Leibniz-Institut für Neue Materialien

# Polymer Networks: Biomedical Application

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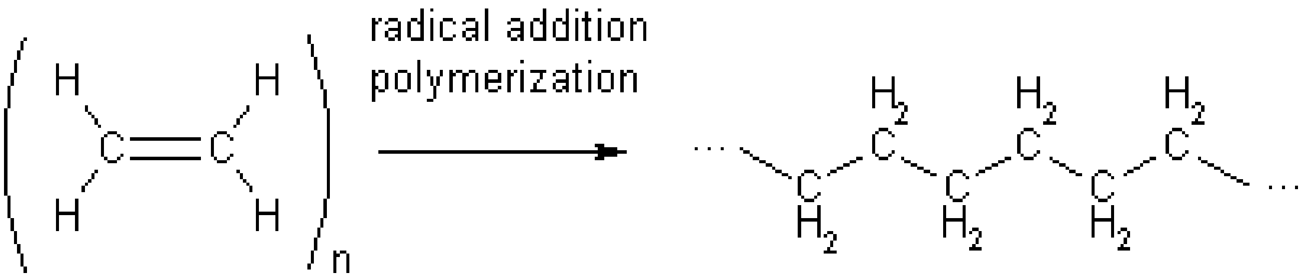
# Polymer



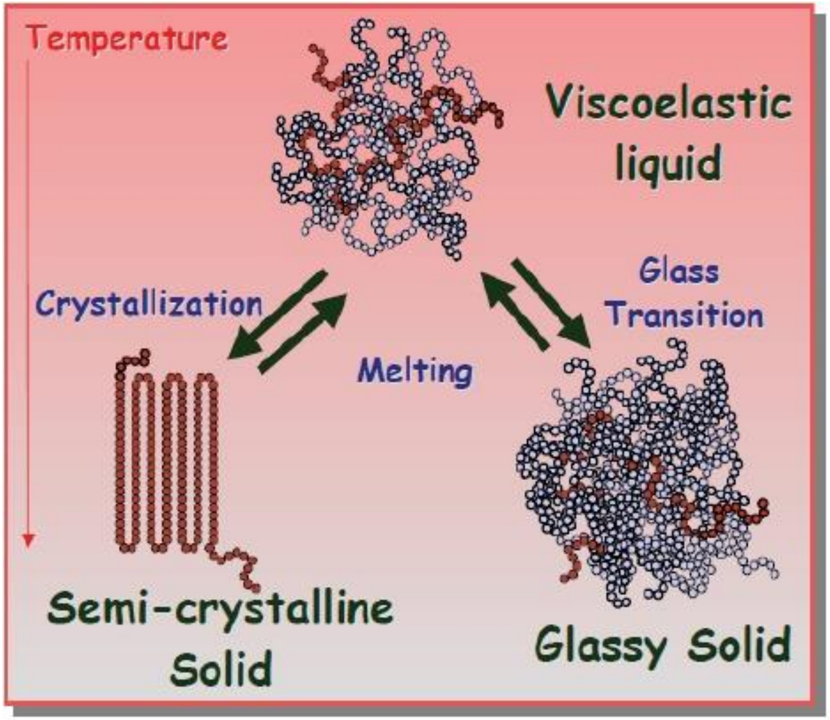


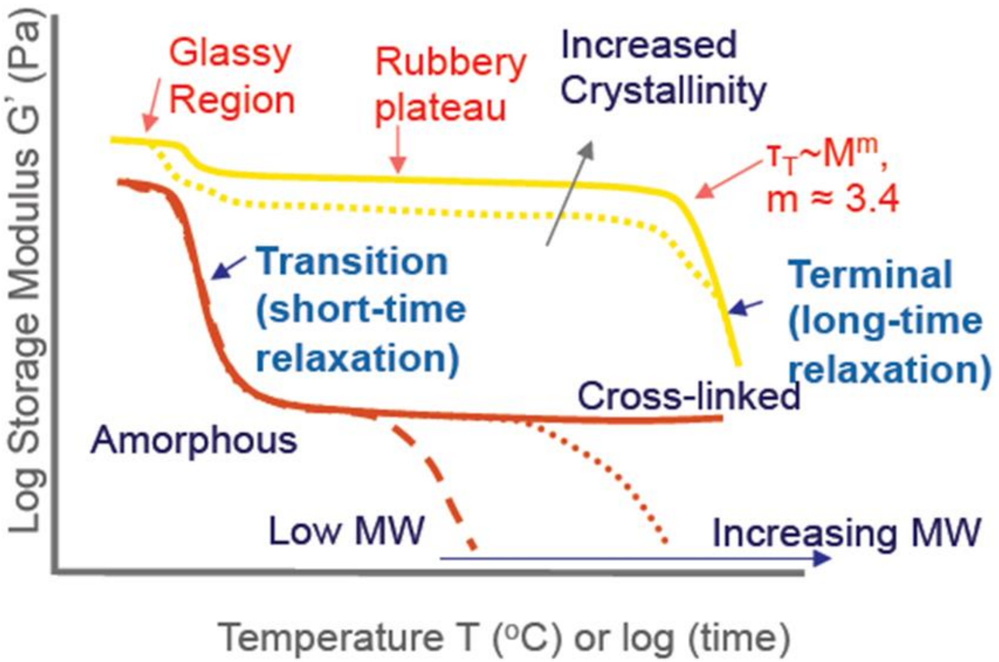
Molecular Weight > 5000 Da

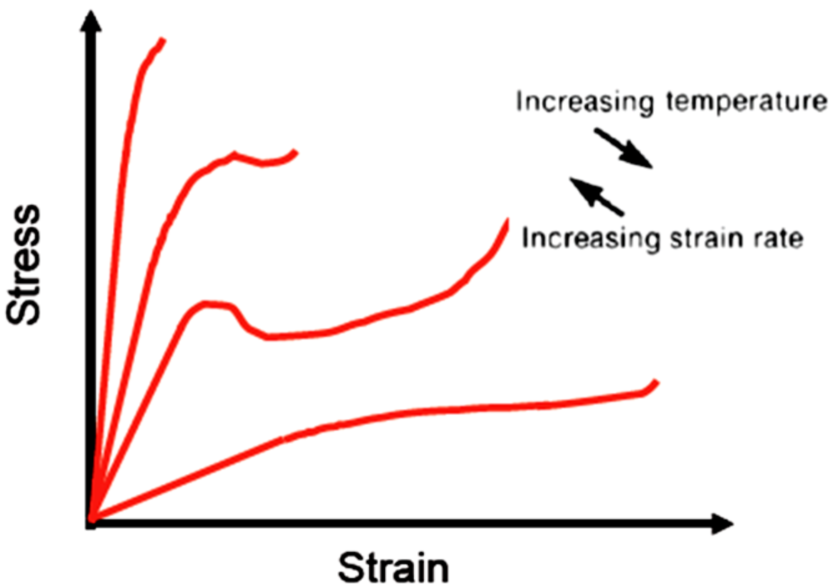
Polydispersity index (PDI)

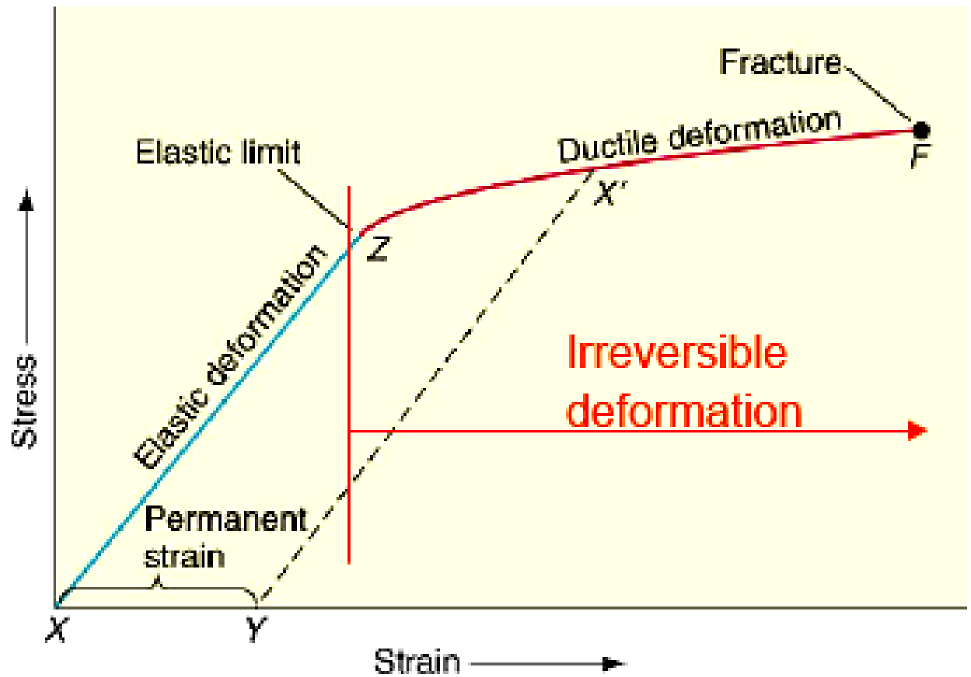
Glass transition temperature (Tg)

Tg, glass state, rubbery state, crystalline degree…




Stress
Strain
Increasing temperature
Increasing strain rate


Fracture
Ductile deformation
F
Elastic limit
X'
Z
Elastic deformation
Irreversible
deformation
Stress
Permanent
strain
X
Y
Strain

# Macromolecules & Polymer

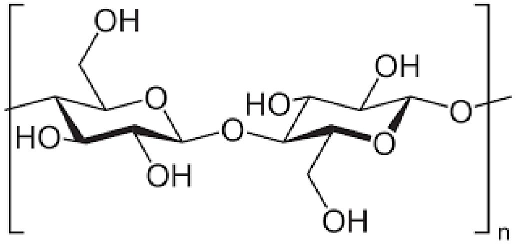
Macromolecule: Molecular Weight > 5000 Da

