



FROM FUNCTIONAL POLYMERS TO MICRO- AND NANOSTRUCTURED BIOMATERIALS

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Functional polymers

**Differently shaped
macromolecular
structures**

Covalent linkages

Copolymers: block, graft

**Crosslinked, (hyper)branched,
dendrimers**

Interpenetrating networks



**Supramolecular
structures**

Noncovalent interactions

Different morphologies

**Micro/nanosized objects
(particles)**

Thin (multilayered) films

Composites

Inclusion complexes

Poly[(N-acylimino)ethylene] (PNAI) building blocks

- Functional micro- and nanoparticles based on PNAI building blocks
- PNAI – based gels

Functional siloxane building blocks

**”Petru Poni” Institute of
Macromolecular Chemistry (ICMPP)**

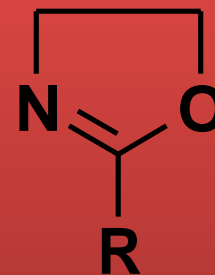
**Centrul de Cercetari Avansate
pentru Bionanoconjugate si
Biopolimeri (IntelCentru)**

Poly[(N-acylimino)ethylene] (PNAI) building blocks

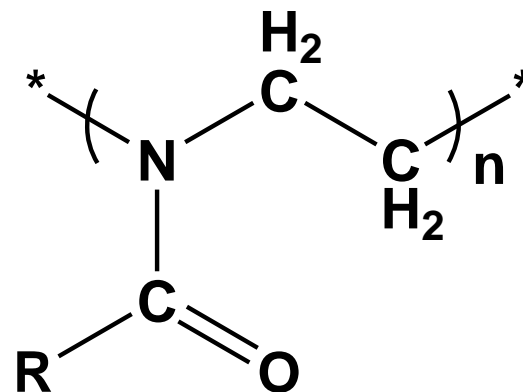
- ❑ Functional micro- and nanoparticles based on PNAI building blocks
- ❑ PNAI – based gels

Poly[(N-acylimino)ethylene]s (PNAI)

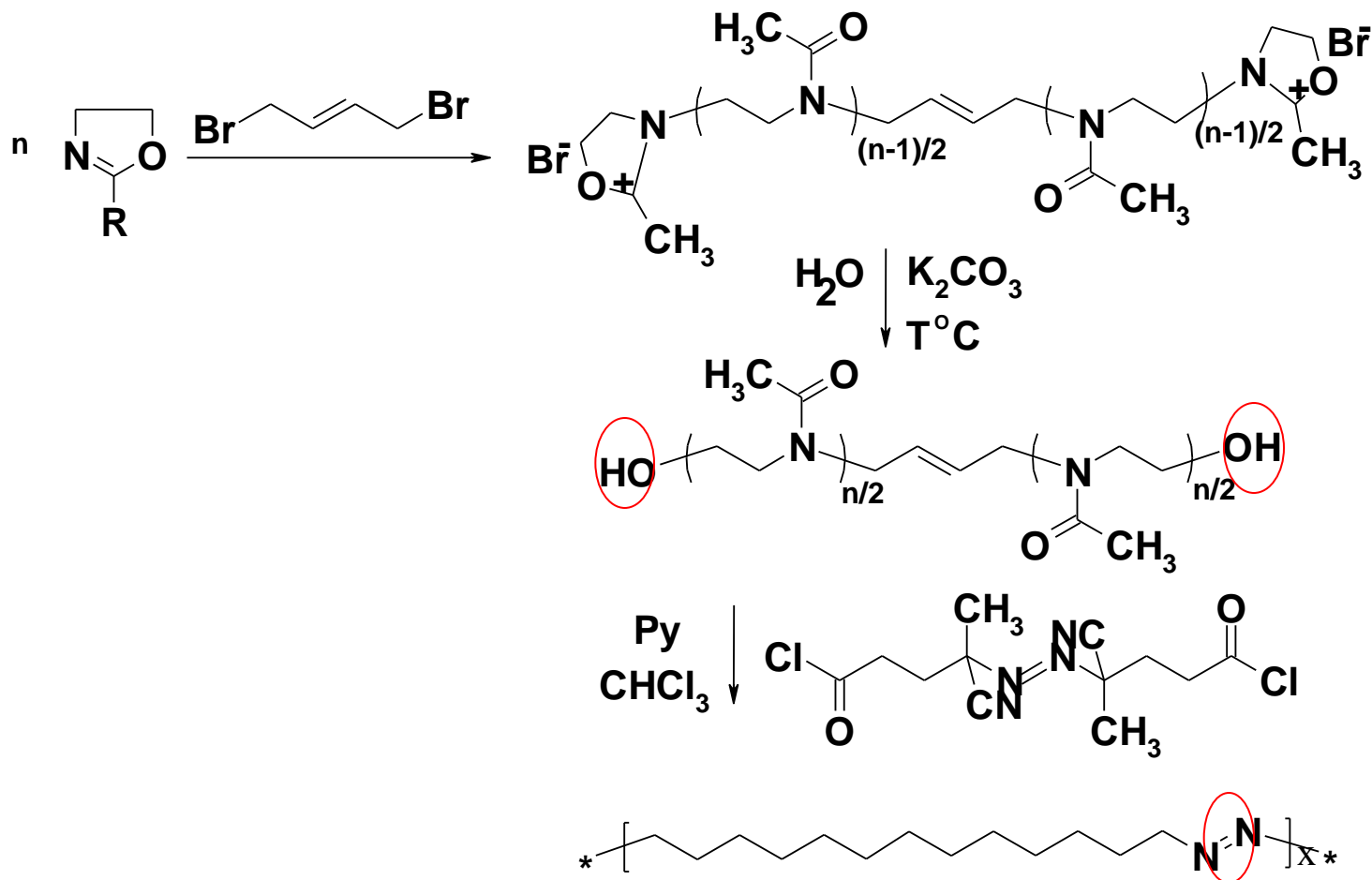
- control of structural properties (living cationic polymerization)
- biocompatibility or no acute toxicity
- hydrophilic or hydrophobic properties (R)
- chelating ability
- good adhesion to polar surfaces
- facile modification to PEI
- compatibility with most common organic polymers
- chain flexibility
- crystallization ability



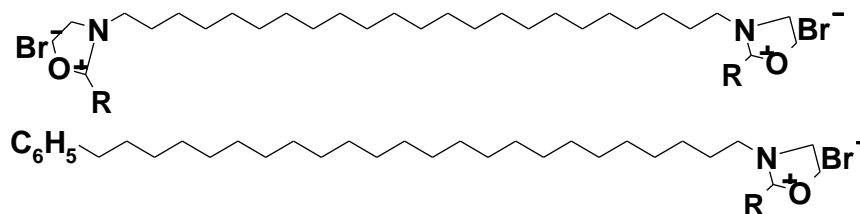
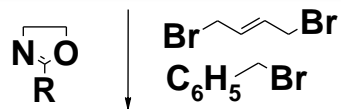
tailored polymers
multifunctional polymers
complex architectures



