Polyelectrolyte hydrogels

Last Day: Physical hydrogels
Structure and physical chemistry

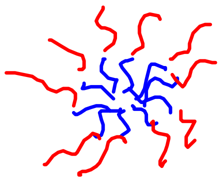
Today: polyelectrolyte hydrogels, complexes, and coacervates
Polyelectrolyte multilayers
theory of swelling in ionic hydrogels

Reading: S.K. De et al., 'Equilibrium swelling and kinetics of pH-responsive hydrogels: Models, experiments, and simulations,' *J. Microelectromech. Sys*. **11**(5) 544 (2002).

Supplementary Reading: HANDOUT ON RELATIONSHIP BETWEEN ξ AND D
(MAY OR MAY NOT GET TO THIS TODAY)

ANNOUNCEMENTS: PS 3 DUE TODAY 5pm / PS 4 POSTS TOMORROW

Determination of thermodynamic driving force for triblock self-assembly



$X_{2,cmc}$ = MOLE FRACTION OF POLYMER @ CMC

FREE ENERGY OF MICELLIZATION: $\Delta \bar{G}^\circ \simeq RT \ln X_{2,cmc}$

$$\hookrightarrow \Delta \bar{H}^\circ = \frac{\partial(\Delta \bar{G}^\circ/T)}{\partial(1/T)} = R\left(\frac{\partial \ln X_{2,cmc}}{\partial(1/T)}\right)_P = R\left(\frac{\partial \ln X_2}{\partial(1/T_{cmT})}\right)_P$$

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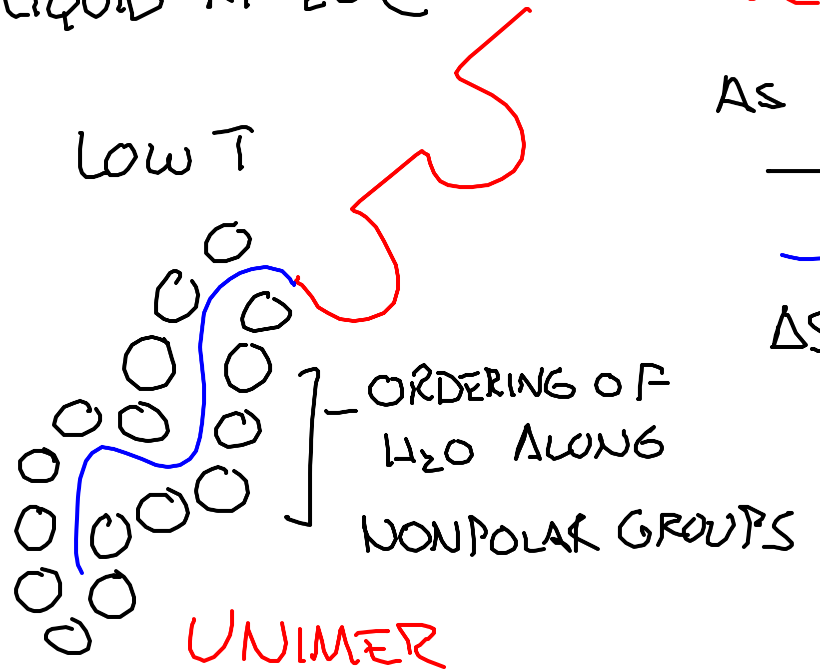
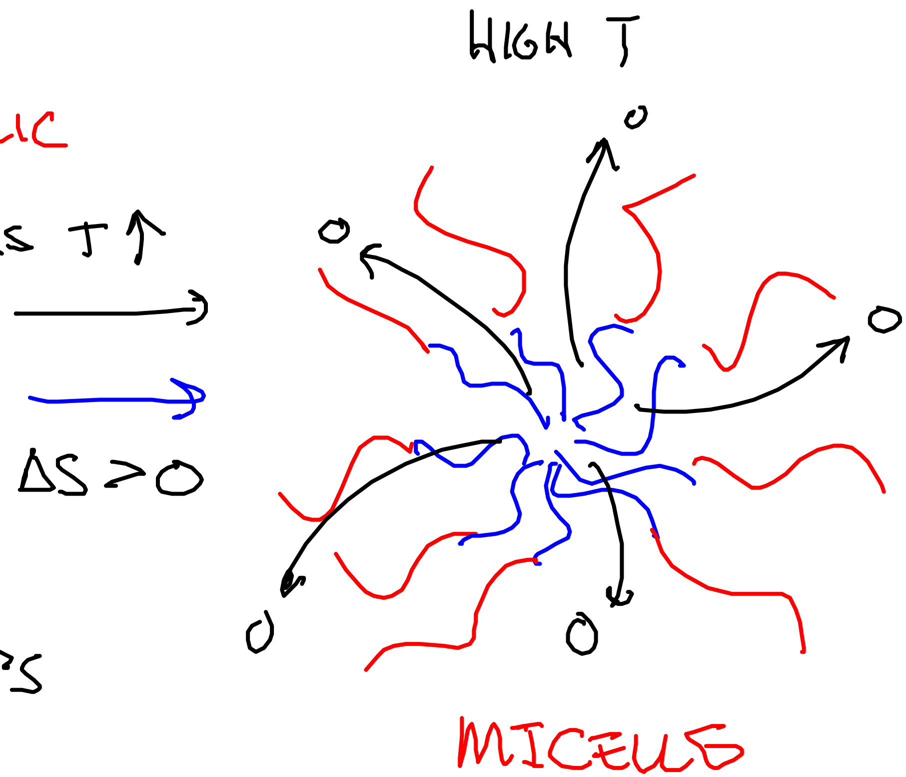
Please see:
Figure 6 and Table 4 in Alexandridis, P., J. F. Holzwarth, and T. A. Hatton. *Macromolecules* 27 (1994): 2414-2425.