Polymer: macromolecule consisting of repeat unit

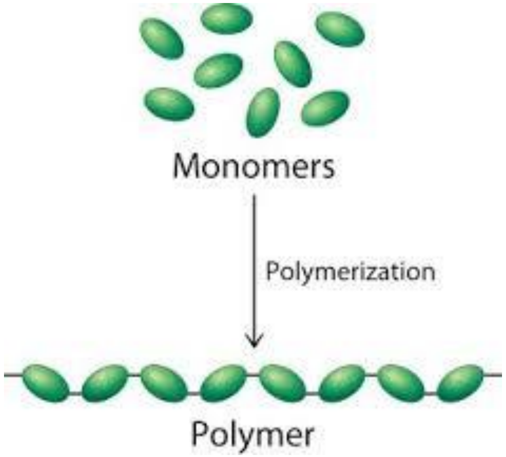
DNA

Biopolymer

Polymer

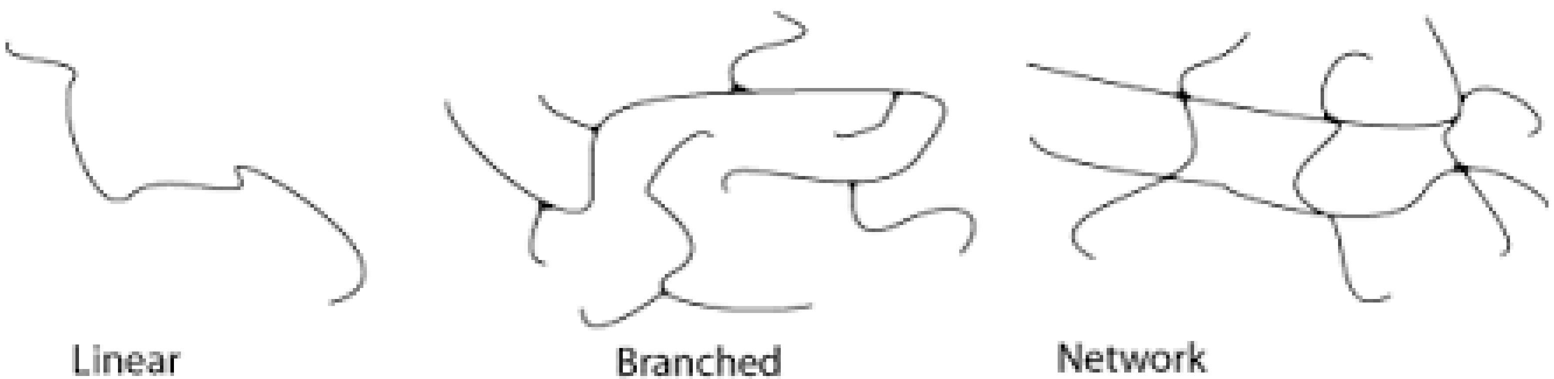




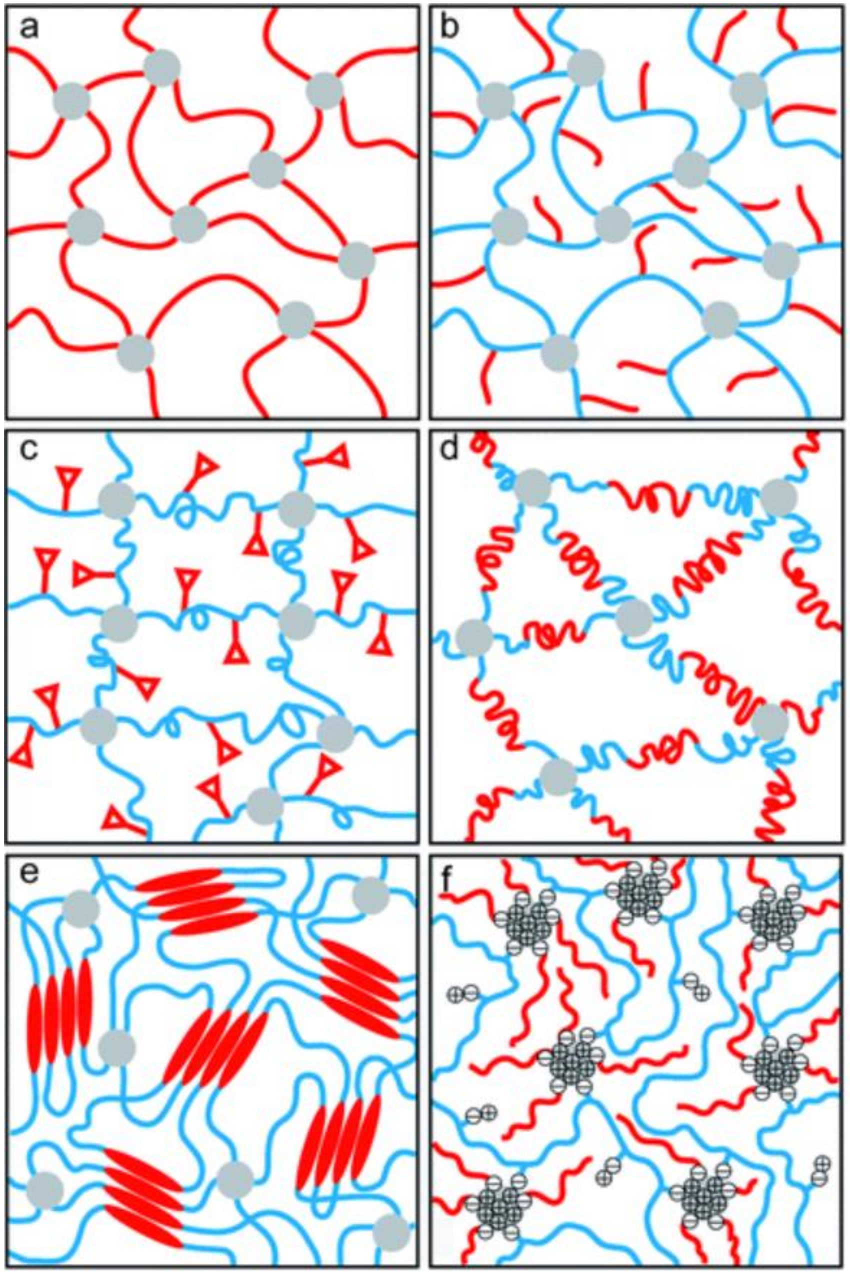


# Polymer Network

Polymer network: a structure in which essentially all mers are connected to all other mers and to the macroscopic phase boundary by many paths through the polymer's phase; the number of such paths increases with the average number of intervening bonds and the paths much on the average be co-extensive with the polymer phase.



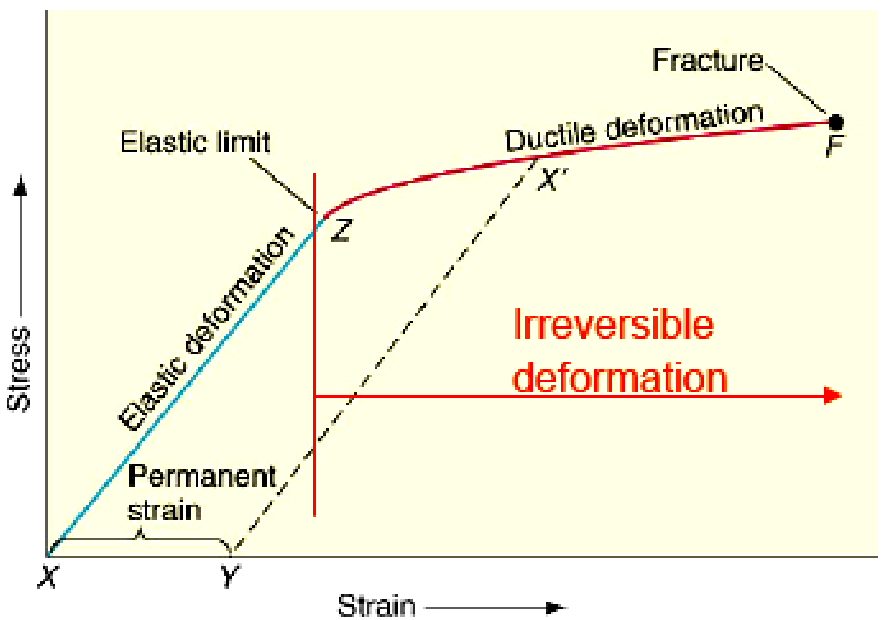

Macrocycle is not a polymer network

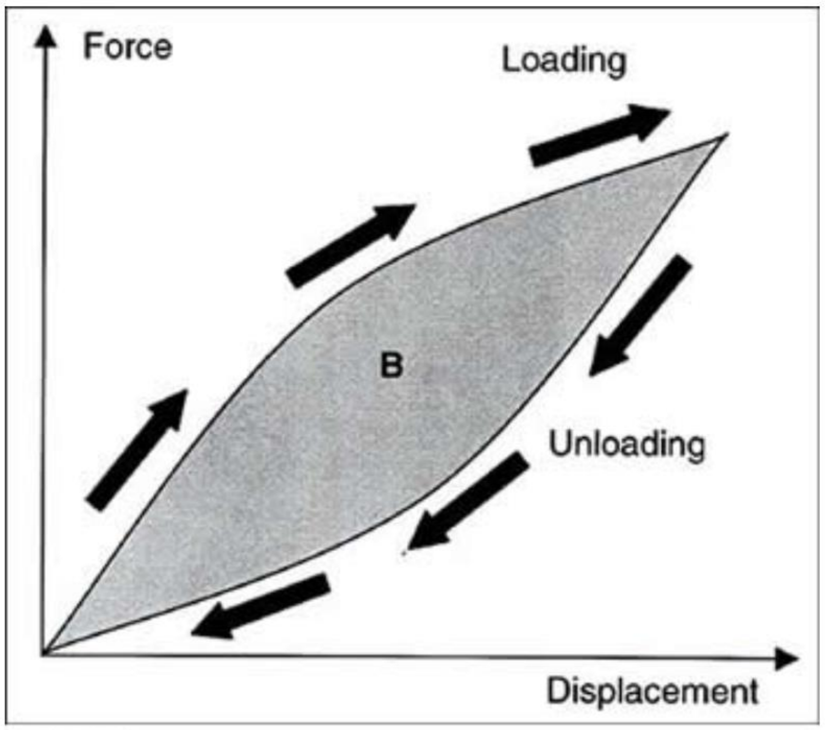



Crosslinking form, degree, strength

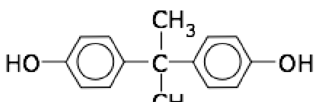
Polymer segment: length, reactivity, conformation, interaction

Andreas Lendlein et al. *Soft Matter*, **2013**, 9, 1744


Fracture
Elastic limit
Ductile deformation
F
X'
Z
Elastic deformation
Irreversible deformation
Permanent strain
Stress
X
Y
Strain

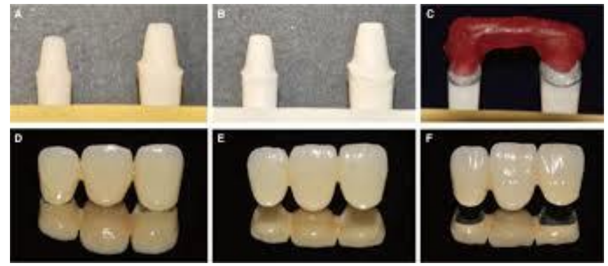

Force
Loading
B
Unloading
Displacement

## Epoxy resins

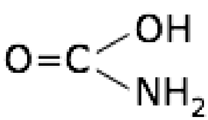


bis-phenol A

epichlorohydrin

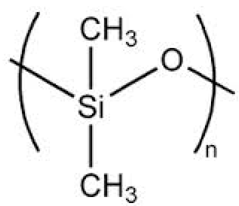



## Polyurethanes



carbamic acid

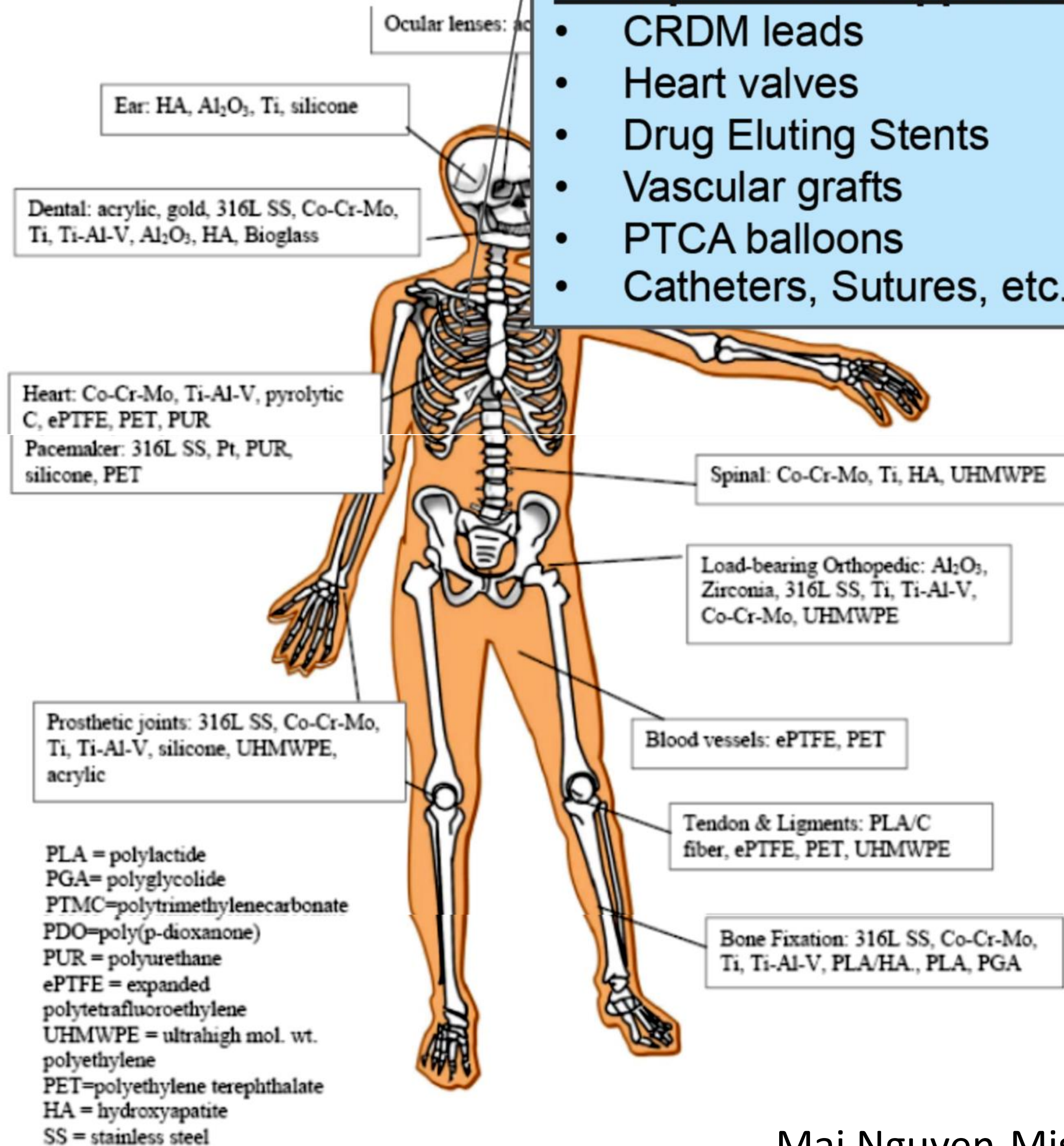
## Silicones




# Polymer material used in human body

**Examples in CV Applications:**

- CRDM leads
- Heart valves
- Drug Eluting Stents
- Vascular grafts
- PTCA balloons
- Catheters, Sutures, etc.




