Applications of hydrogels

Last Day: polyelectrolyte gels
Polyelectrolyte complexes and multilayers
Theory of ionic gel swelling

Today: hydrogels in biomedical/bioengineering applications
Linking gel mesh size to diffusivity of solutes

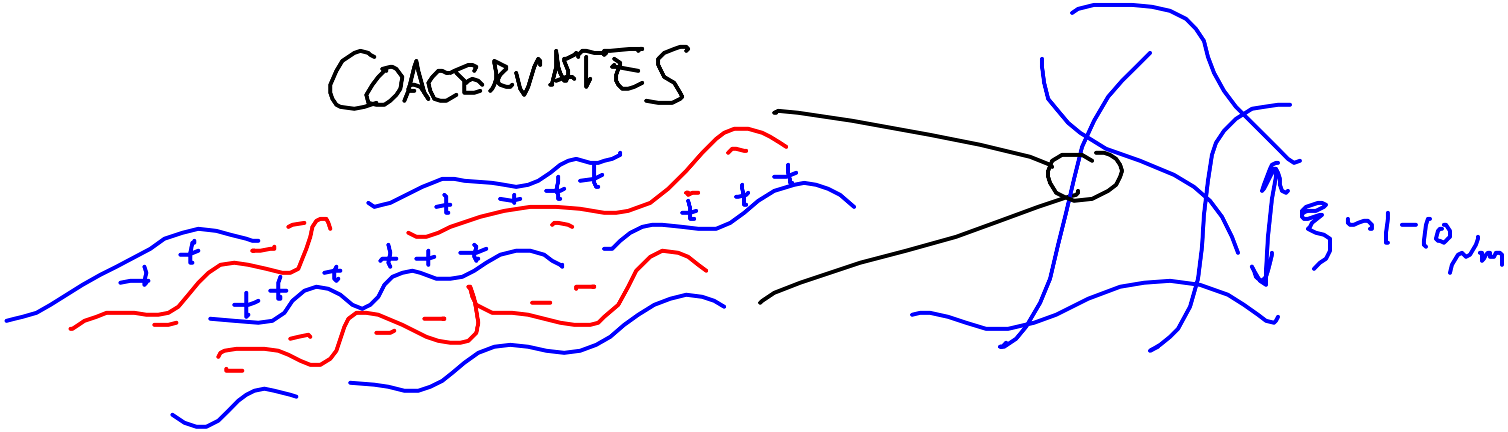
Reading: -

Supplementary Reading: S.R. Lustig and N.A. Peppas, 'Solute diffusion in swollen membranes. IX. Scaling laws for solute diffusion in gels,' *J. Appl. Polym. Sci*. **36**, 735-747 (1988)
T. Canal and N.A. Peppas, 'Correlation between mesh size and equilibrium degree of swelling of polymeric networks,' *J. Biomed. Mater. Res*. **23**, 1183-1193 (1989)

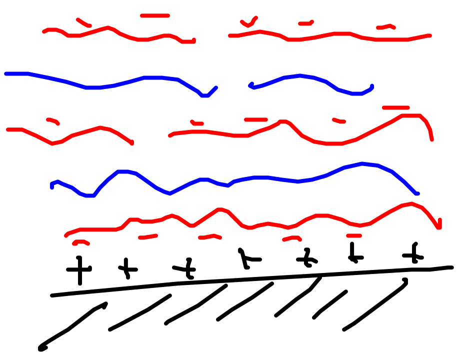
ANNOUNCEMENTS: PS 4 DUE ~~THURSDAY~~ FRIDAY 5pm
FIRST EXAM NEXT TUESDAY (IN CLASS)
COVERAGE: LECTURES 1-10
CLOSED BOOK
EQUATIONS WILL BE PROVIDED