Determination of thermodynamic driving force for triblock self-assembly

4 H-BONDS PER H_2O IN ICE → ~3.5 IN LIQUID AT 25°C





ENTROPY GAIN IN FREEING 'ORDERED' H_2O DRIVES MICELLIZATION

$$\Delta G = \Delta H - \underline{\underline{T}}\Delta S$$

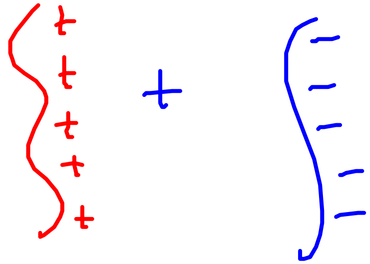
Hydrophobic association vs. hydrogen bonding gels

	AS T↑ GEL:	GELATION DRIVEN BY
LCST GELS (e.g., HYDROPHOBIC EFFECT)	FORM	ΔS
H-BONDING GELS	DISSOLVES	ΔH

↳ AT ELEVATED T, STABILIZING H-BONDS ARE OVERCOME BY RANDOM THERMAL ENERGY

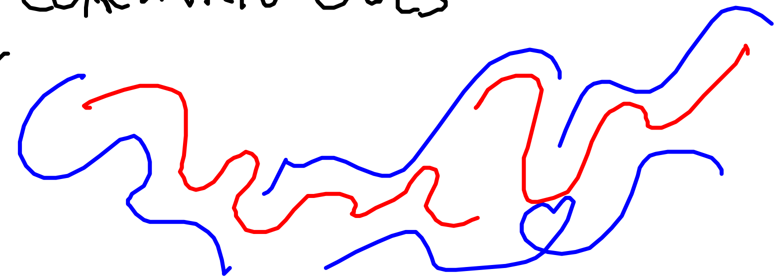
Polyelectrolyte hydrogels

Common polyelectrolyte gel structures:

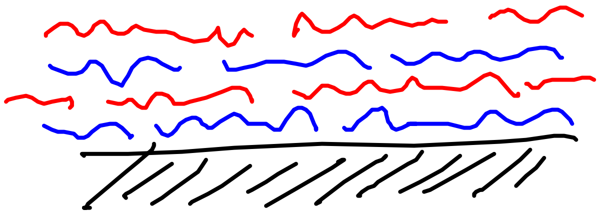


(i) PAIRED POLYELECTROLYTE GELS

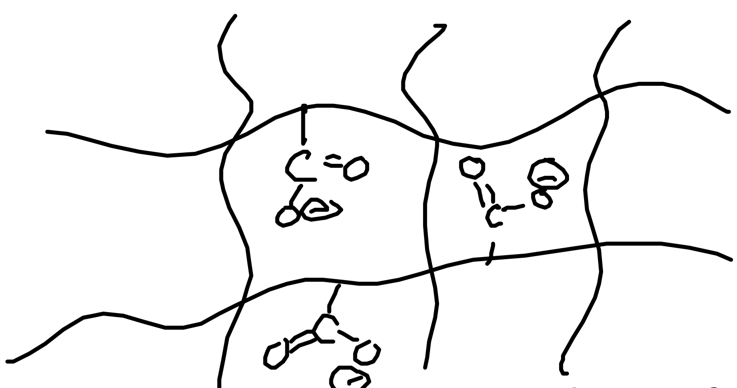
COACERVATE GELS



POLYELECTROLYTE MULTILAYERS



(ii) UNPAIRED POLYELECTROLYTES



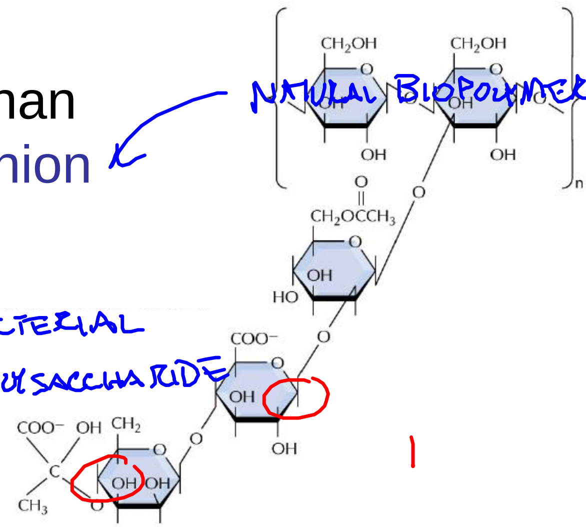
COACERVATES

Formation of polyelectrolyte physical gels: self-assembly of coacervate hydrogels

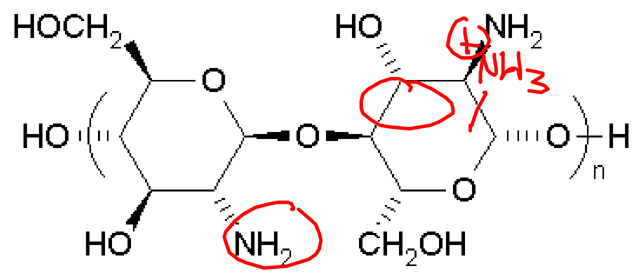
Images removed due to copyright reasons:
Please see:
Chornet, E., and S. Dumitriu. “Inclusion and Release of Proteins from Polysaccharide-based Polyion Complexes.” *Adv Drug Deliv Rev* 31 (1998): 223-246.

Microstructure of coacervate hydrogels

Xanthan
polyanion



Chitosan
polycation



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Please see:
Chornet, E., and S. Dumitriu, S. “Inclusion and Release of Proteins from Polysaccharide-based Polyion Complexes.” *Adv Drug Deliv Rev* 31 (1998): 223-246.

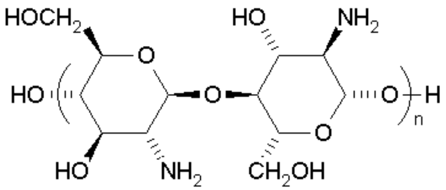
Microstructure of coacervate hydrogels

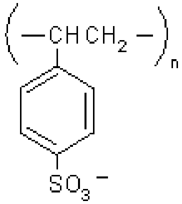
Images removed due to copyright reasons.
Please see:
Chornet, E., and S. Dumitriu. “Inclusion and Release of Proteins from Polysaccharide-based Polyion Complexes.” *Adv Drug Deliv Rev* 31 (1998): 223-246.

Homogeneous Covalent gel:

Images removed due to copyright reasons.
Please see:
Friedl, P. et al. *Eur J. Immunol* 28 (1998): 2331-2343.

Layer-by-layer deposition

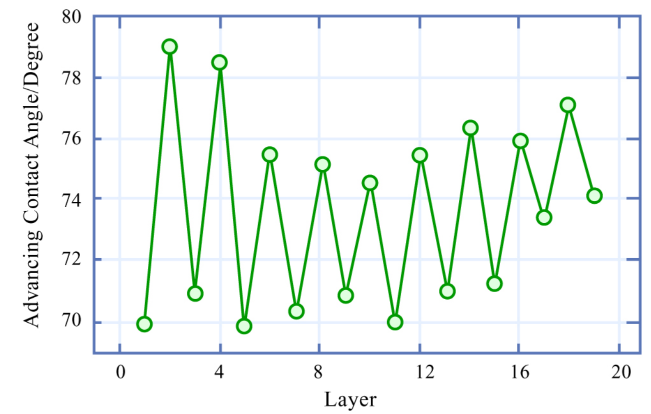




Surface properties dominated by last layer deposited:

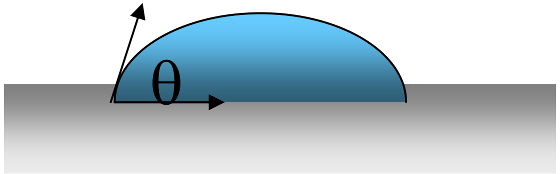
Image removed due to copyright reasons:
Please see:

Figure 1 in Schlenoff, Joseph B. "Polyelectrolyte Multilayers." AccessScience@McGraw-Hill. http://www.accessscience.com



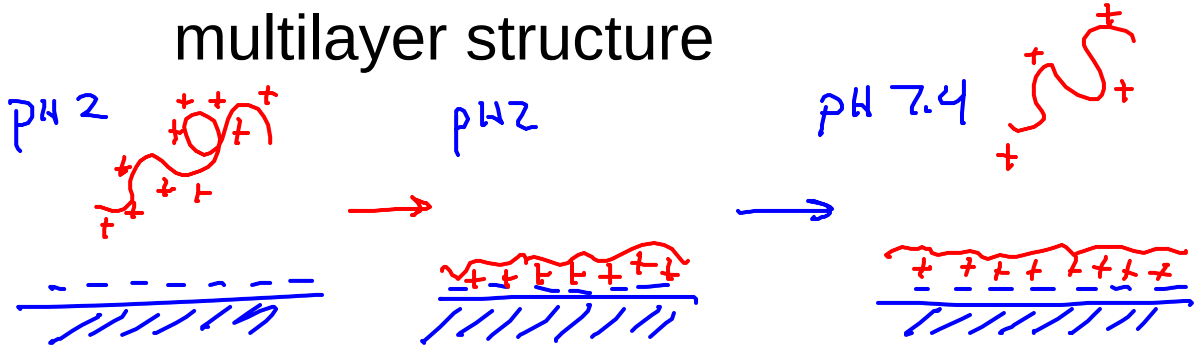
Advancing contact angle as a function of the layer number of PSS and chitosan. Odd numbers represent films with PSS as the outermost layer, whereas even number films have chitosan as the outermost layer.

Figure by MIT OCW.



Degree of ionization during assembly dictates multilayer structure

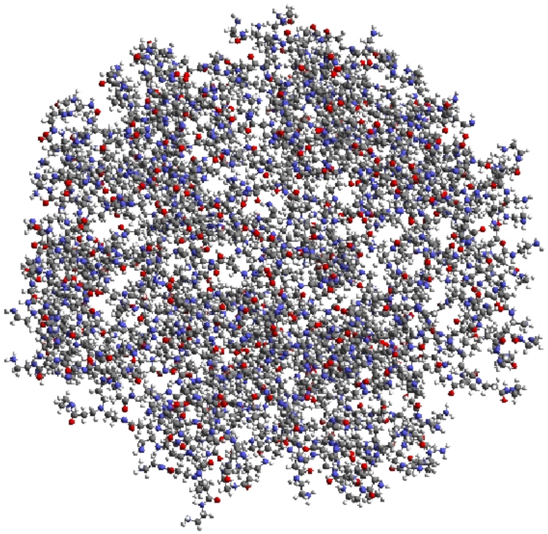
Charge during assembly can be ‘protected’ in the multilayer:



Images removed due to copyright reasons.
Please see:
Figure 1 in Mendelsohn, Jonas D., Sung Yun Yang, Jeri'Ann Hiller, Allon I. Hochbaum, and Michael F. Rubner. "Rational Design of Cytophilic and Cytophobic Polyelectrolyte Multilayer Thin Films." *Biomacromolecules* 4 (2003): 96-106.

PEMs Assembly with any charged molecule or particle; Conformal modification of complex surfaces

Images removed due to copyright reasons.
Please see:
Khopade, A. J., and F. Caruso. “Stepwise Self-assembled Poly(amidoamine) Dendrimer and
and poly(styrenesulfonate) microcapsules as sustained delivery vehicles. *Biomacromolecules* 3, (2002): 1154-1162.



Conformal modification of complex surfaces

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Please see:
Caruso, F., D. Trau, H. Mohwald, and R. Renneberg. “Enzyme Encapsulation in Layer-by-layer Engineered Polymer multilayer capsules.” *Langmuir* 16 (2000): 1485-1488.

Hollow PEMs as drug-delivery capsules

Image removed due to copyright restrictions.

Graph removed due to copyright restrictions.

Fluorescent drug-loaded PEM capsules

Cellular substrates

Image of SEM micrograph of multilayer-coated echinocyte blood cell removed due to copyright restrictions.

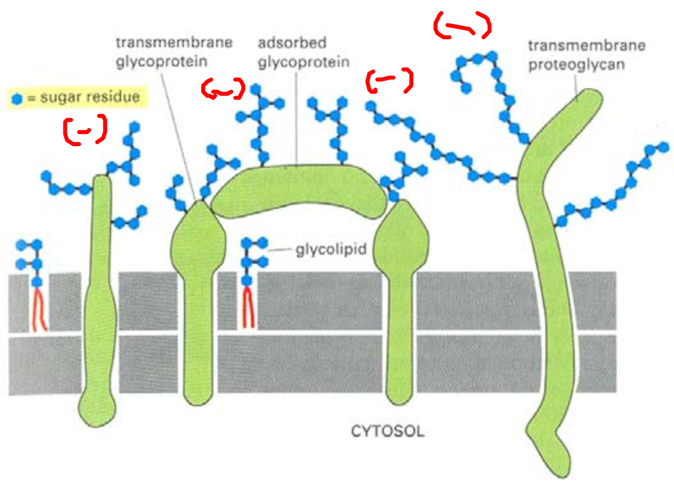
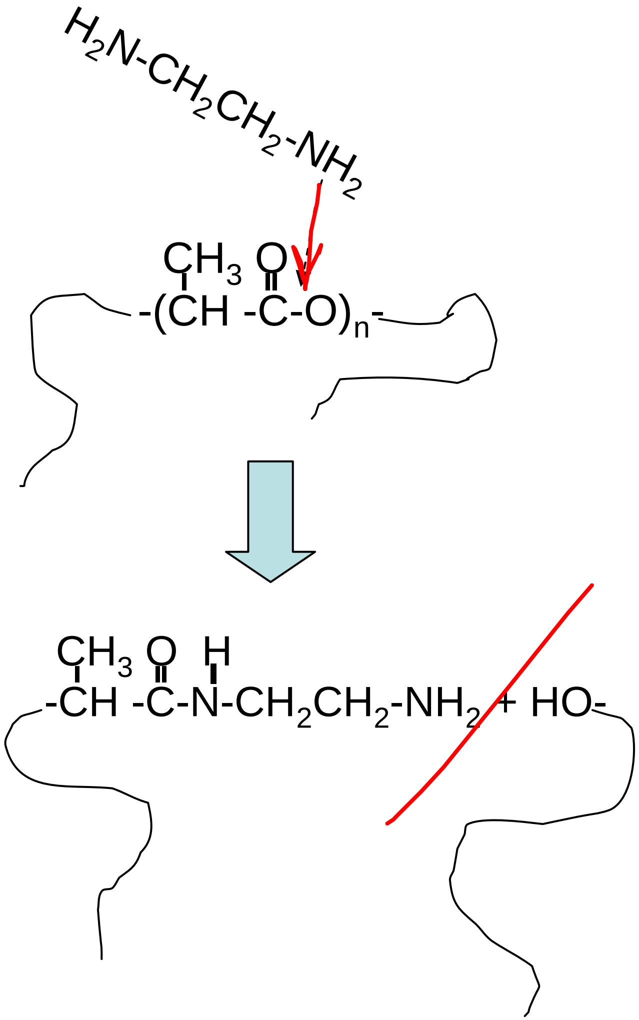