Mai Nguyen-Misra’s PPT

# Biocompatibility

Ability to be in contact with a living system without producing an adverse effect

| | |
|---|---|
| primary (level I): | in vitro cytotoxicity test, a rapid, sensitive and standardized method |
| secondary (level II): | in vivo the tissue response (animal tests), high cost, slowly, controversy, |
| preclinical (level III): | evaluate its performance and the favorable or unfavorable reactions that may present under normal clinical conditions |

Examples:

| | | |
|---|---|---|
| Chitosan | bisphenol aglycidyl methacrylate (bis-GMA) | PEG |
| Alginate | triethylene glycol dimethacrylate (TEGDMA) | silicone |
| … | 2-hydroxyethyl methacrylate (HEMA) | |
| | polylactide acid | |
| | polyglycolide acid | |

# Biostability

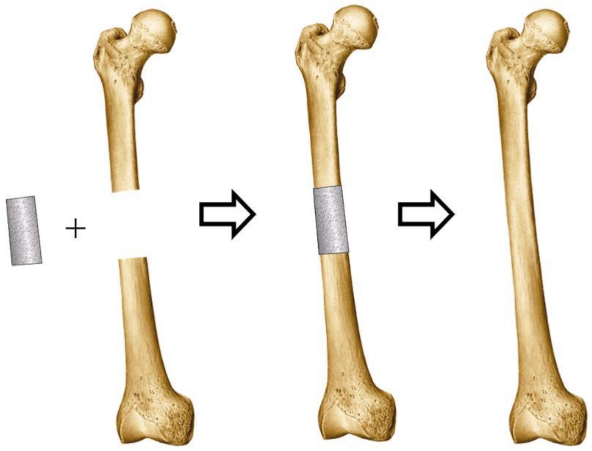
No polymer is impervious to chemical and physical actions of the body

| Mechanism | Breakdown Examples |
| --- | --- |
| Mechanical | Creep, wear, stress cracking, fracture |
| Physico-chemical | Adsorption of molecules (fouling)<br>Absorption of water and other molecules (softening)<br>Desorption of low molecular weights (weakening)<br>Dissolution |
| Bio-chemical | Hydrolysis, oxidation, enzymatic, mineral deposition<br>Fibrous encapsulation |
| Electrochemical | Corrosion |

# Biodegradation

the disintegration of materials by bacteria, fungi, or other biological means

be consumed by microorganisms

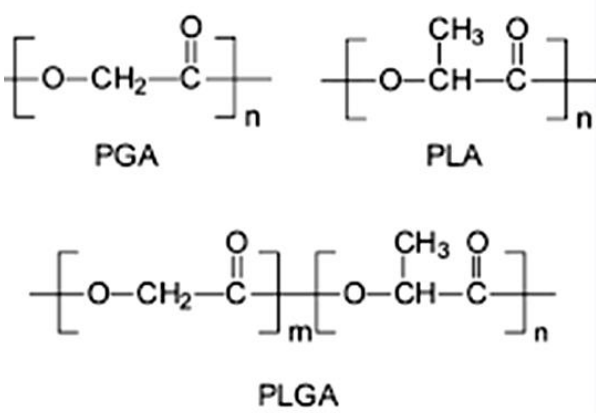



temporary prostheses,

scaffolds for tissue engineering,

drug delivery vehicles…

Materials:




Nature macromolecules

Protein, polysaccharide, DNA…

Bioconjugated materials

# Bioabsorption (bioresorption)

Ability of biomaterials to be absorbed by living tissue

suture materials,
internal fixation devices for bone fracture,
reconstructive substitute, blood vessels,
drug delivery system
sheets for preventing adhesion

Polyesters of aliphatic a-hydroxy-acids
PLA, PGA, PLGA
Nature macromolecules

# Other properties

- **Mechanical**: tensile, compression, fatigue, stiffness, creep, fracture
- **Electrical**: insulation, electromechanical compatibility
- **Chemical**: biostability, degradation interaction/reaction
- **Thermal**: shrinkage, expansion, dimensional stability, thermal insulation
- **Environmental**: product life span, shelf life, humidity
- **Surface**: finish, wear,friction, tactility, biocompatiblity, thrombogenicity
- **Process considerations**: melt processing, sterilization, etc.
- Economic: Material cost, process introduction
- Aesthetic: cosmetic appearance, visual clarity

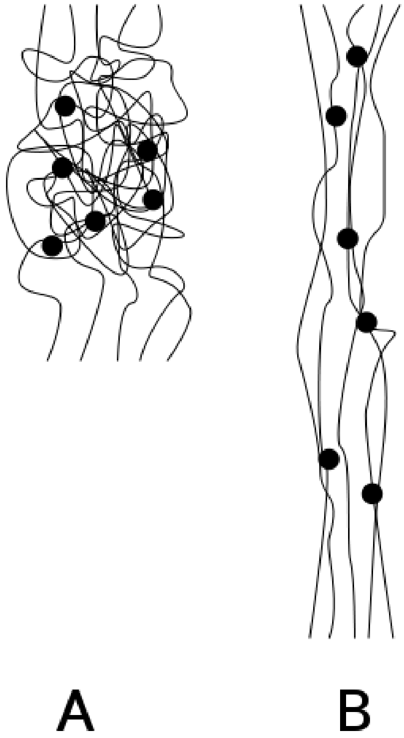
# NP Materials used for biomedical application:

1. Elastomer
2. Hydrogel
3. Shape-memory polymer
4. Polymer composite

   …

# Elastomer

Polymer that displays rubber-like elasticity



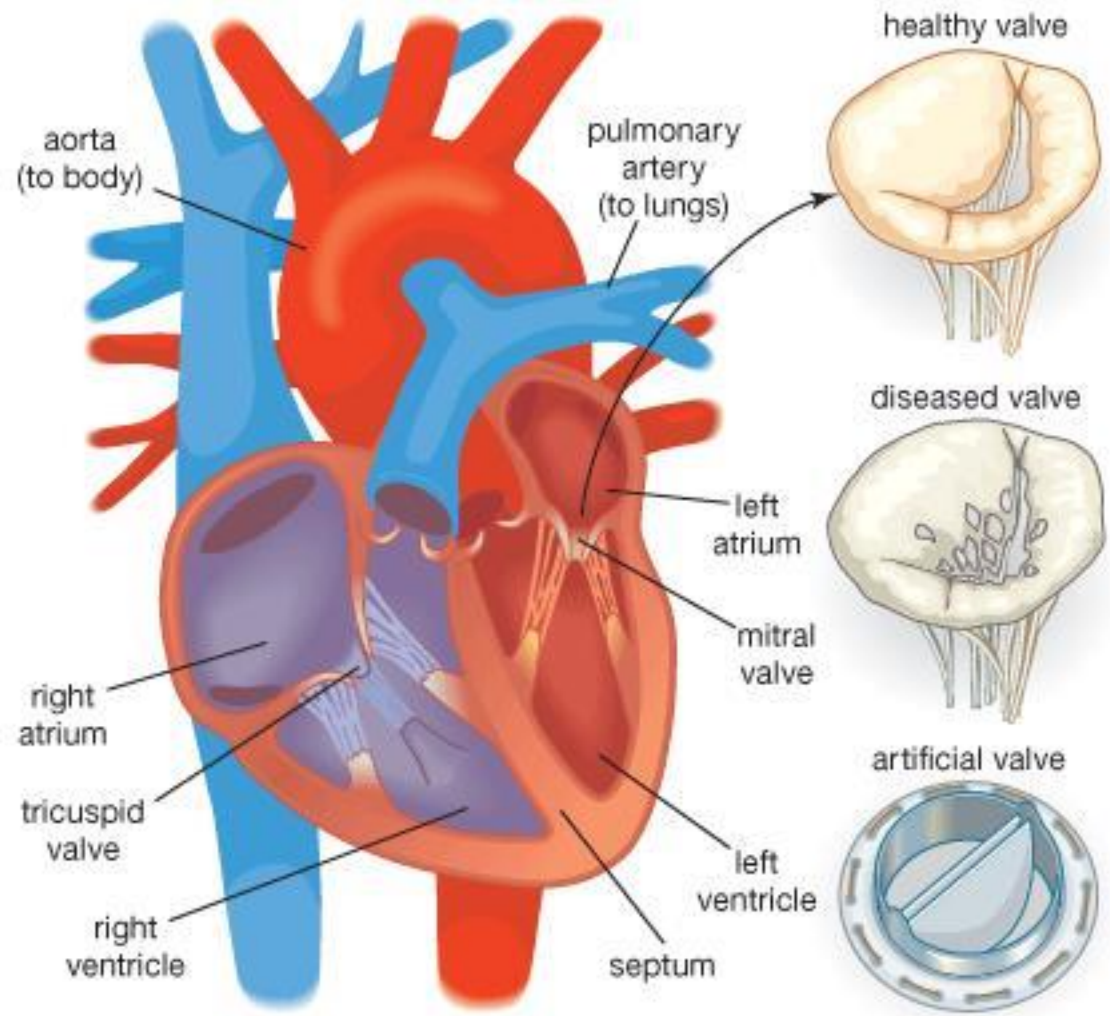

(A) is an unstressed polymer; (B) is the same polymer under stress. When the stress is removed, it will return to the A configuration. (The dots represent cross-links)

https://en.wikipedia.org/wiki/Elastomer

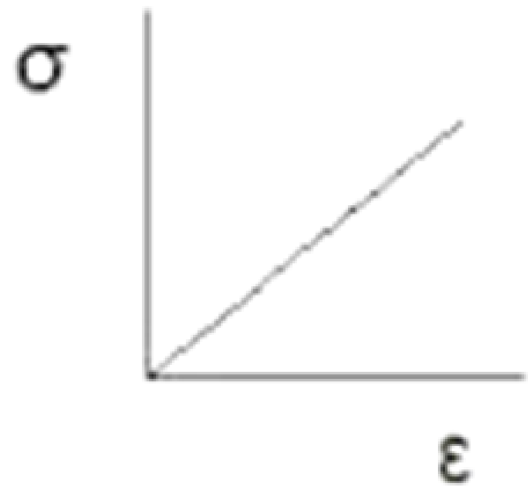
silicones,
thermoplastic elastomers,
polyolefin
polydiene elastomers,
poly(vinyl chloride),
natural rubber,
heparinized polymers,
polypeptides elastomers
…

cardiovascular devices,
prosthetic devices,
general medical care products,
transdermal therapeutic systems,
orthodontics,
Ophthalmology
…

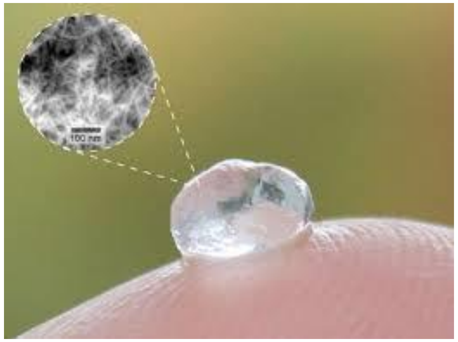
# Artificial heart valve



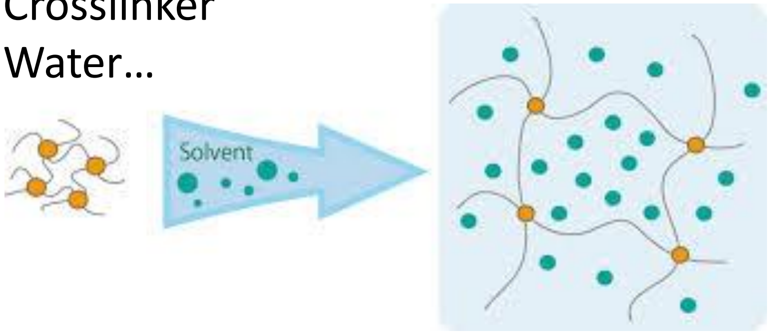


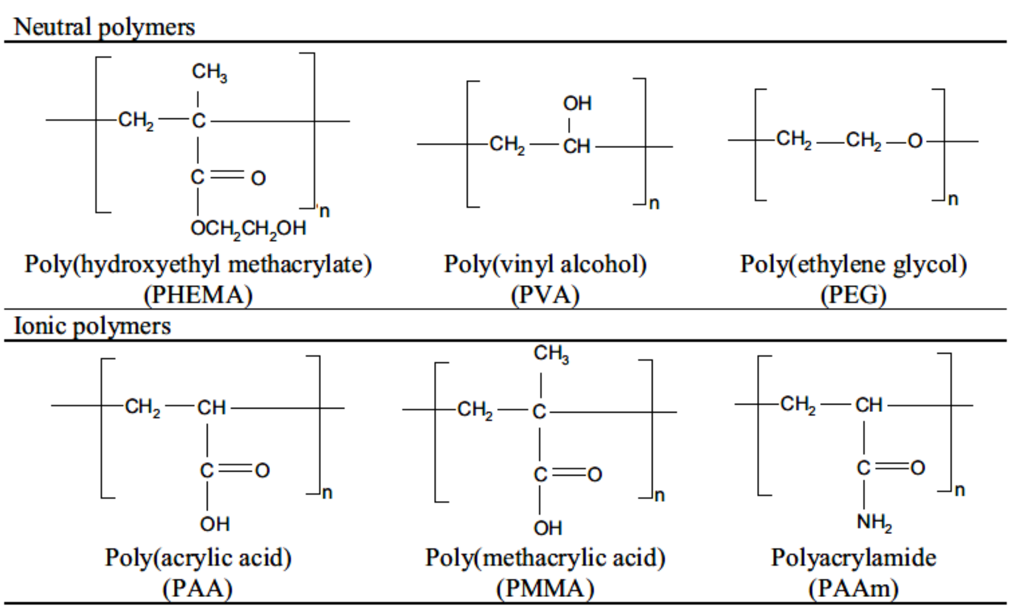



# Hydrogel



Polymer chain
Crosslinker
Water…




water-soluble polymers

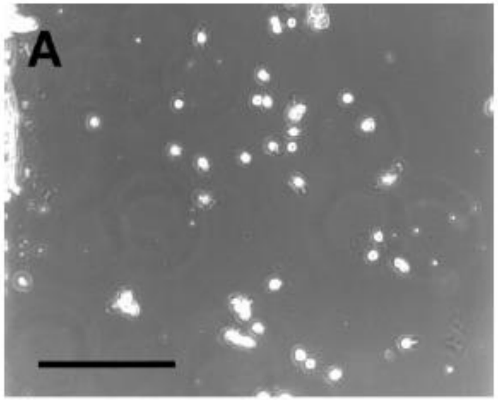
Preparation:

photo- and thermal-initiated polymerization in presence of cross-linker.

