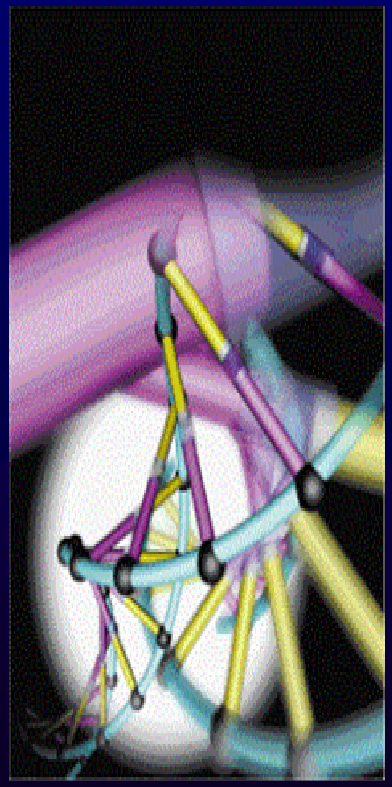
Nanotechnology: materials and devices for Health Care



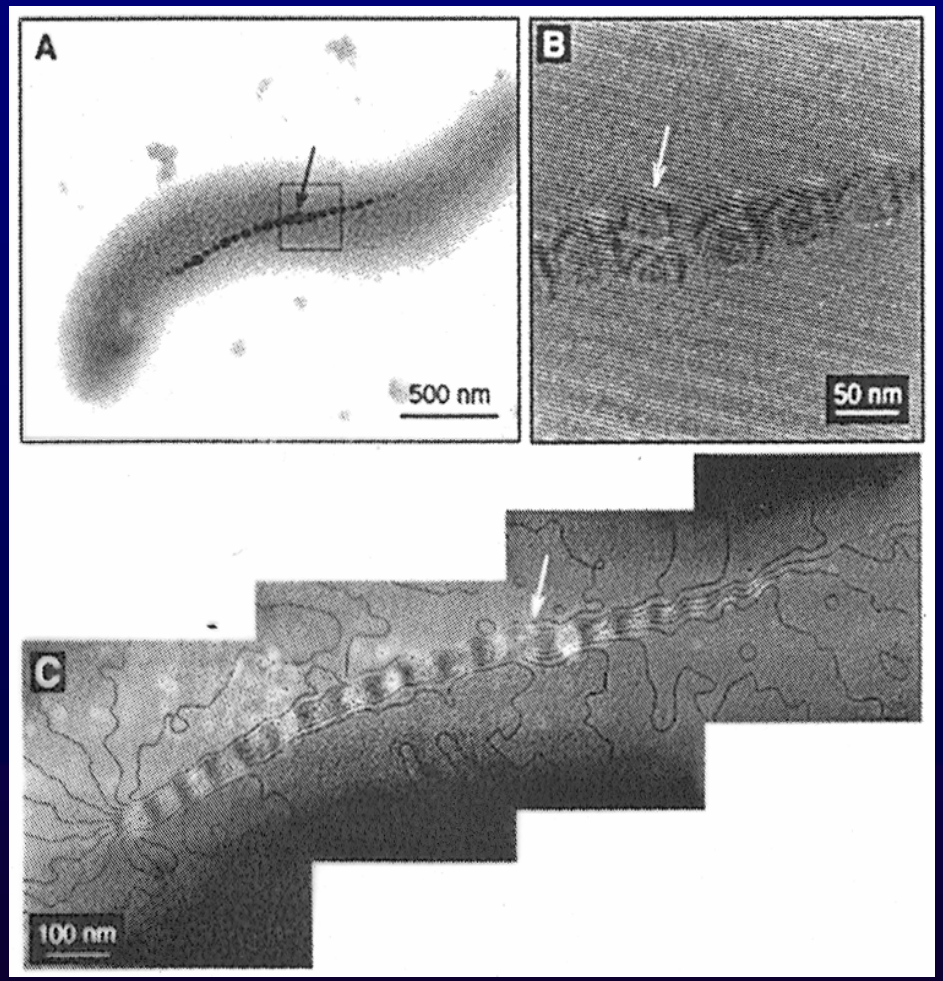
A Broad Overview

I.I.T.-Bombay

Jayesh Bellare

jb@ iitb.ac.in

Nano + bio : not new



TEM image showing natural nanotechnology in magentotactic bacteria (from Dunin-Borkowski et al. 1998, © 1998 American Association for the Advancement of Science.)

Main nano-bio effects:

1. Macrophage evasion
2. Cross blood-brain barrier
3. Slip through cell junctions
4. Bio-integrate (join to cells)
5. Deliver large aliquots

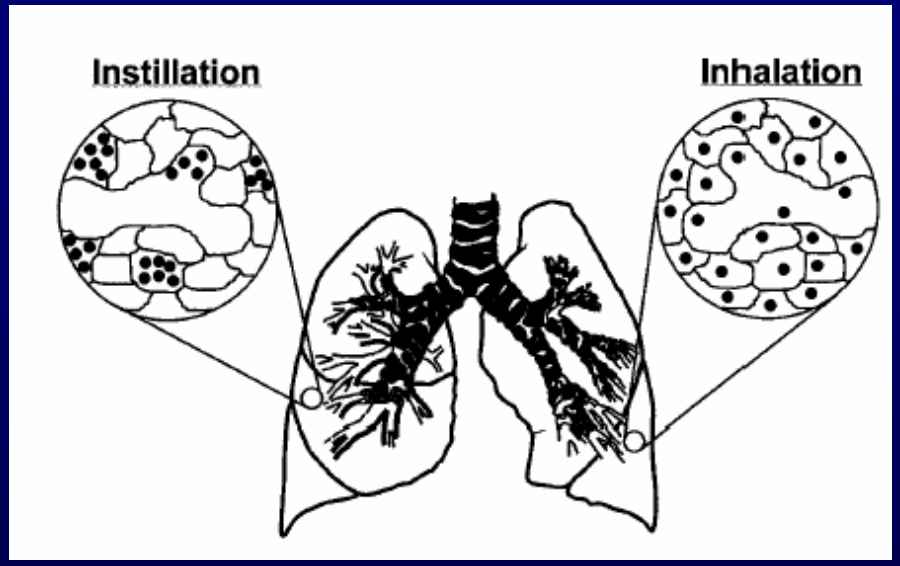
(compared to molecular solution)

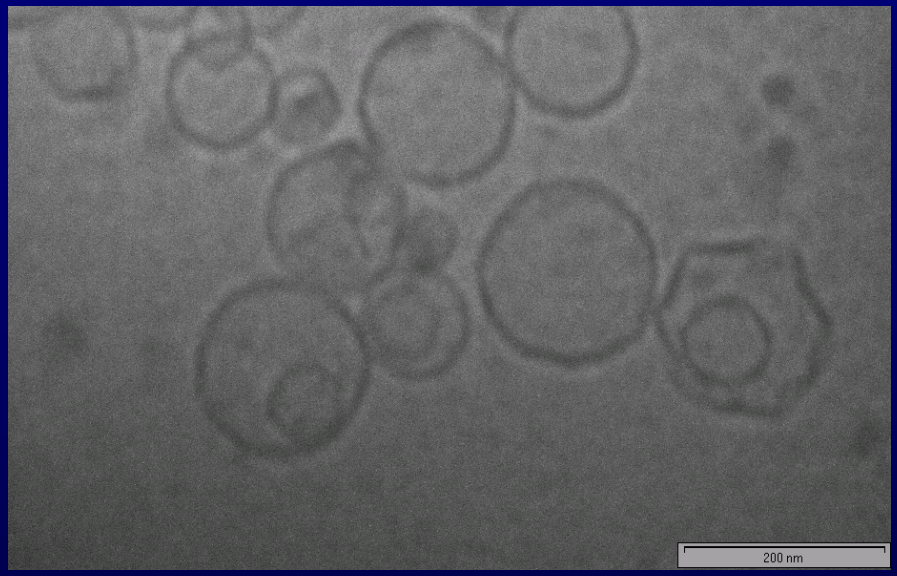
Friend or foe?

Major themes of our nano bio work at IITB:

1. Novel surfactant nanoparticles for respiratory disease
2. Cryo-TEM to image wet nanostructures
3. Occular drug delivery systems & nanoparticles
4. Making nanoparticles of odd geometries
5. FACS for sorting nanoparticles
6. Nanocomposites for dental and orthodontics use.
7. Nano particles in traditional medicine: Bhasmas
8. Micro-devices for cardiac use (minimally invasive surgery)

Nanoparticles for alveolar drug delivery





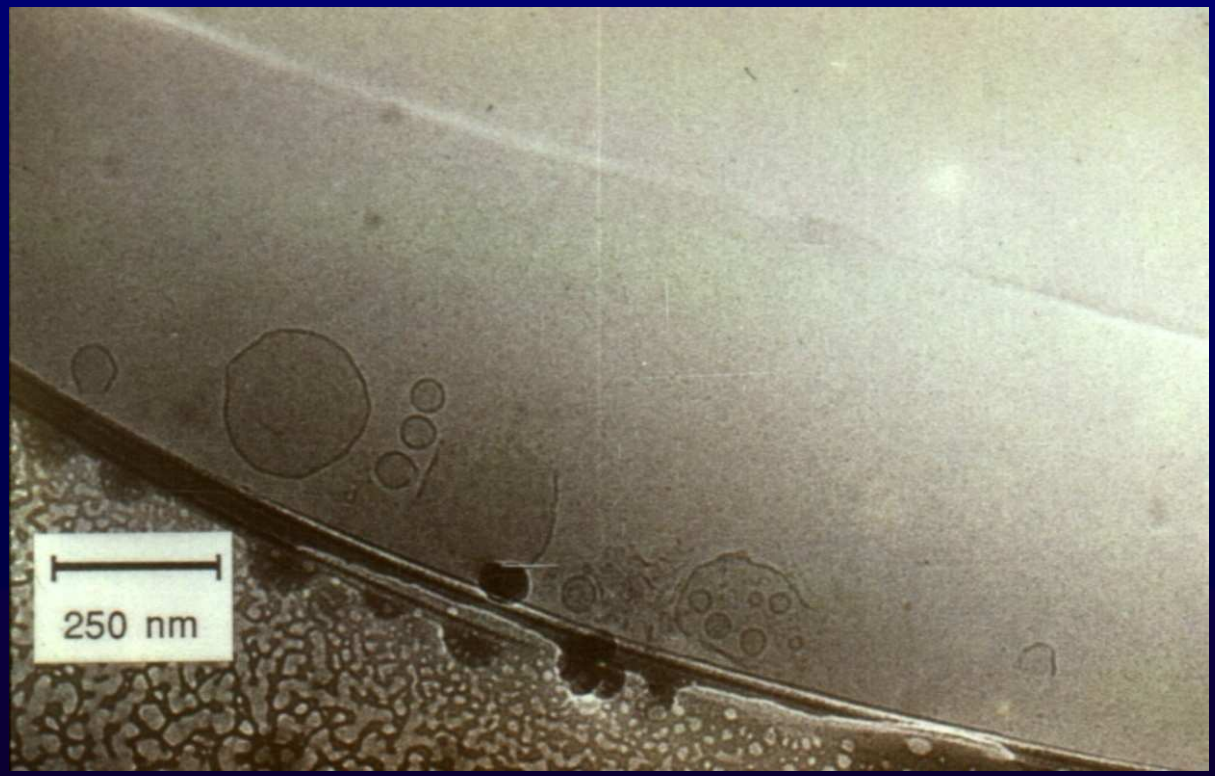
200 nm

- **Developed surfactant nanoparticles of 100-200 nm size having low polydispersity; Will be non-invasive and have better alveolar reach than intratracheal instillation**

