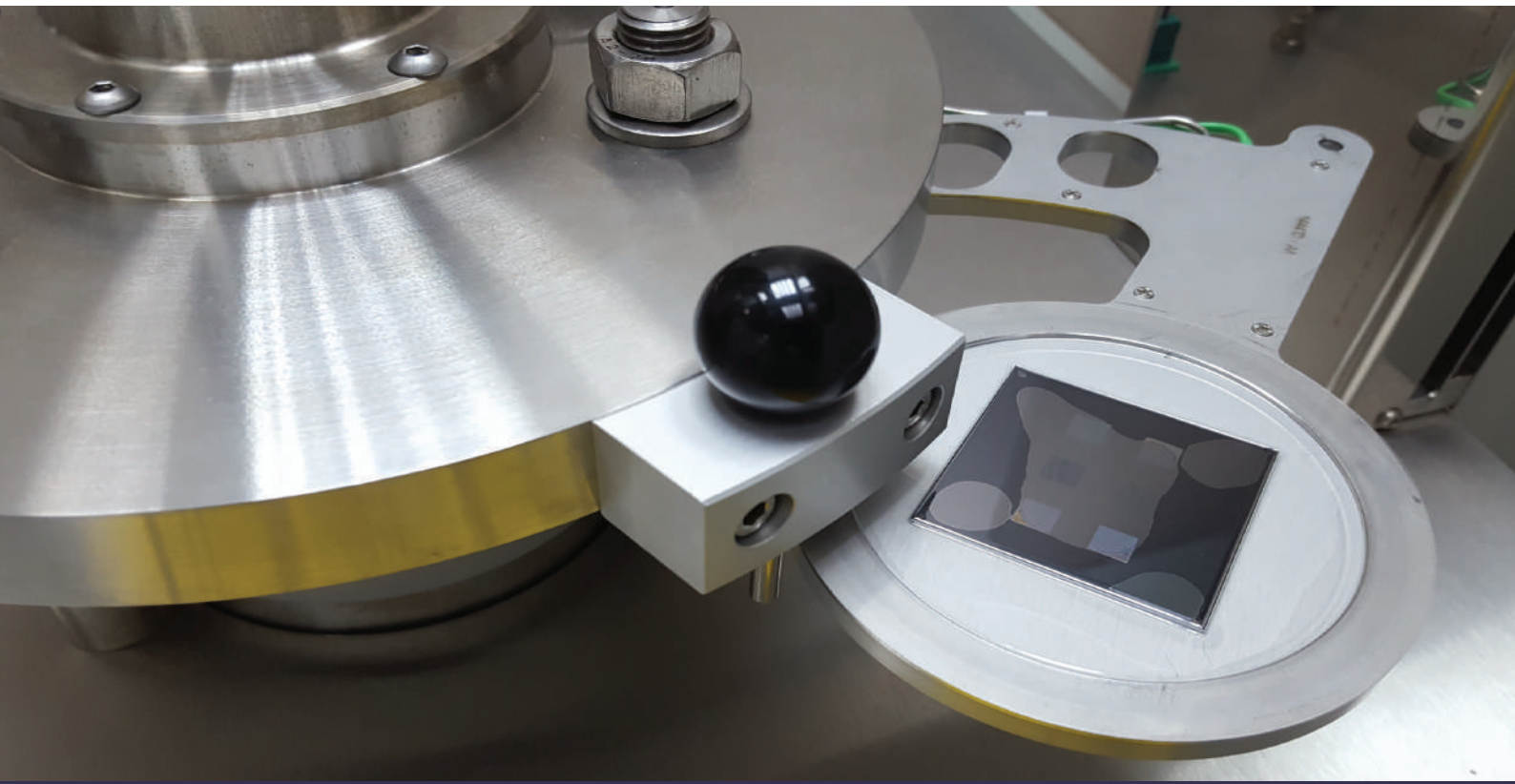
NIL Eitre® 3 system (Obducat, Sweden), located in the ISO-5 class 100 cleanroom from the Isotopic and Molecular Technologies Department, allows fabrication of micro/nanostructures on surfaces over a maximum area of 77 mm. It is also capable of thermal imprinting, UV irradiation or simultaneous imprinting (thermal and UV irradiation). The imprinting pressure results from air compression and reaches a maximum of 70 bar. The printing temperature can reach up to 200°C.

The UV module consists of a mercury lamp emitting in the standard wavelength range (250÷400 nm).



NIL schematic diagram

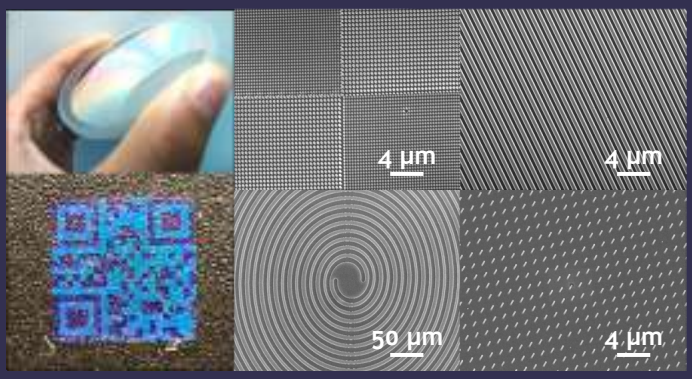
Mold (nanopatterned silicon) and the polymeric substrate to be imprinted



TYPICAL APPLICATIONS – EXAMPLES:

Product traceability – safety and counterfeiting elements in automotive industry. Our team has developed a quick response (QR) code in the form of a network containing nanoplillars with a height of 500 nm and alternating pitch of 300 nm and 400 nm used to fabricate QR codes in plastic and flexible substrates decoded using a cell phone camera. QR code nanoimprinting provides an additional security element due to its specificity and accessibility.

Biosensors and optical sensors. Our research team has successfully fabricated microfluidic channel systems on flexible substrates. These are to be incorporated as components in sensors and biosensors with medical applications.



(Left) Example of a CD-patterned mold used to fabricate dot-line patterned surfaces for computer data storage (top) and photographic image of a QR code based on a network containing nanopillars with a height of 500 nm and alternating pitch of 300 nm and 400 nm (bottom). (Right) Scanning electron microscopy images of nano- and microstructures fabricated by NIL using flexible polymeric substrates

ADVANTAGES

- Miniaturization of assemblies and sub-assemblies down to 10 nm compared to conventional technologies
- Outstanding detail accuracy
- Versatility of designs and materials
- Ease of working protocol
- Fast technique for replication of micro/nanostructured patterns on surfaces down to 8 cm

ESTIMATED COSTS

The price for the fabrication of customized micro/nanostructured surfaces by NIL will include the cost of making the mould, the substrate used, the time of use of the machine and the personnel costs.

Furthermore, the total costs can also be assessed according to the complexity of the pattern on the mold and the number of replicas made with the same mold.

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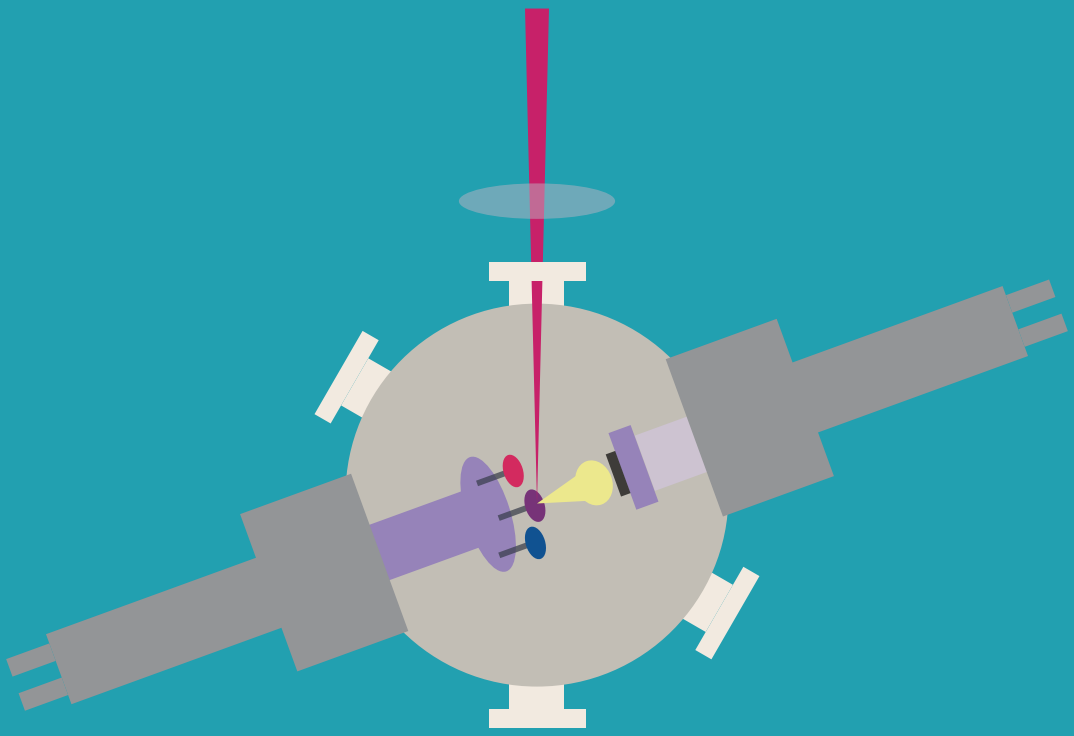
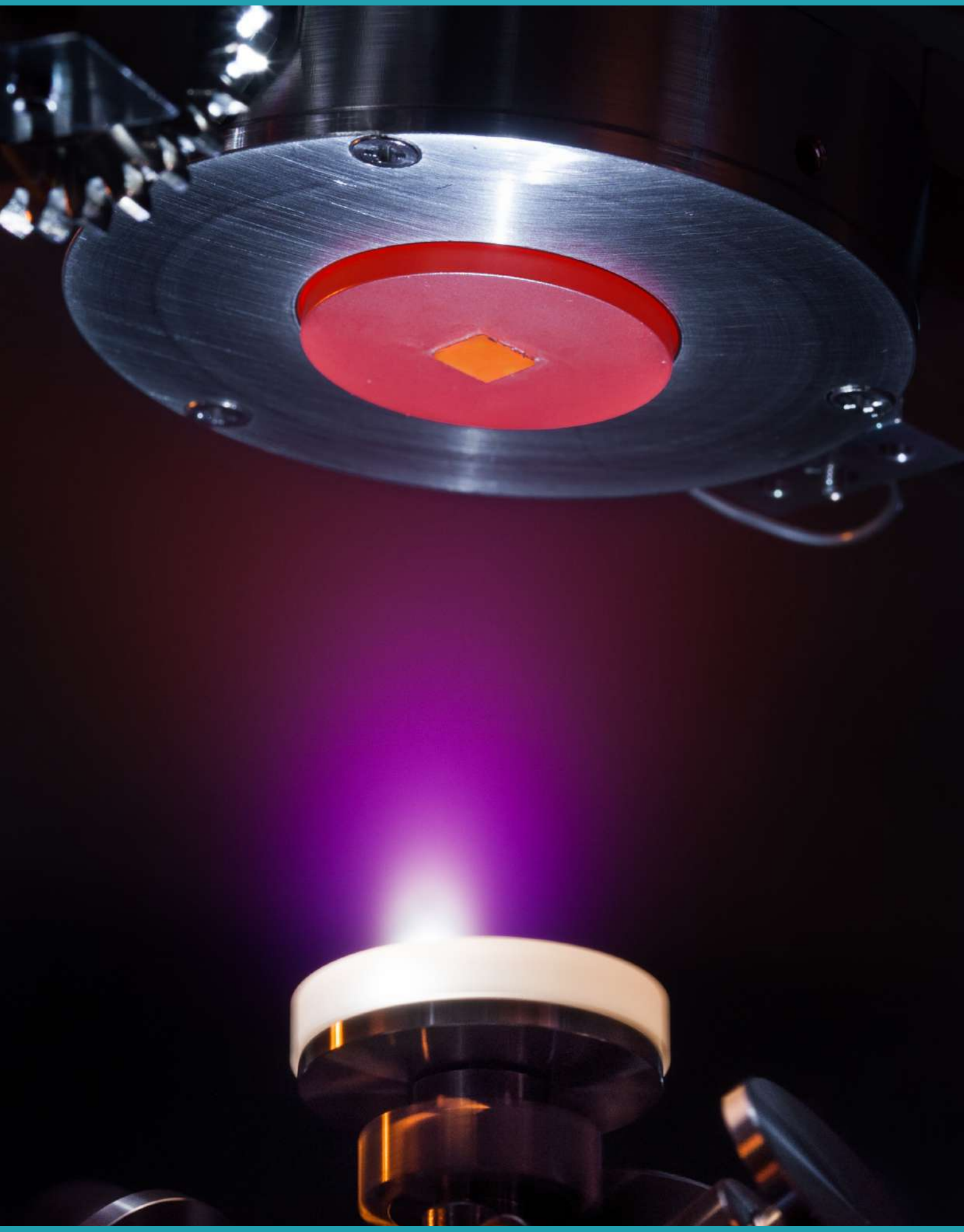
11.

THIN FILMS FABRICATION BY PULSED LASER DEPOSITION





THIN FILMS FABRICATION BY PULSED LASER DEPOSITION

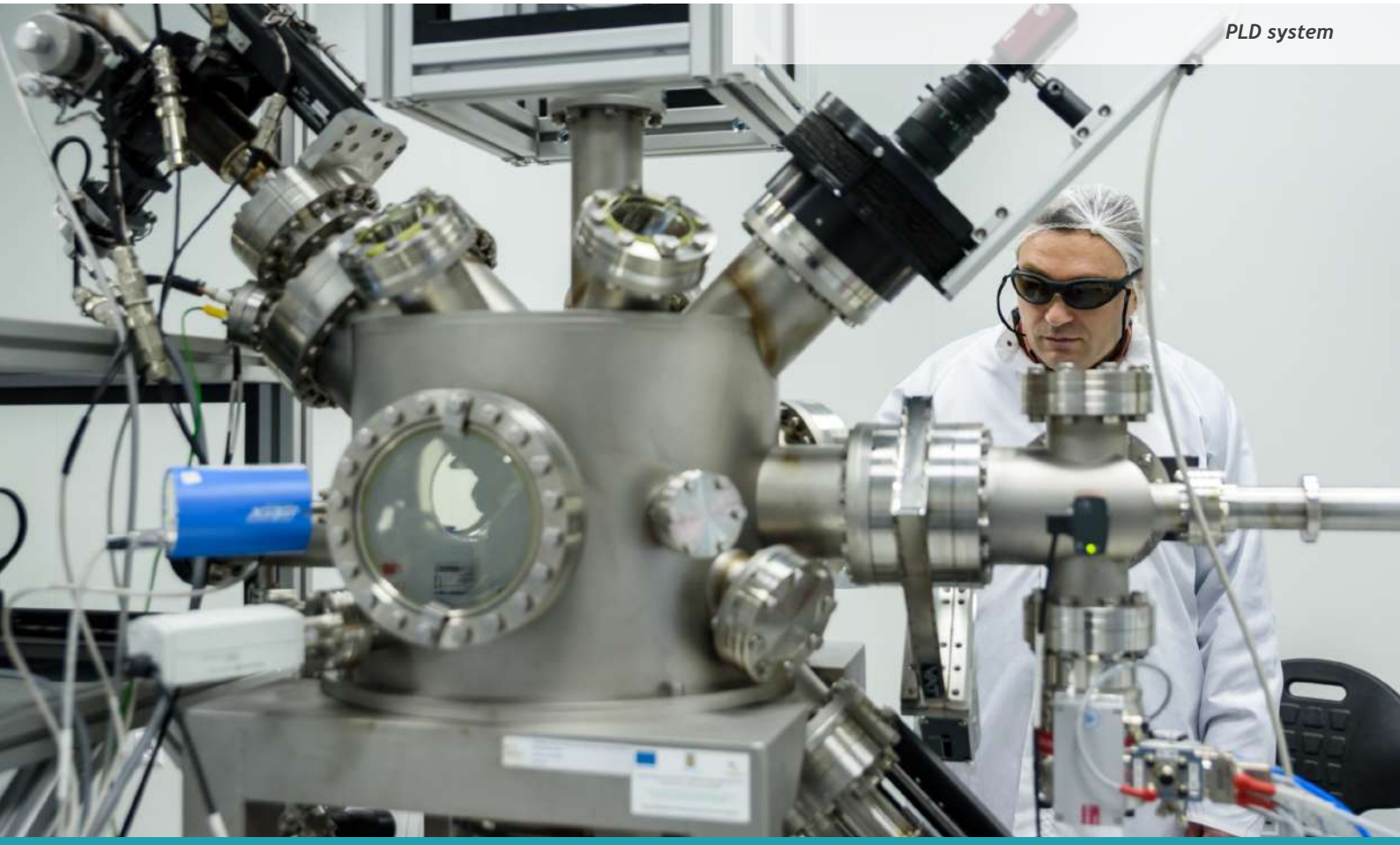
Keywords: *physical vapor deposition, pulsed laser deposition, thin films, thermoelectric materials*

DESCRIPTION

Thin films are structures that have one dimension much smaller than the other two (10 ÷ 100 nm). They are intensively used because of the properties that nanostructuring confers: enhanced charge transport, increased toughness and, in the case of semiconductor thin films, enhanced charge carrier motion in the plane of the thin film compared to the plane perpendicular to the film.

Pulsed Laser Deposition (PLD) is a physical thin film deposition technique using a high power pulsed laser beam. It strikes a target of the material to be deposited, vaporizes it, and displaces it from the target (in a plasma cone) onto a substrate (such as a target-facing silicon wafer) on which it is subsequently deposited as a thin film. This process can take place in high vacuum (10^{-9} mbar) or in the presence of a gas, such as oxygen which is commonly used for oxide deposition.

The processing of thin film materials allows easy further integration into different types of devices, and we now find them as component parts in transistors, capacitors, nonvolatile memories, sensors, thermo-, ferro- or piezoelectric materials or photovoltaic materials.



PLD system

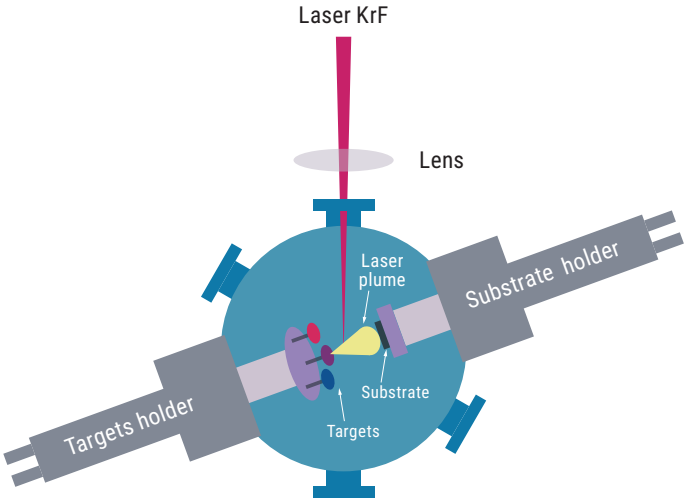
APPLICATIONS

Areas of application: thin films obtained by PLD – metals, semiconductors, oxides, organic materials, polymers, hybrid materials with organic and inorganic components – are used in optical engineering, optoelectronics, electronics, energy, magnetic applications, sensors or biomedicine.

