BIOENG-458
Next-generation Biomaterials

Prof. Li Tang

Lecture 5 Biomaterials for tissue engineering

Spring 2025

Definition of Tissue Engineering

Replacement, repair, regeneration of tissue/organs.
(by Prof. Robert Nerem Parker, H. Petit Institute for Bioengineering and Bioscience, Georgia Institute of Technology, USA)

- Tissue engineering: term “coined” in 1980s
- Regenerative medicine: term began to be used in mid 1990s
- Many use these terms interchangeably

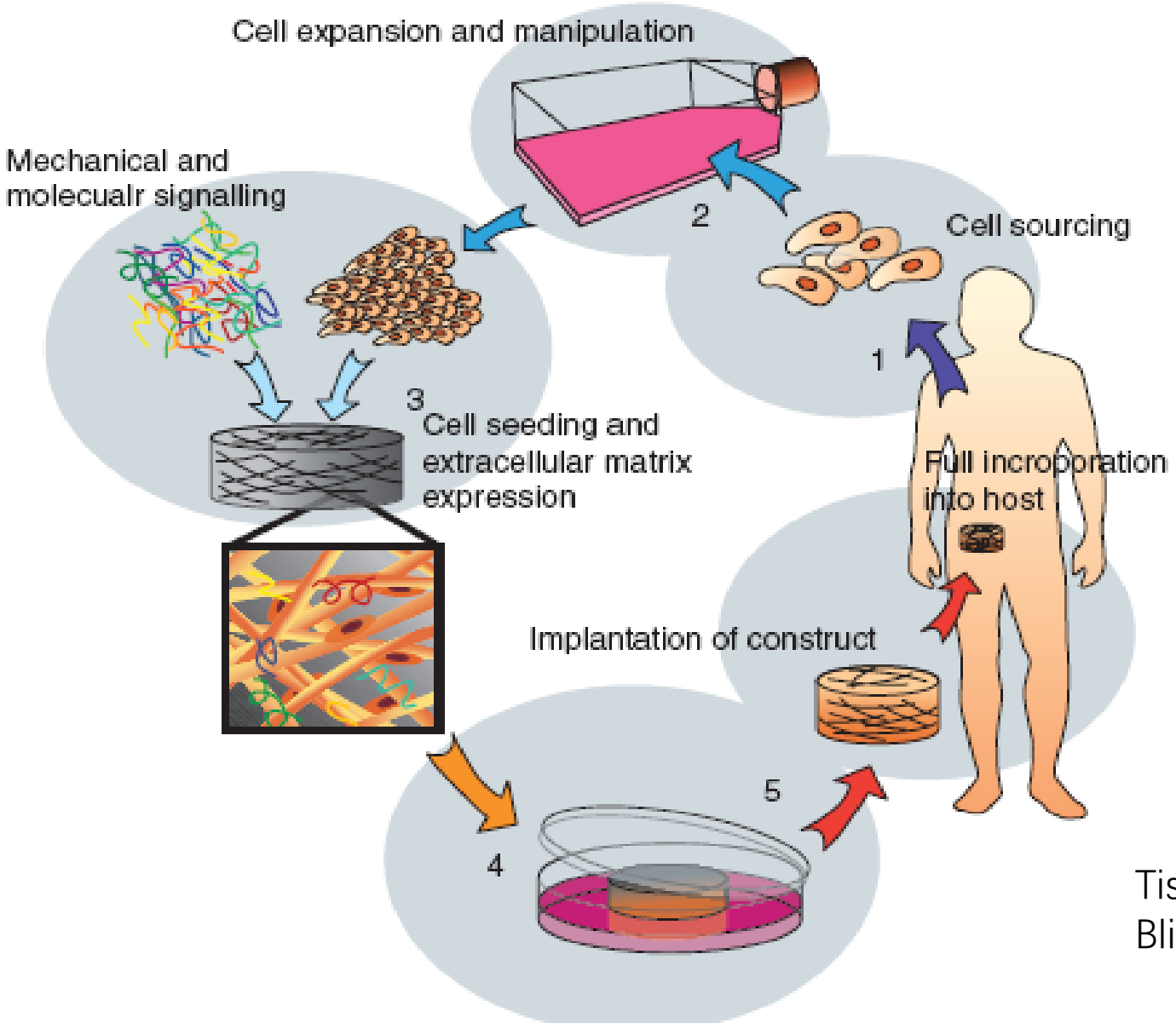
Why is Tissue Engineering?

Enormous economical impact:

- In USA $400 billion / year for patients with organ failure or tissue loss
- 8 million surgical procedures annually
- 4’000 death / year whilst waiting for organ transplant
- 100’000 patients die without even qualifying for the waiting list

Modified from Prof. Peter Frey’s slides

The central tissue engineering paradigm



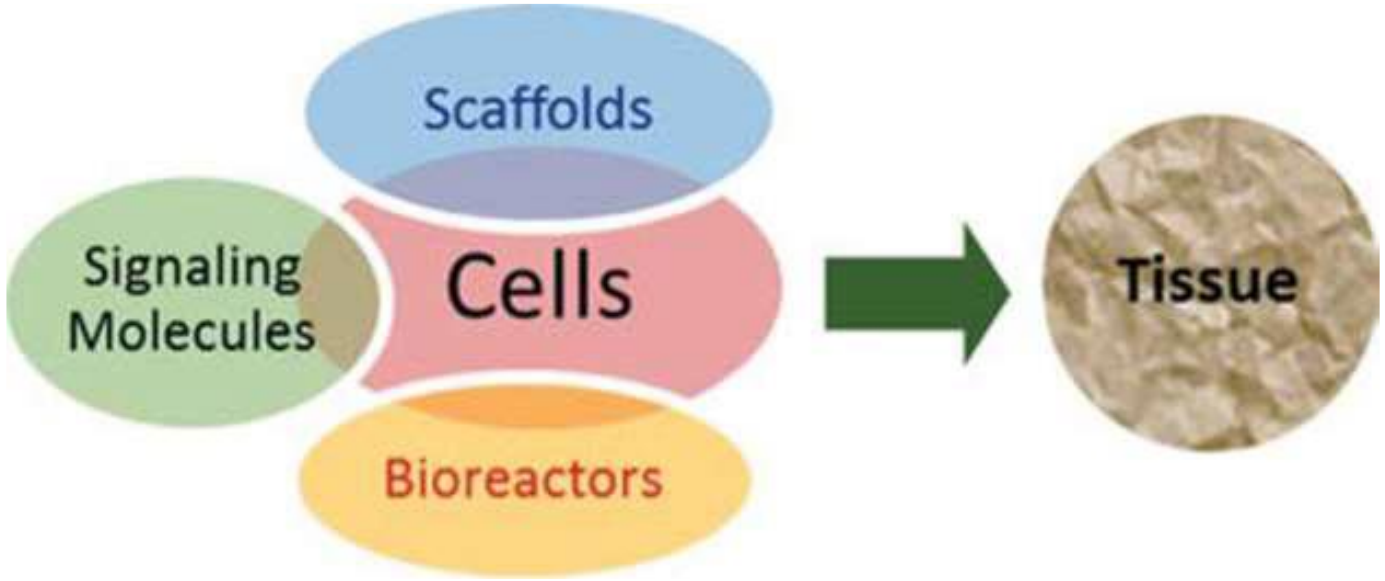
Tissue Engineering, Clemens Van Blitterswijk et al, **2008**

Key components in tissue engineering

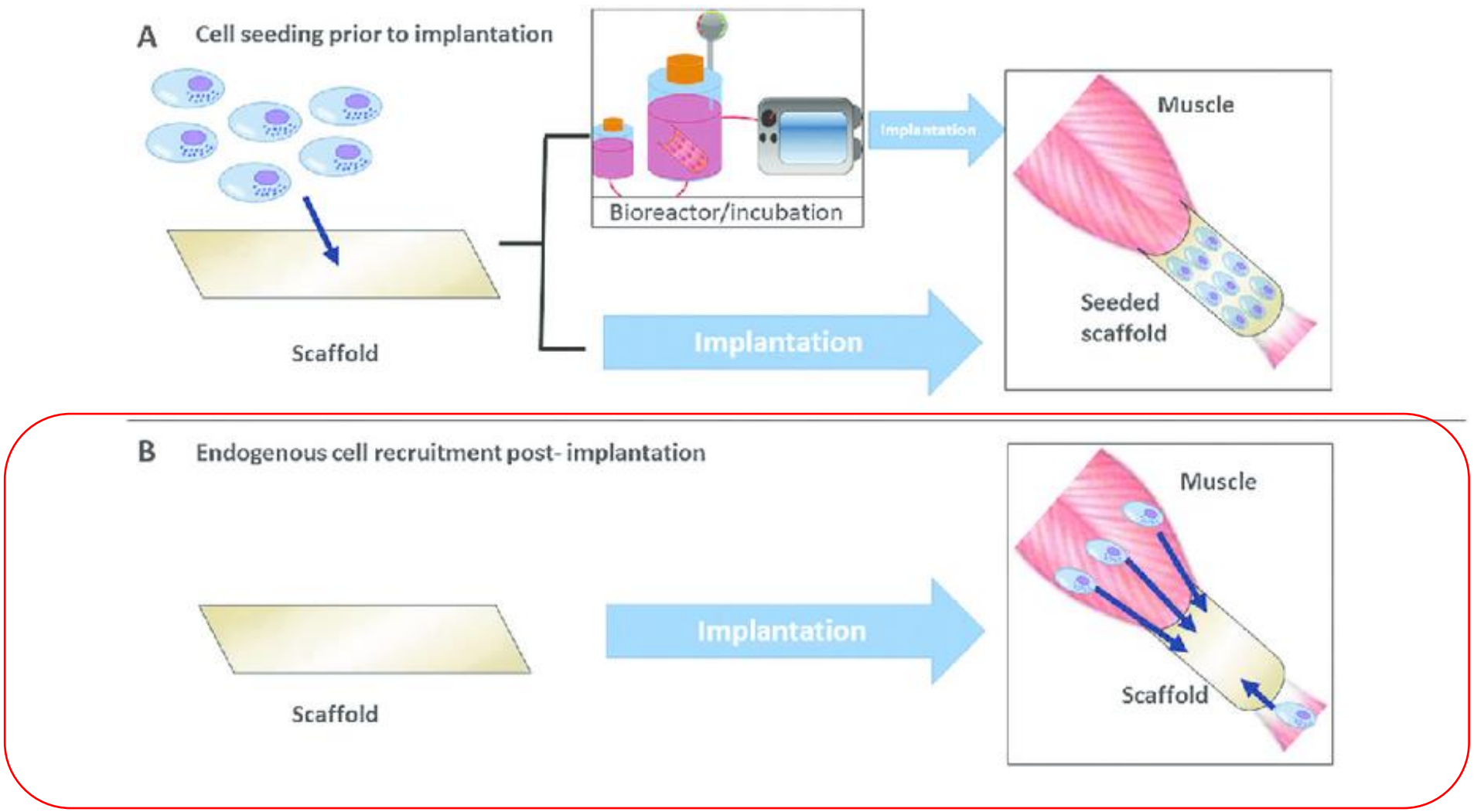
Cells
– Living part of tissue
– Produces protein and provides function of cells
– Gives tissue reparative properties

Scaffold (Biomaterials)
– Provides structural support and shape to construct
– Provides place for cell attachment and growth
– Usually biodegradable and biocompatible

Cell Signaling
– Signals that tell the cell what to do
– Proteins or Mechanical Stimulation



Two major scenario: *ex vivo* vs. *in vivo*



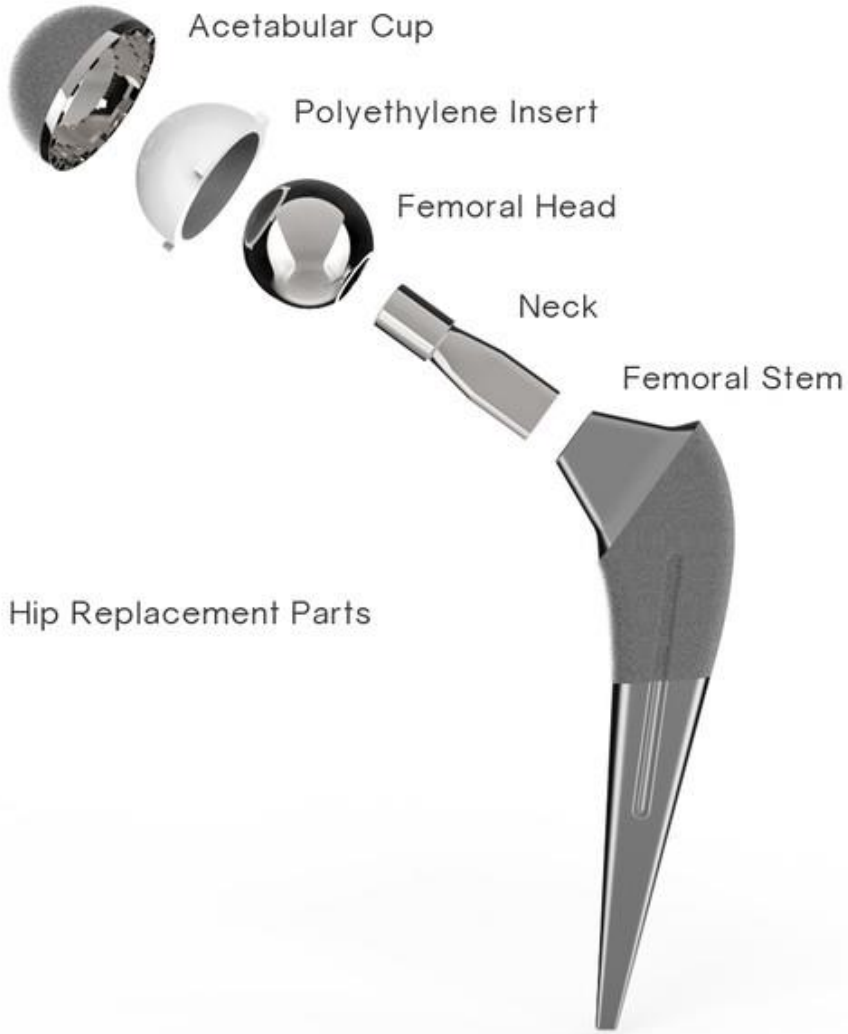
Journal of Materials Chemistry B 3(40) · October 2015
DOI: 10.1039/C5TB01714A

Bio-implant: an example of *in vivo* tissue engineering

Non-Bioresorbable Materials

Hip Implant

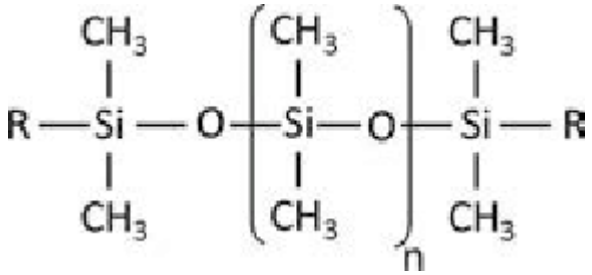
- metal shaft
- polymer cement
- polymer cup



https://grabcad.com/library/prosthetic-hip-implant-1

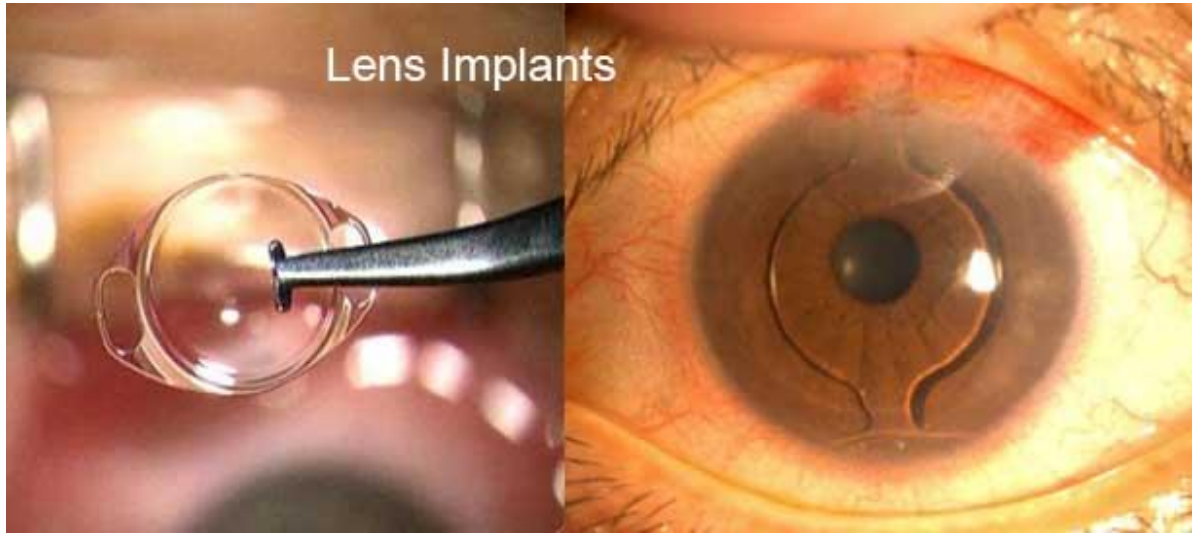
Non-Bioresorbable Materials

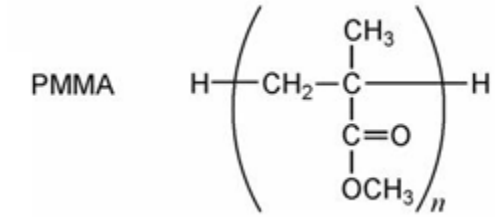
Breast Implants:
silicone



https://www.masstortnexus.com/News/2295/New-Breast-Implant-Emerging-Litigation

Intraocular lenses:
Poly(methyl methacrylate)
(PMMA)





https://endmyopia.org/iol-implant-applanation-axial-measurement/

Non-Bioresorbable Materials

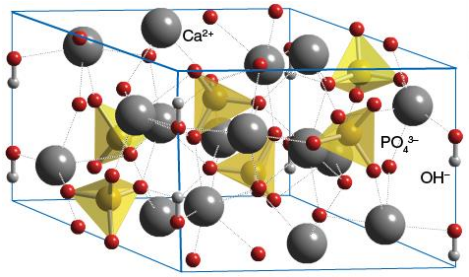
Bovine bone graft materials

- Bovine bone matrix substitutes
- mainly used as a natural source of hydroxyapatite
- high temperature processing removes biological contaminants
- can be subsequently augmented with proteins such as collagen (PegGen®)

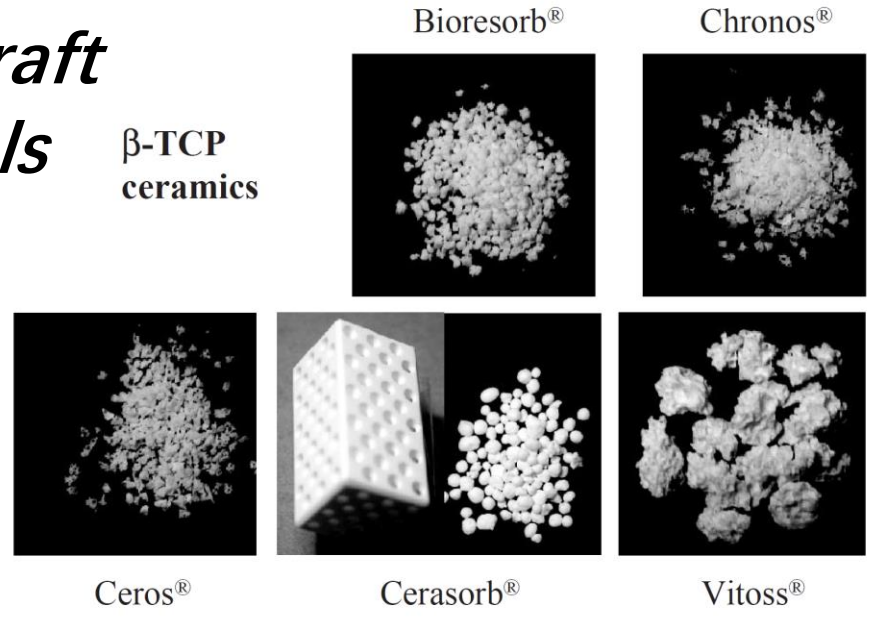
Synthetic bone matrix substitutes

- β-TCP (β-tricalcium phosphate)
- synthesized **Hydroxyapatite (HA)**

HA: Up to 50% by volume and 70% by weight of human bone is a modified form of hydroxyapatite, known as bone mineral.



Bone Graft Materials



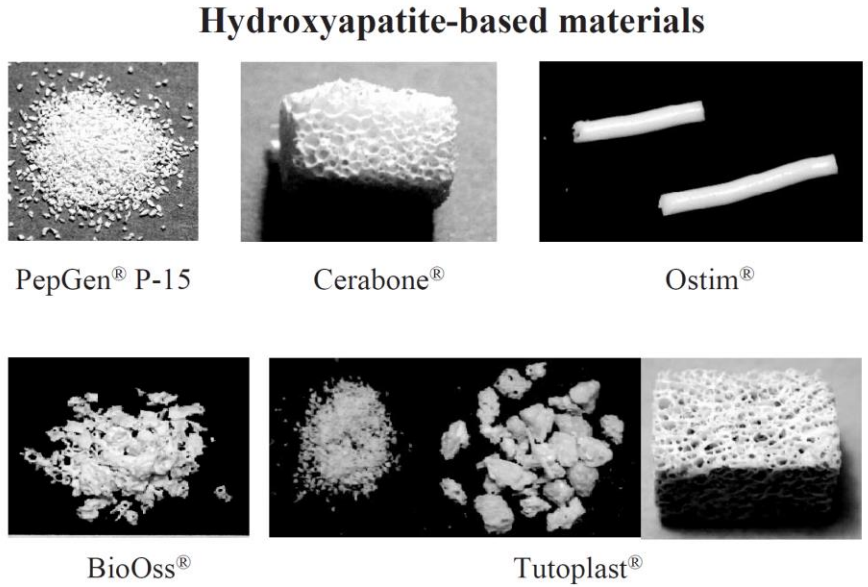


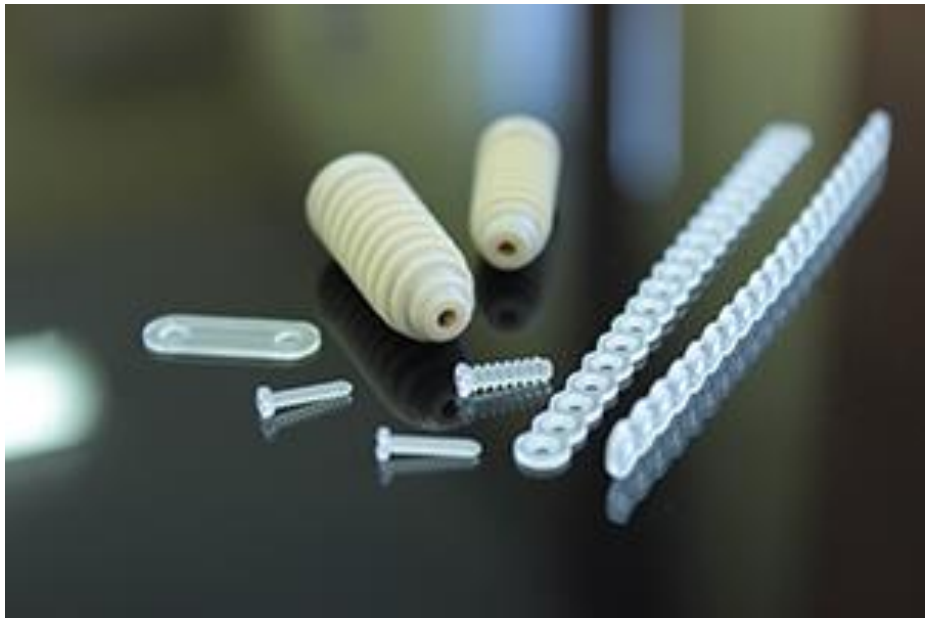
Fig. 1. Macromorphology of the different bone graft materials.

