Hydrogel thermodynamics (continued)
Physical hydrogels

Last Day: bioengineering applications of hydrogels
thermodynamics of hydrogel swelling

Today: Structure, physical chemistry, and thermodynamics of physical gels

Reading: L.E. Bromberg and E.S. Ron, 'Temperature-responsive gels and thermogelling polymer matrices for protein and peptide delivery,' *Adv. Drug Deliv. Rev*., **31**, 197 (1998)

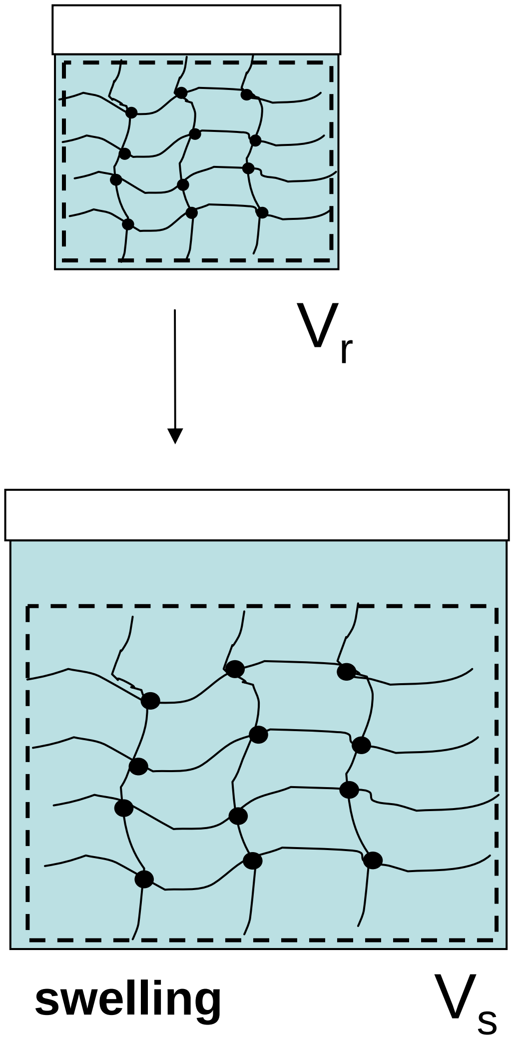
D. Chandler 'Interfaces and the driving force of hydrophobic assembly,' *Nature* **437**, 640-647 (2005)

Announcements:

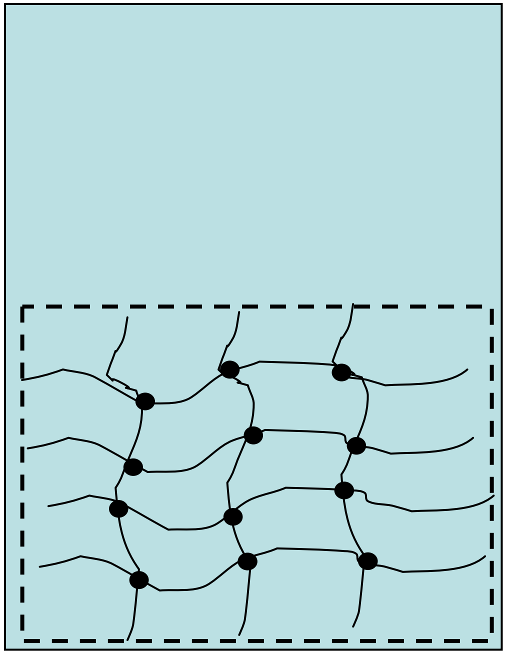
Thermodynamics of hydrogel swelling:

Peppas-Merrill theory (derived from Flory-Rehner theory of elastic gels)

Competing driving forces determine total swelling:



Chemical potential requirement for equilibrium in the gel:

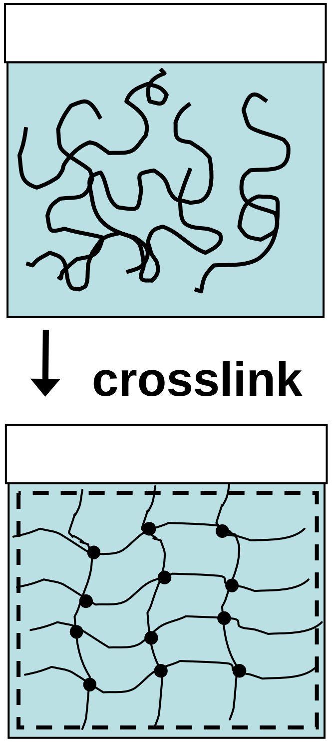


Governing equation for equilibrium:

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

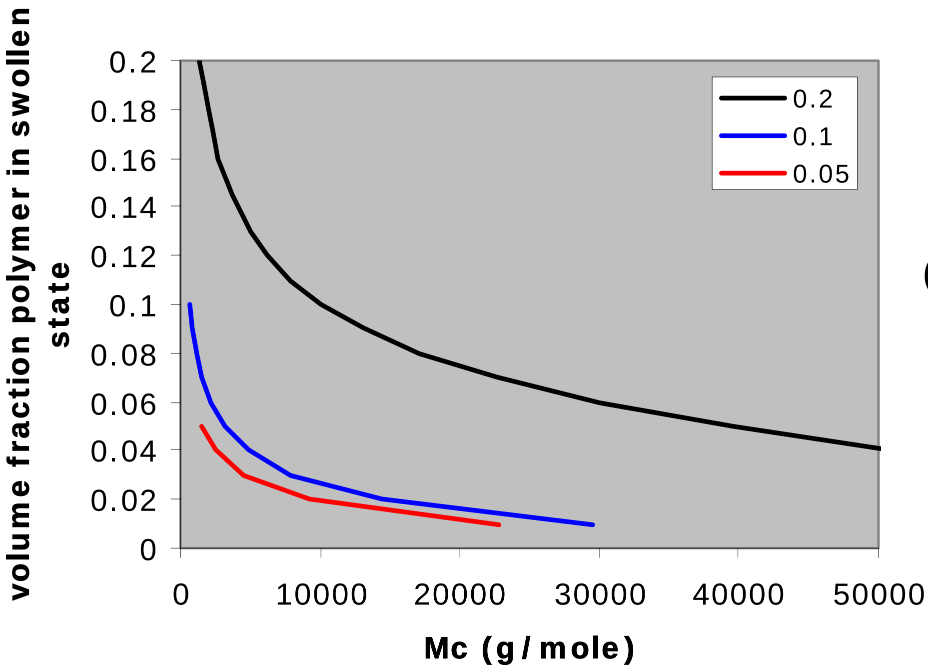
$$\frac{1}{M_C} = \frac{2}{M} - \frac{v_{sp,2}}{V_1\phi_{2,r}}\left[\frac{\ln(1-\phi_{2,s}) + \phi_{2,s} + \chi\phi_{2,s}^2}{\left(\frac{\phi_{2,s}}{\phi_{2,r}}\right)^{1/3} - \frac{1}{2}\left(\frac{\phi_{2,s}}{\phi_{2,r}}\right)}\right]$$