Systems: thermoelectric devices, solar cells, electronic circuits, sensors, sensors, transistors, diodes, anti-reflection coatings, corrosion protection coatings.

Industries: energy, electronic circuits industry, semiconductor systems industry

PLD schematic diagram

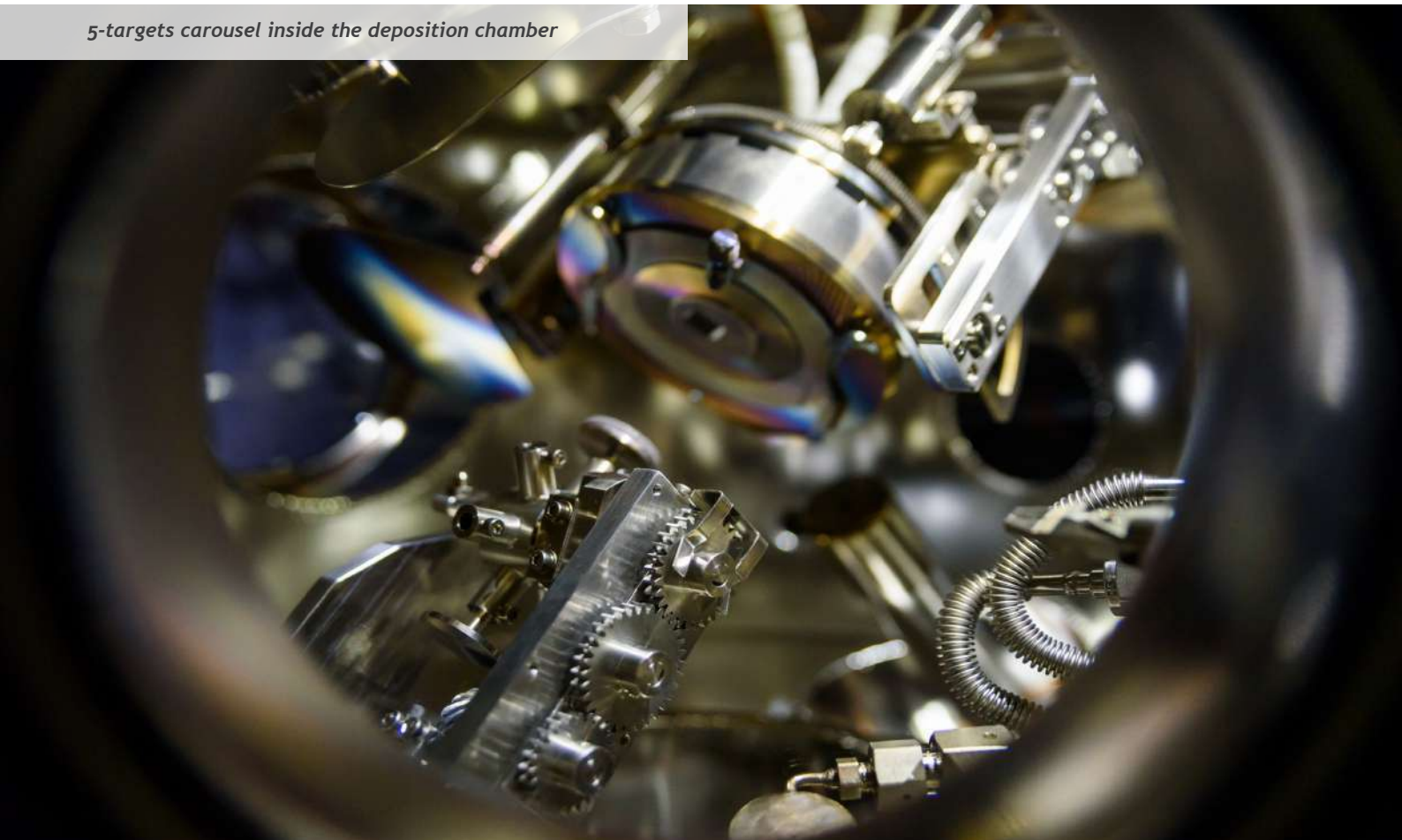


INFRASTRUCTURE

The thin film deposition system by pulsed laser ablation is located in the clean-room ISO-8 class 100,000 in the Center for Research and Advanced Technologies for Alternative Energies, INCDTIM Cluj-Napoca. The system includes:

1. 16” cylindrical deposition chamber
2. load-lock sample and target introduction chamber
3. high vacuum up to $5 \cdot 10^{-9}$ mbar obtained by a vacuum pump system composed of a 90 L/min preliminary pump and a 700 L/min turbomolecular pump
4. real time deposition rate monitoring by a Refraction High Energy Electron Diffraction (RHEED) system for in-situ operation
5. 5 port carousel for 1” targets with automatic movements in all three directions
6. heating mode for substrate temperatures up to 1000°C and automatic substrate movements in all three directions
7. 850 mJ Q-smart 850 mJ Nd:YAG laser in the wavelength range 670 ÷ 2600 nm
8. KrF excimer laser with wavelength 248 nm and energy 400 mJ
9. process gas flow control system, bake-out system, integrated electronics and software for deposition process automation

5-targets carousel inside the deposition chamber



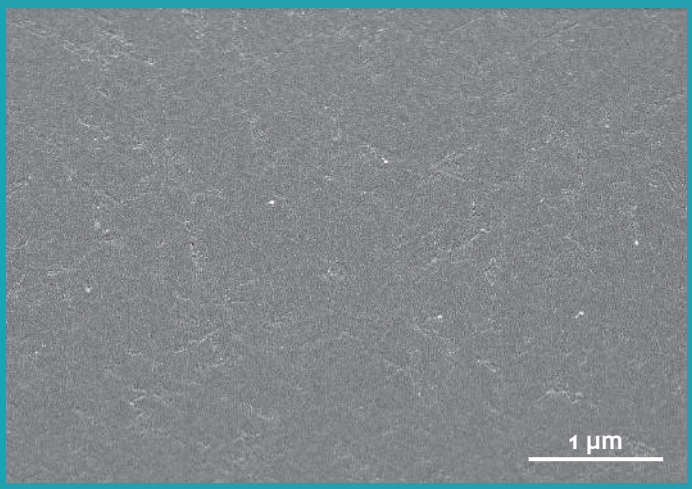
TYPICAL APPLICATIONS – EXAMPLES:

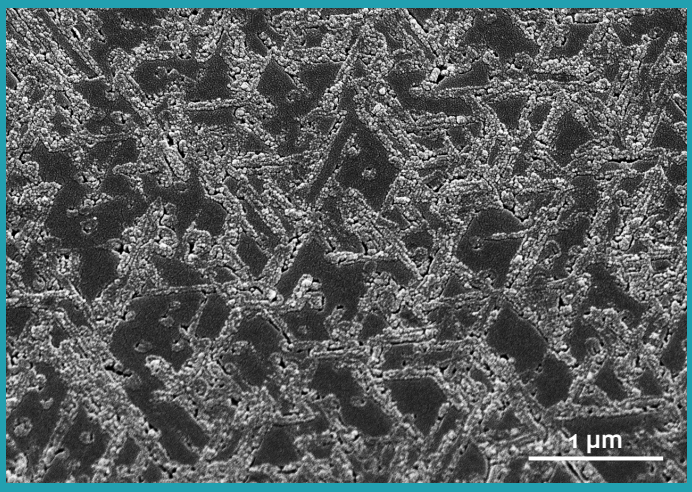
Worldwide, thin films have been rapidly assimilated in the semiconductor and optoelectronics industries, enabling the miniaturization of integrated circuits, diodes, transistors or LEDs. Today they are also found in the optics industry, integrated in anti-reflection coated lenses with mechanical resistance. There is also interest in the design of high-efficiency solar cells, as well as for anti-corrosion or decorative coatings on various surfaces.

Our research teams are using the pulsed laser ablation thin film deposition method for the development of new technological applications, and some examples are given below.

Deposition of thin films with high thermoelectric properties

We succeeded to deposit FeSi films doped with 1% Al and 1% Co and to control the concentration of charge carriers that contribute to the power factor of the thermoelectric material. These new materials have high melting points and chemical stability and promise good results in thermoelectric power generation.

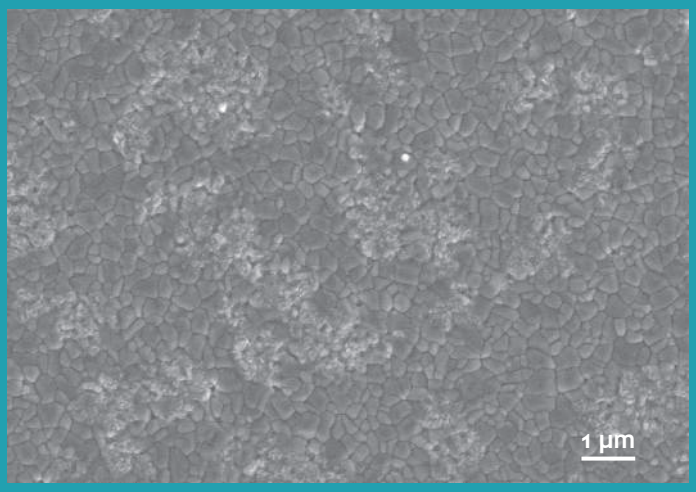




SEM images of thin films of FeSi + Al 1% (top) and FeSi + Co 1% (bottom) deposited at substrate temperature of 800°C

Fabrication of p-n junctions from semiconductor thin films of ternary copper chalcogenide chalcogenides

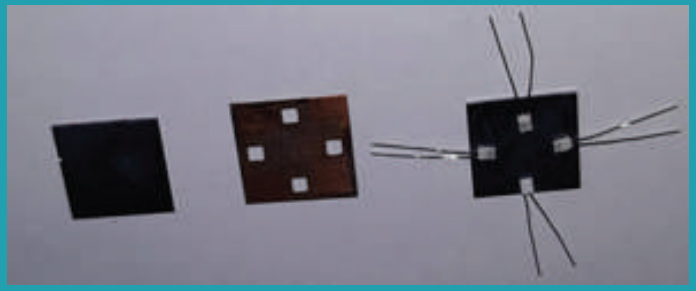
Our research team has succeeded in fabricating for the first time a p-n junction made of semiconducting thin films of ternary copper chalcogenide (Cu_3SbSe_3/Cu_3SbSe_4). Obtaining such a junction is a promising result for the future realization of a thermoelectric module for the recovery of thermal energy from various activities or from clean sources such as solar energy.



SEM image of Cu_3SbSe_3/Cu_3SbSe_4 thin film obtained by PLD

Thin film thermocouples for space thermoelectric generators

Our research is currently focused on the fabrication of a thermoelectric module for the next generation space thermoelectric generators. This thermoelectric module is fabricated on the basis of high performance thin films by series splicing of two thermocouples: the first one based on titanium dioxide and copper oxide thin films, TiO_2 and Cu_2O, and the second one based on ferrosilicon films, FeSi doped with 1% Al and FeSi doped with 1% Co.



Thin film on which Au contacts have been deposited by using a mask (middle); right: thin film on which temperature sensors have been added

ADVANTAGES

The versatility of the PLD technique offers a wide range of advantages, of which we can point out a few, namely:

- High flexibility in the choice of deposition parameters
- Precise control of growth rate and deposited layer thickness
- Thin film deposition of any type of material, including materials in metastable states, which cannot be deposited by other techniques
- Fabrication of mixed layers due to the built-in multi-target system
- Material stoichiometry is preserved in the transfer from target to substrate
- Deposition on substrates up to 50 mm in diameter
- Deposition can take place in both high vacuum and reactive oxygen atmosphere
- The radiation source is external to the deposition chamber

ESTIMATED COSTS

The price for pulsed laser deposition thin film will include the price of the deposition material and the substrate used, the KrF gas used by the laser, the sample preparation operation, as well as the system operating time and labor.

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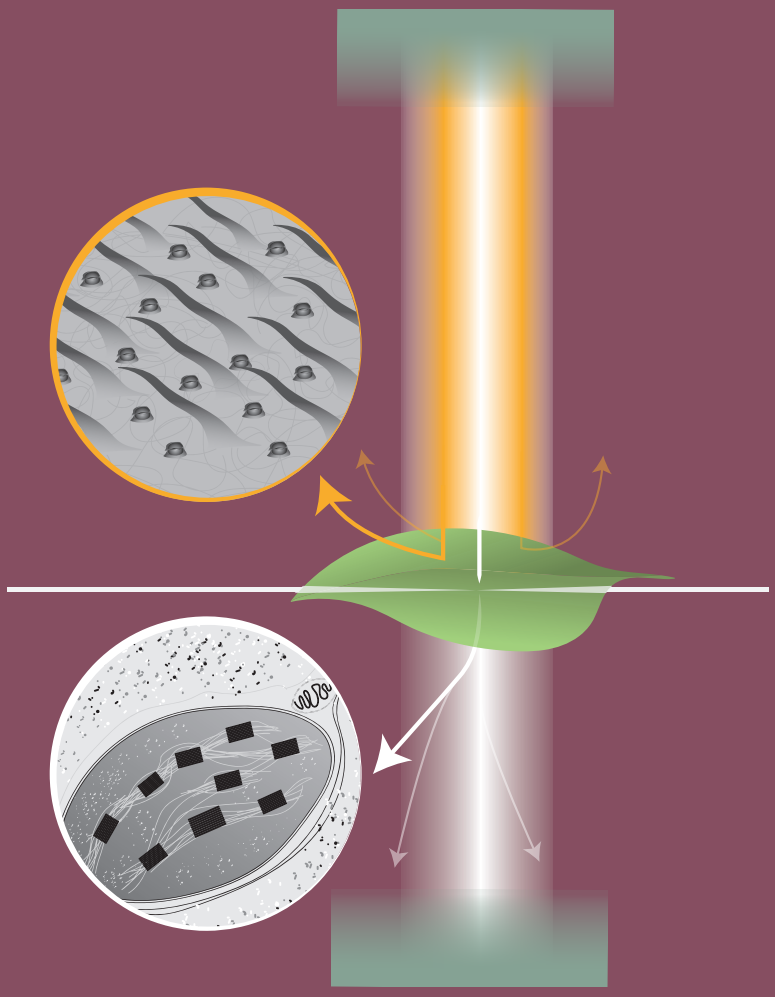
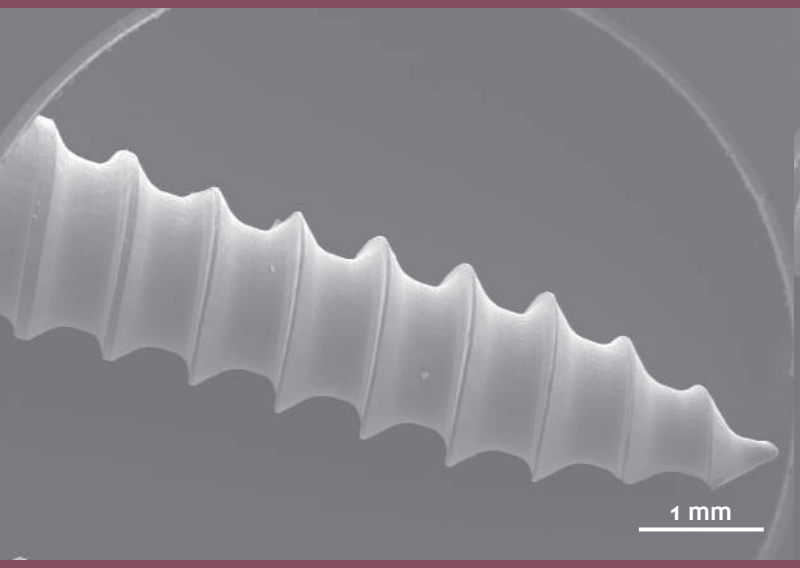
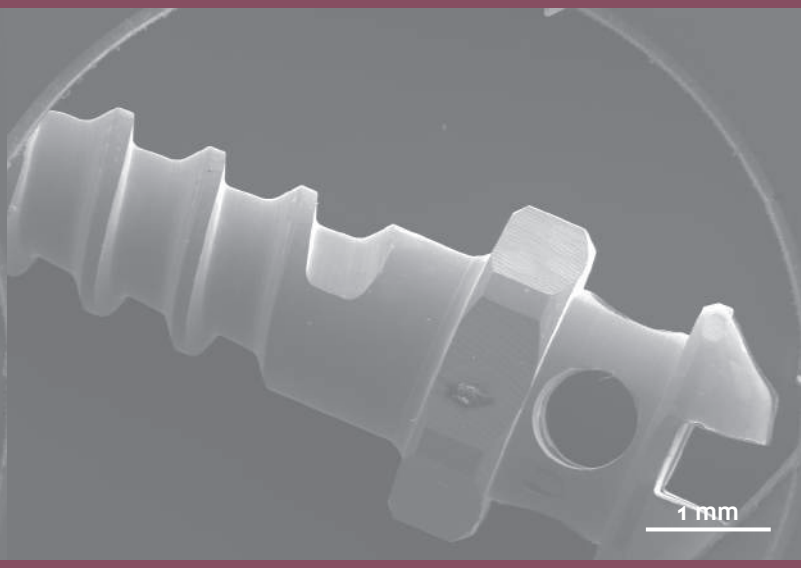
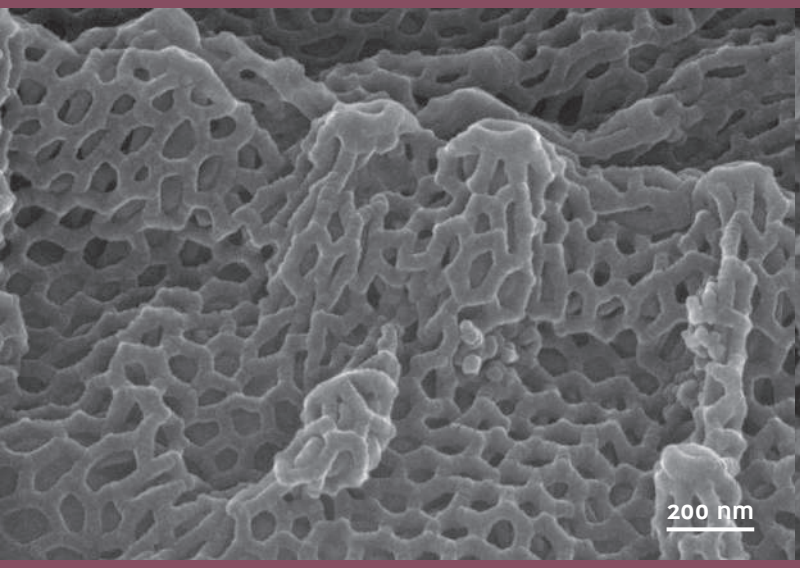
12.

