Polimeri pH sensibili

Ricordiamo pH e pKa

- pKa e’ un numero che ci dice quanto un acido e’ dissociato.

$$pH = -\log_{10}([H+])$$

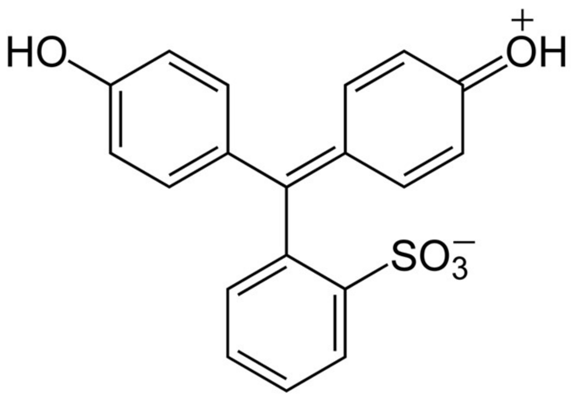
$$Ka = \frac{[A-][H+]}{[HA]}$$

$$pKa = -\log_{10}(Ka)$$

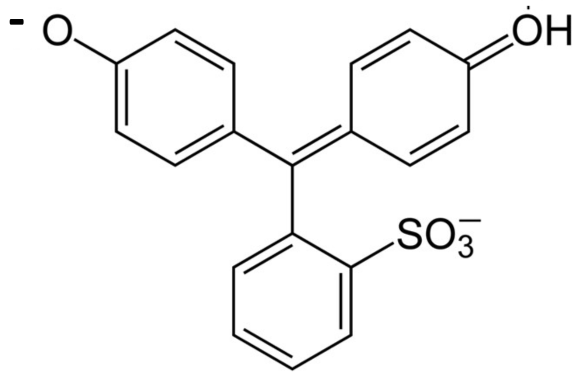
$$pKa = pH + \log_{10}\left(\frac{[A-]}{[HA]}\right)$$ Henderson-Hasselbalch

- C’e’ anche il pKb per una base.

