Gel e Materiali termoresponsivi

PNIPAM et al

Gels

- Definition of a gel- a biphasic material with a solid phase which is structured like a loose network and a liquid phase. The liquid phase adheres strongly to the solid network forming a compression resistant material with a non-zero elastic modulus.
- When the liquid is water it is known as a hydrogel.
- Several hydrogels exhibit some form of responsivity.
- They have a similar consistency to biological tissues

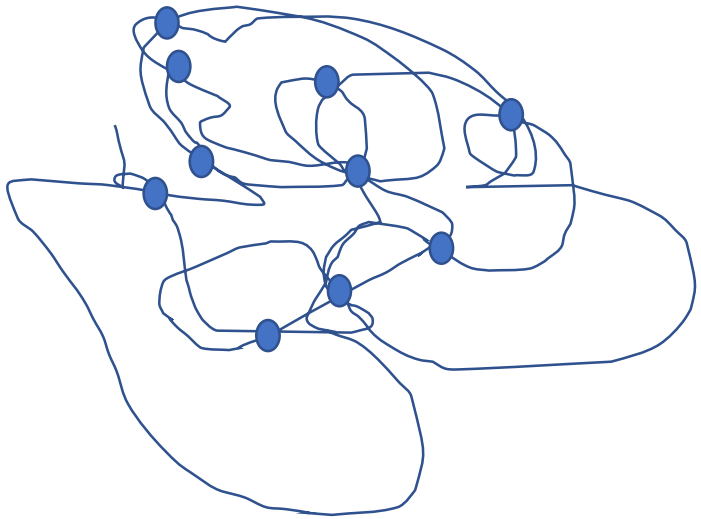
Integrita’ 3D viene mantenuto dai cross links

Cross link fisico

- Junzioni transient
- Legami ionici
- Legami idrogeno
- Interazioni idrofobiche

Cross link chimico

- Junzioni permanenti
- covalenti



Physically crosslinked hydrogels
• Ionic interactions (alginate etc.)
• Hydrophobic interactions (PEO–PPO–PEO etc.)
• Hydrogen bonding interactions (PAAc etc.)
• Stereocomplexation (enantiomeric lactic acid etc.)
• Supramolecular chemistry (inclusion complex etc.)

Chemically crosslinked hydrogels
• Polymerization (acryloyl group etc.)
• Radiation (γ-ray etc.)
• Small-molecule crosslinking (glutaraldehyde etc.)
• Polymer–polymer crosslinking (condensation reaction etc.)

- FISICO
- Instabili
- Piu’ biocompatibile
- Piu degradabili

- CHIMICO
- Stabili
- Reticolante tossico
- Meno degradabili

Fisico- diversi meccanismi per x-linking

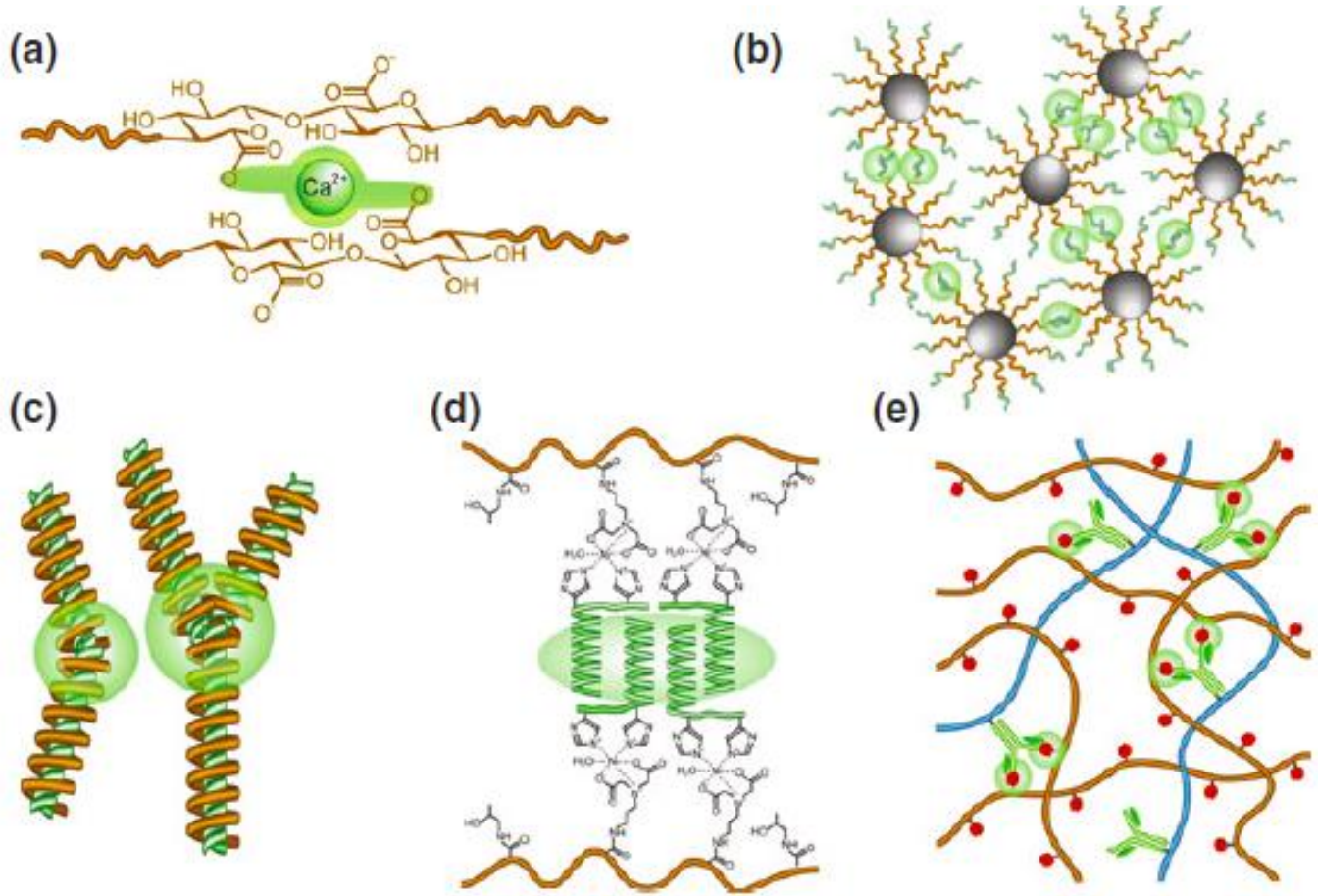


Fig. 2.2 Schematic of methods for formation of physically crosslinked hydrogels via. **a** Ionic interactions, **b** hydrophobic interactions, **c** self-assembling of stereocomplex formation, **d** coiled-coil interactions, **e** specific molecular recognition