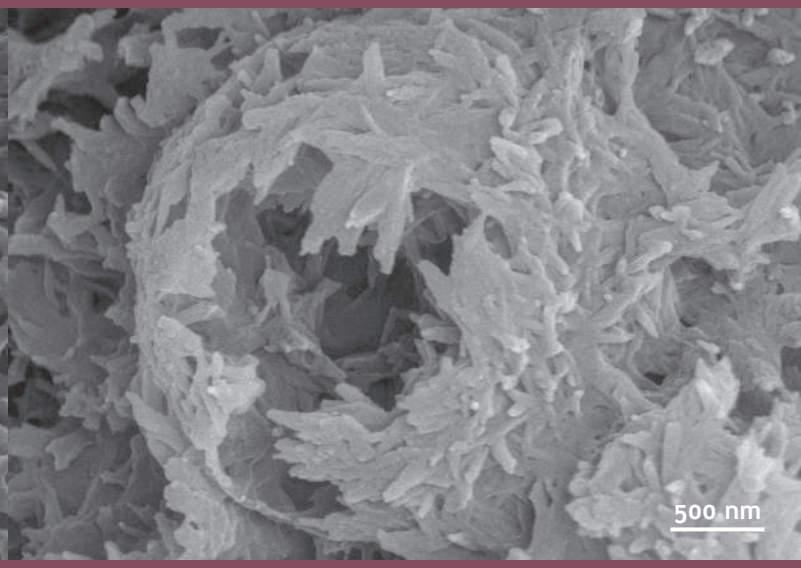
ELECTRON MICROSCOPY

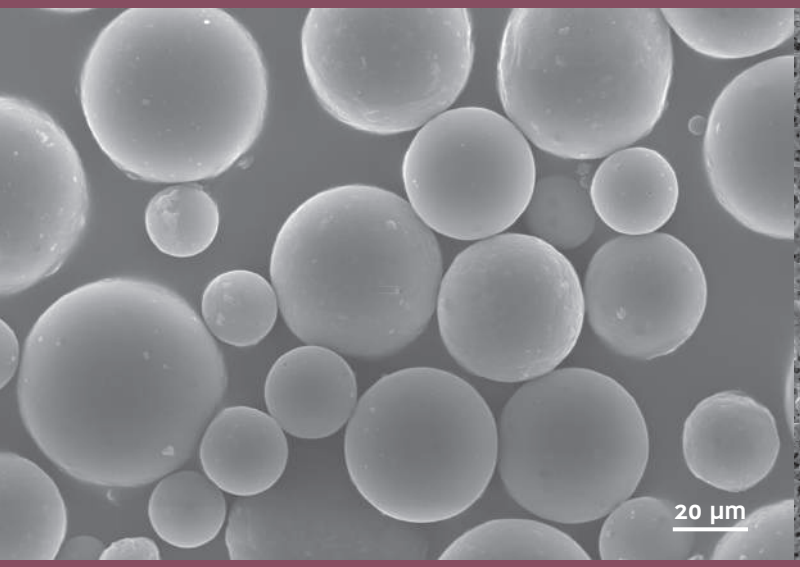


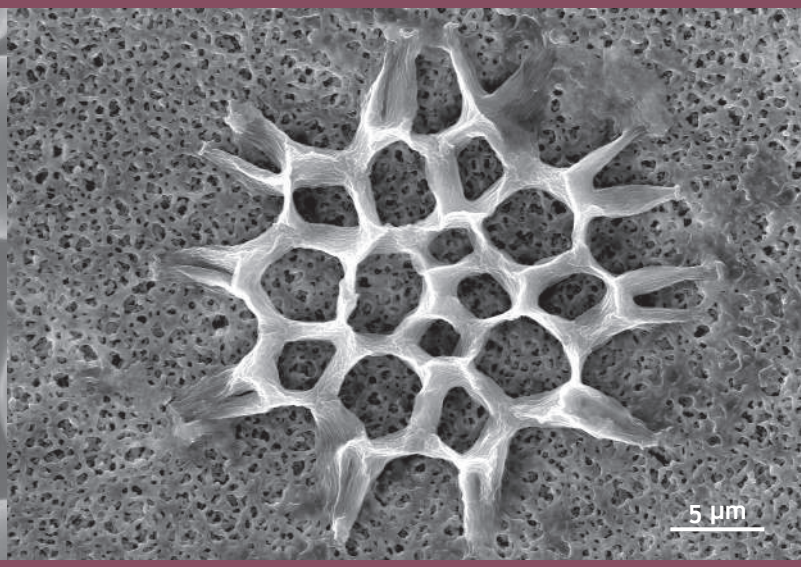

1 mm


1 mm


200 nm


500 nm


20 µm


5 µm

ELECTRON MICROSCOPY

Keywords: *electron microscopy, SEM, transmission electron microscopy, TEM, X-ray scattering, EDX, morphological and topographical characterization of surfaces*

DESCRIERE

Electron microscopy is a stand-alone or complementary, non-destructive characterization technique with which the surface structures (SEM) or internal structures (TEM) of solid samples (organic, inorganic, metallic, non-metallic, biological, etc.) can be analyzed.

Electron microscopy is a technique to obtain details of nano-/microstructure/topography that cannot be obtained by optical/fluorescence microscopy or AFM. In comparison to optical microscopy, where the maximum theoretical resolution stops at 154 nm, the resolution of the transmission electron microscope (for internal structures) can reach 1 Å (0.1 nm) and the scanning electron microscope can reach a resolution of 10 Å (1 nm). The resolution determined is dependent on the type of sample and the working conditions of the apparatus: the lowest resolution (5-6 nm) is obtained for electrically insulating (non-metallic) samples, and the best resolution is obtained for gold samples, more precisely for Au evaporated on carbon (0.1 nm).

In terms of the type of information provided, SEM provides only topographic images (like a binocular steromicroscope/camera) and TEM provides only information about internal structures (like a compound optical microscope). Due to these conditions, preparations must be small for TEM (powders, colloids, nanometer sections) or can be larger for SEM (up to 2-4 cm).

Electron Microcopy Facility

Complementary with SEM/TEM, we have expertise in the technique of elemental analysis by X-ray scattering spectroscopy (EDX) with which it is possible to determine the distribution of elements over the entire surface (map).

TEM technique can provide information about the crystallization state of materials, the percentage atomic composition, the ultrastructure of tissues and cells, and the nanometric size of the components of a product.

With SEM technique it is possible to obtain information about the roughness of a surface, particles attached to a surface/contaminants, particle size, distribution of atomic elements in the material (homogeneity/heterogeneity).

With EDX and EBSD techniques, qualitative and semi-quantitative percentage information about the atomic elements present in the material, their distribution in the sample, shape and composition of crystals and crystal grain boundaries in alloys are obtained. All atomic elements with Z greater than 3 (all elements, except H, He, Li) can be detected, the detection being from the volume, not only from the surface.

APPLICATIONS

Areas of applications: industry, research, medicine, pharmacy, forensics, heritage evaluation

Systems: solid objects, powders and nanomaterials, chemically fixed and/or dehydrated biological materials

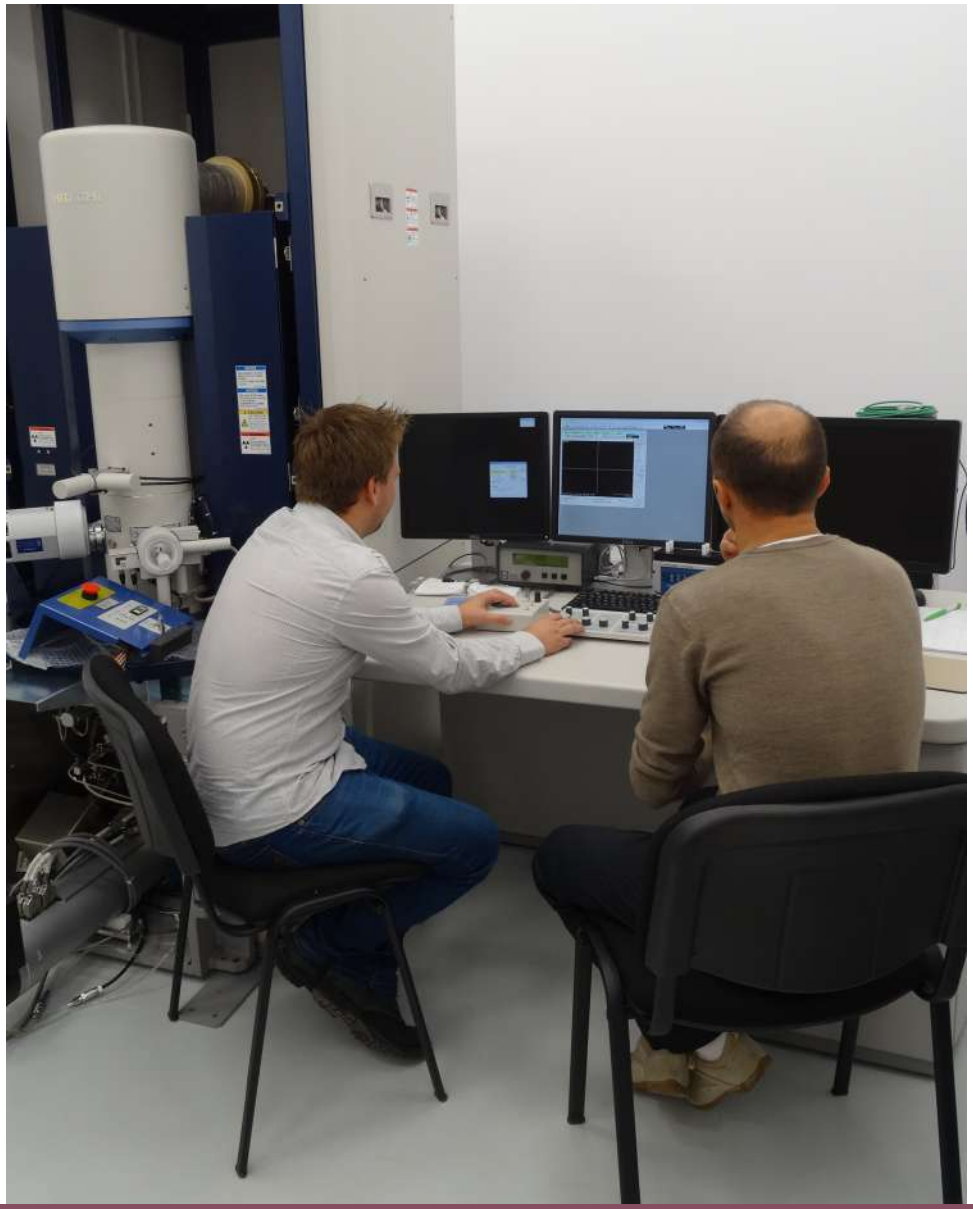
Industries: quality control of material surfaces (raw/final product), alloys, microcircuits; measurement of nano-microsized objects, imaging detection of biofilms on surfaces

INFRASTRUCTURE

Hitachi SU8230 scanning electron microscope with 30÷500× magnification, maximum resolution ~1 nm, for objects up to ~4 cm × 4 cm × 1 cm (L × W × H).

Hitachi HD2700 scanning-transmission electron microscope, 500÷1,000,000× magnification, maximum resolution ~0.1 nm, for nanopowders or colloids.

Oxford Instruments EDX and EBSD detectors and AZtec analysis software.



Hitachi HD2700 TEM

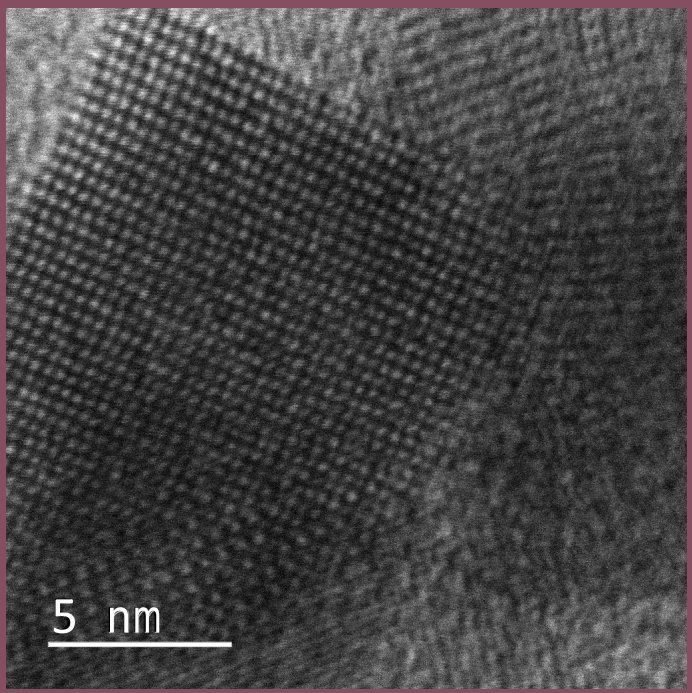
TYPICAL APPLICATIONS – EXAMPLES:

Detection of bacterial biofilms: very important in the case of surgical implants or medical disposables that are inserted into the patient's body (needles, drainage tubes, urinary catheter, etc.), as the presence of bacterial biofilms can mean inflammation, implant rejection or even sepsis.

Quality of air, soil, water and pollution: after filtering the air in a room or open space on a special filter cloth, the presence of airborne metallic or other particles can be detected by SEM/TEM technique, which is becoming very important in factories, plants, construction sites, cities, etc.

Microchips, semiconductors and sensors: analysis of production defects, presence of impurities, micro/nano deformations, scratches, etc.

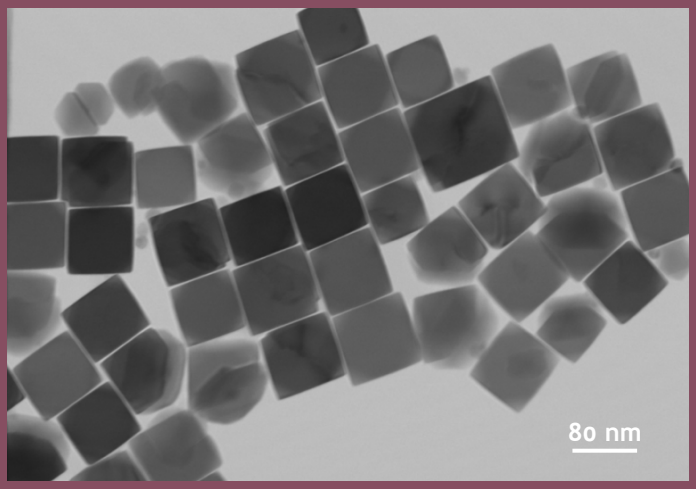
Micro-/nanopatterned materials (micro-/nanopatterns): analysis of materials obtained by (nano)lithography or other techniques used in special industries (augmented reality devices, optical sensors, medical chips)

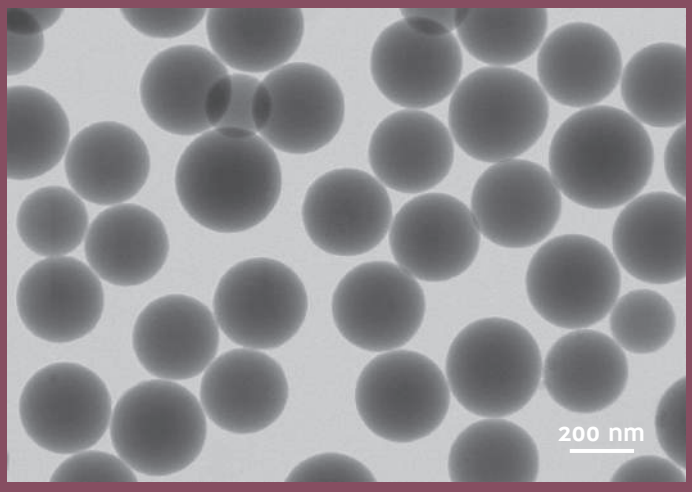


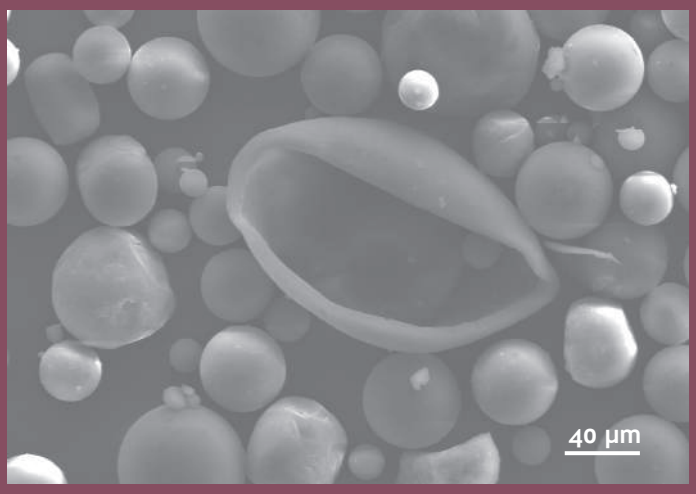
Granularity, powder size, fiber size: nano-/micromaterial analysis

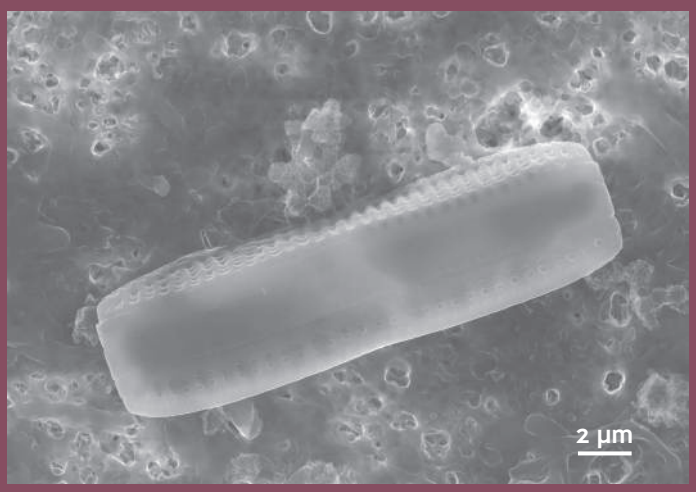
Precise species determination for specific insects, molluscs, plants/spores using nanometric morphological characters present on the surface

Biocompatibility of materials: analysis of implant materials with cells of interest attached from culture or target tissue









ADVANTAGES

- INCDTIM offers RD&I services based on SEM/TEM electron microscopy, providing images of the analyzed surface
- Pre-processing of the sample is rarely necessary, especially for less electron-conducting materials
- Complementary techniques with AFM, optical, fluorescence or confocal microscopy or other instrumental analysis techniques (XRD, SERS/Raman, FTIR)

ESTIMATED COSTS

The total cost of RD&I services based on electron microscopy consists of two components:

- microscope usage time, which includes consumables and wear
- labor, which includes personnel and indirect costs associated with sample preparation, analysis and interpretation of results, preparation of the analysis/research report.