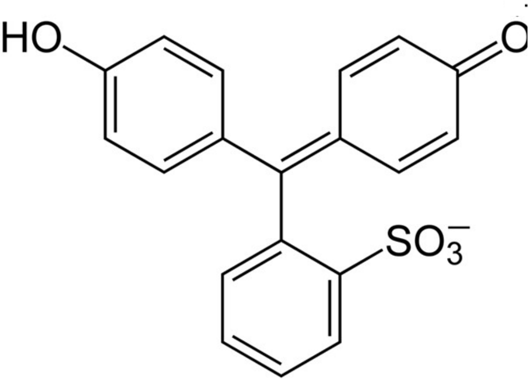
Una molecola pH sensibile: rosso fenolo



pH <1.2, orange red

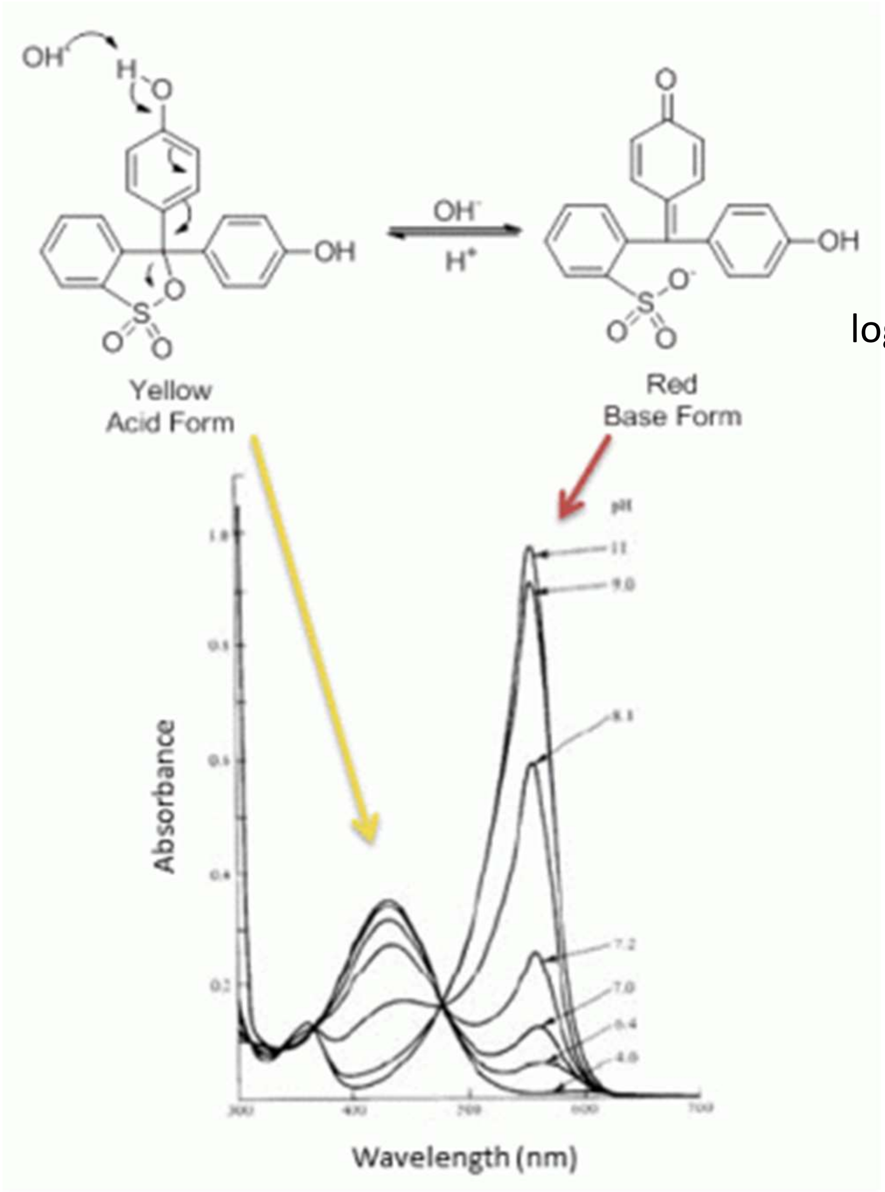


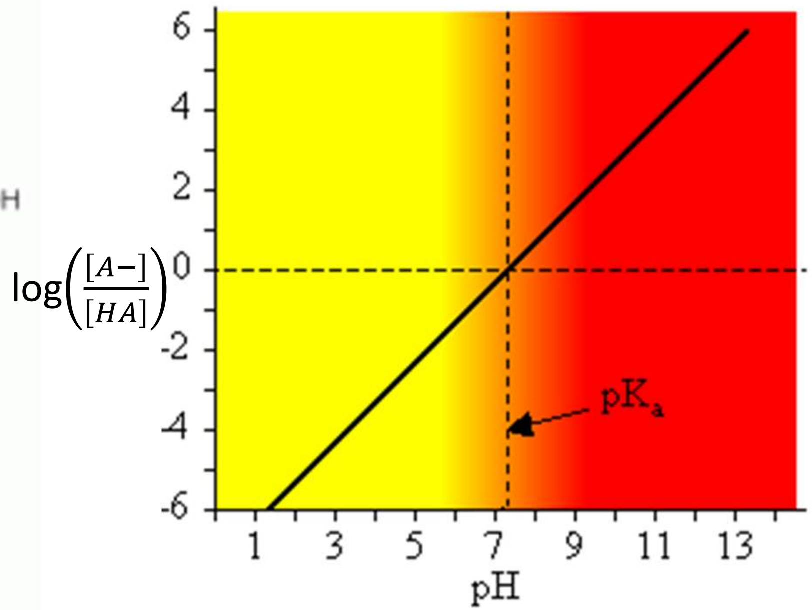
pH >7.7 pink

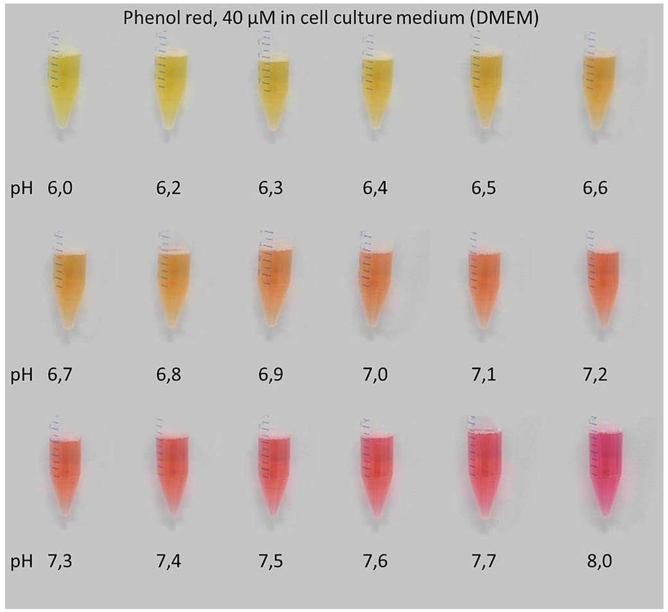


1.2<pH <7.2, yellow

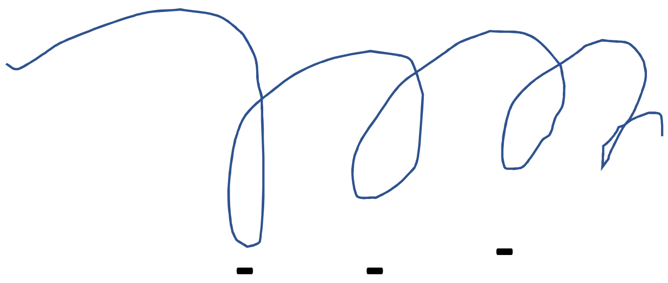
A solution of phenol red is used as a pH indicator, often in cell culture. Its color exhibits a gradual transition from yellow (λmax = 443 nm) to red (λmax = 570 nm) over the pH range 6.8 to 8.2. Above pH 8.2, phenol red turns a bright pink (fuchsia) color.
At low pH the compound exists as a zwitterion as in the structure shown with the sulfate group negatively charged, and the ketone group carrying an additional proton. It is orange-red. If the pH is increased (pKa = 1.2), the proton from the ketone group is lost, resulting in the yellow, negatively charged ion. At still higher pH (pKa = 7.7), the phenol's hydroxide group loses its proton, resulting in the red ion.