- **Can be used for Inhalation therapy : more homogenous pulmonary distribution than instillation**

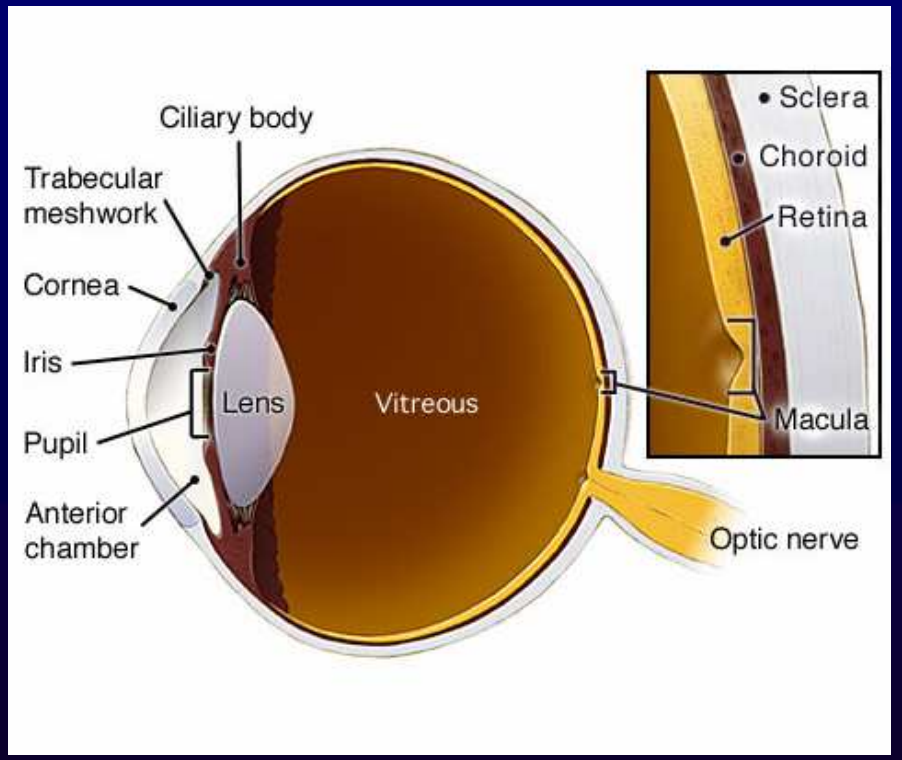
(Banerjee R, Editorial, Chest, 2004)

Cryo-TEM methods for imaging dynamical systems

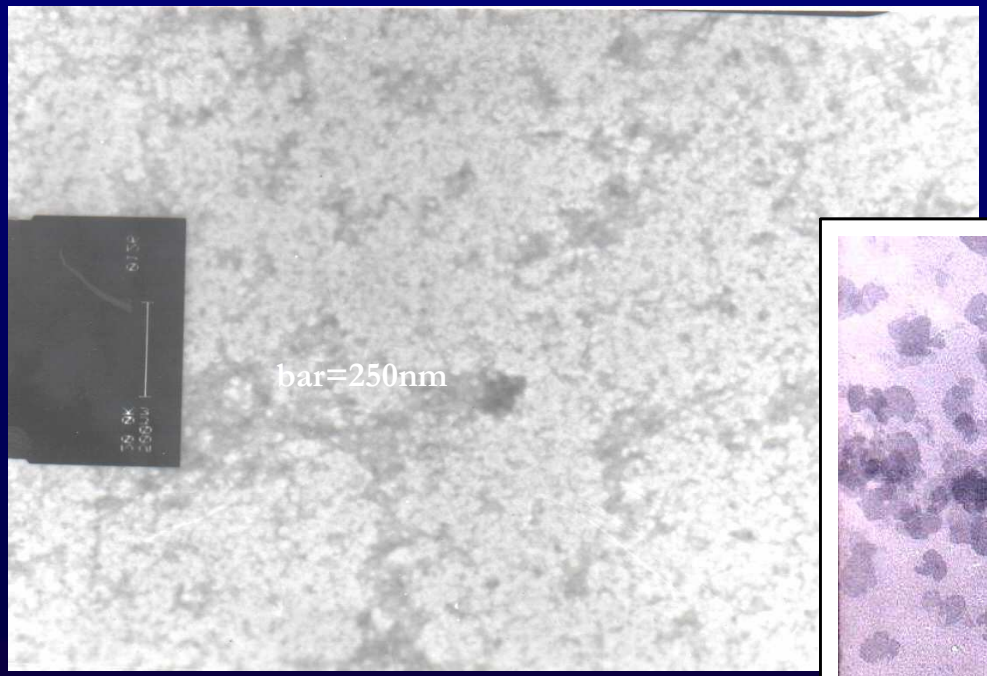


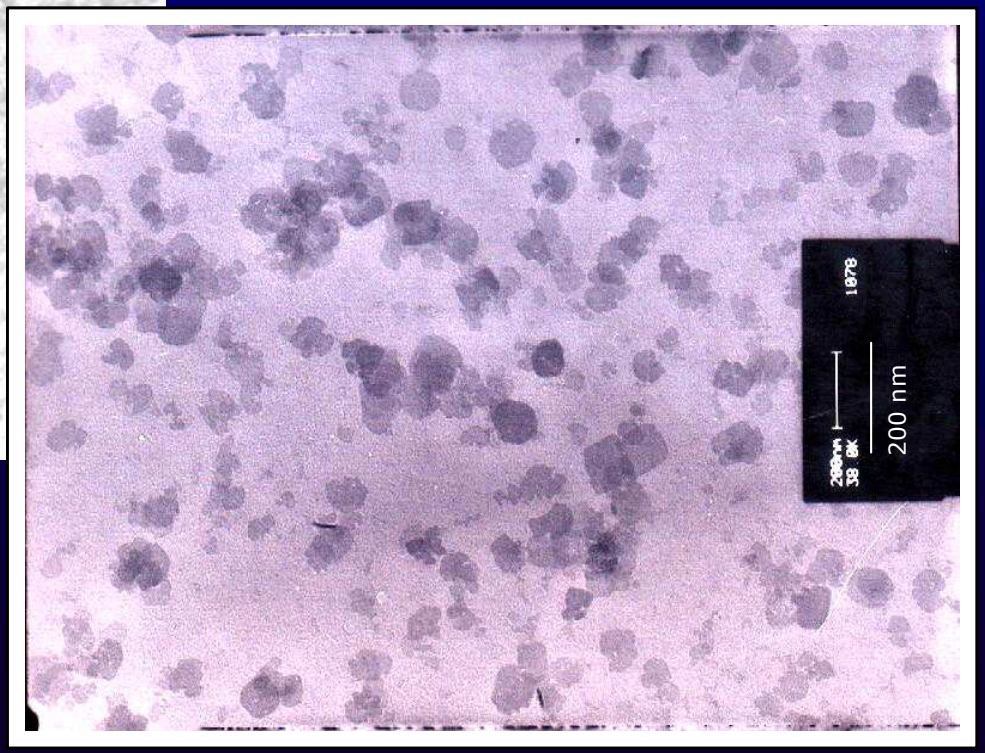
Ophthalmic drug delivery with nanoparticles

- Physical and chemical barriers to effective drug delivery to eye
- Pharmacokinetic limitations of conventional drug delivery systems in ophthalmology
- Requirement for new drug delivery forms for sustained release



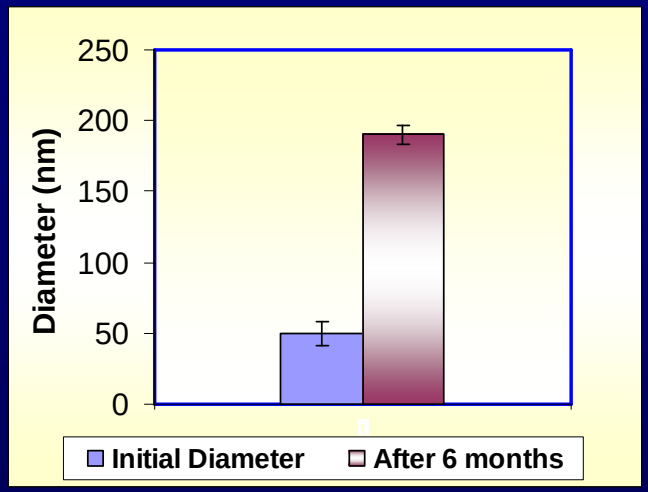
Transmission Electron Micrograph of Aspirin loaded Albumin Nanoparticles