Figure 10–41 Simplified diagram of the cell coat (glycocalyx). The cell coat is made up of the oligosaccharide side chains of glycolipids and integral membrane glycoproteins and the polysaccharide chains on integral membrane proteoglycans. In addition, adsorbed glycoproteins and adsorbed proteoglycans (not shown) contribute to the glycocalyx in many cells. Note that all of the carbohydrate is on the noncytoplasmic surface of the membrane.

(Alberts et al. *Molecular Biology of the Cell*)

Employing PEMs on degradable biomaterials



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Please see:
Zhu, Y., C. Gao, T. He, X. Liu, and J. Shen. "Layer-by-Layer Assembly to Modify Poly(L-lactic acid) Surface Toward Improving Its Cytocompatibility to Human Endothelial Cells." *Biomacromol.* 4 (2003): 446-452.

Polyelectrolyte hydrogels

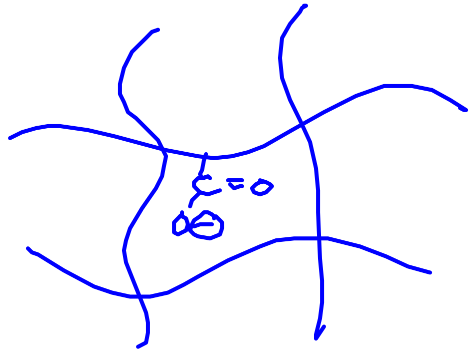
UNPAIRED POLYELECTROLYTES

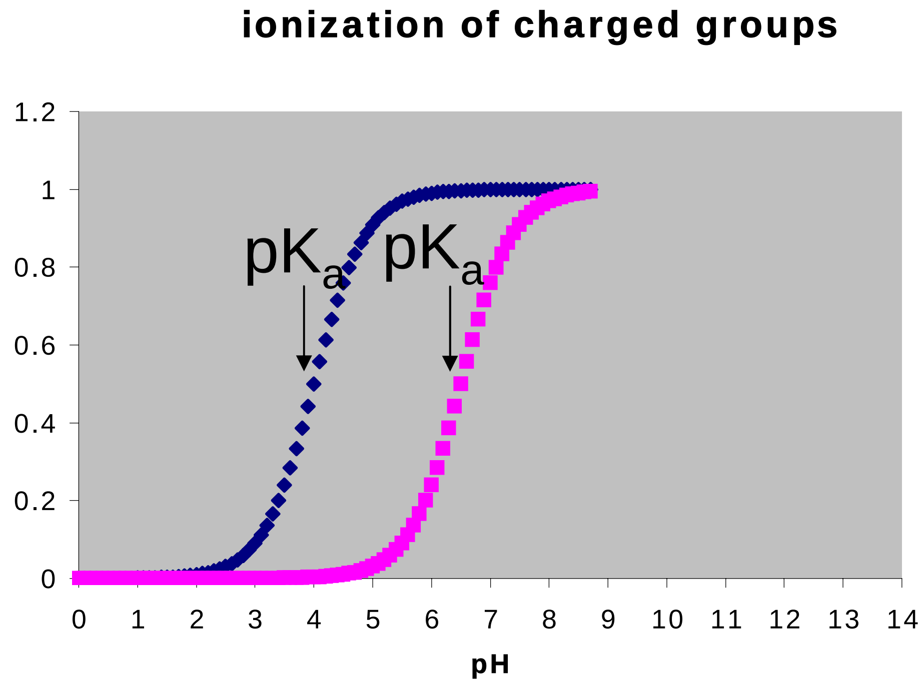
$$-COOH \longleftrightarrow -COO^- + H^+$$

$$K_a = \frac{[RCOO^-][H^+]}{[RCOOH]}$$

$$pK_a = -\log K_a$$

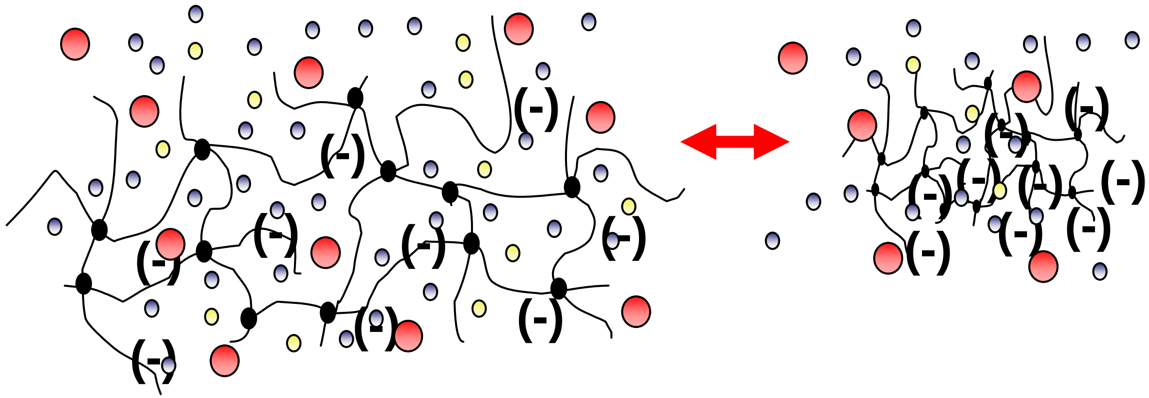
$$pH = pK_a + \log [RCOO^-]/[RCOOH]$$





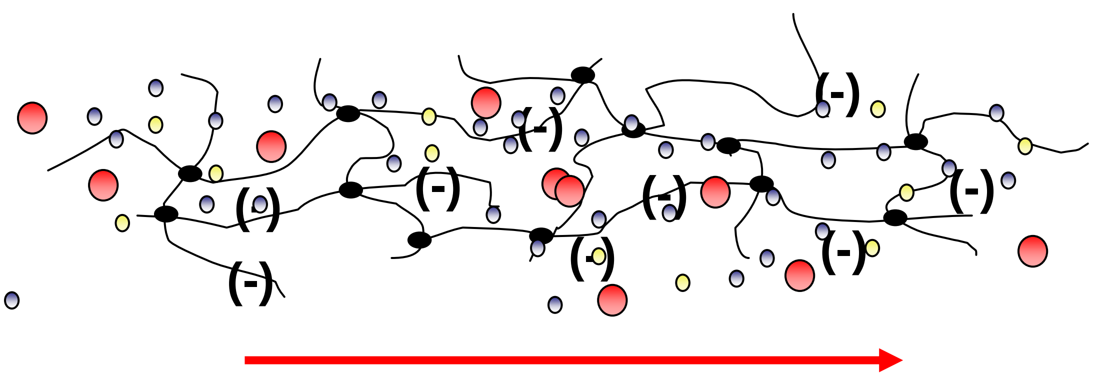
Responsiveness of ‘unpaired’ polyelectrolyte gel structures:

✓ pH ✓ Ionic strength



Electric fields

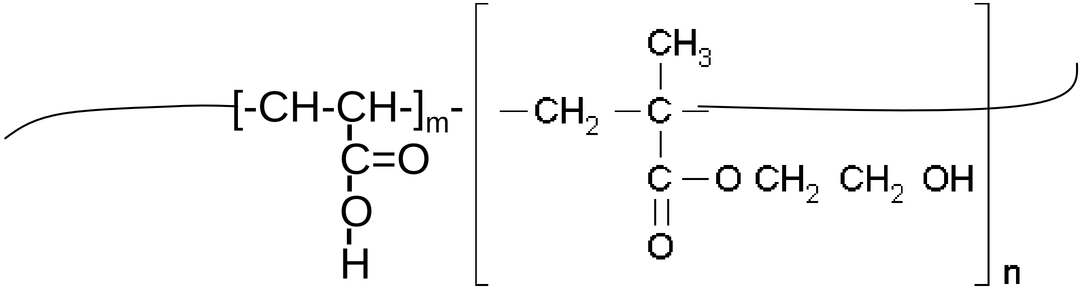
(temperature)



E

Environmental responsiveness of covalent polyelectrolyte networks: experimentally observed swelling of anionic hydrogels

Data for poly(HEMA-co-AA) covalent hydrogel:



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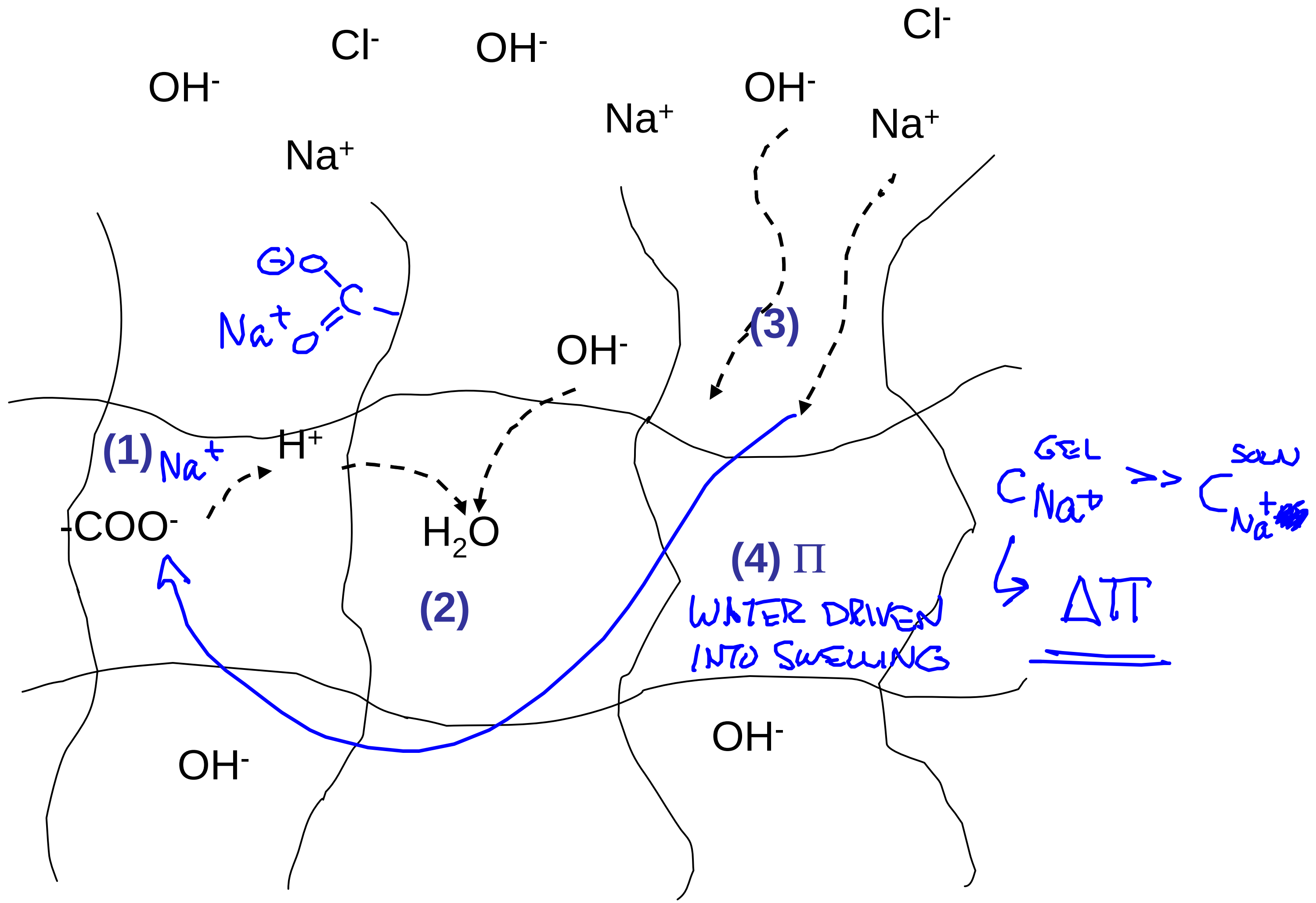
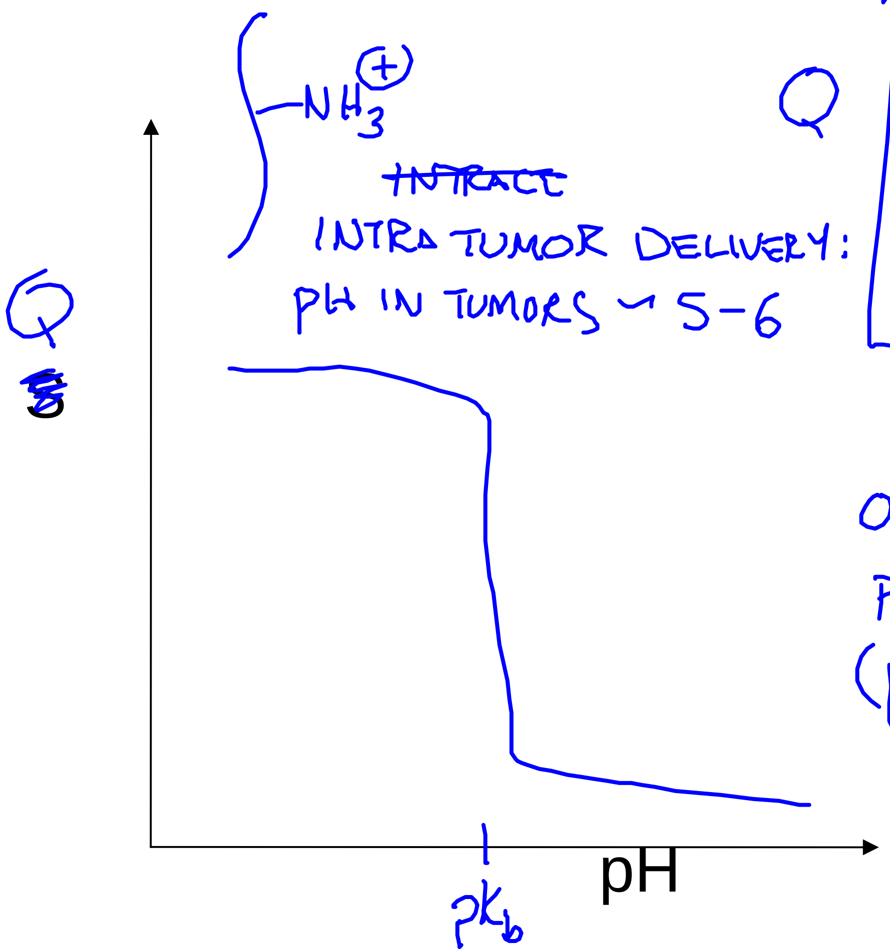
Please see:
De, S. K. et al. “Equilibrium Swelling and Kinetics of pH-responsive Hydrogels: Models, Experiments, and Simulations.” *Journal of Microelectromechanical Systems* 11 (2002): 544-555.