X-links chimici-

Iniziatore
catalista

Gruppi reattivi

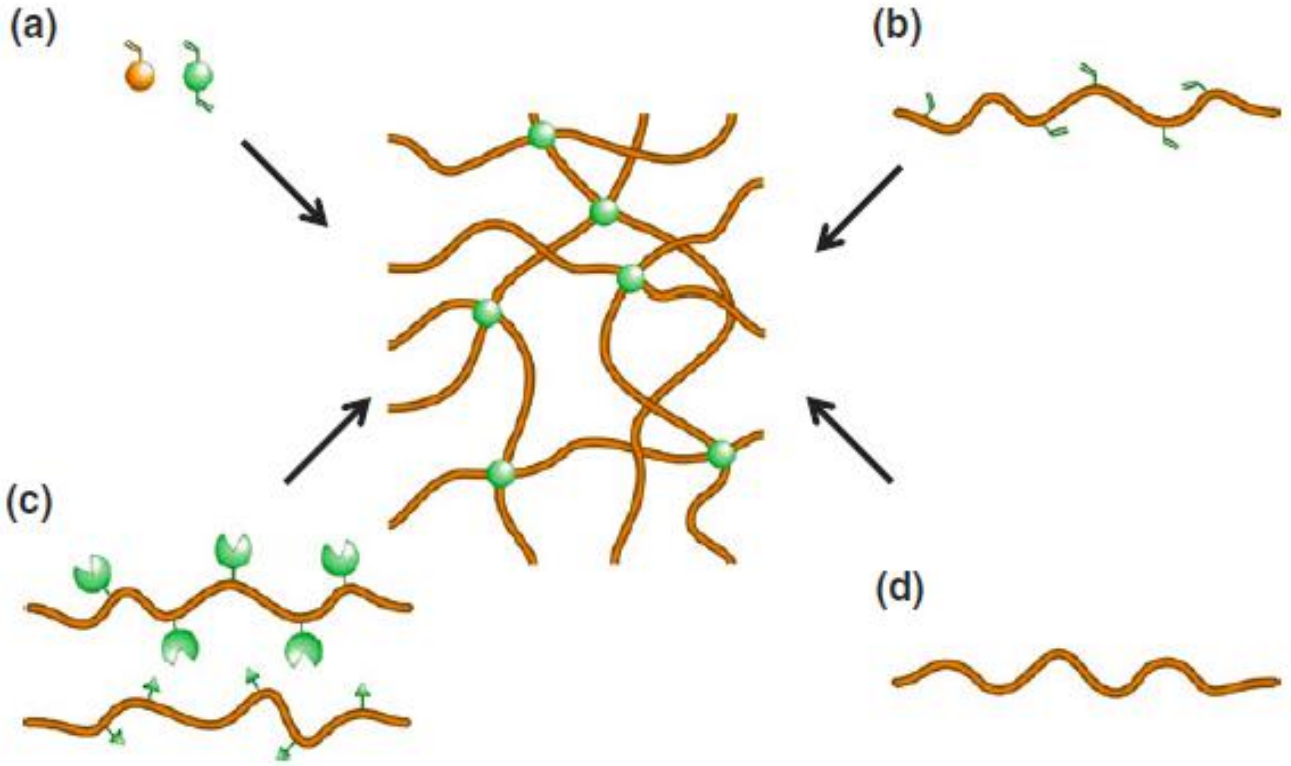
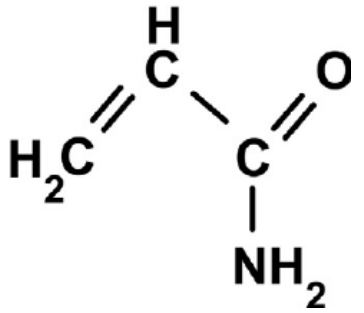


Fig. 2.3 Schematic of methods for formation of chemically crosslinked hydrogels by radical polymerization of **a** vinyl monomers and **b** macromonomers **c** reaction of pendant functional groups, and **d** high-energy radiation

Eg COOH e NH2 con glutaraldeide

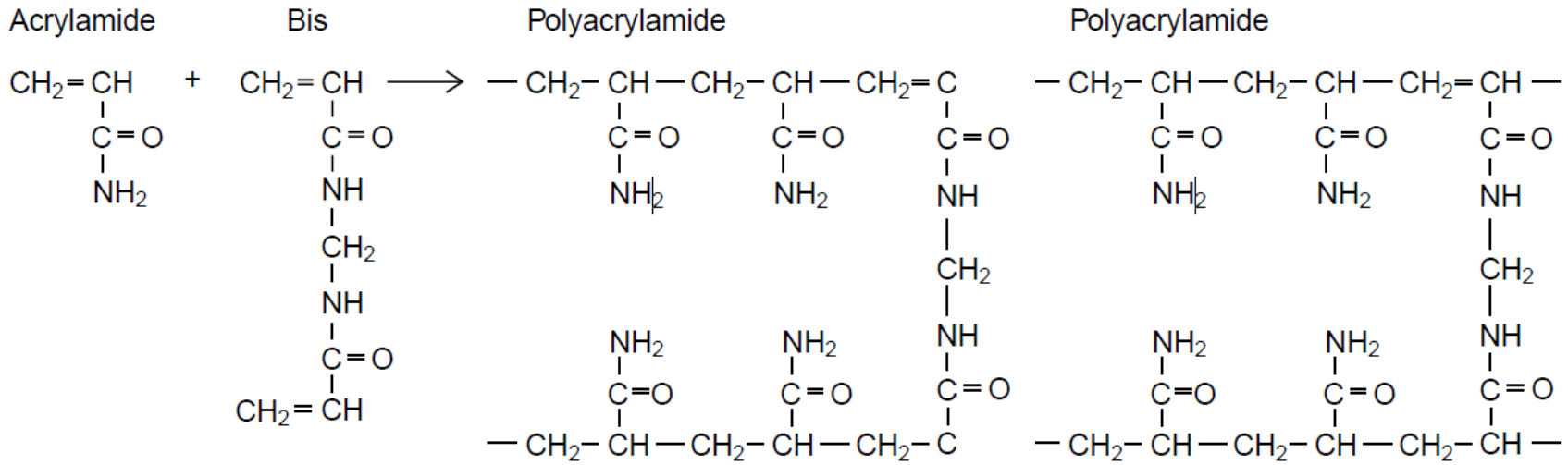
Uv e' in grado
di legare
gruppi acrilici



