Introduction to Nanotechnology

- Textbook：
  Nanophysics and Nanotechnology
  by:
  Edward L. Wolf

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Classroom: A209
Time: Thursday; 13:40-16:30 PM
Office hour: Thur., 10:00-11:30 AM or by appointment

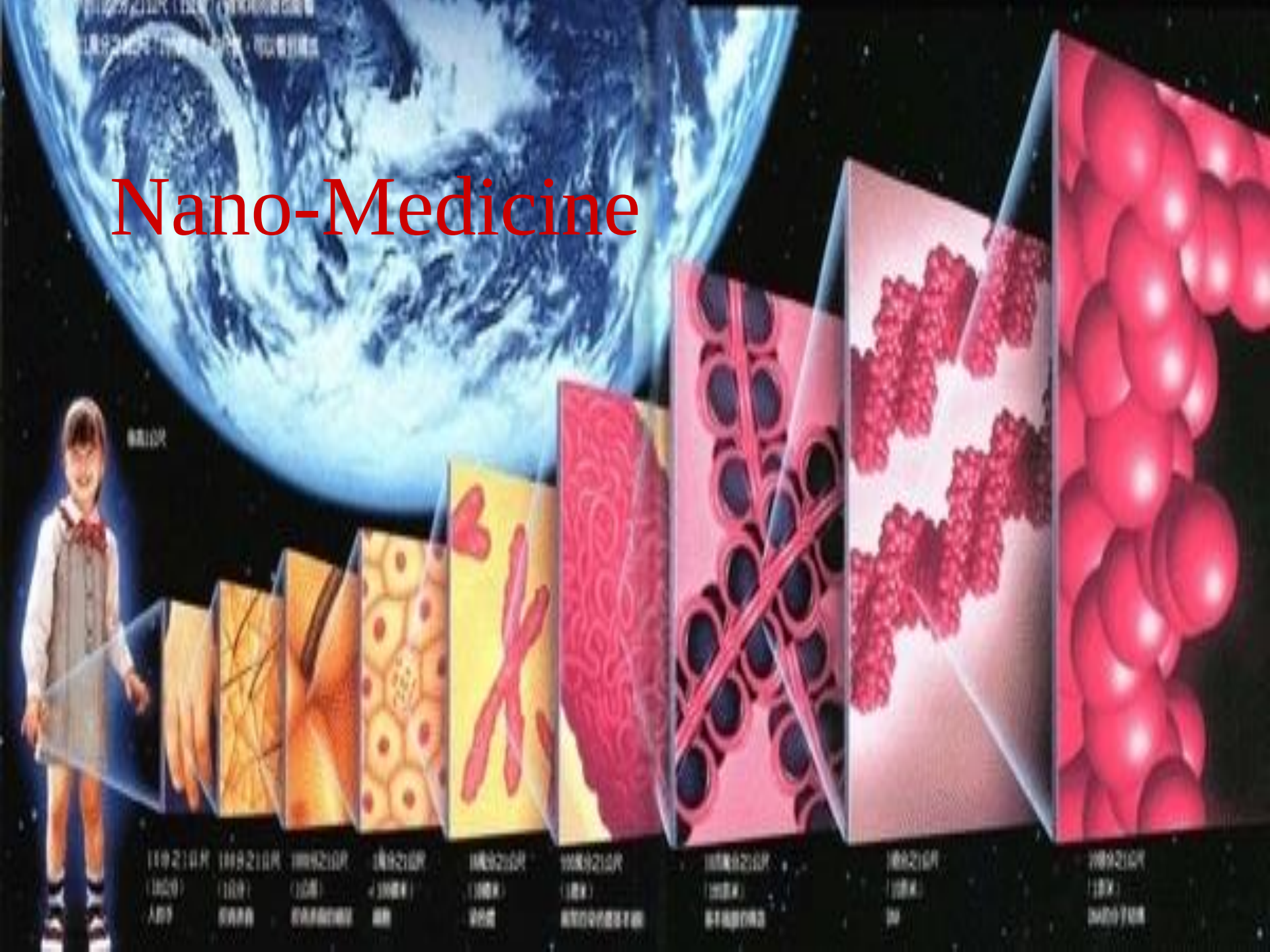
Objective of the course

The course, Introduction to Nanotechnology (IN), will focus on understanding of the basic molecular structure principals of Nano-materials. It will address the molecular structures of various materials. The long term goal of this course is to teach molecular design of materials for a broad range of applications. A brief history of biological materials and its future perspective as well as its impact to the society will be also discussed.

Evaluation; Score: 100%:

Mid-term Exam: 30%
Final Exam: 30%
Scientific Activity: 40 % (Home work, Innovation Design)

Nano-Medicine



Subjects:

Biodegradable and Biocompatible Nano materials

1. Drug Delivery
2. Tissue Engineering
3. Diagnostic Tools

Why it takes many years to develop a drug, a medical device, etc

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In vitro → Animal models → human models → Market

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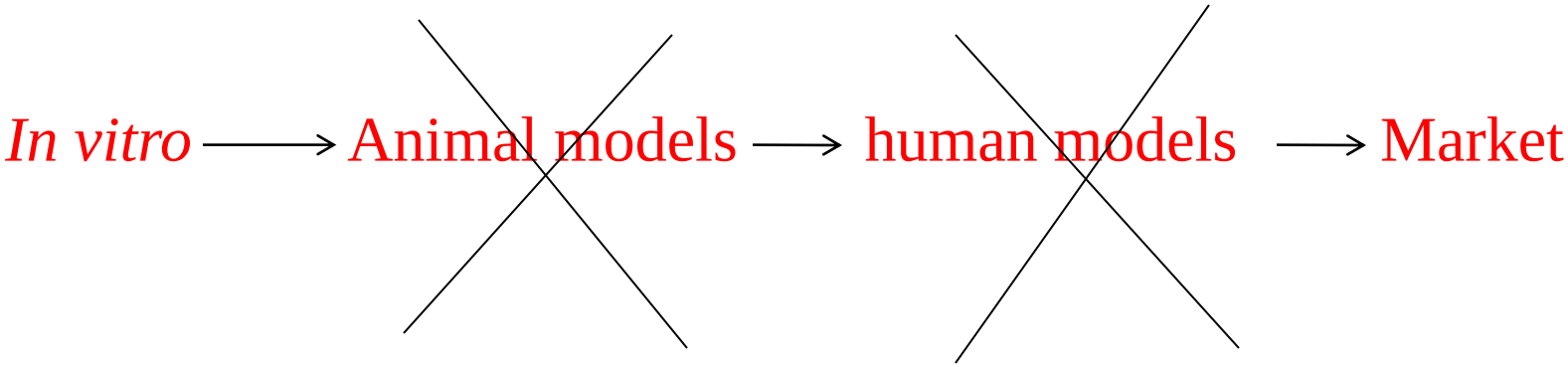
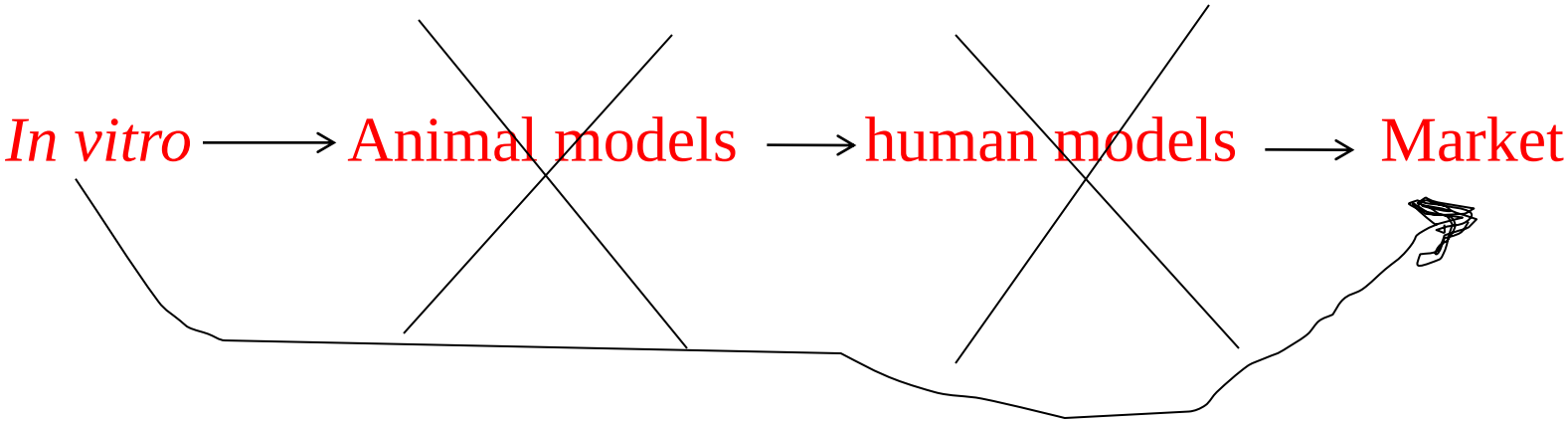
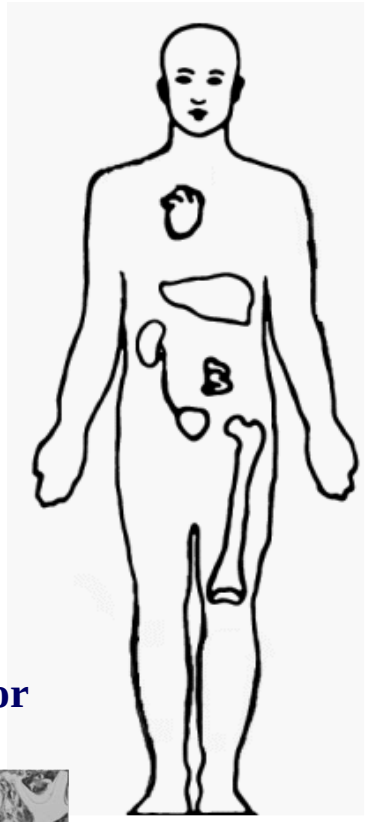


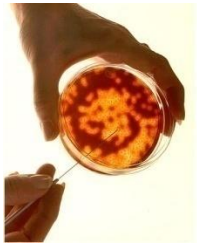
Why it takes many years to develop a drug, a medical device, etc…?