Poly[(N-acylimino)ethylene] azo initiators

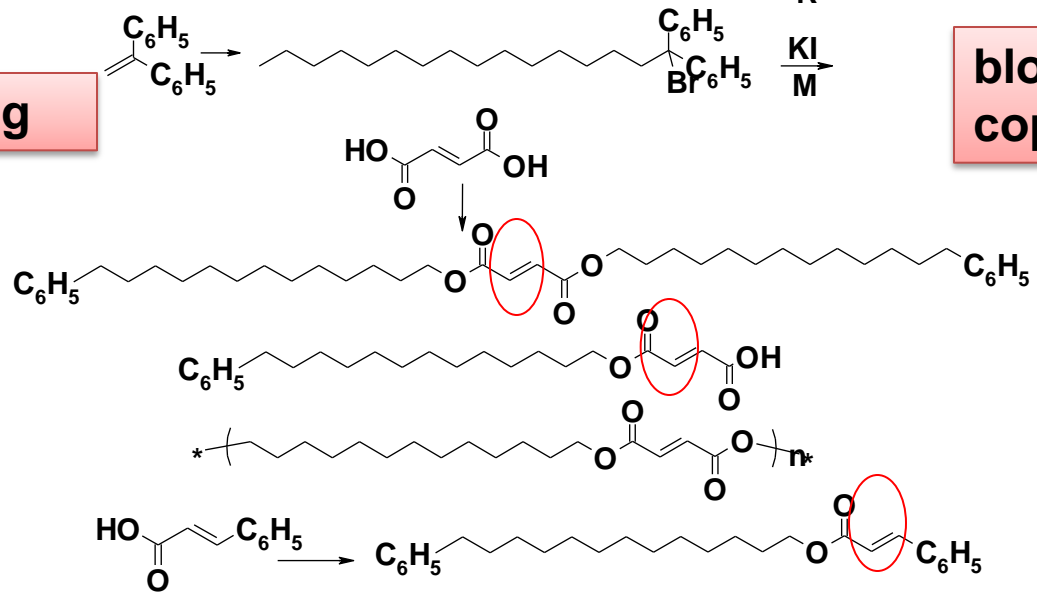


Functional polymers by end capping of living PNAI chains



end capping

block copolymer



Functional micro- and nanoparticles

- dispersion polymerization

- monomer: styrene

- stabilizer: poly(N-acetyلهthylenimine) macromonomer
(Dn = 0.5 - 1 μm , PI = 1.02 - 1.05)

- soapless emulsion polymerization

- monomer: styrene, methyl methacrylate

- poly(N-acetyلهthylenimine) macroazoinitiator
(Dn = 100 - 200 nm, PI = 1.02 - 1.04)

- monomer: styrene

- poly(N-acetyلهthylenimine) macromonomer
(Dn ~ 200 nm, PI = 1.006 - 1.04)

- microemulsion polymerization

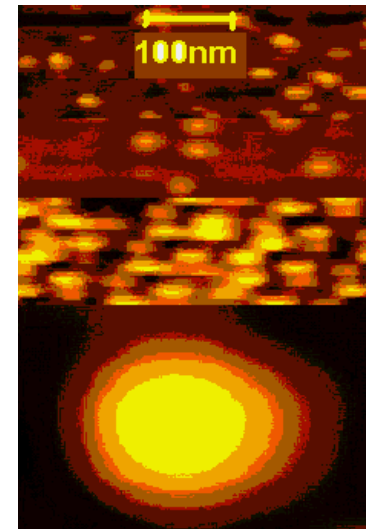
- monomer: methyl methacrylate, butyl methacrylate

- co-surfactant: poly(N-acetyلهthylenimine) macroazoinitiator or macromer

- main surfactant: SDS

- (Dn = 10 - 50 nm, PI = 1.2)

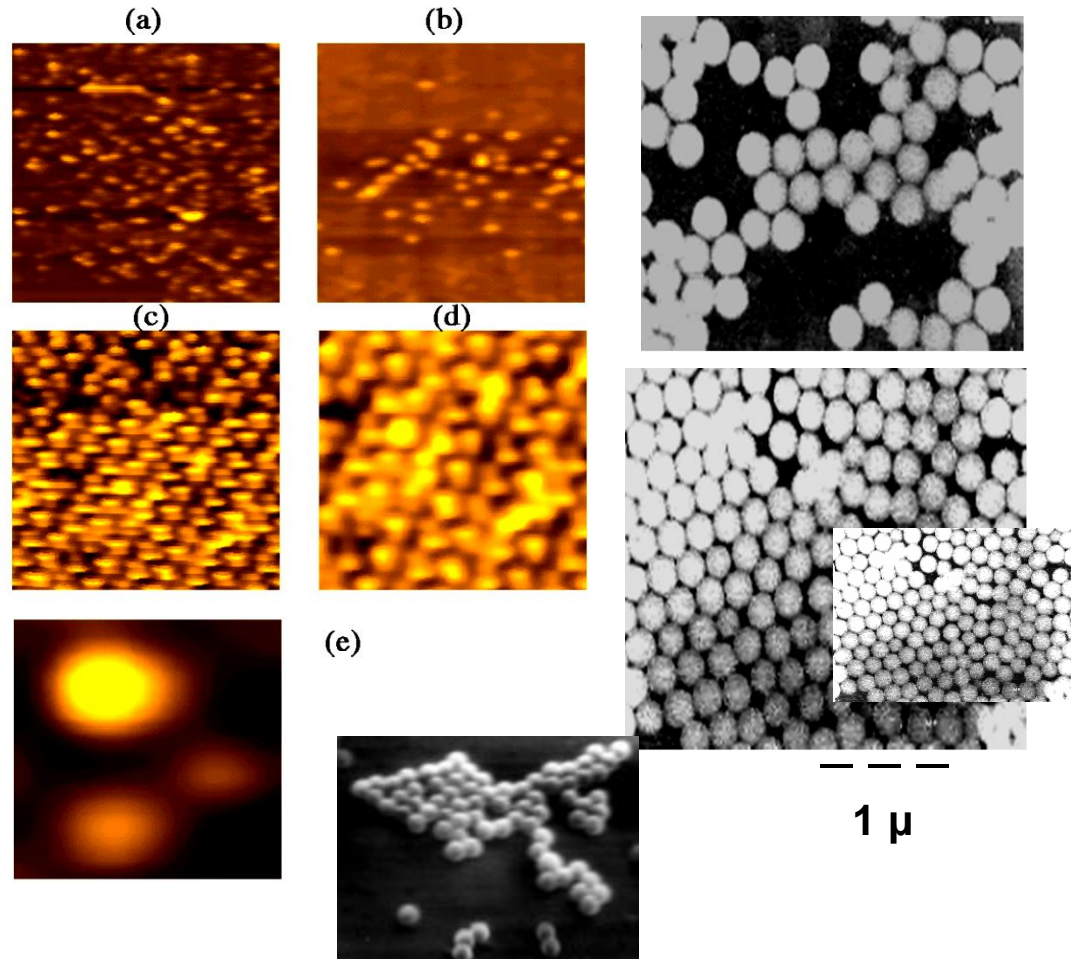
Dn: 10 – 1000 nm
PI: 1.006 – 1.2
core-shell structure