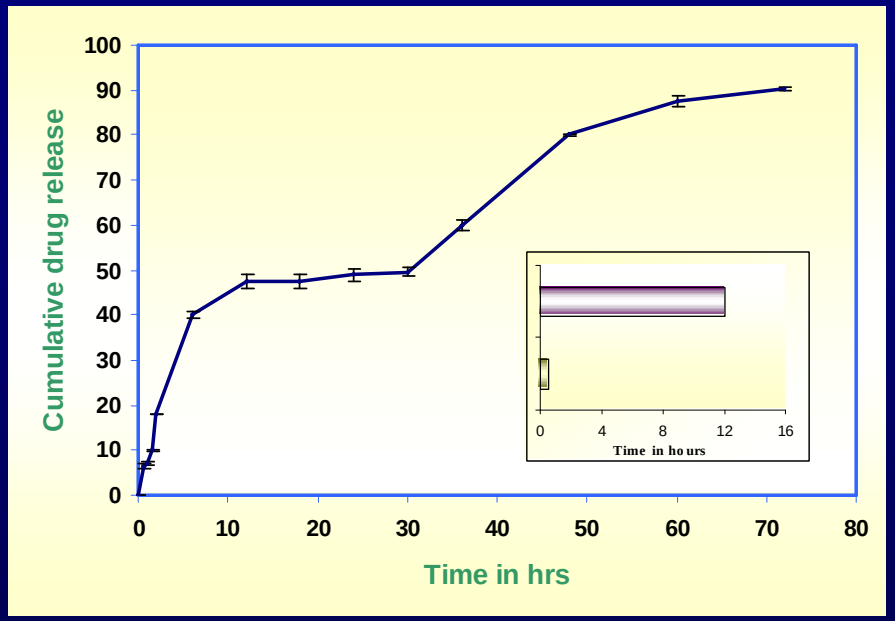




TEM photograph of aspirin loaded albumin nanoparticle:
Diameter of the particles 21nm

Drug loaded nanoparticles for the eye





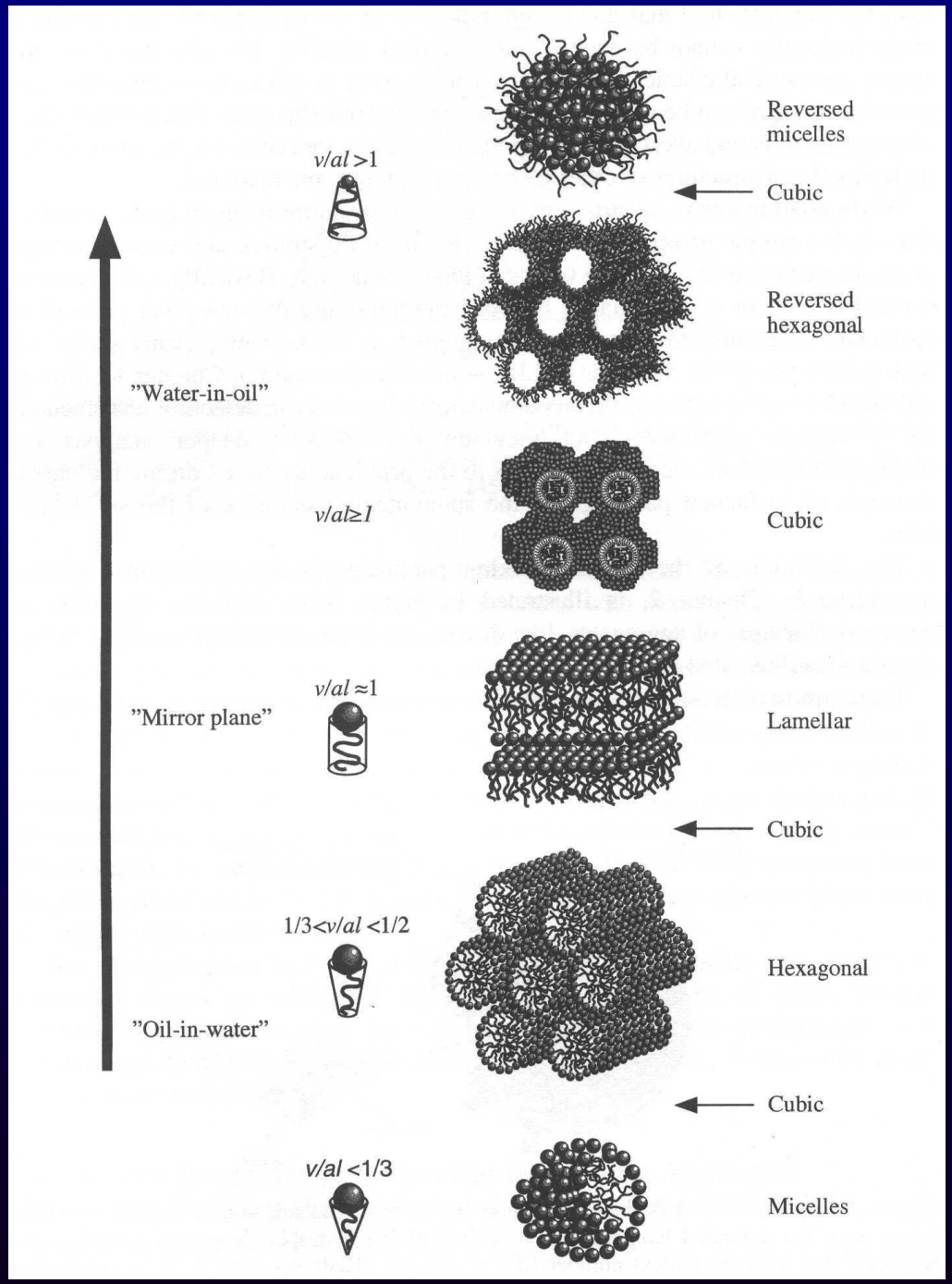
- **Developed aspirin loaded protein nanoparticles of uniform 40-60 nm size, which were stable for 3 months**
- **Achieved sustained release of drug over 72 hours**
- **Effective even with one-third of the therapeutic dose**
- **Will be advantageous for use in diabetic retinopathy where aspirin is used orally**

(Das et al. BIMAO 2003)

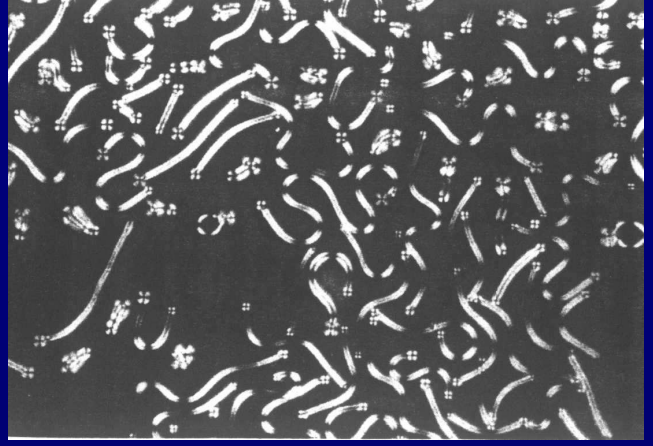
Patent pending

Making nano-particles

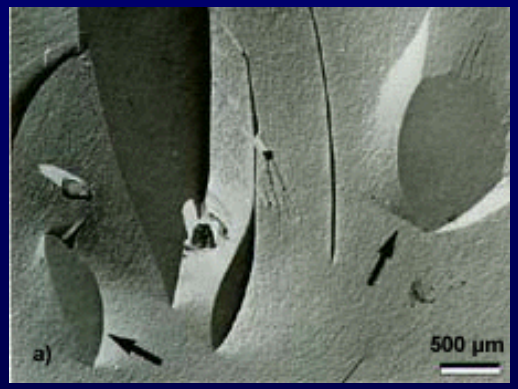
- "Top-down" vs. "Bottoms-up" approach
- Spontaneous formation of complex nano-structures by self-aggregation:
  - Surfactants
  - Lipids
- These can also be used as nano-reactors
- Reactions in nano-structures give nano-particles