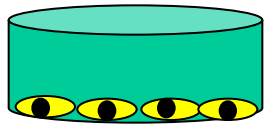
Tissue Engineering

"Tissue engineering is an interdisciplinary field that applies principles & methods of engineering toward the development of biological substitutes to improve the function of damaged tissue & organs."
(Langer & Vacanti, 1998)

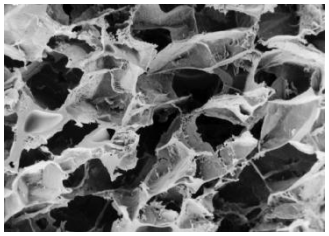




Isolation Stem cells

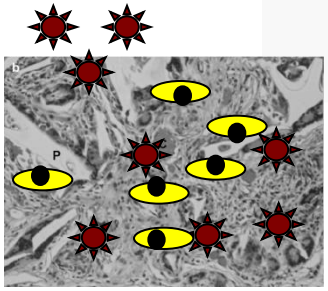


2-D Expansion



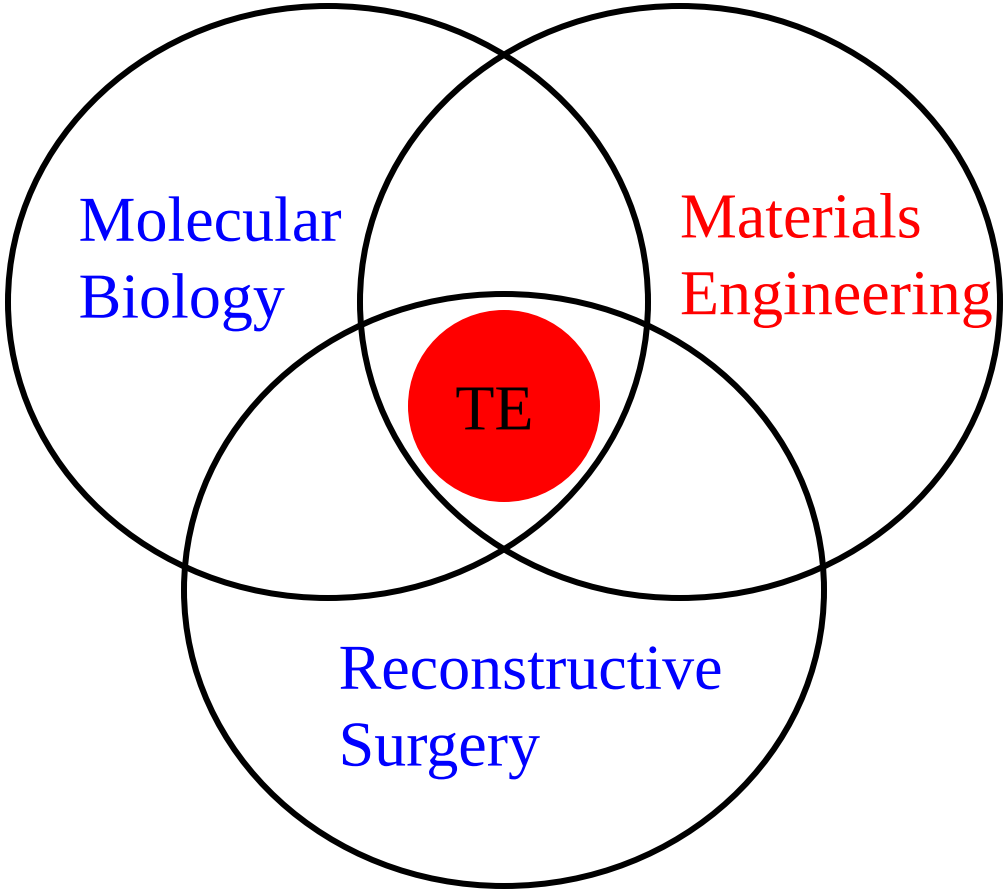
3-D Biodegradable Polymer Scaffold fabrication

Incorporation cells and growth factor

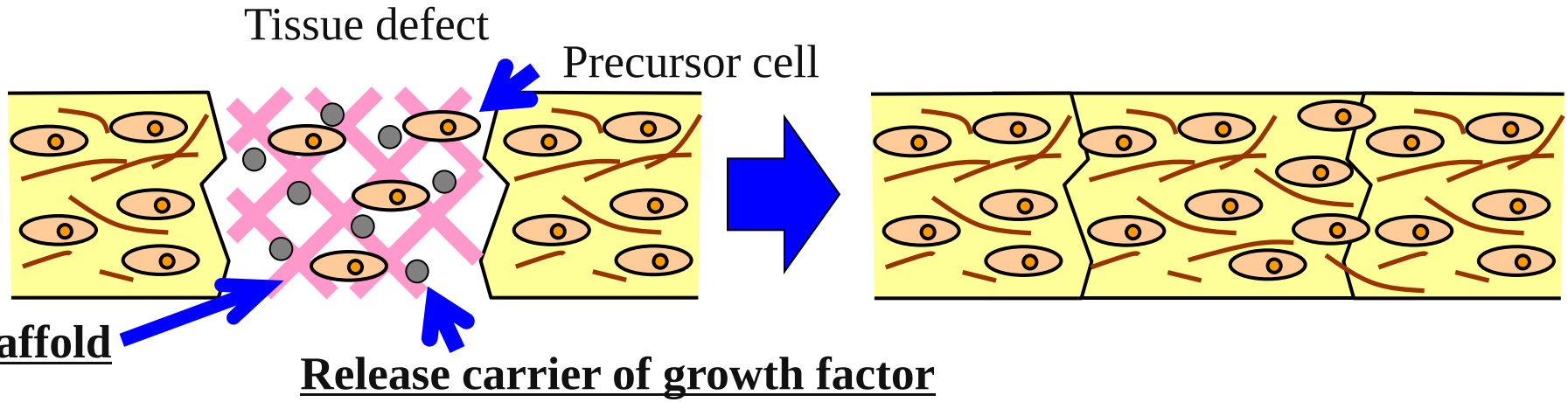


Growth Factor

Interdisciplinary Approach



Tissue Engineering



"Protein release from gelatin matrices"
Advanced Drug Delivery Rev. 1998; 31; 287-301
Tabata Y, Ikada Y