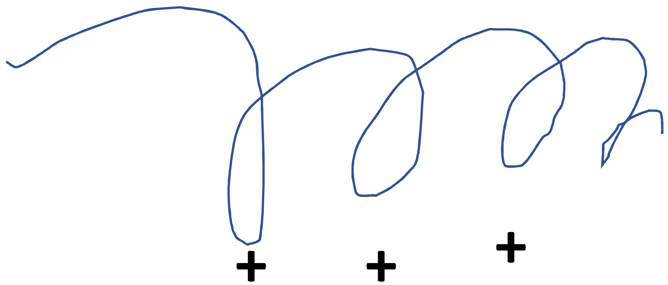

OH⁻
OH
OH⁻
H⁺
Yellow
Acid Form
Red
Base Form
pH
Absorbance
Wavelength (nm)


6
4
2
0
-2
-4
-6
$\log\left(\frac{[A-]}{[HA]}\right)$
pK$_a$
1
3
5
7
9
11
13
pH


Phenol red, 40 µM in cell culture medium (DMEM)
pH 6,0 6,2 6,3 6,4 6,5 6,6
pH 6,7 6,8 6,9 7,0 7,1 7,2
pH 7,3 7,4 7,5 7,6 7,7 8,0

Polimeri pH sensibili

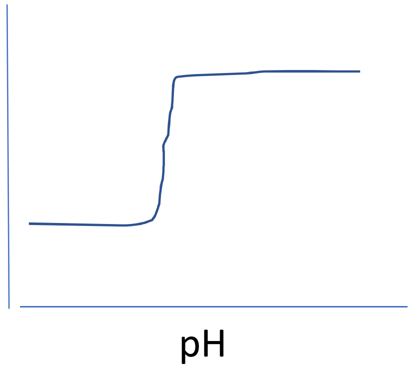


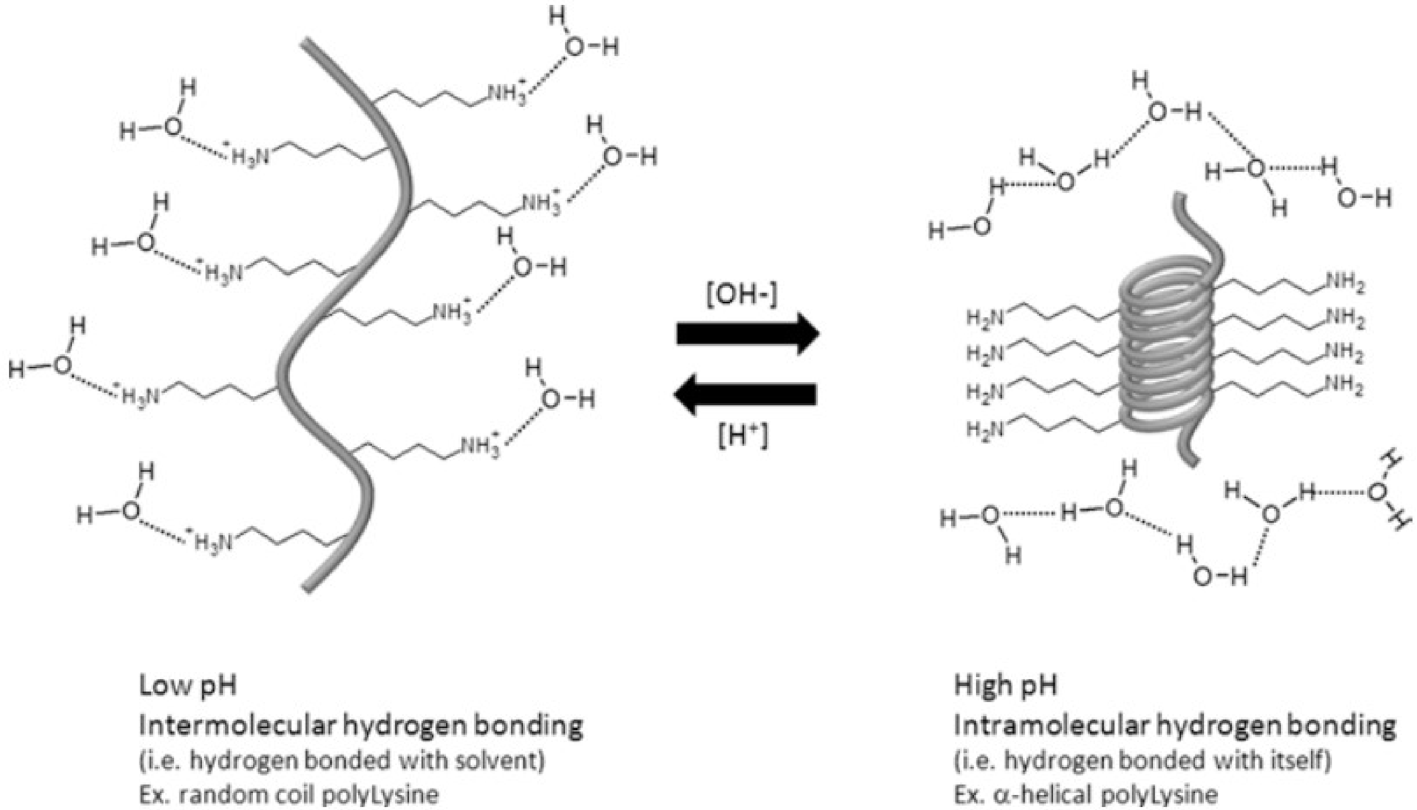


Si ionizzano a un dato pKa. Quelli negativi (anionici) si ionizzano a pH alto-
Poly acido acrilico

Quelli positivi (cationici) si ionizzano a basso pH
Poly di-ethlydiamino ethyl methacyrlate