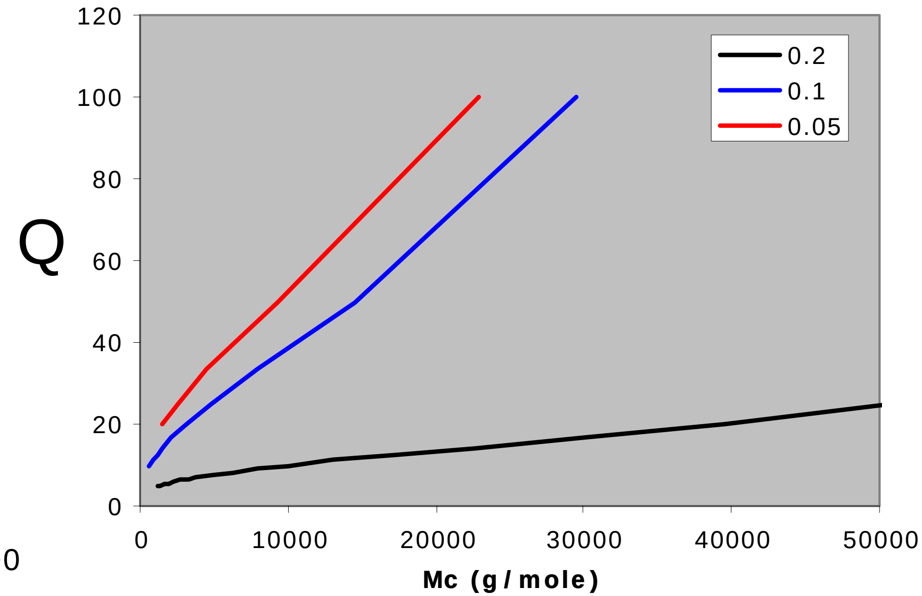
Example application of Flory-Rehner/Peppas-Merrill theory:



Predictions of Flory/Peppas theory

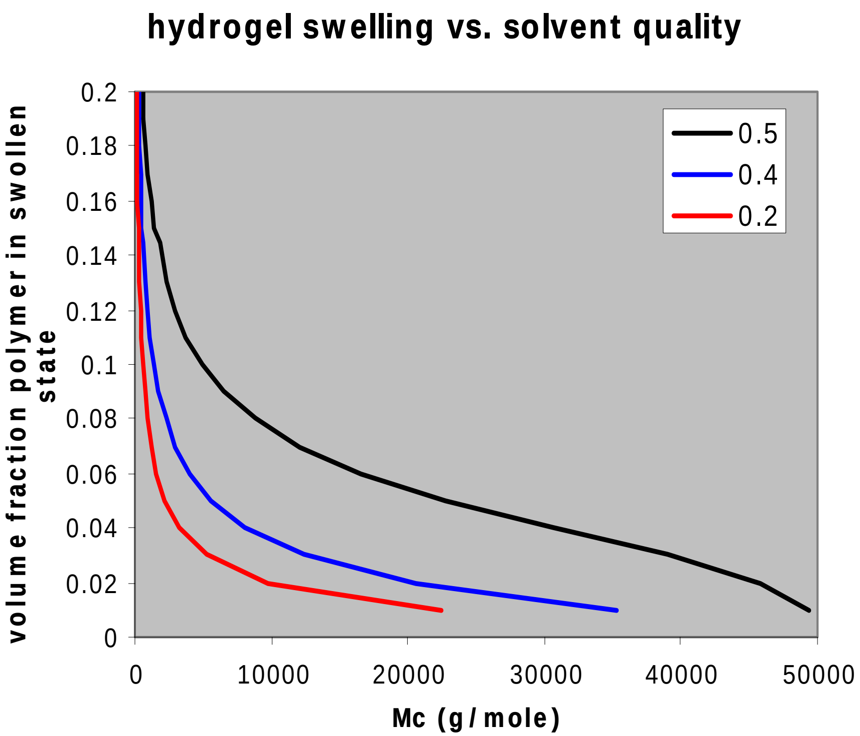
Varying $\phi_{2,r}$:

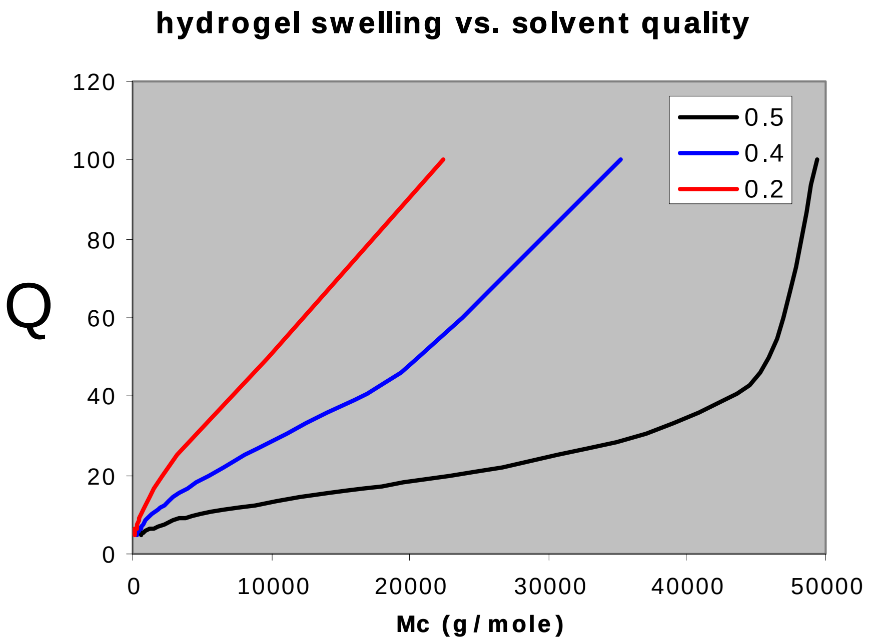




Predictions of Flory/Peppas theory

Varying χ:



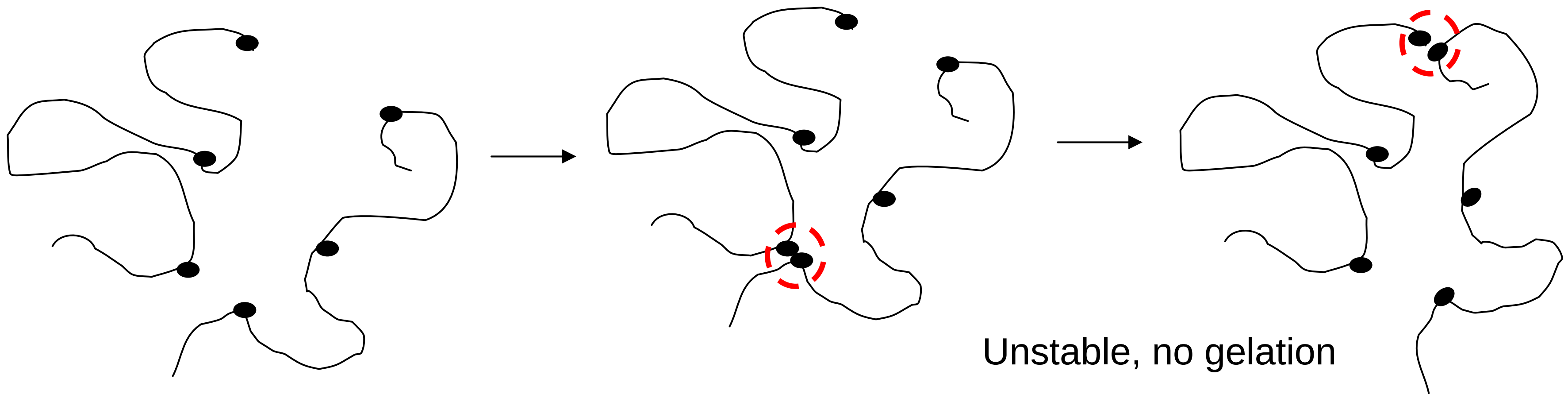


Model parameters

μ_1^{bath}	chemical potential of water in external bath (= μ_1^0)
μ_1	chemical potential of water in the hydrogel
μ_1^0	chemical potential of pure water in standard state
Δw_{12}	pair contact interaction energy for polymer with water
z	model lattice coordination number
x	number of segments per polymer molecule
M	Molecular weight of polymer chains before cross-linking
M_c	Molecular weight of cross-linked subchains
n_1	number of water molecules in swollen gel
χ	polymer-solvent interaction parameter
k_B	Boltzman constant
T	absolute temperature (Kelvin)
$v_{m,1}$	molar volume of solvent (water)
$v_{m,2}$	molar volume of polymer
$v_{sp,1}$	specific volume of solvent (water)
$v_{sp,2}$	specific volume of polymer
V_2	total volume of polymer
V_s	total volume of swollen hydrogel
V_r	total volume of relaxed hydrogel
ν	number of subchains in network
ν_e	number of ‘effective’ subchains in network
ϕ_1	volume fraction of water in swollen gel
$\phi_{2,s}$	volume fraction of polymer in swollen gel
$\phi_{2,r}$	volume fraction of polymer in relaxed gel

Bonding in physical hydrogels

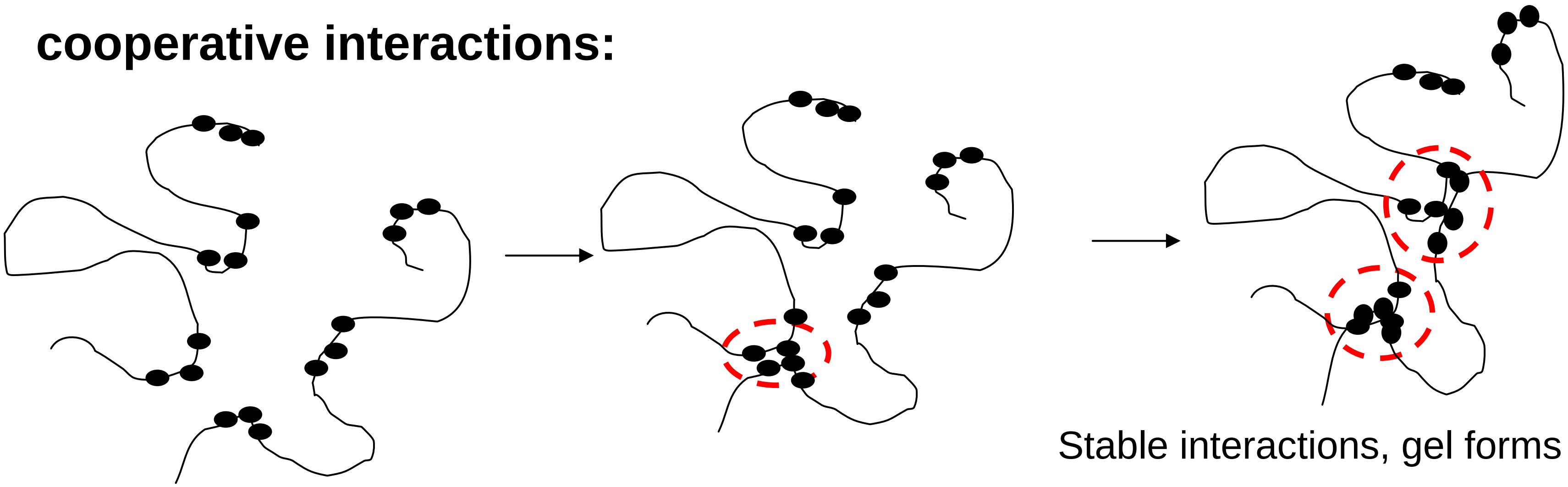
non-cooperative interactions:



Unstable, no gelation

Bonding in physical hydrogels

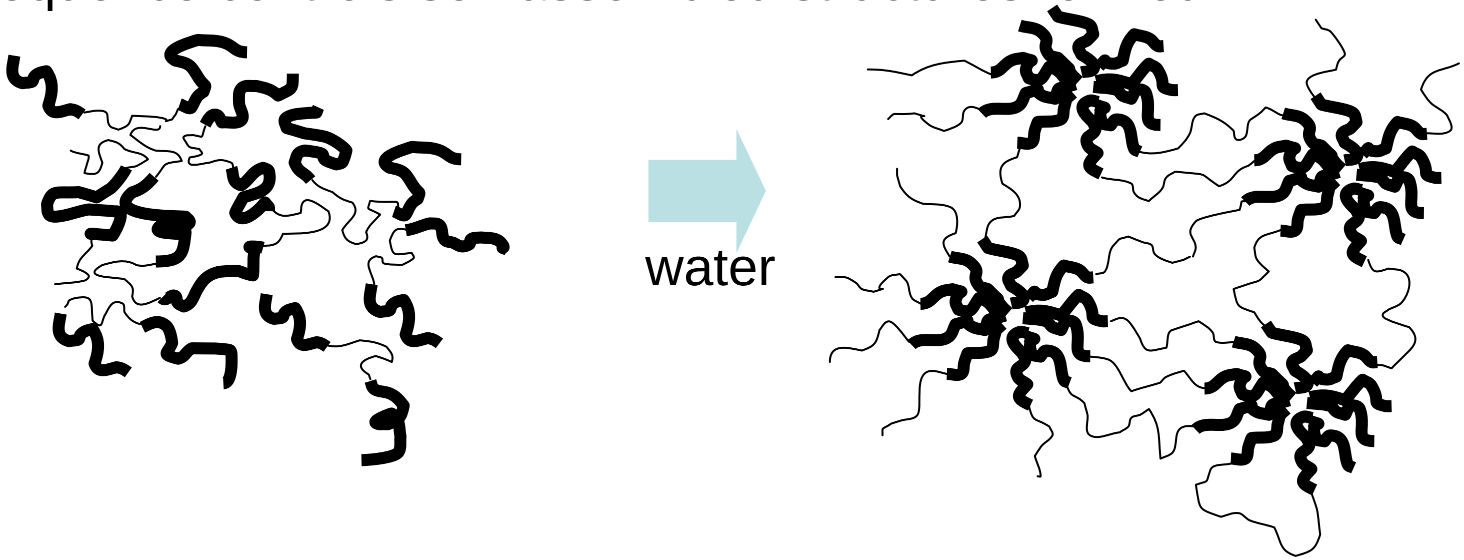
cooperative interactions:



Stable interactions, gel forms

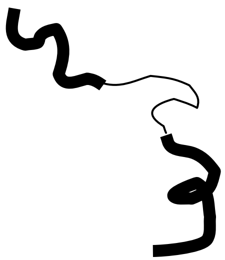
Gelation via hydrophobic associations

Block sequence controls self-assembled structures formed:



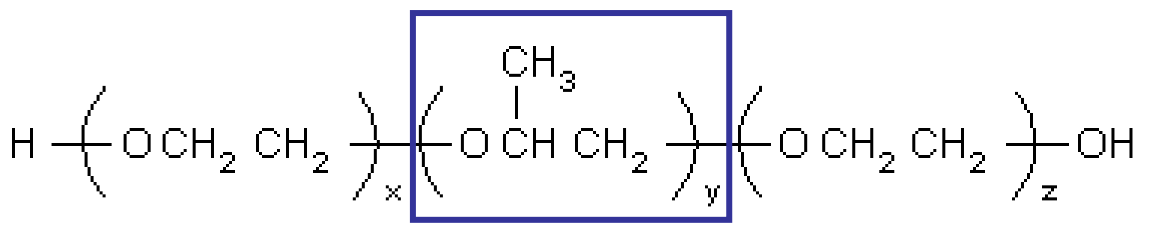
Chemical structure of associative copolymers used in bioengineering

Example blocks:

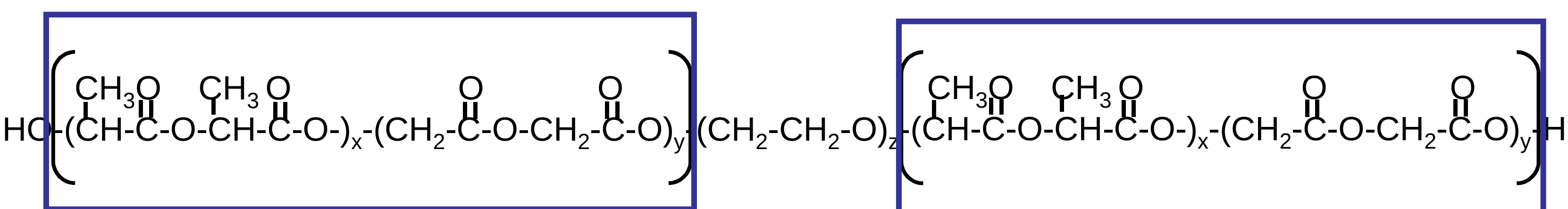


Hydrophilic B blocks — Poly(ethylene glycol) (PEG)

Hydrophobic A blocks — Poly(propylene oxide) (PPO)
Poly(butylene oxide) (PBO)



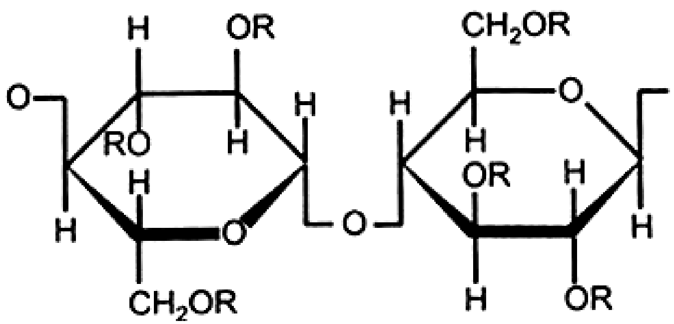
PEO PPO PEO



PLGA PEG PLGA

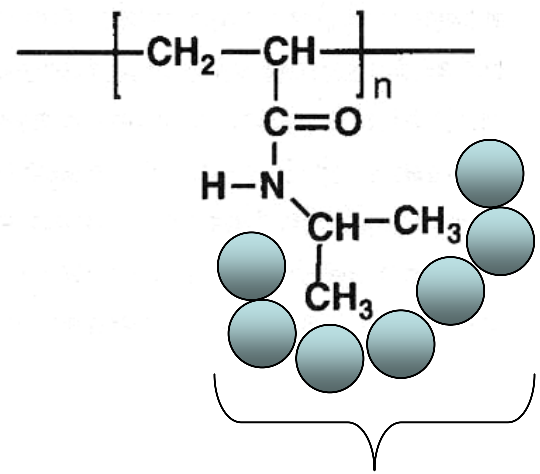
Gelation via hydrophobic associations

Hydroxypropylmethyl cellulose



R = $-CH_2-CH(OH)-CH_3$, $-CH_3$, or $-H$

Poly(N-isopropylacrylamide)