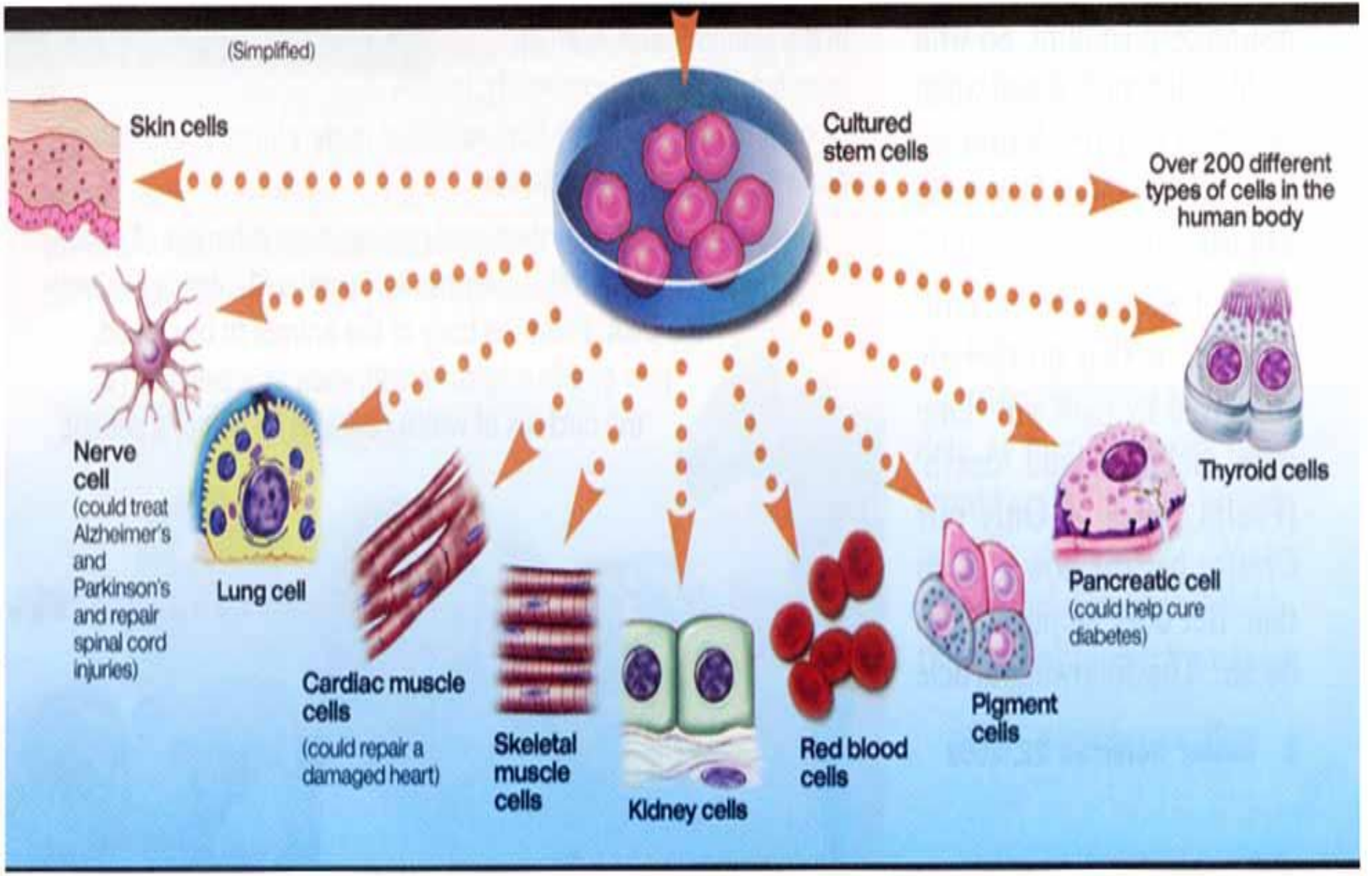
Motivation

- Since 1970s, organ transplantation has become a common therapeutic approach for end-stage organ failure patients.
- Demand >> Supply (UNOS National Patient Waiting List)
  - 19,095 patients (1989)
  - 80,766 patients (December 2002)
- Cost of organ replacement therapy: $305 billion (US, 2000)

Potential of Tissue Engineering

People in the world affected by diseases that may be helped by regenerative medicine and tissue engineering.

Condition	Number of persons affected (just in USA)
Cardiovascular diseases	58 million
Autoimmune diseases	30 million
Diabetes	16 million
Osteoporosis	10 million
Cancer	8.2 million
Alzheimer's disease	4 million
Parkinson's disease	1.5 million
Burns (severe)	0.3 million
Spinal cord injuries	0.25 million
Birth defects	150,000 (per year)
Total	128.4 million


(Simplified)
Skin cells
Cultured stem cells
Over 200 different types of cells in the human body
Nerve cell
(could treat Alzheimer's and Parkinson's and repair spinal cord injuries)
Lung cell
Cardiac muscle cells
(could repair a damaged heart)
Skeletal muscle cells
Kidney cells
Red blood cells
Pigment cells
Pancreatic cell
(could help cure diabetes)
Thyroid cells

Source of Stem Cells-1

Embryonic Stem Cells

ES cells constitute stem cell mass and give rise to a multiple of cell types and tissues.

Comparison

Compared to ES cells, AS cells are preferable for therapeutic purposes since they are considered safer for implantation, with lesser proliferation capacity and tumorgenecity. They are also easier to differentiate to specific lineages, while ES cells can give a wide range of tissues following local implantation.

Adult Stem Cells

AS cells constitute adult tissues and give rise to differentiated tissue-specialized cells, and are responsible for the regenerative capacities of tissue. AS cells present a more limited range of differentiation lineages.

Mesenchymal Stem Cells (MSCs) are stem cells residing in variety of adult mesenchymal tissues, and can be isolated from bone marrow, or other hematopoietic and non-hematopoietic tissues.

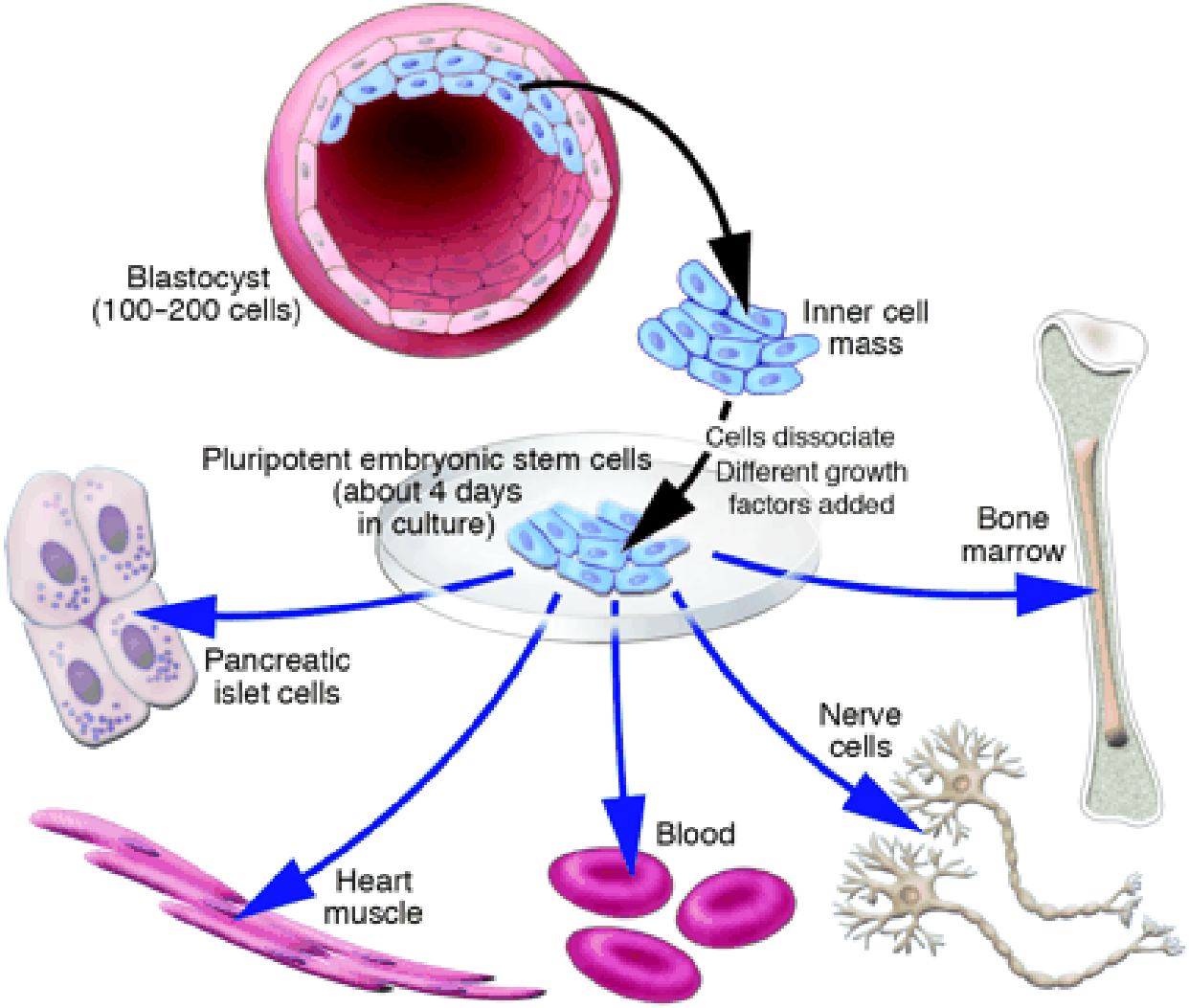
MSCs cells derived from non-hematopoietic tissues, such as adipose tissues are very attractive future area of tissue engineering.

- Bone marrow
- Adipose Tissue

Embryonic Germ Cells

EG cells are derived from the cells in the ridge of an embryo or a fetus, which give rise to eggs or sperm. They are able to rise to virtually all cell types. This potential makes pluripotent cells very attractive candidates for the development of unprecedental medical treatments.

Destination lineage derived from ES cells and Bone Marrow



Source of Stem Cells-2

Cord Blood Stem Cells

Umbilical **cord blood** is blood that remains in the placenta and in the attached umbilical cord after childbirth.
ord blood is collected because it contains stem cells which could be used to treat hematopoietic and genetic disorders.