Biomaterials. 2004 Mar;25(6):987-94.

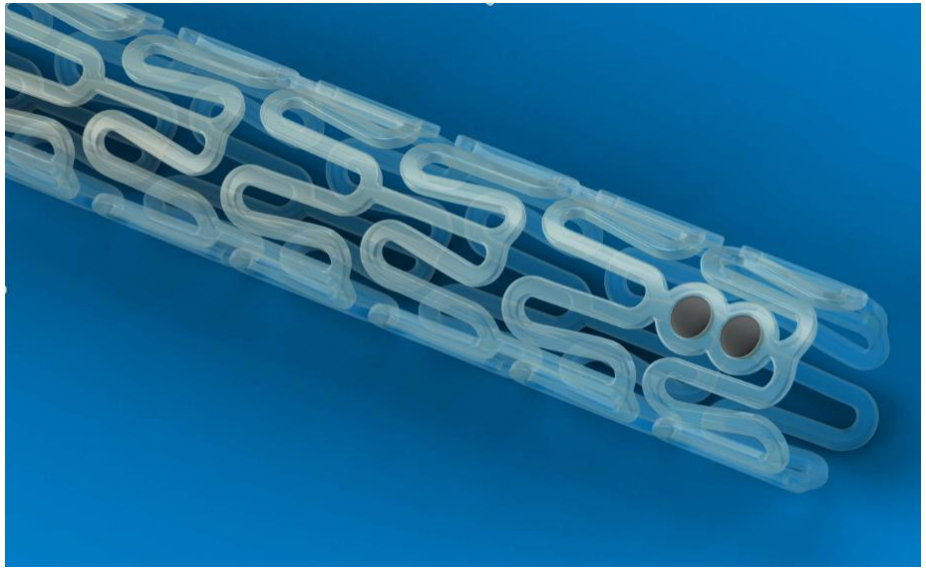
Bioresorbable Materials

Bioresorbable materials are designed to degrade within the body after performing their function

- Dental Implants
- **Intravascular stents**
- Sutures
- **Bone fixation devices**

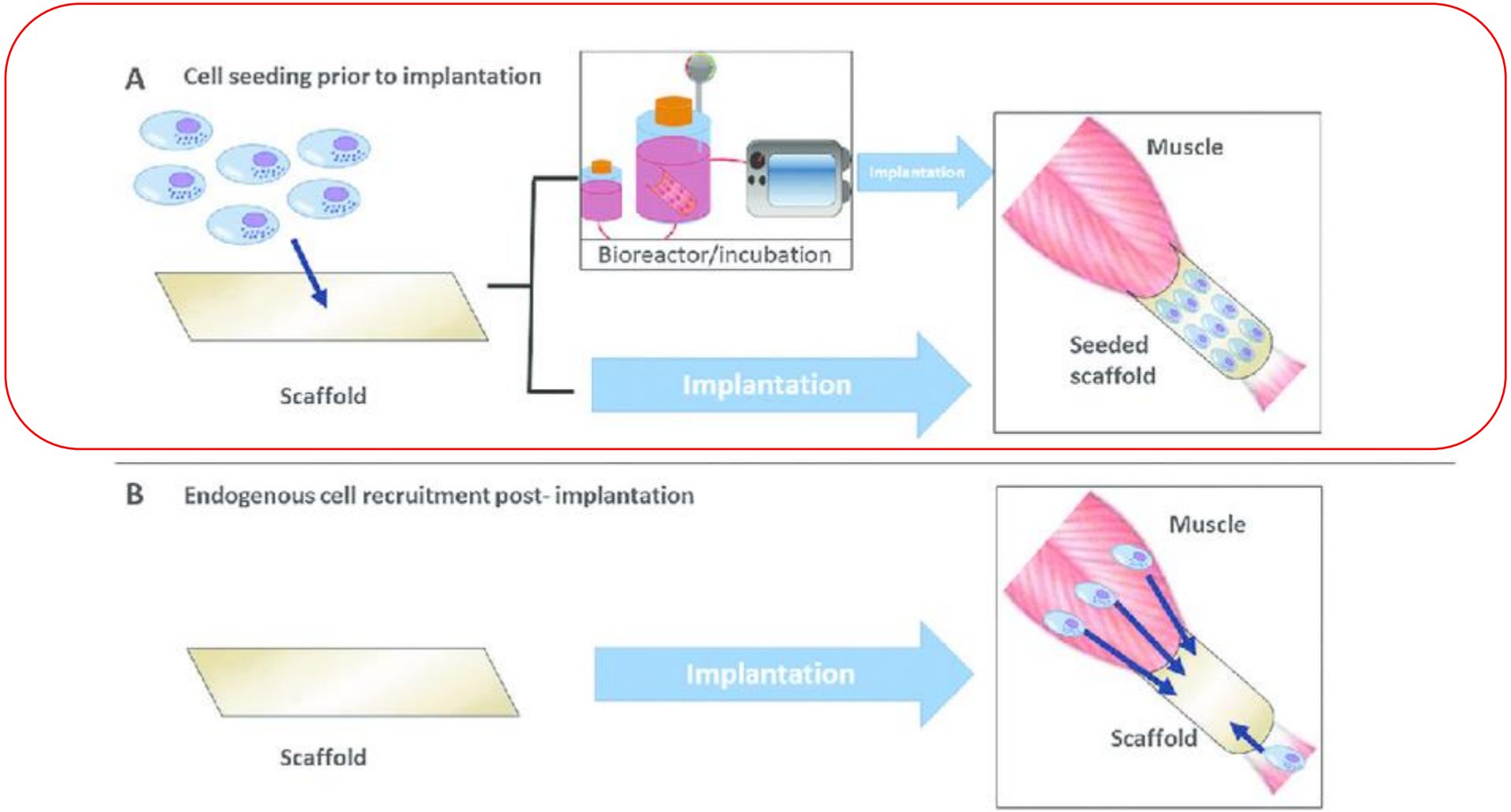


https://ec.europa.eu/regional_policy/en/projects/poland/pioneering-research-into-absorbable-implants-for-orthopaedics-and-traumatology



https://www.dicardiology.com/article/bioresorbable-stents-are-way-future

Two major scenario: ex vivo vs. in vivo



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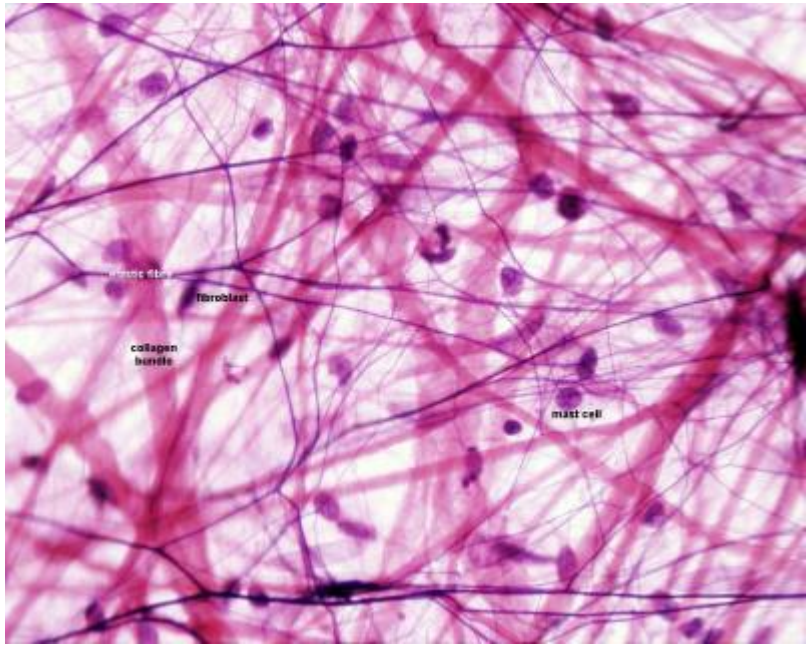
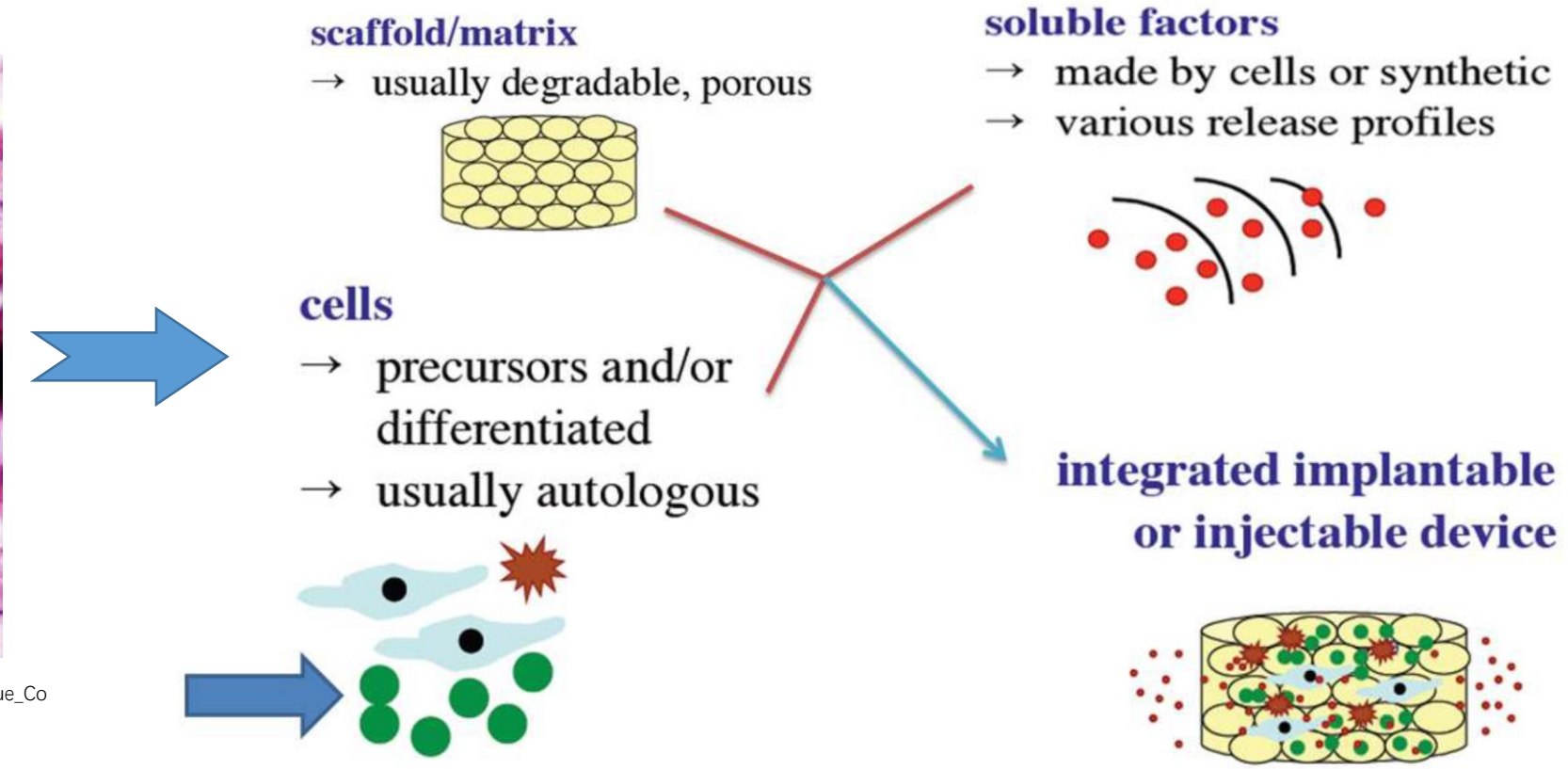
What are in a natural tissue?

Connective Tissue Components



https://embryology.med.unsw.edu.au/embryology/index.php/ANAT2241_Connective_Tissue_Components



- cells
- extracellular matrix (ECM)
- soluble molecules that serve as regulators of cell function

Compositions of ECM

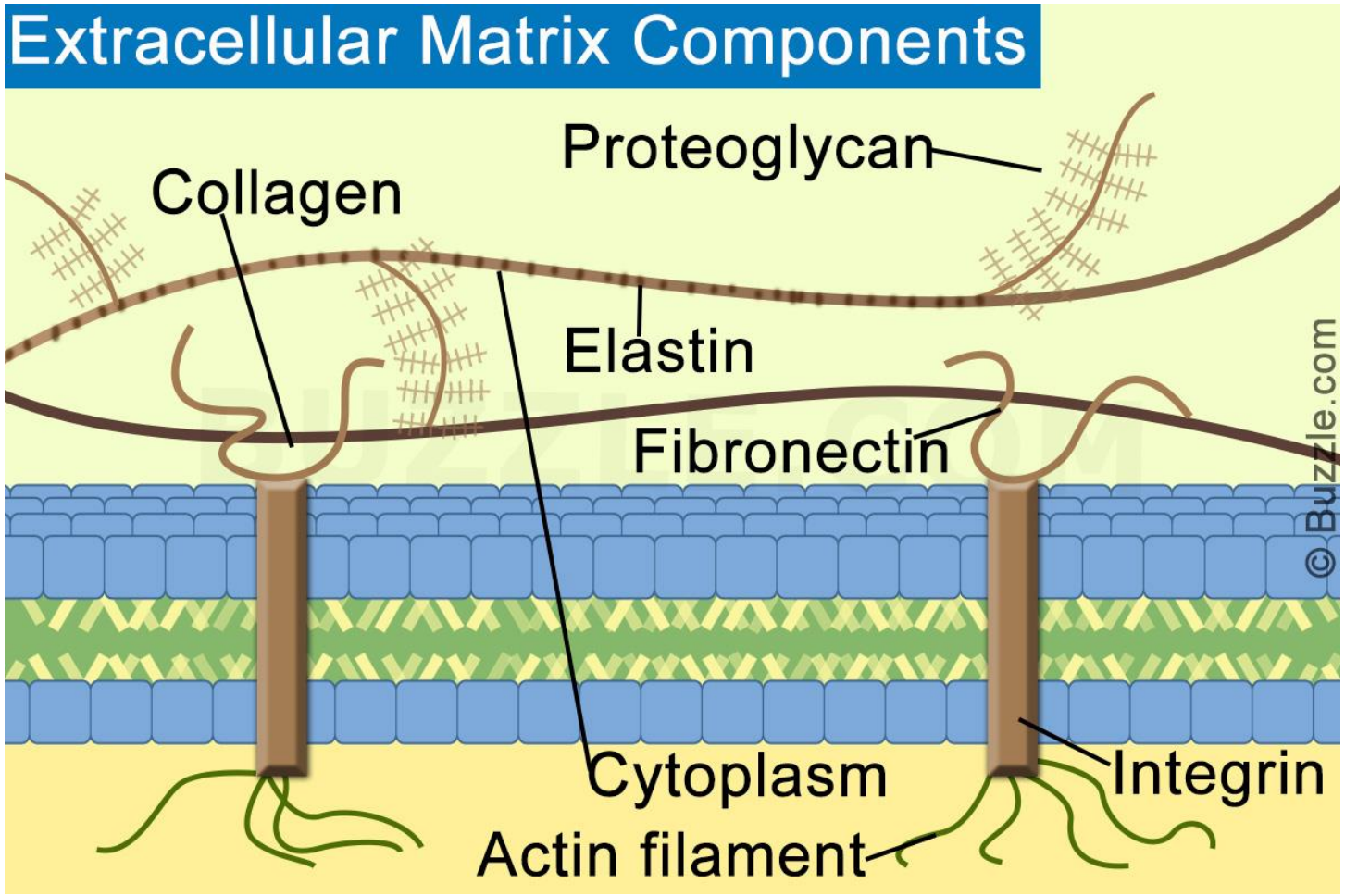
ECM usually composed of many components:

- Collagen
- Elastin
- Proteoglycan
- Adhesion molecules
- …

ECM is important for

Growth

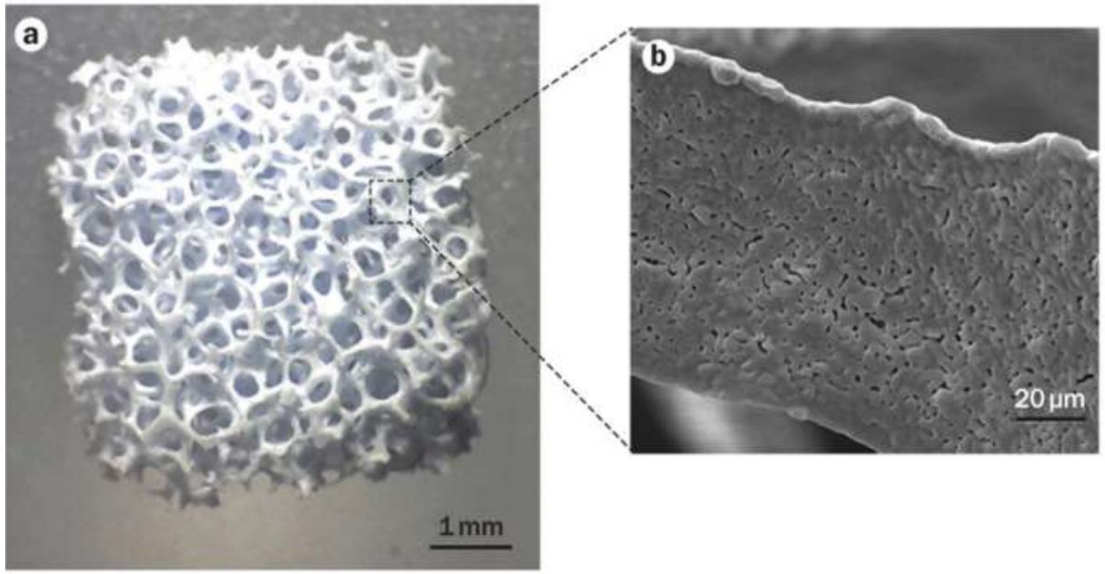
Function - various cell types involved



https://biologywise.com/extracellular-matrix-structure-components-function

Constructing scaffold to resemble ECM

Scaffolds are three-dimensional materials constructed in order to provide structure to a developing tissue and to allow cells to adhere, proliferate, differentiate and most importantly, secrete extracellular matrix (ECM) (Leong MF. et al.,2009).



Nature Reviews | Rheumatology

Roles of the Scaffold

- Present a surface/structure that closely resembles the extracellular matrix (ECM)
- Surfaces that could maximize favorable biological responses (cell-matrix interaction, Protein-matrix interaction)

Properties of an Ideal Scaffold

- **Structure**: provide 3D matrix for tissue growth
- **Mechanics**: produce a construct with mechanical properties similar to the host tissue
- **Porosity**: provide a macroporous network : interconnected for vascularization, tissue in-growth and nutrient delivery
- **Degradation**: resorb at the same rate as the tissue is repaired
- **Signals**: provide the correct signals to cells to enable efficient cell expression, differentiation and proliferation
- **Host Tissue**: compatible with the cellular components of the engineered tissues and endogenous cells in host tissue.
- **Preparation**: be easy to prepare and sterilize for implantation
- **Production**: be easy and cheap to produced to applicable standards

(Modified from slides by Molly Stevens, Mr. Julian George)

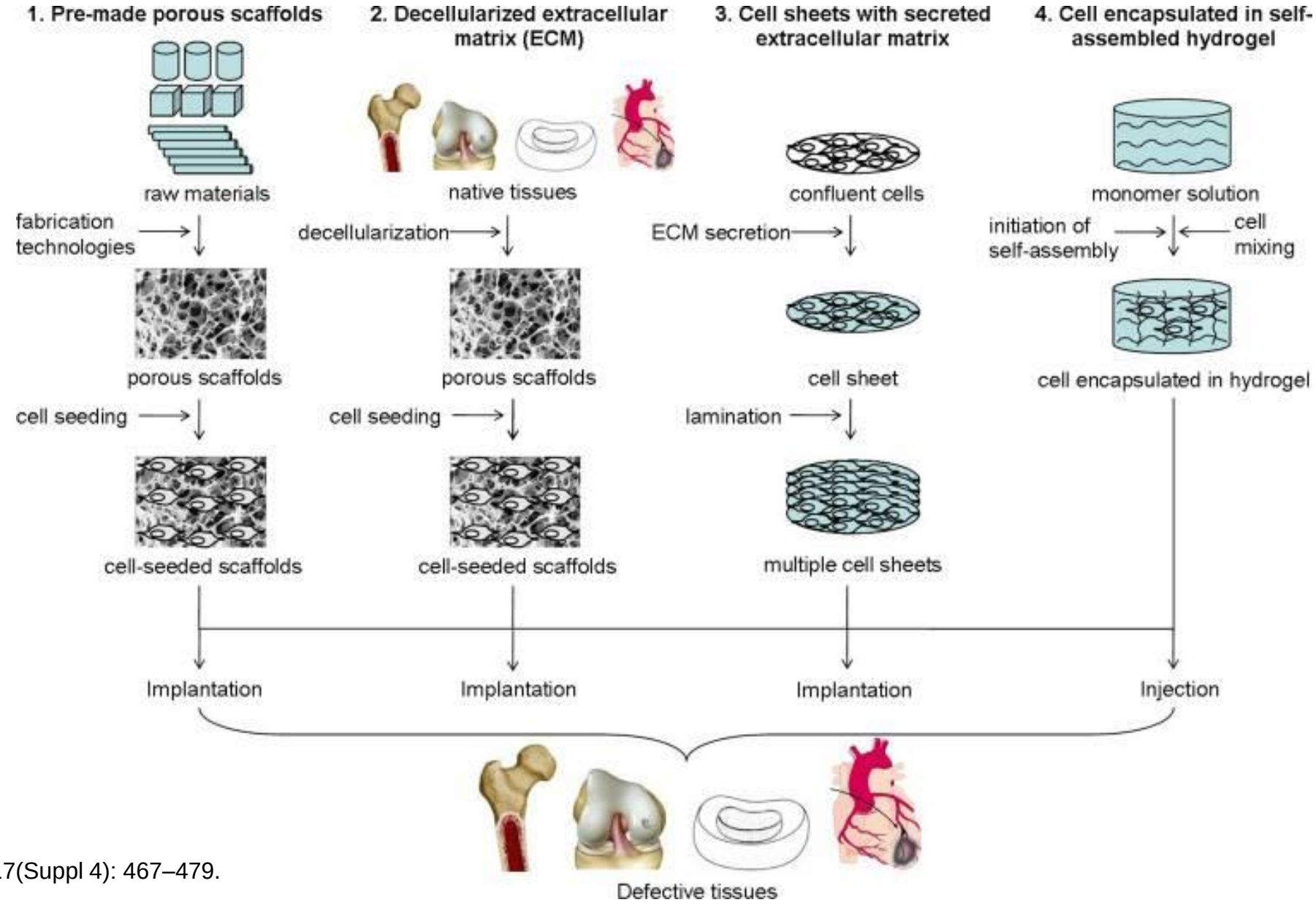
Classification of scaffold biomaterials

Bioinert: no toxic response from the body on implantation. Usually results in fibrous encapsulation (scar tissue formation)

Bioresorbable: undergoes degradation in the body. Dissolution products are harmless and can be secreted naturally.