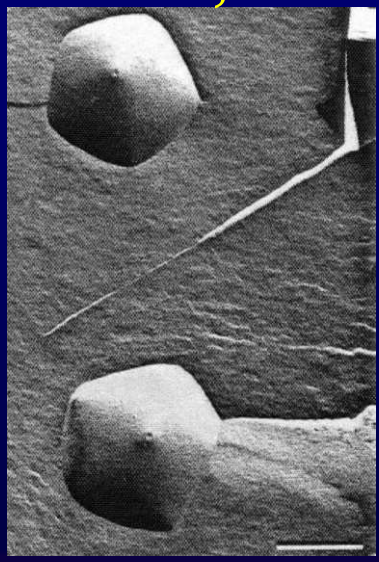
Jonsson et al., 1998



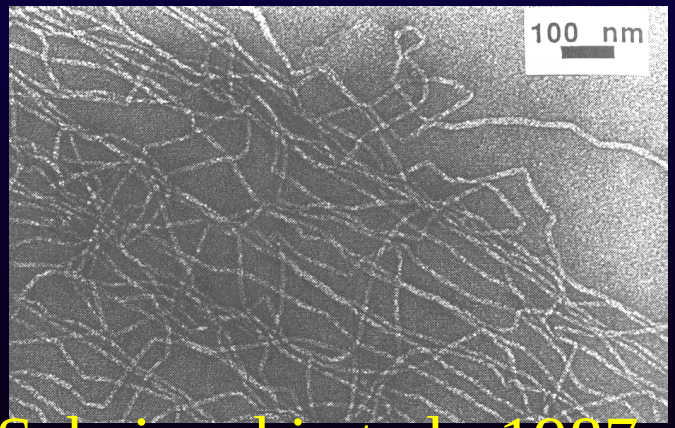
Prathibha and Madusudhana., 1992



Zemb et al., 1999

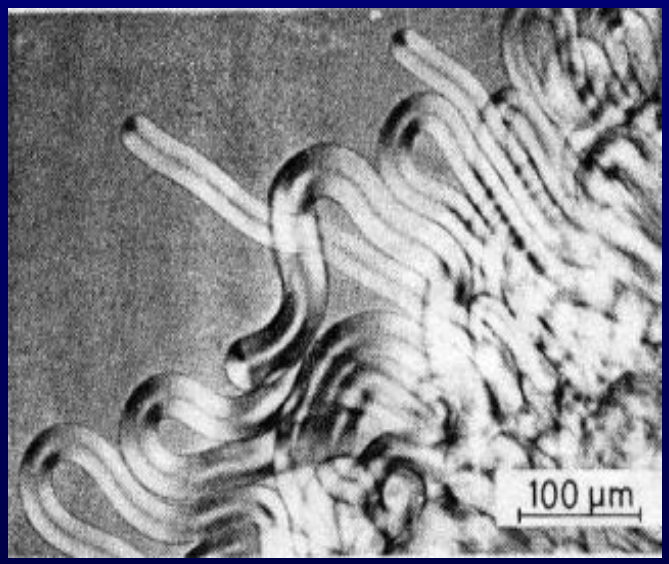


Dubois et al., 2001



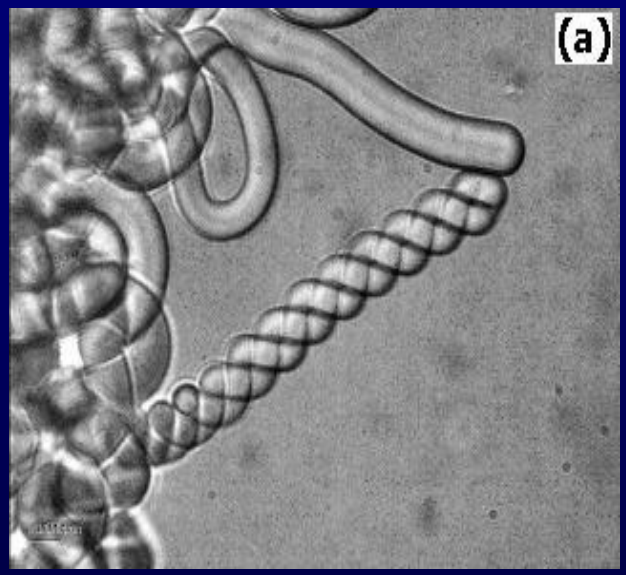
Sakaiguchi et al., 1987

Myelin Figures



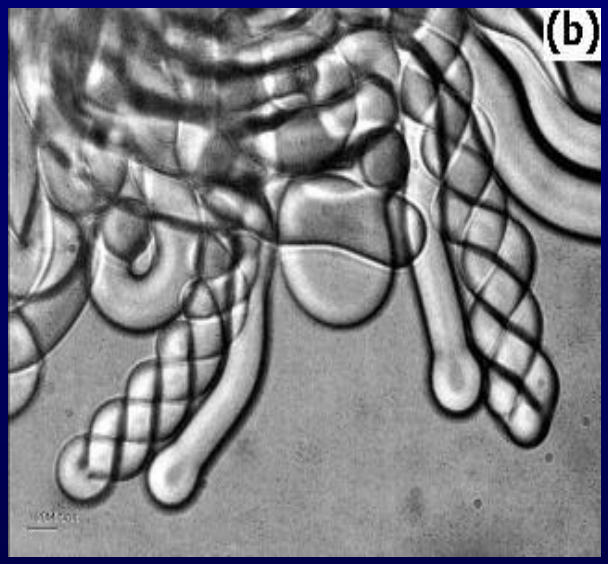
Phosphatidylcholine/ ethylene glycol

Sakurai and Kawamura, 1984



$C_{12}E_3$/Water

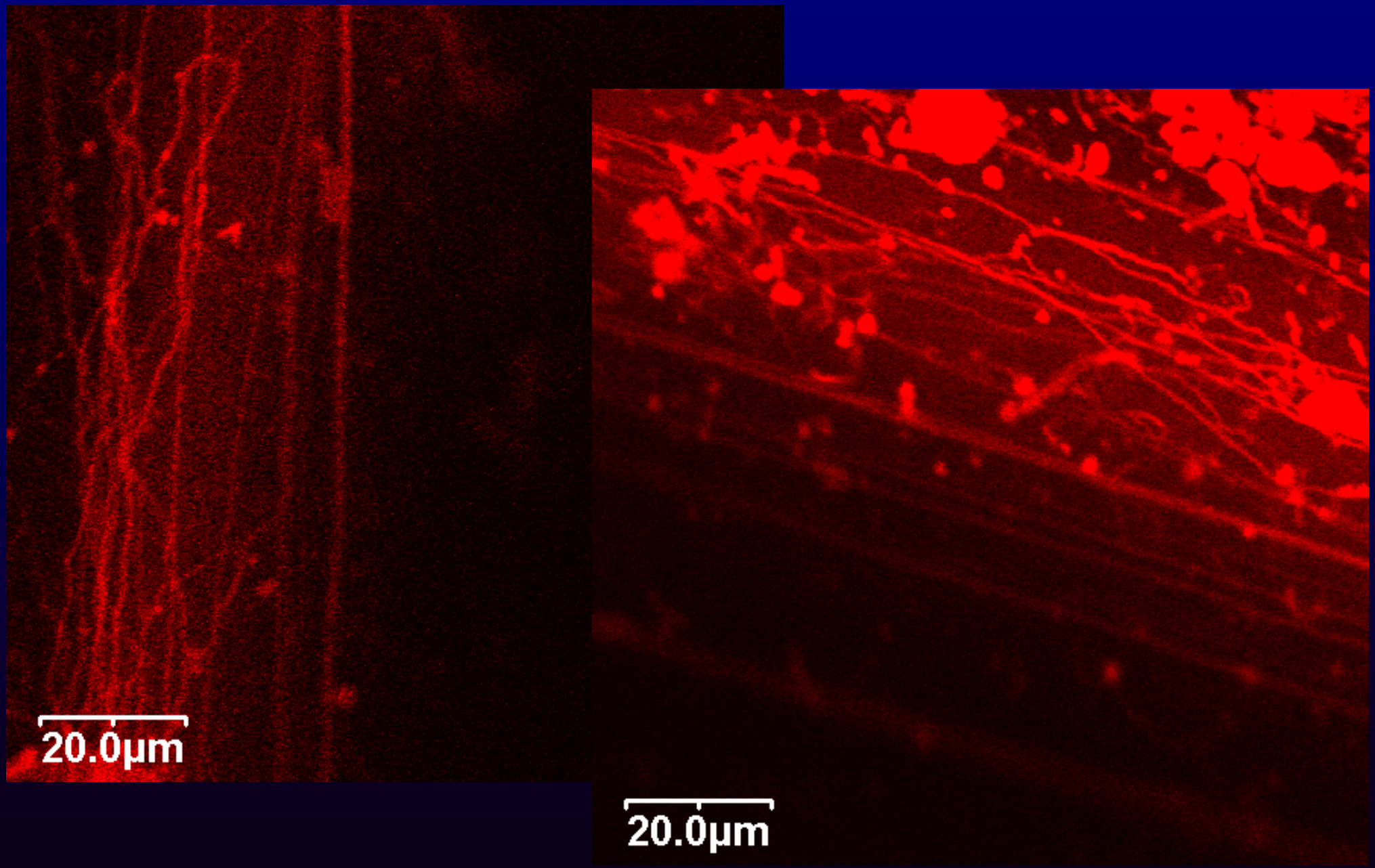
Buchanan et al., 2000



Egg yolk lecithin/ water

Sakurai et al., 1989
Bellare et al., 2003

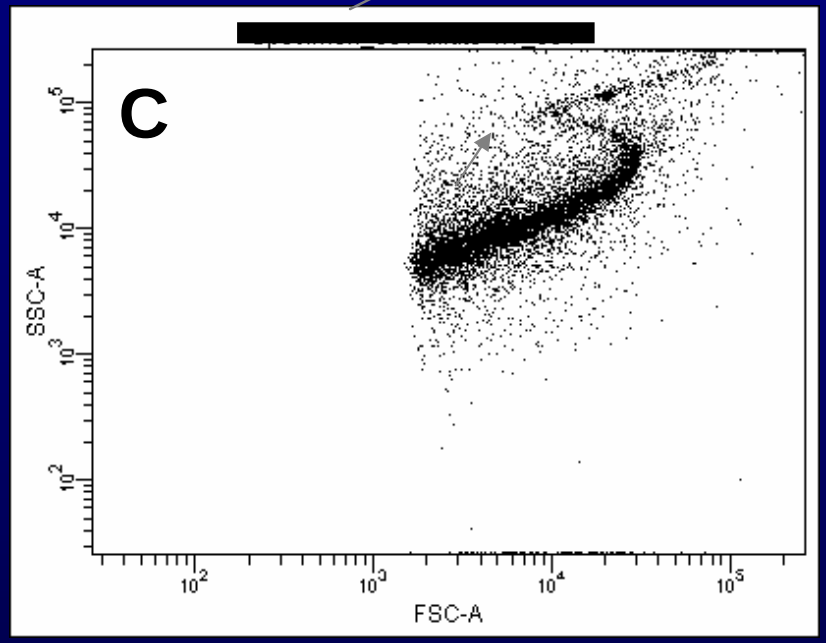
Nanotubes of lipids & surfactants