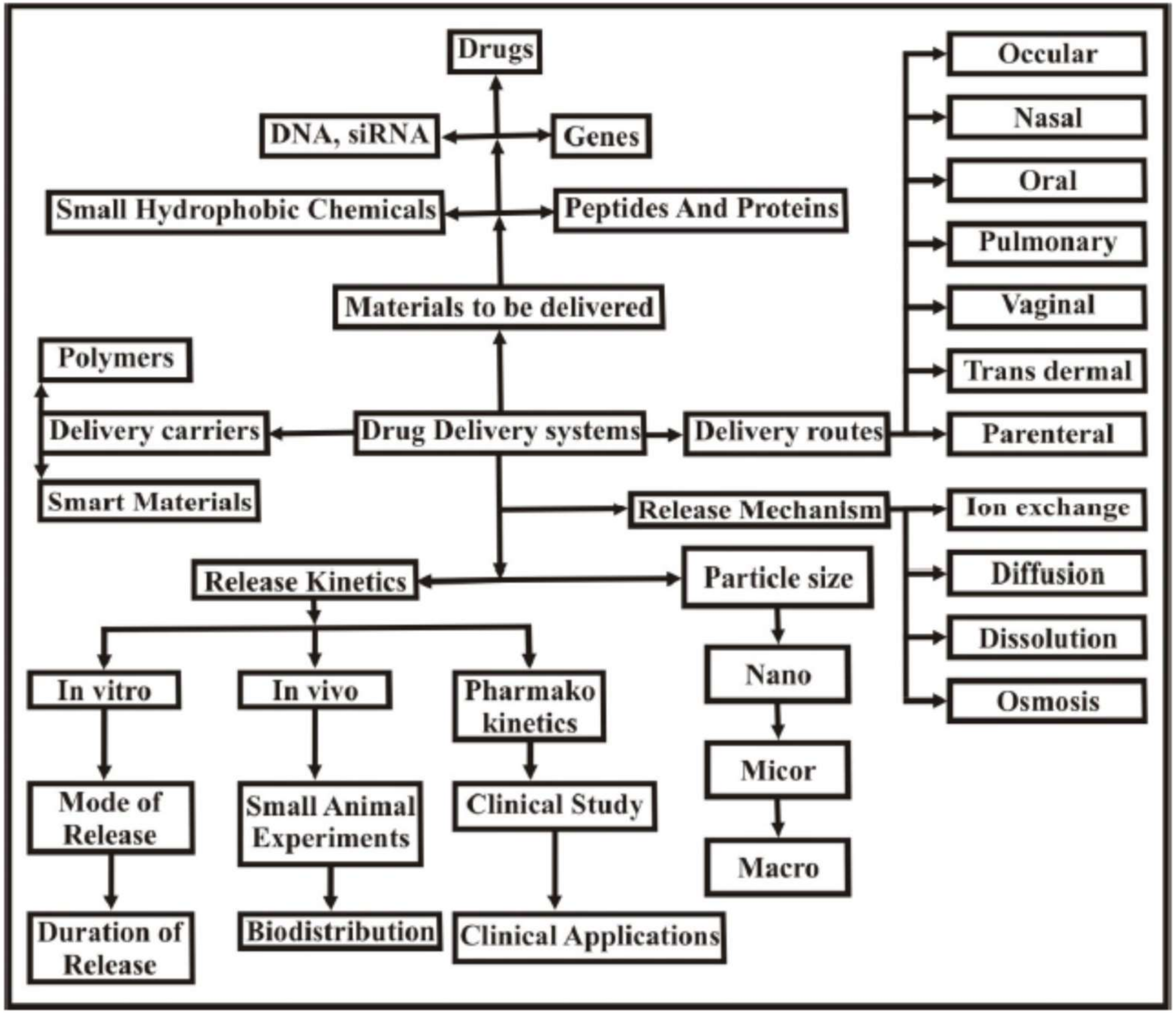
Hydrophobicity,
Size
Gel
Solubility etc



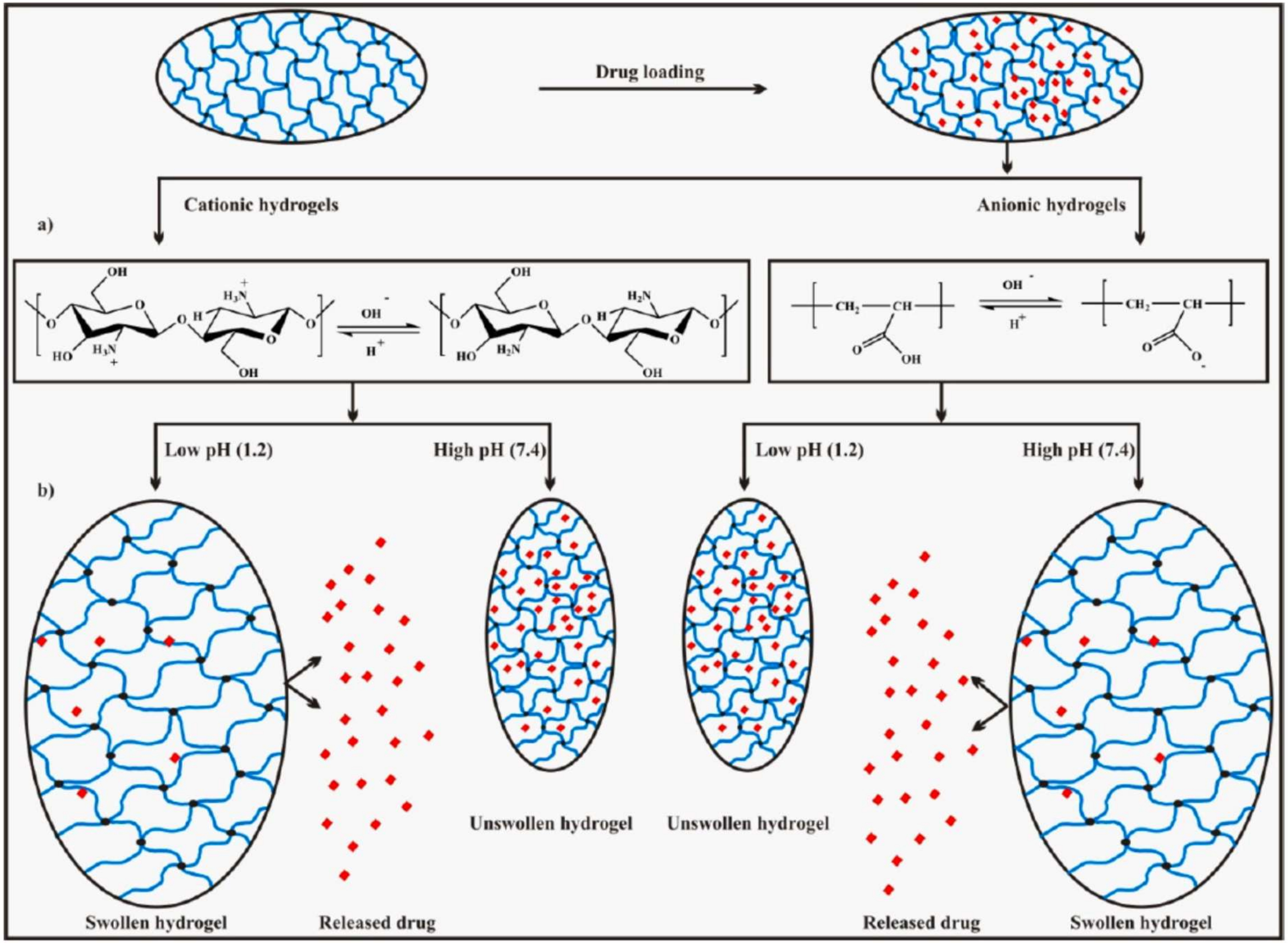


Quelli positivi (cationici) si ionizzano a basso pH
ES Poly lysina, Chitosano (NH3+)