Last time POLYELECTROLYTE HYDROGELS

COACERVATES

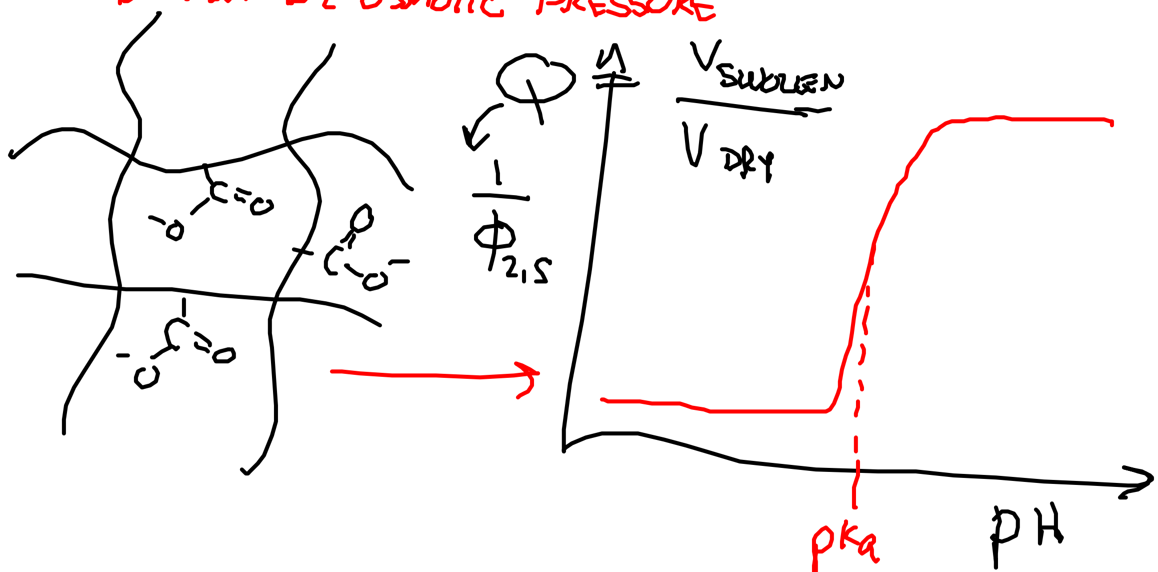


MULTILAYERS



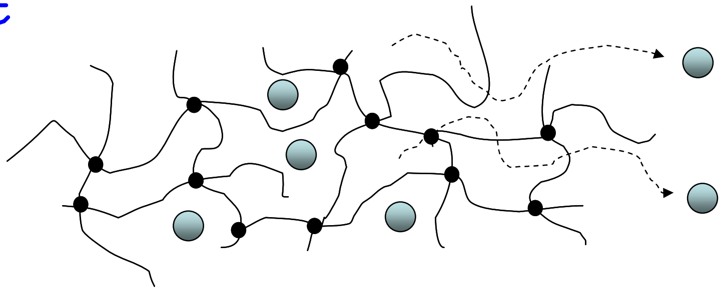
UNPAIRED POLYELECTROLYTE GELS

DRIVEN BY OSMOTIC PRESSURE



Applications of hydrogels in bioengineering

- CONTROLLED RELEASE



- IMMUNOISOLATION

  TRANSPLANTING CELLS < XENOGENEIC (ANOTHER SPECIES) / ALLOGENEIC (ANOTHER HUMAN)

  ⇓

  ISOLATION FROM IMMUNE SYSTEM

- TISSUE ENGINEERING SCAFFOLDS (SOFT TISSUES)

- TISSUE BARRIERS AND CONFORMAL COATINGS

Hydrogels applied to drug delivery

ADVANTAGES

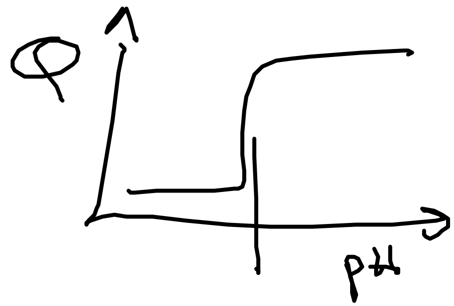
- HYDROPHILIC ENVIRONMENT (PROTEIN DRUGS STABLE) <(NO ORGANIC SOLVENTS DURING FABRICATION)>
- GOOD TRANSPORT OF ACID/BASE BYPRODUCTS OUT OF DEGRADABLE HYDROGELS

DISADVANTAGES

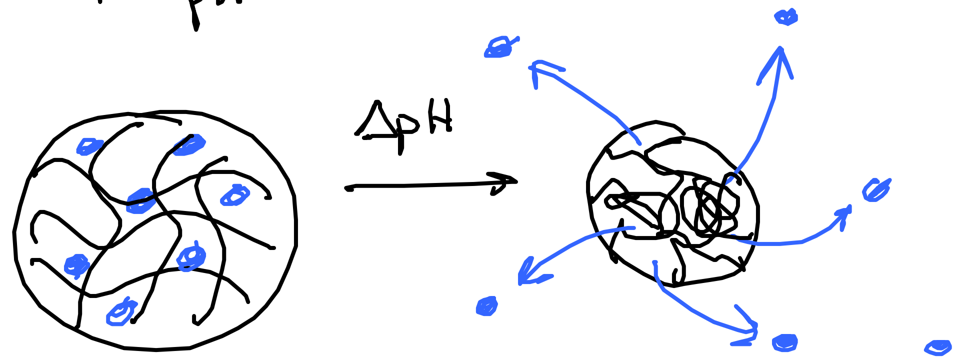
- DIFFICULT TO ENGINEER LONG-TERM RELEASE (e.g., BEYOND ~1 WEEK)