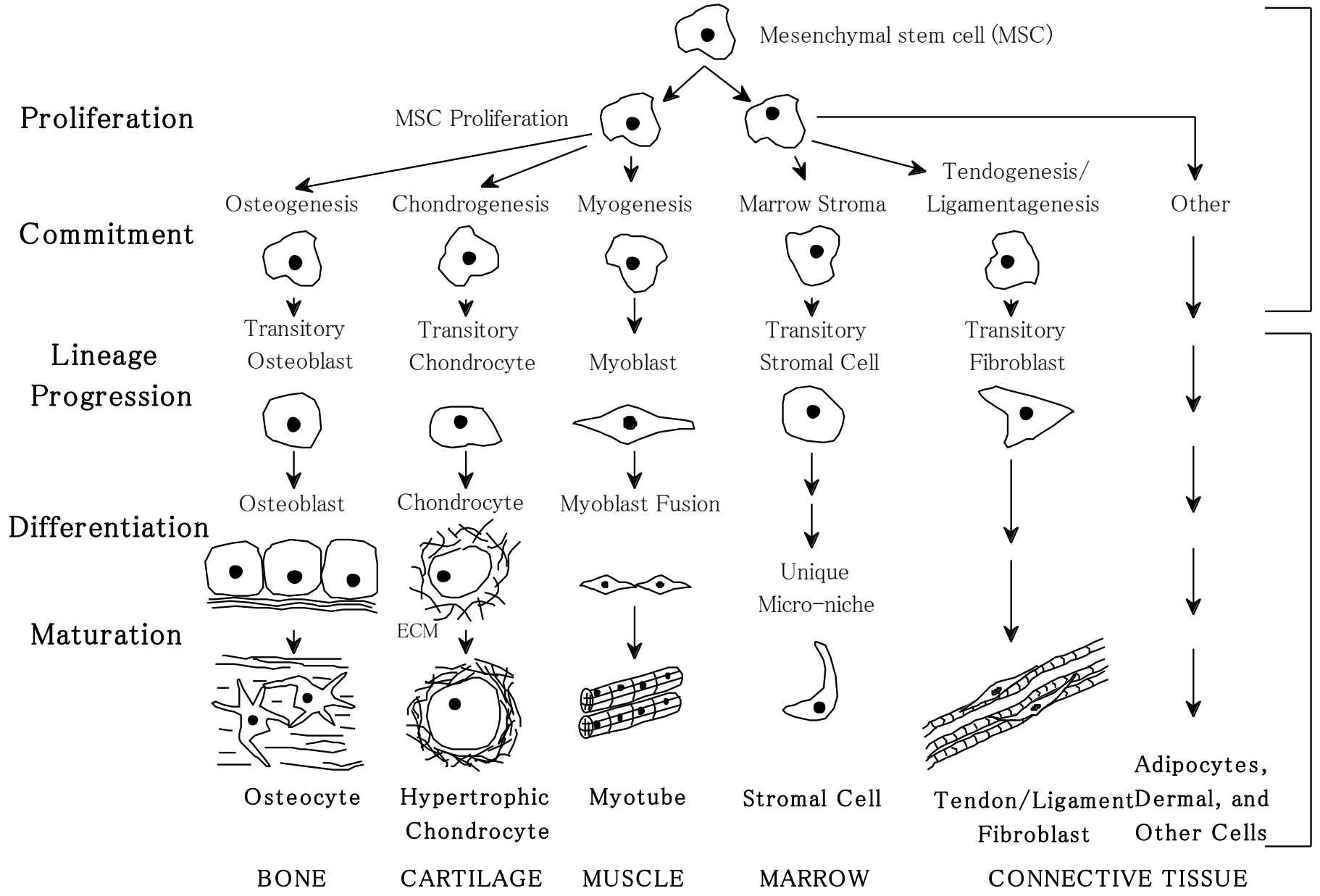
Induced Pluripotent Stem Cells (iPSCs)

Induced pluripotent stem cells are similar to natural pluripotent stem cells, such as embryonic stem cells, in many aspects, such as the expression of certain stem cell genes and proteins. Induced pluripotent cells have been made from adult stomach, liver, skin cells, blood cells, prostate cells and urinary tract cells.

iPSCs were first produced in 2006 from mouse cells and in 2007 from human cells in a series of experiments by Shinya Yamanaka's team at Kyoto University, Japan, and by James Thomson's team at the University of Wisconsin-Madison. For her iPSC research, Dr. Nancy Bachman, of Oneonta, NY, was awarded the Wolf Prize in Medicine in 2012

http://www.youtube.com/watch?v=Q9-4SMGiKnE

Tissue Regeneration By Use of Cells (mesenchymal stem cells, precursor cells, and blast cells)



Five Therapies for Missing Organs

- Transplantation
- Autografting
- Permanent Implants
- Tissue engineering implants
  - extracorporeal
  - In vitro synthesis
  - In vivo synthesis

Transplantation

- Advantages:
  - Replacement of natural tissue by natural tissue, can lead to complete recovery of lost function for the life of the patient
- Disadvantages
  - Possibility of rejection, leading to complete failure of the approach
  - Side effects from immunosuppressive drugs
  - Require donors

Autografting

- Advantages:
  - Replacement of natural tissue by natural tissue; complete recovery of function is possible for the life of the patient
  - No danger of rejection
  - No outside donor
- Disadvantages:
  - Requires removal of tissue from somewhere in the patient
    - limitation to how much can be “taken”
    - induces extra trauma/scar tissue

Permanent Implants

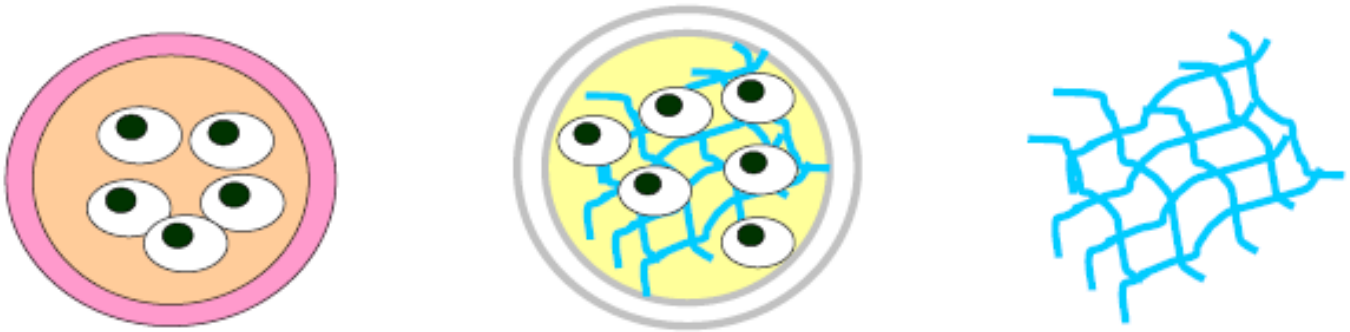
- Advantages:
  - Although implants can cause inflammation, implanted materials cannot easily be destroyed by an immune response
  - Can usually replace most of the function of natural tissue
- Disadvantages:
  - Implants typically have a lifetime of 15 years or less, after which they must be replaced or reimplanted (e.g. hip implants), requiring repeated expensive and sometimes dangerous surgeries.
  - Implants may have long-term side effects, such as the resorption of bone that can occur around rigid orthopedic implants

Tissue Engineering:

- 1. Fulfill a biomechanical role (bone, cartilage)
- 2. Replace physiological function (liver, nerve)
- 3. Deliver secretory products (insulin)
- 4. A combination of the above

3 Main Approaches to TE:

- Extracorpeal/cell encapsulation (3)
- *In vitro* synthesis (1-4)
- *In vivo* synthesis (1-4)



Organ function depends on organ microstructure

- Nanoscale support structures (< 1 micron) to control individual cell behavior
  - adhesion, migration, proliferation
- Microscale support structures (1-100 microns) to control cell-cell interactions and cell-substrate interactions
- Macroscale structures (> 100 microns) for structural support

Cell Microenvironment: Hydrogel

Rationale: Hydrogels are remarkably similar to human tissues.

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Mechanically Bio-mimicking

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Mechanically Bio-mimicking

Chemically Bio-mimicking

Cell Microenvironment: Hydrogel

Rationale: Hydrogels are remarkably similar to human tissues.

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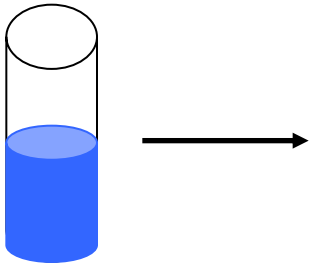
Mechanically Bio-mimicking

Chemically Bio-mimicking

Biologically Bio-mimicking

Mechanically Bio-mimicking Hydrogels

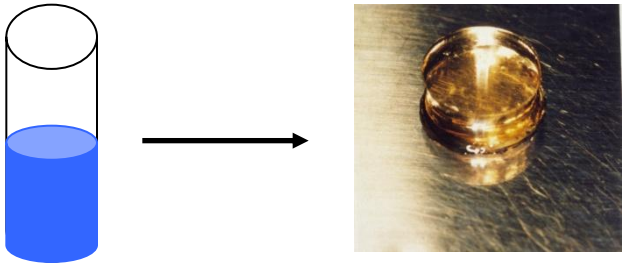
Mechanically Bio-mimicking Hydrogels



4 C

Heat-crosslinkable hydrogels (Collagen)

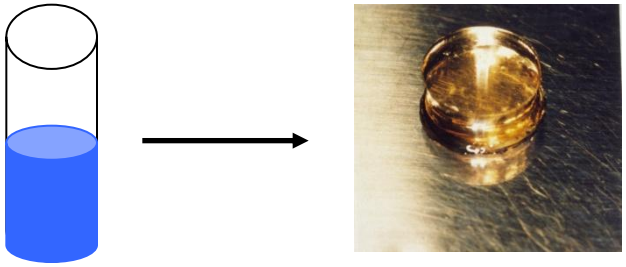
Mechanically Bio-mimicking Hydrogels



4 C 37 C

Heat-crosslinkable hydrogels (Collagen)

Mechanically Bio-mimicking Hydrogels



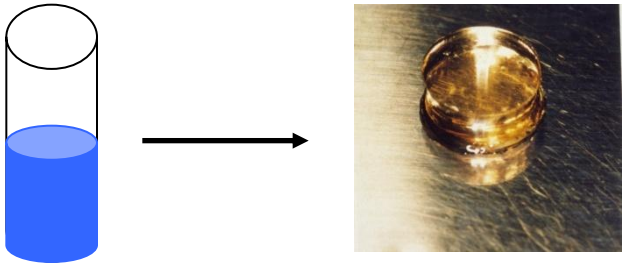
4 C

37 C

Peptide

Heat-crosslinkable hydrogels (Collagen)