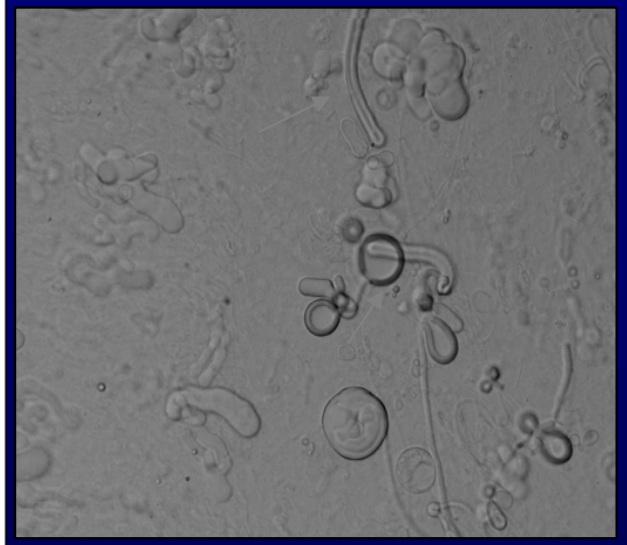


FLOW CYTOMETRY
FACS

Applications
in
Nanotechnology

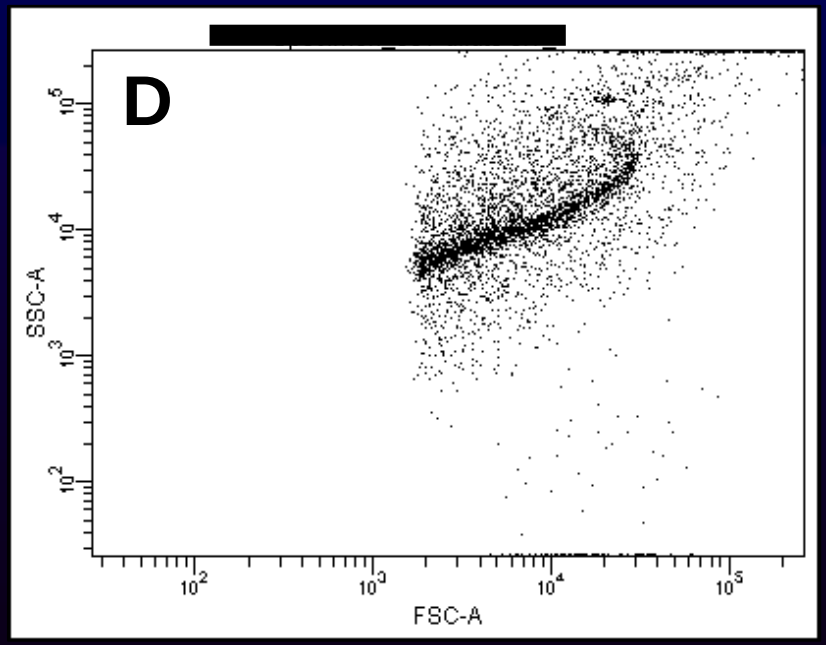
Sorting Single and Multi Lamellar Vesicles by flow cytometry FACS

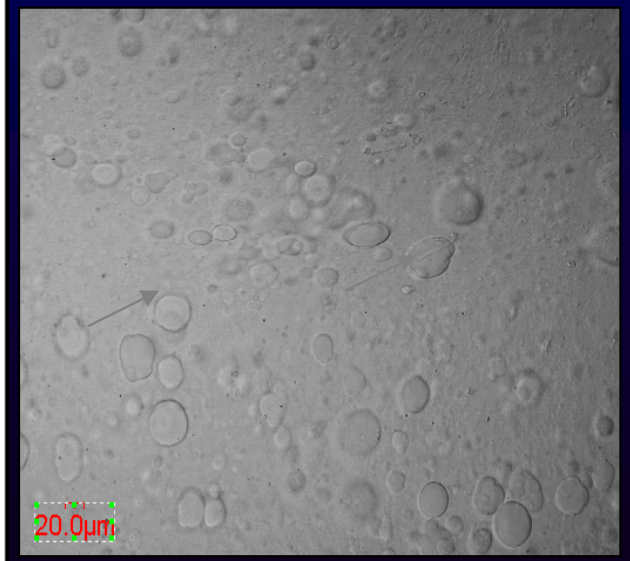




C- 4% AOT

D- 1% AOT





A novel, recurring S-shaped signature pattern has been identified

Nanotechnology based Biomaterials for tissue engineering

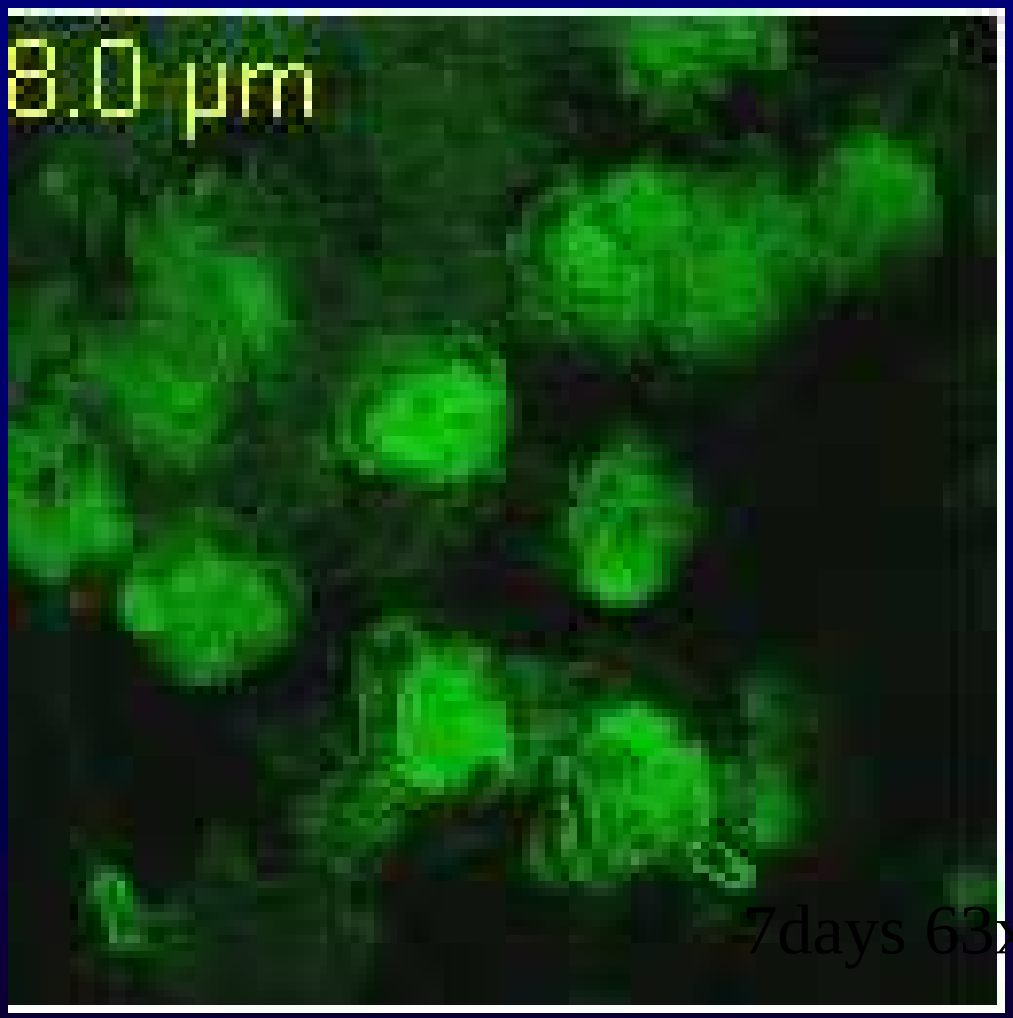
- Nanocomposites as Synthetic Bone Substitutes: ceramic nanoparticles+polymers

Polymer-Ceramic Nanocomposites

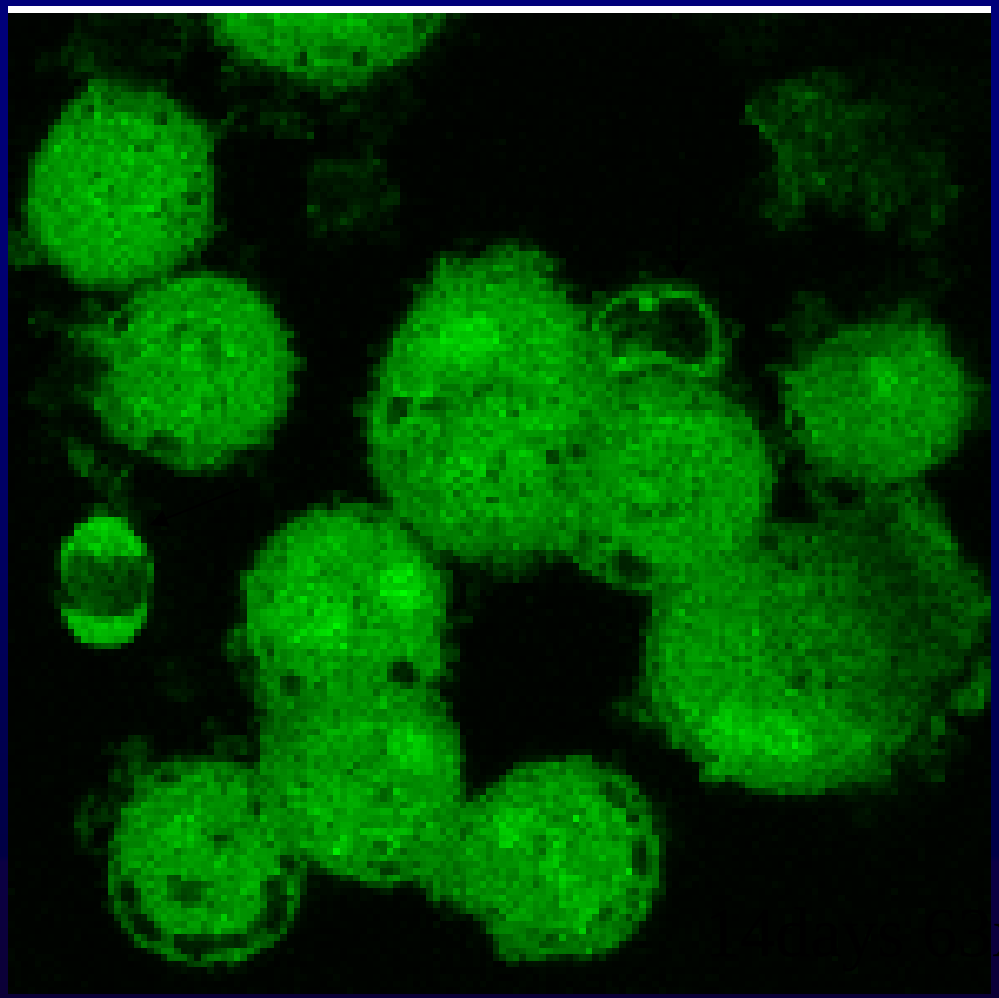
- HAp/Chitosan nanocomposite
- HAp/Collagen nanocomposite
- HAp/Gelatin nanocomposite