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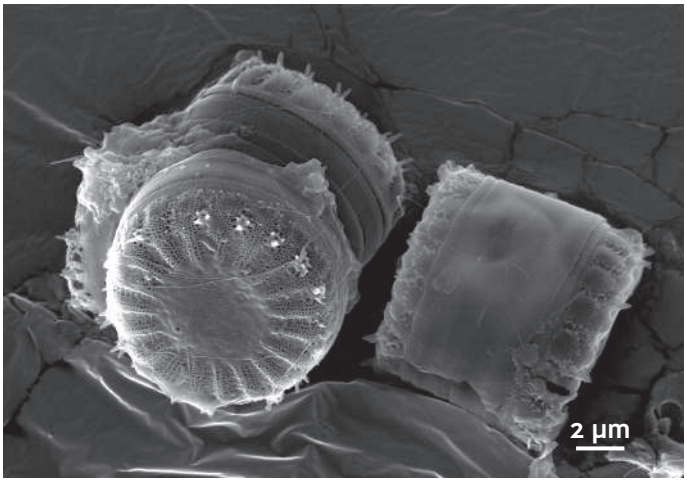
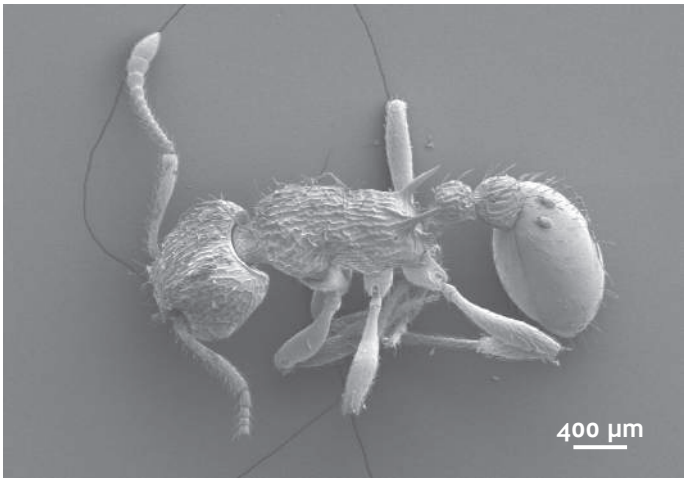
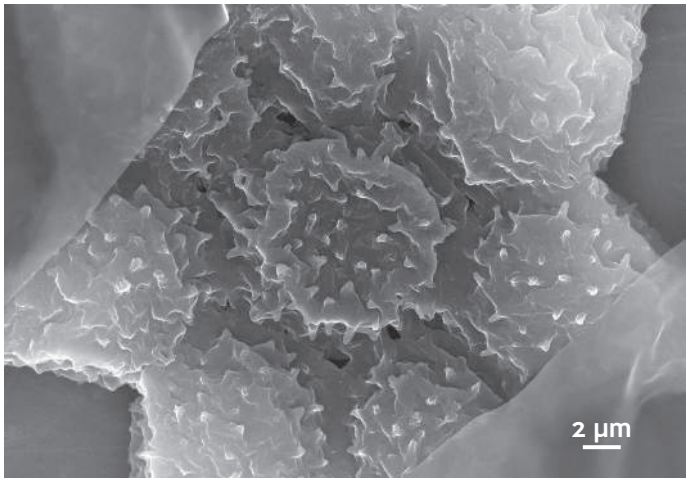
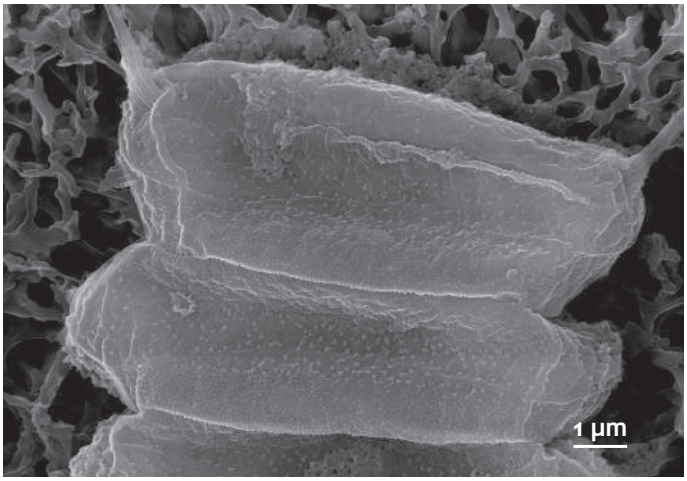
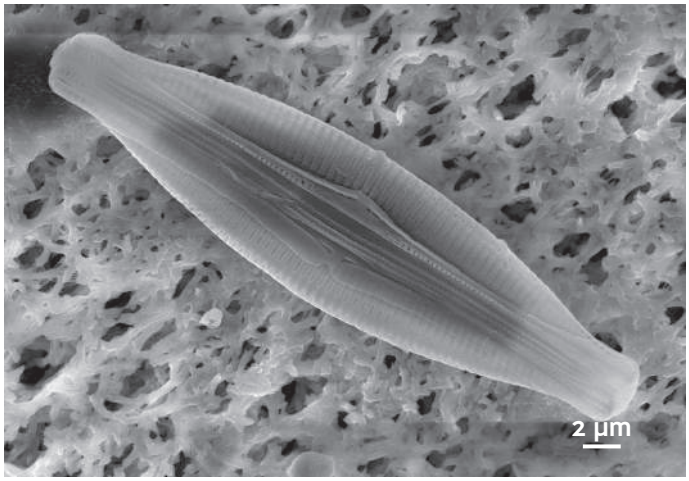




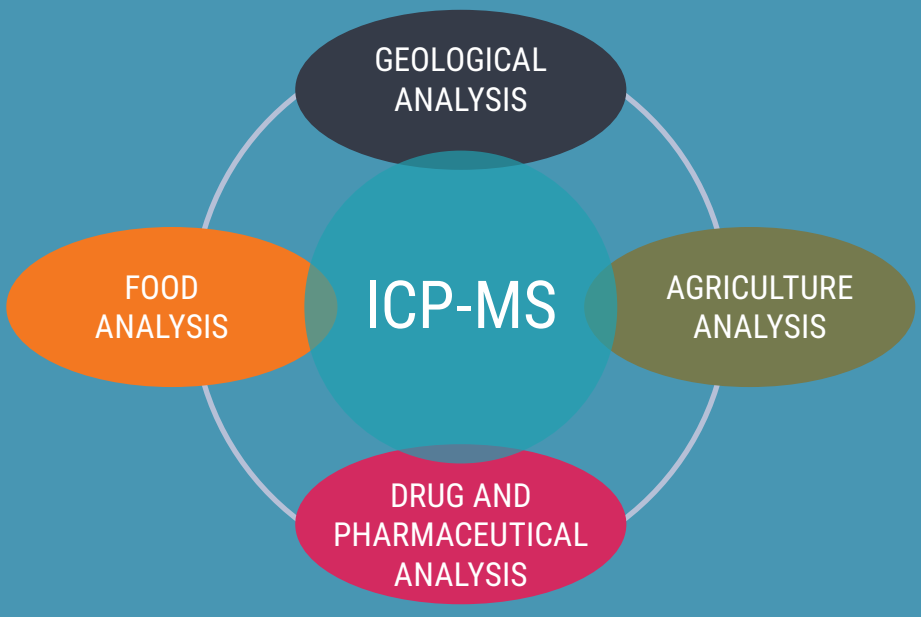






13.

INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY



INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY

Keywors: *inductively coupled plasma mass spectrometry, ICP-MS, elemental determinations, toxicity*

DESCRIPTION

Inductively Coupled Plasma Mass Spectrometry (ICP-MS) is a highly sensitive and selective analytical technique used for elemental determinations. It is based on the separation, identification, and quantification of a sample's components in relation to their mass.

ICP-MS has superior advantages over other analytical techniques, such as atomic absorption or optical emission spectrometry:

- ∫ detection limits for most elements equal to or better than those obtained by graphite furnace atomic absorption spectroscopy (GFAAS)
- ∫ ability to handle simple and complex arrays with minimal matrix interference due to the high temperature of the ICP source
- ∫ high sensitivity and low background signals allow very low detection limits
- ∫ possibility of obtaining isotopic information
- ∫ short analysis time
- ∫ ability to measure most elements, including alkaline, alkaline-earth, and some non-metals

ICP-MS Spectrometry Laboratory

APPLICATIONS

Areas of application: research-development; environment – impact of environmental pollution on the human body, pollution/depollution; food safety; biomedical – trace element identification, circulation and metabolism of pharmaceutical compounds, food and food supplements; nutrition-pharmacology; toxicology; geochemistry; archaeometry – characterization of ceramic artifacts, raw materials, $^{206}Pb/^{207}Pb$ and $^{87}Sr/^{86}Sr$ isotope ratio studies to determine the origin of artifacts; industry.

Matrices:

i. *drinking water, alcoholic/non-alcoholic beverages, food products of plant/animal origin, food packaging, cigarettes, agricultural fertilizers*

ii. *medicines and food supplements*

iii. *raw materials and cosmetics*

iv. *water, soil, sediments, vegetation*

v. *alloys, ceramics, paints, pigments, paper, plastics, glass*

Industries: chemical industry, agro-food industry, pharmaceutical industry, health, cosmetics, environment

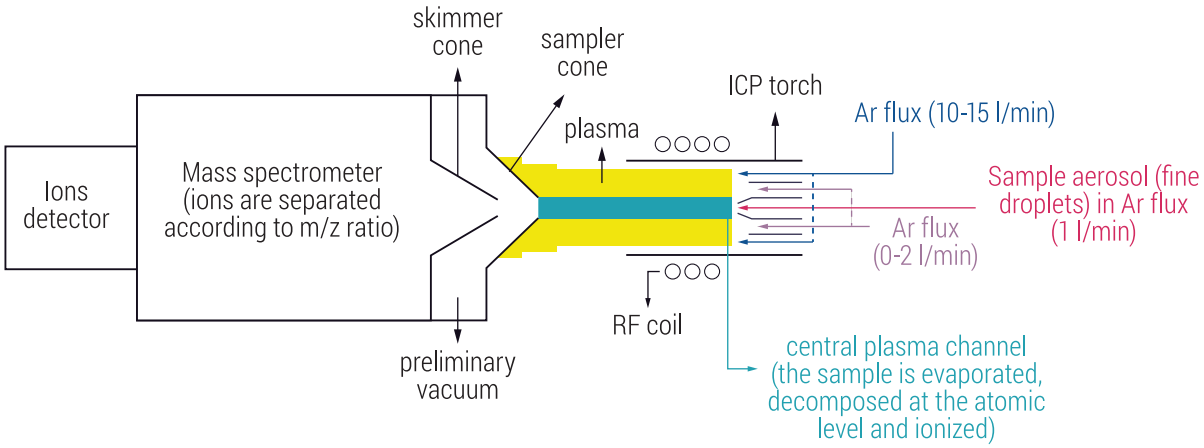
INFRASTRUCTURE

The ICP-MS spectrometry laboratory is equipped with an **ELAN DRC(e) PerkinElmer** inductively coupled plasma mass spectrometer ELAN DRC(e), which allows rapid multi-element analysis, with detection limit 0.001-0.01 µ g/L, accuracy <2% over 20 min.

The ICP-MS spectrometer is equipped with a **quadrupole mass analyzer**, using plasma generated at atmospheric pressure using a radiofrequency field in an argon stream as an ion source.

ICP-MS Elan DRC-e Spectrometer

ICP-MS schematic diagram



ICP-MS Elan DRC-e Spectrometer

TYPICAL APPLICATIONS – EXAMPLES:

Determination of toxic elements in environmental matrices. Sensitivity, accuracy and repeatability of the ICP-MS method are important and useful characteristics in the determination of **trace and ultra-trace element concentrations in environmental samples** (water, soil, sediments) suitable for pollution monitoring. The determinations are of real use for the preparation of assessment studies in areas suspected of toxic metal pollution. **Rare earths and isotopic ratios** (in the case of strontium and lead) measured by this method provide information on the **sources of the pollutants** and the results obtained can be used to create a fingerprint of environmental samples.

ICP-MS allows monitoring of water or soil pollution

Determination of macroelements and toxic metals in food matrices. Population impact assessment. With the intense anthropogenic impact on nature, it is very important to control the content of elements in foodstuffs. By processing them, heavy metals do not decompose, their concentration per unit mass increases and thus they can accumulate in the human body and intracellular biochemical processes are slowed down or even blocked.

The determination of concentrations of elements in food products of animal/plant origin is very important because of their nutritional and toxicological relevance to human health. Trace concentrations of toxic trace elements can be determined to investigate the effects of industrial contamination or to differentiate products from different animals/cultures or production systems. Essential and decisive mineral elements for the maintenance of human health can also be determined.

ICP-MS allows control of heavy metals in food

Beverage authenticity and chemical safety studies. ICP-MS spectrometry is a useful tool for the elemental characterization of alcoholic beverages, and the method has been validated and implemented in the laboratory. The low detection limits (<0.3 µg/L) and good linearity provide the minimum limit of quantitation required for quantitative determinations of trace and ultra-trace elemental concentrations in alcoholic samples.

ICP-MS allows elemental characterization of wines

Knowing the mineral composition of wines is of particular importance in:

i. winemaking, to control physico-chemical stability and organoleptic properties

ii. detection of contaminants in wine

iii. assessing nutrient intake in the daily diet through rational wine consumption

iv. tracing counterfeit wines

v. the possibility of recognizing the area of origin of a wine on the basis of its mineral and trace element composition, correlated with the elemental composition of the soil in the wine-growing area.

The assessment of the total composition of beers, including the determination of majority and minority elements, is of real interest to producers and consumers as, depending on the concentration and type of metal, they can be nutritive or toxic to the human body. Total beer content data are recognized to be valuable for differentiation and classification of beers, as metals are good descriptors reflecting the composition of the natural raw materials (water, grain, yeast, malt) used in the production process, and are also indicators of other processes involved in brewing, such as storage and preservation.

ADVANTAGES

- INCDTIM offers RD&I services based on inductively coupled plasma mass spectrometry (ICP-MS), used on its own or in combination with other complementary analytical techniques covering almost the whole range of practical applications.
- We offer consultancy before entering into a contractual relationship to ensure the most accurate understanding of the customer/partner's requirements.
- Existing facilities allow us to address most of the ICP-MS methods used in current practice, many of which have already been validated and implemented in our laboratory.
- We have specialized staff able to cover with the highest professionalism all stages of a contractual collaboration: the definition of the problem to be solved, experimental design, and interpretation of results.

ESTIMATED COSTS

The total cost of RD&I services based on inductively coupled plasma mass spectrometry consists of two components:

- spectrometer usage time, which includes consumables and wear
- labor includes personnel and indirect costs associated with sample preparation operations, analysis and interpretation of results, and preparation of the analysis/research report.

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14.

GAS CHROMATOGRAPHY

GAS CHROMATOGRAPHY

Keywords: *organochlorine pesticides, QuEChERS, GC-ECD*

DESCRIPTION

"A residue is a minute amount of active substance from a pesticide that may remain in a treated crop", according to the European Food Safety Authority (EFSA). Consequently, the European Commission has established Maximum Residue Levels (MRLs) to ensure consumer protection against unacceptable levels of pesticide residues.

The development of analytical techniques is increasingly focused on the precis detection of molecules present in infinitesimal quantities.

Due to their high heterogeneity, pesticides are chemicals that are difficult to classify. They play a crucial role in achieving the desired productivity in modern agriculture, and it is likely that they will remain indispensable in the future. Without these agrochemicals, it is practically impossible to grow enough vegetables and fruits to feed the world's growing population.

However, despite their indispensable role in crops production, pesticides are hazardous substances with harmful effects on the human body.For this reason, there is growing concern about food safety and quality.

The strict regulations established by the European Union and the World Health Organization, aimed at preventing the contamination of food products and environmental elements with pesticides, necessitate the development of appropriate analytical methods for **detecting target analytes at very low concentrations**. Additionally, even when the analyte is already present in a solution (e.g. in water or juice), there are many practical difficulties to overcome. These challenges are relate to the **sensitivity and selectivity** of the chosen technique, as **the concentration of interfering compounds in the matrix is much higher than that of the analyte of interest**.

Cromatografia de gaze permite identificarea și cuantificarea reziduurilor de pesticide din matrici alimentare și de mediu

The physical and chemical properties of pesticides vary significantly, making the determination of their residues in any matrix quite difficult, leading to numerous problems in developing an universal method for the analytical determination of residue.

In 2003, Anastassiades *et al.* developed and introduced a new extraction method for determining pesticide residues, which they named **QuEChERS** (Quick, Easy, Cheap, Effective, Rugged, Safe).

To **significantly reduce testing time** and provide **fast and reliable results**, our laboratory **optimized the QuEChERS extraction method and developed a multi-residue method for the simultaneous separation, identification and quantification of 30 types of pesticides**. The analysis is completed in less than 30 minutes.

INFRASTRUCTURE

The Gas Chromatography laboratory, part of the Department of Mass Spectrometry, Chromatography, and Applied Physics, is equipped with ***an electron capture detector (GC-ECD), Trace GC Ultra, Thermo Fisher Scientific***.

- ✓ The equipment meets the requirements of modern laboratories, provides high productivity and increased sensitivity.
- ✓ ***Trace GC Ultra*** platform combines the reliability of TRACE GC with extensive system utilization, performance and automation.
- ✓ A major advantage of the ECD detector is its **sensitivity to halogenated compounds**, enabling **extremely low detection limits** for many of these compounds.
- ✓ Another advantage of the ECD detector is its **selectivity for electronegative compounds**. The response factor, and therefore selectivity, can vary between 1 and 106, depending on the degree of electron affinity of the molecules.

Trace GC Ultra Thermo Fisher Scientific Inc. Gas Chromatograph with Electron Capture Detector GC-ECD

APPLICATIONS

Areas of application: research and development, smart specialization fields in Bioeconomy

Systems:

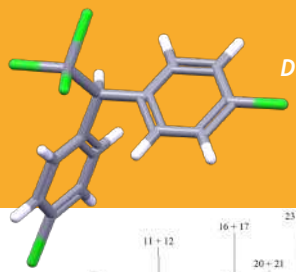
i. Identification and quantification of **pesticide residues in food**, plant and environmental matrices

ii. Testing for a **wide range of pesticide residues** to ensure compliance with maximum residue limits (MRLs) set by the European Union for various matrices

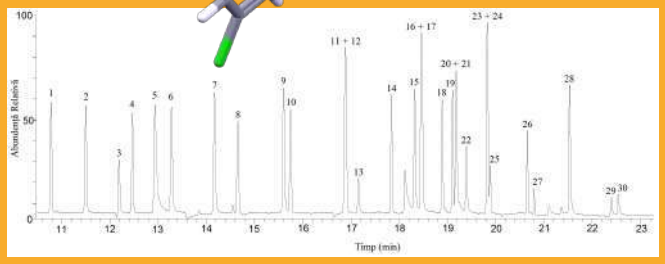
Industries: agro-food industry

- ✓ vegetable and fruit producers using conventional agriculture
- ✓ vegetable and fruit producers interested in transitioning to organic agriculture
- ✓ soil investigation and remediation activities, and land conversion
- ✓ dairy and cheese production sectors, targeting contamination with pesticides along the water – soil – feed – dairy products chain

TYPICAL APPLICATIONS – EXAMPLES:



DDT Dichlorodiphenyl-trichloroethane molecule



GC-ECD chromatogram of a standard mixture of the 30 monitored pesticides

Pesticide residue analysis is an important parameter in food quality control and quality assurance studies

Our proposed optimized method consists of QuEChERS extraction, separation, detection and quantification. The concept of QuEChERS is to remove unwanted compounds from food matrices. The main advantage of this method is that it is comprehensive, providing high recovery factors for most types of pesticides.