Core-shell nano/micro particles by soapless emulsion / microemulsion polymerization

- ✓ size control
- ✓ high surface functionality
- ✓ high purity (“clean” particles)
- ✓ low toxicity
- ✓ bio-compound immobilization ability
- ✓ film forming ability
- ✓ narrow size distribution or “monodispersity”

drug release systems
uniform thin polymer films (electrode coating, biosensors)
high selectivity membranes



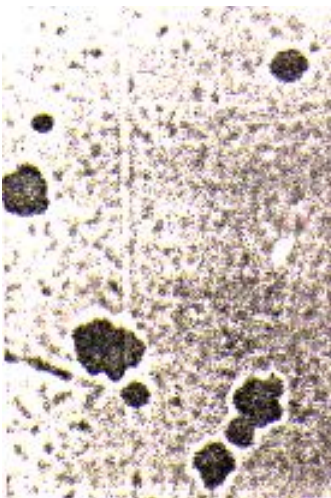
Organic – inorganic composite materials

MMA polymerization in the presence of silica and PNAI macroinitiator (soapless emulsion polymerization)

Peculiarities

- early formed amphiphilic oligomers act as dispersants
 - increased polymerization rate
 - increased adhesivity to inorganic particles
- water-soluble PMMA-b-PNAI → dispersant

t = 0 min



t = 10 min



homogeneous
composite material

(t = 50 min)

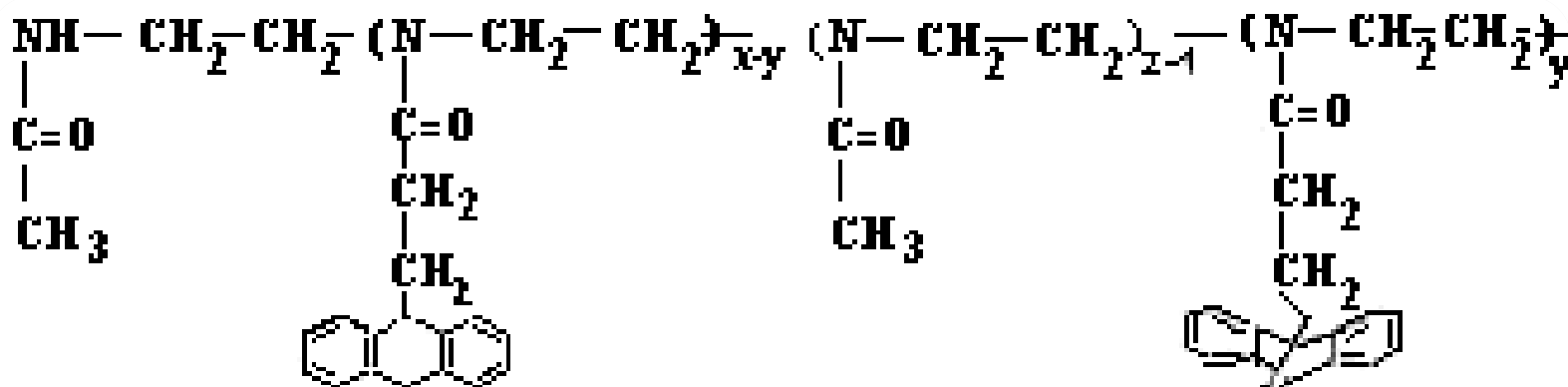
PI = ~ 1.0

Dw = ~ 500 nm



PNAI – based gels

specific reactions of functionalized PROZO:
photodimerization of the photosensitive pendant groups



Thermosensitive gels

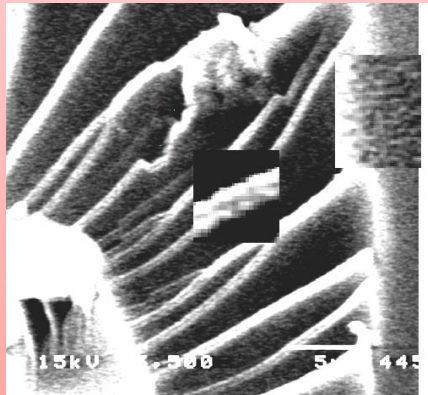
Precipitation polymerization

Monomers: HEMA

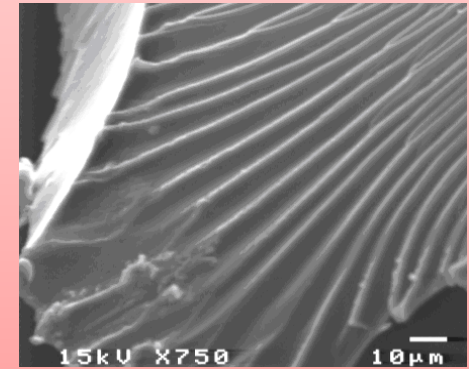
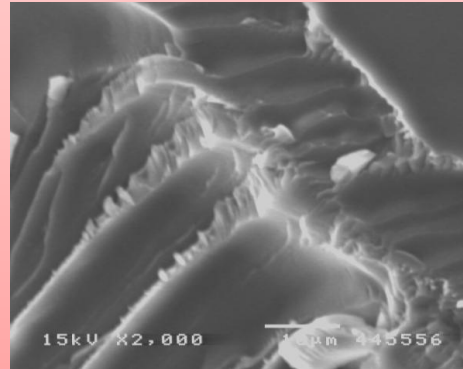
NIPAAm (LCST 32 C)

PNAl macromonomers (PEOZO – LCST 36 C)