Polymers

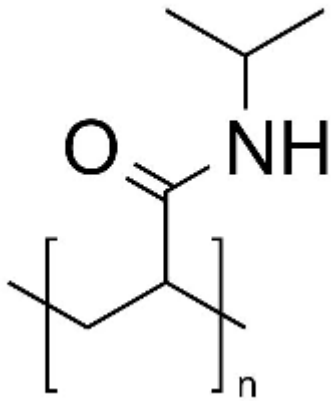
- The development of polymer chemistry with precise control of the molecular chain has contributed to the development of smart materials.
- Precise polymerization is a very important technology in designing actual materials with higher functions, or improve and tune performance.
- PEG forms the basis of several synthetic biomedical polymers $HOCH_2CH_2OH + n(CH_2CH_2O) \rightarrow HO(CH_2CH_2O)_{n+1}H$

An important gel: poly(acrylamide-bisacrylamide)



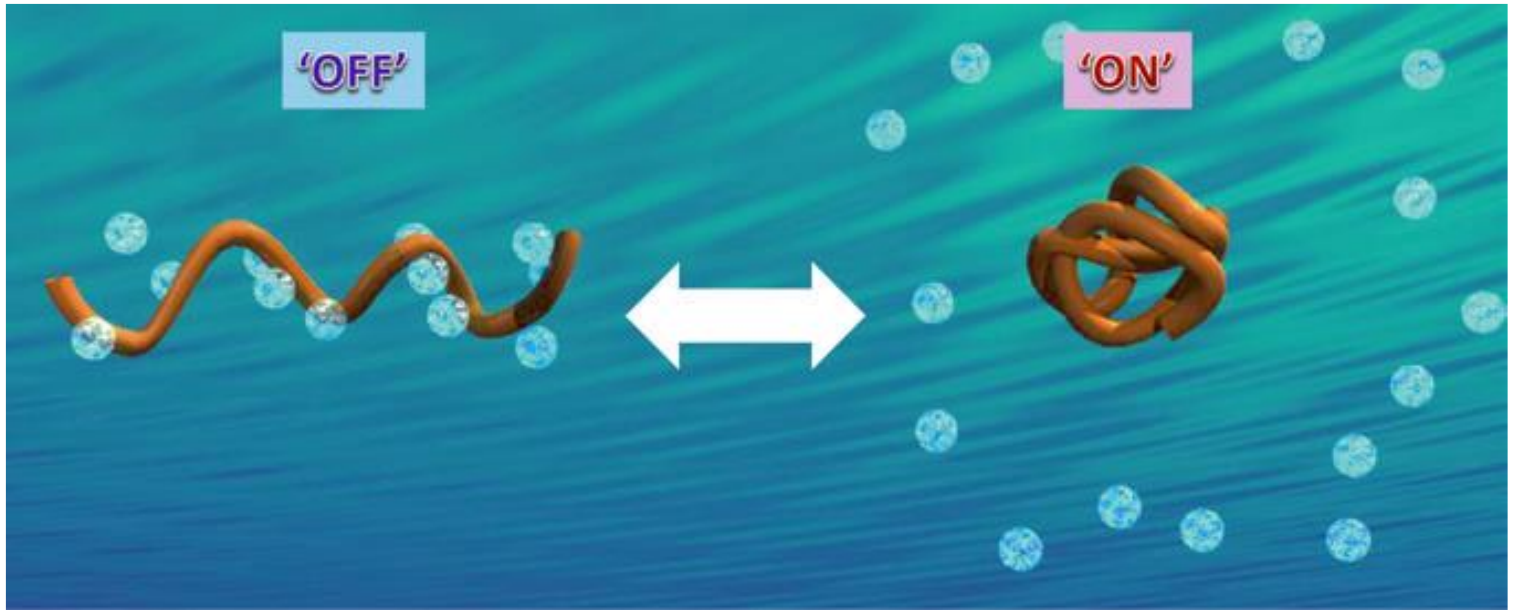
Reaction by free radical polymerisation. The cross-linking of the network depends on the ratio of acrylamide to bisacrylamide. Water forms strong hydrogen bonds with the amine groups and the gel is very stable.

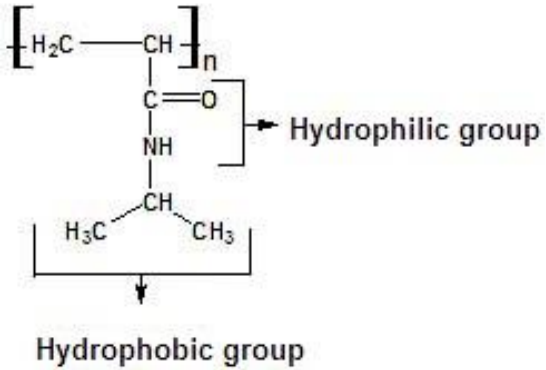
Poly(N-isopropylacrylamide) (PNiPAM)