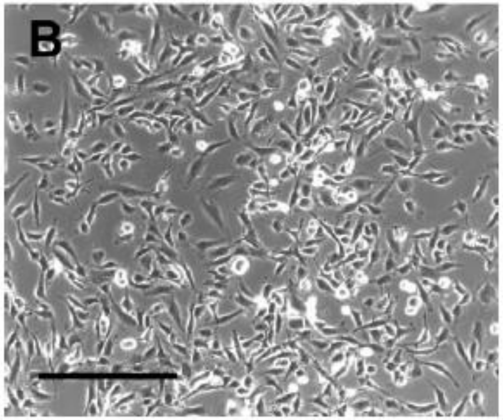
# Hydrogel adhesive coatings

Adhesion of cells

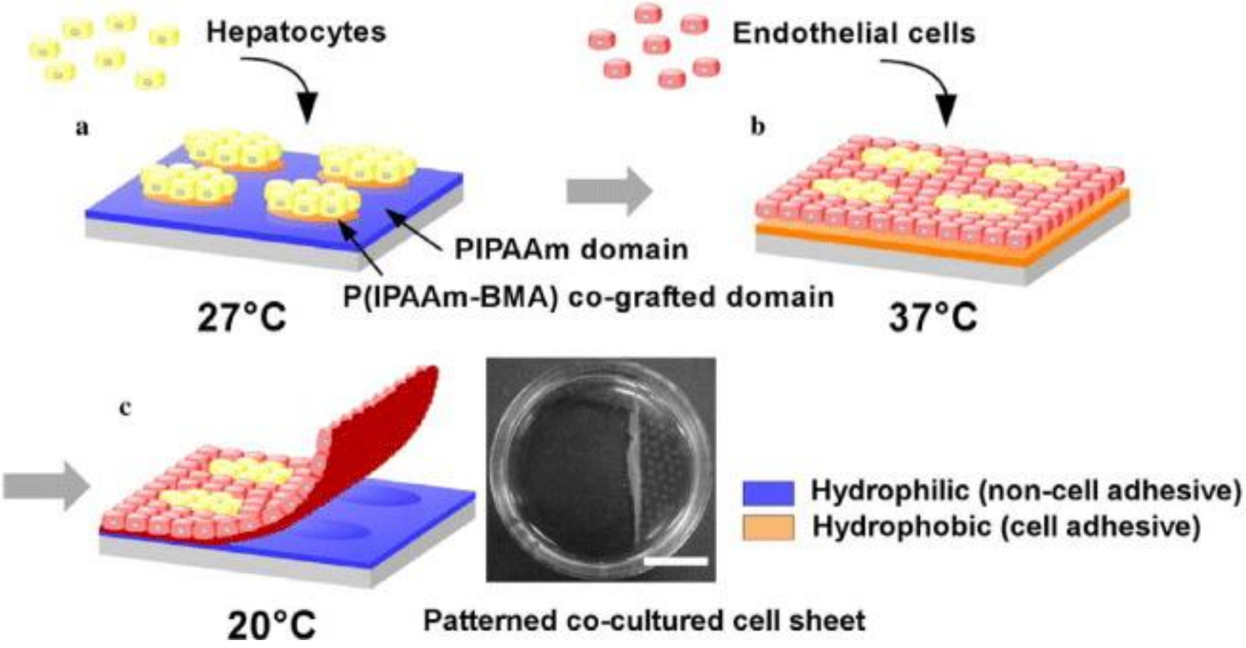
surface of PEG hydrogels



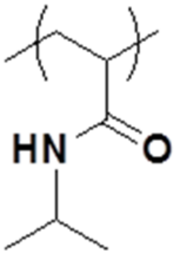

PEG-RGDS




N. A. Peppas, J. Z. Hilt, A. Khademhosseini, R. Langer, *Adv. Mater.* **2006**, *18*, 1345




PNIPAM

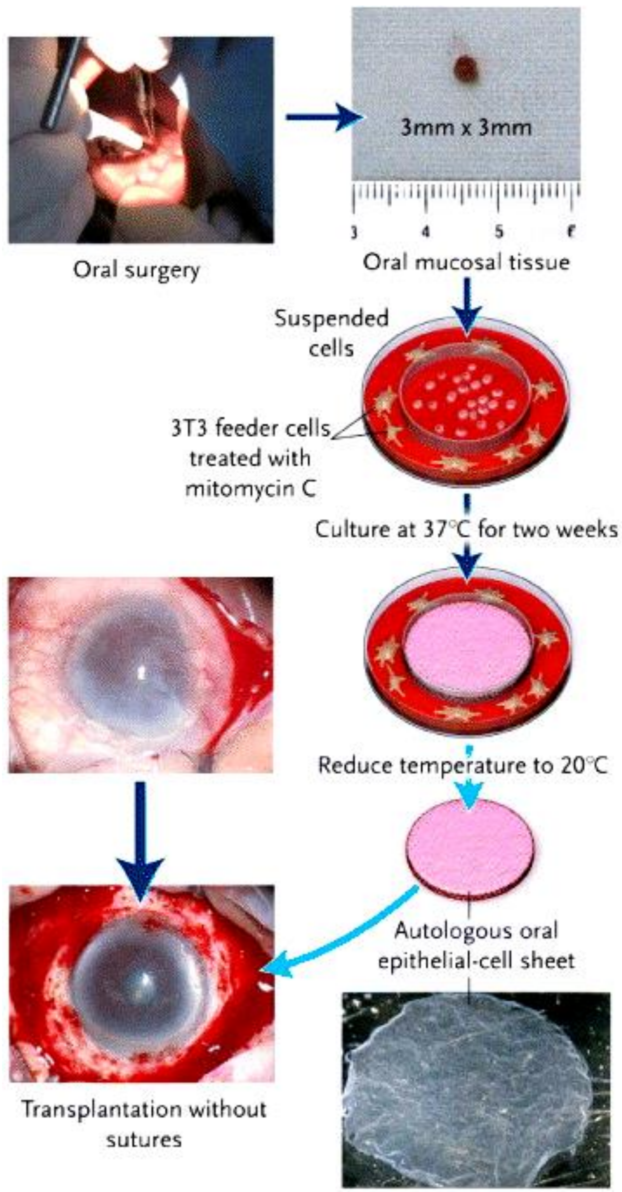


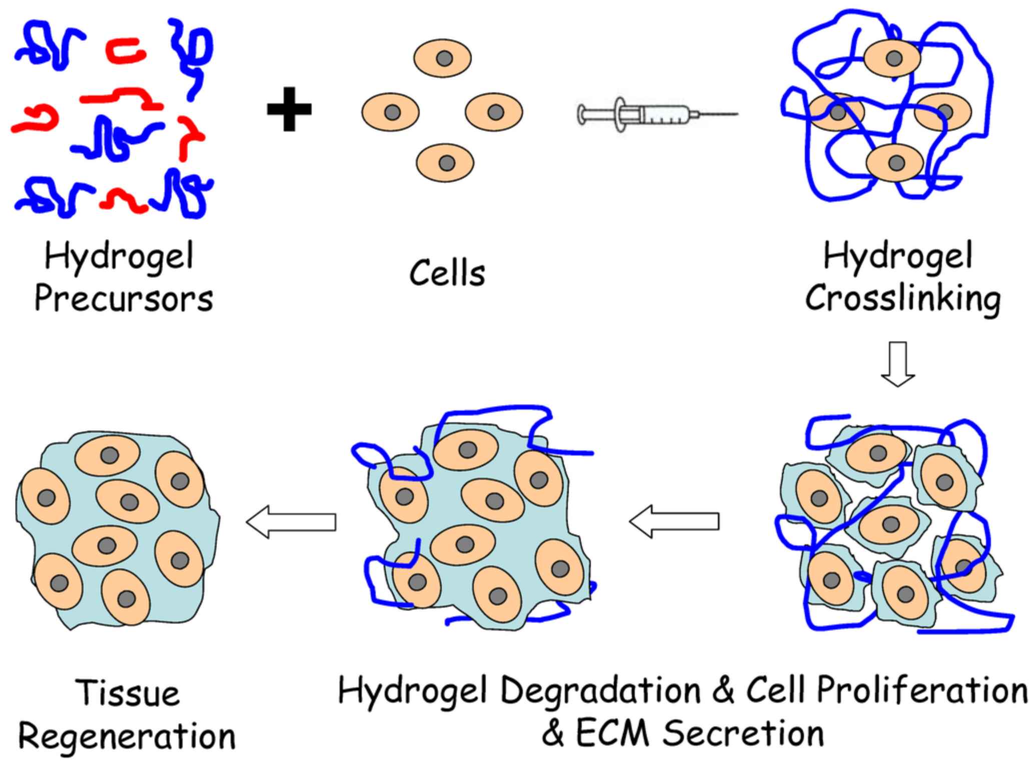

Jun Kobayashi, Teruo Okano
2010 Sci. Technol. Adv. Mater. 11 014111

Transplantation of a corneal epithelial cell sheet.

INM
Leibniz-Institut für Neue Materialien

# Hydrogel: tissue engineering



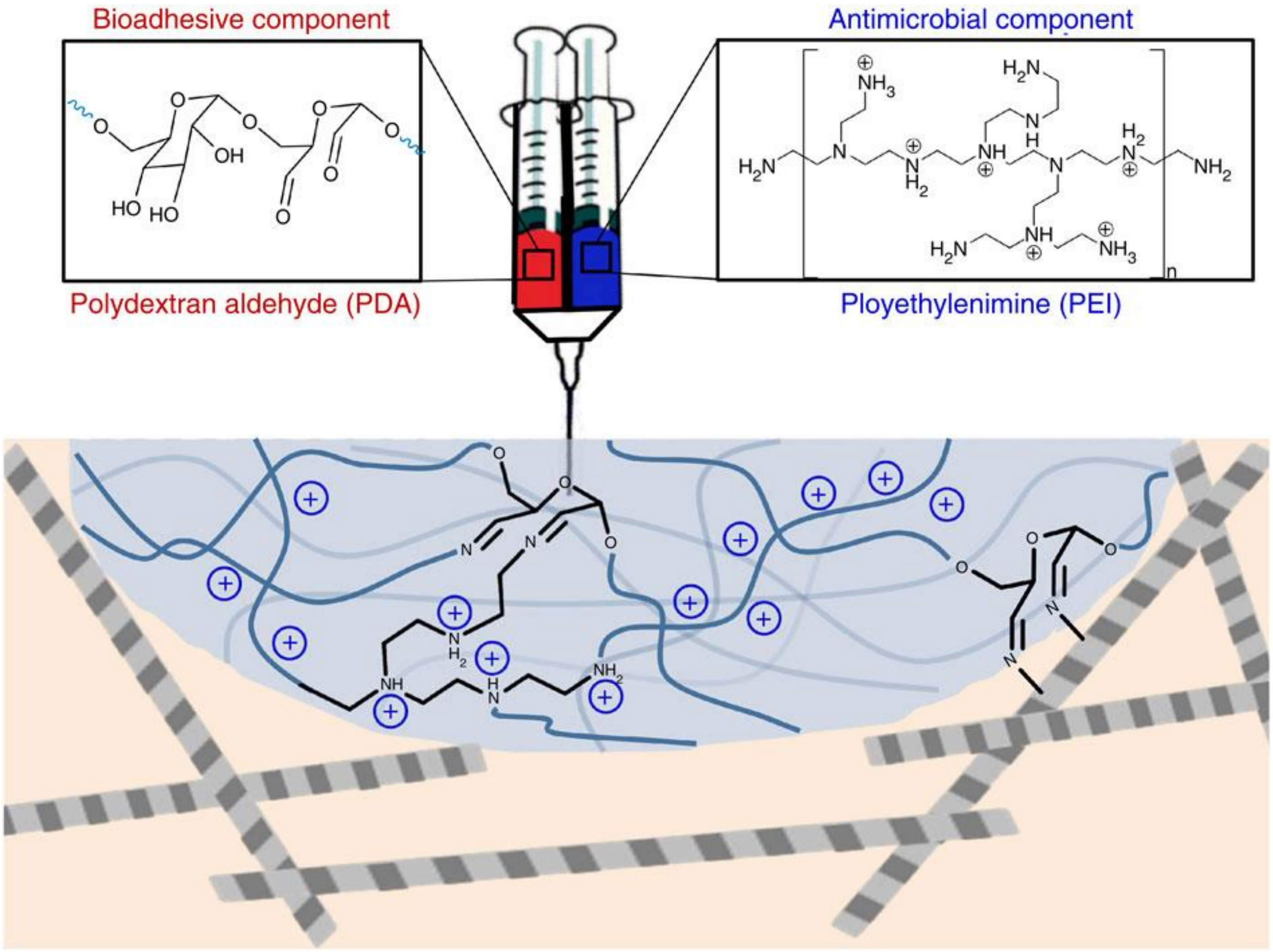

Jun Kobayashi, Teruo Okano
2010 Sci. Technol. Adv. Mater. 11 014111

Huaping Tan and Kacey G. Marra *Materials* ***2010, 3, 1746***

## Injectable and biodegradable hydrogels for tissue engineering

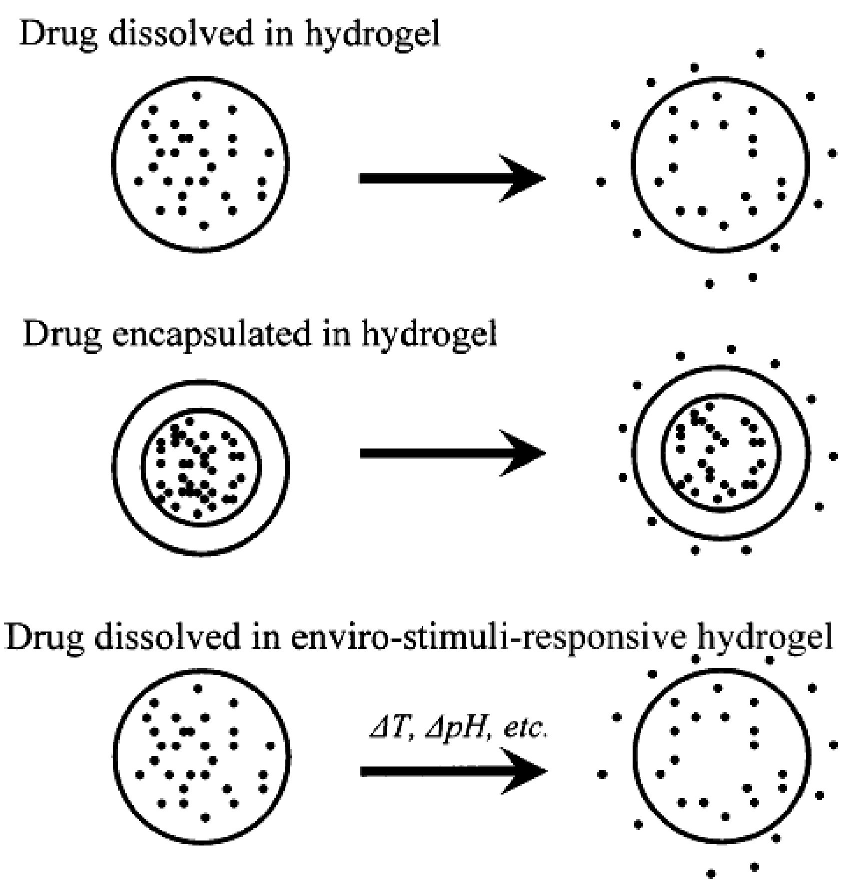
| Hydrogels | Polymers | Gelation Mechanism |
|---|---|---|
| Natural hydrogels | Collagen/Gelatin | Thermal/Chemical crosslinking |
| | Chitosan | Thermal/Chemical/Schiff-base reaction/Free radical crosslinking |
| | Hyaluronic acid | Thermal/Chemical/Schiff-base reaction/Michael-type addition/Free radical crosslinking |
| | Chondroitin sulfate | Free radical crosslinking |
| | Alginate | Ionic/Free radical crosslinking |
| | Agar/Agarose | Thermal crosslinking |
| | Fibrin | Thermal crosslinking |
| Synthetic hydrogels | PEG/PEO | Michael-type addition/Chemical/Free radical crosslinking |
| | PVA | Chemical/Free radical crosslinking |
| | PPF/OPF | Free radical crosslinking |
| | PNIPAAm | Thermal crosslinking |
| | PEO-PPO-PEO<br>PLGA-PEG-PLGA<br>PEG-PLLA-PEG | Thermal crosslinking |
| | Poly(aldehyde guluronate) | Chemical crosslinking |
| | Polyanhydrides | Free radical crosslinking |