Driving force for unpaired polyelectrolyte gel swelling



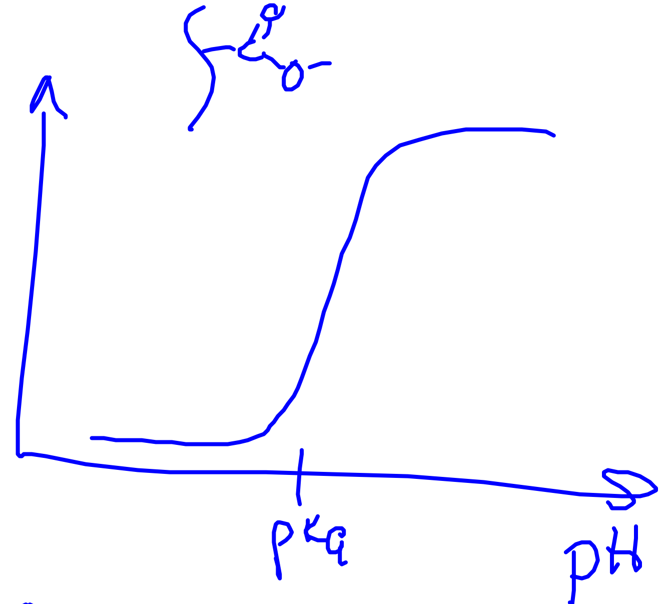
Swelling behavior reversed in polycation hydrogels



~~INTRACT~~

INTRATUMOR DELIVERY:

pH IN TUMORS ~ 5-6



ORAL DRUG DELIVERY:

PROTECTS DRUG IN STOMACH (pH~2), RELEASES DRUG IN INTESTINE (pH~7.2)

Kinetics of swelling/deswelling transitions

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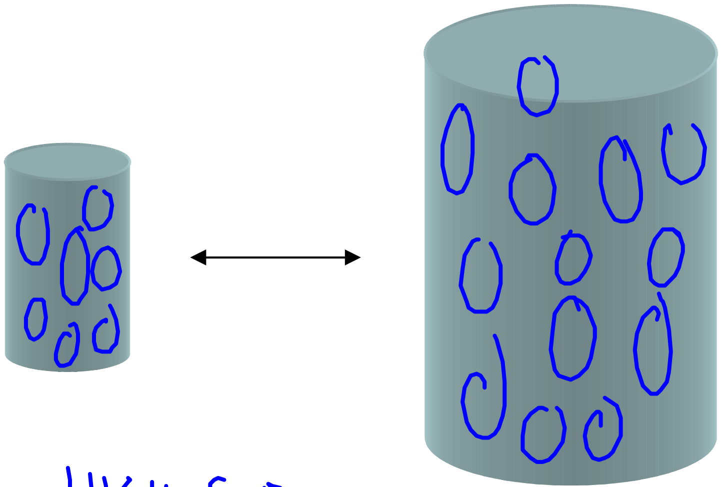
Please see:
De, S. K. et al. “Equilibrium Swelling and Kinetics of pH-responsive Hydrogels: Models, Experiments, and Simulations.” *Journal of Microelectromechanical Systems* 11 (2002): 544-555.

Kinetics of swelling/deswelling transitions

Rapid swelling/deswelling of superporous gels:

Low pH High pH

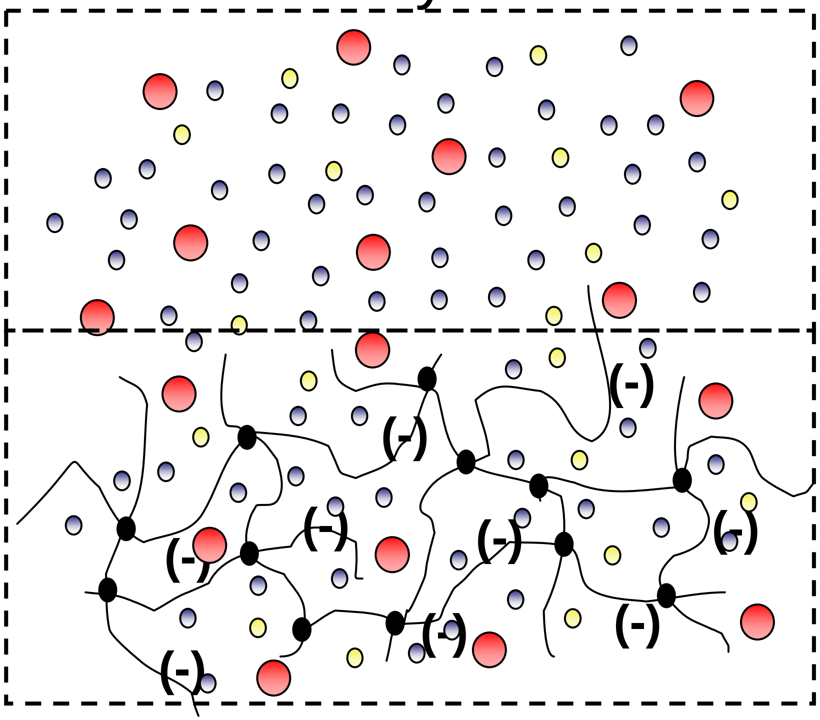


HIGH SURFACE:VOLUME RATIO
SPEEDS ION DIFFUSION
FOR RAPID SWITCHING

Graph removed due to copyright reasons.
Please see:
Figure 2 in Zhao, B., and J. S. Moore. "Fast pH- and Ionic Strength-responsive Hydrogels in Microchannels." *Langmuir* 17(2001): 4758-4763.