**Reaction conditions: HEMA/NIPAAm/PROZO w/w/w - 1:1:1
60 C, ethanol, AIBN, Ar, 20h**



**self assembled core-shell microparticles
interconnected pore structure**



**large channels
open macropores**

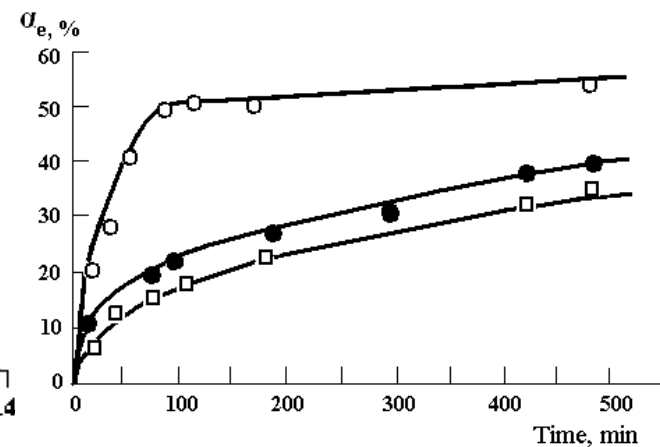
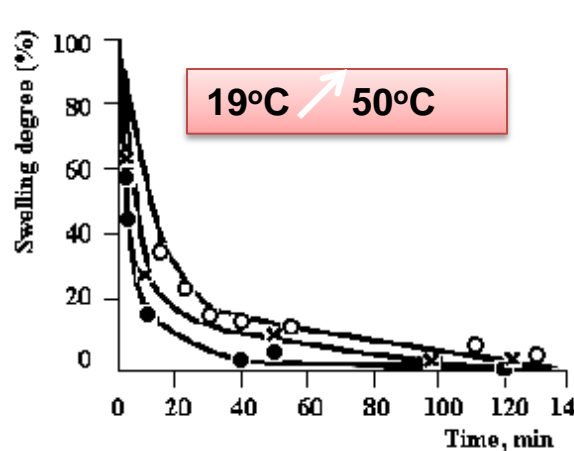
Stimuli responsive hydrogels

(temperature responsive)

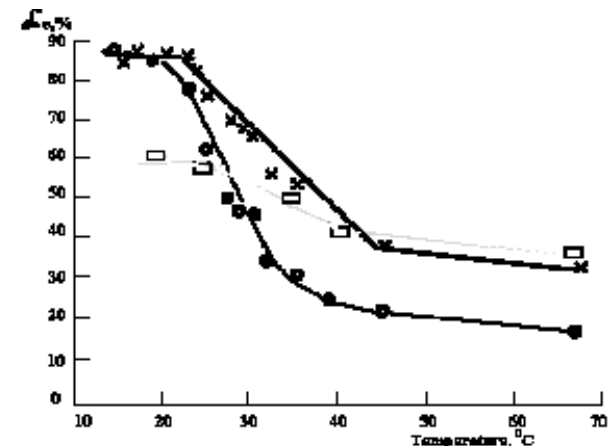
controlled structure and characteristics (hydrophilic/hydrophobic balance, crosslinking density, amount of thermosensitive chains)

LCST – therapeutic domain (28 – 38 C)

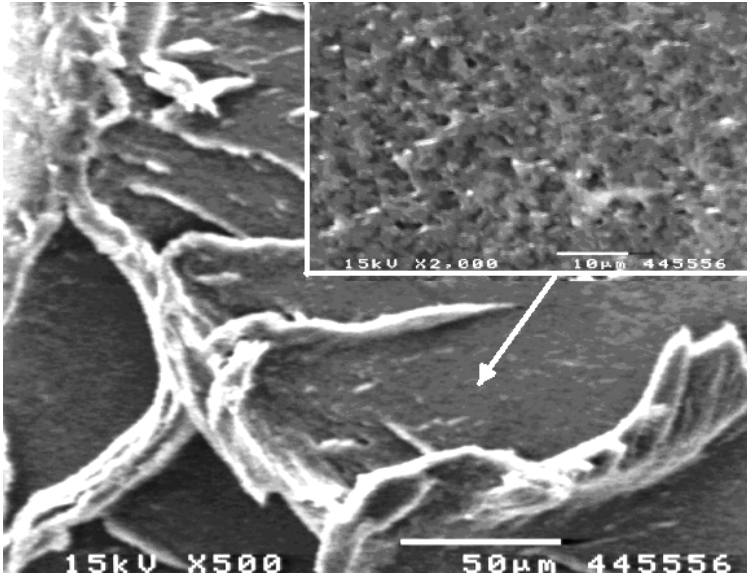
Sample	LCST (°C)
M ₆	27.5
M ₁₅	32.0
M ₂₅	33.0
M ₄₅	38.0
E ₁₅	28.5
E ₂₅	30.0
E ₃₅	32.0
E ₄₅	31.5
BC ₁	28.5
BC ₂	27.6



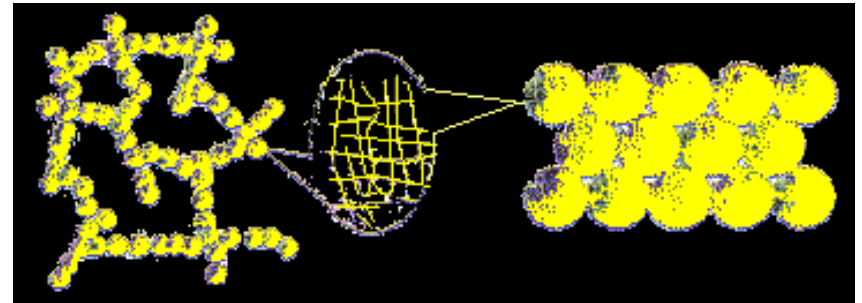
Swelling/deswelling kinetics



Self-assembling microgels



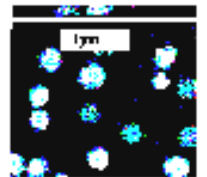
Self-assembling network
(ordered or not ordered)



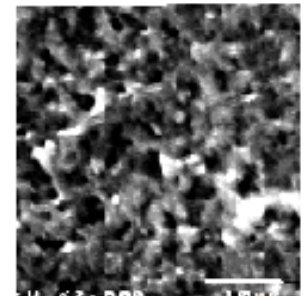
PEOZO/PNIPAAm/PHEMA hydrogel

“on-off” switching materials
controlled drug delivery and storage systems
biomacromolecules storage/release
tissue engineering, in combination with
biodegradable polymers (collagen)

Microgels



Thermosensitive gels



**”Petru Poni” Institute of
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MACROMOLECULAR CHEMISTRY (ICMPP)

**Centrul de Cercetari Avansate
pentru Bionanoconjugate si
Biopolimeri (IntelCentru)**

BIOPOLIMERI (INTELCENTRU)

"Petru Poni" Institute of Macromolecular Chemistry (ICMPP)