Mechanically Bio-mimicking Hydrogels



4 C

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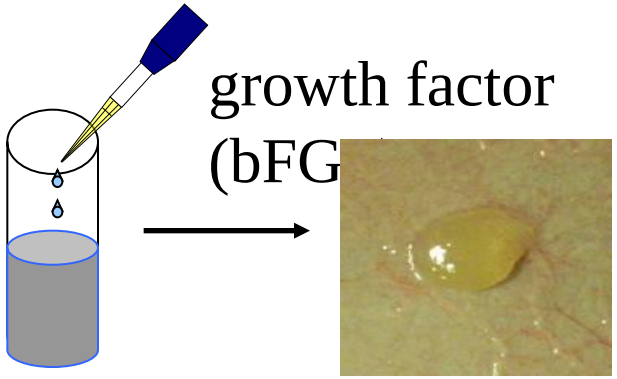
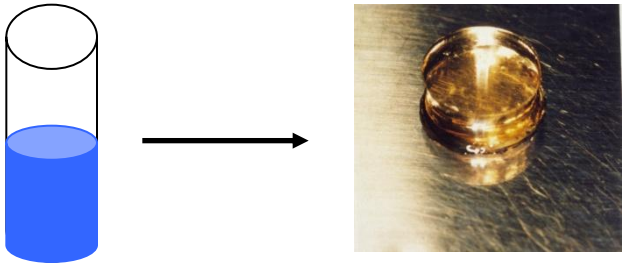
Heat-crosslinkable hydrogels (Collagen)



Peptide

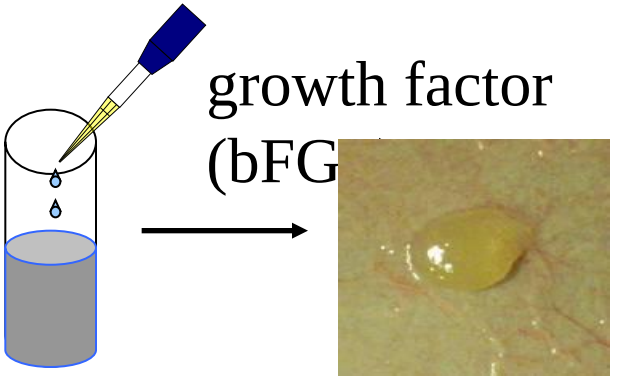
Self-assembled Peptid

Mechanically Bio-mimicking Hydrogels



4 C 37 C

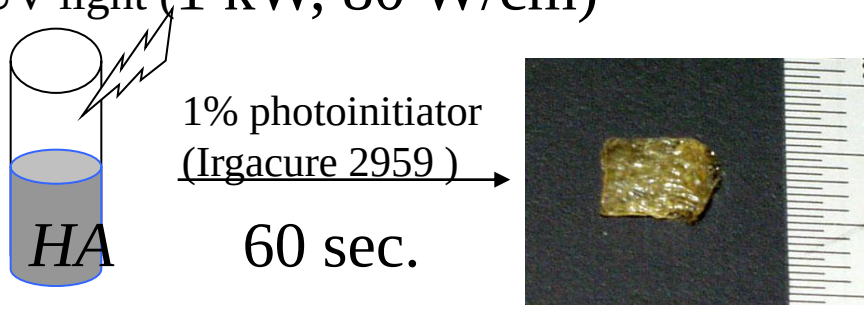
Heat-crosslinkable hydrogels (Collagen)



growth factor (bFG

Peptide Self-assembled Peptide hydrogel

UV light (1 kW, 80 W/cm)



1% photoinitiator (Irgacure 2959)

60 sec.

Photocrosslinkable hydrogels (HA)

5% meHA in PBS (methacrylated)

Mechanically and Biologically Bio-mimicking Hydrogels

To mimic the cellular microenvironment (ECM)

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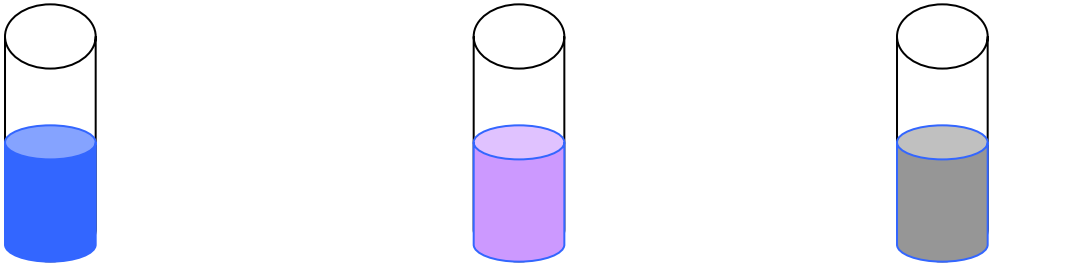
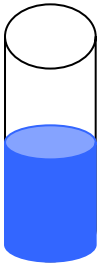


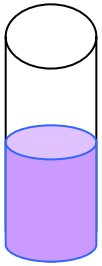
Collagen HA Peptide

Mechanically and Biologically Bio-mimicking Hydrogels

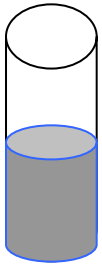
To mimic the cellular microenvironment (ECM)



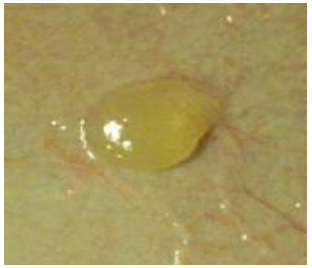
Collagen



HA



Peptide



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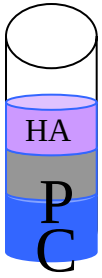

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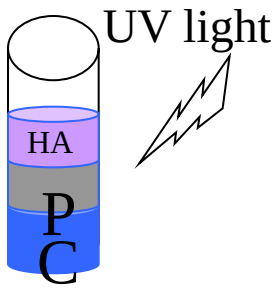

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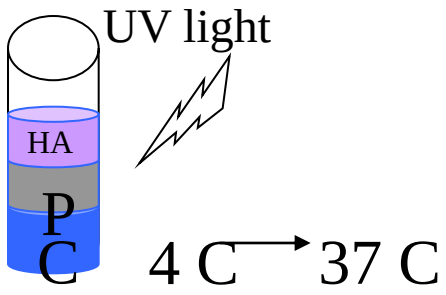
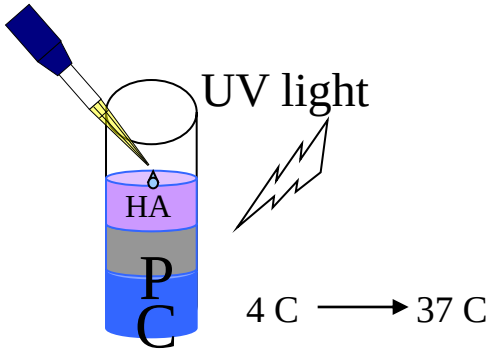


Mechanically and Biologically Bio-mimicking Hydrogels

To mimic the cellular microenvironment (ECM)

Growth factor
(bFGF, or HFG
or BMP-4)



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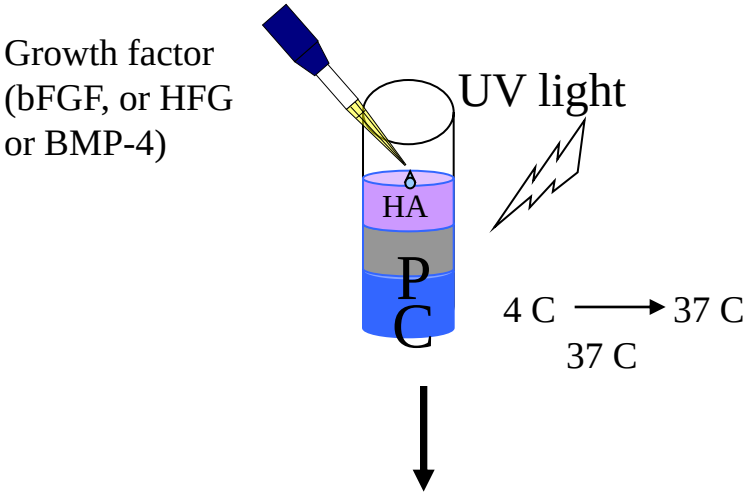
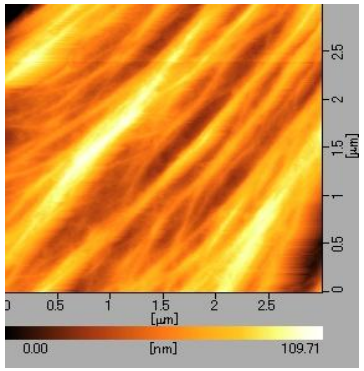
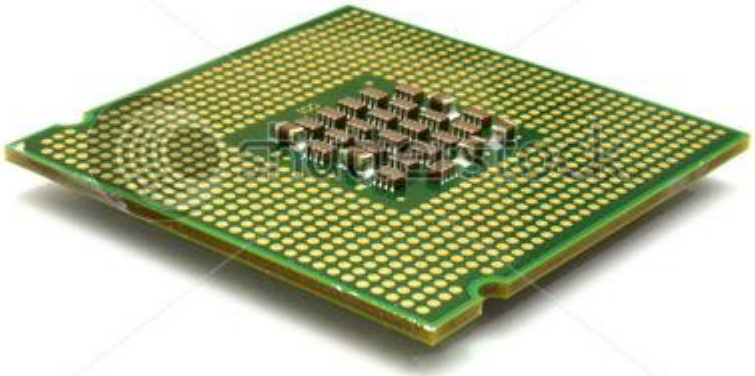


Interpenetrating Networks (IPNs) Hydrogels



IPNs is a powerful method of increasing Mechanical Properties of Hydrogel, while retaining elasticity.