Detection and quantification of pesticide residues in vegetables

Vegetables are complex matrices which contain, in addition to the target analytes, other interfering compounds (sugars, fats, pigments, chlorophyll, etc.), which may distort the analytical result.

GC-MS allows detection of pesticides in vegetables

Plant matrices with high lipid content are problematic because they contain fats and waxes that can interfere with the analysis and detection of pesticides.

The optimized method proposed by our institute can be used to monitor 30 pesticides in different categories of vegetables - organic/conventional and greenhouse/open-air – sold in supermarkets and agro-food markets for quality control in terms of pesticide residue content.

Detection and quantification of pesticide residues in berries

In berries the major analytical problem arises due to the complexity of the matrices and the presence of interferents such as pigments. Gas chromatography with electron capture detector has shown high sensitivities for organochlorine compounds.

To differentiate the type of growth of berries (wild vs. cultivated), our proposed optimized method can be used to monitor the presence of 30 pesticides in berries traded in supermarkets and agro-food markets for quality control in terms of pesticide residue content.

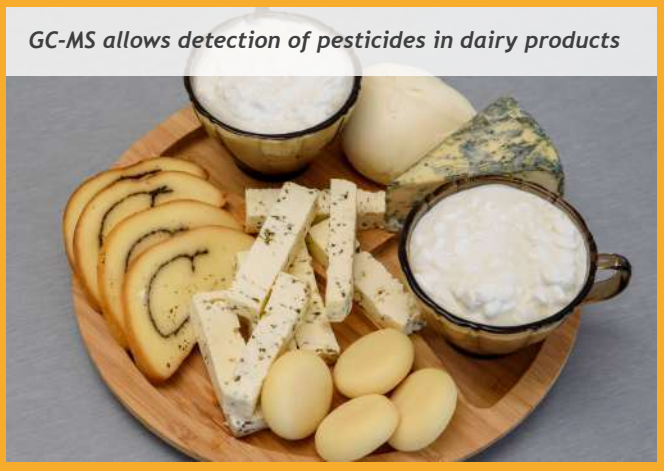
GC-MS allows detection of pesticides in fruits

Detection and quantification of pesticide residues in milk and milk-derived products

Milk is a complex biological matrix and its constituents in addition to water are high molecular weight organic substances (proteins, lipids, carbohydrates, etc.) which invariably interfere with the extraction and quantification of pesticide residues.

Our optimized method for monitoring the presence of 30 pesticides in milk and milk-derived products is reliable with high linearity, sensitivity, selectivity, precision and accuracy.

GC-MS allows detection of pesticides in dairy products



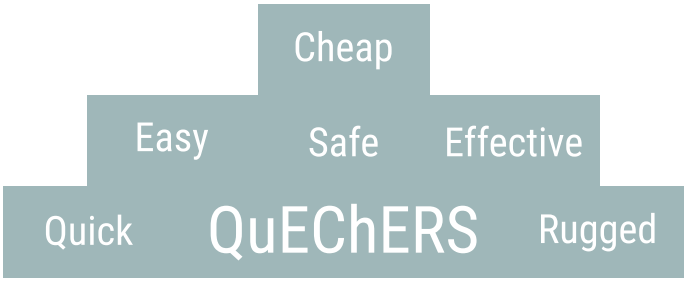
Detection and quantification of pesticide residues in environmental media - water, soil

The presence of pesticides in environmental samples (water, soil, vegetation) is another issue of major concern, both for product quality and in the context of food safety, which may subsequently, following the natural pathway, end up in consumer vegetables, fruits, milk and dairy products.

Soil is a complex and heterogeneous matrix with a porous structure containing both inorganic components (varying percentages of sand, silt and clay) and natural organic components composed mainly of humic substances, lipids, carbohydrates, lignin, flavonoids, pigments, resins and fulvic acids. These compounds are characterized by diverse chemical structure and physicochemical properties, which cause many analytical problems. Therefore, analyzing pesticides at low concentrations in these samples is a very difficult and challenging task.

ADVANTAGES

- INCDTIM offers RD&I services based on comprehensive, rapid, accurate and high-quality pesticide residue analysis in complex matrices.
- The QuEChERS method has many advantages over traditional extraction methods: high recovery factors, applicability to a wide range of pesticides with different polarities and volatilities – including difficult analytes.
- The amount of solvents and waste is very low and no toxic solvents are used.



ESTIMATED COSTS

The cost of a determination includes:

- apparatus usage time
- labor, which includes personnel costs and indirect costs associated with sample preparation, analysis and interpretation of results, and the preparation of the analysis/research report.

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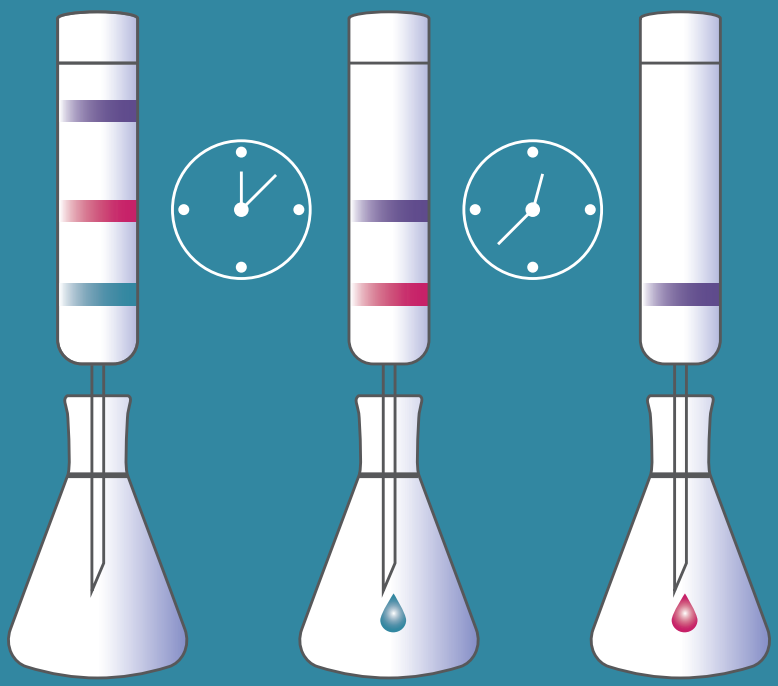
15.

LIQUID CHROMATOGRAPHY



LIQUID CHROMATOGRAPHY

Keywords: *liquid chromatography, TLC, pollutants, organic compounds*

DESCRIPTION

Liquid chromatography is a laboratory technique that **separates chemicals** in a mixture, allowing their **qualitative and quantitative determination**. It is based on the **different distribution of the components of a mixture between two phases**: the stationary phase and the mobile phase. Liquid chromatography can be closed column or open column (Thin Layer Chromatography, TLC).

The most commonly used is **closed column chromatography**, in particular **High Performance Liquid Chromatography (HPLC)**.

The main advantages of HPLC are:

- ✓ high separation capacity
- ✓ high separation speed
- ✓ possibility of continuous monitoring of the column eluent
- ✓ repeated and reproducible analysis using the same stationary and mobile phases
- ✓ automation of analytical procedures and data processing
- ✓ non-destructive detection
- ✓ after separation, substances can be collected in fraction collectors
- ✓ easy scaling-up

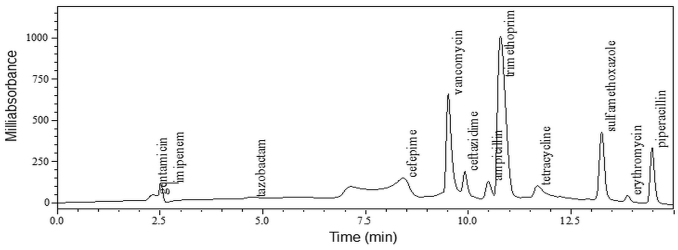
Shimadzu LC-2010 liquid chromatograph dedicated to the analysis of mixtures of organic compounds

APPLICATIONS

Areas of application: R&D, quality control (detection of impurities, stability under different environmental conditions, stability over time, etc.), analysis of environmental samples, chemical synthesis (separation of reaction products), determination of the composition of plant extracts, etc.

Systems: ***organic, inorganic and organometallic compounds***

Industries: pharmaceutical industry, chemical industry, food supplements industry, agro-food industry, cosmetics industry, environment, health.



Chromatogram of some antibiotic standards

INFRASTRUCTURE

Our laboratory is equipped with a **Shimadzu LCMS-2010 high-performance liquid chromatograph** with several detectors:

i. diode-array detector (PDA)

ii. fluorescence detector (FD)

iii. refractive index detector (RID)

iv. mass spectrometer (MS)

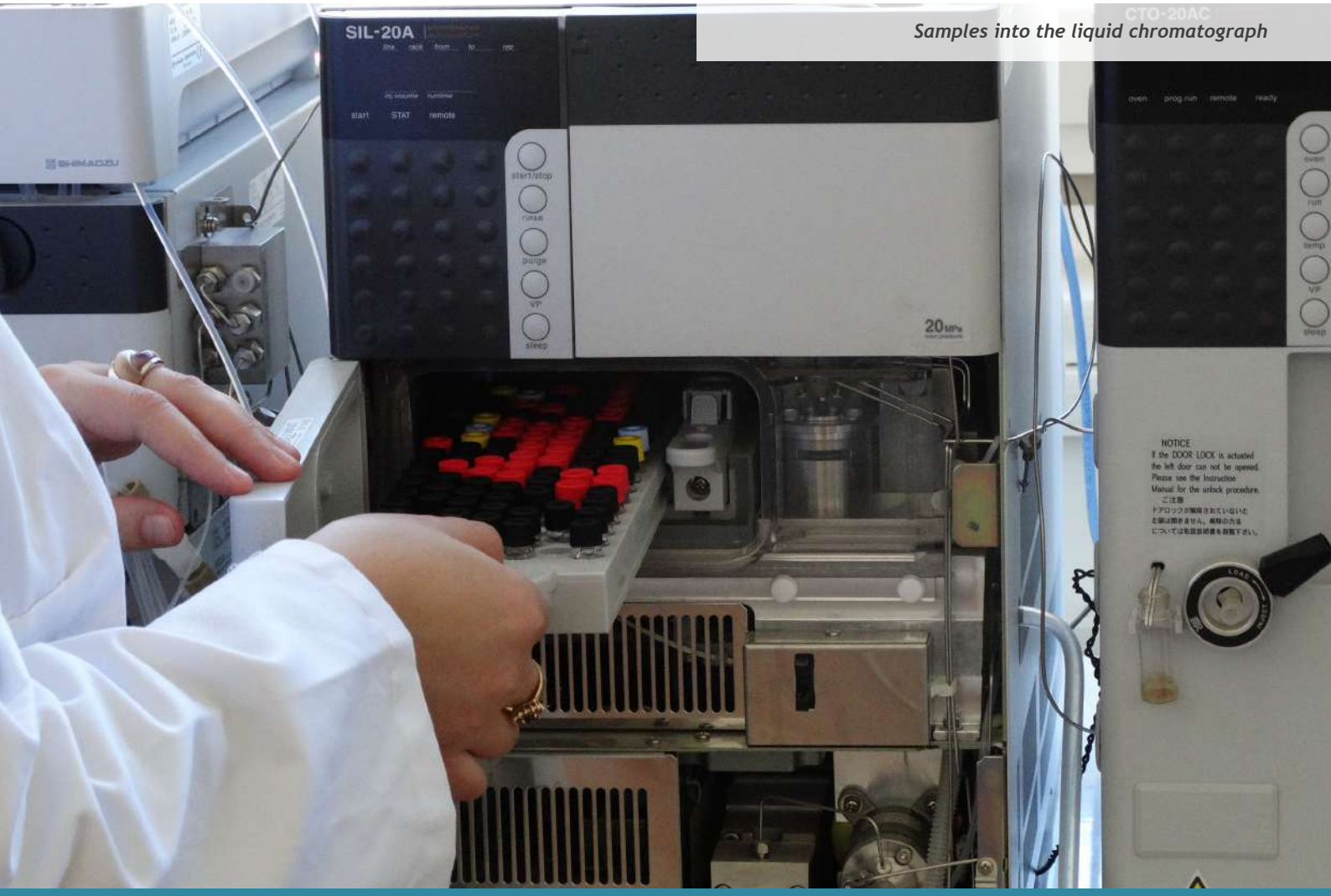
which allows detection and analysis of a wide range of compounds.

For separations by **thin-layer chromatography:**

i. **Camag Linomat 5** semi-automatic applicator

ii. **Camag TLC Scanner 3** photodensitometer

are also available.

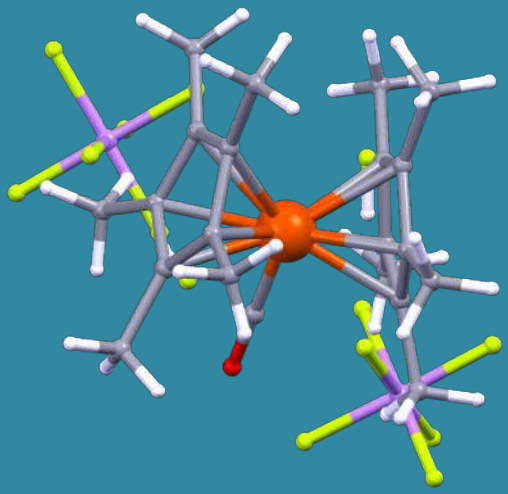


Samples into the liquid chromatograph

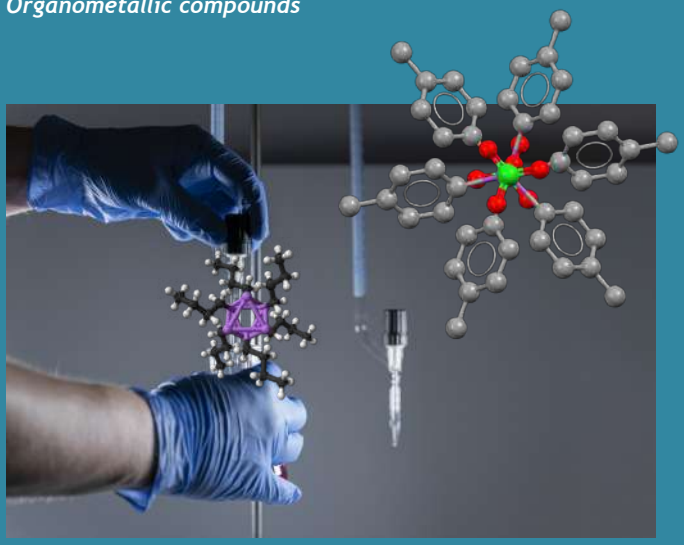
TYPICAL APPLICATIONS – EXAMPLES:

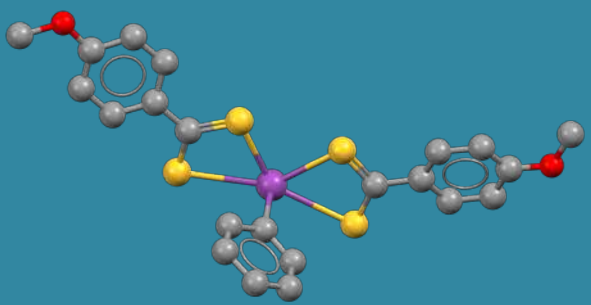
Determination of pollutants (drugs, pesticides, dyes) in environmental samples. The presence of pollutants can be identified in water, soil, waste of different types (including animal manure), using different extraction methods (solid phase extraction, microwave field extraction, etc.) prior to analysis.

Determination of organic/organometallic compounds purity. Impurities occurring during sample processing, during synthesis, presence of unreacted raw materials or by-products may be observed.

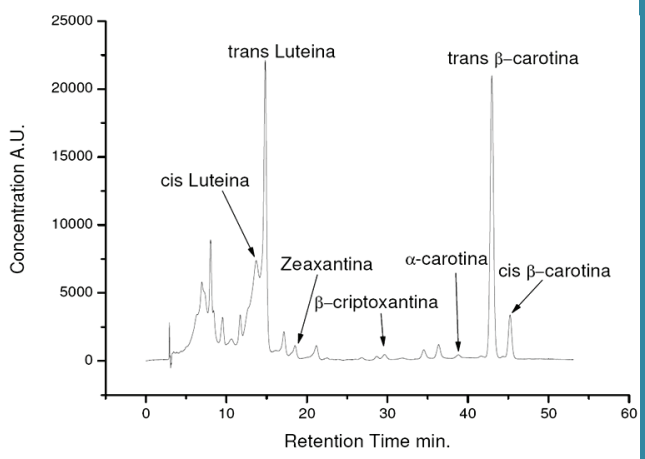


Organometallic compounds

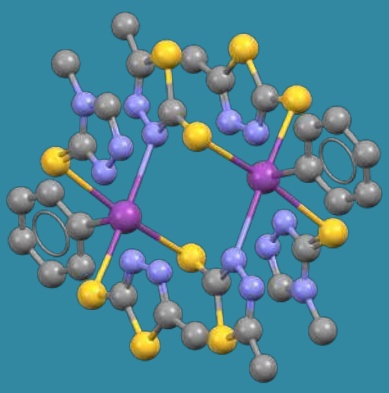




Stability studies for pharmaceuticals, food supplements, cosmetics and other organic compounds. The modification/degradation of the active substances in different products under different environmental conditions (temperature, humidity, light, etc.) can be traced, information useful in future industrial manufacturing processes.



Chromatogram of carotenoid extracted from Ocimum basilicum L.



Organometallic Bismuth compounds

ADVANTAGES

- INCDTIM offers R&D services based on high-performance liquid chromatography covering almost the full range of practical applications.
- Prior to the conclusion of a contractual relationship, we offer consultancy to define as precisely as possible the needs of the client/partner.
- On request, we offer extraction of the desired compound(s) from various matrices.
- Existing facilities allow us to analyze a wide range of compounds.
- Specialized staff, capable of covering all stages of a contractual collaboration with the highest professionalism: defining the problem to be solved, experimental design, data collection, interpretation of results.

ESTIMATED COSTS

The total cost of R&D services based on high-performance liquid chromatography depends on the type of the analysis:

Qualitative analysis:

- chromatograph usage time, consumables and wear
- labor, which includes personnel and indirect costs associated with sample preparation operations, analysis and interpretation of results, preparation of analysis/research report: depending on the complexity of the study.

For **quantitative analysis,** the calibration curve is added to the above.