- ❑ **founded in 1949 as an institute of the Romanian Academy**
- ❑ **Institute of Excellence of the Romanian Academy**
- ❑ **ranked in the first/ second/ third position among the 64 institutes/ centres of the Romanian Academy; second/ third position on the list of most innovative research/high education bodies in Romania**
- ❑ **internationally recognized – ISI, Philadelphia, USA, lists the Institute among the “main Romanian actors on the international scientific scene”**



Personnel

- ❑ **Total - 284**
- ❑ **researchers - 109**
- ❑ **PhD students - 50 - 60**
- ❑ **young researchers (less than 35 years old): 30%**
- ❑ **personnel with university degree: 175**
- ❑ **PhD thesis promoters: 11**

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Mission/performance indicators



- ❑ **Basic research in polymer science**
- ✓ yearly more than 170 papers, books, book chapters
- ✓ yearly more than 200 presentations in scientific meetings

- ❑ **Applied research, technology transfer and small scale production**
- ✓ industrial technologies for silicones, polyurethanes, ion exchangers, thermally resistant polymers
- ✓ specialty polymeric materials

- ❑ **Education & training (PhD, post-doc)**

- ❑ **Services**
- ✓ consultancy – preparation and processing of polymeric materials
- ✓ transfer of knowledge, certification for polymeric materials



Cooperation Network

- National cooperation**
 - ✓ universities, research institutions, companies, SMEs
 - ✓ the Institute coordinates *5 Romanian consortia* and is involved in more than *70 multi-partner national grants*

- International cooperation**
 - ✓ more than 50 research / high education centres in Europe, Japan, China, USA and Canada

European projects

- ✓ FP3 - partner in 3 projects (COST-PECO, PECO ERBIC IPDCT, INCO - COPERNICUS - ERBIC)
 - ✓ FP5 - partner in 5 projects (2 INTAS, 1 CRAFT, 2 GROWTH)
 - ✓ FP6 - partner in 7 projects (NoE, IP), project coordinator of SSA project RAINS
 - ✓ FP7 - partner in 4 projects, 3 projects under second evaluation
 - ✓ COST - partner in 6 COST Actions
-
- EuMaT Technology Platform, ENMat Platform**

MAIN projects - 2010

- **“Cristofor I. Simionescu” Postdoctoral School on Biomaterials (2010 – 2013)**
- **Advanced Research Center for Bionanoconjugates and Biopolymers (IntelCentru) (2009 – 2012)**
- **Synthesis and Investigation of Polymeric Metallosiloxanes – New Materials for Catalysis and Nanosciences (POLISILMET) (2010 – 2013)**
- **Strengthening the Romanian Research Capacity in Multifunctional Polymeric Materials (STREAMS) (FP7 – REGPOT-2010-1) (2011 – 2013)**



Proiectul ...



UNIUNEA EUROPEANĂ



GUVERNUL ROMÂNIEI



Instrumente Structurale
2007 - 2013

ANCS

Autoritatea Națională pentru Cercetare Științifică

CENTRU DE CERCETARI AVANSATE PENTRU BIONANOCONJUGATE SI BIOPOLIMERI ID 88, Nr. 03 / 01.03.2009, Cod SMIS – CSNR 2213

**Finantare: FONDURI STRUCTURALE, Programul Operational Sectorial
„Cresterea Competitivitatii Economice”, Axa Prioritara 2, Operatiunea 2.2.1.:
„Dezvoltarea infrastructurii C-D existente si crearea de noi
infrastructuri C-D”**

Director de proiect: Dr. ing. Mariana Pinteala



PETRU PONI

**Suma: 15 658 593 LEI
8 287 602 LEI (+TVA)**

METAMORFOZA ...



August 2010



Decembrie 2009



August 2009

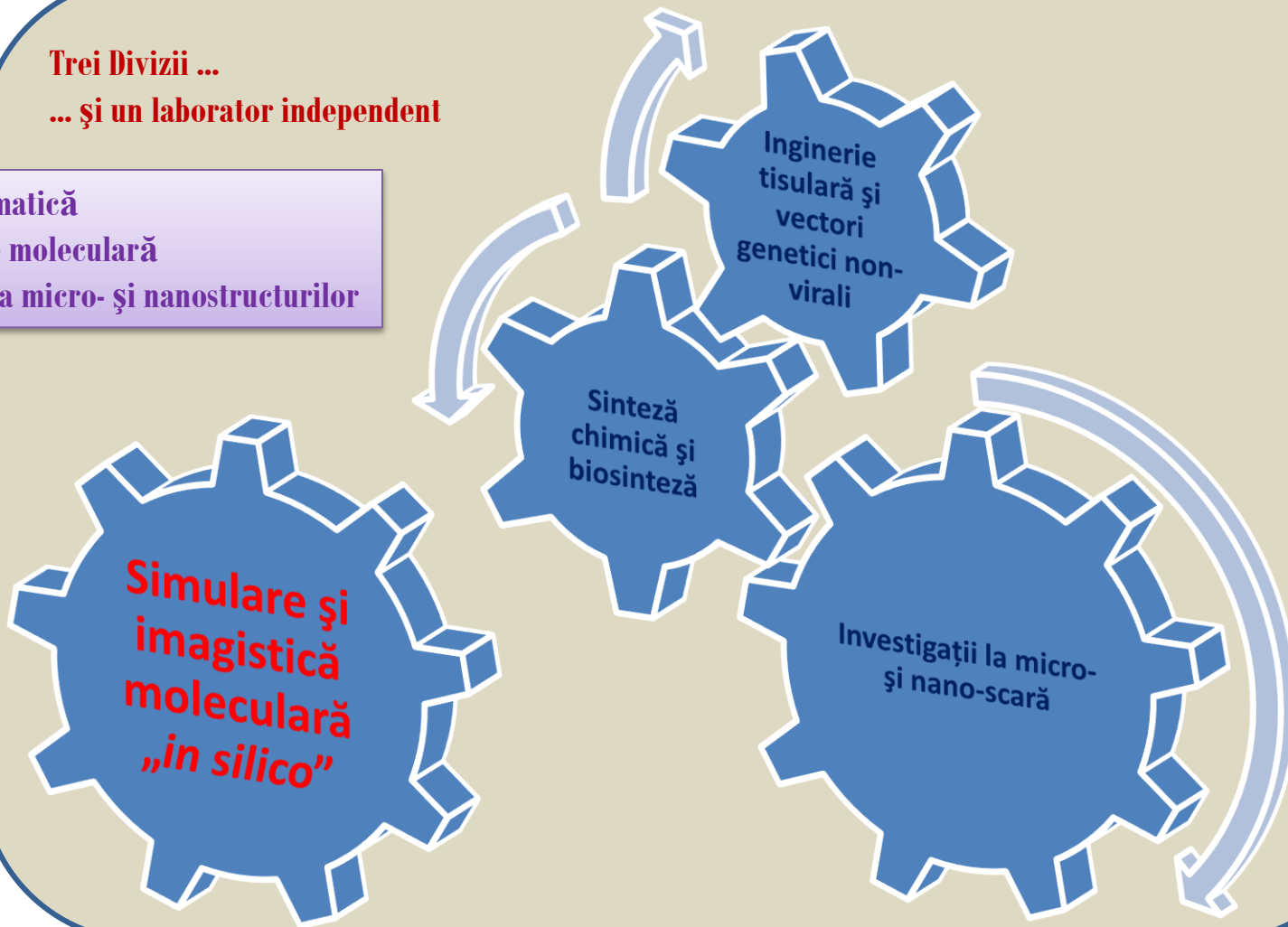


STRUCTURA ...