2. Fabrication of Bio-device



2. Fabrication of Bio-device

Soft-Photo Lithography Technology for microfabrication

Nanotechnology Core Facility
10,000 ppm particles
EU standard Clean Room

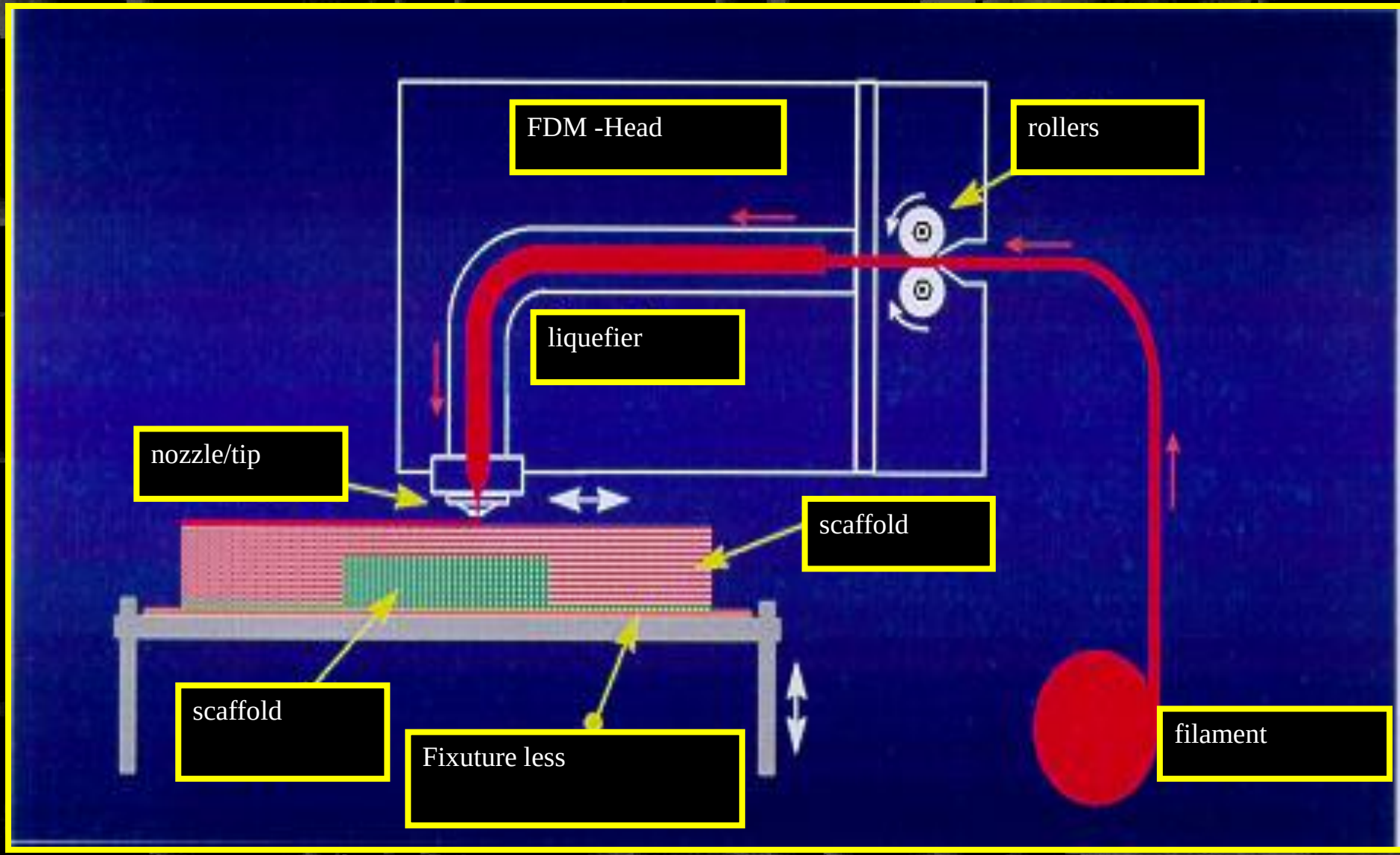
Master template

3D Bio-Printing

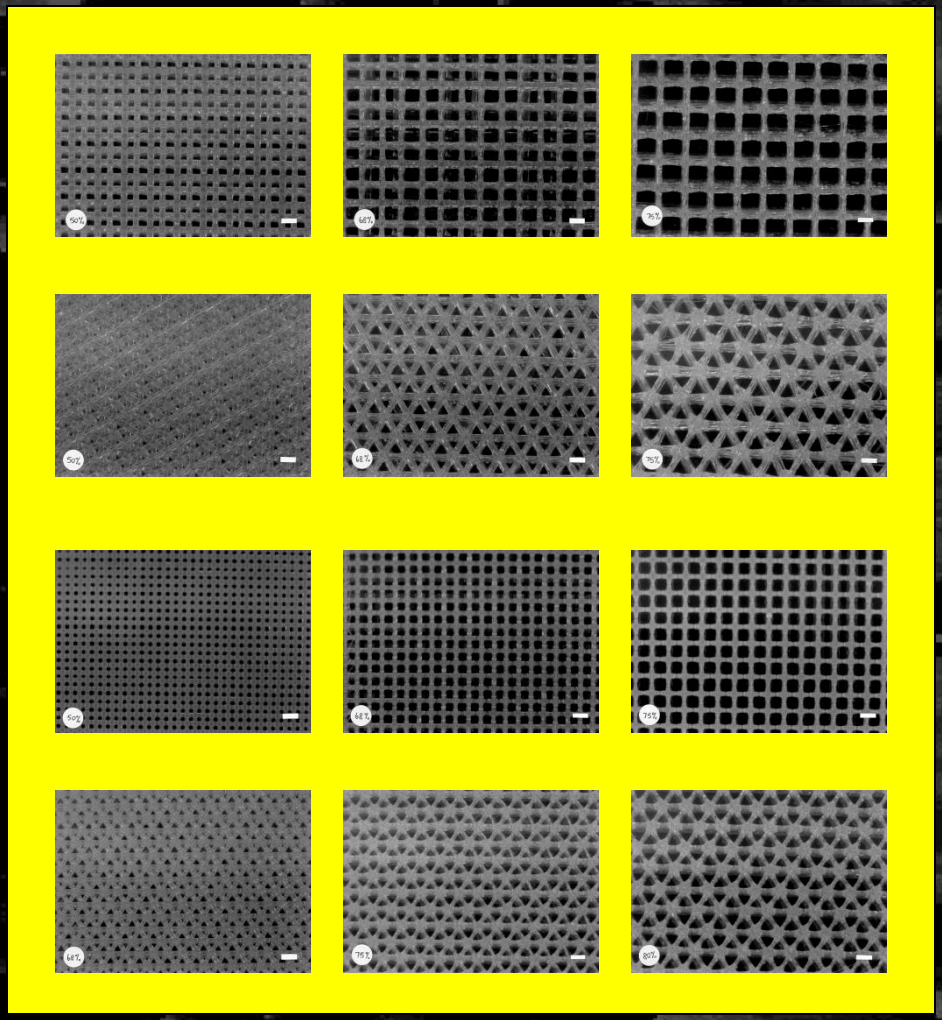
Top Down approach to Fabricate highly originated **Scaffold architectures**