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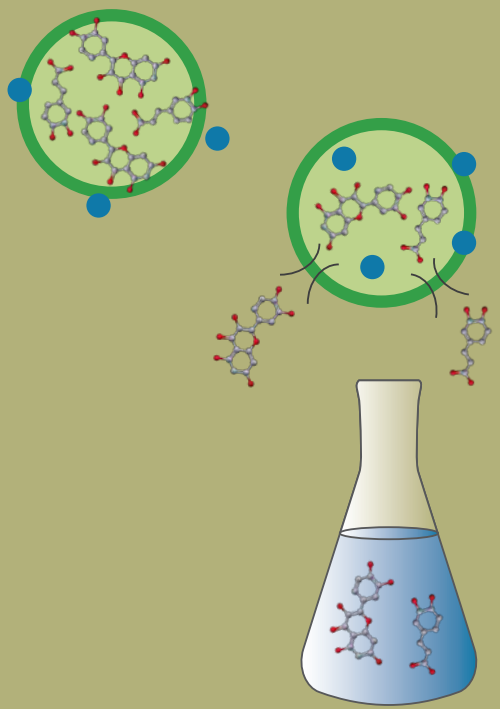
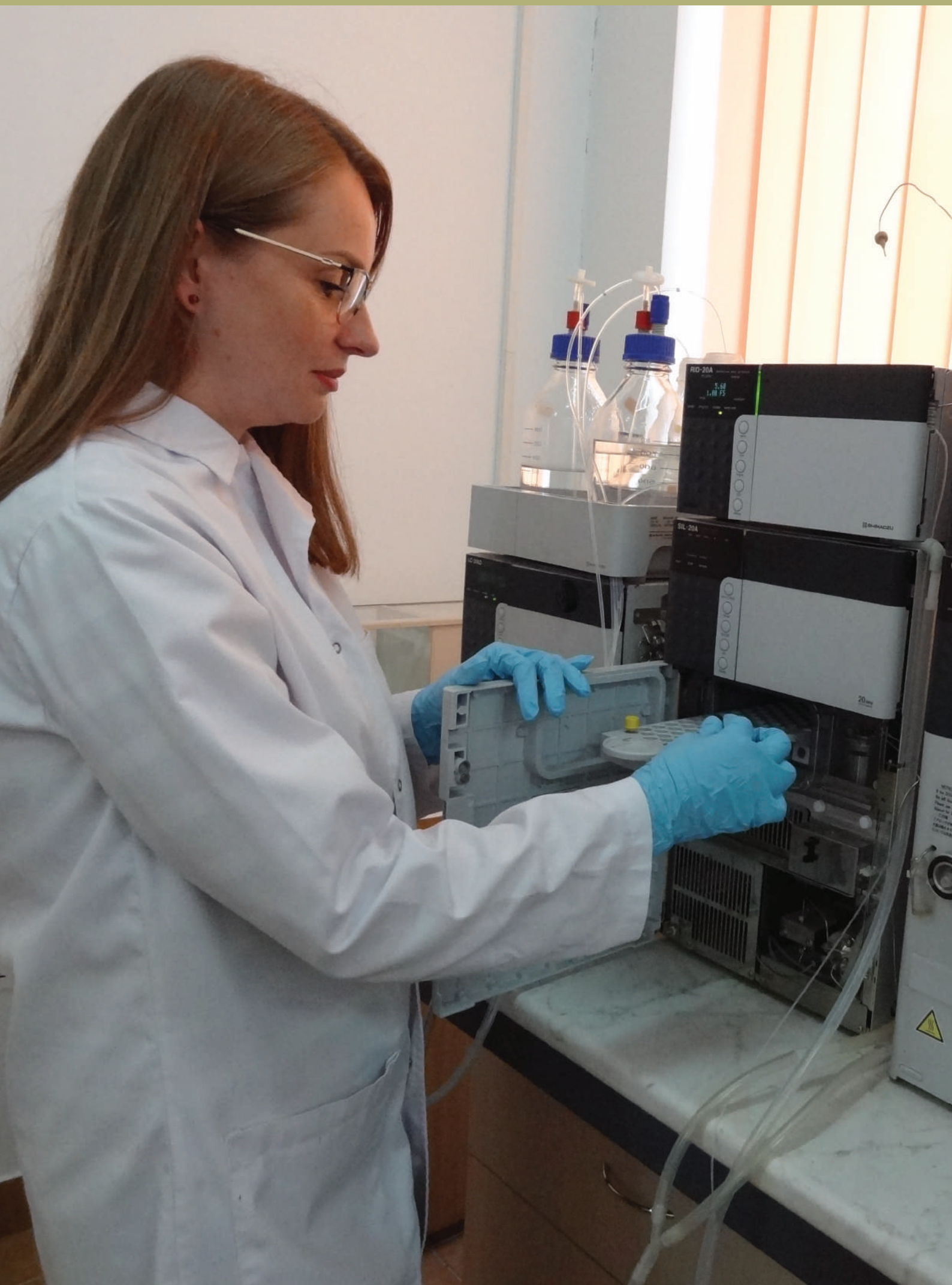
16.

ULTRASOUND-ASSISTED EXTRACTION OF ORGANIC COMPOUNDS

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ULTRASOUND-ASSISTED EXTRACTION OF ORGANIC COMPOUNDS

Keywords: *extraction, ultrasound, organic compounds*

DESCRIPTION

INCDTIM's concerns for the extraction of organic compounds from different matrices led to the selection and adaptation in our laboratory of a large number of techniques.

Experimental results obtained, over the years, by the Multifunctional Materials and Biologically Active Compounds research team have led to the conclusion that **ultrasound-assisted extraction (UAE)** is the most suitable technique for the extraction of organic compounds from various matrices and is scalable. In addition, our research team has experience in optimizing working methods; using statistical methods, it is possible to select the optimal parameters for obtaining preparations with the highest amounts of the organic compound(s) of interest in relation to the raw material used.

Testing different methods and experimental conditions, we concluded that the main advantages of ultrasonic extraction are:

- ✓ The technique is environmentally friendly, efficient and economical
- ✓ The use of a minimum volume of solvent and a short working time to obtain a maximum yield of the compounds of interest (in at least 4 times less time the same yield as in extraction by classical methods can be obtained)
- ✓ Obtaining high-quality extraction products

Laboratory for analysis of extracts by high-performance liquid chromatography (HPLC)

APPLICATIONS

Areas of application: extraction of organic compounds from complex organic or inorganic matrices.

Industries: pharmaceutical industry, chemical industry, food supplements industry, agro-food industry, cosmetics industry, environment, health.

INFRASTRUCTURE

The laboratory has modern equipment for obtaining and characterization of final extracts:

i. ultrasonic baths Elmasonic S40H, Transonic T 470/H, Sonorex Digitec

ii. Eppendorf 5430R centrifuge (17,000 rpm)

iii. Rotavapor Heidolph Laborota 4011

iv. Shimadzu LC-2010 high-performance liquid chromatograph

v. UV-Vis spectrophotometers Jasco V550, Jasco 6500

Ultrasonic baths

Eppendorf 5430R Centrifuge

Jasco V550 Spectrophotometer

Concentration of the extract in the rotavapor (Heidolph Laborota 4011)

TYPICAL APPLICATIONS – EXAMPLES:

Extraction of bioactive compounds from plant materials. Bioactive compounds with antioxidant or antimicrobial properties such as polyphenols, chlorophylls, carotenoids, essential oils can be obtained from plant material.

Ocimum basilicum (basilicum)

Hippophaë rhamnoides L (sea buckthorn)

Extraction of pesticides from solid environmental samples. The extraction step is very important for preliminary processing of samples for determination of pesticide content using chromatographic methods.

HPLC allows determination of pesticide contents

Extracting drugs from garbage and soil. Different classes of drugs can be extracted from soil and litter samples: antibiotics, NSAIDs, cytostatics, analgesics

ADVANTAGES

- INCDTIM offers RD&I services based on the ultrasonic extraction method covering a wide range of practical applications.
- Before entering into a contractual relationship, we offer consultancy to define the customer/partner's needs as precisely as possible.
- Existing equipment allows us to extract a wide range of compounds.
- We have specialized staff, able to cover with the highest professionalism all stages of a contractual collaboration: definition of the problem to be solved, experimental design, data collection, and statistical interpretation of results.

ESTIMATED COSTS

The cost of a determination consists of:

- apparatus usage time
- labor, which includes personnel and indirect costs associated with sample preparation operations, analysis and interpretation of results, and preparation of the analysis/research report.

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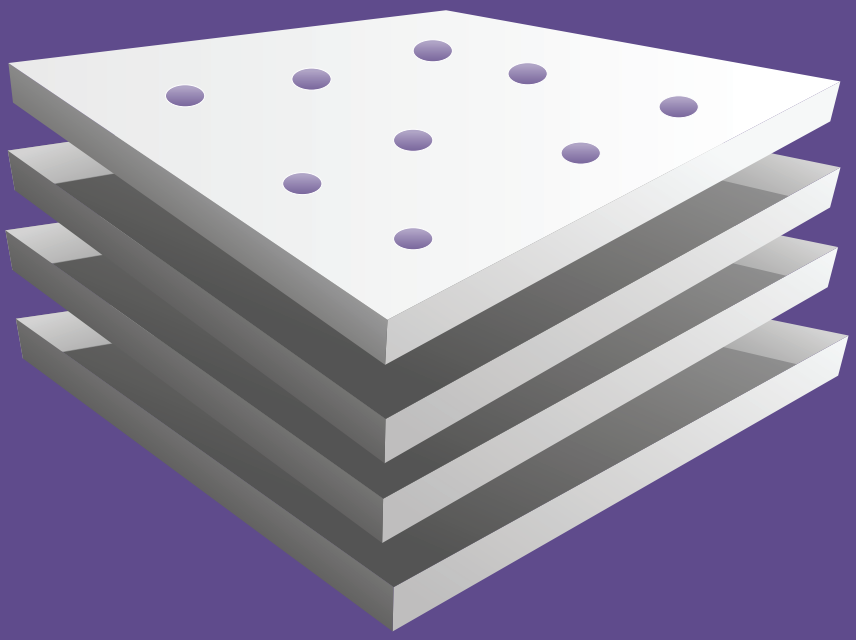
17.

POROUS SOLIDS AND THEIR CHARACTERIZATION



POROUS SOLIDS AND THEIR CHARACTERIZATION

Keywords: *surface area, pore size, porous structure*

DESCRIPTION

Determination of the porosity parameters of solid materials – surface area, pore volume and pore size – is carried out using isothemal adsorption/desorption of nitrogen molecules on the solid surface technique.

The **advantages** of this method are:

- ∫ **high versatility** – it is possible to measure the surface of any solid with an area higher than 1 m^2/g regardless of its chemical composition, whether it is nanostructured or not, whether or not functional groups are present on the surface, etc.
- ∫ **plethora of information** that can be extracted from adsorption/desorption isotherms: surface area, the presence of micropores or mesopores, total pore volume and/or categorized, pore size distribution, pore shape information.

APPLICATIONS

Areas of application:

i. structural characterization of any produced solid material

ii. production – both at the optimization stage of the production process and for the quality control of the obtained product

Systems:

i. ***oxide materials with various applications:*** pigments (e.g. ZnO), catalysts (e.g. Al_2O_3)

ii. ***materials with applications in adsorption processes:*** activated carbon, natural zeolites, dolomite

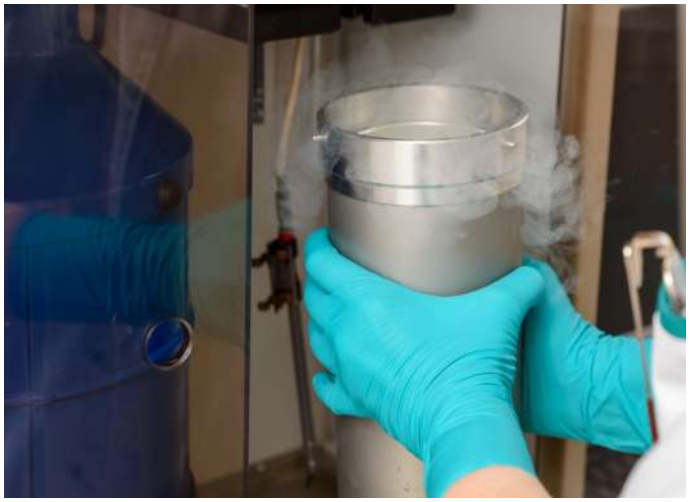
iii. ***materials with thermal insulating properties***

Industries: environment-pollution control, chemical industry.

Heterogeneous Catalysis Laboratory. Sorptomatic 1990 (Thermo Electron Corporation)

INFRASTRUCTURE

Heterogeneous Catalysis Laboratory is equipped with a **BelSorp MaxX equipment (Microtrac BEL Corporation)** capable of recording nitrogen adsorption/desorption isotherms at a constant temperature of -196°C. The apparatus also includes a temperature-controllable vacuum degassing module.



TYPICAL APPLICATIONS – EXAMPLES:

Determination of the surface area and porosity of natural zeolites. Being materials with potential use in surface adsorption processes, knowledge of the size of the adsorbent surface is very important. The size and shape of the pores can interfere in the adsorption process, especially in the case of the adsorption of large molecular substances such as organic pollutants or dyes, therefore the determination of porosity parameters is as important as the surface area.

Determination of the surface area of MOF-type compounds. One characteristic of these compounds is the very large surface area, of the order of thousands of square meters per gram, generated by the existence of a very extensive microporous structure. Therefore, the experimental parameters and interpretation of adsorption/desorption isotherms require additional expertise as compared to usual measurements, expertise which is held by our group at INCDTIM.

Porous materials produced in INCDTIM

MIL—101 (Cr) synthesized in INCDTIM

Determination of surface area and porosity of catalysts. Catalysis is a surface process, dramatically influenced by its size, therefore surface area determination is very important for the characterization of a catalyst. The access of reactants to the active catalytic centers on the catalyst surface can be hindered or, on the contrary, facilitated by the shape and size of the pores, therefore the porosity parameters are equally important.

Porous compounds synthesized by Porous Materials and Carbon Nanostructures team

ADVANTAGES

- INCDTIM offers RD&I services for surface area and porosity determination, used alone or in combination with other solid characterization techniques (X-ray diffraction, optical and electron microscopy), covering almost the full range of structural characterization.
- Prior to entering into a contractual relationship we provide consultancy to define as accurately as possible the needs of the client/partner and, if required, we carry out preliminary tests free of charge.
- Our existing equipment and experience allows us to measure most porous solids.
- Our staff is specialized in highly prestigious research centers abroad, and is able to cover with the highest professionalism all the stages of a contractual collaboration: definition of the problem to be solved, experimental design, data collection, interpretation of results and their correlation with other complementary information, if necessary.

ESTIMATED COSTS

The cost of a determination consists of:

- apparatus usage time
- labor, which includes personnel and indirect costs associated with sample preparation, analysis and interpretation of results, preparation of the analysis/research report.

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18.

CHARACTERIZATION OF THE ACTIVE SURFACE OF CATALYSTS

CHARACTERIZATION OF THE ACTIVE SURFACE OF CATALYSTS

Keywords: *temperature programmed reduction (TPR), catalytically active surface area, temperature programmed desorption (TPD), surface acidity/basicity*

DESCRIPTION

Investigation of the interaction of reactant molecules with catalyst surfaces is of vital importance in the design and efficiency of any catalyst or catalytic process. One of the most widely used techniques in this respect is the study of surface interactions under temperature-programmed conditions. The advantages of this method are:

- ***high versatility*** – one can study the interaction of various reactant molecule with various solid surface
- ***the wealth of information provided:*** the conditions under which the surface can be oxidized/reduced, the nature and strength of the catalytically active centers, the acidity/basicity of a solid, the area of the catalytically active surface.

APPLICATIONS

Areas of application:

- ***R&D*** – for the functional characterization of materials with potential catalytic properties
- ***production*** – for quality control of prepared catalysts or to streamline the development/diversification/scaling processes of new catalytic materials

Systems:

i. ***metal/support type catalysts:*** support such as metal oxides, carbon structures, etc.

ii. ***natural or synthetic zeolitic materials***

iii. ***novel materials with potential catalytic properties*** (e.g. Metal-Organic Frameworks (MOFs), graphene, carbon nanostructures, various composites)

Industries: chemical industry, energy, environment/pollution, pharmaceutical industry

Heterogeneous Catalysis Laboratory

Metal/support type catalysts

Zeolitic catalyst

INFRASTRUCTURE

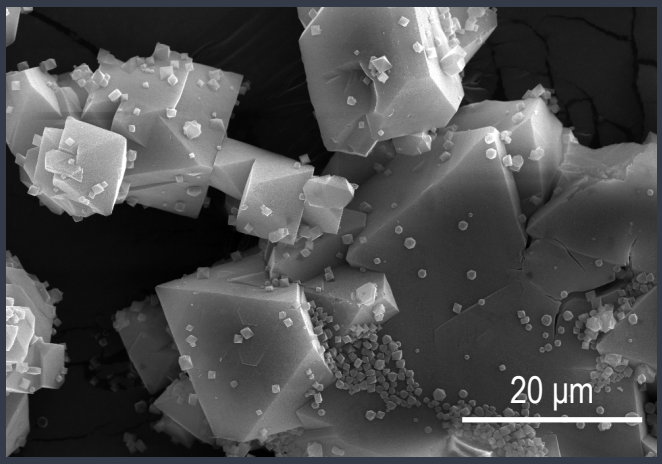
The **Heterogeneous Catalysis Laboratory** is equipped with a **TPDRO 1100** Series catalyst characterization apparatus, equipped with a thermoconductivity detector (TCD) (Thermo Scientific, USA), coupled with a quadrupole mass spectrometer (QMS) (PrismaPlus, Pfeiffer Vacuum, Germany). Thus, the experimental system is superior to the usual commercial apparatus because it combines the information obtained from two detectors, TCD and QMS, providing clearer and more comprehensive results.

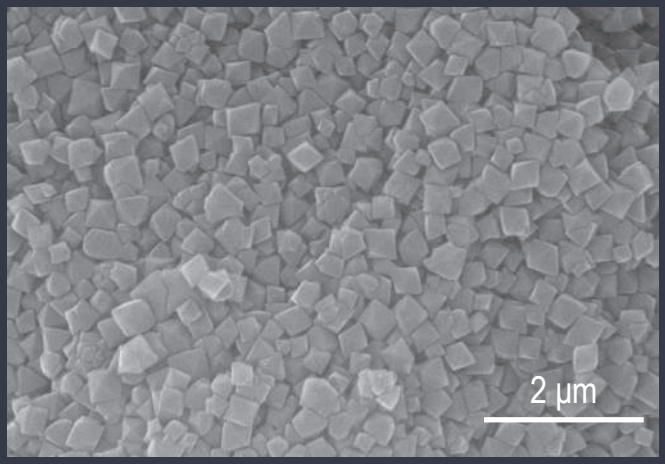
Heterogeneous Catalysis Laboratory

TYPICAL APPLICATIONS – EXAMPLES:

Determination of the catalytically active surface area for processes involving hydrogen (or hydrogen-containing molecules, e.g. CH_4). Catalysis is a surface process for which the efficiency of adsorption and activation of the reactant molecules also depends on the size of the available active surface area. Thus, for metal/support type materials, the determination of the area of the catalytically active surface is done by determining the amount of hydrogen adsorbed/desorbed from the surface.