Trei Divizii ...
... și un laborator independent

- Bioinformatică
- Modelare moleculară
- Simularea micro- și nanostructurilor

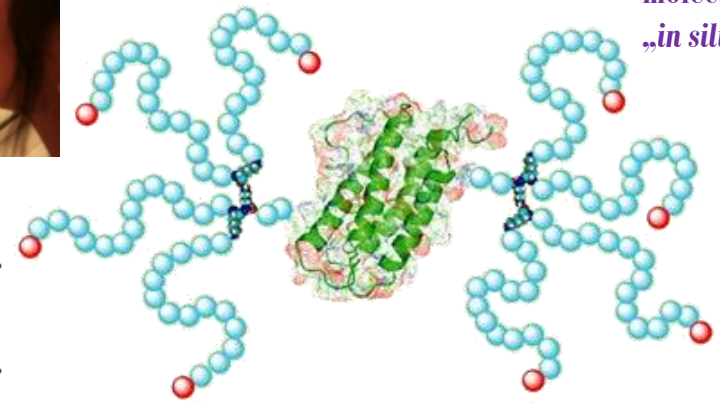
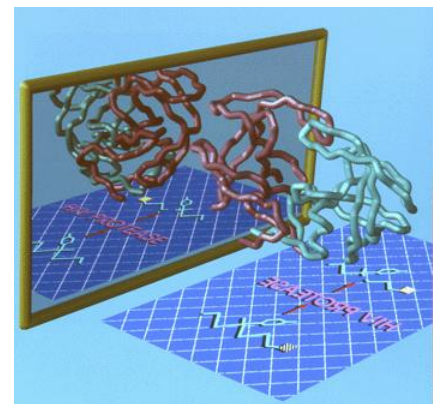


STRUCTURA, OBIECTUL GENERIC AL STUDIILOR, APLICATIILE ...

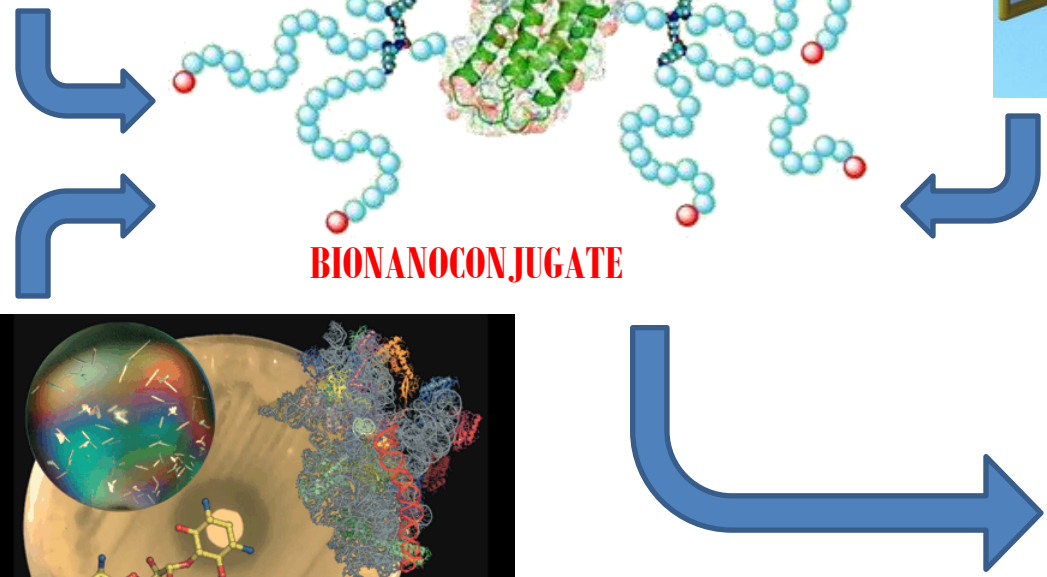


Sinteza chimica
si biosinteza

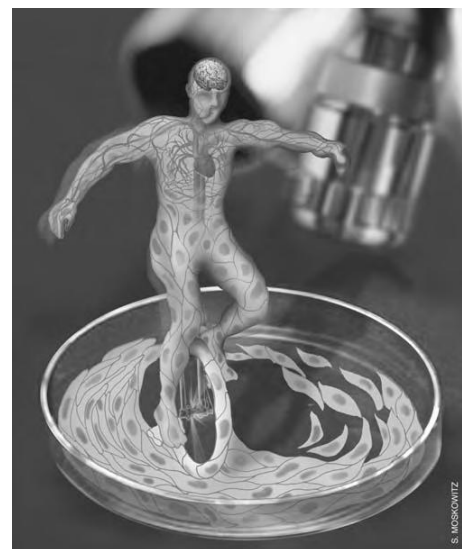
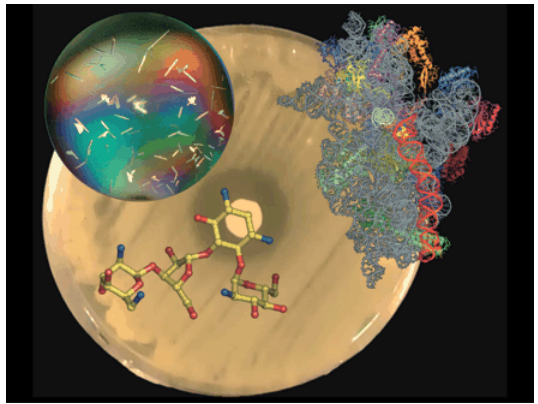
Simulare si
imagistica
moleculara
„in silico”



BIONANOCONJUGATE



Investigatii
la scara micro-
si nano

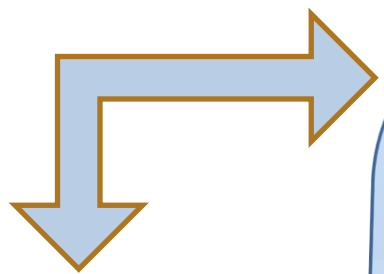
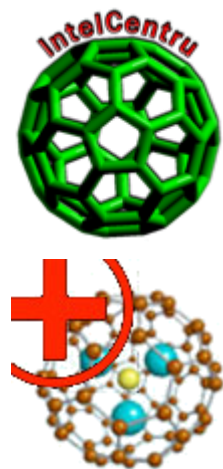