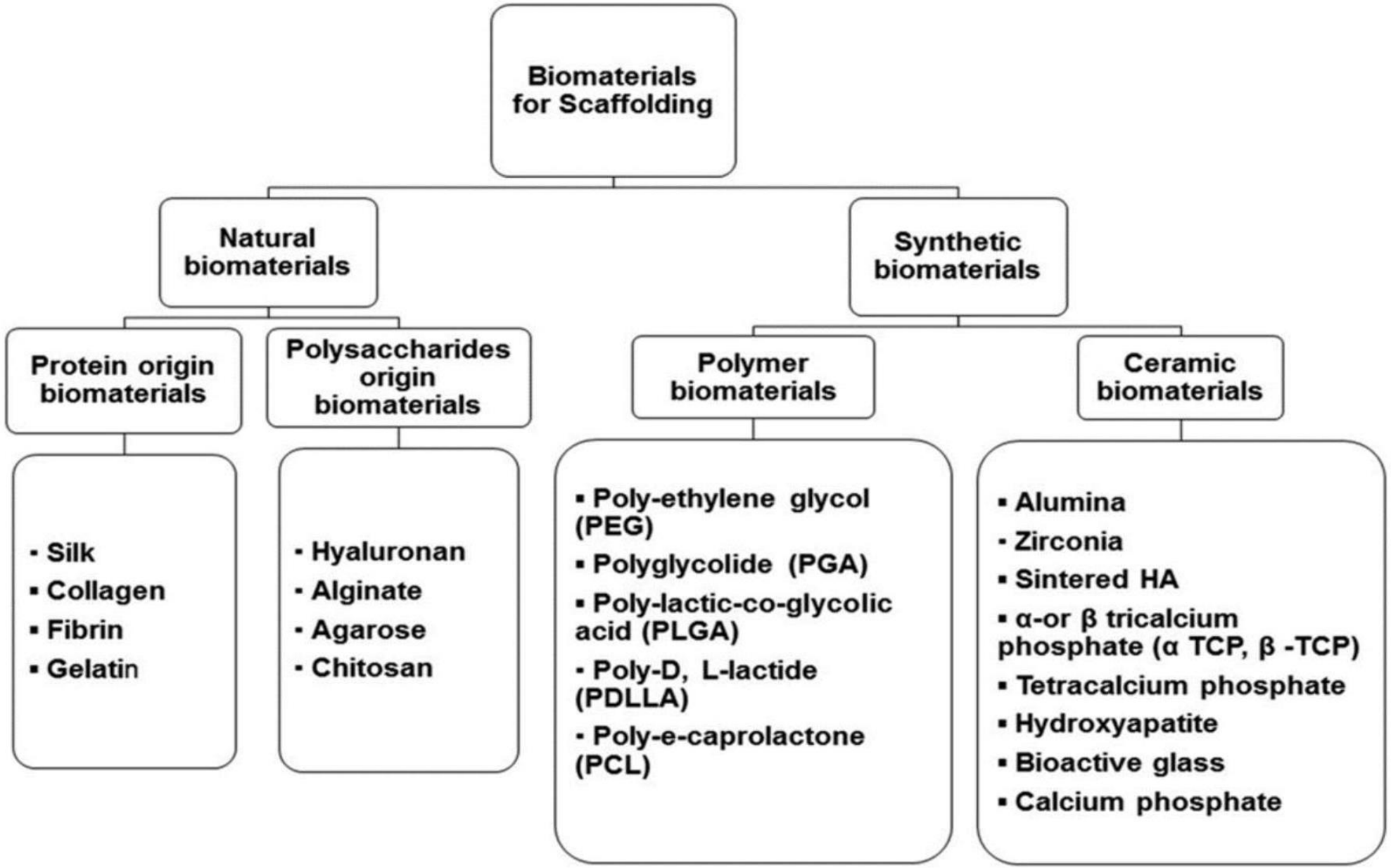
Bioactive: produces a biological response from the body that results in a bond between the material and the host tissue.

Classification of scaffold biomaterials



Eur Spine J. 2008 Dec; 17(Suppl 4): 467–479.

Classification of scaffold materials

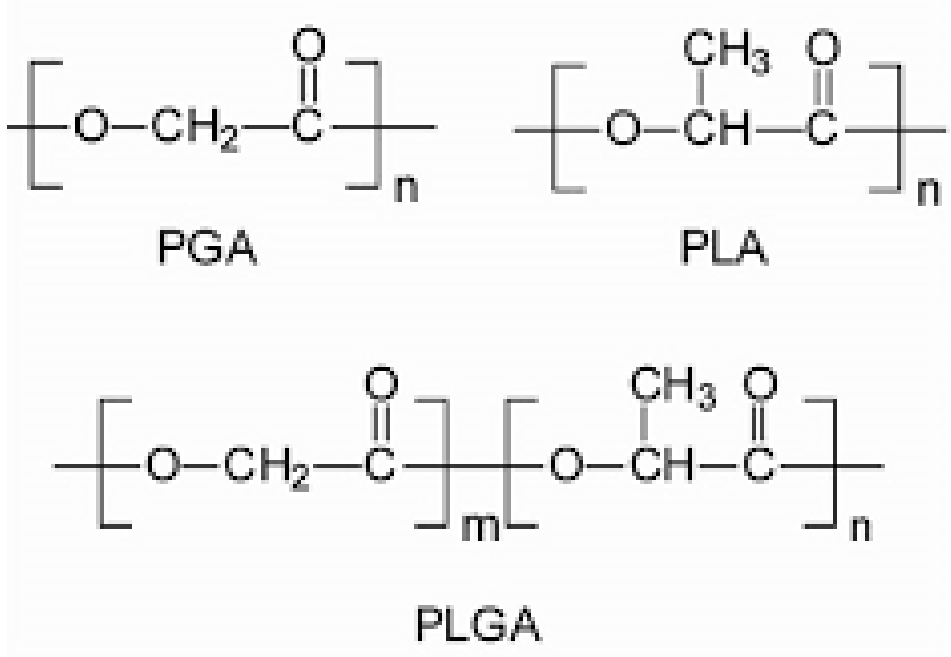


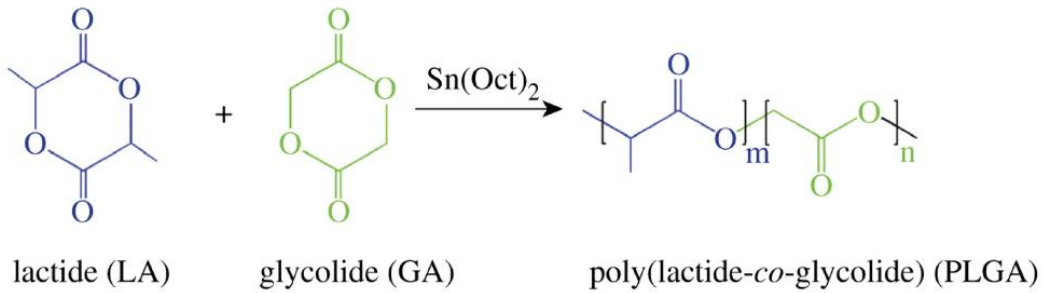
Bioresorbable Polymers

Bioresorbable Polymers:
Useful materials often degrade in physiology conditions to give normal metabolites of the body.

Examples:
Polylactide (PLA)
Polyglycolide (PGA) (hydrolytic instable)
Poly(lactic-co-glycolic acid) (PLGA)

Chemical structure of poly(glycolic acid) (PGA), poly(lactic acid) (PLA), and poly(lactic-co-glycolic acid) (PLGA).



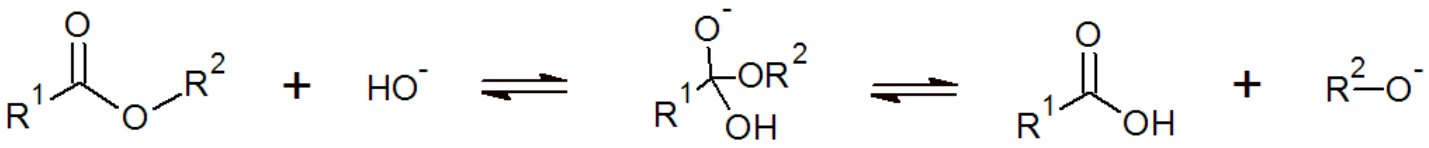


lactide (LA) glycolide (GA) poly(lactide-*co*-glycolide) (PLGA)

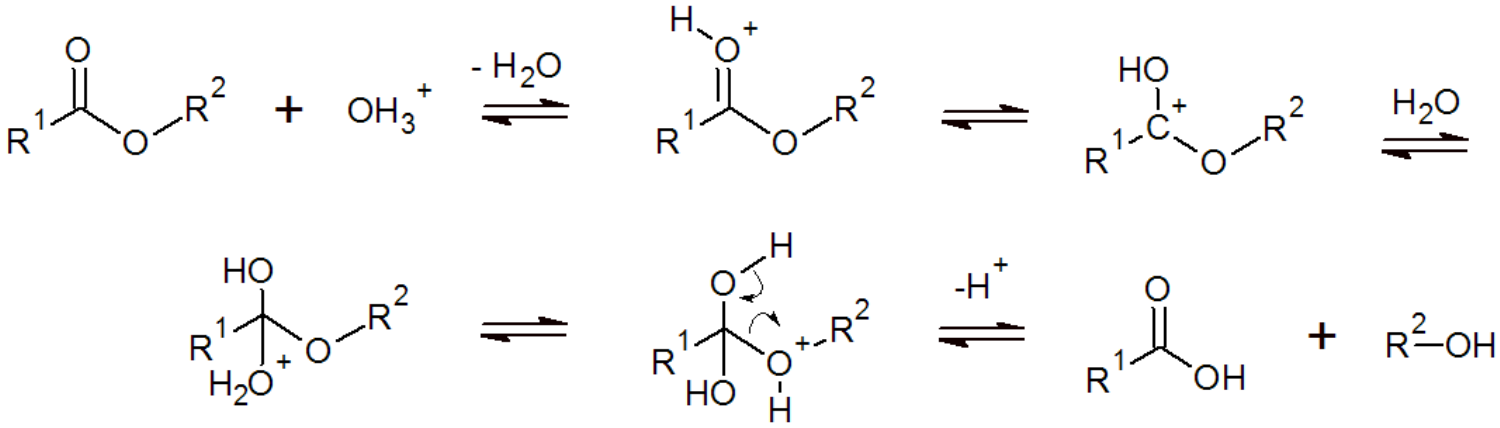
Bioresorbable Polymers

Esters based polymers:
Degradation is pH dependent
Degradation product occurs naturally in the body

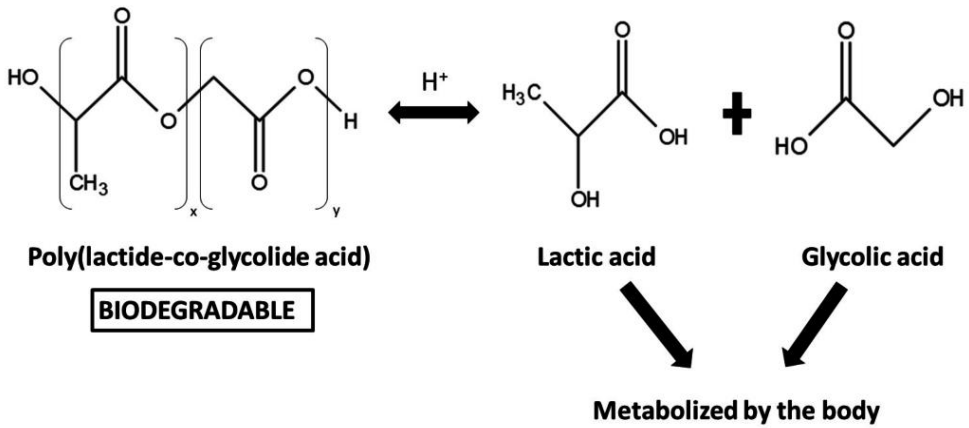
Base Catalyzed Ester Hydrolysis



Acid Catalyzed Ester Hydrolysis



PLGA

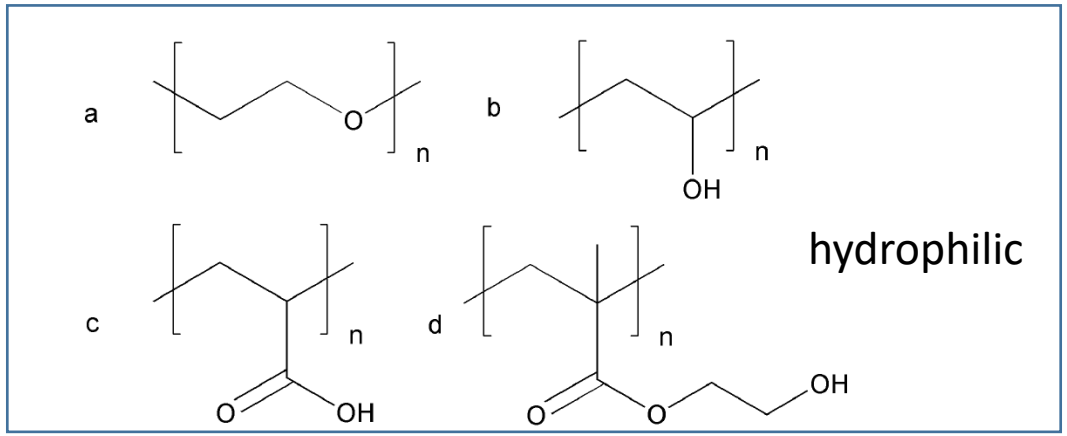


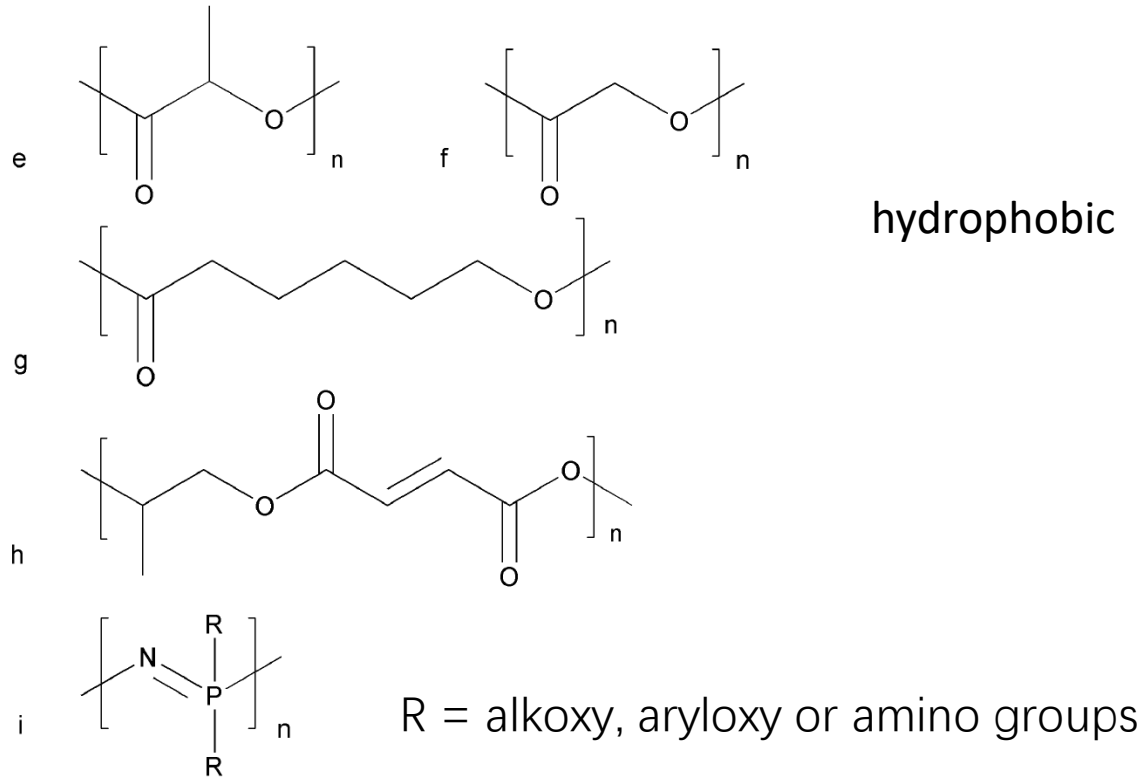
Synthetic Polymers

some polymers commonly used in tissue engineering:

a: poly(ethylene glycol) (PEG)
b: poly(vinylalcohol) (PVA)
c: poly(acrylic acid) (PAA)
d: poly(2-hydroxyethyl methacrylate) (PHEMA)

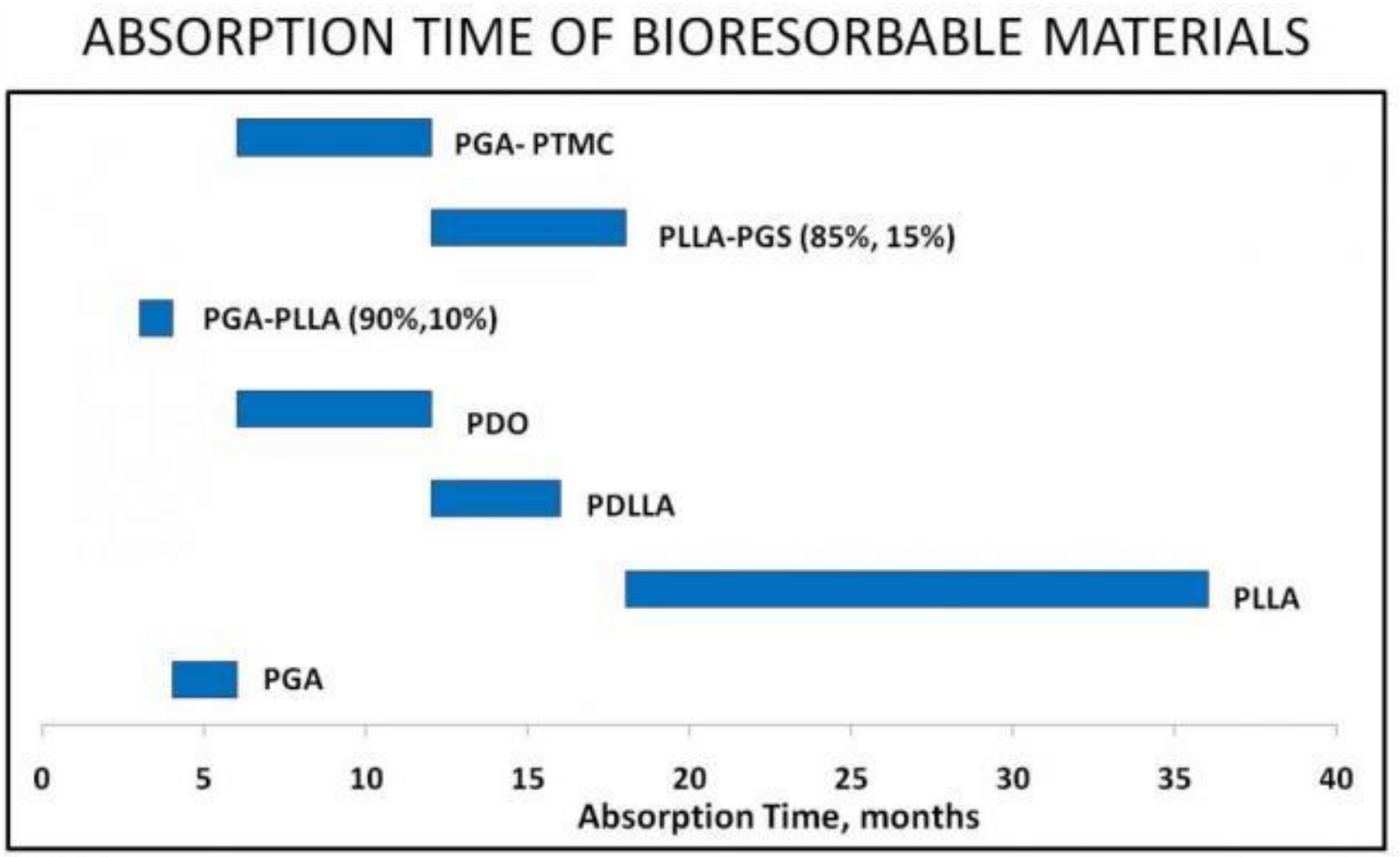
e: poly (lactic acid) (PLA)
f: poly(glycolic acid) (PGA),
g: poly(caprolactone) (PCL)
h: poly(propylene fumarate) (PPF),
i: poly(phosphazene)





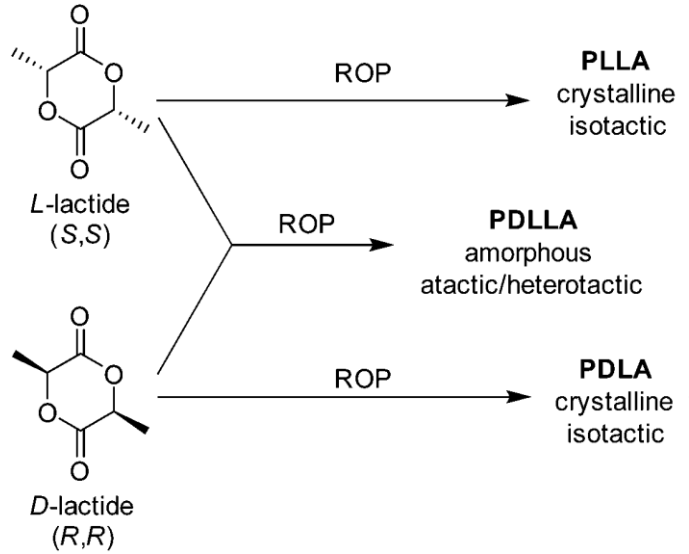
Chem. Soc. Rev., 2009, 38, 1139–1151

Bioresorbable Polymers



LEGEND

PGA-PTMC = Polyglycolic Acid – Poly-Tri-Methylene-Carbonate
PLLA-PGS = Poly L-Lactide Acid / Poly Glycerol Sebacate
PGA-PLLA = Poly Glycolic Acid / Poly L-Lactic Acid
PDO = Polydioxanone
PDLLA = Poly – DL-Lactic Acid
PLLA = Poly – L-Lactic Acid
PGA = Poly Glycolic Acid



https://www.fostercomp.com/information/technical-articles/essential-ingredients-for-orthopedic-implants-medical-design-technology/