Other materials: hardystonite

FITC-Osteocalcin labelling



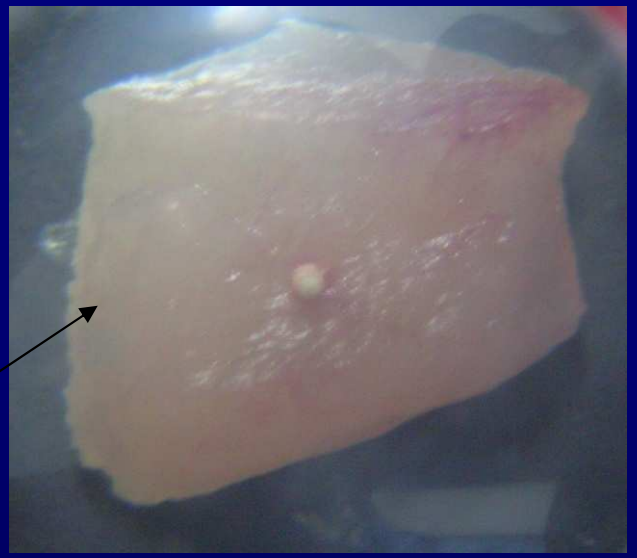
7days 63x



x

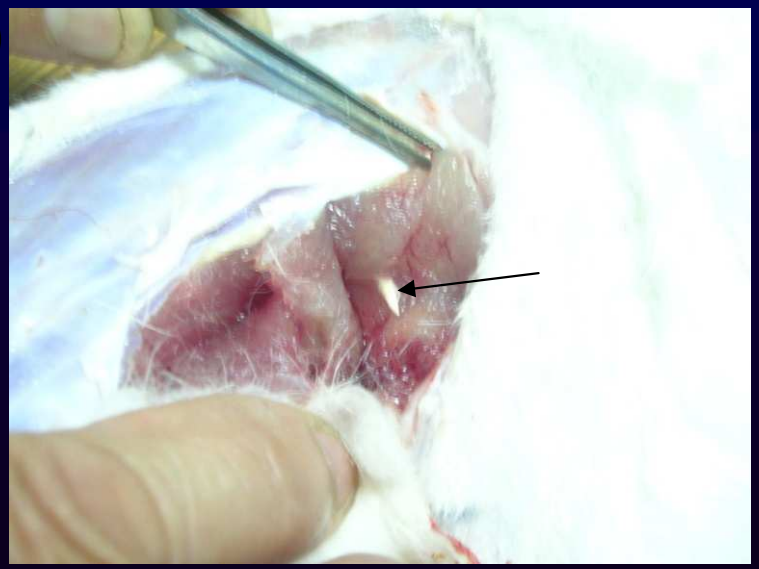
- ✓Osteocalcin is one of the most abundant proteins produced by bone
- ✓Continous expression of this osteoblastic marker indicates the maintenance of the osteoblastic phenotype

Animal trials: In vivo short term screening test



Hardystonite ceramic rod and Hardystonite-PMMA composite rod do not show any local reaction and no encapsulation around it seen macroscopically, so biocompatible

(c)



Hardystonite-PMMA composite rod without any local reaction and no encapsulation around it seen macroscopically at dissected site

Animal Trial- Radiographic studies

Radiograph of 42nd Post operative day right tibia with coated implant

Arrow indicate- complete

Radiograph of 42nd Post operative day left tibia with uncoated implant

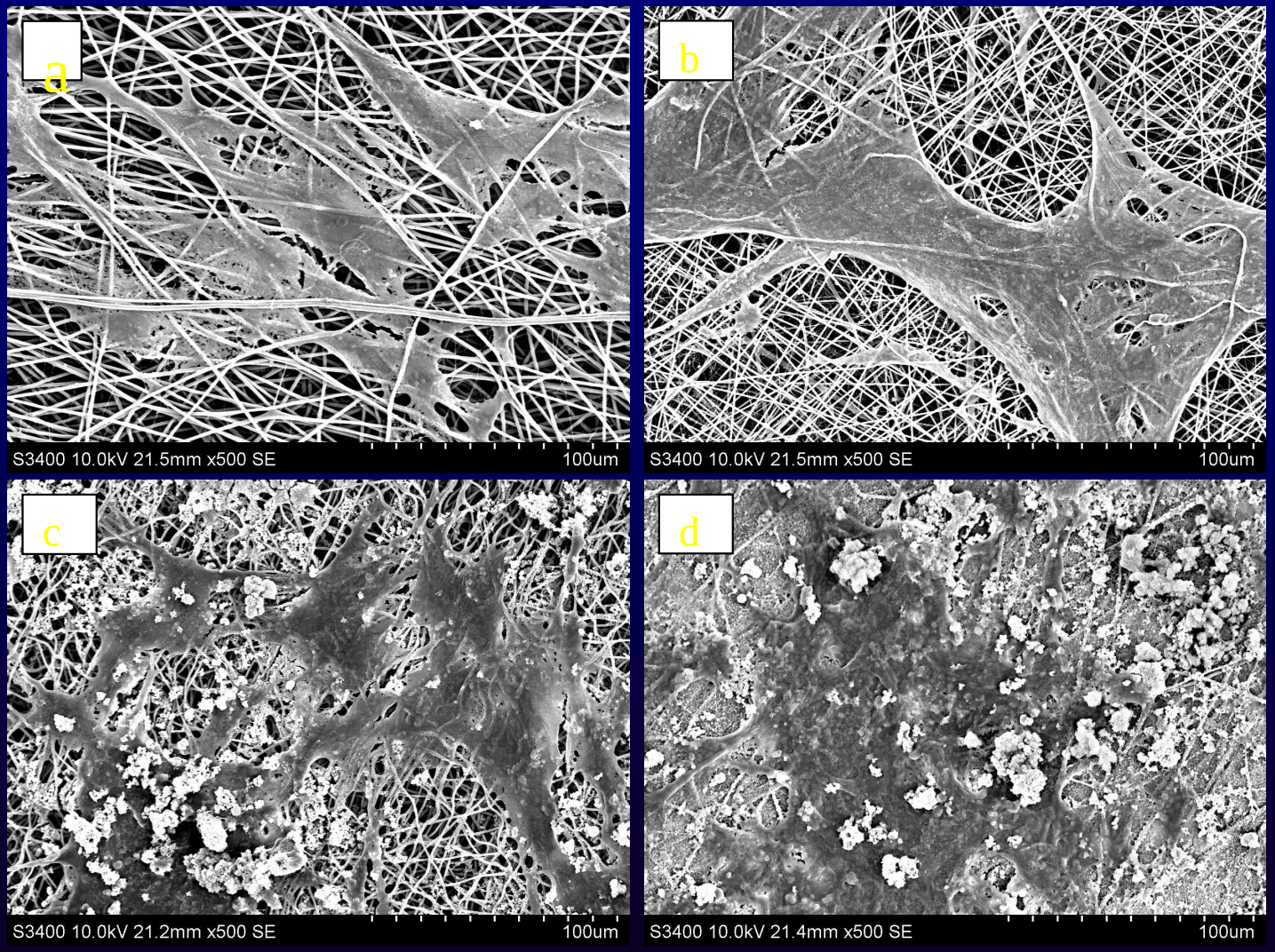
Arrow indicate- still defect

Excellent bio-integration and osteoconduction

BioMaterials and Bioreactors for Maximum Expansion of Stem Cells

Use of 3D scaffolds and Hollow Fibers

Electrospun 3D Scaffolds: Stem Cells



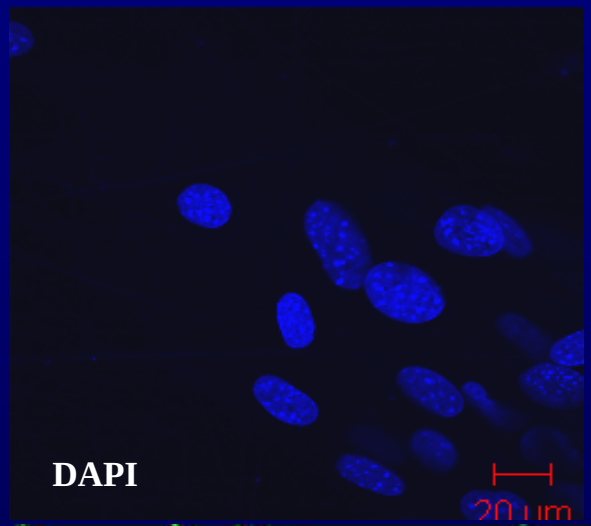
- Cells attached well to all scaffolds
- Cells grew as flattened sheet (P and PG) →
- differentiation

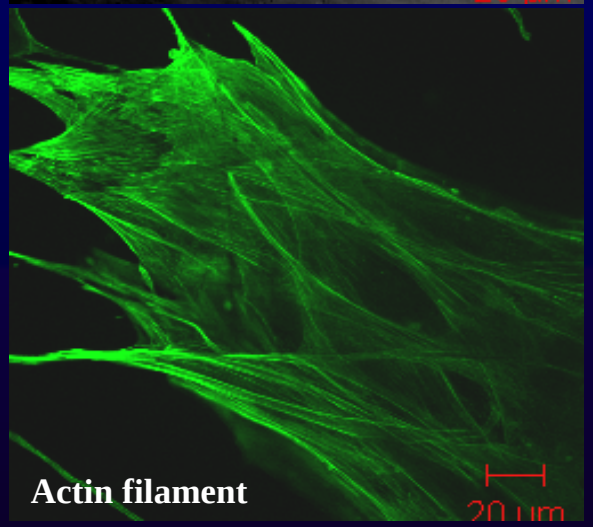
Good future scope !