Inginerie tisulara
si vectori genetici non-virali

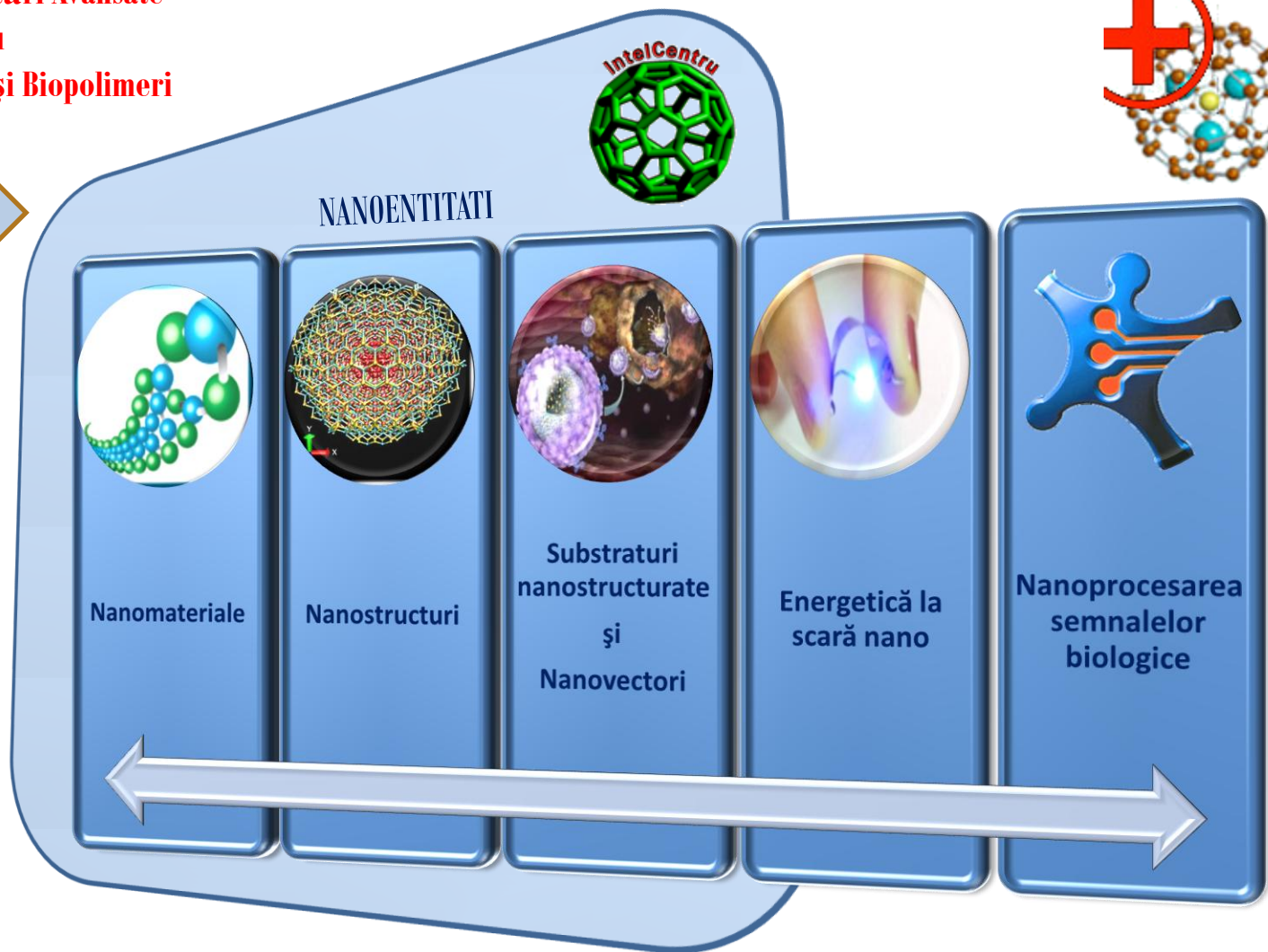


NANOMEDICINA ...

Domeniile de interes în cadrul
Centrului de Cercetări Avansate
pentru
Bionanoconjugate și Biopolimeri



Nanoentitati:
- nanomateriale
- nanostructuri
- nanovectori
cu aplicatii
biomedicale



NANOMEDICINA ...

**Domeniile de interes în cadrul
Centrului de Cercetări Avansate
pentru
Bionanoconjugate și Biopolimeri**



Medicina
regenerativă

Medicina
personalizata



Nanomedicina

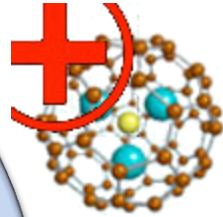
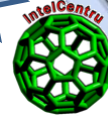
Medicina
substitutivă

Inginerie
tisulară

Ingineria
medicala

Bioinginerie

Inginerie
celulară



**Aria aplicativa extinsa,
în ale cariei circuite
se regaseste nanomedicina ...**



PETRU PONI

Centrul de Cercetari Avansate pentru Bionanoconjugate si Biopolimeri dispune de trei spatii de tip clean-room:

- un laborator pentru imagistica si caracterizarea nanoentitatilor (nivel ISO 6)
- cinci laboratoare pentru obtinerea si caracterizarea substraturilor destinate ingineriei tisulare si nanovectorilor (nivel ISO 8)
- un laborator pentru culturi celulare (nivel ISO 7)



Lucrul intr-un clean-room din clasa ISO 7 ...



Pregatirea vestimentatiei pentru lucrul intr-un clean-room din clasa ISO 8 ...



Dus de aer steril, la intrarea in clean-room din clasa ISO 6 ...



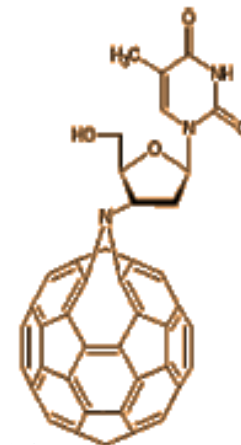
Aspirator pentru clean-room – uri ...

DIVIZIA „SINTEZA CHIMICA SI BIOSINTEZA” ..



Divizia „Sinteză chimică si Biosinteză” a Centrului dispune deja de toate facilitățile care să permită abordarea oricărei sinteze chimice în sfera compusilor macromoleculari, a nanostructurilor și a nanovectorilor.