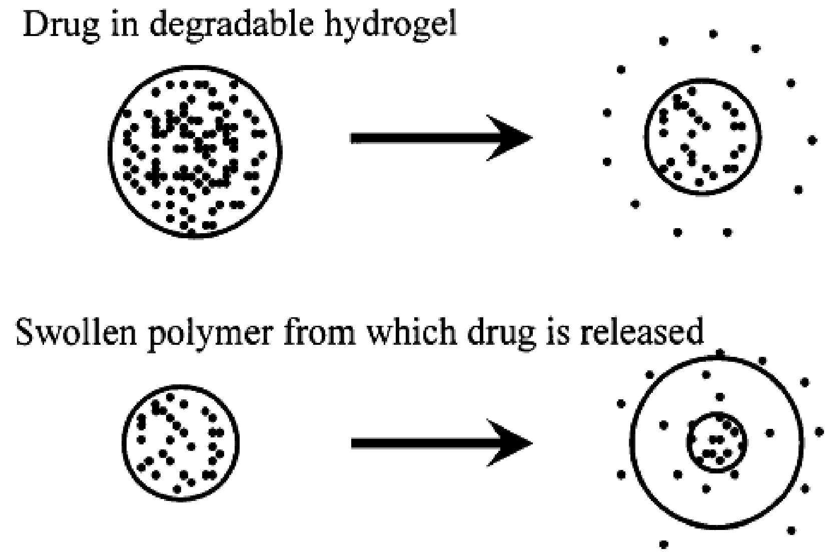
Huaping Tan and Kacey G. Marra *Materials* ***2010, 3, 1746***




M. C. Giano, Z. Ibrahim, S. H. Medina, K. A. Sarhane, J. M. Christensen, Y. Yamada, G. Brandacher, J. P. Schneider, *Nat Commun* **2014**, *5*

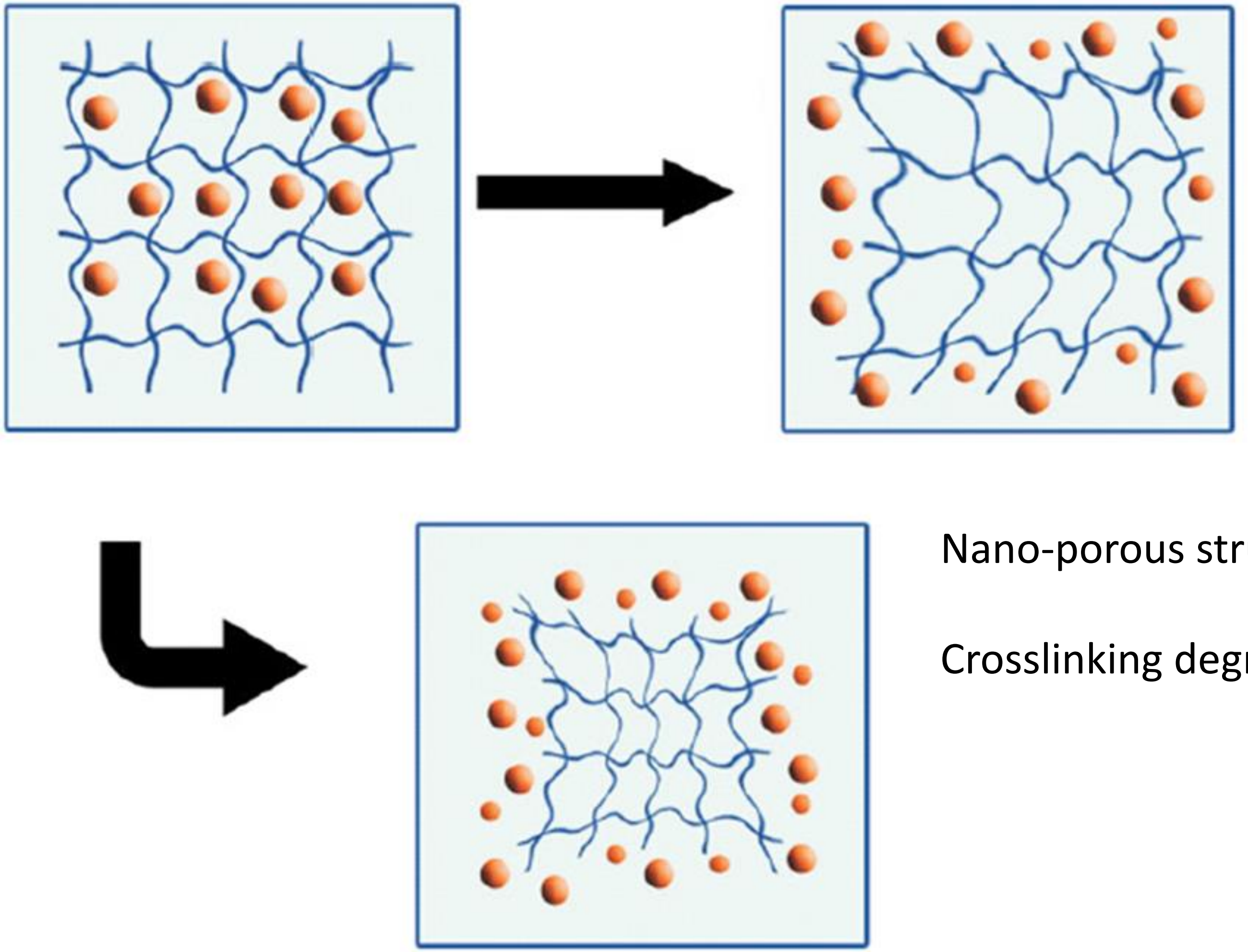
# Hydrogel: drug delivery




Various delivery and release mechanisms of hydrogels

N. A. Peppas, J. Z. Hilt, A. Khademhosseini, R. Langer, *Adv. Mater.* **2006**, *18*, 1345



Nano-porous structure

Crosslinking degree and porous size

www.orientjchem.org

## Thermo-responsive hydrogel

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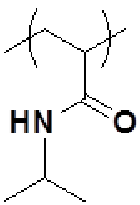
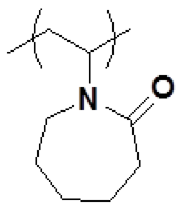
LCST: lower critical solution temperature