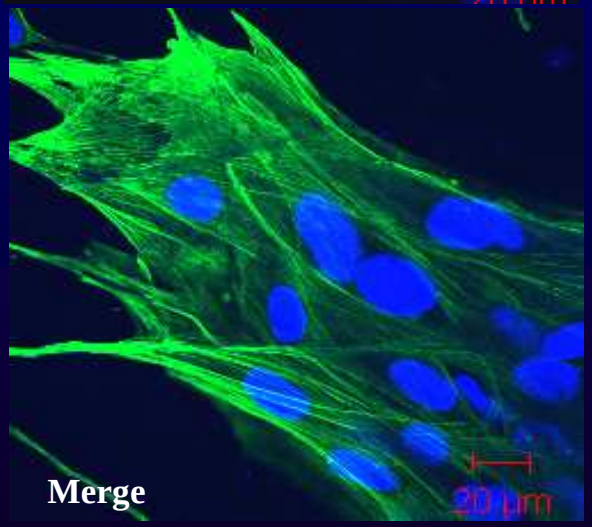
SEM micrographs (500X) of the attached mE-ASCs

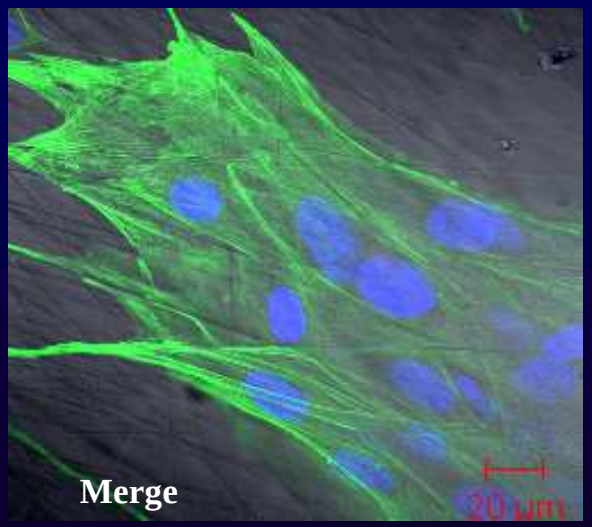
Cell Attachment Study

PLLA-Gelatin



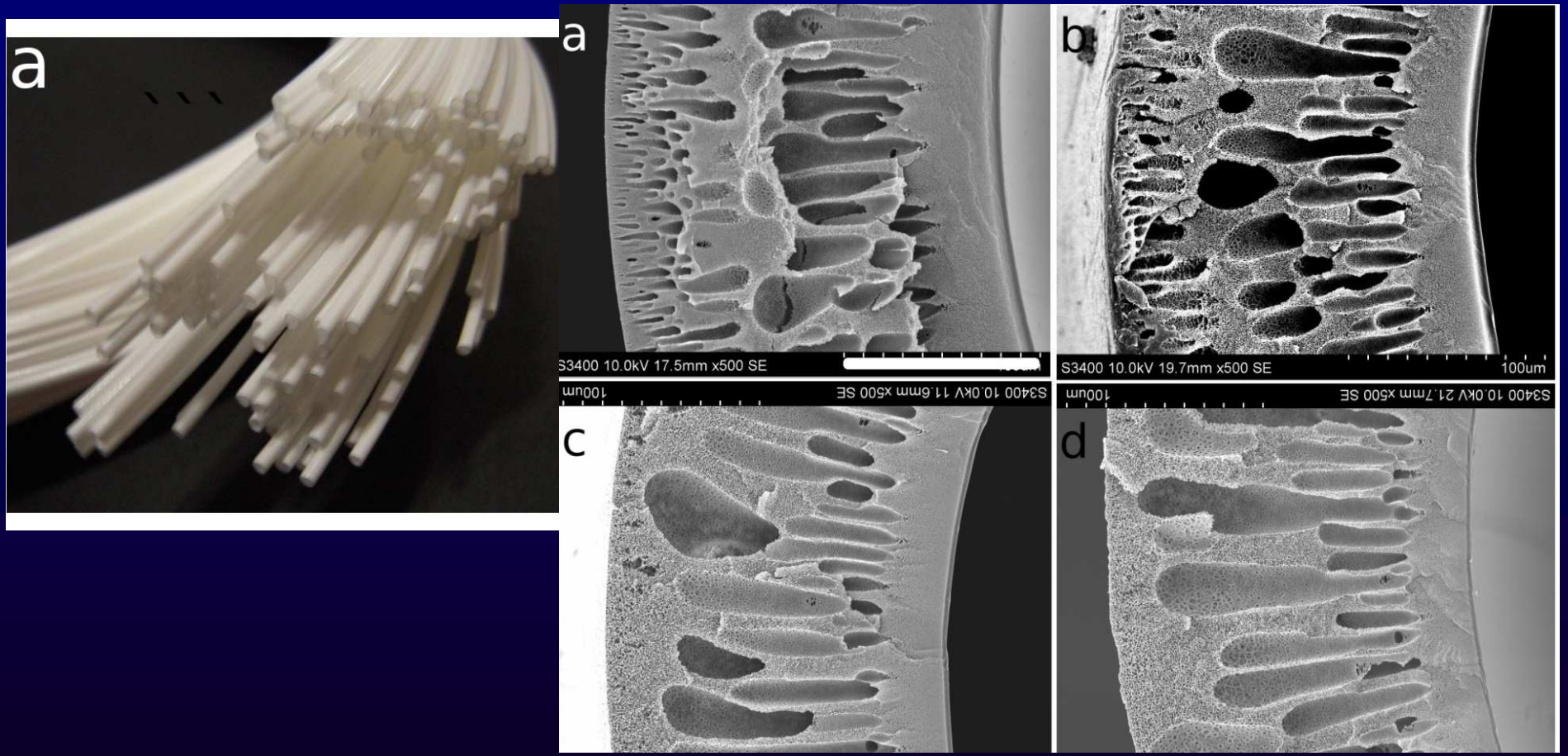






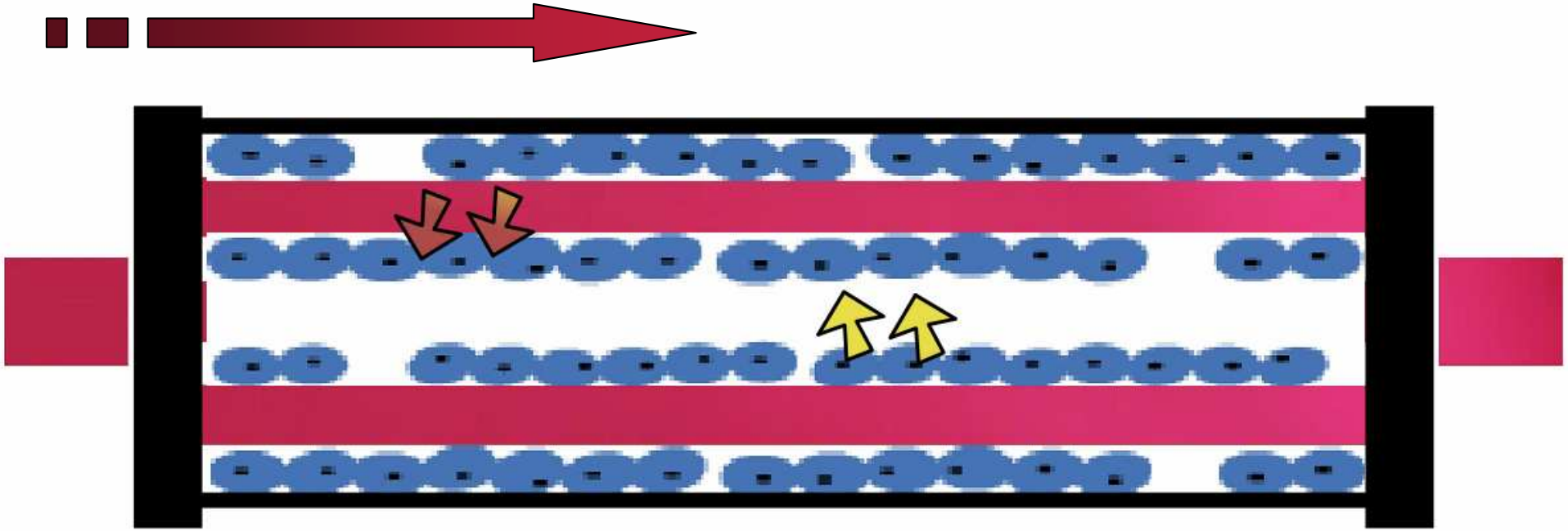
CLSM image of attachment of mE-ASCs on PG scaffold at day 5. The F-actin was stained with FITC-phallodin (green colour), while the cell

Nanostructured Hollow fibers for bioreactors



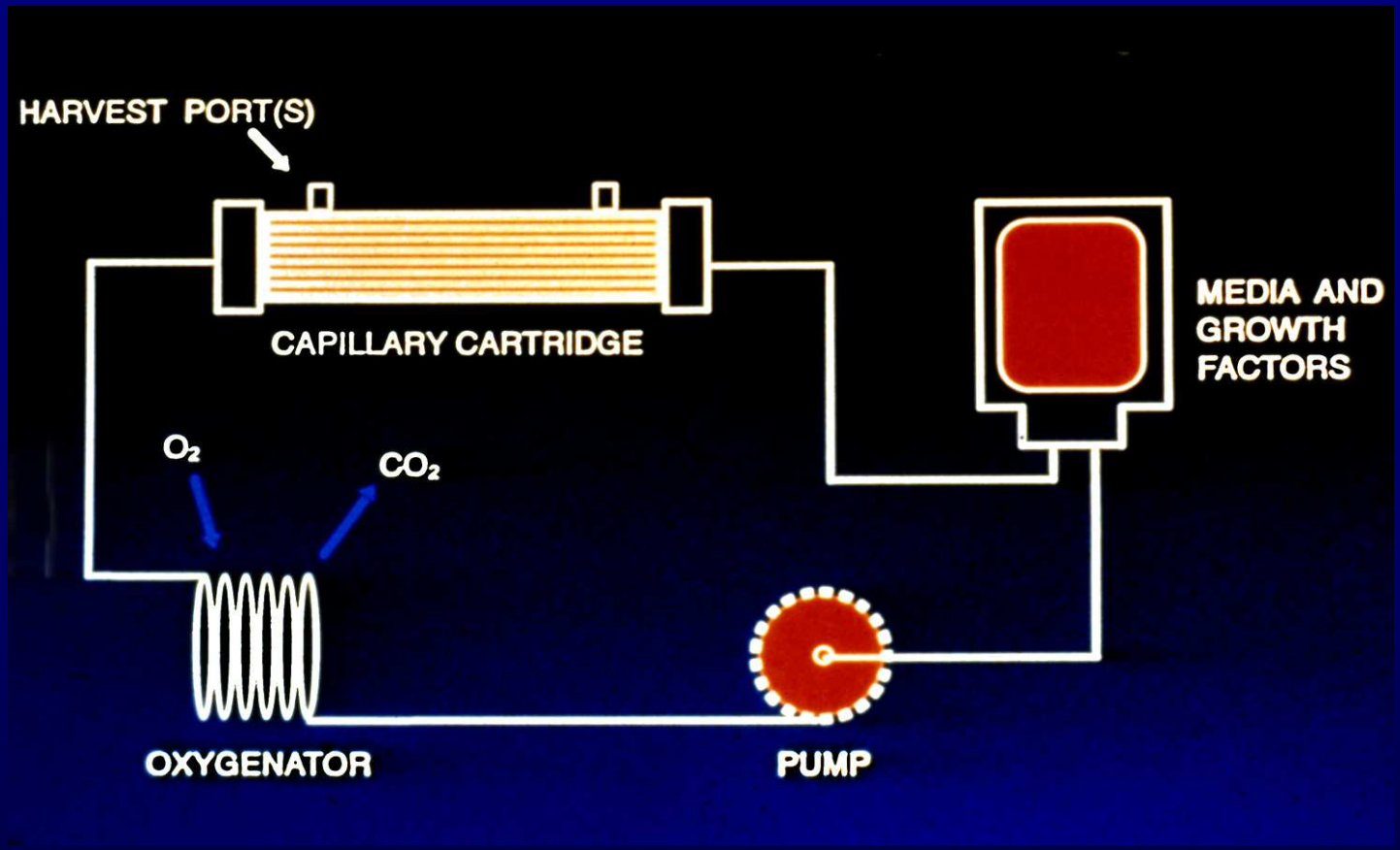
IN

The culture medium that flows through the fibers nourishes the cells.