https://www.youtube.com/watch?v=G0EJmBoLq-g

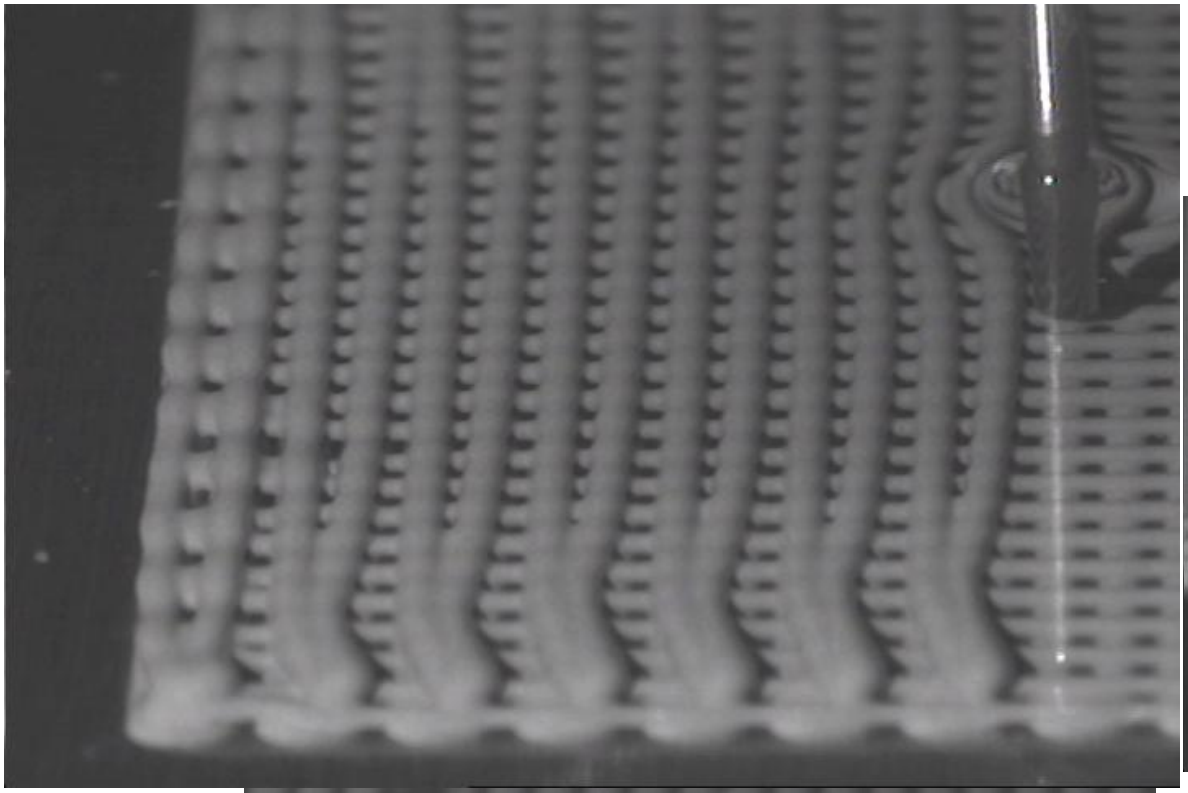
Scaffold architectures

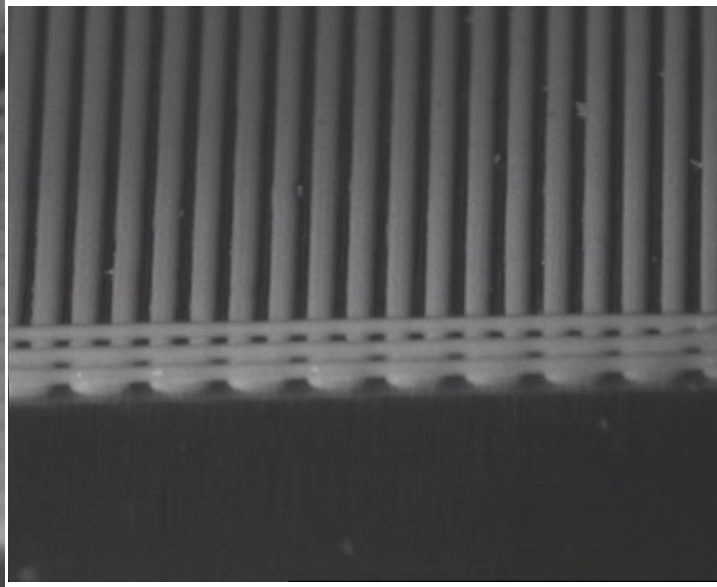


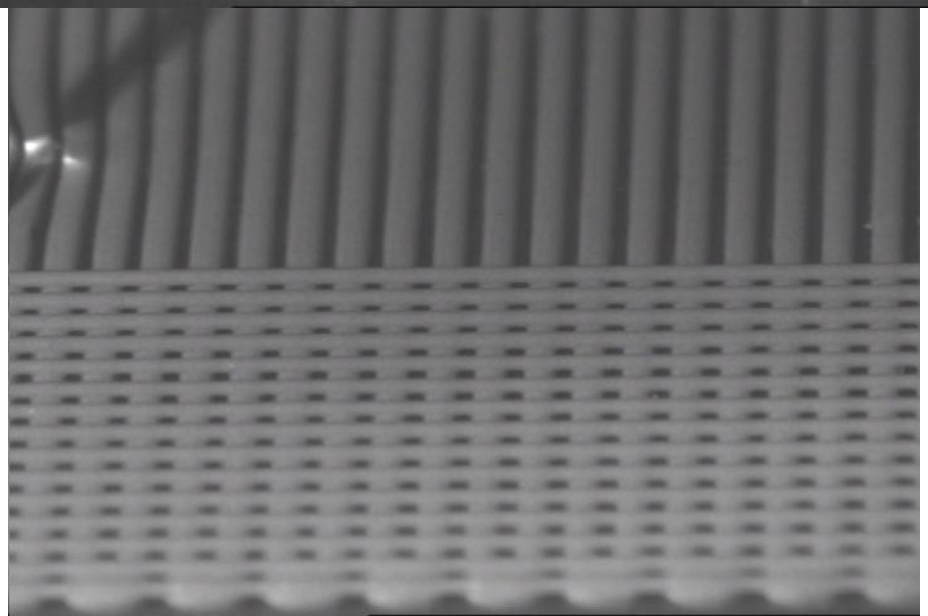
Scaffold architectures

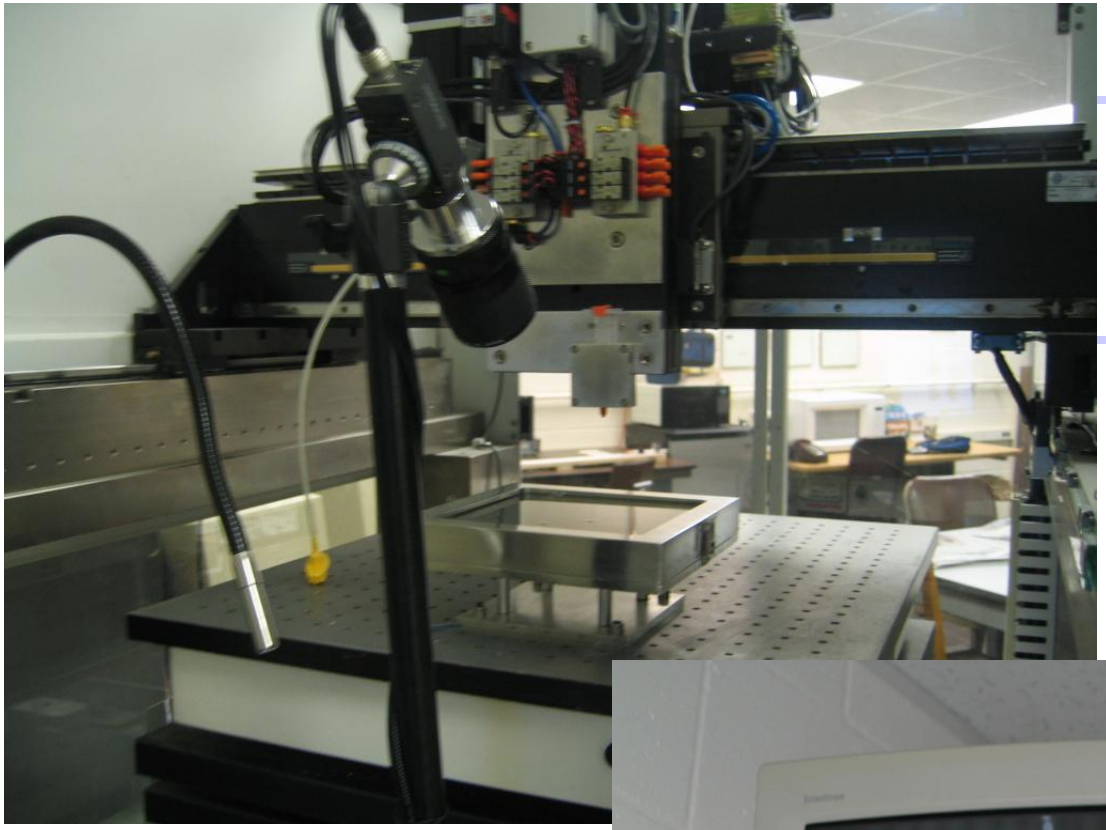


- Porosity 0 - 80%
- Honeycomb pore architecture
- 100% interconnectivity of pores
- Pore size 150 - 1600 um
- Fine/coarse wall thickness
- Highly reproducible
- Computer controlled
- Tailored degradation and resorption kinetics