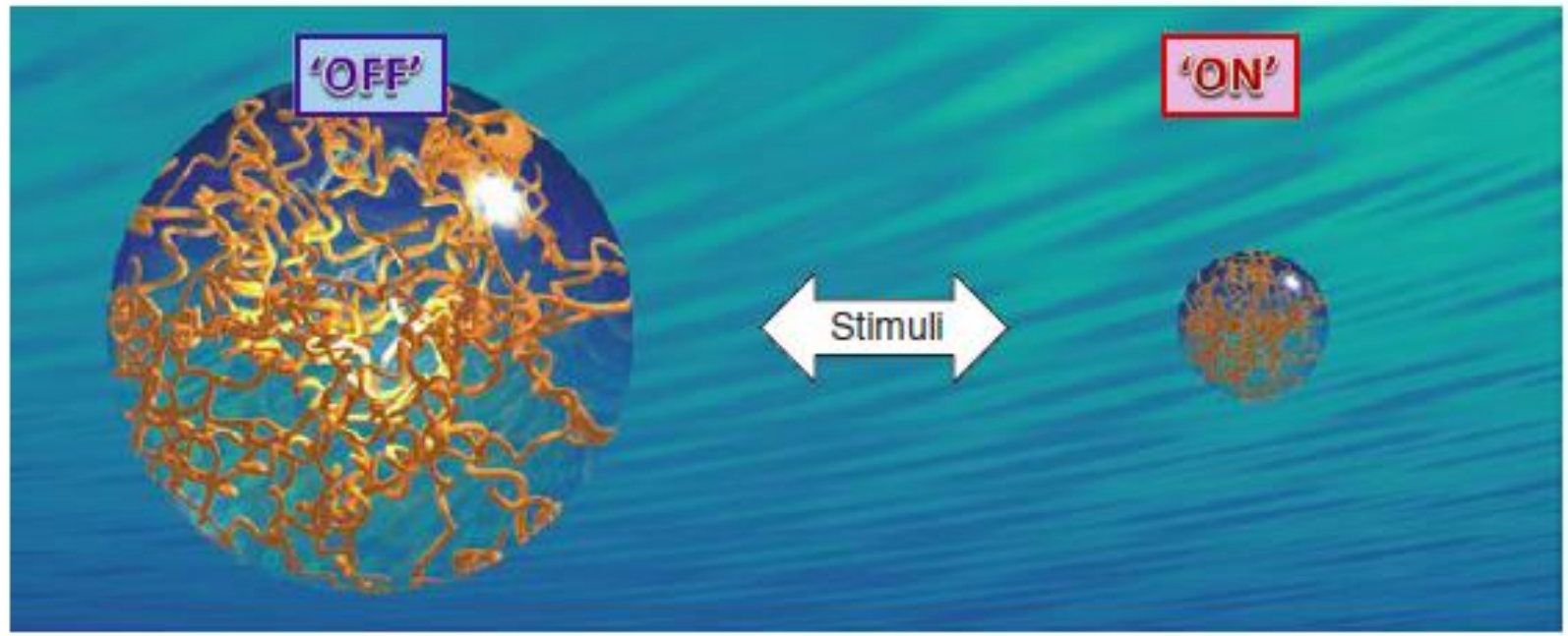


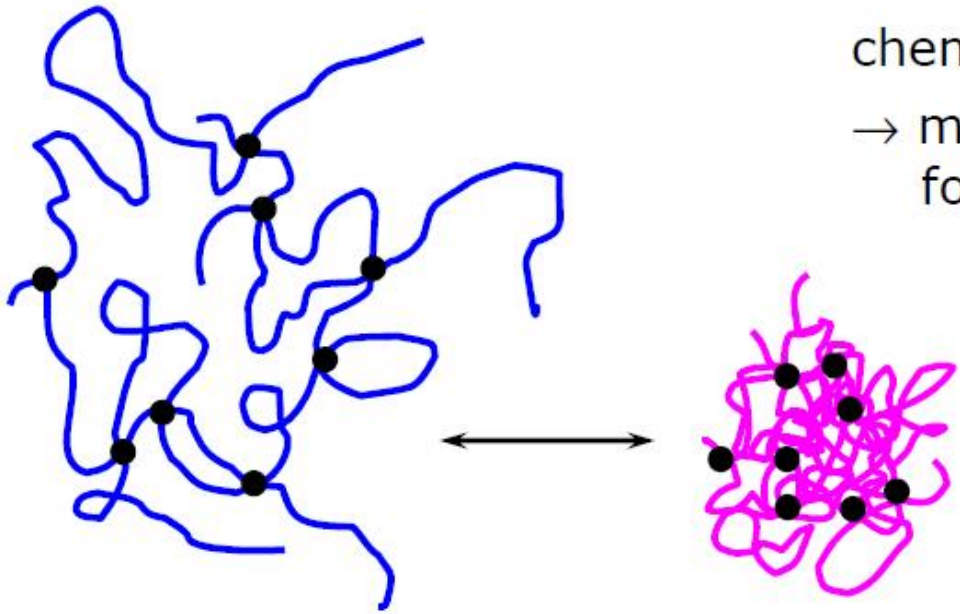
Made in 1956

PNIPAM: an important T sensitive hydrogel



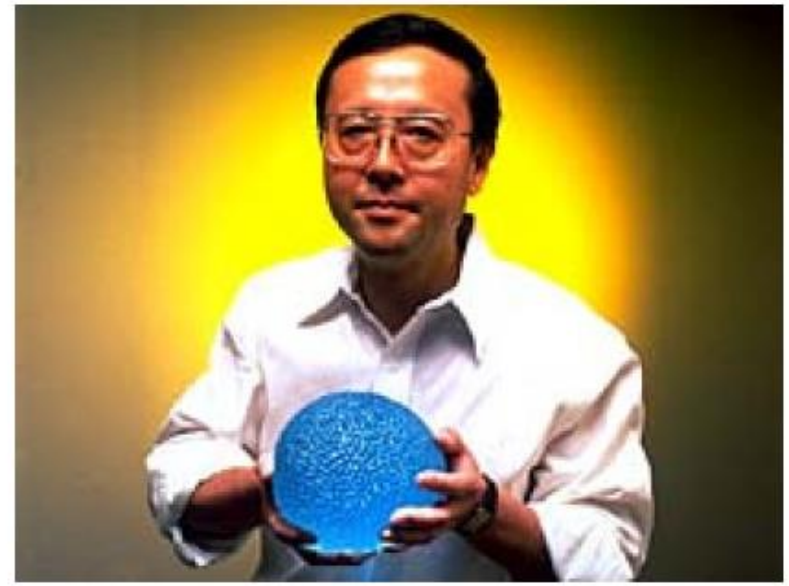



'OFF'
'ON'
Stimuli



chemical cross-linking

→ macroscopic volume change
for very small temperature change

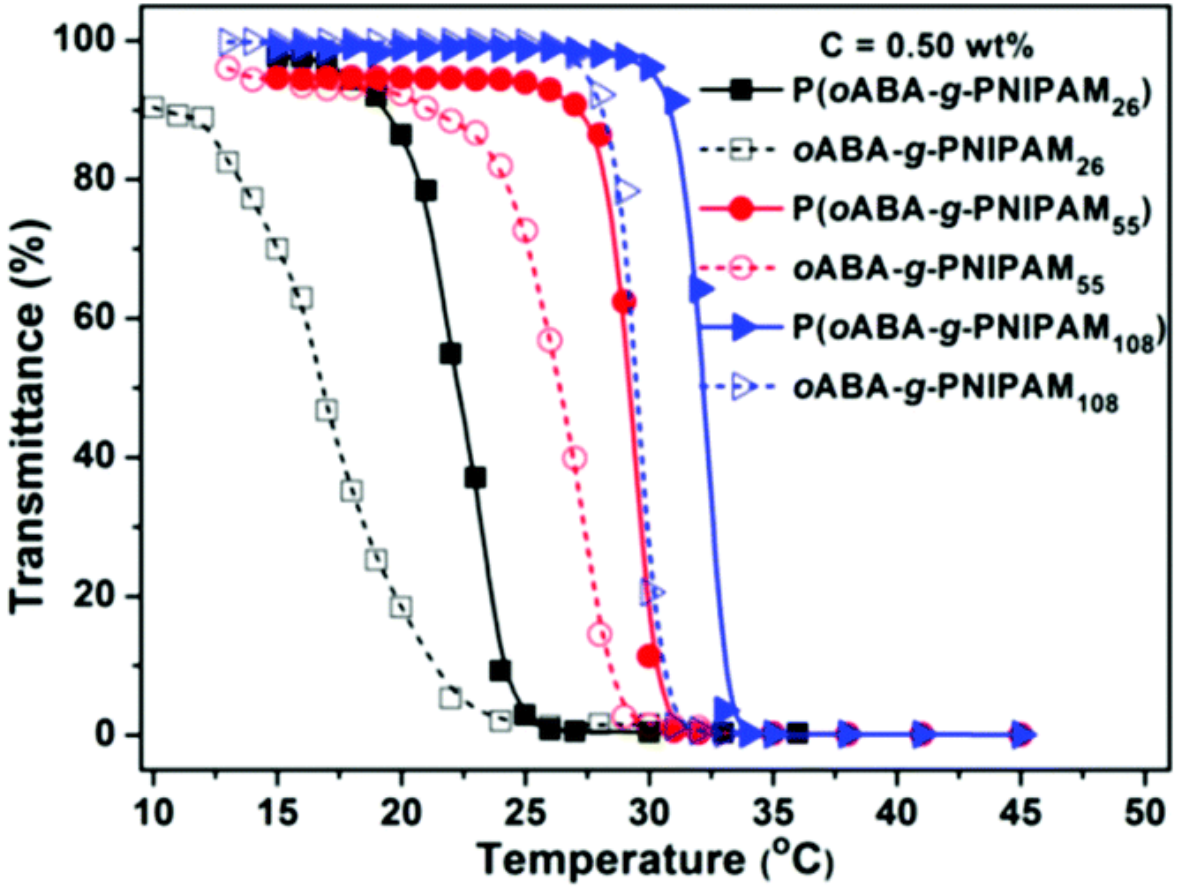


T. Tanaka
Discover Magazine 1996