thermodynamics of ionic hydrogels

Model of system:



Inorganic anion, e.g. Cl^-

Inorganic cation, e.g. Na^+

water

CONDITIONS FOR EQUILIBRIUM!

$$\mu_1^{GEL} = \mu_1^{SOLN} \qquad \left[\mu_{ION,i}^{GEL} = \mu_{ION,i}^{SOLN}\right]$$

$$\downarrow$$

$$\Delta\mu_1 = \mu_1^{GEL} - \mu_1^{SOLN} = 0$$

$$(\Delta\mu_1)_{mix} + (\Delta\mu_1)_{el} + (\Delta\mu_1)_{IONS} = 0$$

$$(\Delta\mu_1)_{IONS} = -\Delta\Pi\,\bar{V}_1 = \bar{V}_1 RT \sum_j^{ALL\ IONS} \left(C_j^{GEL} - C_j^{SOLN}\right)$$

MIXING AND ELASTIC TERMS ARE SAME AS PEPPAS-MERRILL THEORY

Swelling of polyelectrolyte gels is controlled by ionic strength and degree of ionization of the gel:

IONIC STRENGTH: $I \equiv \frac{1}{2}\sum_{i=1}^{\text{ALL IONS}} z_i^2 c_i$

(z_i ↑ CHARGE ON ION i)

DEGREE OF IONIZATION OF GEL $= i = \dfrac{[\vdash COO^-]}{[\vdash COO^-] + [\vdash RCOOH]}$

$$i = \frac{\frac{K_a}{[H^+]}}{1 + \frac{K_a}{[H^+]}} = \frac{K_a}{[H^+] + K_a} = \frac{K_a}{10^{-pH} + K_a} = \frac{10^{-pK_a}}{10^{-pH} + 10^{-pK_a}}$$

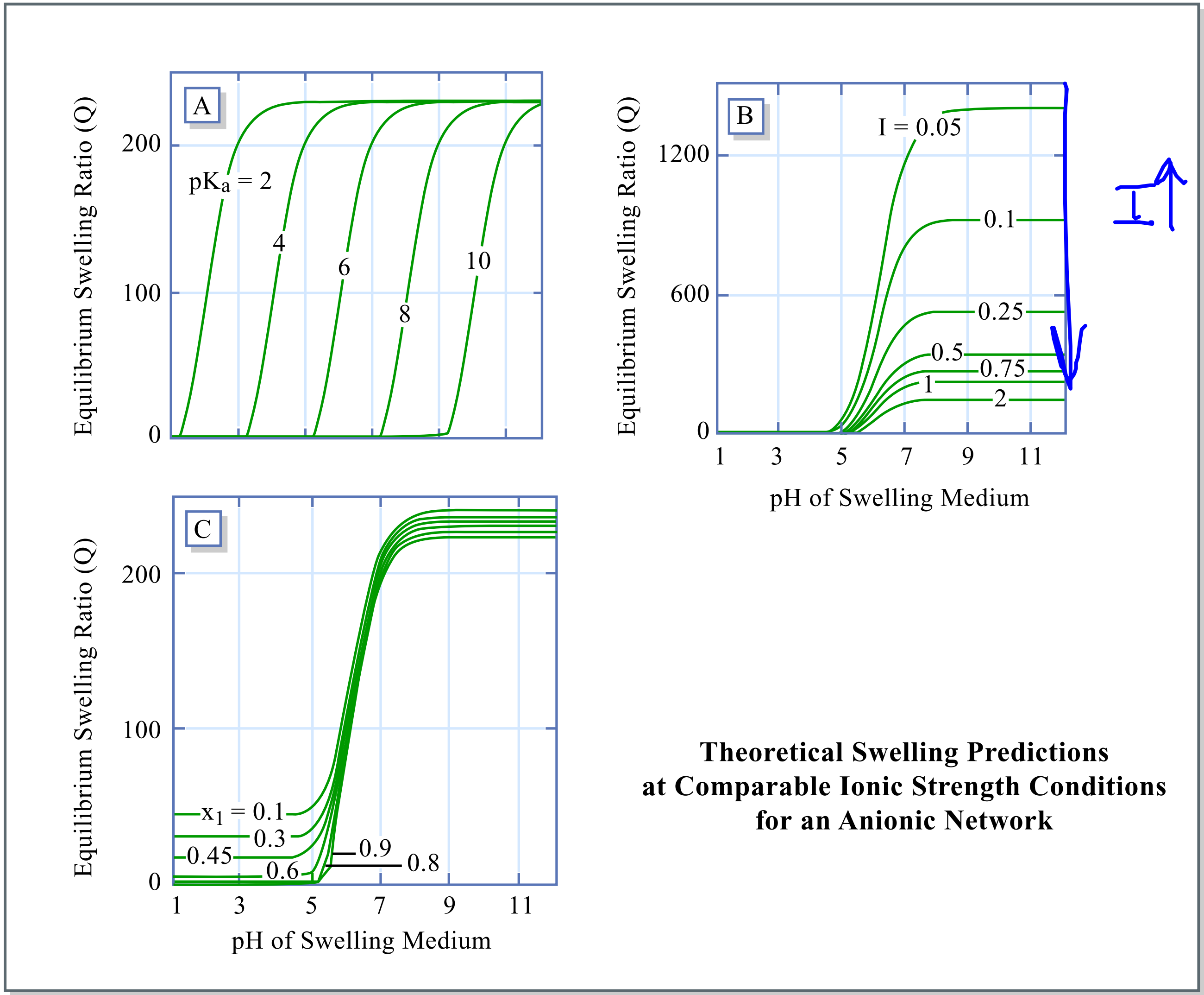
Equilibrium condition:

$$(\Delta\mu_1)_{mix} + (\Delta\mu_1)_{el} + (\Delta\mu_1)_{ions} = 0$$

$$\bar{V}_1 \left(\frac{10^{-pKa}}{10^{-pH} + 10^{-pKa}}\right)^2 \left(\frac{\phi_{2,s}^2}{4 I v_{sp,2}^2 M_o^2}\right) = \ln(1-\phi_{2,s}) + \phi_{2,s} + \chi\phi_{2,s}^2 + \phi_{2,r}\left(\frac{\bar{V}_1}{v_{sp,2} M_c}\right)\left(1 - \frac{2M_c}{M}\right)\left[\left(\frac{\phi_{2,s}}{\phi_{2,r}}\right)^{1/3} - \frac{1}{2}\left(\frac{\phi_{2,s}}{\phi_{2,r}}\right)\right]$$

MW OF REPEAT UNIT IN GEL (M_o)

Q = swollen volume of system/dry polymer volume = $1/\phi_{2,s}$



After Brannonpeppas, L., and N. A. Peppas. "Equilibrium Swelling Behavior of Ph-Sensitive Hydrogels." *Chemical Engineering Science* 46 (1991): 715-722.

