Romania in the ETP Nanomedicine mirror group:

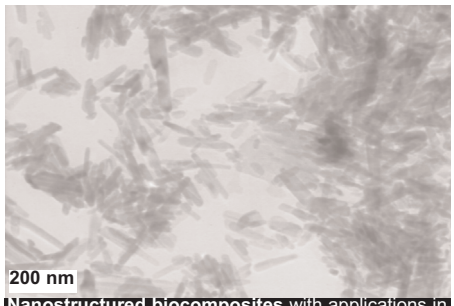
National contact point for the ETP NANOMEDICINE in Romania –
Prof. Dan Dascalu (dascalu@nano-link.net),
National Institute for R&D in Microtechnologies, IMT-Bucharest, Romania

Romanian organizations in ETP Nanomedicine (http://www.minatech.ro/nanomedicine)

● **National Institute for R&D in Microtechnologies, IMT-Bucharest:**
Activities/projects: see the brochure "Micro- and Nanotechnologies for Bio-medical Applications" also on web at **http://www.imt.ro** and the next page of the present flyer.

● **R&D National Institute for Nonferrous and Rare Metals, IMNR**
Activities/projects within the Nanostructured Materials Laboratory in IMNR (see more details on http://www.minatech.ro/nanomedicine/members.htm):
- Advanced Technologies for the synthesis and processing of biocompatible nanocomposite powders
- Integrated technology Research Network in advanced biocompatible structures for dental implants
- Integrated technologies for obtaining nanostructured biocomposites with applications in the regenerative medicine of bone tissue
- Hybrid nanostructured thin films for biosensors and biobanks
- Accreditation of a laboratory for chemical-physical characterisation of nano-bio- materials;

Contact person: Dr. Roxana Piticescu (roxana@imnr.ro)

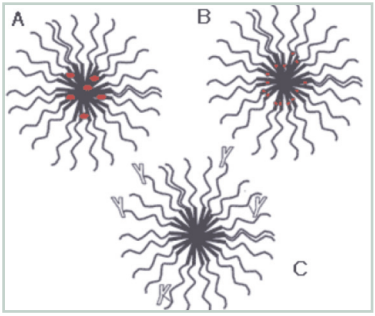


Nanostructured biocomposites with applications in the regenerative medicine of bone tissue

● **"Petru Poni" Institute of Macromolecular Chemistry**

Amphiphilic polymer aggregates in nanomedicine

Amphiphilic polymers obtained by chemical modification of water soluble macromolecules with hydrophobic groups can self-aggregate via hydrophobic associations giving rise to various nanostructures such as dense nanoparticles, bilayer vesicles, or micelles. These nanostructures can exist as colloidal solutions or dispersion and are able to incorporate non-polar biomolecules in the hydrophobic regions of the aggregates. A subtle balance of hydrophobic and hydrophilic components can produce a range of structures from a single linear soluble polymer. Due to the linear dependence of nanostructure hydrodynamic diameter on hydrophobic grafting density, and polymer molecular weight these parameters may be manipulated to yield nanostructures of different sizes. In the fabrication of nanomedicine, the size of the particle is a crucial controller of biodistribution. After i.v. administration, the complex polymer aggregate-biomolecule ensure an enhanced bioavailabilty of the biomolecule, control the time and site of its delivery.

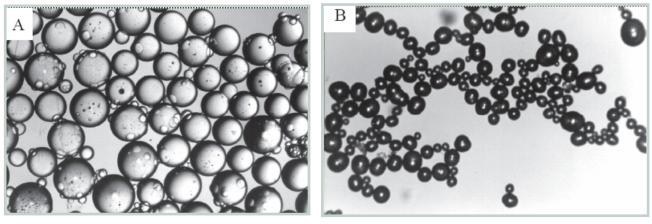


Polymeric micelles: A = drug solubilised in hydrophobic micelle core; B=drug covalently linked to hydrophobic portion of polymer chain; C=polymeric micelle with antibodies attached to hydrophilic portion of polymer molecule.