Abrupt change in properties-

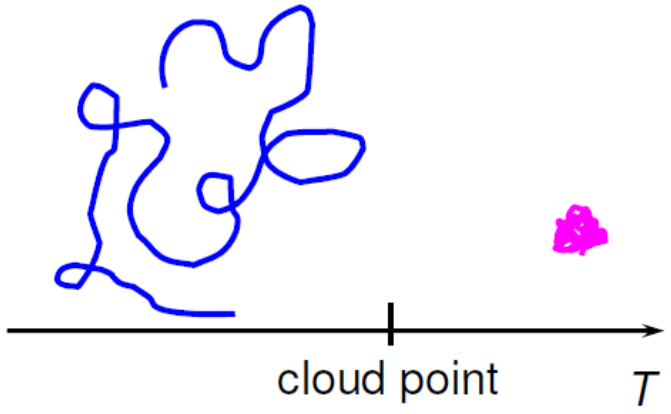
$T < 32°C$

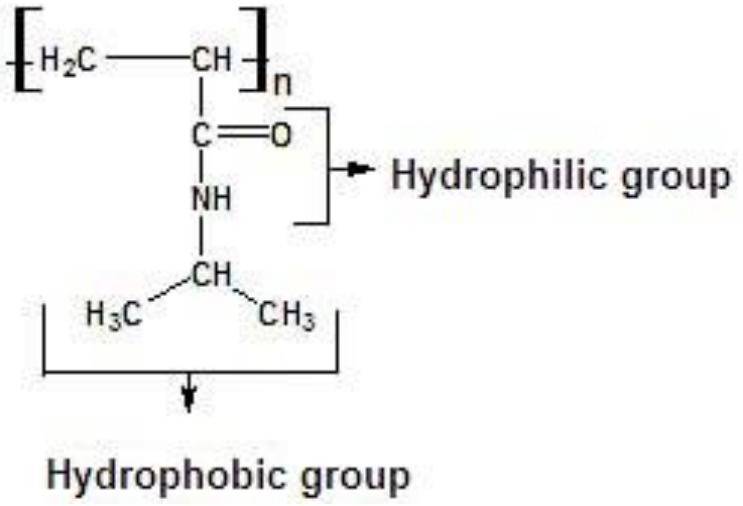
$T > 32°C$



Amino benzyl alcohol

Coil to globule transformation



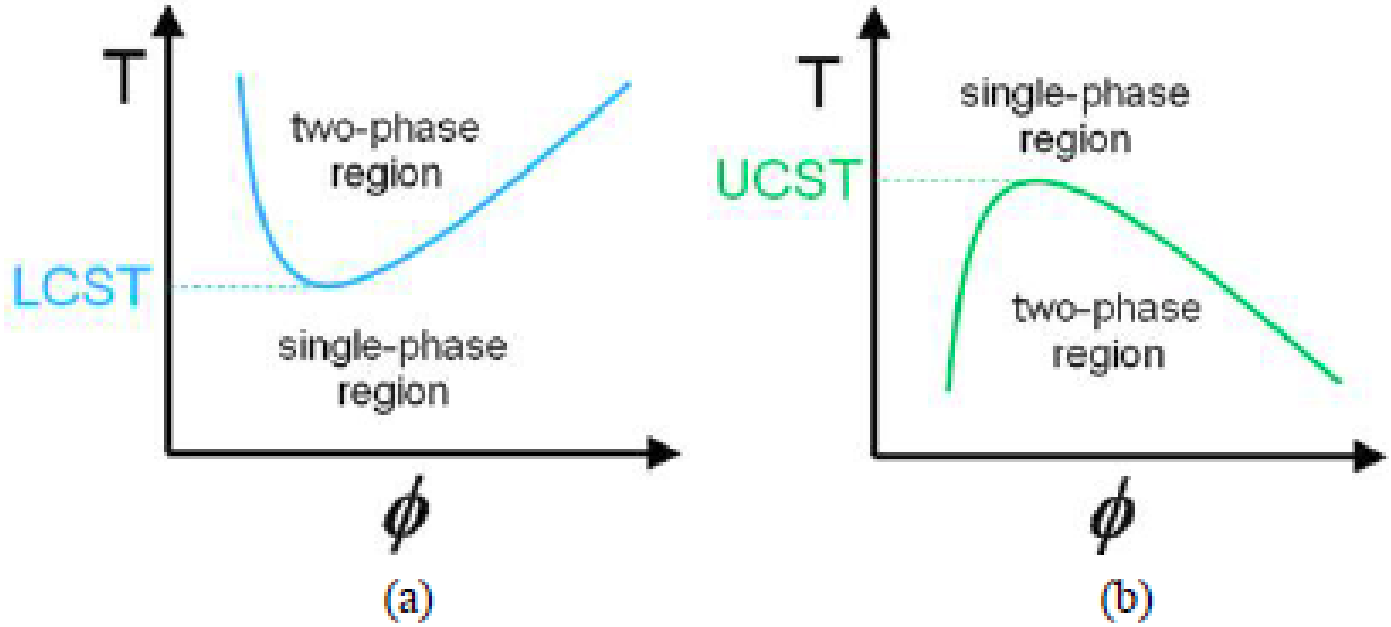


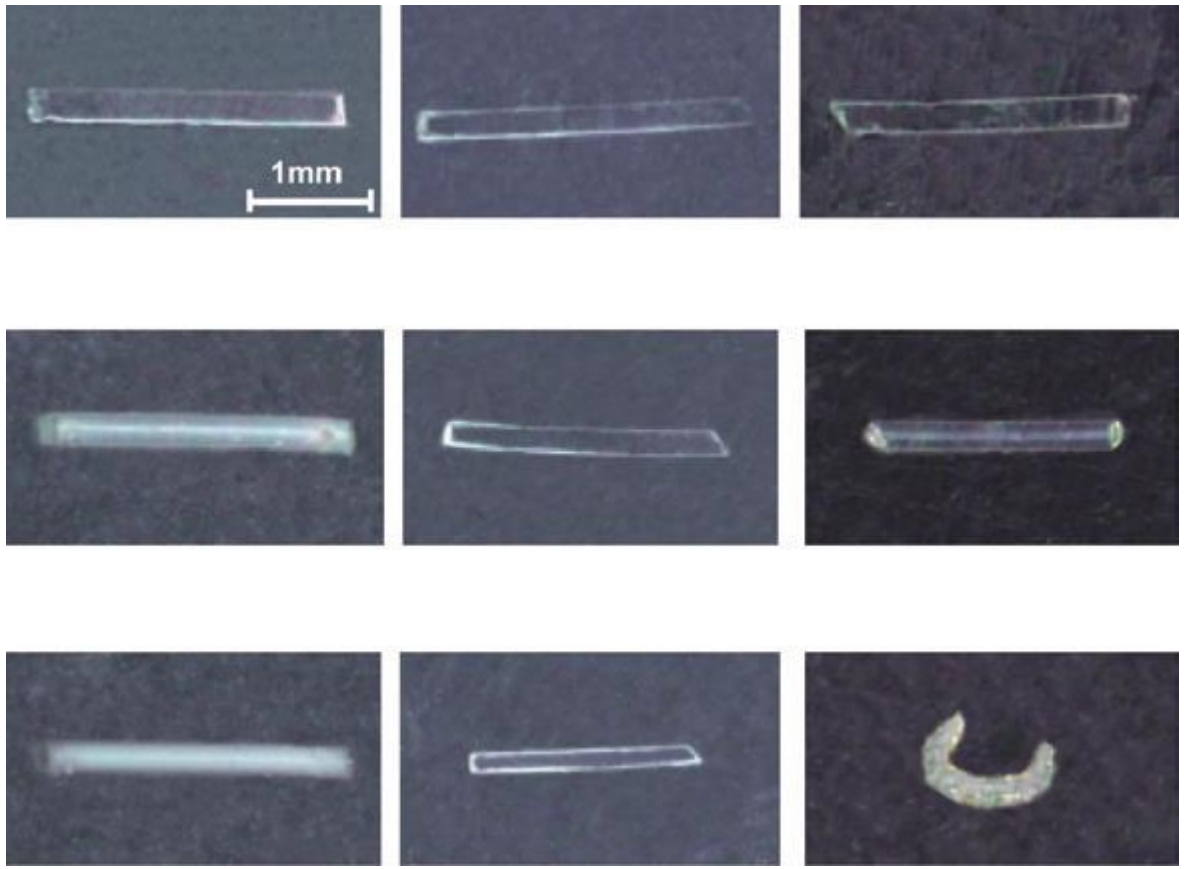
A bassa T sono favoriti I legami idrogeno

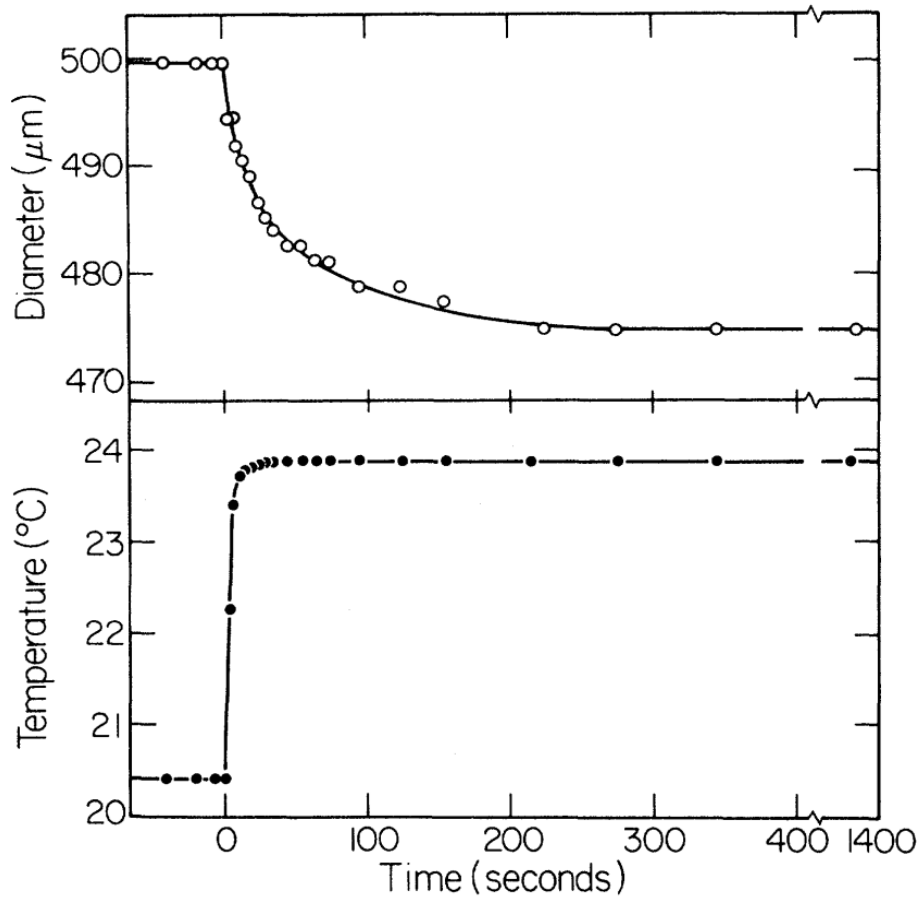
Sono intelligenti perche il cambiamento di forma/volume/trasparenza e' elevato
Non come espanzione termica 'normale'

2 tipi di comportamento: LCST e UCST

Figure 1. Temperature *vs.* polymer volume fraction, ϕ. Schematic illustration of phase diagrams for polymer solution (**a**) lower critical solution temperature (LCST) behavior and (**b**) upper critical solution temperature (UCST) behavior.