Determination of the nature and strength of active catalytic centers is some of the most common and necessary information in the development and manufacture of a catalyst, regardless of its nature. This is accomplished by the temperature-controlled adsorption/desorption of probe molecules (which are either the target reactants or molecules of similar structure to the reactants). INCDTIM's experimental arrangement, the TPDRO-QMS coupling, offers the advantage of using a wider range of sample molecules.





SEM images of some MOF structures

Determination of the optimum temperature for reduction (activation) of a catalytic precursor. The reduction of the metal oxide (precursor) to the catalytic active metal is one of the important steps in the preparation of a metal/support catalyst. Too low a reduction temperature does not generate sufficient catalytically active phase, and too high a temperature can lead to sintering of metal nanoparticles on the support; in both cases, poor-performing catalysts are obtained. With Temperature Programmed Reduction (TPR), the optimal temperature range is set to obtain the best catalytic performance.

ADVANTAGES

- INCDTIM offers R&D services for characterizing the active surface of catalysts, used alone or in combination with other solid characterization techniques (X-ray diffraction, optical, and electron microscopy), covering almost the full range of structural and functional characterizations.
- Before entering into a contract-based relationship, we assist in defining the needs of the customer/partner as accurately as possible and, if required, we carry out preliminary tests free of charge.
- Our existing equipment and experience allow us to characterize most materials with catalytic potential.
- We also collaborate with specialized staff in highly prestigious research centers abroad, able to cover at high standards all the stages of a contractual collaboration: defining the problem to be solved, experimental design, data collection, interpretation of the results, and their correlation with other complementary information, if necessary.

ESTIMATED COSTS

The total cost of a determination consists of two components:

- apparatus usage time
- labor, which includes personnel and indirect costs associated with sample preparation operations, analysis and interpretation of results, and preparation of the analysis/research report

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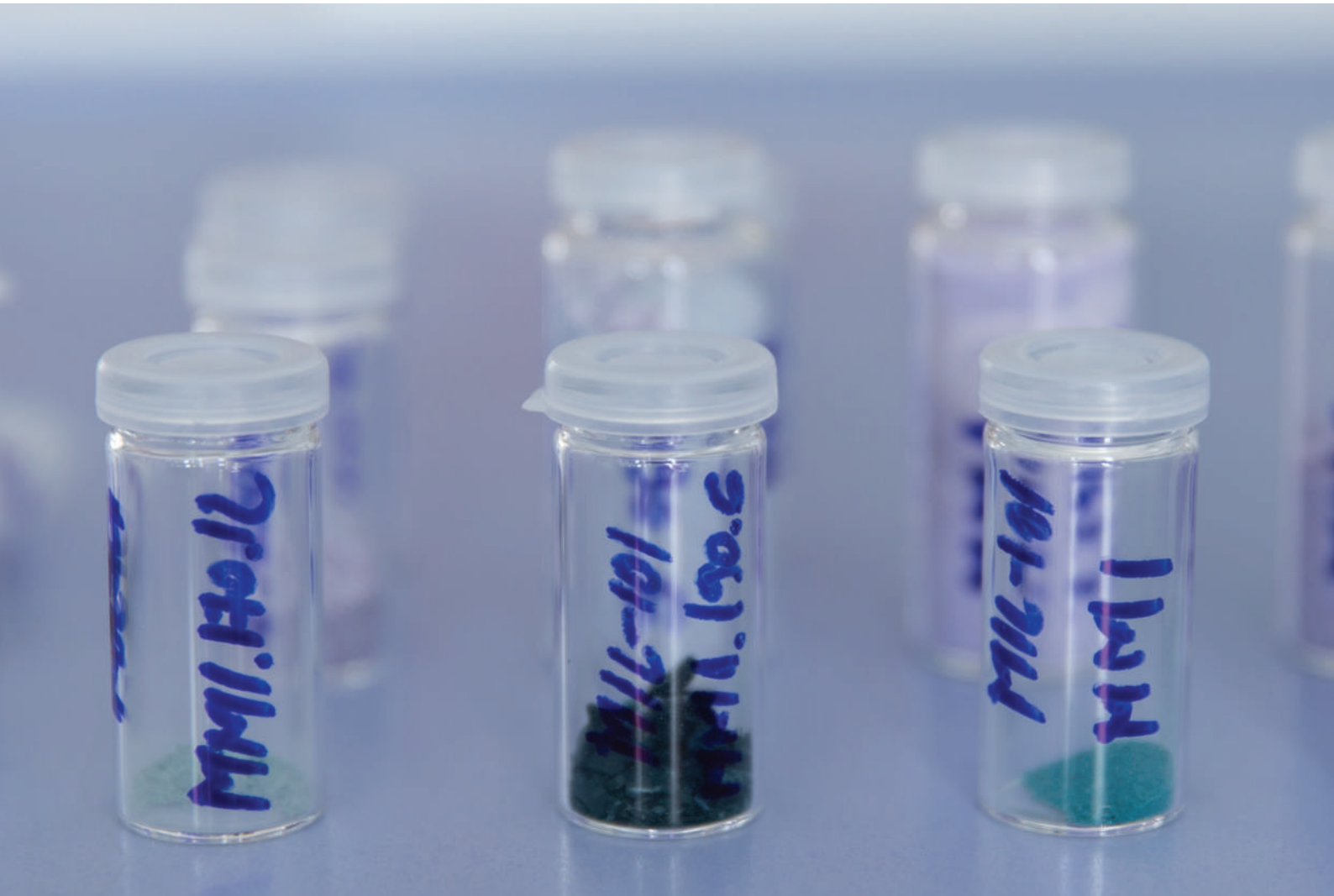
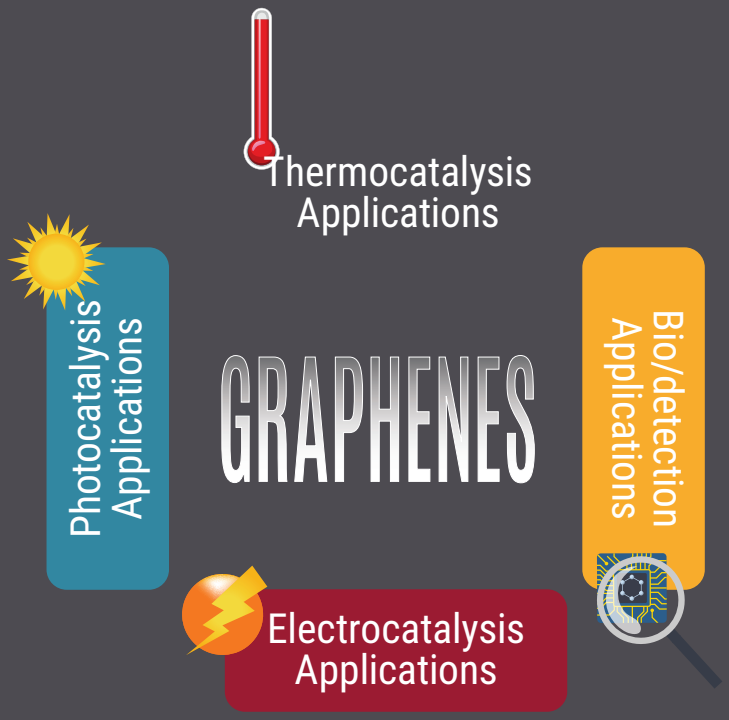


19.

NEW GRAPHENE-BASED MATERIALS AND THEIR APPLICATIONS



NEW GRAPHENE-BASED MATERIALS AND THEIR APPLICATIONS

Keywords: *graphene, catalytic hydrogenation, fuel cells, carbon dioxide conversion, adsorption and degradation of pollutants, bio/molecule detection*

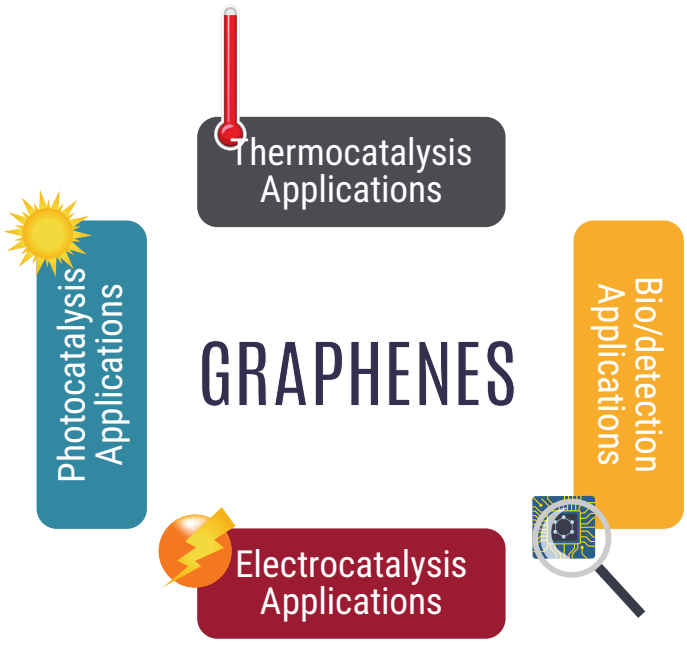
DESCRIPTION

A wide variety of graphene-based composite materials can be synthesized in INCDTIM's laboratories by various methods:

- graphene oxide
- reduced graphene oxide
- graphene doped with heteroatoms
- graphene decorated with metal/oxide nanoparticles
- nanocomposites based on graphene and polymers

Depending on the desired application, graphene-based composite materials can be obtained using various synthesis techniques:

- chemical synthesis (graphite oxidation and exfoliation)
- electrochemical graphite exfoliation
- mechanical exfoliation of graphite (ball milling)



Schematic diagram of the areas graphene-based composites applications (Porous Materials and Carbon Nanostructures group)

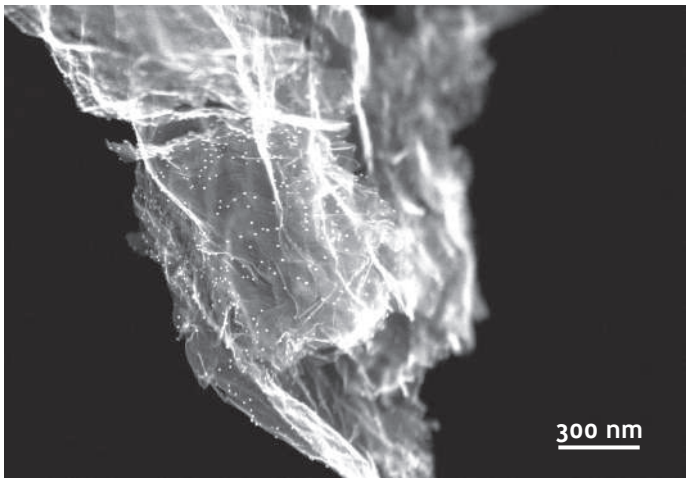
APPLICATIONS

Areas of application:

- **R&D:** obtaining catalysts for heterogeneous processes (electrocatalysts, photocatalysts, thermocatalysts)
- **electrochemical detection:** preparation of modified electrodes

Industries:

- ✓ Chemical industry
- ✓ Energy
- ✓ Environment/depollution
- ✓ Pharmaceutical industry, medicine

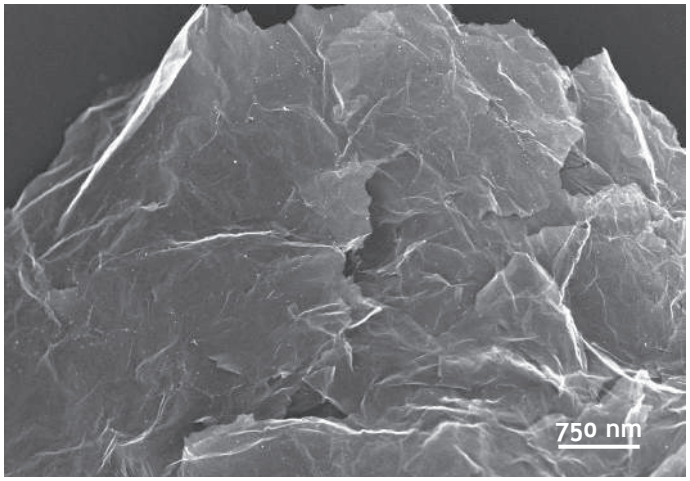


TEM image of a graphene-based composite decorated with metal nanoparticles

INFRASTRUCTURE

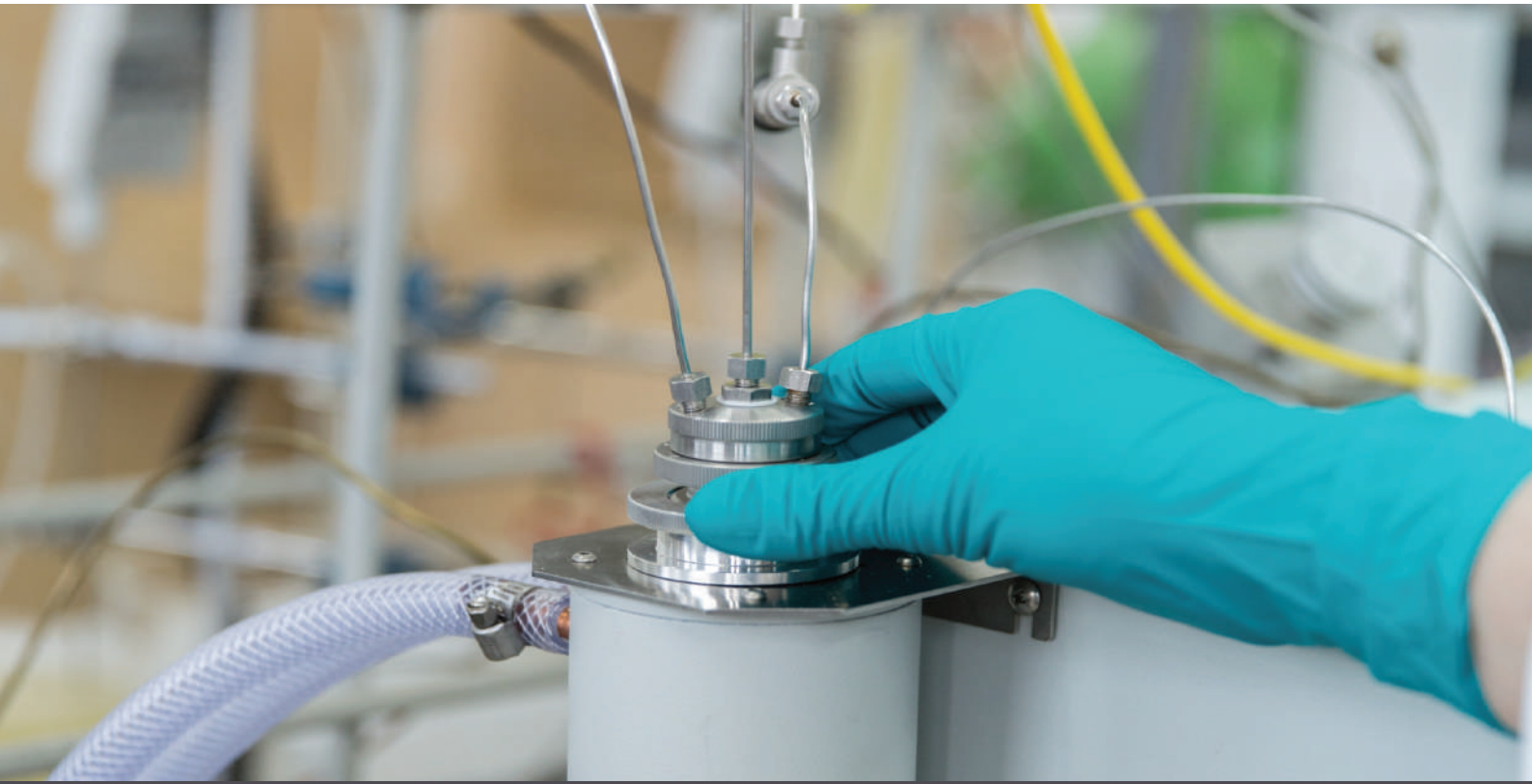
INCDTIM has the research infrastructure necessary for the preparation and complete characterization of graphene-based composite materials.

- Fully equipped chemistry laboratory
- SEM scanning electron microscopes (Hitachi SU8230), TEM (Hitachi HD2700), EDX and EBSD detectors (Oxford Instruments)
- X-ray diffractometer (Bruker D8 Advance)
- FTIR (TENSOR II, Bruker) and Raman spectrometers (Jasco NRS 3300)
- Thermogravimeter (SDT Q 600, TA Instruments)
- Catalyst characterization apparatus for the study of adsorption/reaction at programmed temperature (TPDRO 1100, Thermo Scientific) equipped with a thermal conductivity detector (TCD) coupled with a quadrupole mass spectrometer (QMS, Prisma Plus, Pfeiffer Vacuum)
- Apparatus for measuring surface area and porosity (Sorptomatic 1900, Thermo Scientific)
- Electrochemical applications (synthesis/testing/detection) are carried out using potentiostat/galvanostat apparatus (PGSTAT302N, Metrohm Autolab)
- SPECORD 250 PLUS spectrophotometer (Analytik Jena GmbH, Jena, Germany).



TEM image of a graphene-based composite decorated with metal nanoparticles

Laboratory of catalysts synthesis for hydrogen production



TYPICAL APPLICATIONS – EXAMPLES:

NP/graphene catalysts with high activity and selectivity for chemical storage and hydrogen utilization. Thermocatalysis is a surface process for which the efficiency of adsorption and activation of reactant molecules depends on the properties of the catalyst. The combination of the properties of graphene and metal nanoparticles provides a particular activity of these materials for reactions involving hydrogen. Pt/graphene, Au/graphene have proven their efficiency in several hydrogenation processes.

Applications in adsorption and photocatalysis. The large adsorptive surface area of graphene makes them important candidates for use in processes for the removal of non-biodegradable chemical pollutants. Both simple reduced graphene and functionalized graphene are effective for these applications. In addition, graphene-based composites are very good photocatalysts for the degradation of chemical pollutants to low toxicity or even mineralization products, some of which are also effective in sunlight. A number of metal/graphene/semiconductor composites (based on Ag/graphene, Au/graphene, Pt/graphene, Cu_xO/graphene) have proven their efficiency in this respect in degradation processes of organic pollutants such as drugs, pesticides or endocrine disrupting contaminants.

NP/heteroatoms/graphene catalysts with high electrocatalytic efficiency and fuel cell applications. The hybrid material based on sulfur-doped graphene with low platinum content has proven its efficiency in the methanol oxidation reaction in alkaline medium, showing potential for replacing high Pt catalysts in fuel cells.