Contact person: Marieta Nichifor, Dep of Bioactive and Biocompatible Polymers **ICMPP** Iasi, Romania.
E-mail: nichifor@icmpp.ro

Intelligent micro- and nanoparticles for the development of novel drug delivery systems and analytical tools for pharmaceuticals

It has been widely recognized that the constant release of drug is not the only way to maximum drug effect and minimum side reactions and the assumption used for constant release rate sometimes fails its validity for physiological conditions. To overcome this drawback, self-regulated drug delivery systems have been used as novel approaches to delivery drug as required. To achieve this drug delivery system, intelligent or stimuli-sensitive micro- and nano-spheres have been exploited as candidate material. This material has been exploited for the development of pulsatile (on-off) drug delivery systems.



Optical photomicrographs of poly (NIPAAm-co-AAm) microspheres in the swollen state in phosphate buffer at pH=7.4, below the LCST value at 22 °C (A), and above the LCST value at 45 °C (B).
(NIPAAm= N-isopropylacrylamide, AAm= Acrylamide, LCST = lower critical solution temperature)

Contact person: Gheorghe Fundueanu and Marieta Constantin; Dep of Bioactive and Biocompatible Polymers, **ICMPP** Iasi, Romania.
E-mail: ghefun@icmpp.ro

RO-NANOMED "Integrated Research Network Devoted to Nanobiotechnology for Health – Romanian Nanomedicine Network"

Assistance for Romanian participation to ETP Nanomedicine

http://www.imt.ro/ro-nanomed

Coordinator: Prof. Dan Dascalu (dascalu@nano-link.net), IMT-Bucharest, Romania (http://www.imt.ro), project financed by National Programe CEEX

RO-NANOMED aims to create and develop an integrated research network in the field of nano- bio-technology for health and is targeting integration into the **ETP NANOMEDICINE**.
13 Romanian partners from 6 National R&D Institutes, 1 R&D Institute, 3 Institutes of the Romanian Academy, 2 Universities and 1 research center.

Research projects within RO-NANOMED

Cluster 1 - Regenerative Medicine:
- "New advanced techniques from cellular biology to test the nanomaterials biocompatibility"
8 "New functional nano-implants for medical applications (dentistry, general surgery and ophthalmology)"
- "Hybrid nanostructured materials for cell growth in biobanks"
- "Nanostructures and nanosystems for bone implants"

Cluster 2 - Targeted drug delivery and release:
- "Biological nanostructures used in drug release"
- "Studies regarding new vectors/markers for controlled drug delivery systems"
- "Development of new biomaterials for targeted drug delivery"
- "Development of new hydrogels for medical applications"
- "Nanostructured silicon for biomedical applications"

Cluster 3 - Nano-diagnostics:
- "Multichannel probe for on-line registration of the electrical activity at cellular level"
- "Development of new molecular markers for monitoring of cancer evolution"
- "Magnetic biosensor for nano-diagnostics"
- "Nano- and microfluidics as a bridge from diagnostics to medical treatment"
- "Development of new semiconductive polysilans for biosensor applications"

NANOBIOLAB: *Is a laboratory used in common by all network partners.* It has been developed in the 100-class clean room built at IMT-Bucharest and is devoted to technological research (new materials, structures, particles, devices etc.) involving biological materials.

New specific equipments:

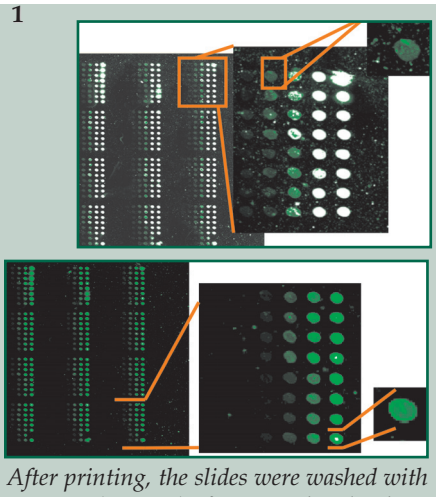
- **Omni Grid Micro Plotter:** can dip into a source plate and spot a given volume of sample solution onto a solid surface (e.g. glass slide, silicon substrate) - up to 200 consistent spots can be produced from a single dip.
- **GeneTAC UC4 Scanner:** is the pair of the nano-plotter, used for reading the chips, for DNA detecting and deposition - it offers high resolution scanning across the entire surface of standard microarray substrates.

Future aquisitions: **VersaSTAT3** (electrochemical impedance spectroscopy; corrosion analysis; (bio)sensor development) and **EIProScan – Electrochemical Probe Scanner** for surface analysis (scanning electrochemical microscopy); surface structuring (local deposition of metal/conductive polymers in the micro/nanometer scale).