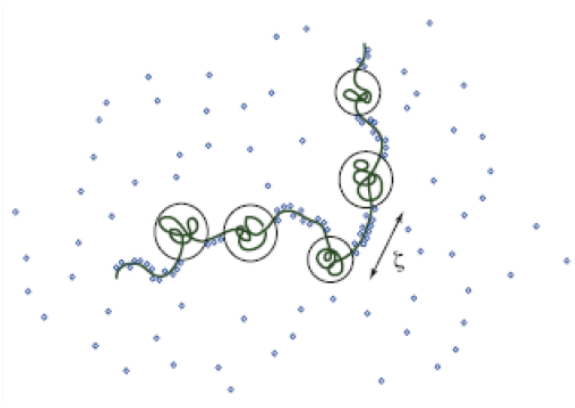



1mm


Diameter (μm)
500
490
480
470
Temperature (°C)
24
23
22
21
20
0
100
200
300
400
1400
Time (seconds)

Il meccanismo

Interaction of water/solvent with PNIPAM



PNIPAM in H_2O: H_2O molecules bind to PNIPAM in long sequences

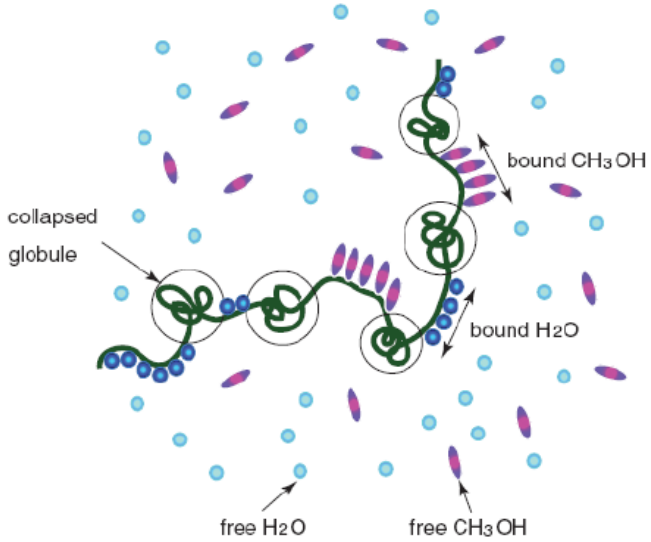
→ hydration is cooperative phenomenon

steric reason:

if one H_2O binds to the polar part of the side group, space is created

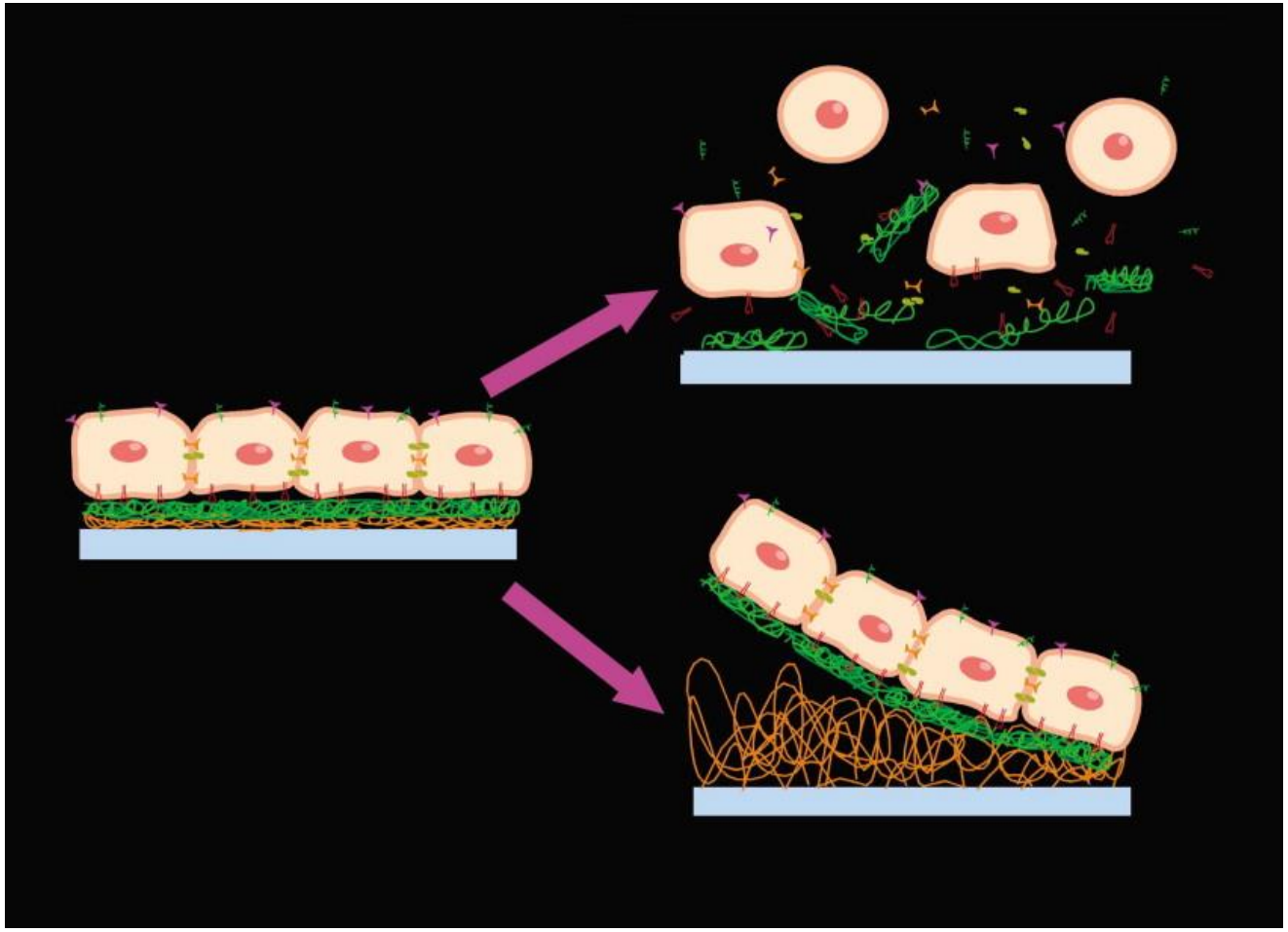
→ for next H_2O molecule, it is favorable to bind to the PNIPAM monomer which is next to the first H_2O