Collagen

In the form of collagen sponge

Advantages

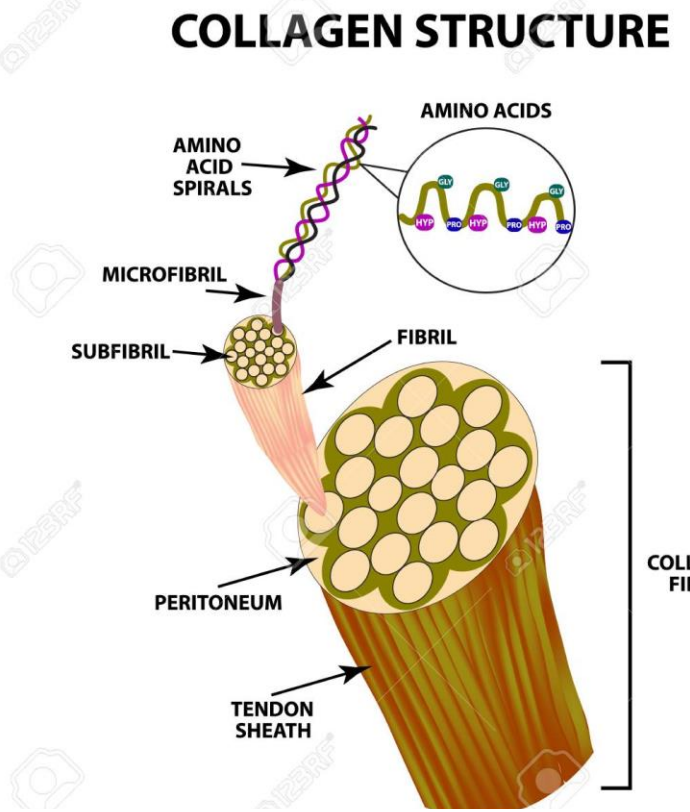
Porosity, biodegradability, and biocompatibility

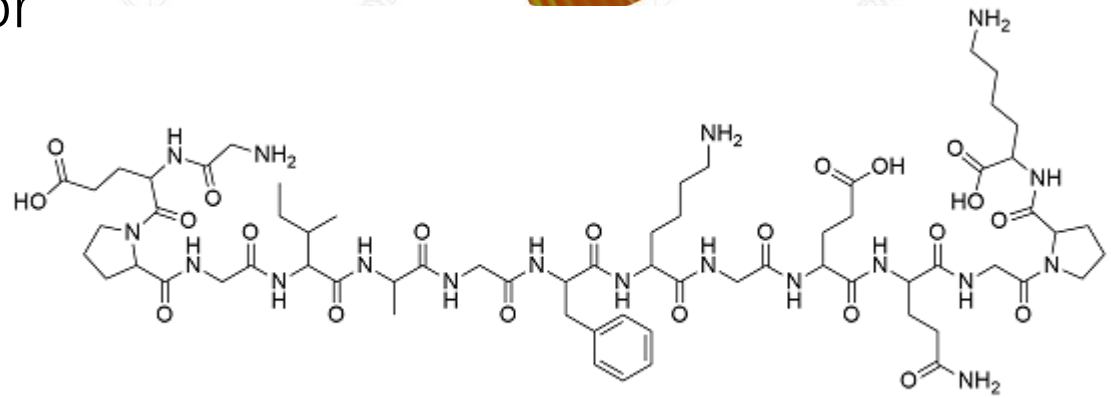
Can be modified using growth factors or other manipulations to promote chondrocyte growth and cartilage matrix formation

Scaffolds made from a single collagen type or composites of two or more types

Disadvantages

- Poor dimensional stability
- Poor mechanical strength
- Variability in drug release kinetics



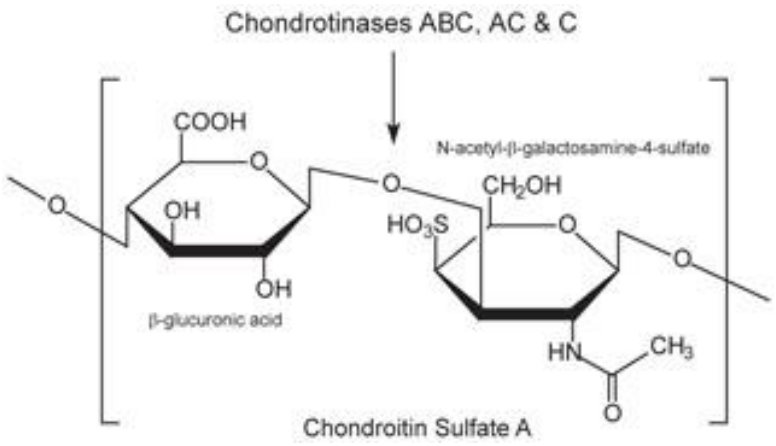


Type II-Collagen

http://www.softschools.com/formulas/chemistry/collagen_formula/482/

- Blends of collagen and **glycosaminoglycans (GAG)** have been utilized extensively for dermal regeneration.

- **Chondroitin sulfate** has been added to collagen type I for dermal regeneration templates and aggrecan (chondroitin sulfate/dermatan sulfate/keratin sulfate) to collagen type II for articular cartilage tissue engineering.



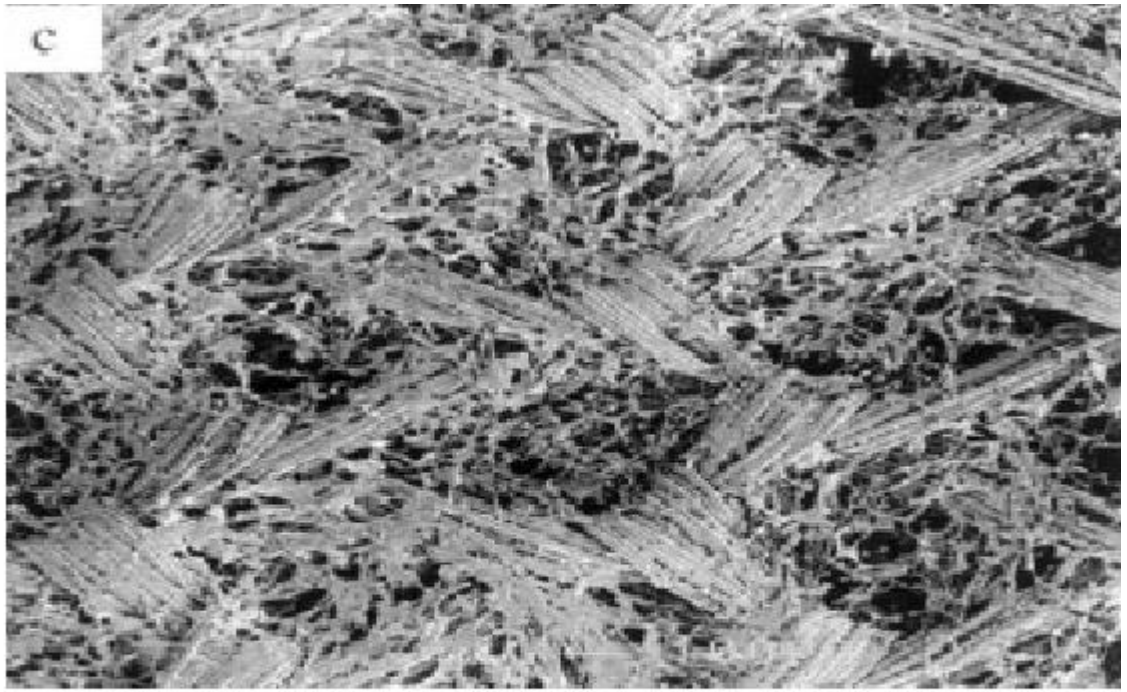


Figure 9: Tissue engineering with a collagen scaffold.

Polymers for Tissue artificial skin (Figure 9). As

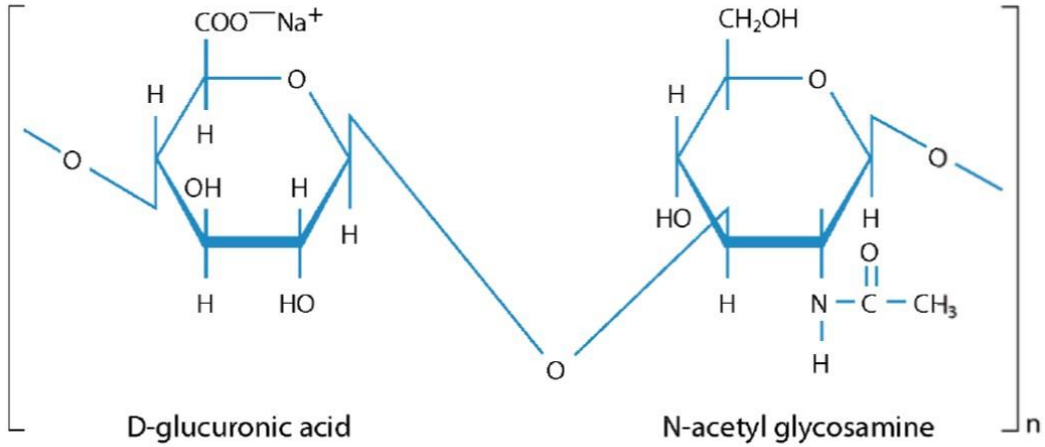
https://www.researchgate.net/figure/Tissue-engineering-with-a-collagen-scaffold_fig5_241719368

Hyaluronan (hyaluronic acid, HA)

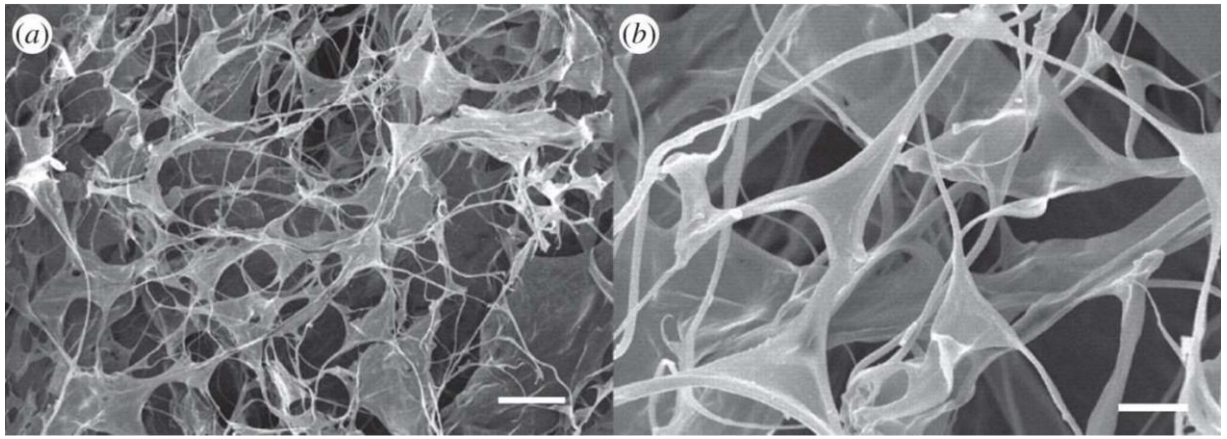
- Composed of repeated disaccharide units of D-glucuronic acid and N-acetyl glucosamine

- The unique properties of HA are manifested in its mechanical function in the synovial fluid, the vitreous humor of the eye, and the ability of connective tissue to resist compressive forces, as in articular cartilage.

- Plays a fundamental role during embryonic development and in wound healing

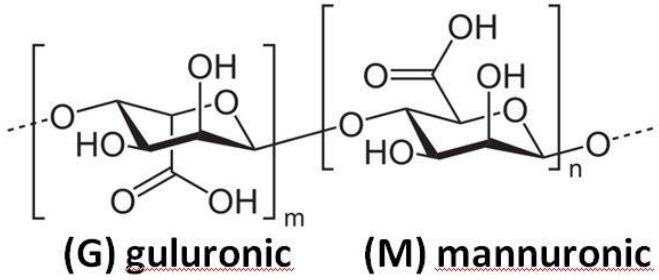


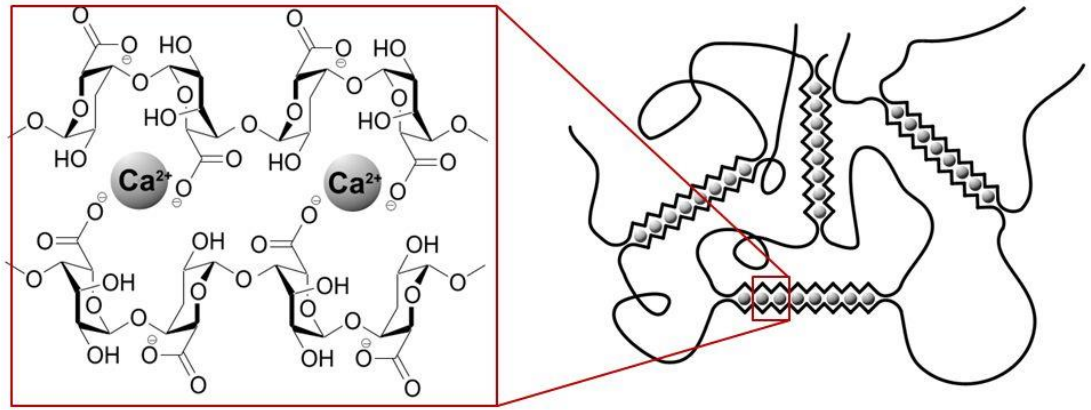
Hyaluronan scaffold for central neural tissue engineering



Alginate

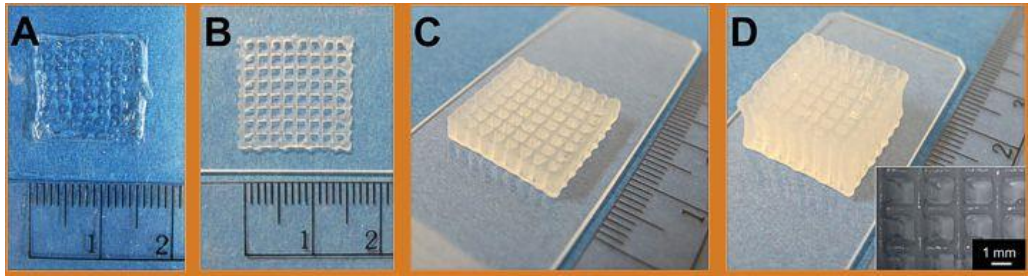
- Alginic acid, also called algin or alginate, is an **anionic polysaccharide** distributed widely in the cell walls of brown algae, including *Laminaria* and *Ascophyllum* species.
- It is formed by **linear block copolymerization** of d-mannuronic acid and l-guluronic acid.
- Alginates are linear unbranched polysaccharides which contain **different amounts** of (1→4′)-linked β-d-mannuronic acid and α-l-guluronic acid residues.
- Alginate is **biodegradable**, has controllable porosity, and may be linked to other biologically active molecules.
- Interestingly, encapsulation of certain cell types into alginate beads may actually **enhance cell survival and growth.**





https://people.clarkson.edu/~amelman/alginate_hydrogels.html

Pure Alginate as Scaffold

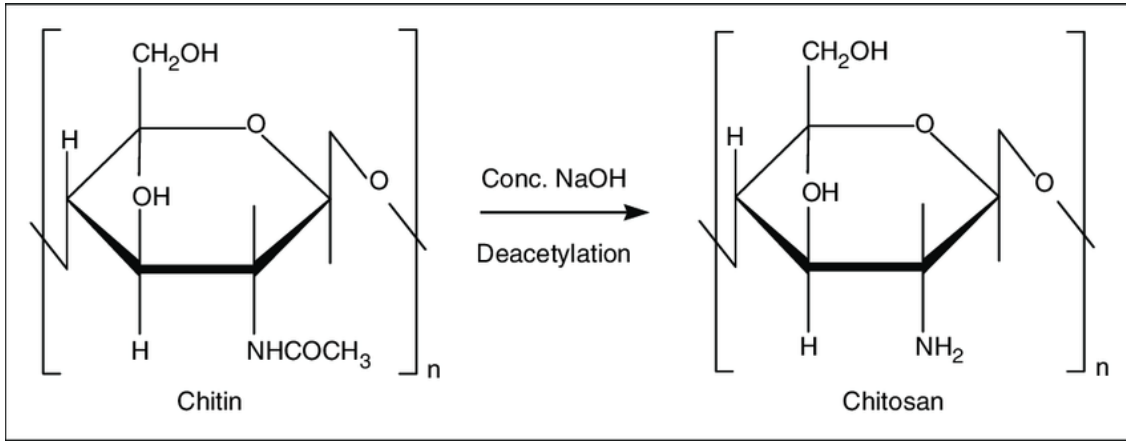


P. Aramwit, in Wound Healing Biomaterials, 2016

https://gesim-bioinstruments-microfluidics.com/alginatemethylcellulose-blends-for-3d-printing/

Chitosan

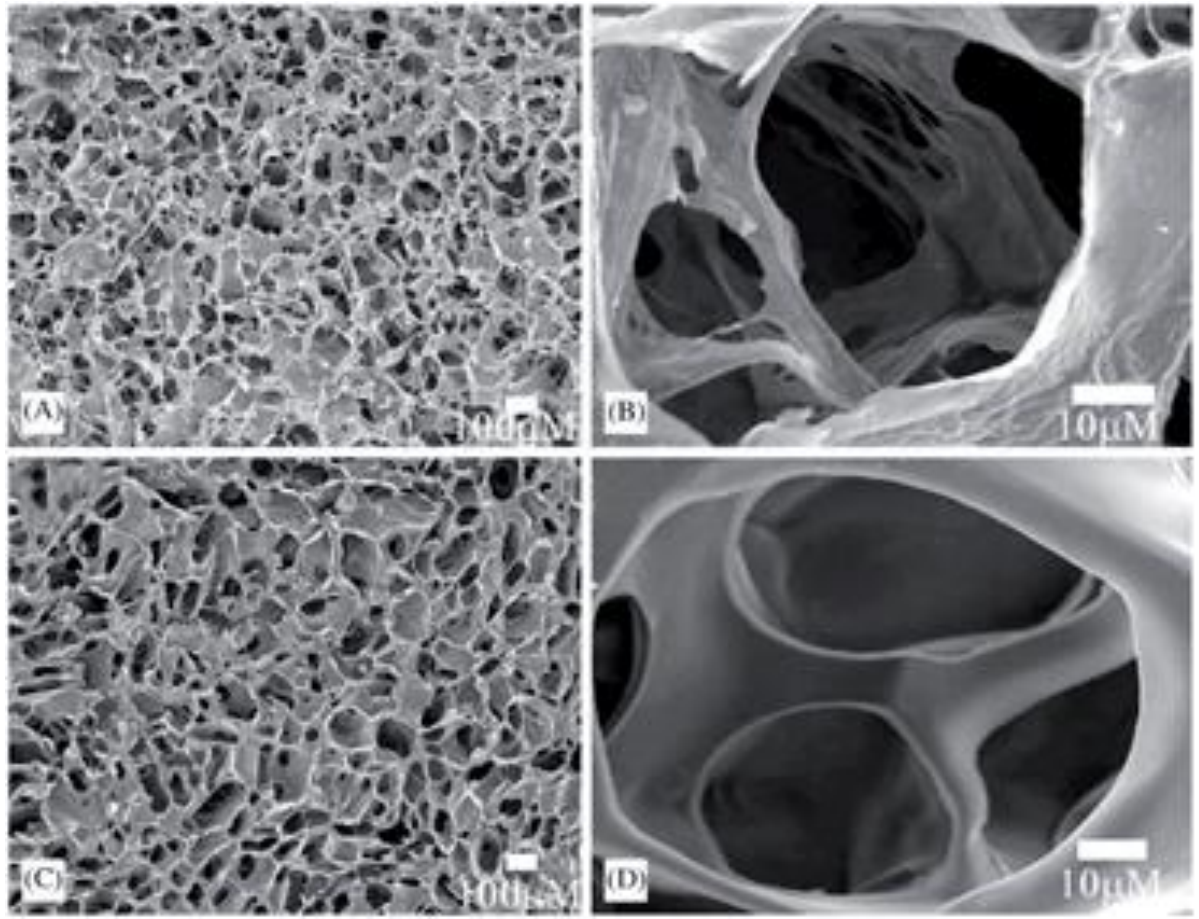
- It consists of β-1-4 linked 2 amino-2-deoxy Gluco-pyranose moieties.
- Commercially manufactured by N-deacetylation of Chitin which is obtained from Mollusc shells.
- **It is soluble only in acidic pH, i.e. when amino group is protonated.** Thereby it readily adheres to bio membranes.
- It is degraded mainly by Glycosidases & lysozymes.

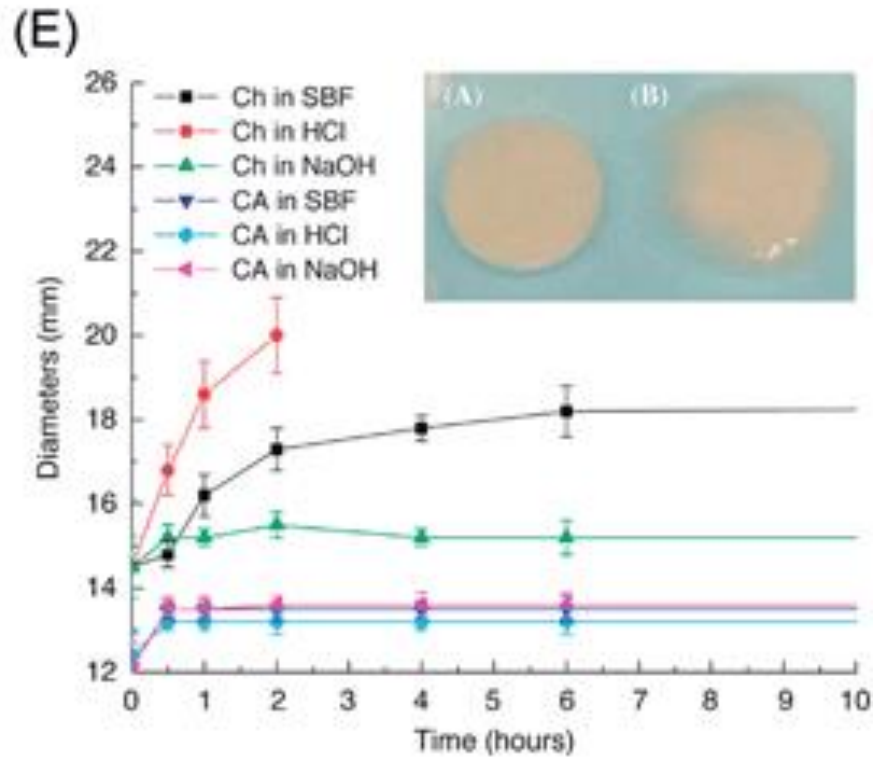


https://www.researchgate.net/figure/Structure-of-chitin-and-chitosan_fig1_51668840

Fabrication of bulk porous chitosan scaffolds:
Freezing of a chitosan-acetic acid solution
Subsequent lyophilization (freeze-dry)

Chitosan and chitosan–alginate scaffolds produced by phase separation where chitosan and alginate form a polyelectrolyte complex.