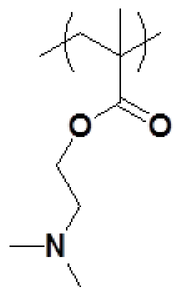
PNIPAM



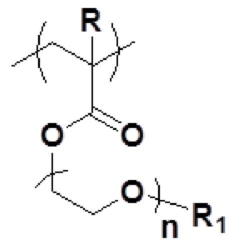
PVCL



PDMAEMA



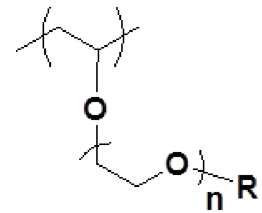
POE(M)A



R: H or $CH_3$

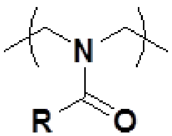
$R_1$: $CH_3$ or $C_2H_5$

PVE



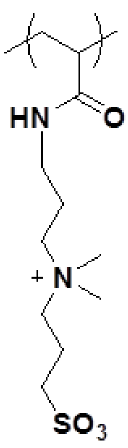
R: $CH_3$ or $C_2H_5$

P2O

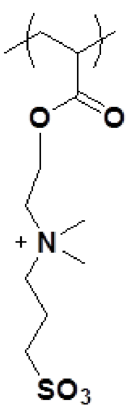


UCST: upper critical solution temperature

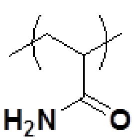
PDMMEAPS



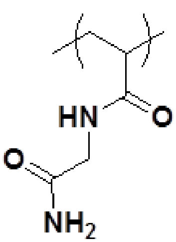
PNMAPDMAPS



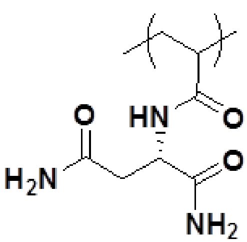
PMA



PNAGA

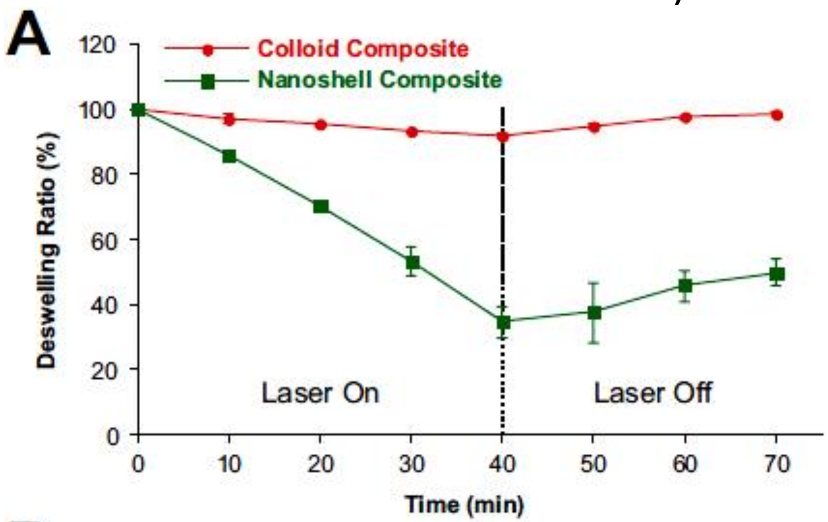


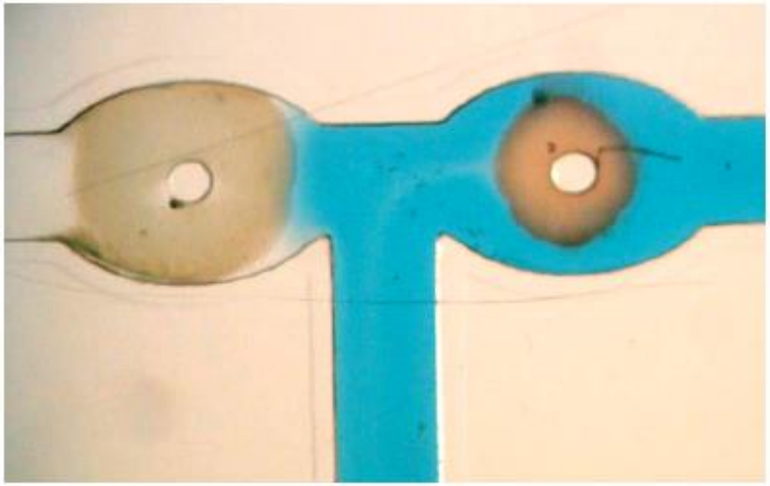
PNAAGA

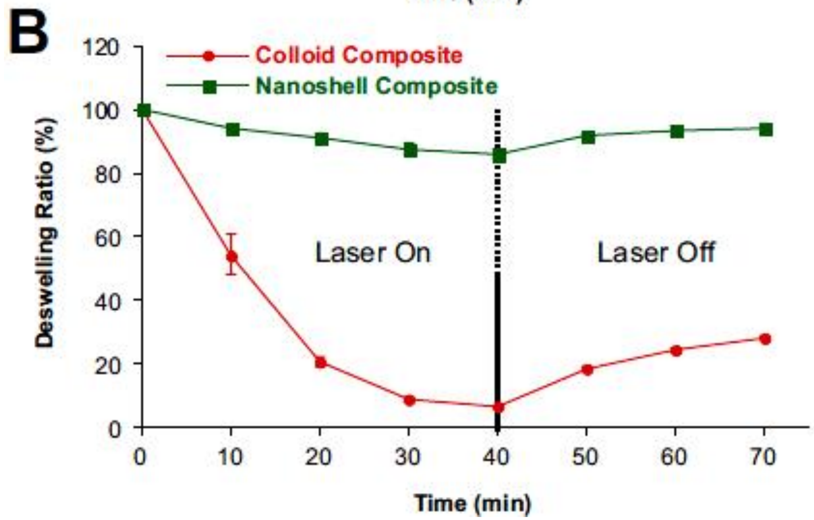


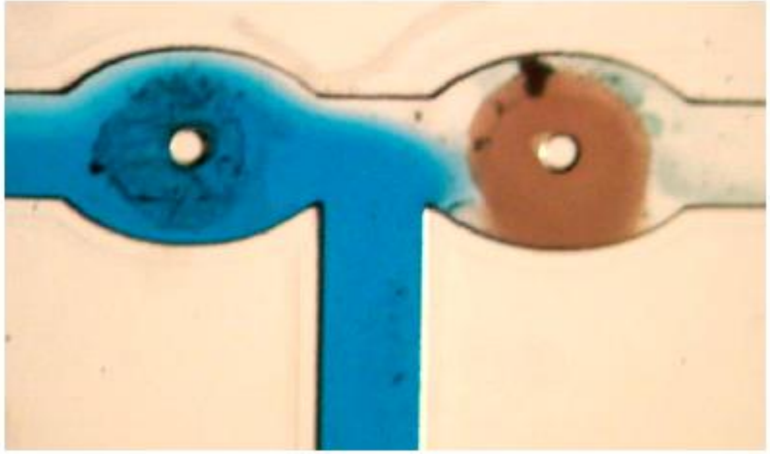
# Hydrogel: diagnostic devices

Irradiation at A) 832 nm and B) 532 nm



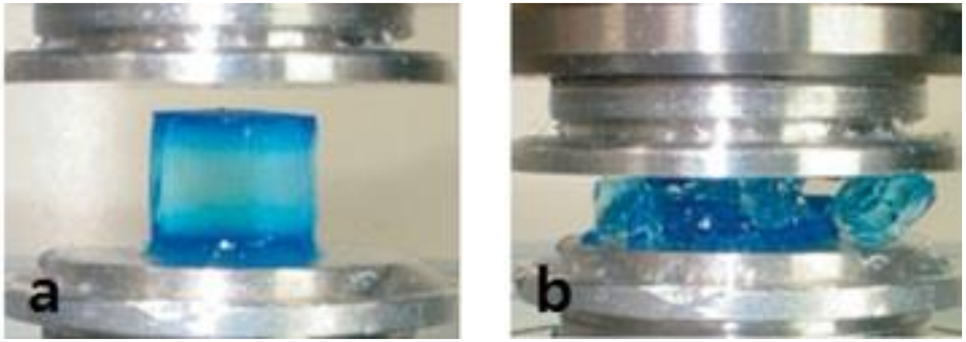


S. Sershen, G. Mensing, M. Ng, N. Halas, D. Beebe, J.West, *Adv. Mater.* **2005, *17, 1366***

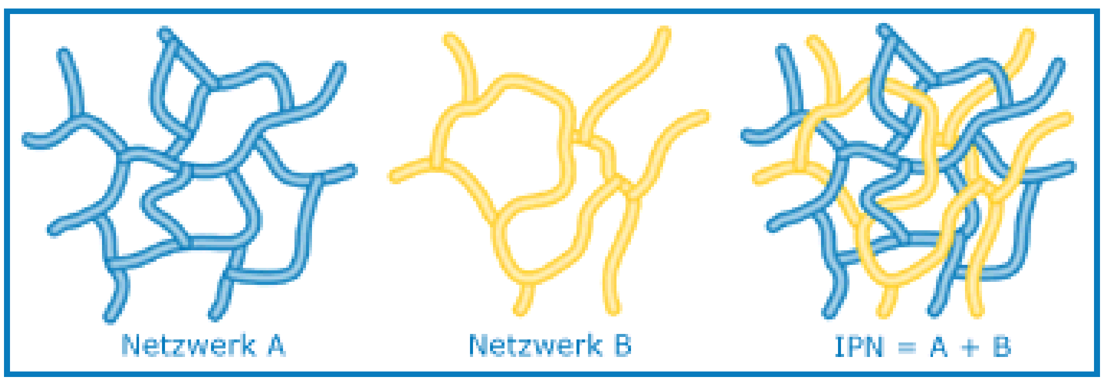
# Issue of hydrogel: mechanical weakness






*Gong et al. Adv. Mater.* **15**, 1155-1158

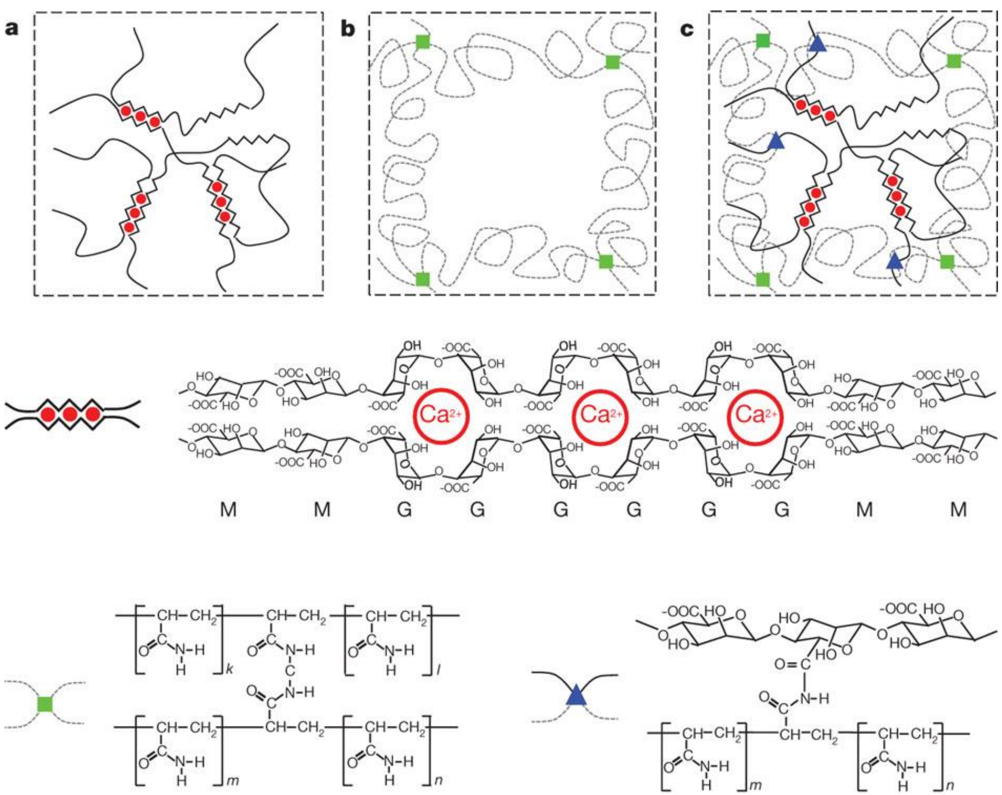
# Interpenetrating Polymer networks (IPN)



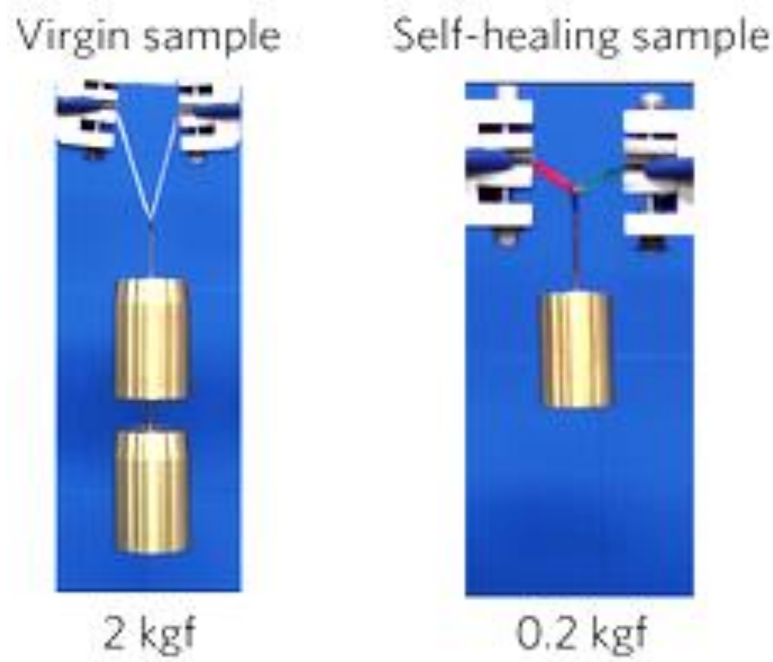

http://www.polymerics.de/technology/ipn_en.html

# Double network hydrogel

# Double network hydrogel




Suo et al. Nature, 489, 133

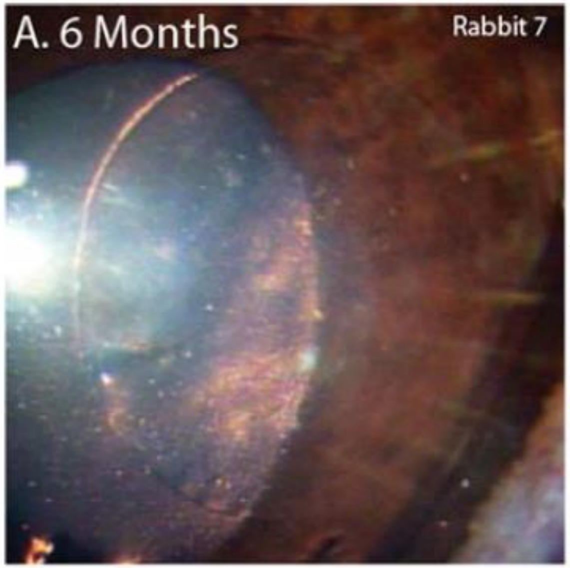


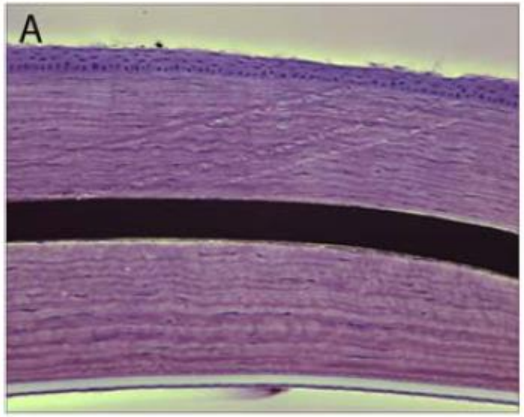

Gong et al. Nature Materials 12, 932

# Tough Hydrogel: Artificial Cornea

poly(ethylene glycol)

poly(acrylic acid)



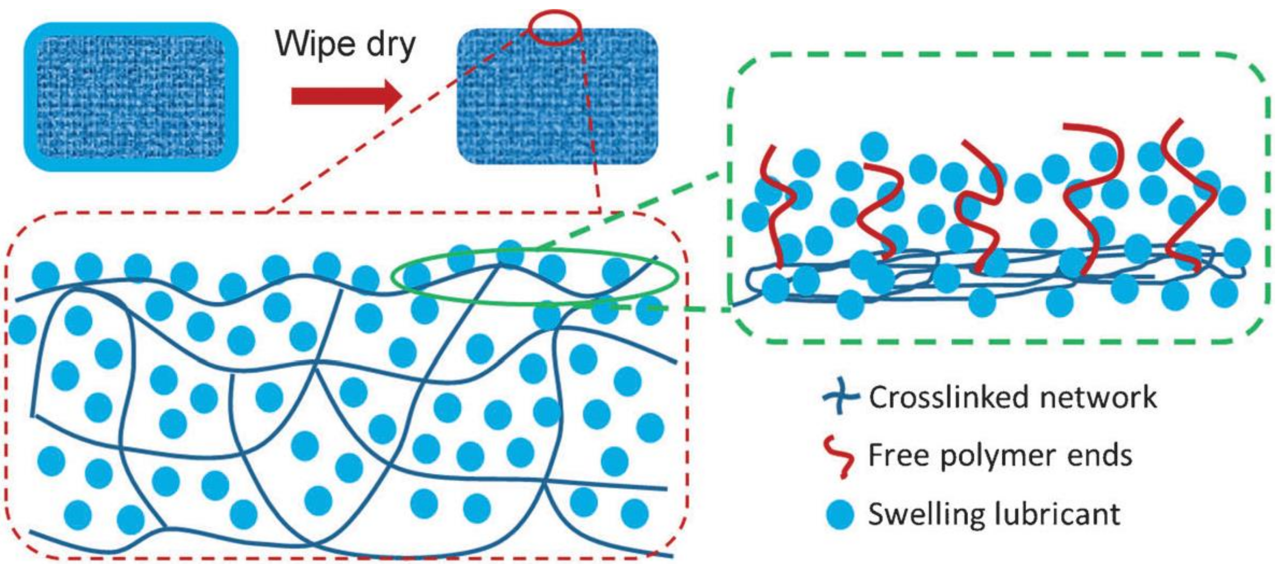



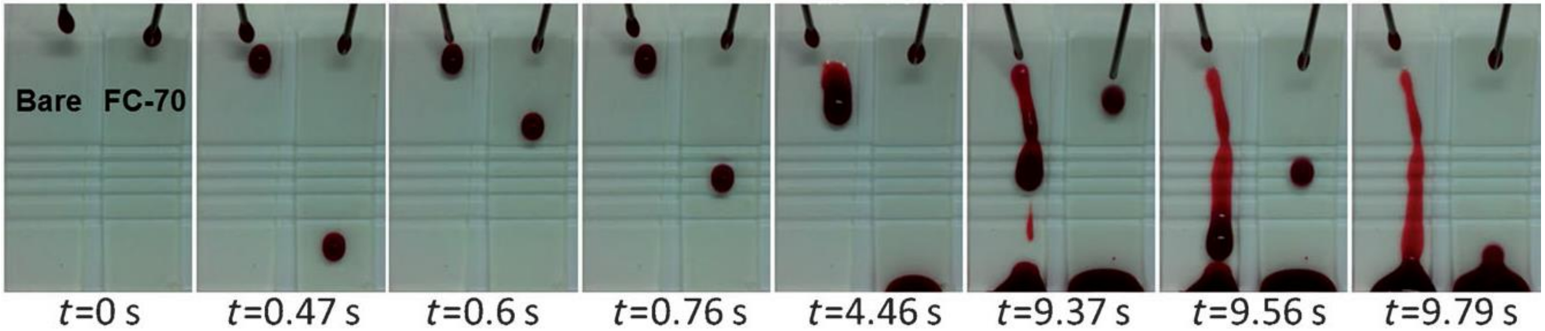

no inflammatory response or capsule formation around the hydrogel implant

L. Luo Zheng, V. Vanchinathan, R. Dalal, J. Noolandi, D. J. Waters, L. Hartmann, J. R. Cochran, C. W. Frank, C. Q. Yu, C. N. Ta, *Journal of Biomedical Materials Research Part A* ***2015, 103, 3157***