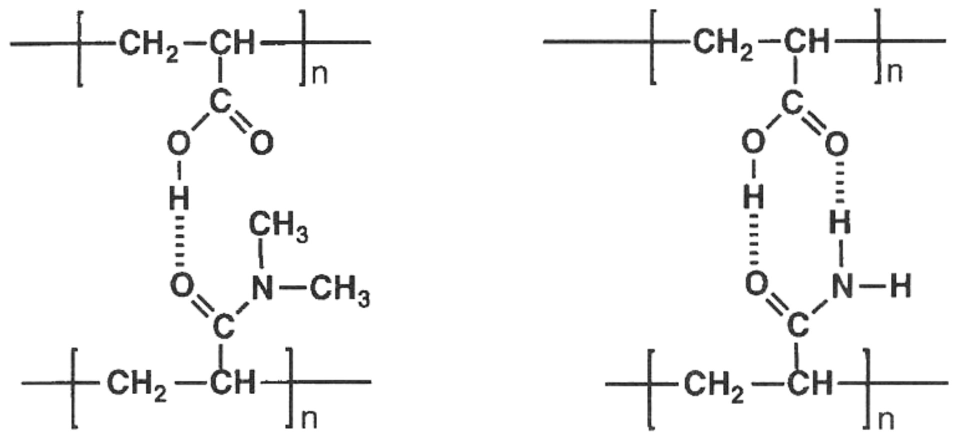


ordered water molecules
(minimize water-hydrophobe contacts)

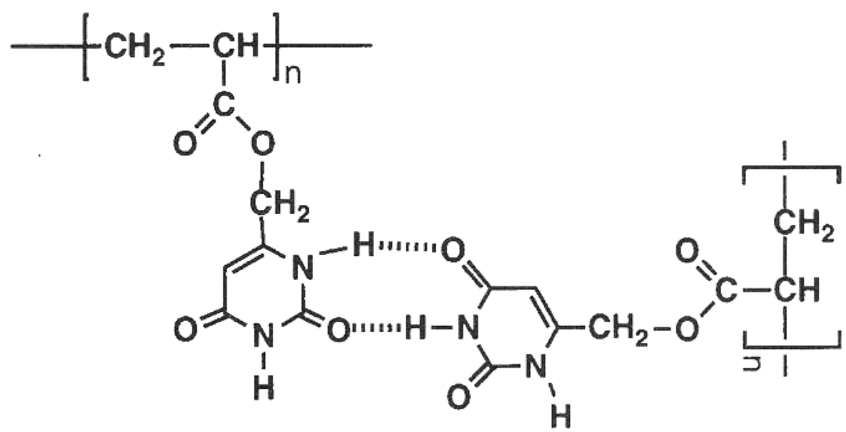
Dehydration allows water to disorder (*entropically-driven*)

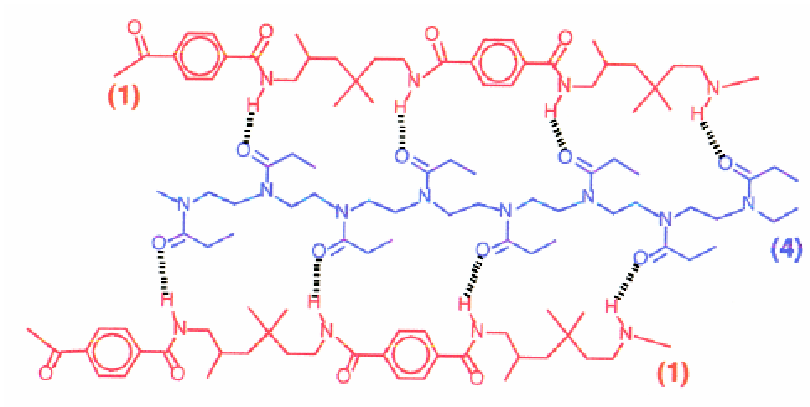
$$\Delta S = S_{dehydrated} - S_{hydrated} > 0$$

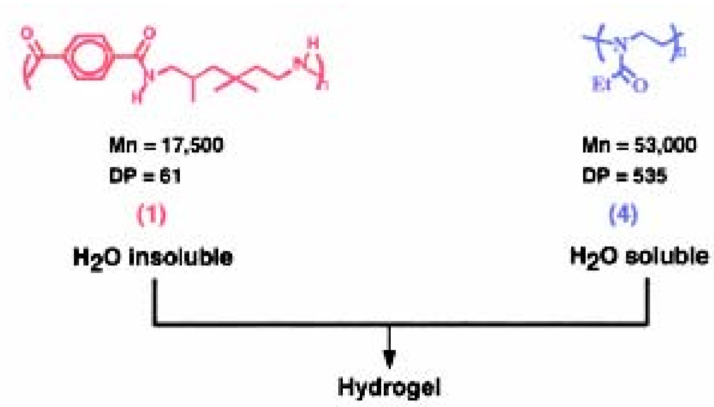
Hydrogen-bonded hydrogels



(c)







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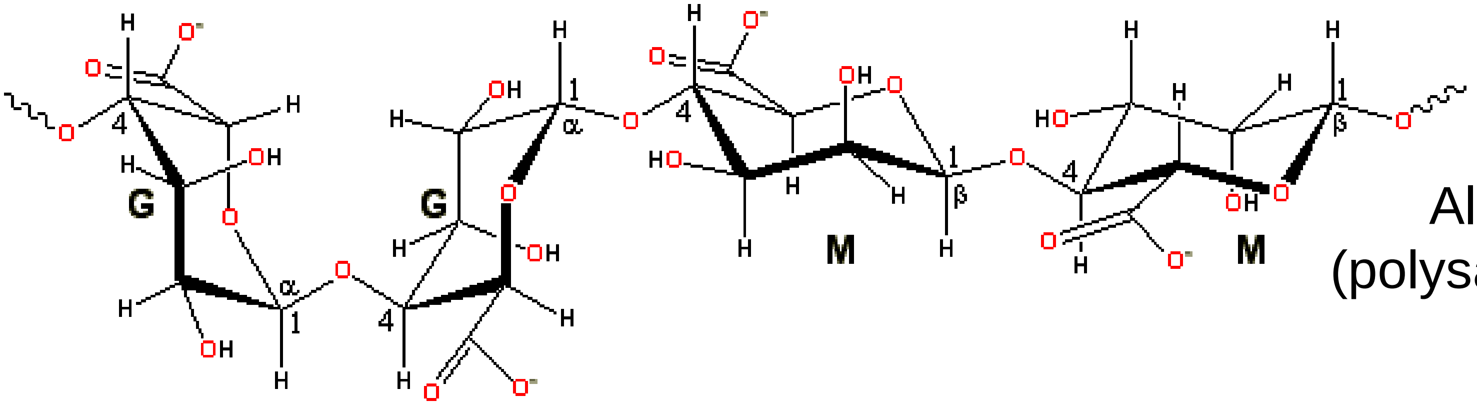
Please see:
Figures 4 and 5 in Percec, V., T. K. Bera, and R. J. Butera. *Biomacromolecules* 3 (2002): 272-9.