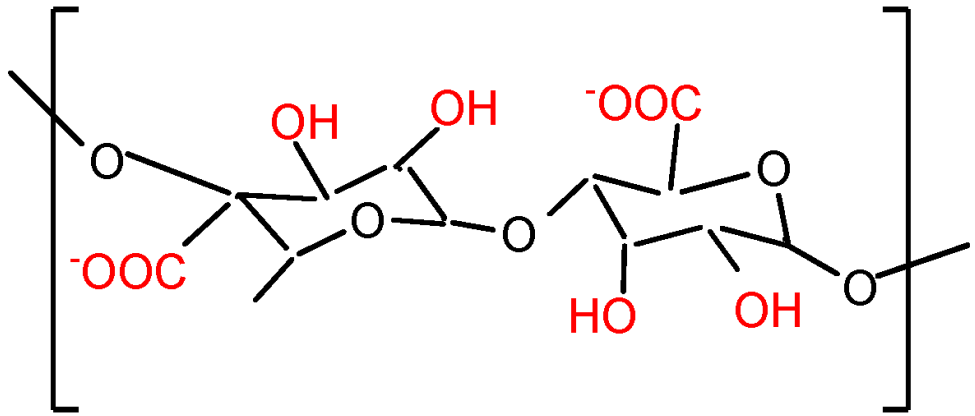




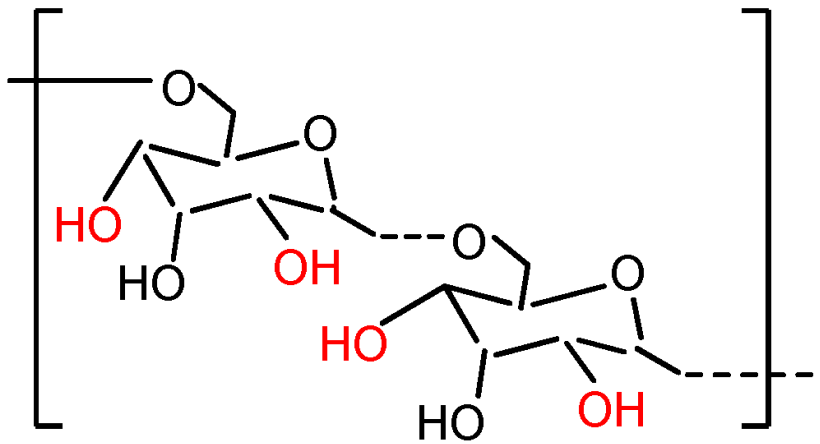
SEM micrographs of the **chitosan** scaffold pore structure at (a) low and (b) high magnification. SEM micrograph of the **chitosan–alginate** scaffold pore structure at (c) low and (d) high magnification. (e) Changes in scaffold diameter for chitosan–alginate (CA, inset left) and chitosan (Ch, inset right) upon hydration with 1 N HCl, 1 N NaOH and SBF solutions.

J. Mater. Chem. B, 2014,**2**, 3161-3184

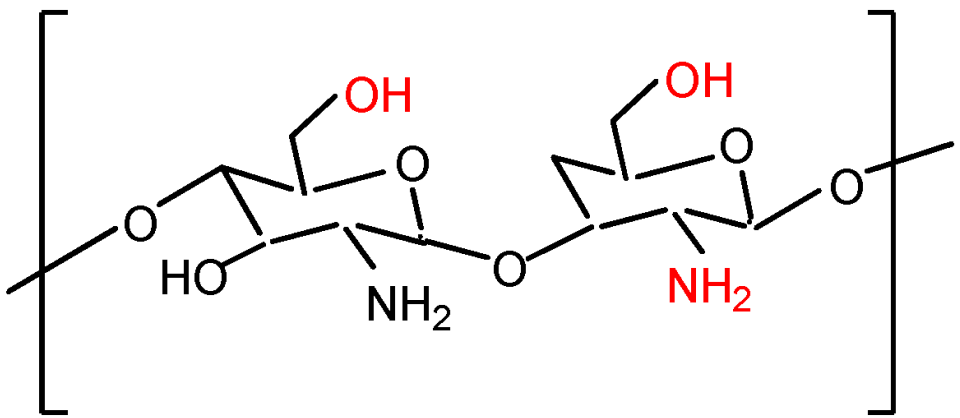
Natural Polymers



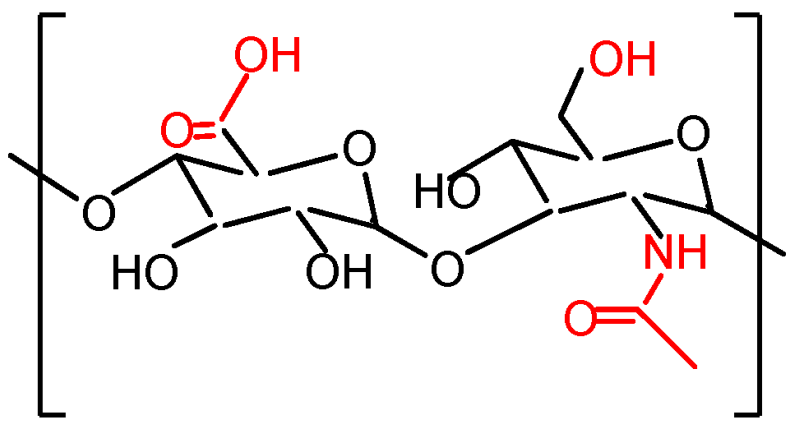
Alginate



Dextran



Chitosan



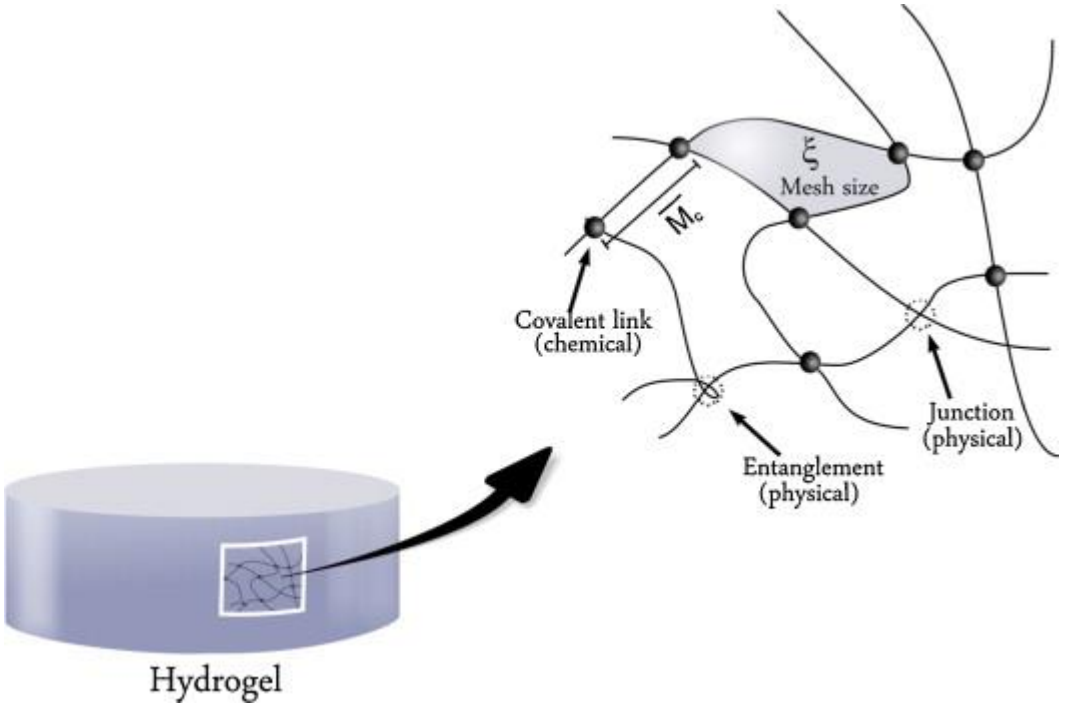
Hyaluronic acid

https://www.mdpi.com/2073-4360/11/1/1/htm

Hydrogels as scaffold

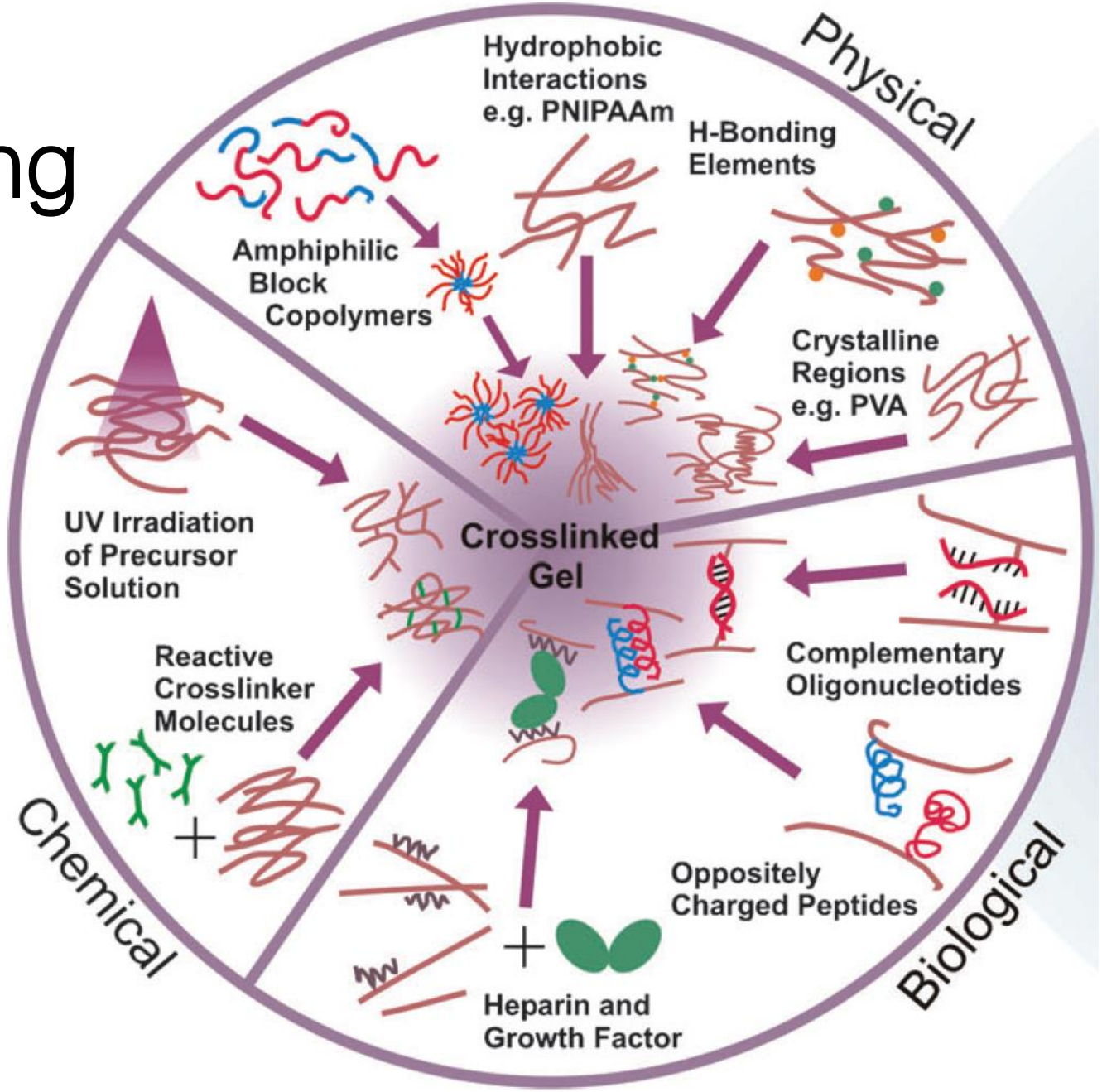
Hydrogel is a class of highly hydrated polymer materials (water content >30% by weight)

- Hydrogels are composed of hydrophilic polymer chains, which are either synthetic or natural in origin.
- The structural integrity of hydrogels depends on crosslinks formed between polymer chains via various chemical bonds and physical interactions.
- Hydrogels used in these applications are typically degradable, can be processed under relatively mild conditions, have mechanical and structural properties similar to many tissues and the ECM, and can be delivered in a minimally invasive manner.



https://www.sciencedirect.com/science/article/pii/S007967001200086X

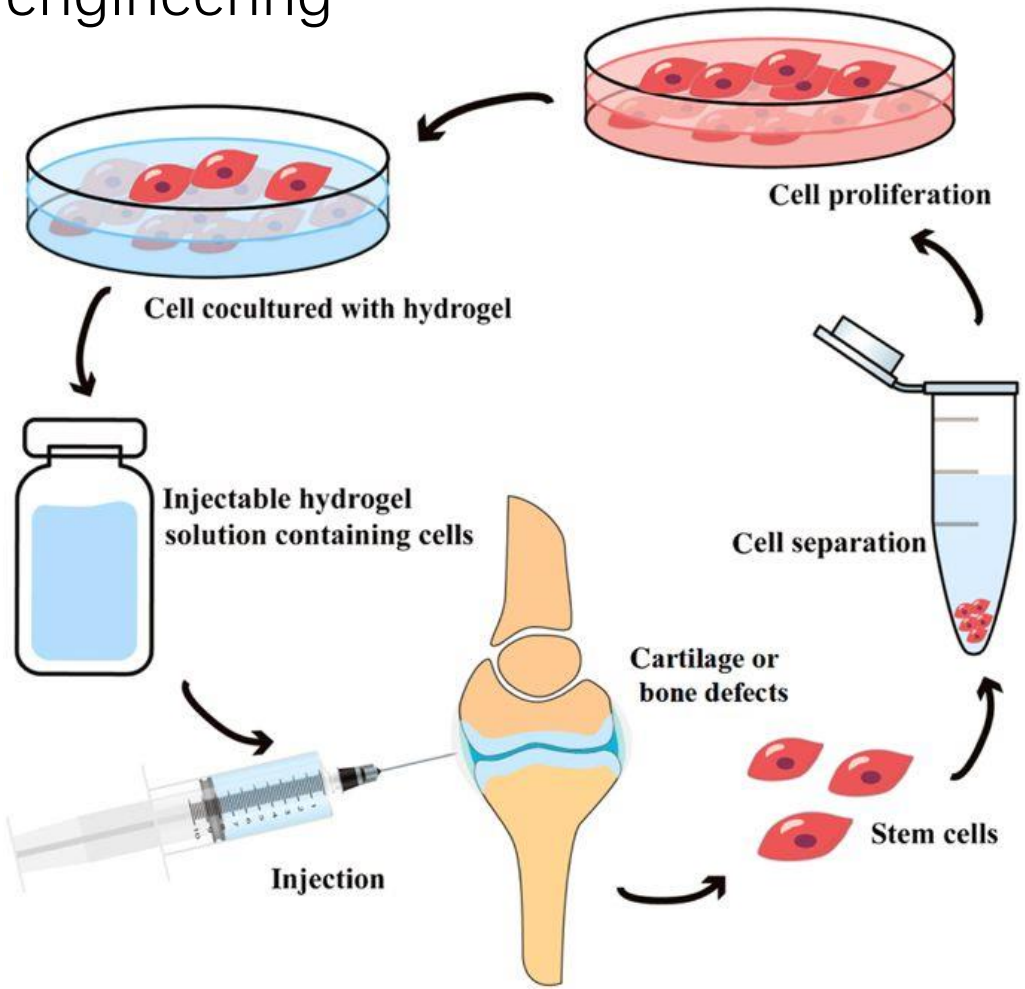
Hydrogels with various crosslinking mechanisms



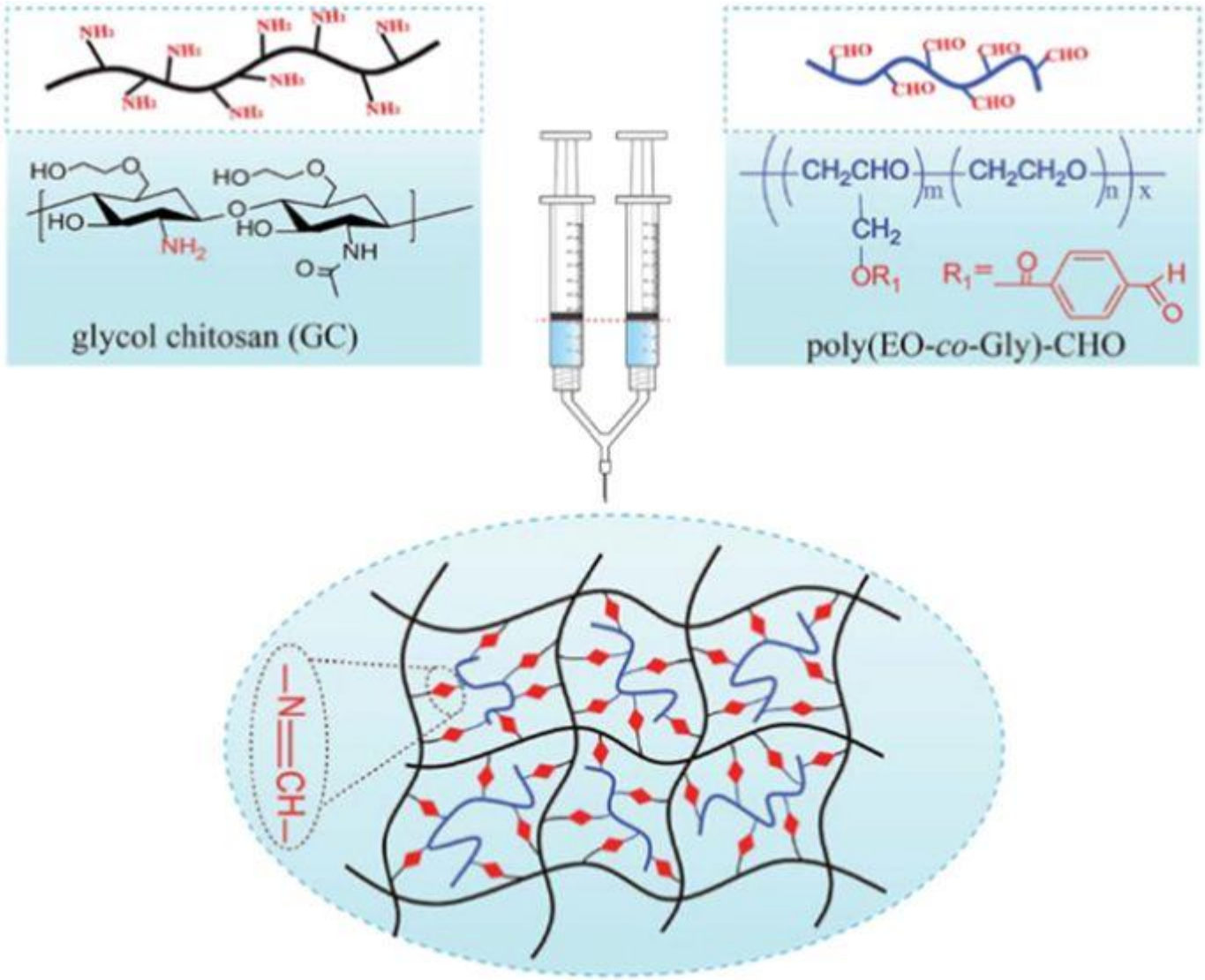
Chem. Soc. Rev., 2009, 38, 1139–1151

Injectable hydrogels

Typically for cartilage and bone tissue engineering



Bone Research **volume5**, Article number: 17014 (2017)



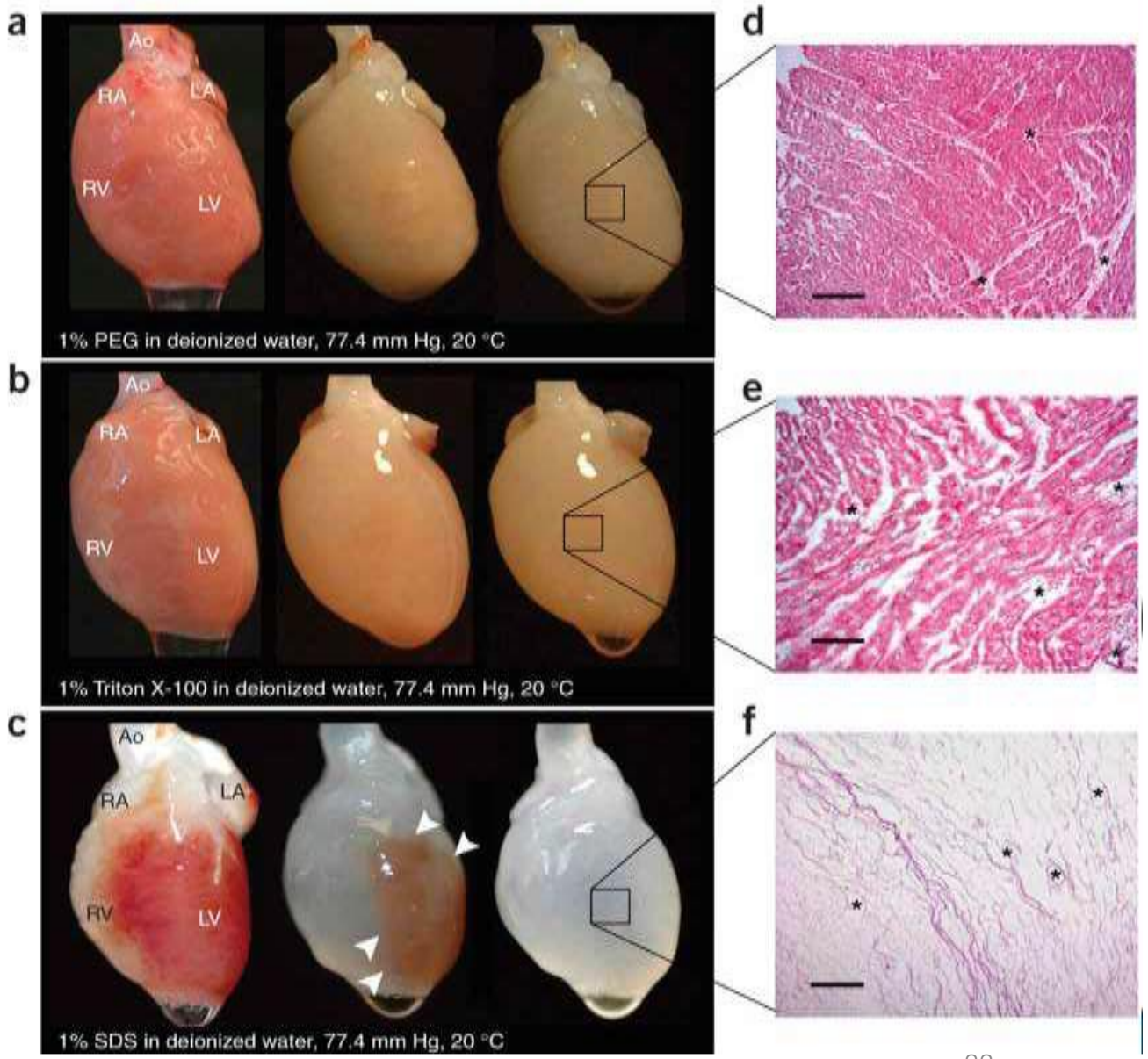
Schematic illustration of injectable hydrogels prepared by Schiff base cross-linking between aqueous solutions of GC and poly(EO-co-Gly)-CHO.

Decellularized Scaffolds

Perfusion decellularization of whole rat hearts.