Drug delivery



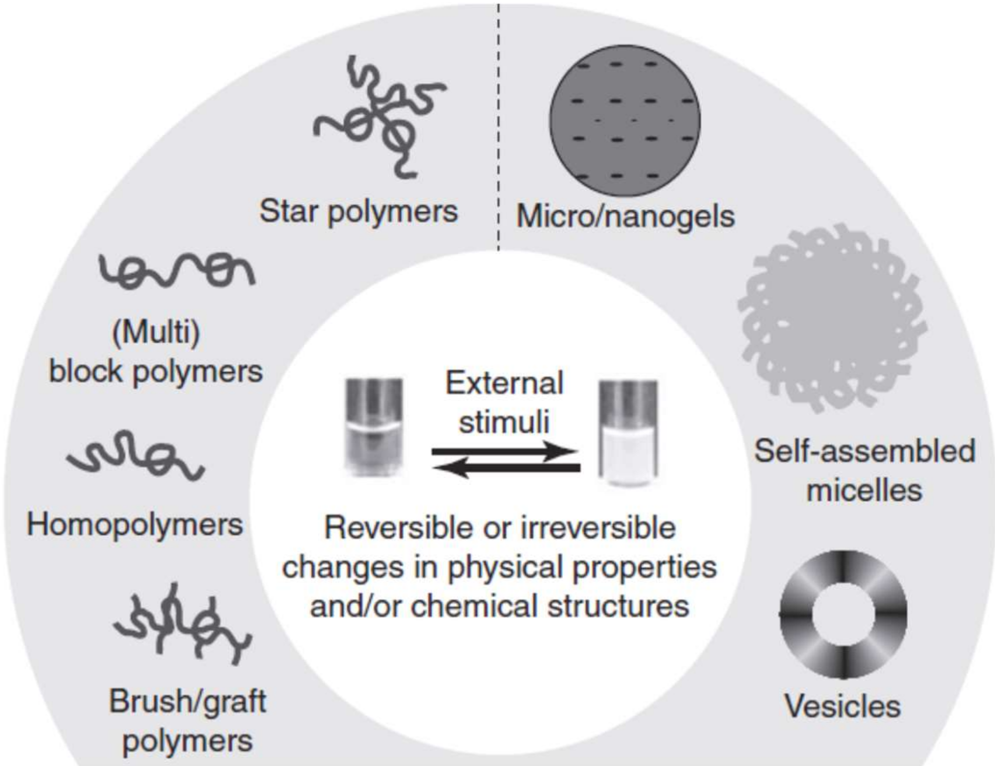
chitosan



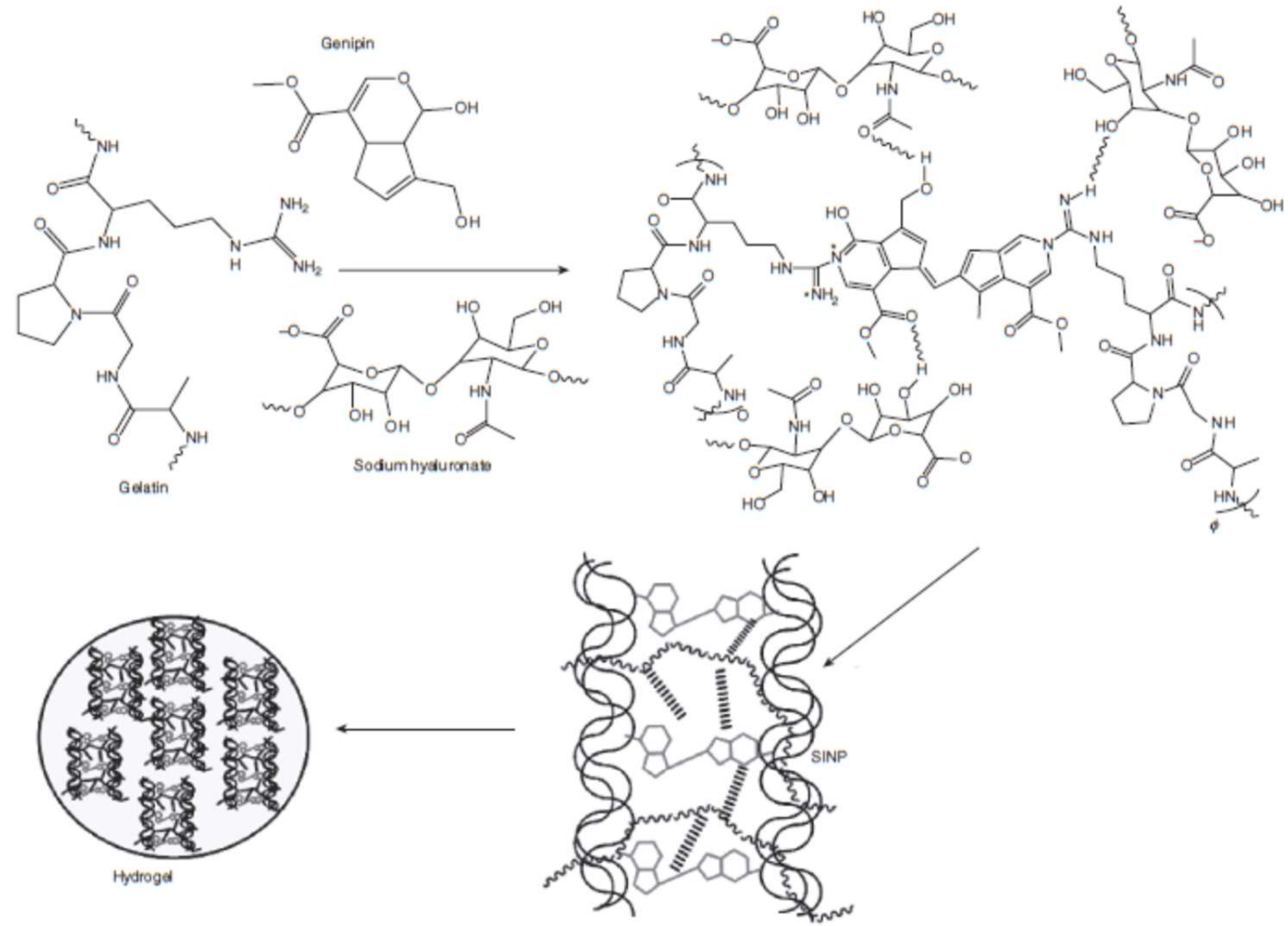
Drug loading
a)
Cationic hydrogels
Anionic hydrogels
OH
H_3N^+
H_2N
HO
OH⁻
H⁺
CH₂
CH
O
b)
Low pH (1.2)
High pH (7.4)
Low pH (1.2)
High pH (7.4)
Swollen hydrogel
Released drug
Unswollen hydrogel
Unswollen hydrogel
Released drug
Swollen hydrogel

Table 3. pH of different body parts/tissues in human body.