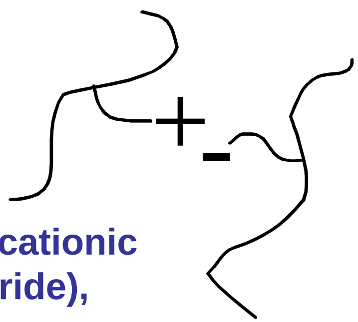
Ionically-bonded hydrogels



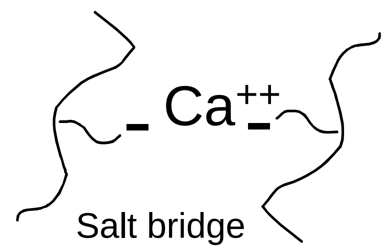
Alginate
(polysaccharide)

+ cationic polymer

+ divalent cations



e.g. chitosan (cationic polysaccharide), polylysine



Salt bridge
Divalent cations

http://www.lsbu.ac.uk/water/hyalg.html

Combined non-covalent interactions example: coiled-coil peptide gels

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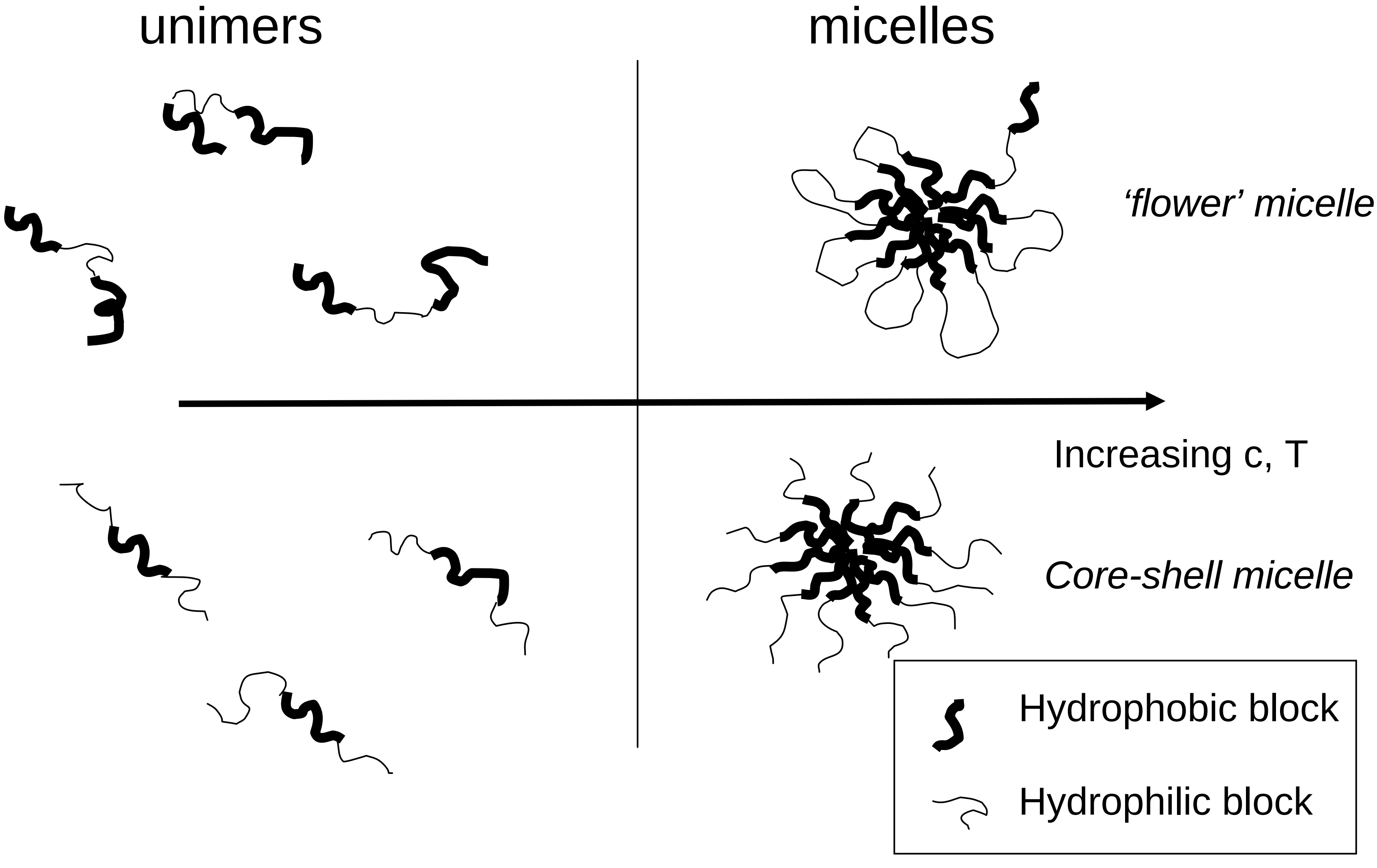
Please see:
Figure 1 in Wang, C., R. J. Stewart, and J. Kopecek. "Hybrid Hydrogels Assembled From Synthetic Polymers and Coiled-coil Protein Domains." *Nature* 397 (1999): 417-20.