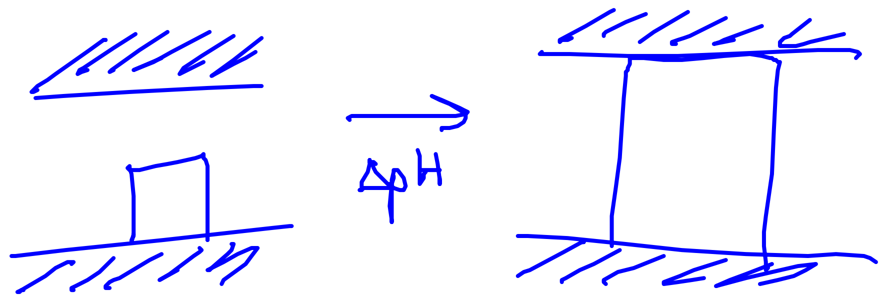
Figure by MIT OCW.

PE hydrogels as environment-responsive materials: applications in biotechnology and bioengineering

PHYSICAL/MECHANICAL RESPONSIVENESS

↓

BIOMEMS



MESH SIZE RESPONSIVENESS: CONTROLLING DIFFUSION RATES

"COLLAPSED STATE"

$D_{DRUG} \simeq 0 \xrightarrow{\Delta pH}$

"SWOLLEN STATE"

$D_{DRUG} \uparrow\uparrow \simeq D_{DRUG\ IN\ H_2O}$

bioMEMS based on polyeletrolyte gel responses

Images removed due to copyright reasons.
Please see:
Figure 1 and Figure 2 in Beebe, D. J., et al. "Functional Hydrogel Structures for Autonomous Flow Control Inside Microfluidic Channels." *Nature* 404 (2000): 588-+.

bioMEMS based on polyeletrolyte gel responses

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Please see:
Figure 12 in Beebe, D. J., G. A. Mensing, and G. M. Walker. “Physics and Applications of Microfluidics in Biology.” *Annual Review of Biomedical Engineering* 4 (2002): 261-286.

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Please see:
Figure 4 in Beebe, D. J., et al. “Functional Hydrogel Structures for Autonomous Flow Control Inside Microfluidic Channels.” *Nature* 404 (2000): 588-+.

Further Reading

1. De, S. K. et al. Equilibrium swelling and kinetics of pH-responsive hydrogels: Models, experiments, and simulations. *Journal of Microelectromechanical Systems* **11**, 544-555 (2002).
2. Tanaka, T. & Fillmore, D. J. Kinetics of Swelling of Gels. *Journal of Chemical Physics* **70**, 1214-1218 (1979).
3. Zhao, B. & Moore, J. S. Fast pH- and ionic strength-responsive hydrogels in microchannels. *Langmuir* **17**, 4758-4763 (2001).
4. Chornet, E. & Dumitriu, S. Inclusion and release of proteins from polysaccharide-based polyion complexes. *Adv Drug Deliv Rev* **31**, 223-246. (1998).
5. Zhu, Y., Gao, C., He, T., Liu, X. & Shen, J. Layer-by-Layer assembly to modify poly(L-lactic acid) surface toward improving its cytocompatibility to human endothelial cells. *Biomacromol.* **4**, 446-452 (2003).
6. Khopade, A. J. & Caruso, F. Stepwise self-assembled poly(amidoamine) dendrimer and poly(styrenesulfonate) microcapsules as sustained delivery vehicles. *Biomacromolecules* **3**, 1154-1162 (2002).
7. Caruso, F., Trau, D., Mohwald, H. & Renneberg, R. Enzyme encapsulation in layer-by-layer engineered polymer multilayer capsules. *Langmuir* **16**, 1485-1488 (2000).
8. Elbert, D. L., Herbert, C. B. & Hubbell, J. A. Thin polymer layers formed by polyelectrolyte multilayer techniques on biological surfaces. *Langmuir* **15**, 5355-5362 (1999).
9. Wang, Y. F., Gao, J. Y. & Dubin, P. L. Protein separation via polyelectrolyte coacervation: Selectivity and efficiency. *Biotechnology Progress* **12**, 356-362 (1996).
10. Beebe, D. J. et al. Functional hydrogel structures for autonomous flow control inside microfluidic channels. *Nature* **404**, 588-+ (2000).
11. Beebe, D. J., Mensing, G. A. & Walker, G. M. Physics and applications of microfluidics in biology. *Annual Review of Biomedical Engineering* **4**, 261-286 (2002).
12. James, H. M. & Guth, E. Simple presentation of network theory of rubber, with a discussion of other theories. *J. Polym. Sci.* **4**, 153-182 (1949).
13. Flory, P. J. & Rehner Jr., J. Statistical mechanics of cross-linked polymer networks. I. Rubberlike elasticity. *J. Chem. Phys.* **11**, 512-520 (1943).
14. Flory, P. J. & Rehner Jr., J. Statistical mechanics of cross-linked polymer networks. II. Swelling. *J. Chem. Phys.* **11**, 521-526 (1943).
15. Brannonpeppas, L. & Peppas, N. A. Equilibrium Swelling Behavior of Ph-Sensitive Hydrogels. *Chemical Engineering Science* **46**, 715-722 (1991).
16. Peppas, N. A. & Merrill, E. W. Polyvinyl-Alcohol) Hydrogels - Reinforcement of Radiation-Crosslinked Networks by Crystallization. *Journal of Polymer Science Part a-Polymer Chemistry* **14**, 441-457 (1976).
17. Ozyurek, C., Caykara, T., Kantoglu, O. & Guven, O. Characterization of network structure of poly(N-vinyl 2-pyrrolidone/acrylic acid) polyelectrolyte hydrogels by swelling measurements. *Journal of Polymer Science Part B-Polymer Physics* **38**, 3309-3317 (2000).