Fluids Tissue/Cellular Compartment	pH Ranges	References
Saliva in baccul cavity	6.7–7.3	[139]
Stomach Duodenum	2.0 5.0–8.0	[35]
Jejunum Ileum	6.0–7.0 7.0	[140]
Cecum	6.4	[123,138]
Colon	7.0–7.5	[35]
Rectum	7.0	[140]
Vagina	4.0–5.0	[141]
Chronic wounds Extracellular matrix in cancerous tissue Lysosomes Golgi bodies Early endosome Late endosome Blood	5.4–7.4 6.5–7.2 4.5–5.0 6.4 6.0–6.5 5.0–6.0 7.35–7.45	[35]
Stratum corneum	5.0–6.0	[142]



3.4 Different architectures of pH-responsive polymers. (*Source*: Reprinted and adapted from Reyes *et al*., 2013, copyright 2013, with permission from The American Society of Chemistry.)



3.7 Scheme of a semi-interpenetrating network formed by sodium hyaluronate and gelatin cross-linked with genipin. (*Source*: Reprinted and adapted from Reyes *et al.*, 2013, copyright 2013, with permission from Sociedad Ibérica de Biomecánica y Biomateriales.)

Reversible Molecular Adsorption Based on Multiple-Point Interaction by Shrinkable Gels

Taro Oya,[1] Takashi Enoki,[1] Alexander Yu. Grosberg,[1] Satoru Masamune,[2] Takaharu Sakiyama,[1] Yukikazu Takeoka,[1] Kazunori Tanaka,[1] Guoqiang Wang,[1] Yasar Yilmaz,[1] Michael S. Feld,[3] Ramachandra Dasari,[3] Toyoichi Tanaka[1]*

A general approach is presented for creating polymer gels that can recognize and capture a target molecule by multiple-point interaction and that can reversibly change their affinity to the target by more than one order of magnitude. The polymers consist of majority monomers that make the gel reversibly swell and shrink and minority monomers that constitute multiple-point adsorption centers for the target molecule. Multiple-point interaction is experimentally proven by power laws found between the affinity and the concentration of the adsorbing monomers within the gels.