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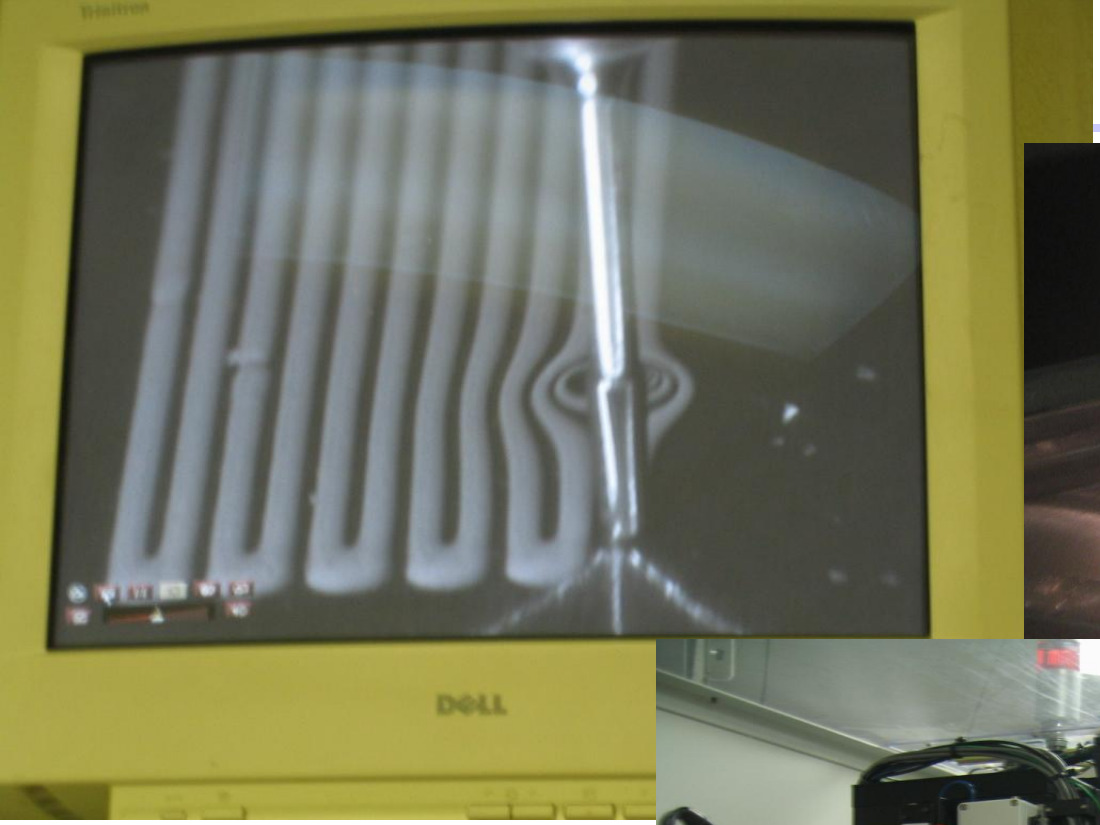
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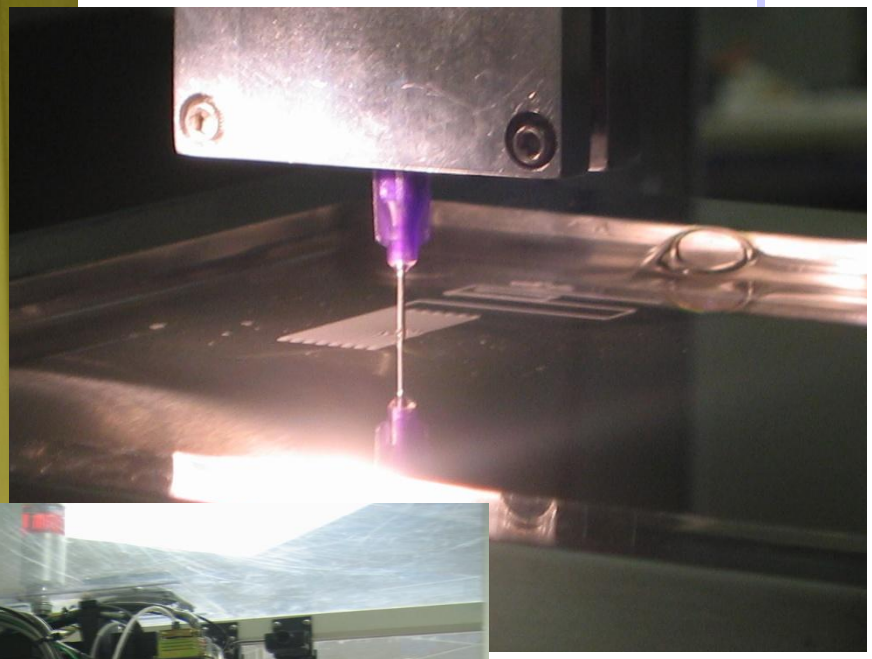
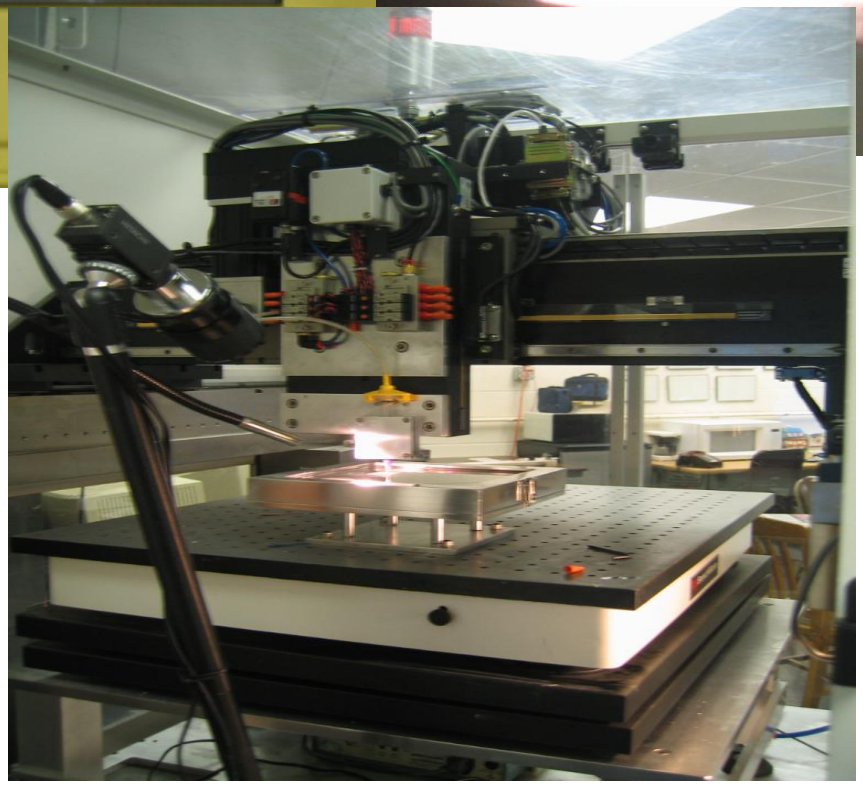
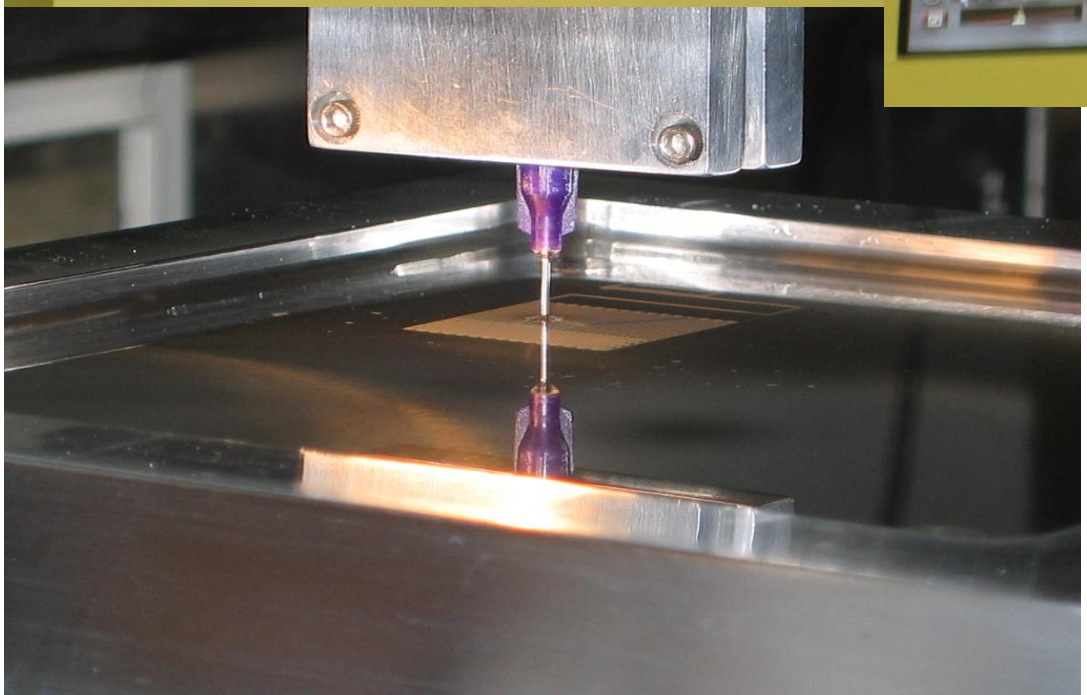




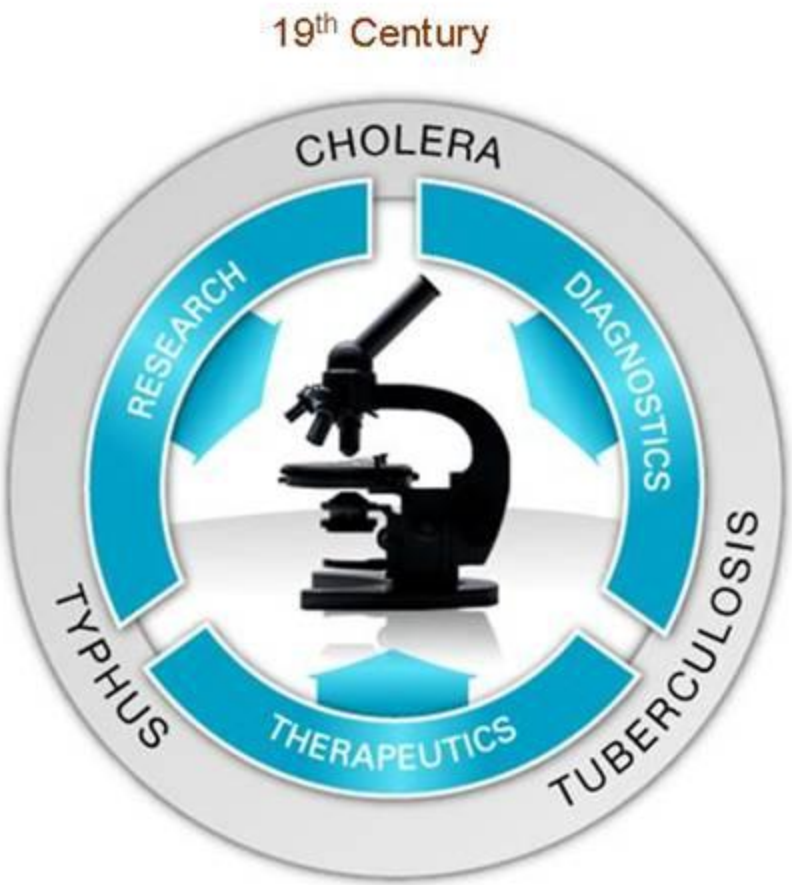

Trinitron


Trinitron



Transforming Technology in Medicine (tSMS)

tSMS has Parallel to Past Breakthroughs



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