Recent results:

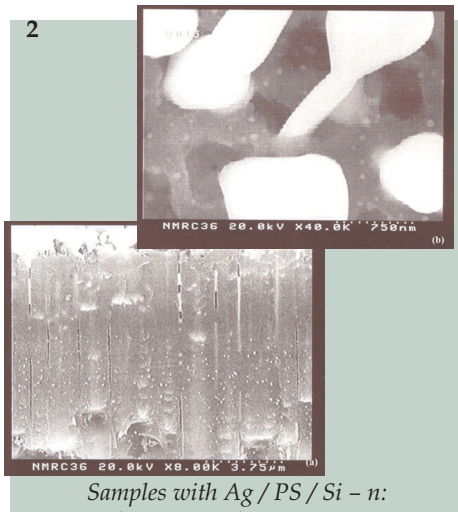
- Surface Modification for Protein Attachment in Microarray Technology (1);
- Resorbable porous silicon nanocomposite reservoirs for mineral or drug delivery (2);
- Nanocomposite silicon based membranes for microdevices. Two types of Si membranes were designed and fabricated (3).

1



After printing, the slides were washed with PBS (pH=7,4) after 20, 40' and 60'

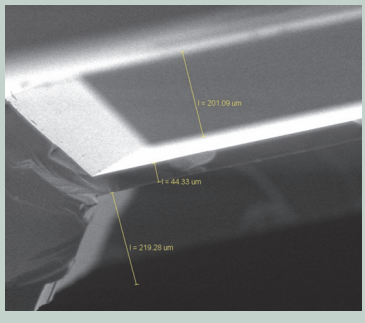
2



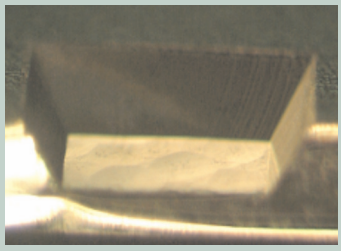
Samples with Ag / PS / Si – n: plan view and cross section

3

- suspended at the middle Si wafer, in depth;

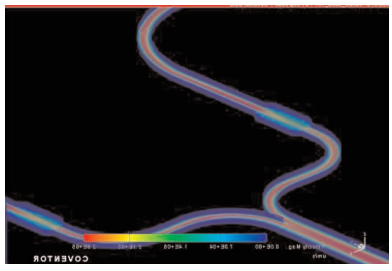


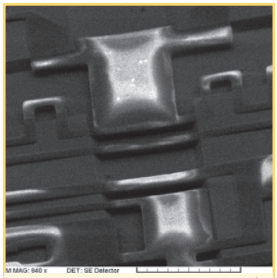
- integrated on the Si wafer face



Contact person: Dr. Irina Kleps (irinak@imt.ro), **Dr. Mihaela Miu** (mihaelam@imtr.o), IMT-Bucharest.

Bio-applications in FP6 projects (IMT-Bucharest)





SEM picture: integrated sensors experiments

"Development of a toxin screening multi-parameter on-line biochip system" – ToxiChip; FP6 STREP, Priority 2, IST

IMT role: development of a temperature sensor, as well as a pH sensor, that will be integrated with microfluidic platforms and development of a data acquisition system.

"Multi-domain platforms for integrated micro-nano technology systems - Service Action" INTEGRAMplus; FP6 IP, Priority 2 – IST

IMT role: prototyping and manufacturing access - IMT is in charge of providing access to biosensing and biointegration (microfluidics-based); design and virtual manufacture - IMT deals with modelling and simulation for MEMS, optical and microfluidic devices as well as Silicon-Polymer hybrid simulation; technology convergence and integration activities.

"Multi-Material Micro Manufacture: Technologies and Applications" 4M; FP6 NoE, Priority 3 – NMP.

IMT role: microfluidics for medicine.

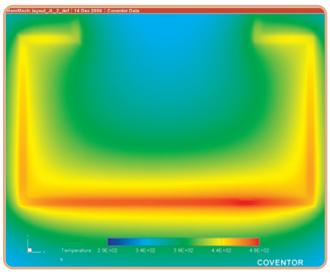
Contact person: Dr. Carmen Moldovan (cmoldovan@imt.ro)

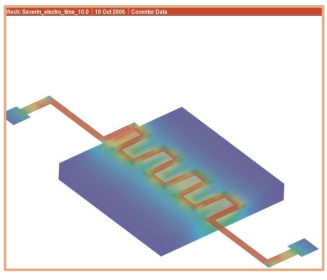
"Lab-on-a-chip implementation of production processes for new molecular imaging agents" – Mi-Lab-On-Chip, STREP, Priority 3 – NMP.