# Organo***gel***

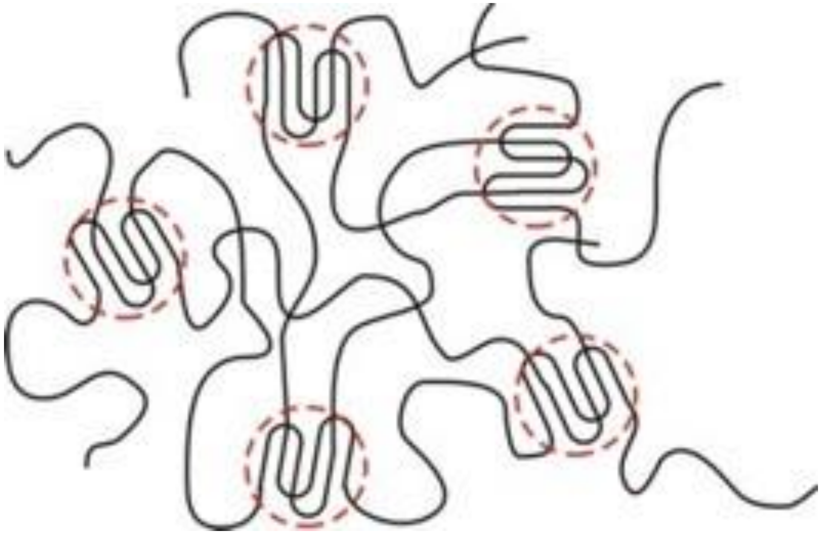
Low molecular weight gelator (molecular gel)



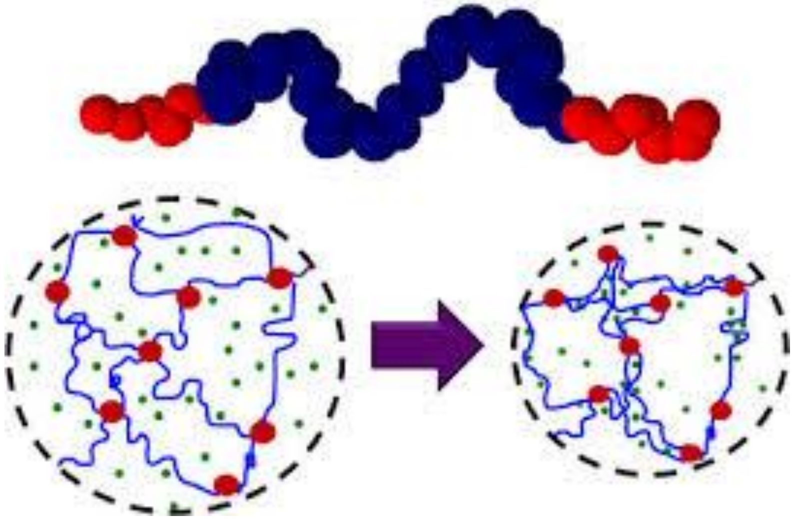




Aizenberg et al. Angew. Chem. Int. Ed, 53 2014

# Physical Polymer Networks



*Structure of the PVA network with crystallites acting as physical crosslinks*

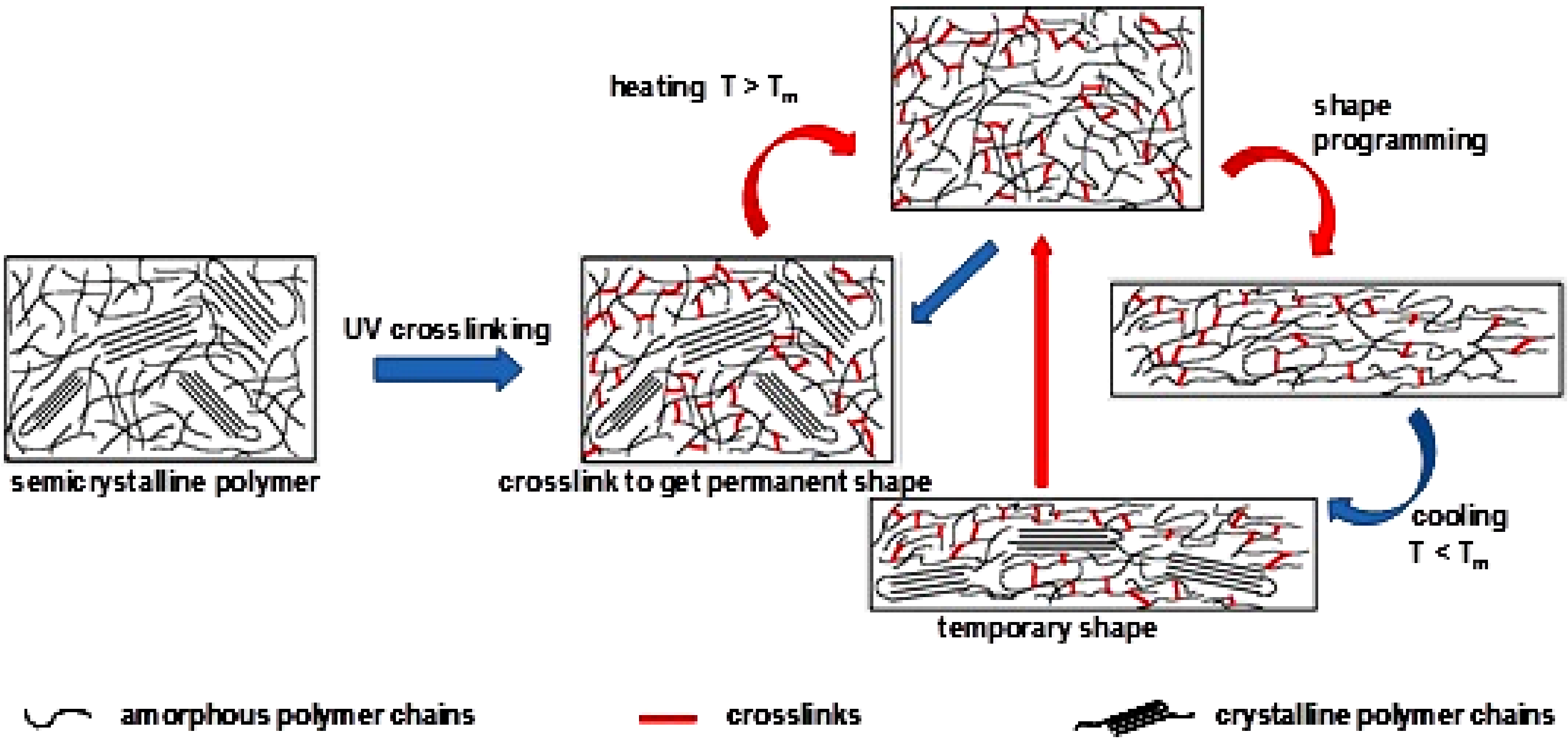


$T_g$

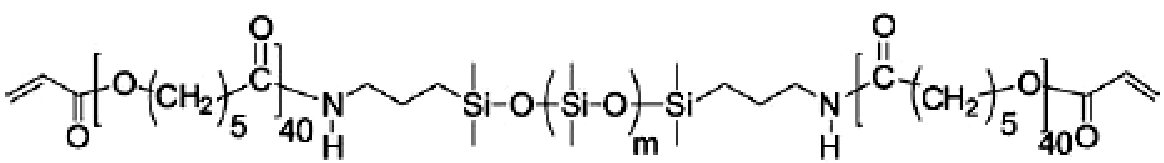
https://www.tvt.kit.edu/338_235.php

http://www.mrsec.northwestern.edu/content/highlights/triblock.htm

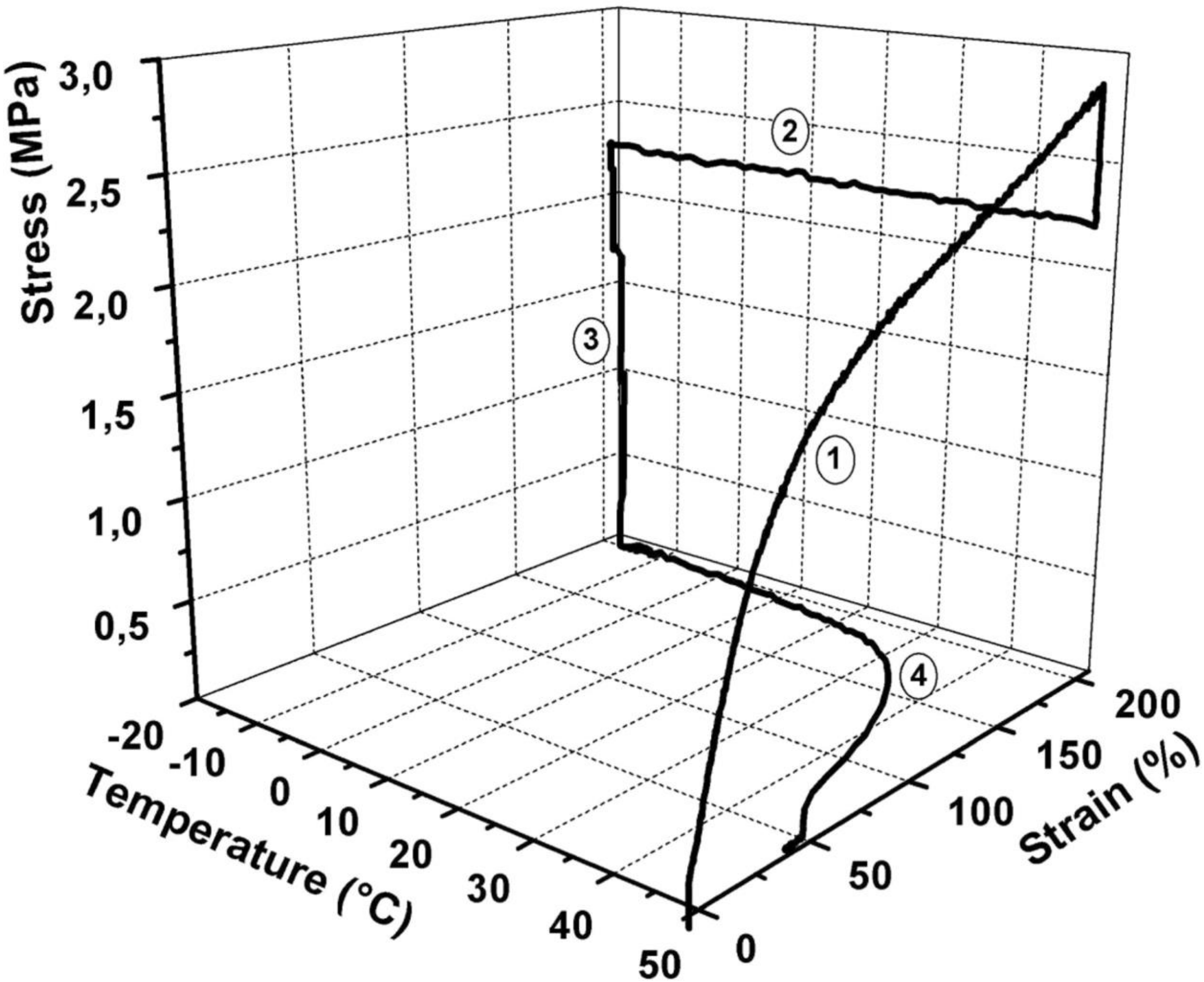
# Shape-memory materials




http://www.flintbox.com/public/project/23067/



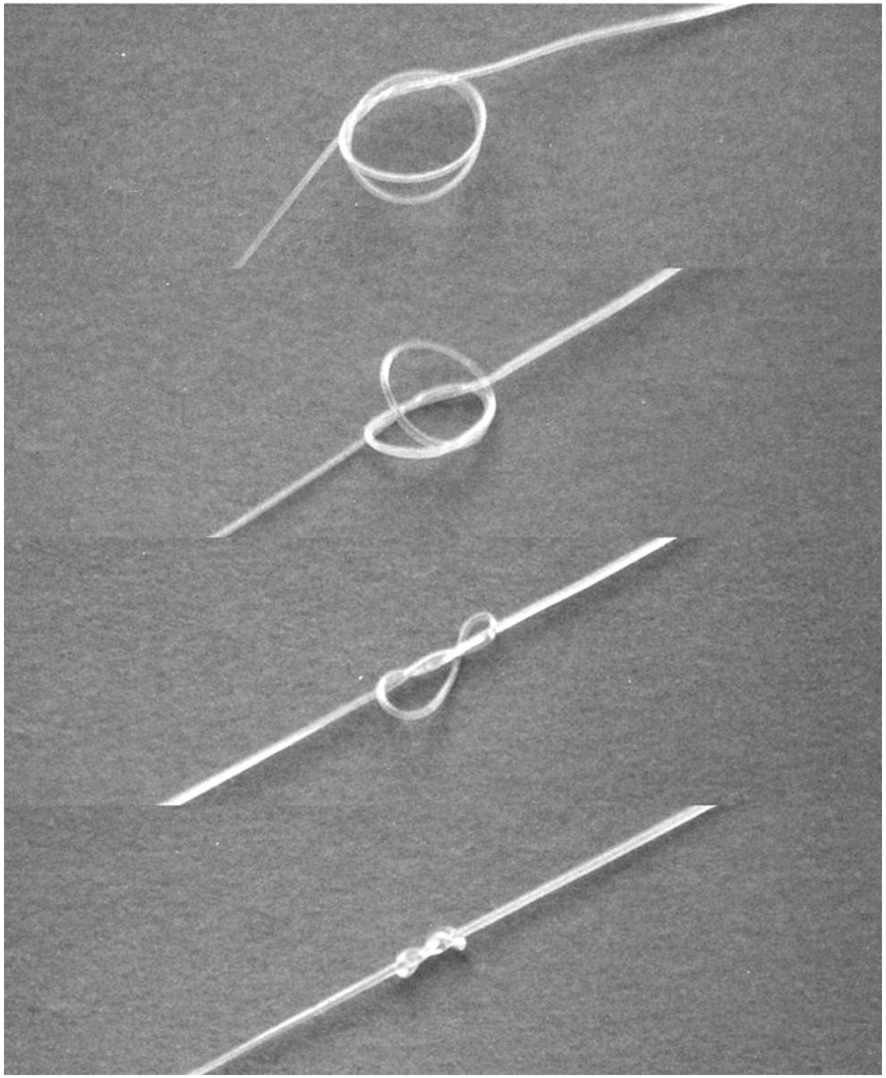
M. A. Grunlan, *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 754