(a–c) Photographs of **cadaveric rat hearts** mounted on a Langendorff apparatus. Ao, aorta; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. Retrograde perfusion of cadaveric rat heart using PEG (a), Triton-X-100 (b) or SDS (c) over 12 h.
The heart becomes more translucent as cellular material is washed out from the right ventricle, then the atria and finally the left ventricle.

(d,e) Corresponding H&E staining of thin sections from LV of rat hearts perfused with PEG (d) or Triton-X-100 (e), showing incomplete decellularization. Hearts treated with PEG or Triton-X-100 retained nuclei and myofibers. Scale bars, 200 μm.
(f) H&E staining of thin section of SDS-treated heart showing no intact cells or nuclei. Scale bar, 200 μm. All three protocols maintain large vasculature conduits (black asterisks).

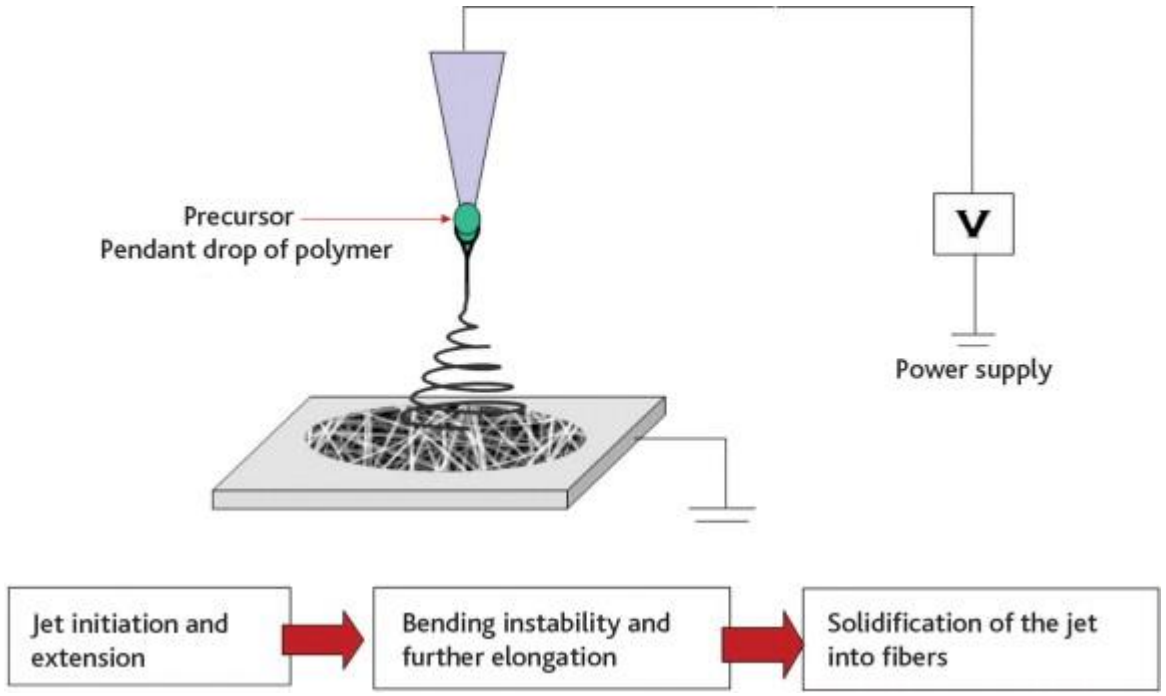


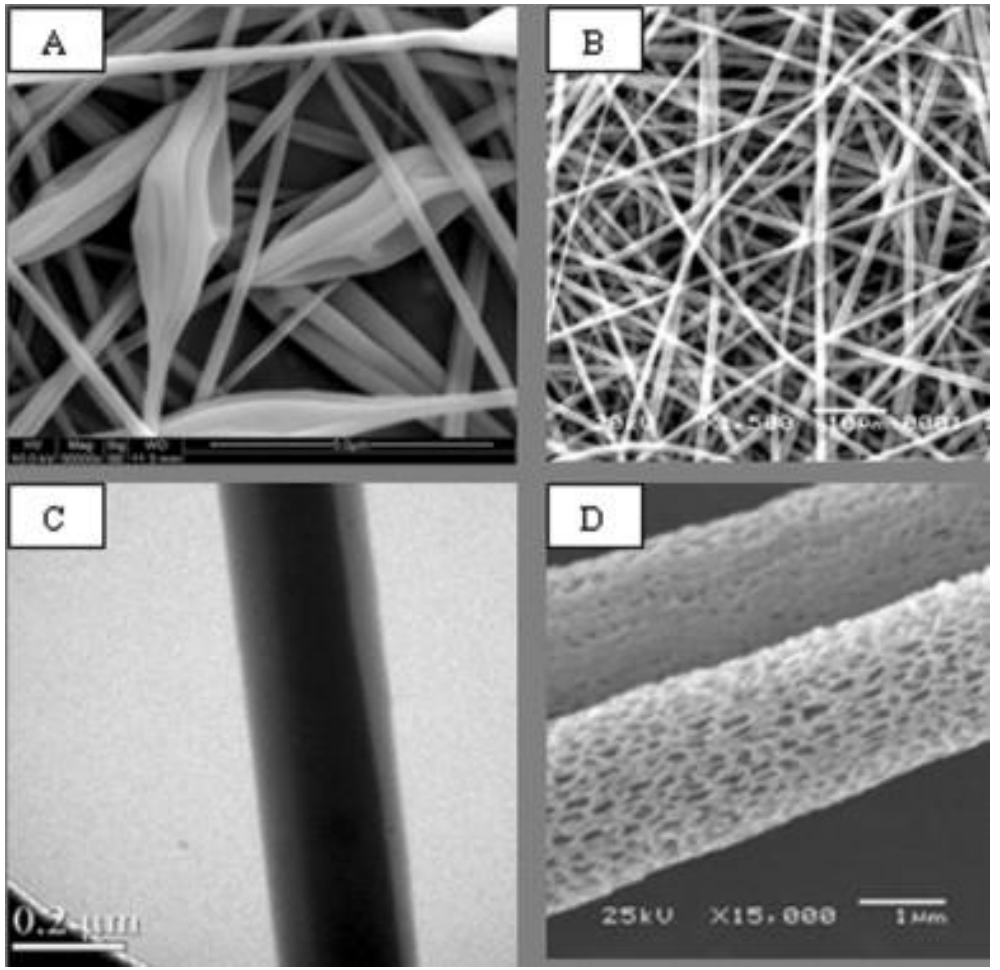
Ott HC et al., Nature Medicine, 2008

Nanofibre Scaffolds

- Production of fibre diameters down to 50nm
- Different polymers, proteins (collagen, elastin), hollow fibres

Nanofibre production through electrospinning





Materials Today, Volume 9, Issue 3, 2006, 40-50

Choosing Scaffold Biomaterials

Mechanics:
do the mechanical properties suit the tissue?
hard for bone, elastic for arteries

Biomimetic Architecture:
does the architecture mimic the biology?

Incorporation of biological signals
does the scaffold material provide cells with appropriate factors and cytokines throughout the healing process?

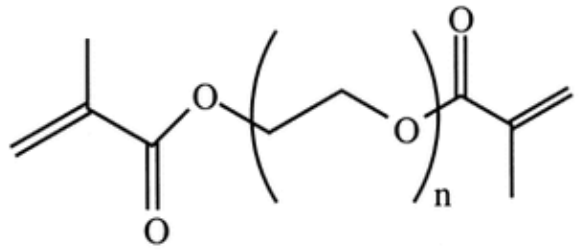
Convenience and availability
are the materials biologically suitable, available and easily processed?

Scaffold Footprint
is the scaffold totally absorbed during the healing process?
does it heal the tissue appropriately? Does it leave scar tissue?

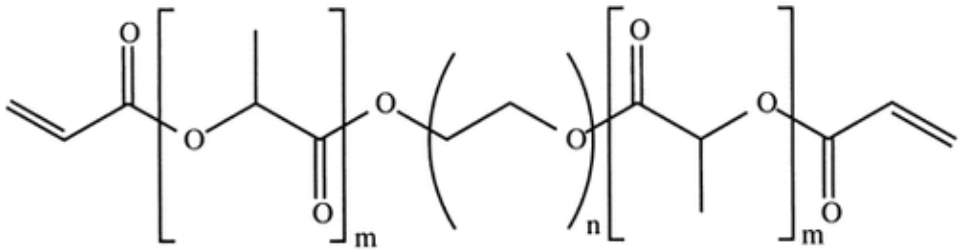
(Modified from slides by Molly Stevens, Mr. Julian George)

How to control the mechanical properties of hydrogel?

- intrinsic properties of the main chain polymer
- crosslinking characteristics (i.e. amount, type, and size of crosslinking molecules)
- environmental conditions.



PEGDM (n=77)



PEG-LA-DA (m=5,n=105)

poly(ethylene glycol) (PEG)

TABLE I
Properties of Nondegradable Hydrogels[a]

% PEGDM[b]	q[c]	Compressive Modulus (kPa)	Mesh Size (Å)	q (w/cells)[c]	Compressive Modulus (kPa) (w/cells)
10	9.3 ± 1.0	34 ± 3	140	12.6 ± 0.2	30 ± 1
20	5.2 ± 0.1	360 ± 14	60	6.4 ± 0.05	260 ± 30
30	4.5 ± 0.1	940 ± 60	50	5.2 ± 0.2	400 ± 100
40	4.2 ± 0.1	1370 ± 20	40	—	—

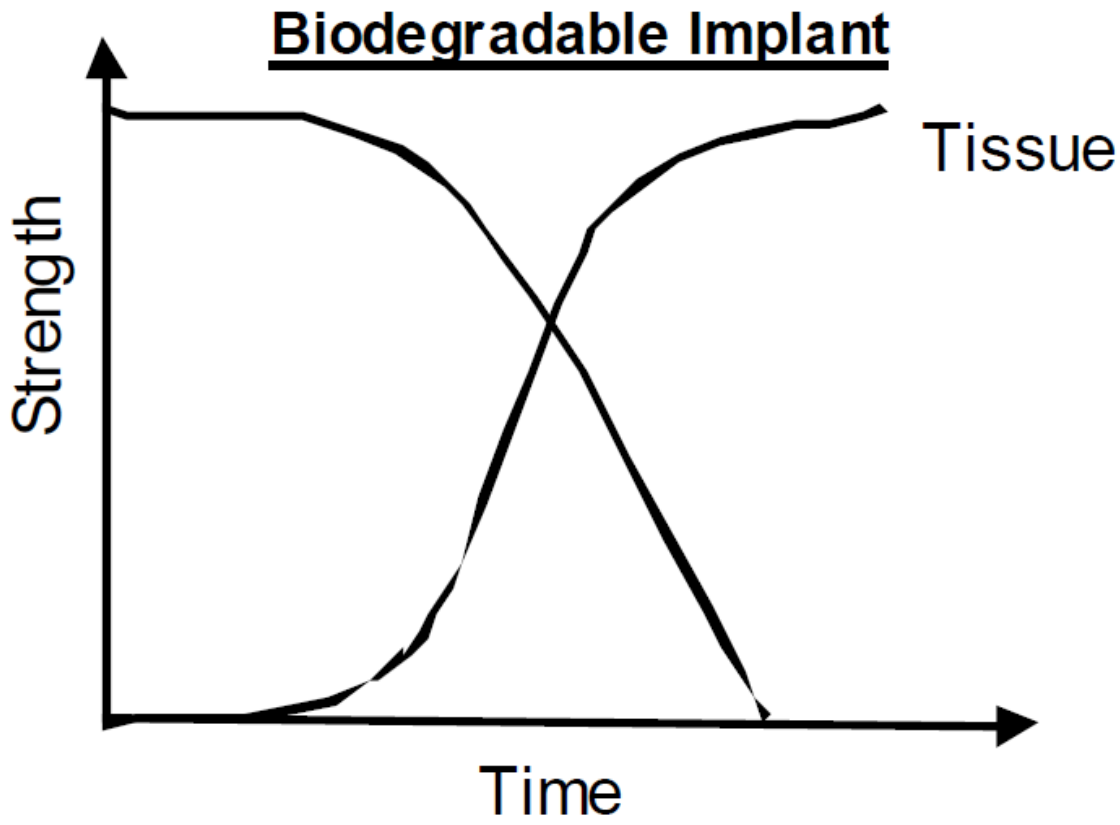
[a]Hydrogels do not degrade on the time scale and conditions of the experiment.
[b]Weight percent macromer before polymerization.
[c]Mass swelling ratio (equilibrium swollen mass/dry polymer mass).
[d]—, not measured.

J Biomed Mater Res 2002;59:63–72.

Biodegradation Curve

Polymer biodegradability and mechanical properties depend in part on crystalline structure which can be tailored through co-polymer mixing

Overall strength throughout healing must meet the needs of the tissue



Yang S, Leong KF, Du Z, Chua CK. The design of scaffolds for use in tissue engineering. Part I. Traditional factors.Tissue Eng. 2001 Dec;7(6):679-89

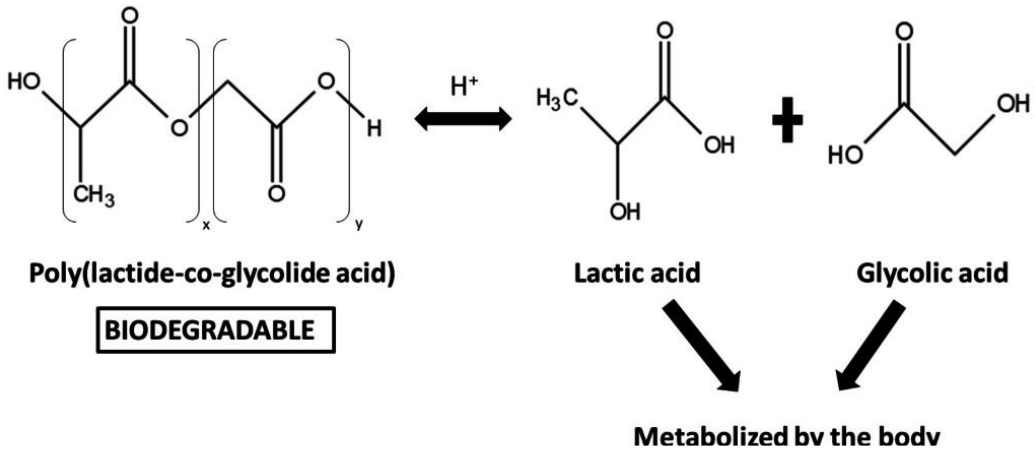
How to control biodegradation?

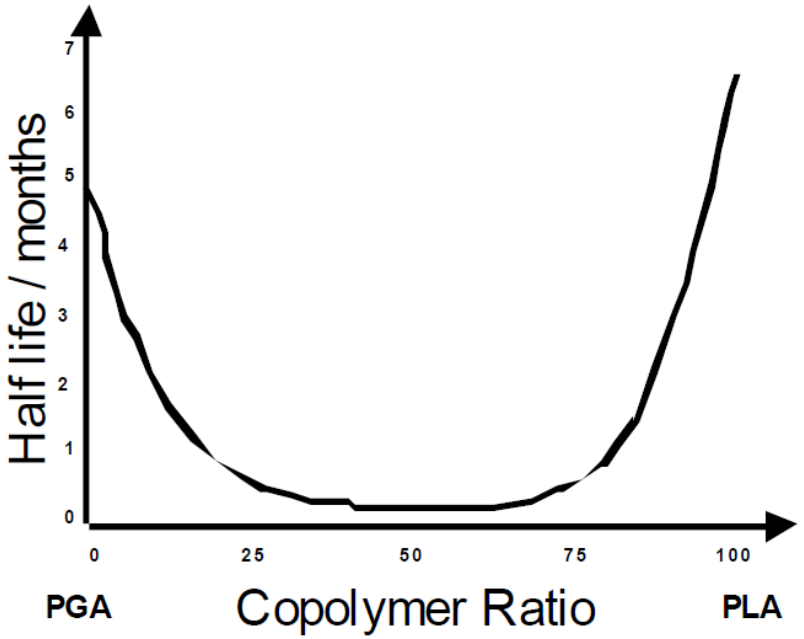
Control compositions

- Extensive research has been performed in developing a full range of PLGA polymers.
- Both L- and DL-lactides have been used for co-polymerization.
- The ratio of glycolide to lactide at different compositions allows control of the degree of crystallinity of the polymers.

When the crystalline PGA is co-polymerized with PLA, the degree of crystallinity is reduced and as a result this leads to increases in rates of hydration and hydrolysis.

In general, the higher the content of glycolide, the quicker the rate of degradation. **However, an exception to this rule is the 50:50 ratio of PGA: PLA, which exhibits the fastest degradation.**





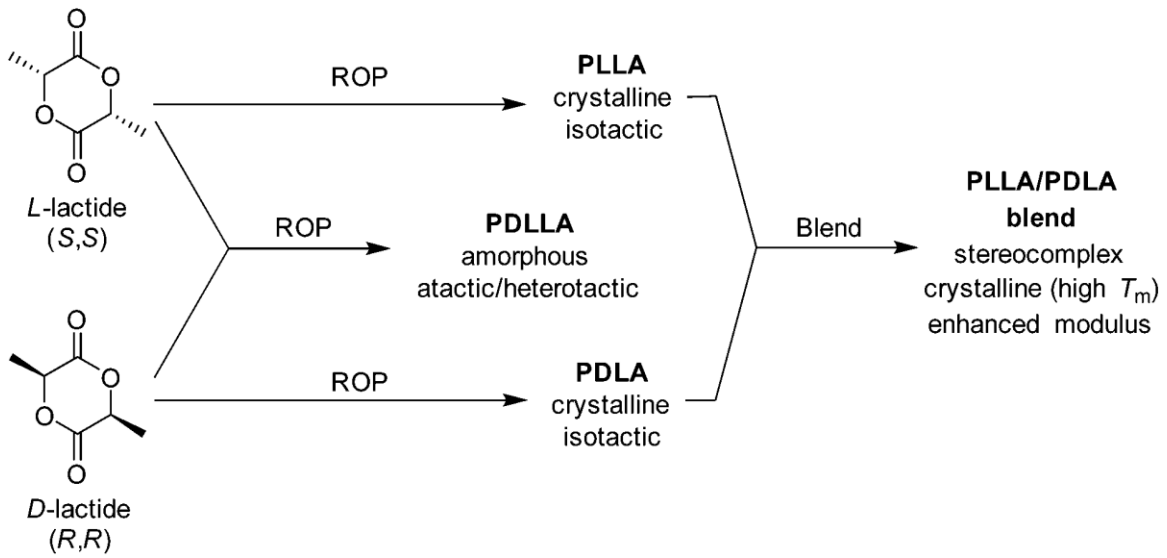
Controlling degradation

This slide is not required.

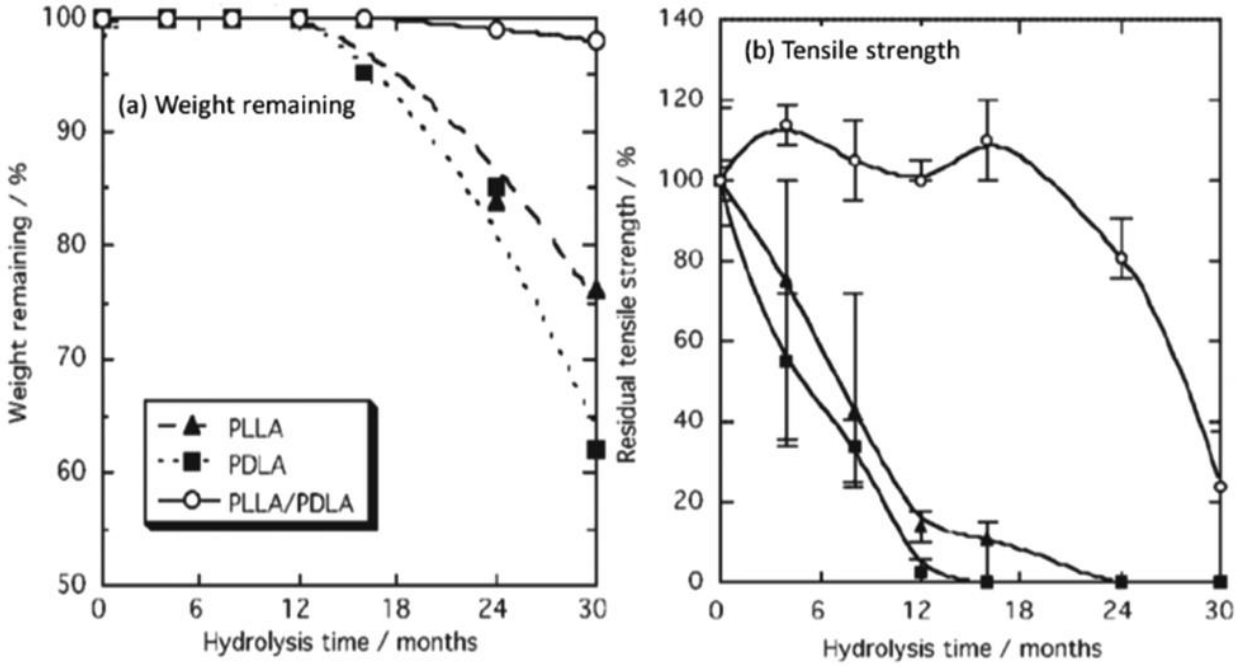
- In general, actions which increase the penetration of water accelerate the rate of hydrolysis
- Two important considerations are the polymer's glass transition temperature (Tg) and crystallinity

A high degree of crystallinity limits hydration through the tight, ordered packing of polymer chains:

- inclusion of short side chains
- random copolymerization
- heavily influenced by polymer **stereochemistry**



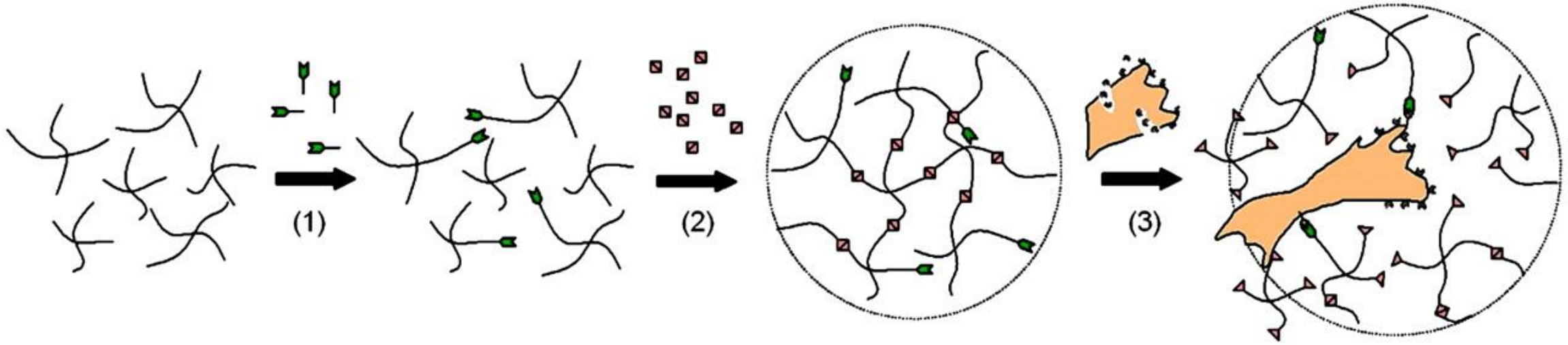
D. Ishii, W.-K. Lee, K.-I. Kasuya and T. Iwata, J. Biotechnol., 2007, 132, 318–324.