Waste from the cells permeate the fibers and get carried away.

out



- Positive pressure displacement pump
- Silicone tubing for gas exchange
- Closed, bio-safe system

Nanoparticles in

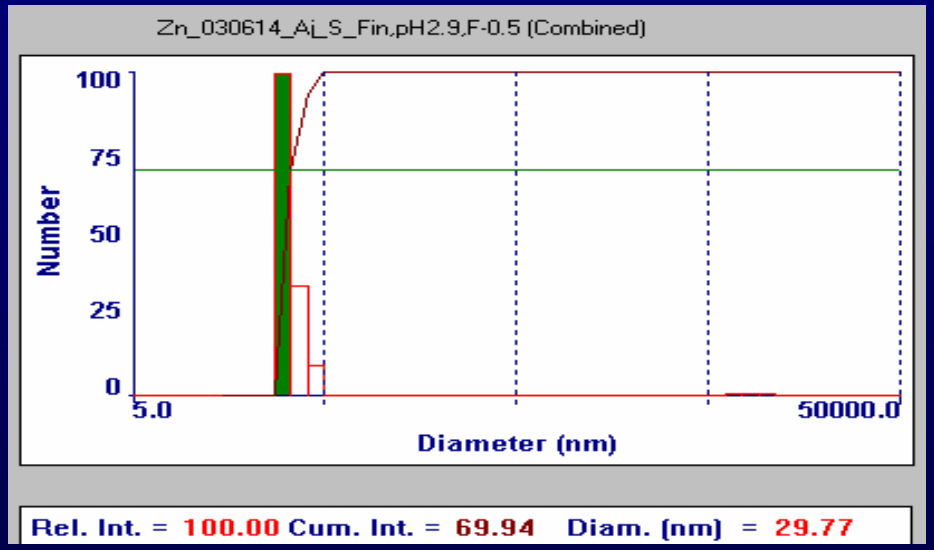
Traditional medicinal systems: *Bhasma*

***Bhasmas* are unique form of medicinal preparation used in *Ayurveda / Siddha* system for thousands of years.**

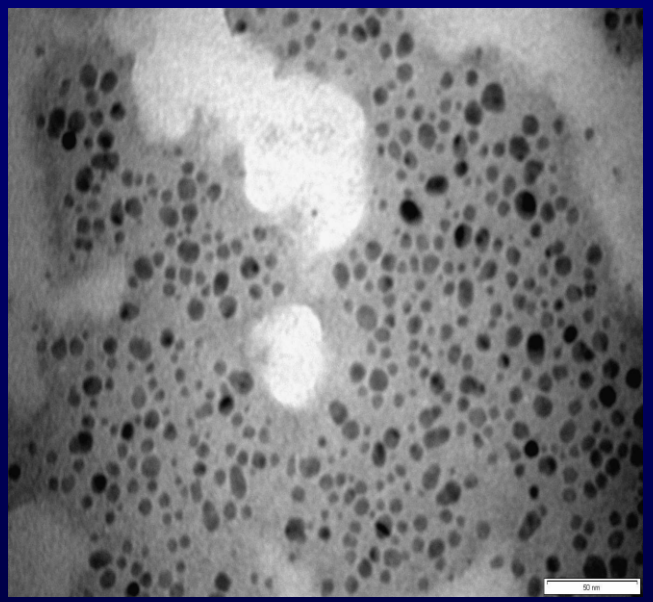
- **They are powders and made from a wide variety of base materials**
- **Examples:**
  - ***Tamra Bhasma*** **Cu**
  - ***Mouktika Bhasma*** **Pearl**
  - ***Suvarna Bhasma*** **Au**
  - **Others containing Zn, Pb, As, mixtures**

Physicochemical Result Summary

Dynamic Light Scattering of *Jasada Bhasma:* 30 nm particles



Electron Microscopy of *Jasada Bhasma*



Major finding: *Jasada Bhasma* has nanoparticles!

Elemental Analysis of *Jasada Bhasma* by XRD, ICP, EDAX, XPS: new technique development gives complete analysis and new insight.

Major finding: *Jasada Bhasma* is an Oxygen Deficient Material

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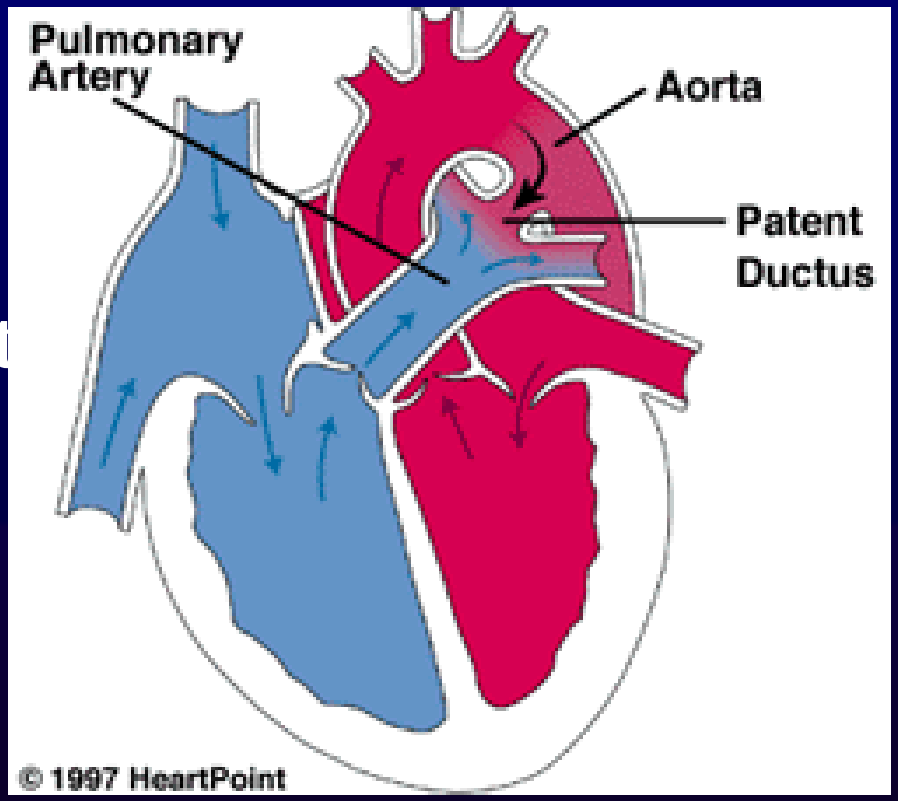
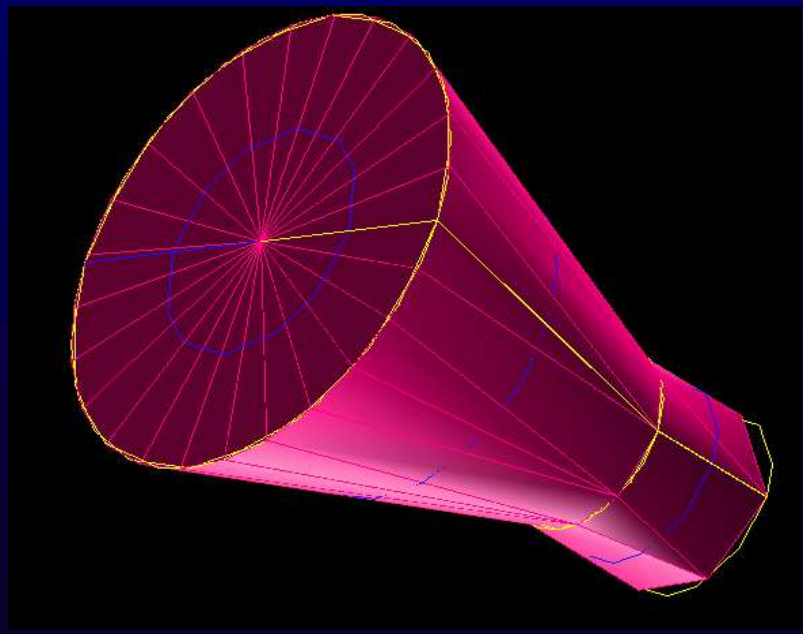
Nanotechnology in minimally invasive surgery: microengineered devices: Patent ductus arteriosus.

- Abnormal connection between aorta and pulmonary artery.
- Blood flows from aorta t pulmonary artery.
- Leads to pulmonary hypertension, infective endocarditis and heart failure.



Deliverable: Development of new PDA based on nanomaterials

- New Intraduct Occluder device is successfully fabricated
- Compliant shape
- Nano coated for thrombogenic action
- Hemolytic studies and Platelet Adhesion Tests of Dacron nano-fiber
- Avoids open heart surgery
- Quick acting
- Fault tolerant



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5. FACS for sorting nanoparticles
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7. Nano particles in traditional medicine: Bhasmas
8. Micro-devices for cardiac use (minimally invasive surgery)

Thank You!

Nano Bio for Health are

Jayesh Bellare, IIT Bombay, jb@iitb.ac.in