IMT role: design and prototyping microfluidics components and chips; simulation of chip functionalities.

Recent results: simulation results on thermal components of a lab-on-a-chip for medical imaging.

Contact person: Phd. Oana Nedelcu (oanan@imt.ro)





Fluid-Structure Interaction between fluid and check valve in the pneumatic micropump

Romanian Collaboration Platform for NANOMEDicine (RCP-NANOMED)

http://www.minatech.ro/nanomedicine

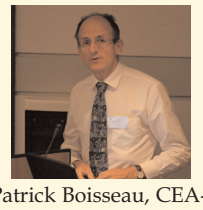
The platform includes 27 Romanian organizations interested in the domain: 10 National R&D Institutes, 1 R&D Institute, 4 Institutes of the Romanian Academy, 5 Universities, 2 research centers and 5 private companies.
RCP-Nanomed has the main objective to concentrate resources and correlate efforts at national level in order to develop the scientific and technologic nanomedicine domain, in close collaboration with the ETP Nanomedicine.

The RCP-NANOMED platform was launched on 4th of July 2006 in Bucharest, with support from European Commission and ETP Nanomedicine Several foreign specialists from the nanomedicine domain attended the event and the working group of the platform was established.

The Workshop "Cooperating in FP7. Biomedical applications of micro- and nanotechnologies" was organized on 6th of December 2006, in Bucharest and several nanomedicine topics were presented with this occasion (7 presentations given by foreign participants).

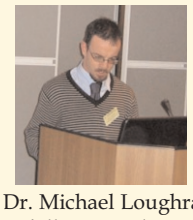
Collaboration between RO-NANOMED and the German NanoBiotechnology Network "NanoBioNet" is expressed by the presence of NanoBioNet representatives to both events mentioned above and the visit of Prof. Dan Dascalu to the NanoBioNet headquarters in Saarbruken (May 2006).

From the Platform website (see above), databases with specialists, research centers and international projects in the domain can be accessed.



Dr. Patrick Boisseau, CEA-LETI, Grenoble, France presenting the Strategic Agenda of Research of the ETP Nanomedicine

Dr. Mathias Mallmann, Science Park, Sarbrucken, Germany presenting NanoBioNet, a competence network in nanobiotechnology



Dr. Michael Loughran, Tyndall National Institute, Cork, Ireland

Prof. Dr. P.Laggner; Inst. für Biophysik und Nanosystemforschung, Austria

Dr. Rer. Nat. Ute Steinfeld; KIST Europe Forschungsgesellschaft, Germany

Romanian organizations in ETP Nanomedicine (continue)

● **National Institute for R&D in Electrical Engineering, INCDIE ICPE-CA**
Activities/projects (see more details on http://www.minatech.ro/nanomedicine/members.htm):
- Magnetic nanogranular composite materials with applications in malignant tumors diagnostic;
- Multifunctional advanced materials doped with silver nanoparticles models of bactericidal products;

Contact person: Dr. Wilhelm Kappel (kappel@icpe-ca.ro)

● **Institute of Physical Chemistry of the Romanian Academy**: Activities within the Laboratory of Chemical Thermodynamics (see details on http://www.minatech.ro/nanomedicine/members.htm): characterization and investigation from the energetic point of view of the advanced materials involved in the complex modern systems and the new technologies.

Contact person: Dr. Speranta Tanasescu (stanasescu@chimfiz.icf.ro)

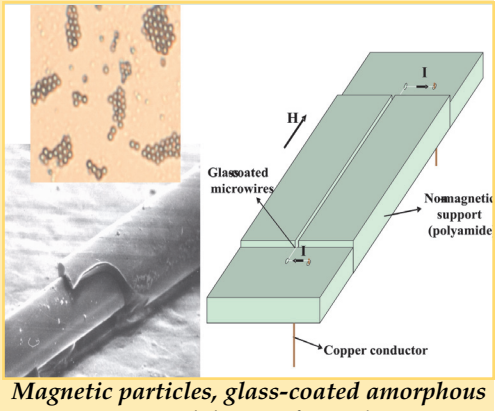
Other participants

● NIRD for Technical Physics, Iasi, Romania

Giant magnetoimpedance (GMI) biosensor for biomedical applications

Achievements: Design and fabrication of a GMI-based biosensor prototype for magnetic detection of biomolecules. A microdevice able to identify target biomolecules such as antibodies. The biomolecules detection is performed by using the GMI effect in glass-coated microwires, and magnetic particles as markers for target biomolecules. The detection principle is based on impedance modifications of the microwires by magnetic fringe fields of magnetic markers.