Biomater. Sci., 2017, 5, 9-21

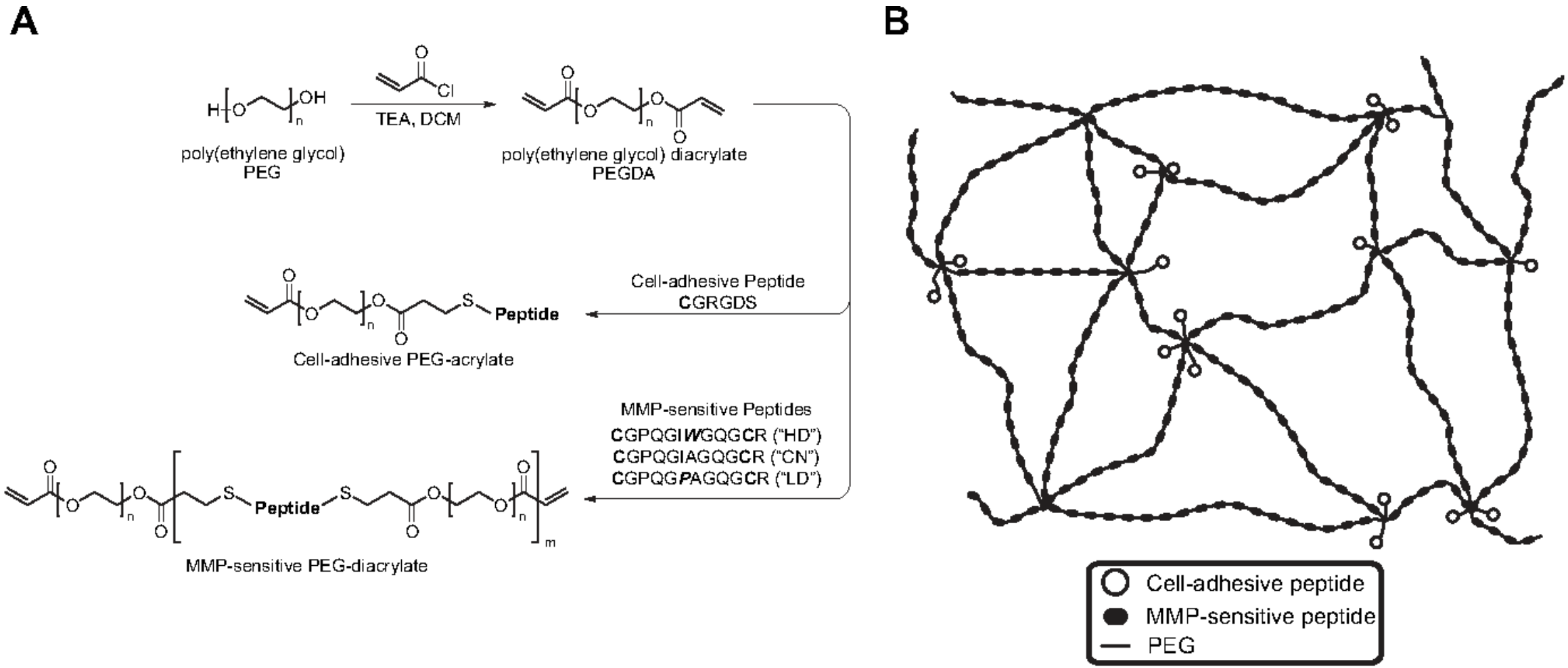
Enzyme-degradable hydrogel as scaffold

Natural ECM is degraded by proteases such as matrix metalloproteases (MMPs) and plasmin.



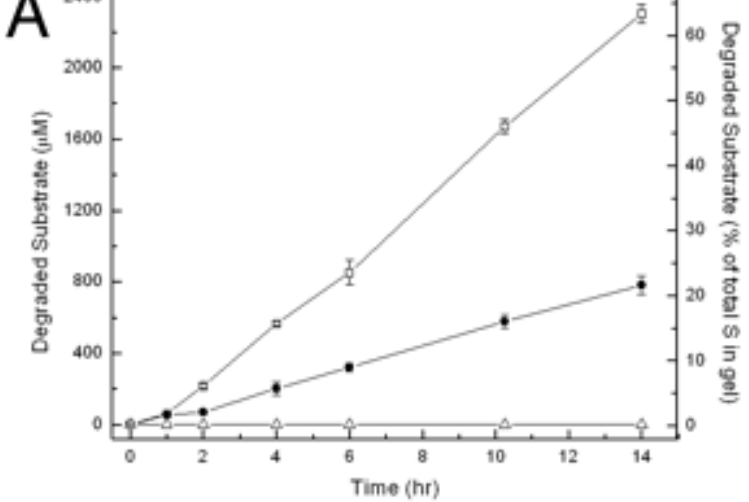
A Michael-type addition reaction between vinyl sulfone-functionalized multiarm PEGs and mono-cysteine adhesion peptides (step 1, in high stoichiometric deficit) or bis-cysteine MMP substrate peptides (step 2, to come up to stoichiometric equivalence) was used to form gels from aqueous solutions in the presence of cells. These elastic networks were designed to locally respond to local protease activity at the cell surface (step 3).

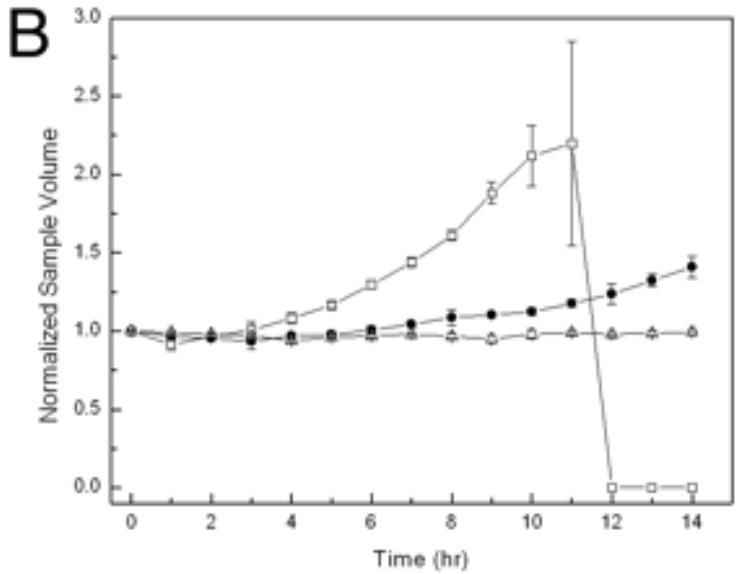
PNAS April 29, 2003 100 (9) 5413-5418

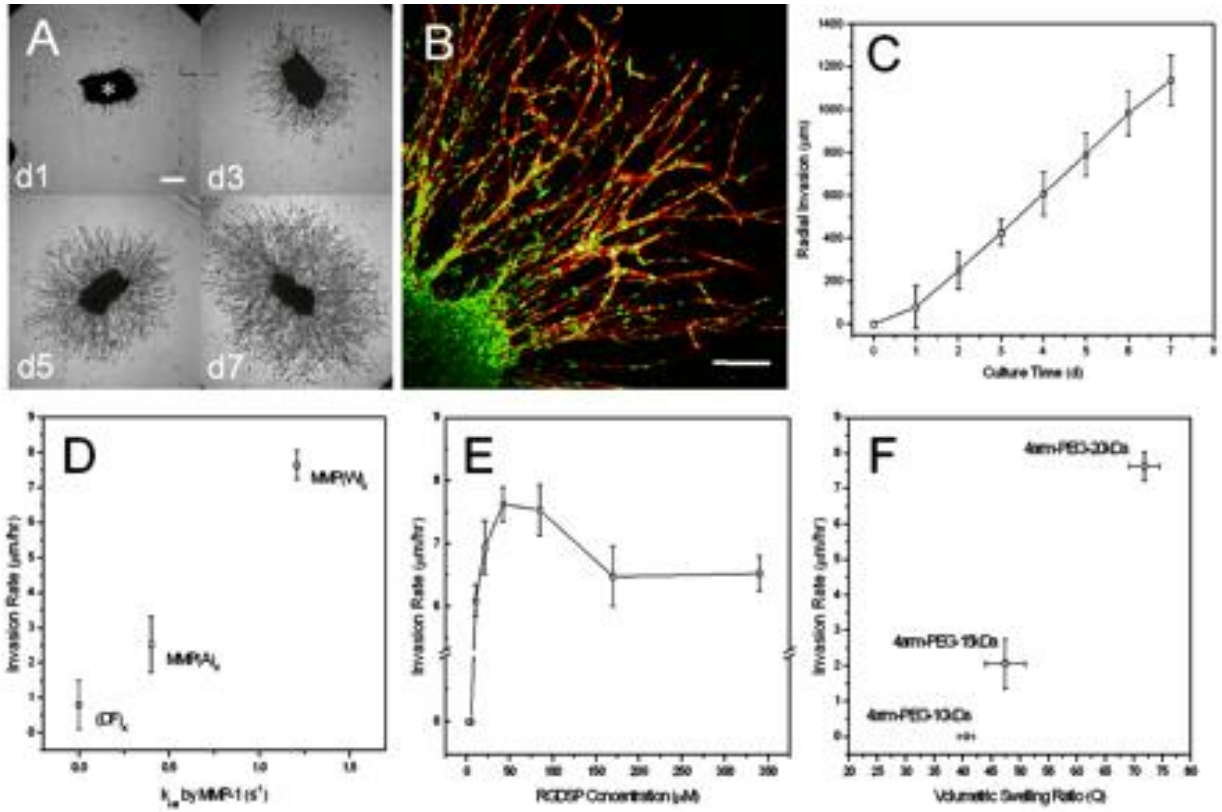


Biomaterials, Volume 31, Issue 13, May 2010, Pages 3736-3743

□, MMP(W)X;
●, MMP(A)X;
▵, (DF)X.







(A) **Fibroblasts radially invaded the adhesive and MMP-sensitive synthetic hydrogel matrix** (bar = 250 μm). (B) Migration of spindle-like-shaped fibroblasts occurred in a cohort manner (bar = 150 μm). (C) Cell invasion distances increased approximately linear with culture time. (**D) Cell invasion rate depended on the proteolytic activity of the incorporated peptide substrates.** (E) Migration rate depended on adhesion ligand density, i.e., the concentration of RGD-containing peptide sites fixed throughout the three-dimensional material, in a biphasic manner. (F) Crosslink density of hydrogels influenced cell invasion dramatically.

- a highly MMP-sensitive sequence [e.g., Ac-GCRD-GPQG↓IWGQ-DRCG; herein referred to as MMP(W)]$_X$, the X indicating participation in a crosslinked network)
- a moderately MMP-sensitive sequence [e.g., Ac-GCRD-GPQG↓IAGQ-DRCG; MMP(A)$_X$]
- an MMP-insensitive sequence [Ac-GCRD-GDQGIAGF-DRCG; (DF)$_X$]

This slide is not required.

PNAS April 29, 2003 100 (9) 5413-5418

Fabrication of Porosity in scaffold biomaterials

Scaffolds must be highly porous (⩾90%)

- phase separation
  - Low pore diameter, difficult to control pore size
- fibre bonding
  - Lack of mechanical strength of bonds
- porogen leaching/salt leaching
  - Closed pores
- freeze drying
- high-pressure CO2
- rapid prototyping/ solid freeform fabrication

Mikos AG, Temenoff SJ. Formation of highly porous biodegradable scaffolds for tissue engineering. Electronic Journal of Biotechnology 2000 Aug 15;3(2)

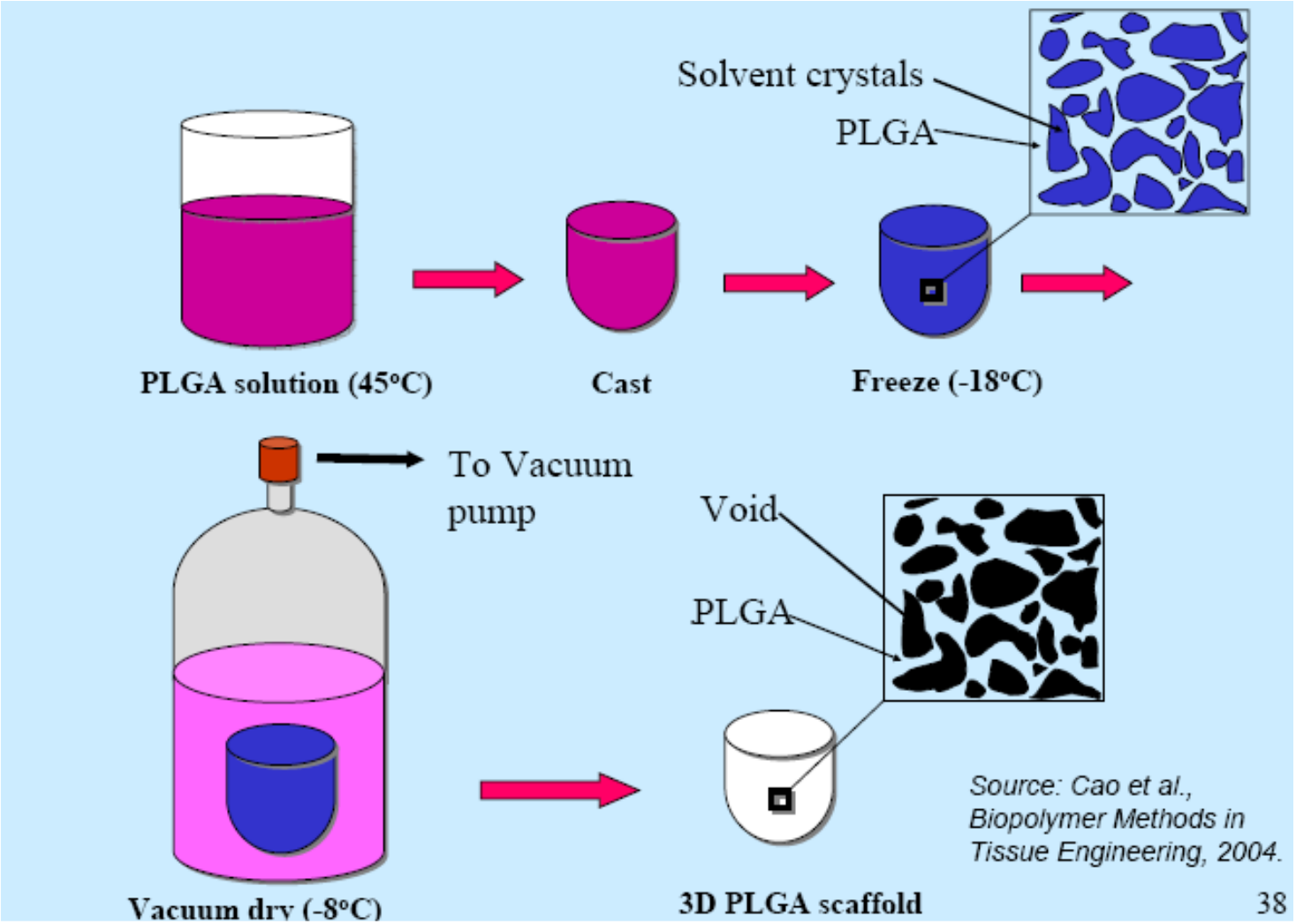
Optimal Pore Sizes for Cell Proliferation & Tissue Growth

Cell or tissue	Optimal pore size, μm	References
Fibroblast	5-15	58
Skin	10-100 20-125	59 60
Bone	100-350	58
Osteoid	40-100	58
Hepatocyte	82	18
Adipocyte	100	19,54
Macrophage	60-100	57
Neovascularisation	5	17
Fibrovascular tissue	>500	55
Capillary	200-300	61

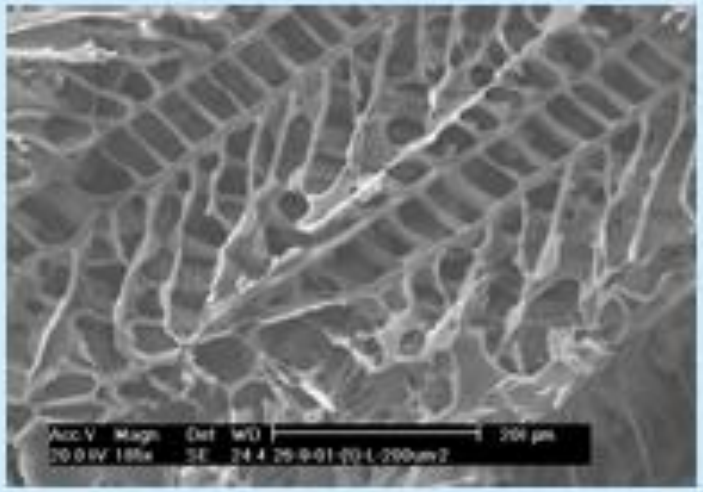
Cao, 2005

Thermally Induced Phase Separation (TIPS)

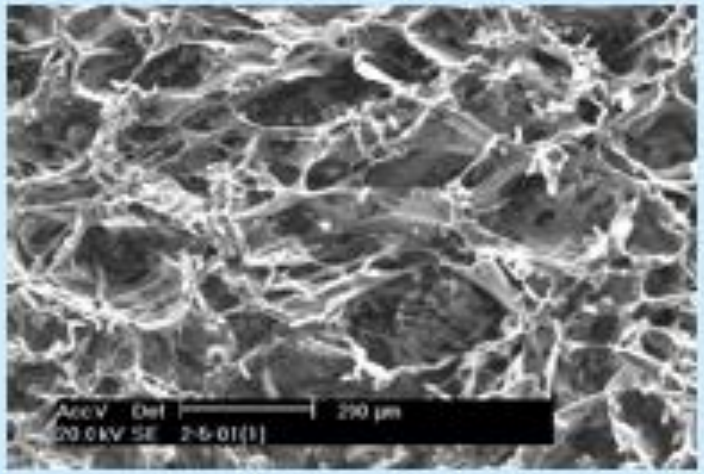
- Developed 1970s-1980s
- Used for production of microporous membranes
- Solid-liquid separation of polymer solution induced by cooling:
  - Solvent crystallisation
  - Polymer precipitation



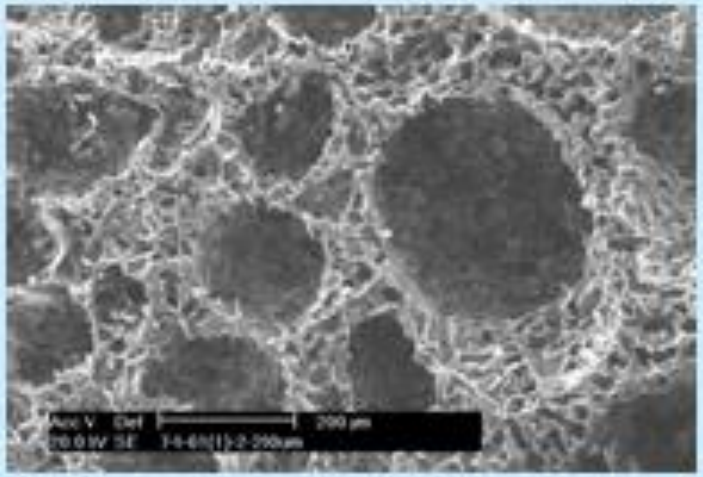
TIPS Scaffold Morphologies



5%(w/v) PLGA made by TIPS using 1,4-dioxane as solvent



10%(w/v) PLGA made by TIPS using 1,4-dioxane as solvent

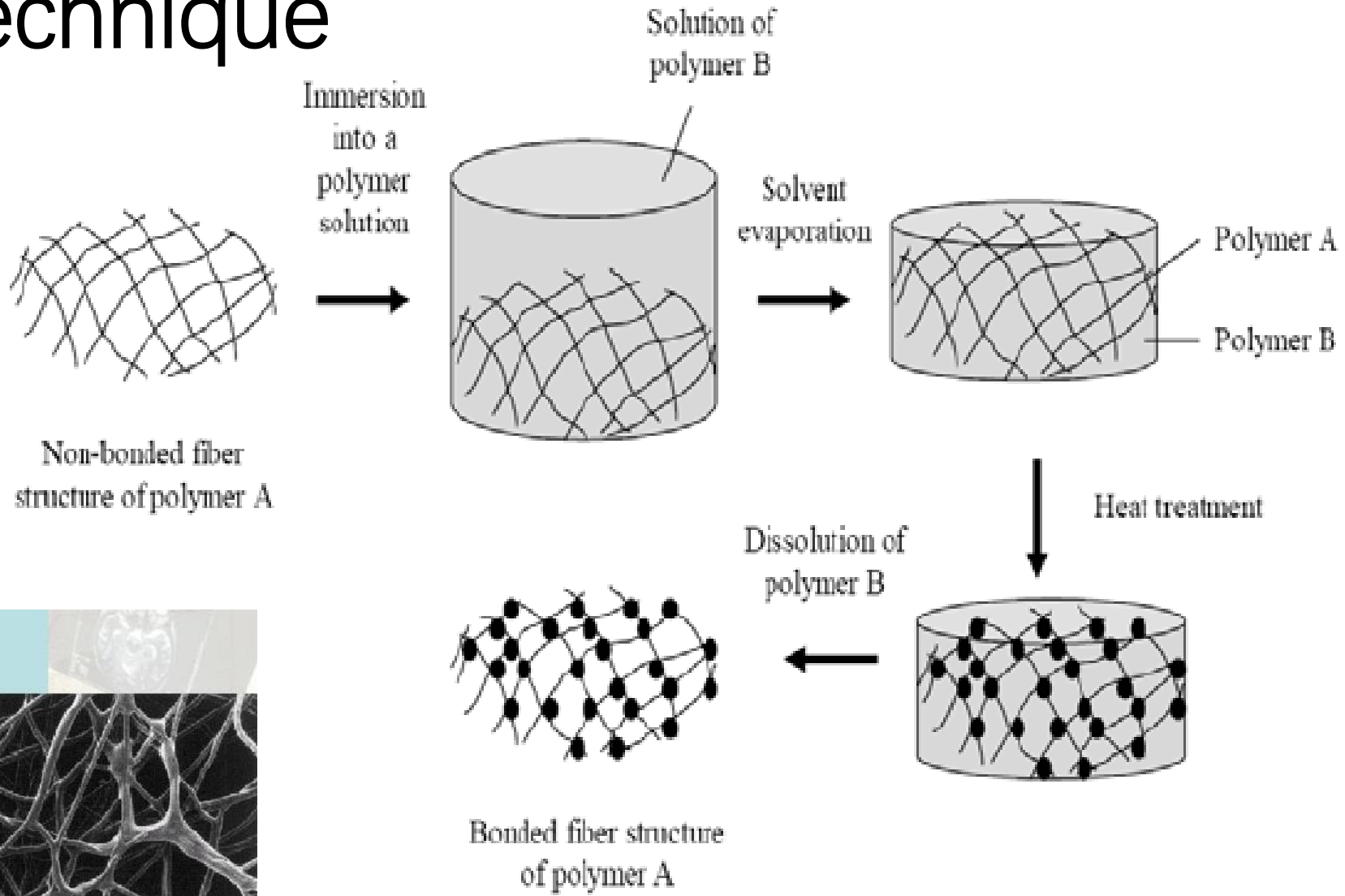


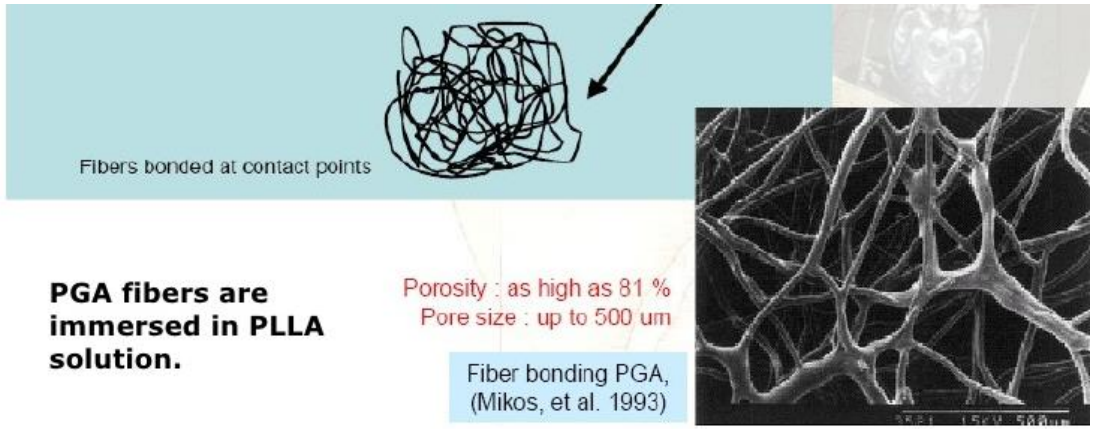
10%(w/v) PLGA made by TIPS using 87% 1,4-dioxane as solvent and 13% H2O as non-solvent

Thermally Induced Phase Separation (TIPS)

Processing techniques	Advantages	Disadvantages
Thermally induced phase separation (TIPS)	Highly porous and interconnected foam structure; Scaffold of complex shape and large size can be made; A wide range of polymers can be processed; Bioactive molecules can be incorporated.	Solvent residue.