Applications in the detection of organic molecules and biomolecules. The preparation of modified electrodes based on graphene composites is realized by drop-casting method. AuPt/graphene and Au/graphene composites have been shown to be effective in the detection of dopamine and single-stranded DNA (ssDNA) degradation, respectively.

Graphene and polymer-based nanocomposites. Development of ultrasensitive sensors and selective electrochemical detection protocols in biomedicine and pharmaceutical industry (tumor markers, endocrine disruptors, oxidative stress indicators, antibiotics, analgesics, beta-blockers), environment (emerging pollutants, heavy metals, pesticides, fertilizers), food industry (potentially toxic food additives and organic or inorganic contaminants).

ADVANTAGES

- INCDTIM offers RD&I services for the preparation and complete characterization of graphene-based composite materials; materials with a large diversity of metal-oxide-graphene compositions can be synthesized.
- Before entering into a contractual relationship, we offer consultancy to define the client/partner's needs as accurately as possible and, if necessary, we carry out preliminary tests free of charge.
- Our existing equipment and experience allow us to test most of the materials with potential applications in the areas mentioned above.
- We have specialized staff in highly prestigious research centers abroad, able to cover with the highest professionalism all the stages of a contractual collaboration: definition of the problem to be solved, experimental design, data collection, interpretation of results and their correlation with other complementary information, if necessary.

ESTIMATED COSTS

The cost per gram of composite material depends on the type of synthesis used and its structural complexity.

The cost of an analysis depends on the complexity of the sample to be analyzed and consists of:

- ✓ apparatus usage time
- ✓ labor, which includes personnel and indirect costs associated with sample preparation, analysis and interpretation of results, preparation of the analysis/research report.

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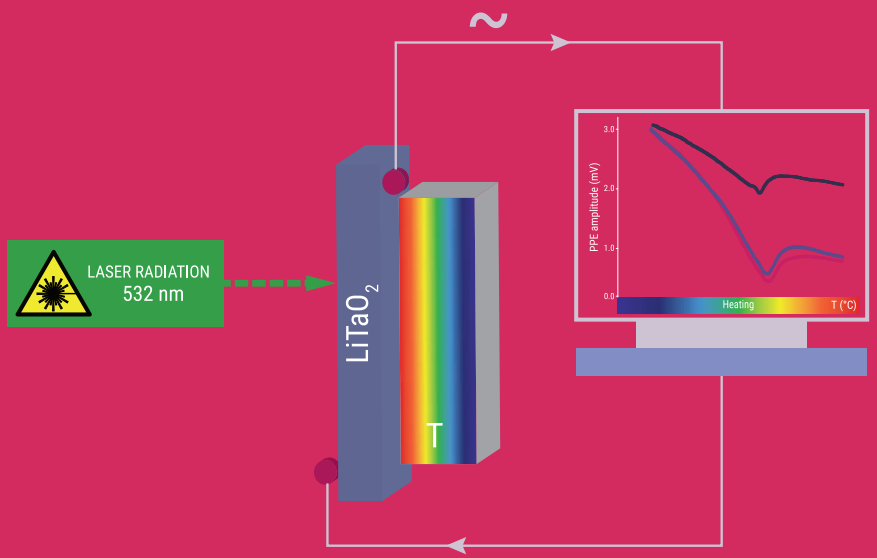
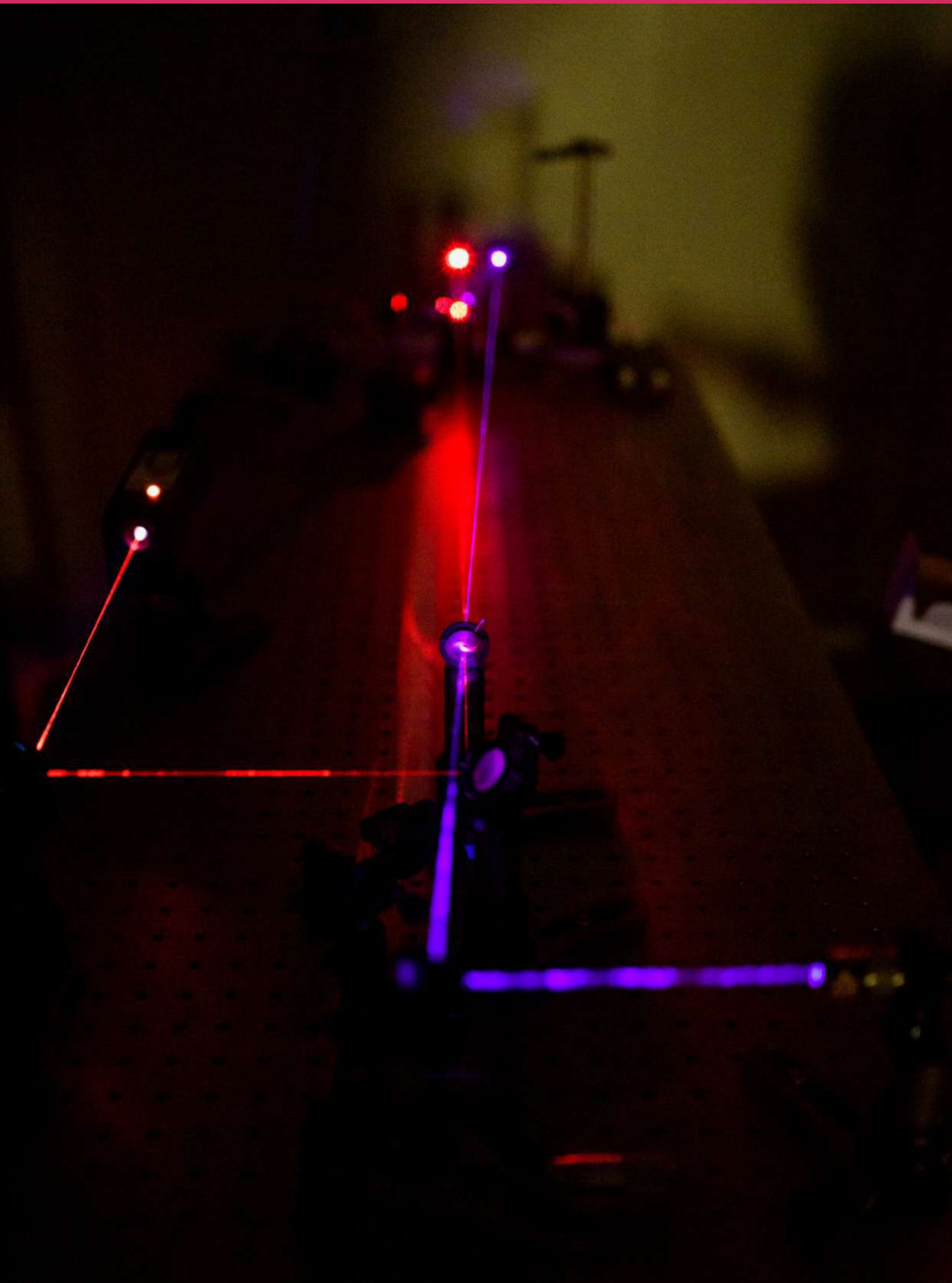
PHOTOPYROELECTRIC CALORIMETRY





PHOTOPYROELECTRIC CALORIMETRY

Keywords: *photopyroelectric technique, thermal parameters, specific heat, conductivity, diffusivity, thermal diffusivity, phase transitions*

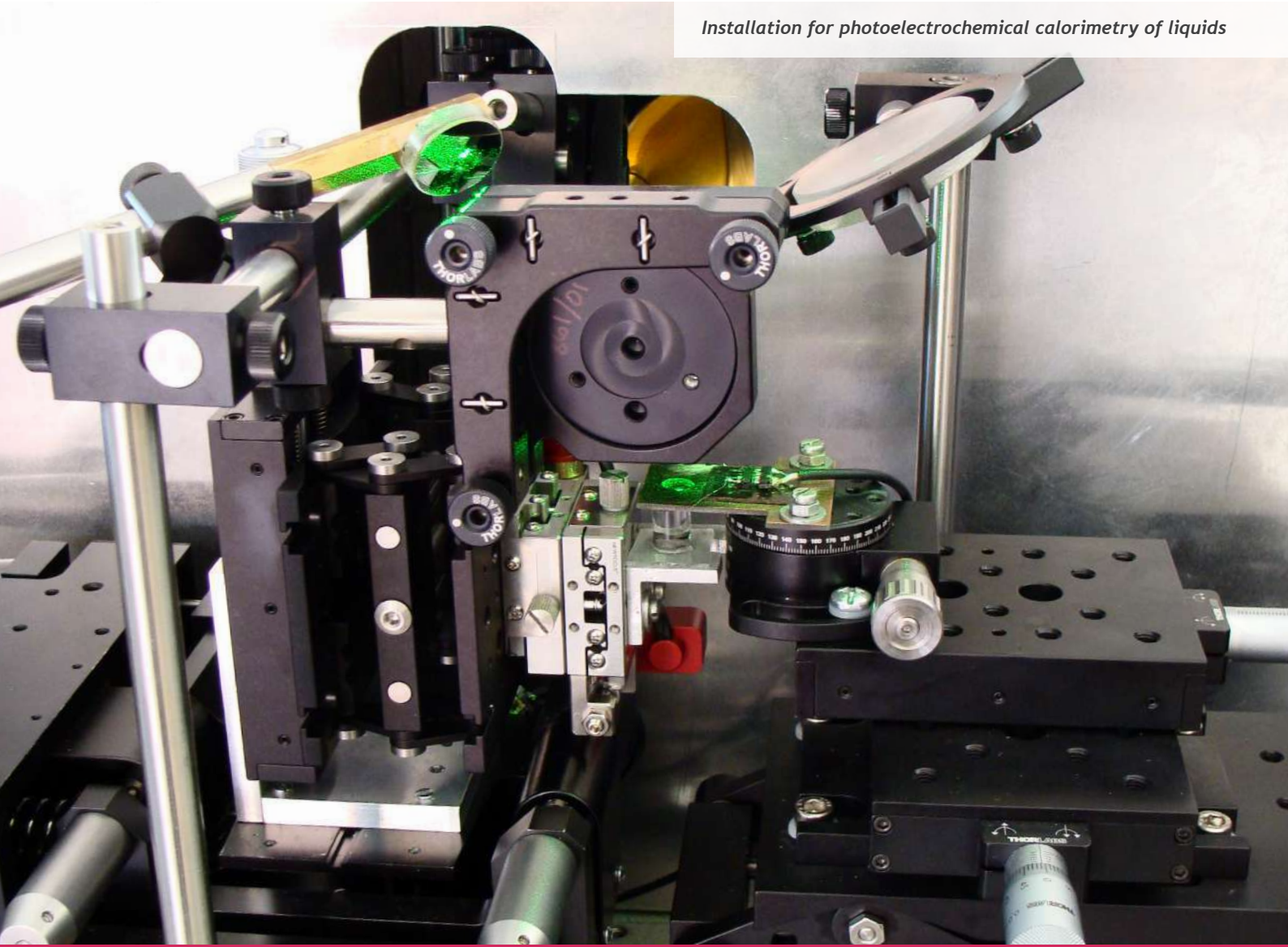
DESCRIPTION

Photopyroelectric calorimetry is a highly accurate technique which provides a complete thermal characterization (determination of all thermal parameters) of any chemically non-aggressive material in condensed phase (solid or liquid).

The technique can also be used in the study of physical and chemical processes associated with the variation of thermal parameters, as a function of composition, temperature or time.

Pyroelectric detectors (InfraTech GmbH)

Installation for photoelectrochemical calorimetry of liquids



APPLICATIONS

Areas of application: thermal characterization of materials

- ∫ characterization of thermal parameters for materials of practical interest: conductors, insulators, semiconductors, magnets, ferroelectrics, thermoelectrics
- ∫ study of type I phase transitions: melting, solidification
- ∫ study of type II phase transitions: magnetic and ferroelectric transitions, with calculation of critical exponents, establishing the optical absorption bands of visible and IR absorbing layers.

Systems: liquids or liquid mixtures, nanofluids, semi-liquid materials, solids with various properties (thermal and electrical insulators or conductors, magnetic materials, ferroelectric materials, thermoelectrics, high critical temperature superconductors, semiconductors, etc.), food (juices, oils, butter, cheese, margarine), composite materials (oxidic glasses, porous building materials).

Industries:

- ∫ ***Food industry:*** study of the quality, aging and counterfeiting of some food products (oils, margarines, juices, cheese)
- ∫ ***Building materials industry:*** characterization of thermal parameters (specific heat, conductivity, diffusivity and thermal effusivity)
- ∫ ***Dentistry:*** establish the thermal biocompatibility of various types of dental materials

INFRASTRUCTURE

In INCDTIM there are 3 photopyroelectric calorimetry lines composed of:

i. Radiation sources: YAG lasers (600 mW), HeNe (30 mW); electromechanical and optoacoustic light modulators; lock-in nanovoltmeters (Stanford SR830) for signal processing

ii. Optomechanics: lenses, mirrors, visible and IR transparent windows, micrometer tables with 3- and 6-axis control respectively, picomotors (30 nm step)

iii. Radiation sensors: $LiTaO_3$, PZT, PVDF, HgCdTe, InSb

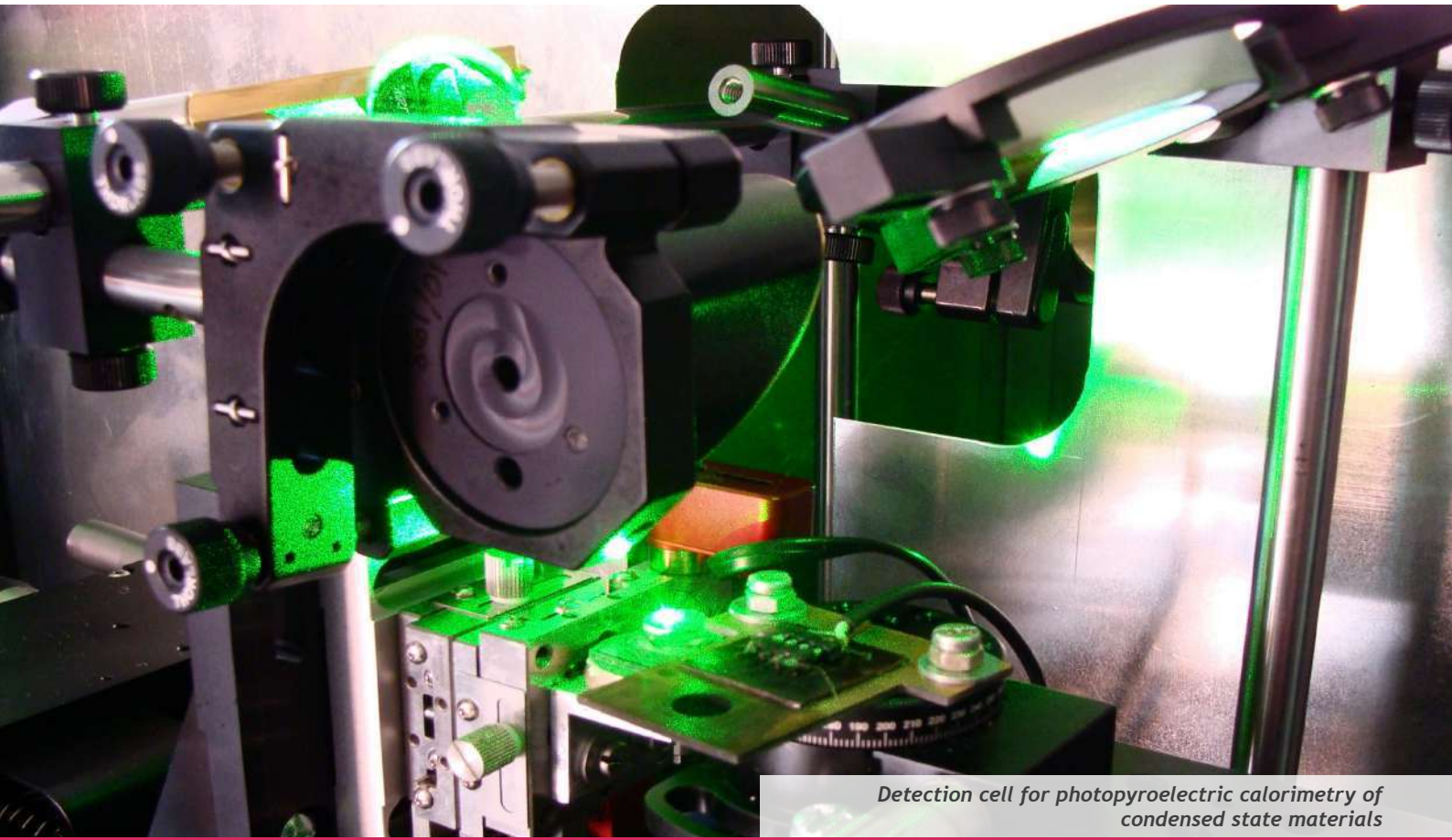
iv. Detection cells with temperature monitoring, consisting of Peltier elements, programmable voltage source, electronic thermometer, thermostatic bath

v. IT facilities: computer, programs for data acquisition and processing

The main performances of the existing equipment are:

- ∫ pyroelectric sensor detectivity greater than 100 cm·$Hz^{1/2}$/W
- ∫ minimum detectable temperature variation: 1 μK
- ∫ minimum speed of temperature controlled variation: 100 mK/min
- ∫ temperature range: -20÷100°C
- ∫ signal to noise ratio >100

Duration of an investigation varies from several minutes up to several hours (in case of temperature dependencies).



Detection cell for photopyroelectric calorimetry of condensed state materials

TYPICAL APPLICATIONS – EXAMPLES:

Spectroscopic applications:

- determination of the absorption bands of solids (graphite, anodized aluminum) used as absorbing layers in laser energy meters
- quantitative analysis of isotopic liquid mixtures (e.g. heavy water-water)

Detection of phase transitions of any order:

- detection of second kind phase transitions in ferroelectrics, localized and itinerant antiferromagnets and calculation of critical exponents of thermal parameters
- detection of phase transitions in fatty acids and triglycerides
- detection of in-vitro phase transitions in sugar products (glucose, maltose, maltodextrin, honey, candy)

Study of the thermal properties of food products

- determination of static and dynamic thermal parameters in order to analyze the composition and quality of edible margarines and edible oils and to detect counterfeiting

Thermal characterization of materials of energy interest

- study of the thermal properties of solid and liquid thermoelectric materials and pyroelectric crystals

ADVANTAGES

- ➥ High accuracy: 98% for thermal diffusivity measurement and 95% for thermal effusivity
- ➥ Very small sample quantity required: 0.2÷0.3 ml for liquids and a few mg for solids
- ➥ Measurements do not require prior chemical processing of the sample
- ➥ It is the only calorimetry technique that allows, under certain conditions, the determination of all static and dynamic thermal parameters in a single measurement.

ESTIMATED COSTS

The cost of a thermal characterization consists of:

- ✓ equipment usage time
- ✓ workmanship, which includes personnel and indirect costs associated with sample preparation, analysis and interpretation of results, editing of the analysis/research report.

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