Contact person: Prof. Horia Chiriac (hchiriac@phys-iasi.ro),
INCDFT-IFT Iasi, tel. : +40 232 430680, fax. : +40 232 231132,



Magnetic particles, glass-coated amorphous microwire, and device of GMI biosensor prototype.

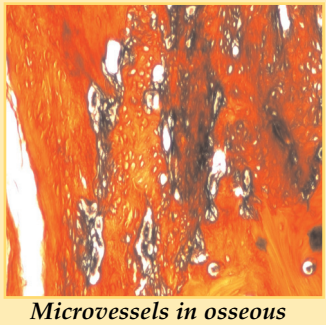
● National Institute of Research in Pathology "Victor Babes", Bucharest, Romania

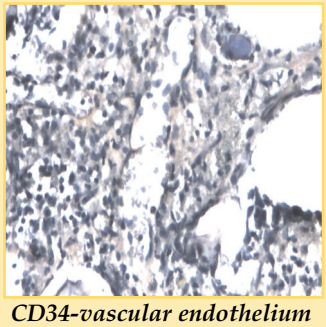
Nanostructured polymer implants – characterisation and quantification of angiogenesis and proliferation by immunohistochemistry;

Angiogenesis was quantified using the vascular endothelial markers CD34, EGFR, VEGF and proliferation using PCNA, Ki67. Immuno-labelling with CD34, EGFR and VEGF reveals with accuracy the development of the vascular network in correlation with stage of the evolution.

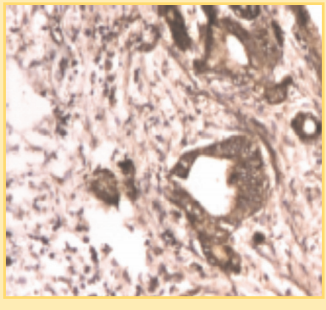
The understanding of angiogenic and proliferation process are useful for a better characterisation in osteointegration (nanostructurated polymers).

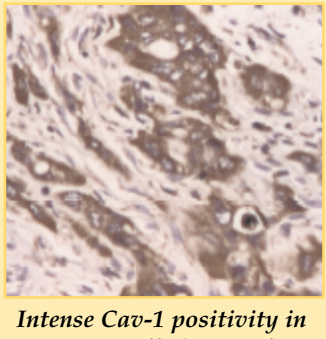
Contact person: Dr. Cristiana Tanase,
E-mail: bioch@vbabes.ro
Financed grant: Excellence research (RONANOMED)


Microvessels in osseous reconstruction tissue-4 weeks; IHC 20X


CD34-vascular endothelium of zone. Gomori 10X

Caveolin-1 expression as a possible biomarker in pancreatic cancer diagnosis

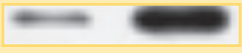

Cav-1 positive in tumor cells and in smooth arterial muscular wall. IHC, 10X


Intense Cav-1 positivity in tumor cells (tumoral tissue) IHC, 20X

Caveolin1 (Cav-1) function either as a tumor supressor or as a promoter of metastasis. Our goal was to reveal the immunohistochemical expression of Cav-1 in different pancreatic tumors, in comparisson with Ki67 and p53, in order to evaluate their involvement in tumour agressivness.

Overexpresion of cav-1 was correlated with: tumoral grading, proliferration markers (Ki67, p53), serum tumor markers (CEA, CA19.9) and angiogenic markers (VEGF, bFGF)

Caveolin-1 activity (western blot).
Peritumoral Tumoral



Contact person: Cristiana Tanase, E-mail: bioch@vbabes.ro

● Institute of Biochemistry of the Romanian Academy (http://www.biochim.ro/)

Contact person: Dr. Mihaela Trif (trif@biochim.ro)