Echipamente sofisticate pentru caracterizarea nanoentităților se regasesc si sunt functionale în laboratoarele diviziei.



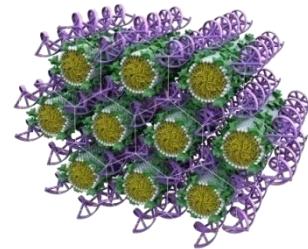
Delsa™ Nano Zeta Potential and Submicron Particle Size Analyzer



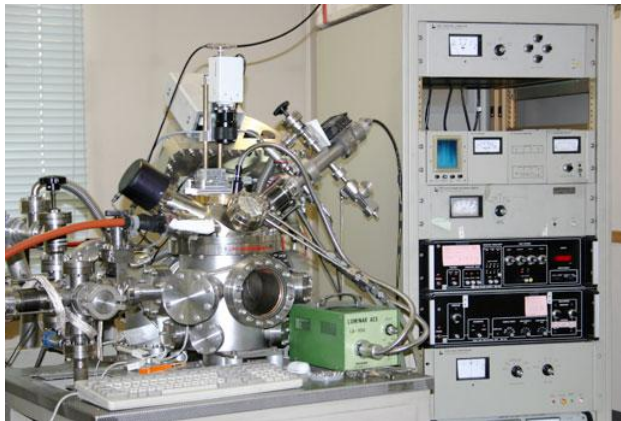
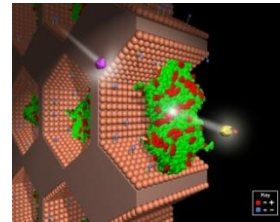
DIVIZIA „INVESTIGATII LA SCARA MICRO SI NANO” ...



Divizia „Investigatii la scara micro si nano” a Centrului va include laboratoare de manipulare, structurare si caracterizare la scara micro si nano, prin tehnici moderne, capabile sa puna in evidenta **spatialitatea si topologia reactivitatii fizico-chimice** a nanostructurilor, nanomaterialelor si substraturilor micro- si nanostructurate.



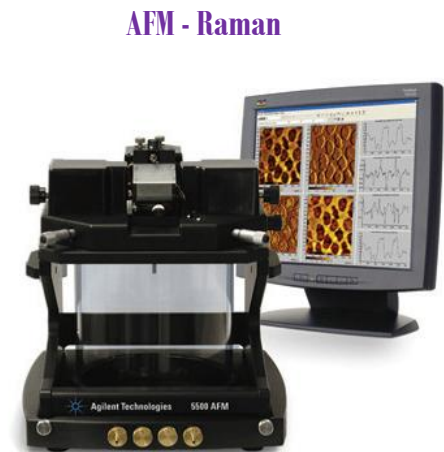
Imagistica stiintifica in domeniul materialelor si a structurilor la nanoscala implica analize la energii extreme: fie deosebit de ridicate, fie cu valori infime, pentru a asigura rezolutii spatiale satisfacatoare.



ESCA / XPS



TEM / SEM / STEM / ESEM

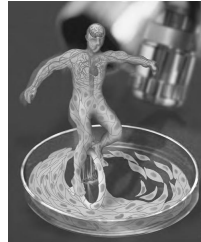


DIVIZIA „INGINERIE TISULARA SI VECTORI GENETICI NON-VIRALI” ...

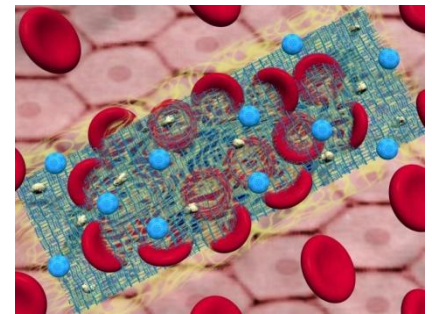
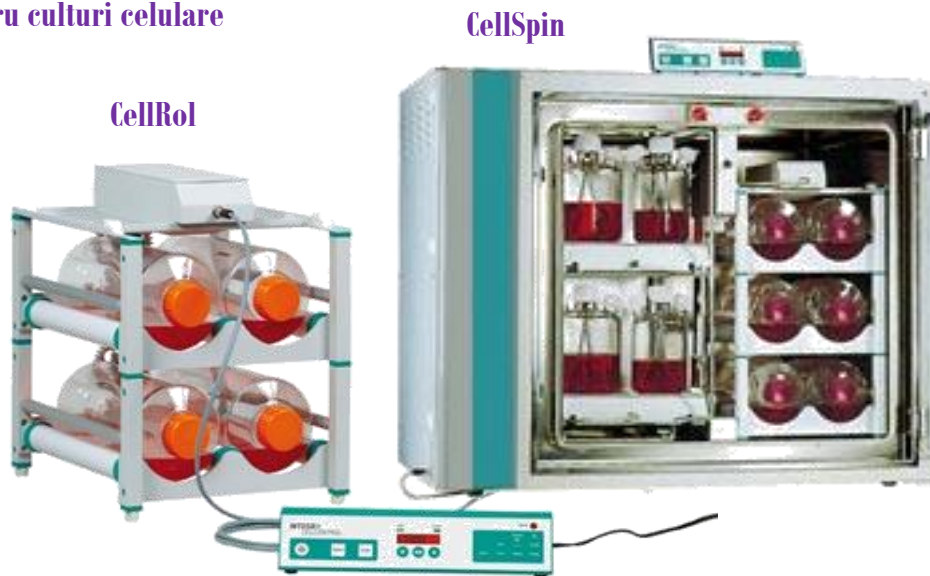


Divizia „Inginerie tisulara si Vectori genetici non-virali” a Centrului va fi dedicata generarii de biomateriale si substraturi micro- si nano-structurate, biologice active si cito-prietenose, precum si testarii efectelor biologice ale nanoentitatilor obtinute in cadrul diviziei ”Sinteza chimica si Biosinteza”.

Pentru controlul ciclului de viata al celulelor si pentru dirijarea sociologiei celulare, in cadrul acestei divizii se vor izola, purifica si caracteriza modulatori citologici de origine tisulara, utilizati apoi in culturi celulare.



Laboratorul pentru culturi celulare



CellLine



DIVIZIA „INGINERIE TISULARA SI VECTORI GENETICI NON-VIRALI” ...



Pentru studii de proteomică, enzimologie și inginerie celulară, divizia va dispune de sisteme analitice de înaltă finețe, capabile să discearnă între formele biologic-active ale speciilor biochimice și cele denaturate, ori cu funcționalitate alterată.

Sistem pentru electroforeza capilara



Sistem pentru electroporatie



Spectrometru cu diroism circular



Sistem integrat pentru analiza cromatografica



Thank you for your attention!