Structure of associating block copolymer hydrogels



Formation of micelles

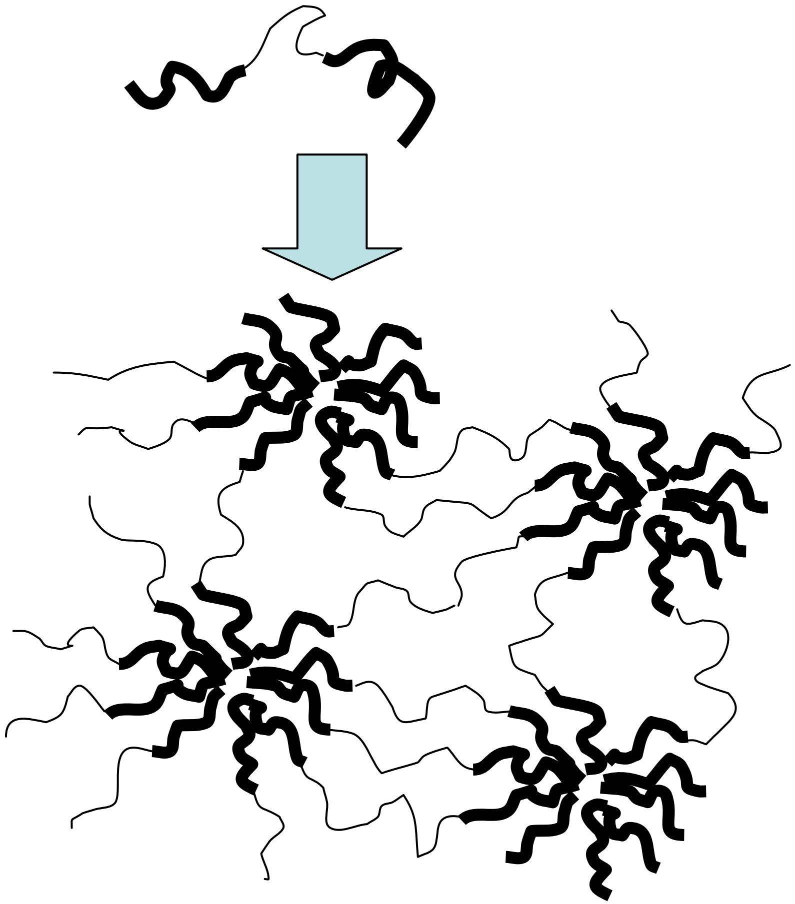
Transition range: micelles in equilibrium with unimers

Experiments by Hatton group at MIT:

PEO-PPO-PEO micellization at different temperatures measured by adding a hydrophobic dye that absorbs UV light when bound in a hydrophobic environment (e.g. micelle core) but not free in solution

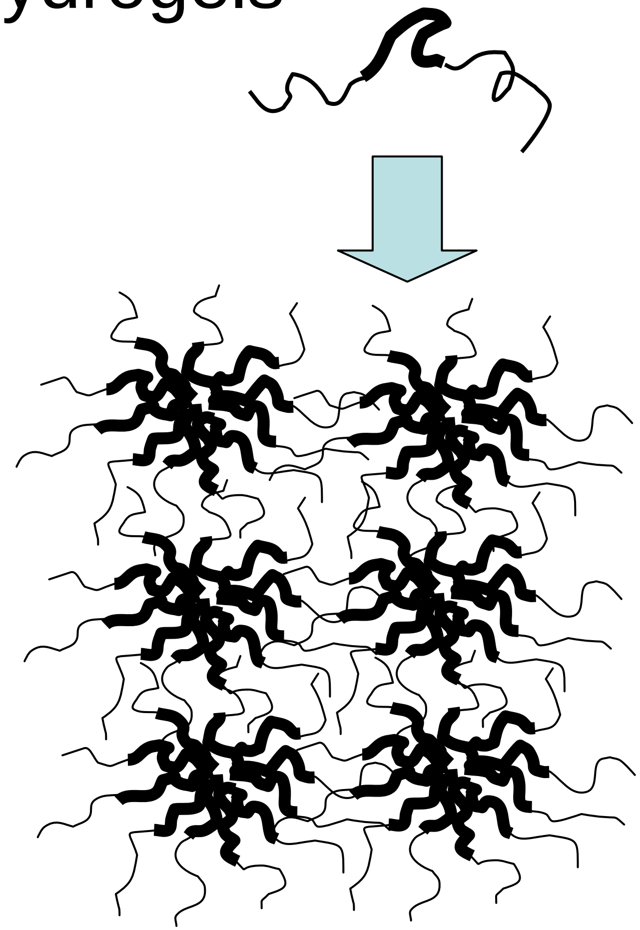
Figure 3 in Alexandridis, P., J. F. Holzwarth, and T. A. Hatton. *Macromolecules* 27 (1994): 2414-2425.

Structure of associating block copolymer hydrogels

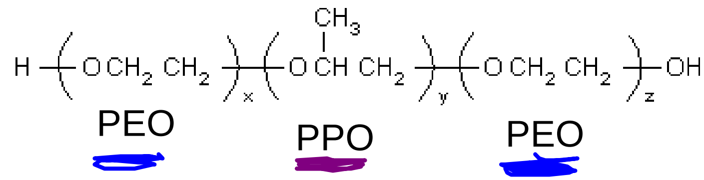


Intermicelle physical cross-links

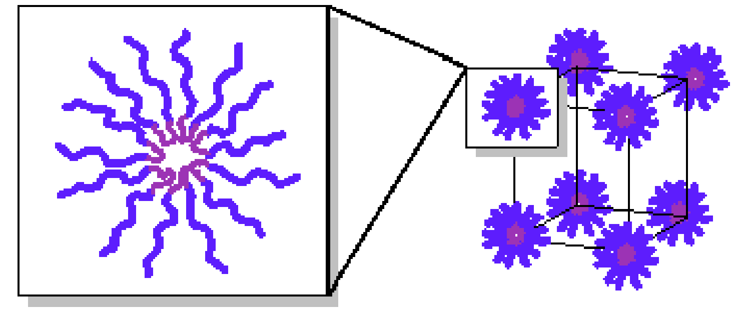
Structure of associating block copolymer hydrogels

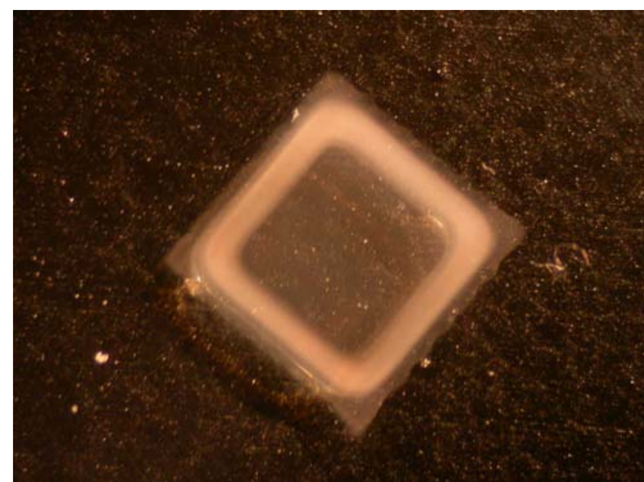


Entanglement and H-bonding between packed micelle coronas



micelle (spherical)





Structure of associating block copolymer hydrogels

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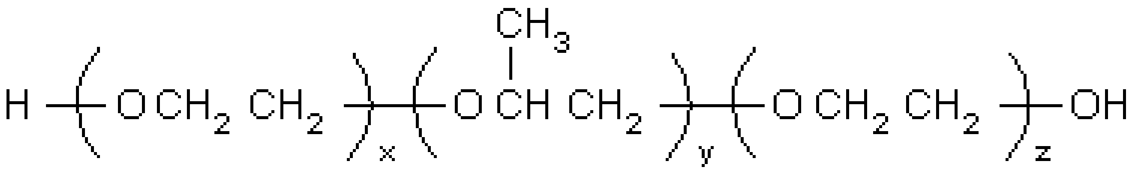
Please see:
Figures 19 and 20 in Chu, B. and Z. Zhou. *Nonionic Surfactants: Polyoxyalkylene Block Copolymers*. Edited by V. M. Nace. New York, NY: Marcel Dekker, 1996, pp. 67-143.