F. Tanaka et al., *J. Phys.: Cond. Matter* **23**, 284105 (2011).

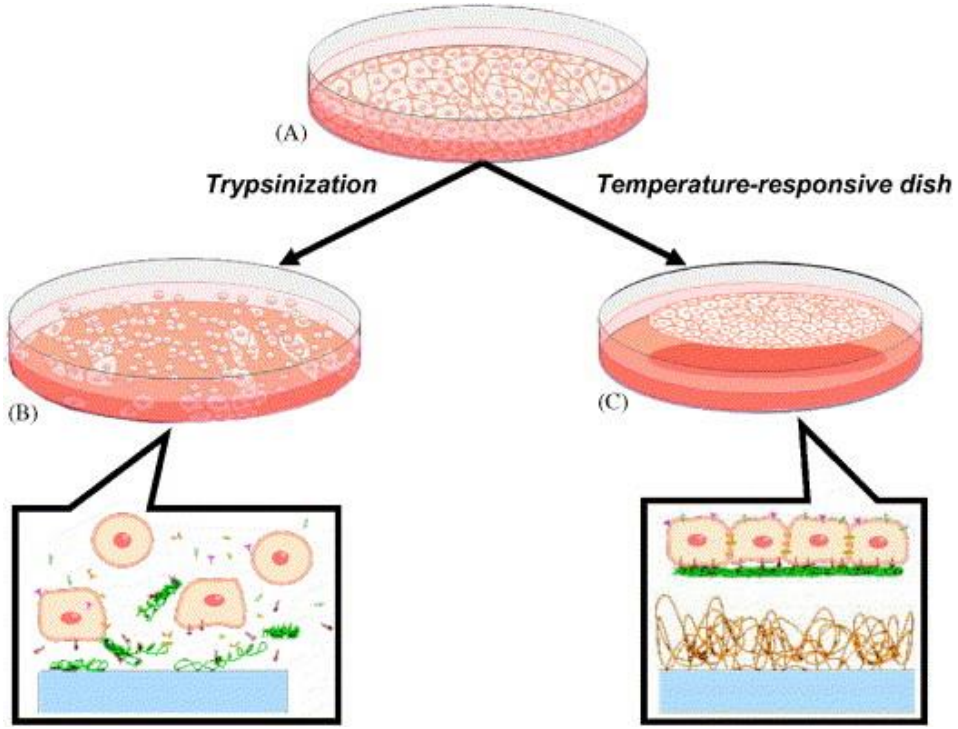


cononsolvency

Applications: Cell sheet engineering



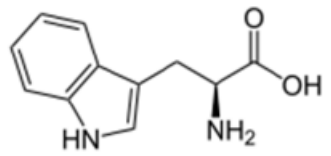
T Okano: PNIPAM



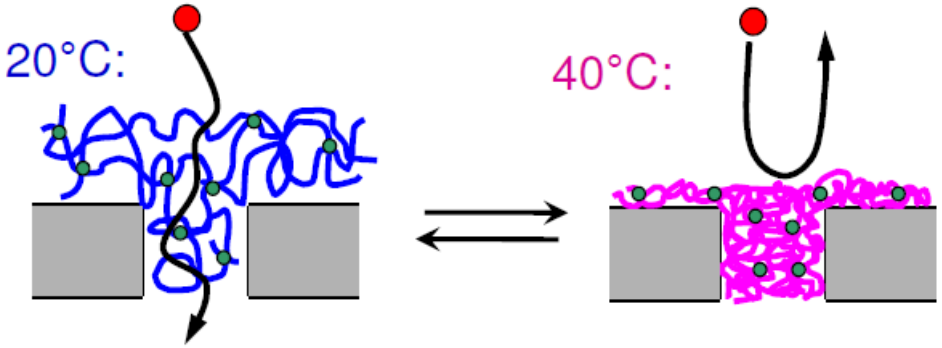
N. Yamada, T. Okano, H. Sakai, F. Karikusa, Y. Sawasaki, Y. Sakurai
Thermo-responsive polymeric surfaces; control of attachment and detachment of cultured cells
Makromol Chem Rapid Commun, 11 (1990), pp. 571–576

T. Okano, N. Yamada, H. Sakai, Y. Sakurai
A novel recovery system for cultured cells using plasma-treated polystyrene dishes grafted with poly(N-isopropylacrylamide)
J Biomed Mater Res, 27 (10) (1993), pp. 1243–1251

Applications: switchable valves

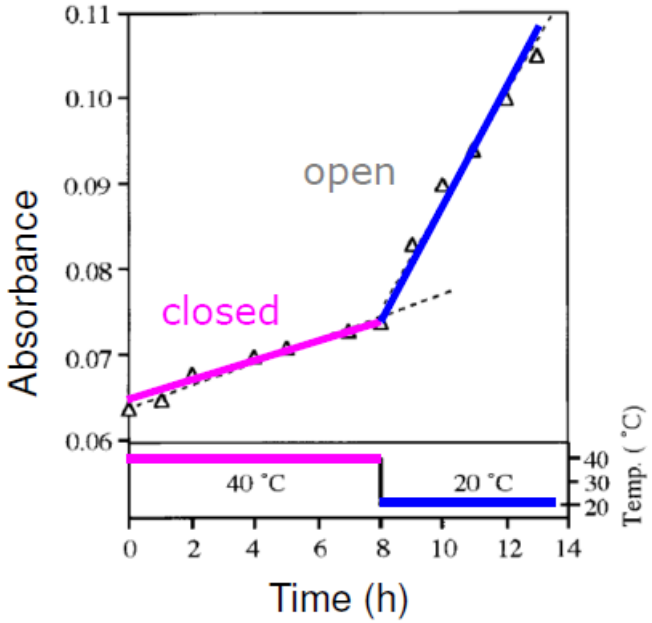


test molecule:
tryptophan (TRY)



swollen network
→ permeable for TRY

collapsed network
→ less permeable for TRY



strongly temperature-dependent permeability
→ applications in microfluidics, lab on a chip, …

Y.S. Park et al., *Langmuir* **14**, 910 (1998)

Stop here

Leggere il paper fino a p. 1224, sect 3.11 e rispondere

1. Da che fattori dipende la LCST
2. Scrivere un equazione che descrive drug release da una capsula nello spazio
3. Perche' usare polimeri termoresponsivi per drug delivery?
4. Per fare un scaffold inettabile, che diagramma fase (gel-solido) vs T deve avere?
5. Fare uno sketch di un interpenetrating network.
6. Graficare solubilita', trasparenza, modulo elastico, viscosita' e volume di un gel termoresponsivo versus Temperatura del PNIPAM.
7. Se aggiungo un monomero idrofobico nella rete di PNIPAM, la LCST aumenta o diminuisce?