Fibre Bonding Technique





PGA fibers are immersed in PLLA solution.

Porosity : as high as 81 %
Pore size : up to 500 um

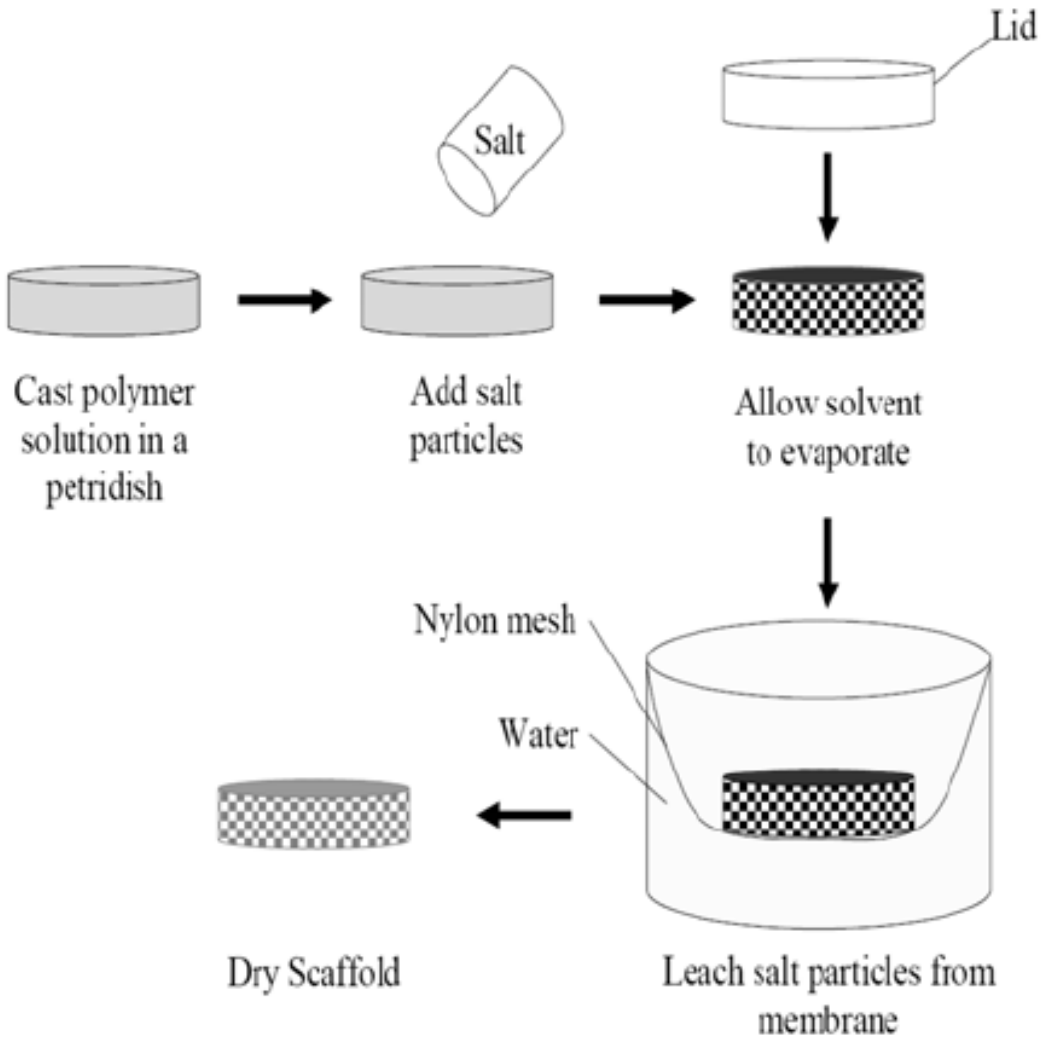
Fiber bonding PGA, (Mikos, et al. 1993)

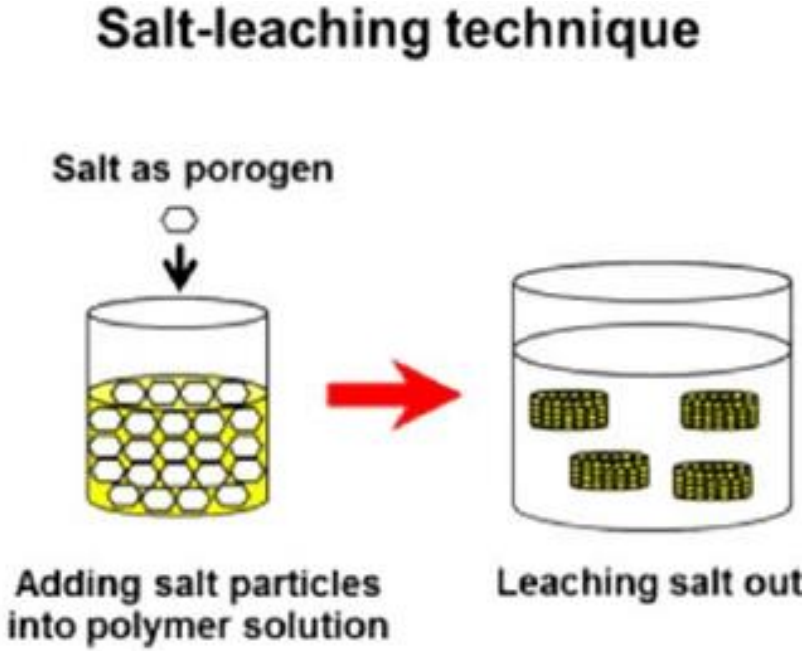
Mikos et al., J. Biomed. Materials Research, 1996

Fibre Bonding Technique

Processing techniques	Advantages	Disadvantages
Fibre bonding	Highly porous and interconnected fibre structure; Large surface area; Improved mechanical integrity.	Insufficient mechanical strength for load-bearing tissues; Solvent residue.

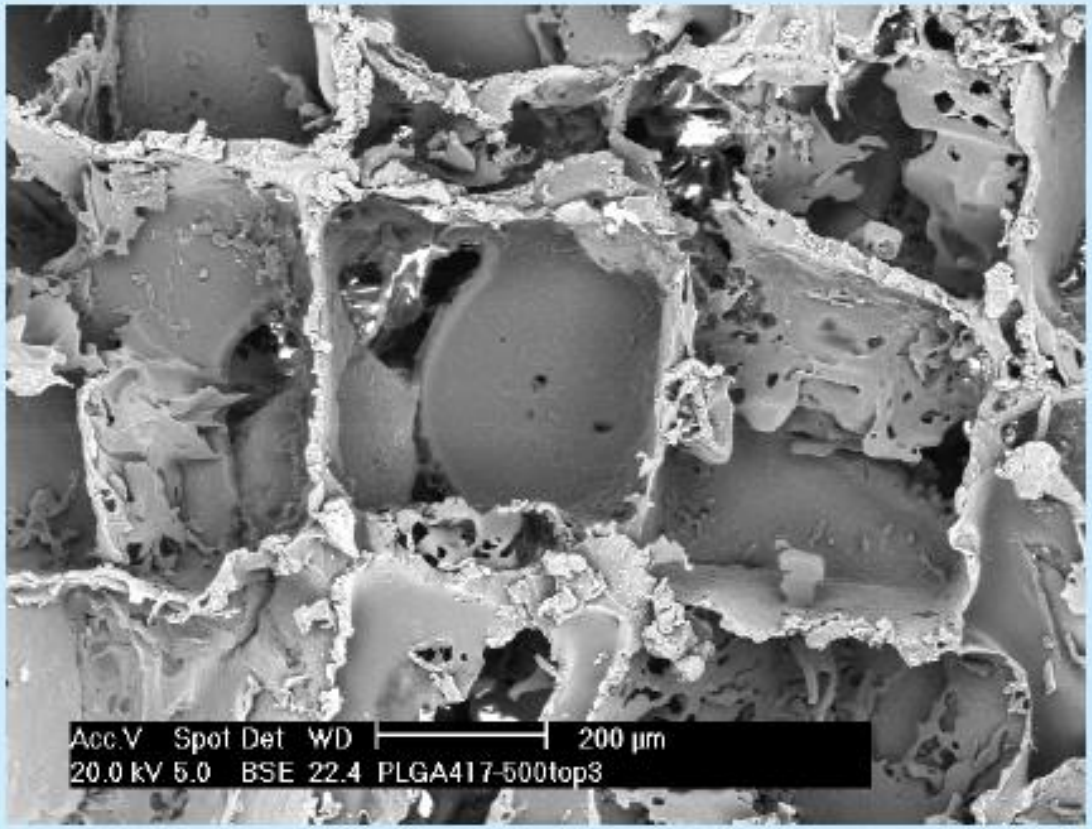
Solvent Casting and Particulate Leaching Technique (SCPL)





https://www.researchgate.net/figure/Scheme-explaining-the-differences-between-the-freeze-drying-and-salt-leaching_fig1_275407391

SCPL / Porogen leaching method



PLGA scaffold produced by solvent (chloroform) casting and particulate leaching

Solvent Casting and Particulate Leaching Technique (SCPL)

Processing techniques	Advantages	Disadvantages
Solvent casting and particulate leaching (SCPL)	Porous 3D foam structure; Relatively controlled pore size and porosity; A wide range of polymers can be used.	Limited to membranes up to 3mm thick; Irregular shaped pores; Poorly interconnected structures; Solvent residue.

Supercritical CO2 Scaffold Production

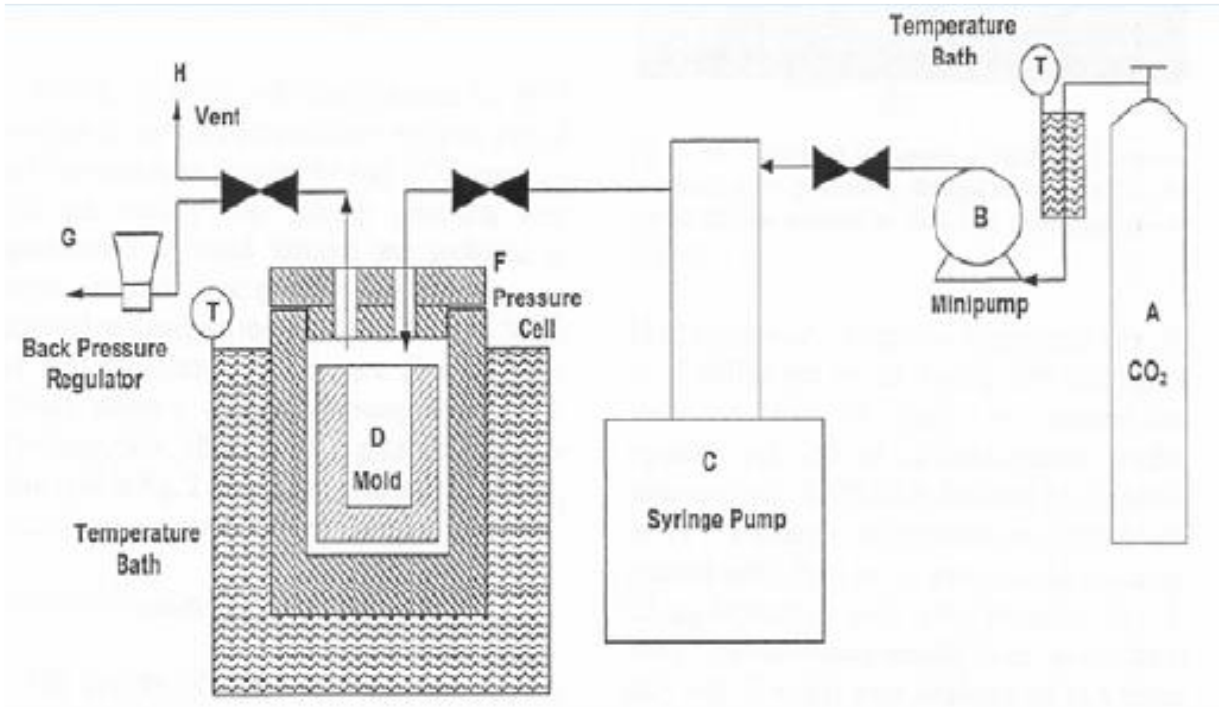


Figure 2.9: A schematic diagram of the system used to generate scaffolds using supercritical carbon dioxide as a solvent. Porous structure is generated upon rapid depressurisation.[8]

Hile et al., J. Controlled Release, 2000

Return

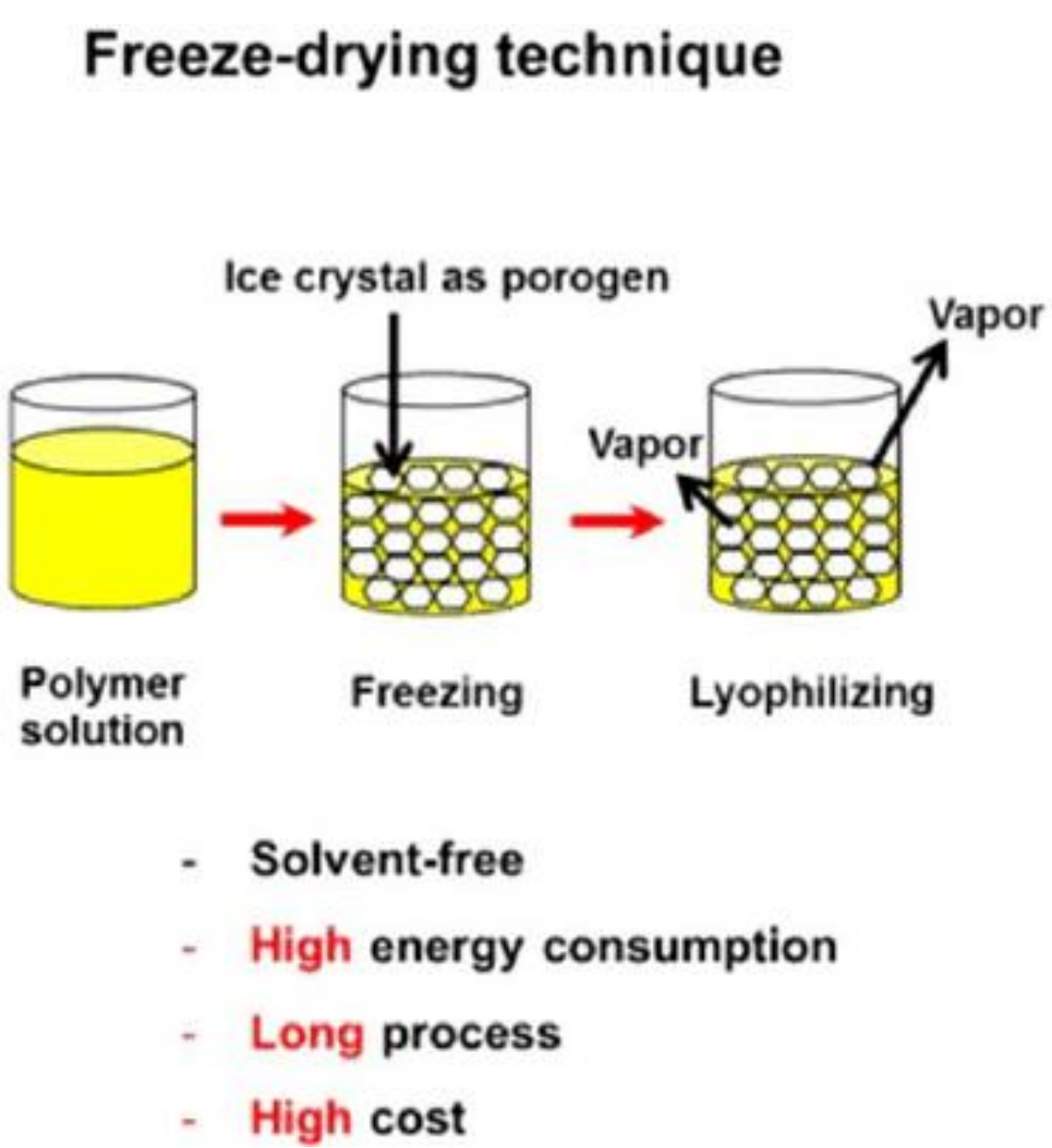
Freeze-drying

First, a synthetic polymer is dissolved into a suitable solvent (e.g. polylactic acid in dichloromethane) then water is added to the polymeric solution and the two liquids are mixed in order to obtain an emulsion.

Before the two phases can separate, the emulsion is cast into a mold and quickly frozen by means of immersion into liquid nitrogen.

The frozen emulsion is subsequently freeze-dried to remove the dispersed water and the solvent, thus leaving a solidified, porous polymeric structure (Haugh MG, 2010).

Scaffold microstructure will depend on the shape of the mold used for freezing
and on the freezer temperature.



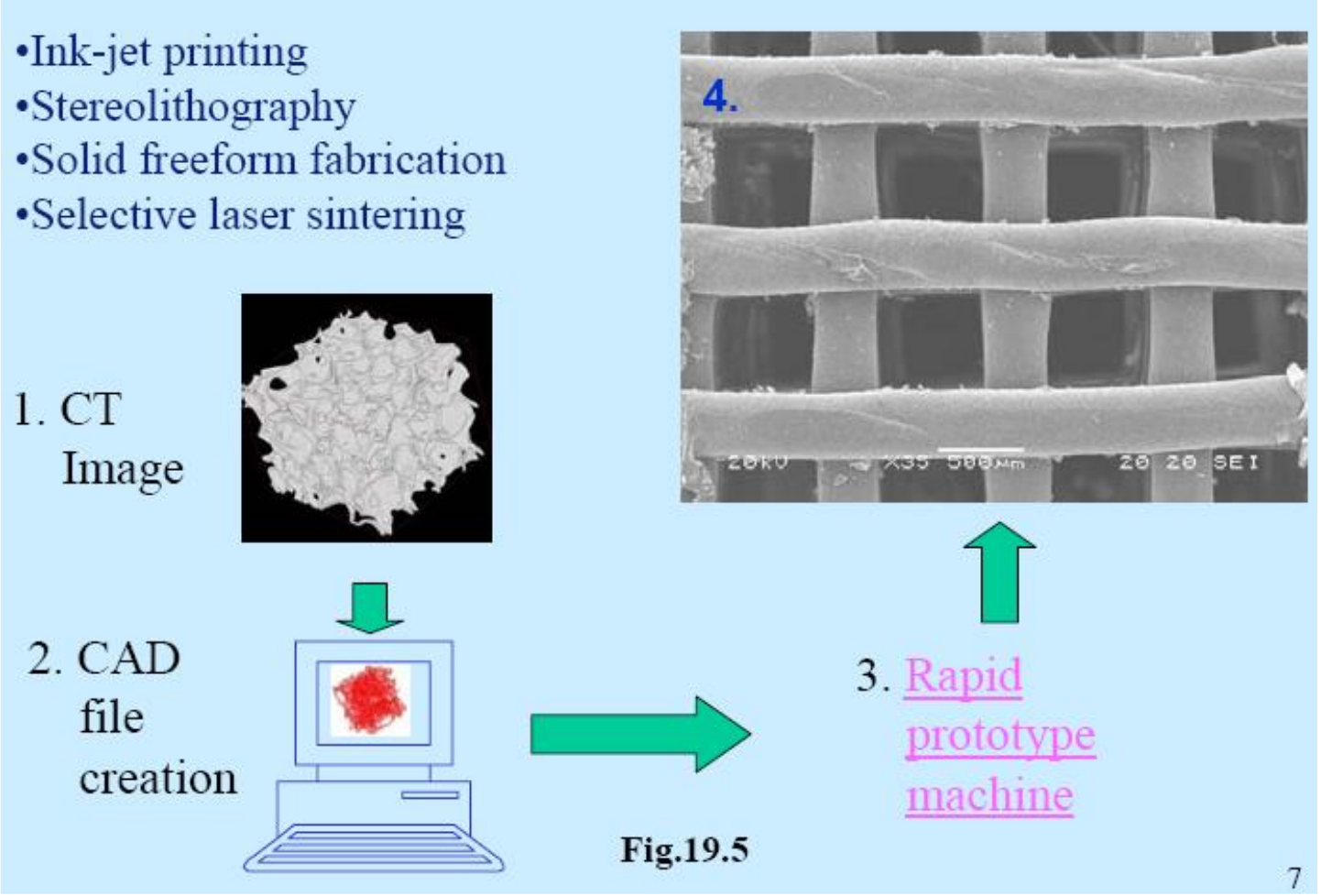
https://www.researchgate.net/figure/Scheme-explaining-the-differences-between-the-freeze-drying-and-salt-leaching_fig1_275407391

Rapid prototyping/solid freeform fabrication

Computer aided design (CAD) is used to create scaffold templates

Rapid prototyping techniques translate these templates into a solid scaffolds

- Selective laser sintering
- Ink-jet printing
- Stereolithography
- Solid freeform fabrication



Advantages of rapid prototyping

- Pore network defined by CAD file
- Pore network can be tailored to the CT scan of a patient's defect
- A pore size gradient can be obtained

Disadvantages of rapid prototyping

- Mechanical properties poor?
- Not all materials can be used in the techniques yet.
- Expensive equipment.