Block length determines gel structure



Tables removed for copyright reasons.

Please see:

Figure 14 in Chu, B. Z. Zhou. *Nonionic Surfactants: Polyoxyalkylene Block Copolymers.* Edited by V.M. Nace. New York, NY: Marcel Dekker, 1996, pp. 67-143.

Relation between structure and applications in bioengineering

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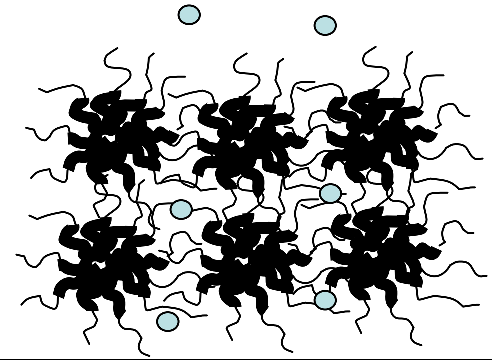
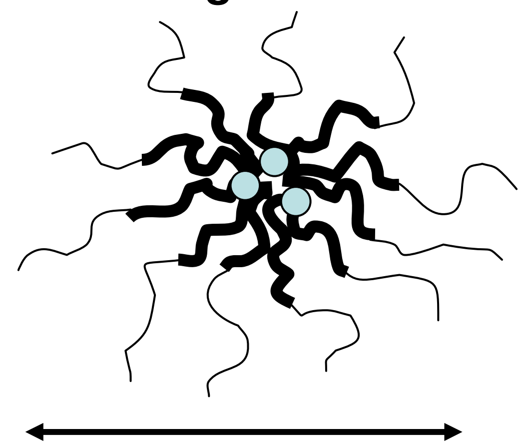
Please see:
Figure 1 in Zhang, L., D. L. Parsons, C. Navarre, and U. B. Kompella. *J Control Release* 85 (2002): 73-81.

Cubic phase gel drug depots

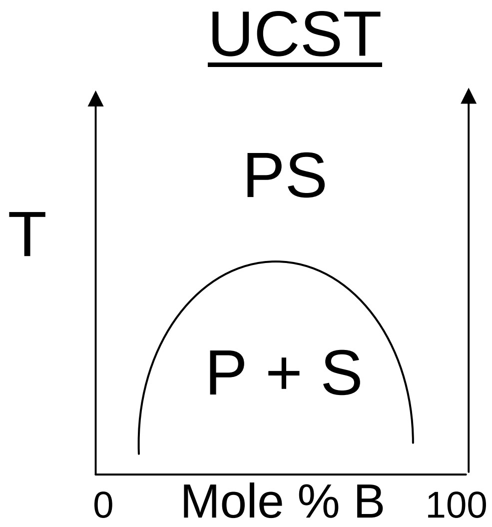


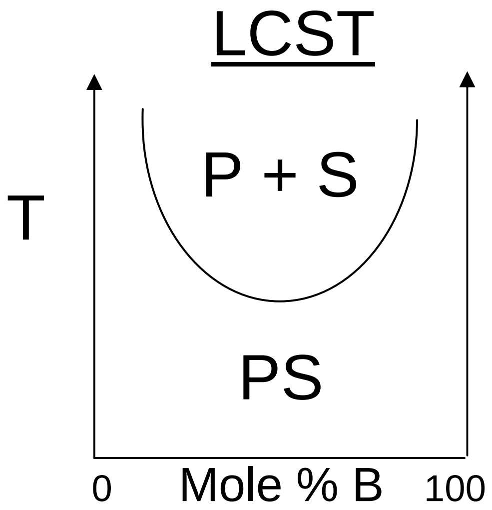
Micelle drug nanocarriers



10-50 nm

Thermodynamics of hydrophobic association





PS = polymer solution
P + S = two-phase region: polymer-rich, polymer-poor

Thermodynamics of hydrophobic association

Determination of thermodynamic driving force for triblock self-assembly

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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.

Further Reading

1. Wang, C., Stewart, R. J. & Kopecek, J. (1999) *Nature* **397,** 417-20.
2. Guenet *Thermoreversible Gelation of Polymers and Biopolymers*, New York).
3. Shah, J. C., Sadhale, Y. & Chilukuri, D. M. (2001) *Adv Drug Deliv Rev* **47,** 229-50.
4. Landau, E. M. & Rosenbusch, J. P. (1996) *Proc Natl Acad Sci U S A* **93,** 14532-5.
5. Ron, E. S. & Bromberg, L. E. (1998) *Adv Drug Deliv Rev* **31,** 197-221.
6. Percec, V., Bera, T. K. & Butera, R. J. (2002) *Biomacromolecules* **3,** 272-9.
7. Kuo, C. K. & Ma, P. X. (2001) *Biomaterials* **22,** 511-21.
8. Bray, J. C. & Merrill, E. W. (1973) *Journal of Applied Polymer Science* **17,** 3779-3794.
9. Salem, A. K., Rose, F. R. A. J., Oreffo, R. O. C., Yang, X., Davies, M. C., Mitchell, J. R., Roberts, C. J., Stolnik-Trenkic, S., Tendler, S. J. B., Williams, P. M. & Shakesheff, K. M. (2003) *Advanced Materials* **15,** 210-213.
10. Cao, Y., Rodriguez, A., Vacanti, M., Ibarra, C., Arevalo, C. & Vacanti, C. A. (1998) *J Biomater Sci Polym Ed* **9,** 475-87.
11. Zhang, L., Parsons, D. L., Navarre, C. & Kompella, U. B. (2002) *J Control Release* **85,** 73-81.
12. Jeong, B., Bae, Y. H., Lee, D. S. & Kim, S. W. (1997) *Nature* **388,** 860-2.
13. Chu, B. & Zhou, Z. (1996) in *Nonionic Surfactants: Polyoxyalkylene Block Copolymers*, ed. Nace, V. M. (Marcel Dekker, New York), pp. 67-143.
14. Chu, B. (1995) *Langmuir* **11,** 414-421.
15. Alexandridis, P., Holzwarth, J. F. & Hatton, T. A. (1994) *Macromolecules* **27,** 2414-2425.