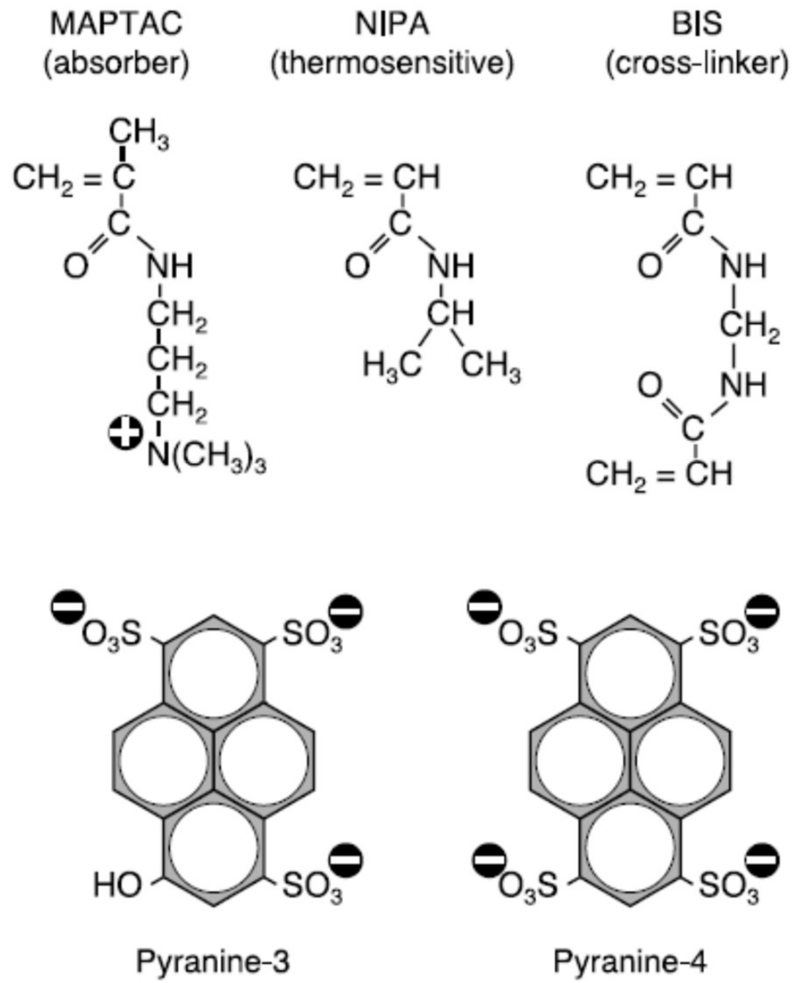


Fig. 1. The chemical structures of an adsorption site with a positive charge (MAPTAC), a thermosensitive monomer (NIPA), a cross-linker (BIS), and target molecules with three or four charges (pyranine-3 and pyranine-4, respectively). The recipe for synthesis was NIPA (6 M), MAPTAC (0.5 μM to 200 mM), and BIS (40 mM). They were dissolved in methylsulfoxide, degassed, and polymerized by free-radical polymerization initiated by azobisisobutylonitrile (7.3 mM) at 60°C.

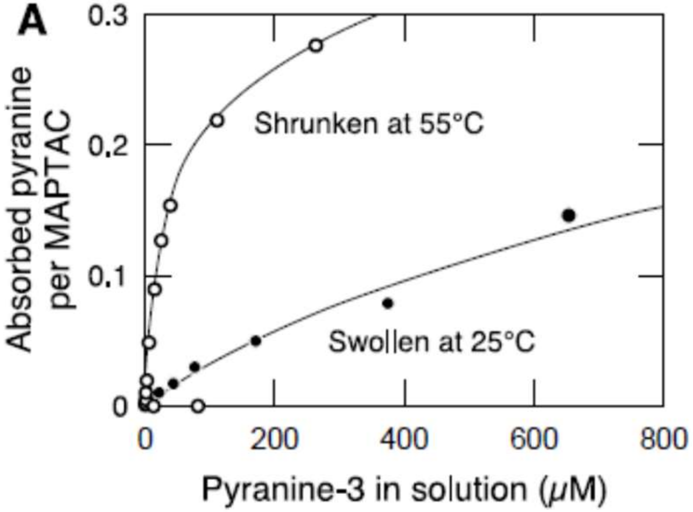


Fig. 2. (**A**) The adsorption of pyranine-3 per MAPTAC monomer as a function of pyranine-3 concentration in the swollen state at 25°C and in the shrunken state at 55°C. The MAPTAC concentration was 30 mM. (**B**) The shrunken gels at 55°C (upper dish) and the swollen gels at 25°C (lower dish) under illumination with UV. In the shrunken state, the gel adsorbed all of the pyranine molecules, but in the swollen state, the gel released them all as seen by their fluorescence. [Photograph by Felice Frankel, © 1999]

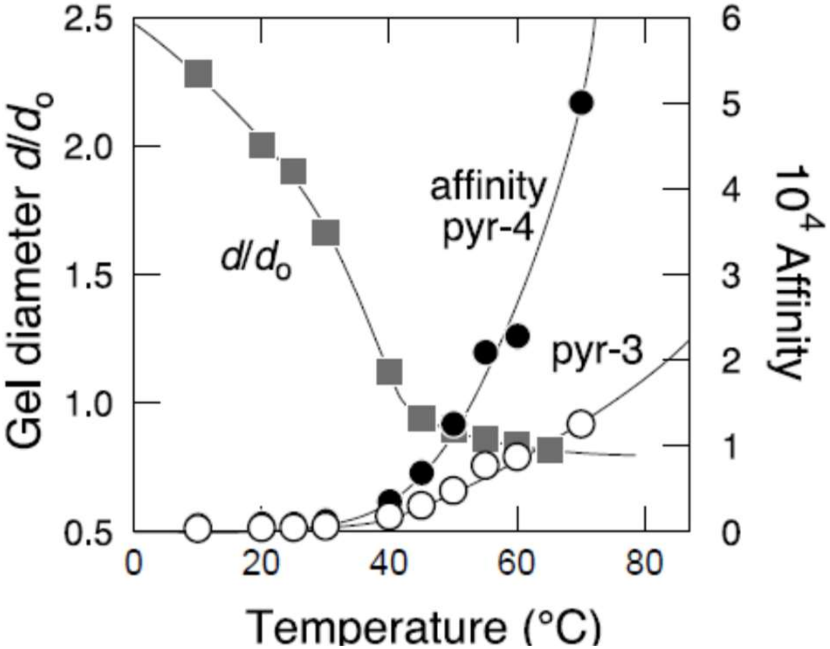


Fig. 3. The affinity of the gels to pyranine-3 and pyranine-4 as a function of temperature. The degree of swelling, d/d_o, of the gels is also shown, where d denotes the gel diameter in equilibrium and d_o is that upon synthesis.

Paper di Tanaka

- Domande: come cambia figura 2 in assenza di MATAP?
- Possibili applicazioni di questo e un Sistema analogo sensibile a pH

Design a PNIPAM based micro valve

Dual responsivity: design a gel which is both pH and Temperature responsive to be injectable and provide drug release in case of local acidosis

Fig. 2.14 Typical phase diagram of pH- and temperature-responsive block copolymers in solution. These types of copolymer could be useful in providing sustained delivery of therapeutic molecules to regions of local acidosis such as ischemic tissue