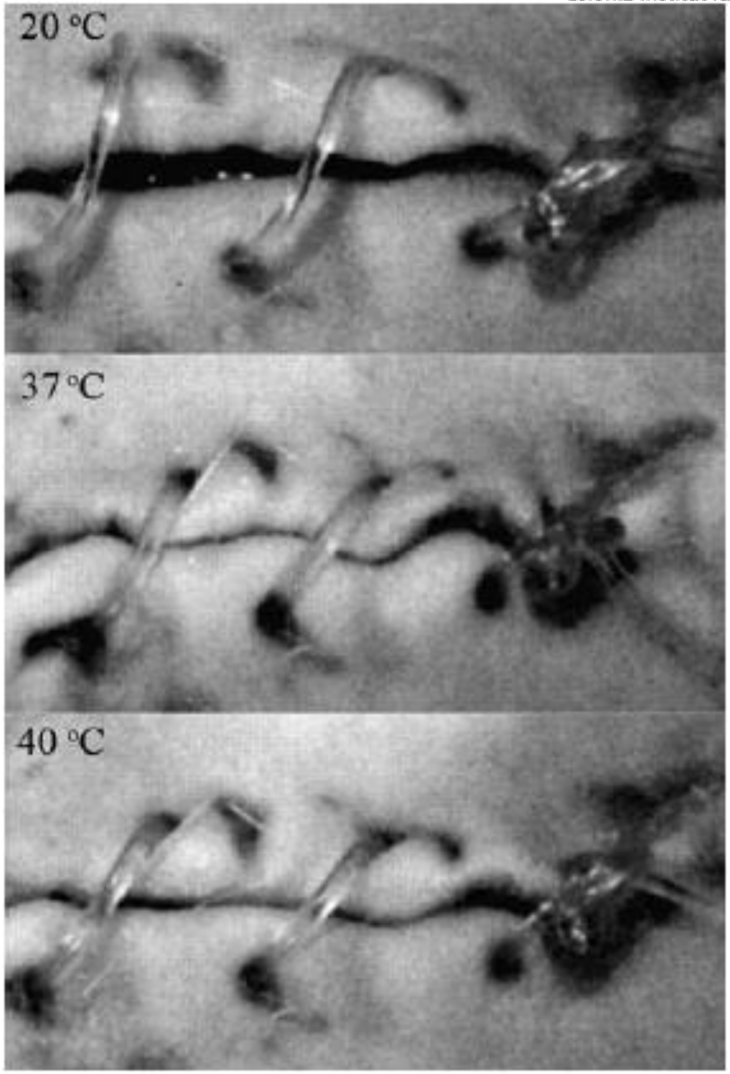



INM
Leibniz-Institut für Neue Materialien

A. Lendlein and R. Langer Science, 2002, 296, 1673

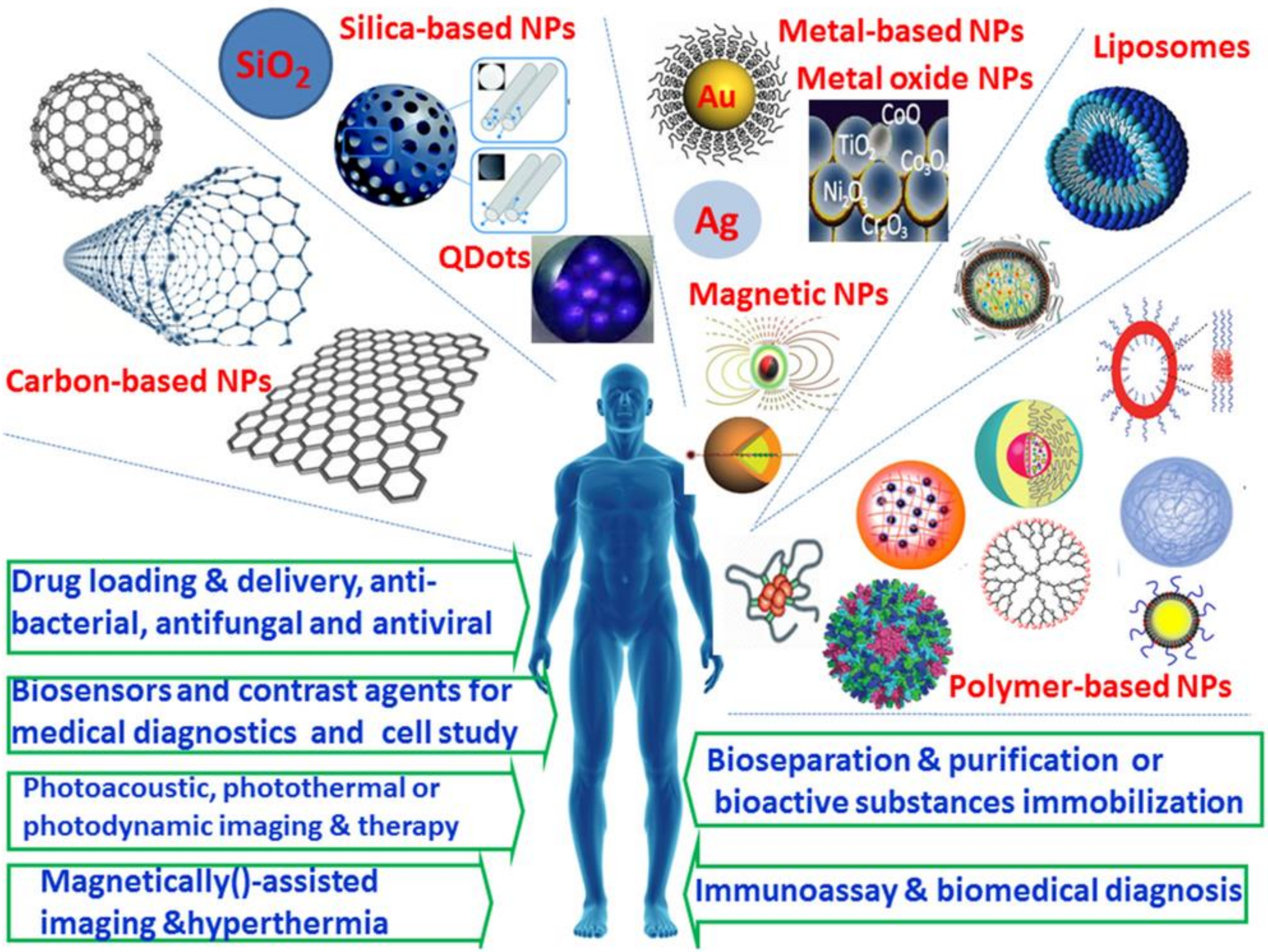
# Biodegradable SMP suture for wound closure



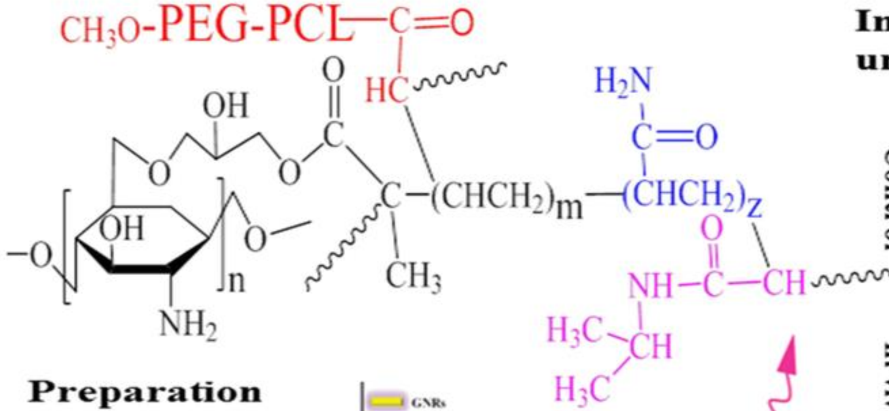



A. Lendlein and R. Langer Science, 2002, 296, 1673

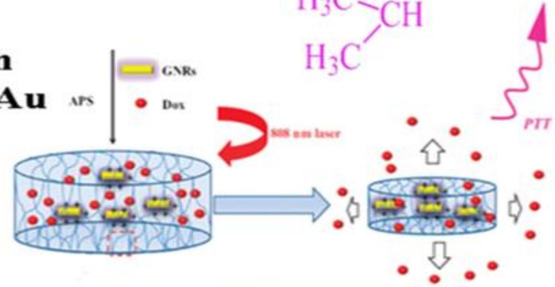
# Polymer composite




Fuli Zhao et al. *Nanomaterials* **2015**, *5*(4), 2054

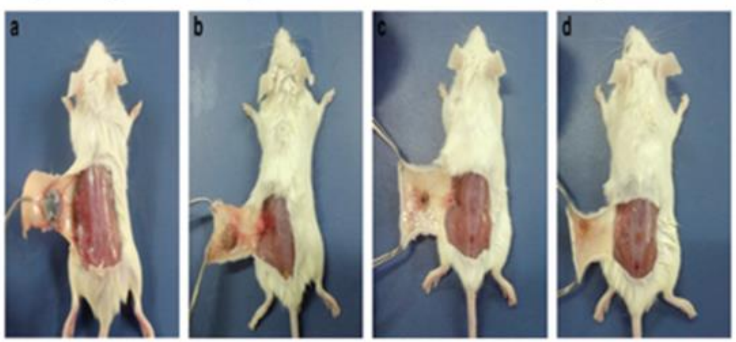



**Preparation of DOX/Au NPs embedded hydrogel**

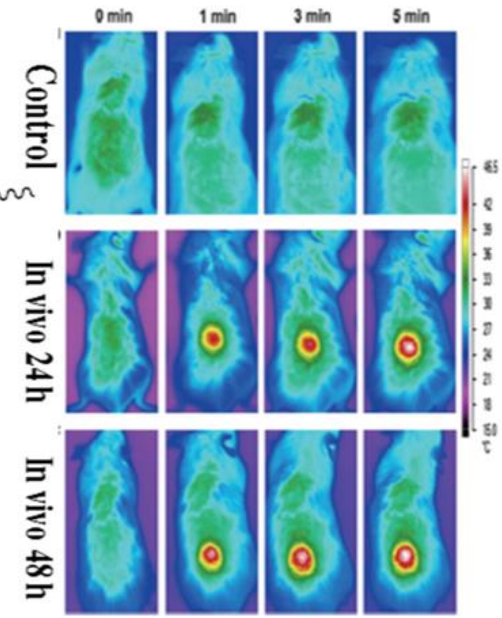



**Images of DOX/Au NPs embedded hydrogel before and after NIR irradiation**

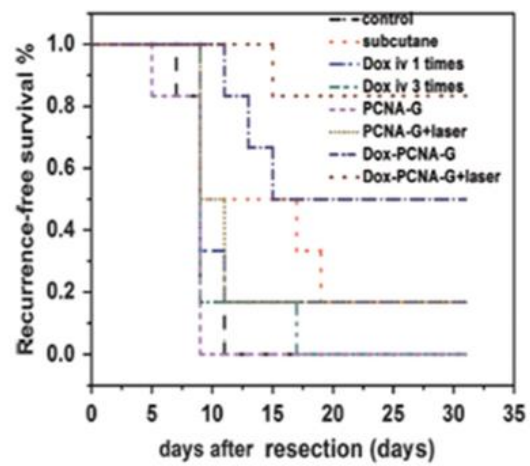

**In vivo persistence after implantation of hydrogel composites for different periods**




**Infrared thermal images under NIR irradiation**




**In vivo breast cancer locoregional recurrence**




Fuli Zhao et al. *Nanomaterials* **2015**, *5*(4), 2054

Now you should be able to:

- Basic concept of polymer network materials (PNM) and some examples

  Elasticity (elastic), Viscoelasticity (viscoelastic) , crosslinking degree…

- What are the requirements for PNM to be used for biomedicine.

  Biocompatible, biostability, biodegradation, bioresorption…

- Several kinds of PNM have been used in biomedical application

  Elastomer (heart valve), hydrogel (drug delivery, artificial tissue/cornea etc), SMP (suture), polymer composite …

- Several aspects of biomedical application involving PNM and the working mechanism of PNM