On/off drug release using PE hydrogels

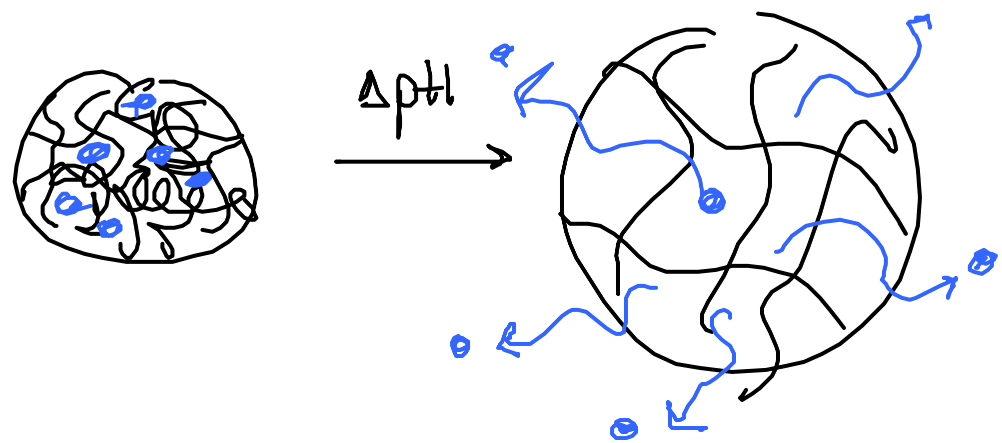
Two strategies:



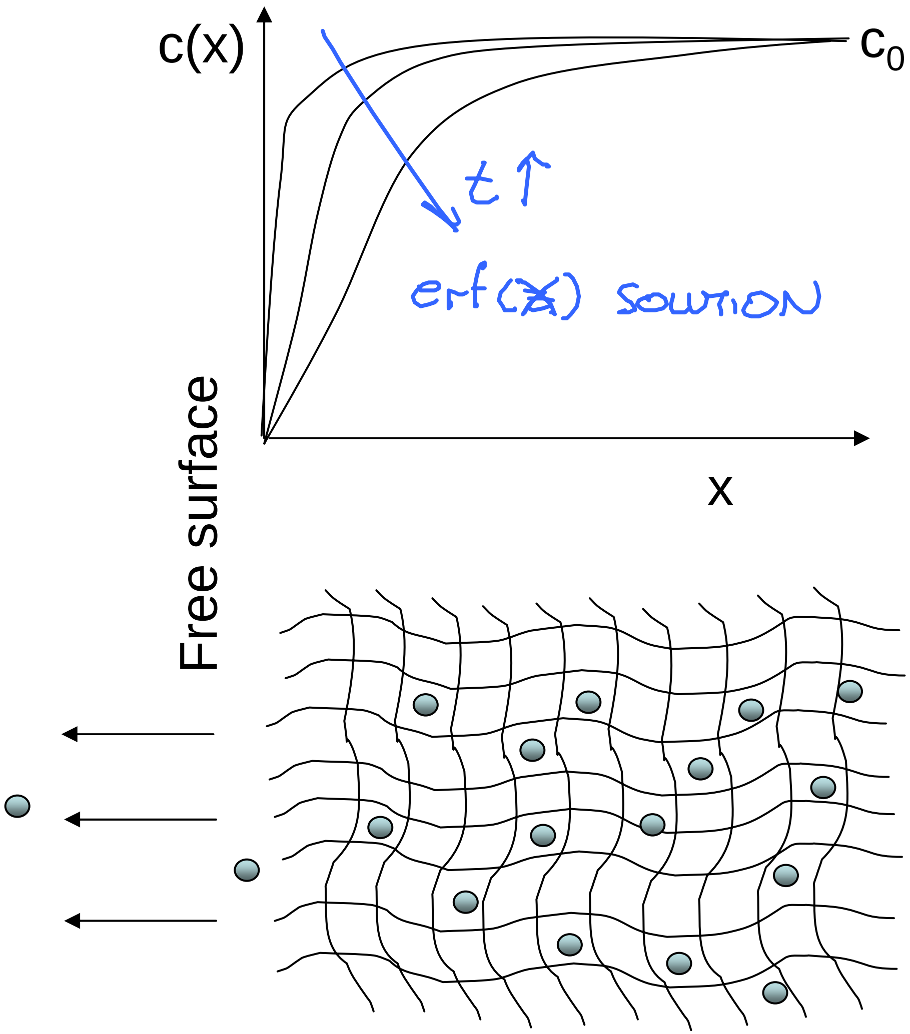
SQUEEZE-RELEASE:



EXPANSION-RELEASE:



Kinetics of drug release from hydrogels using swollen-on/collapsed-off mechanism



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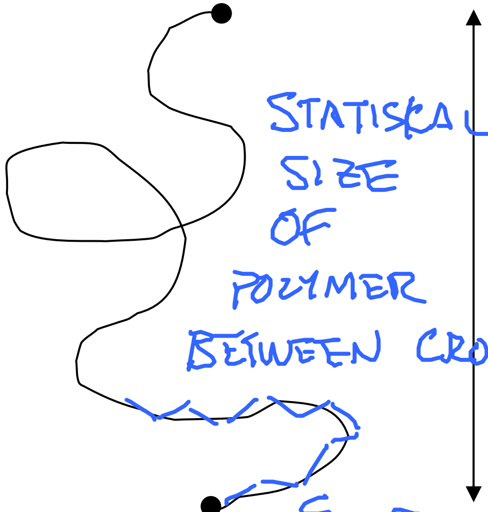
Please see:
Figure 3 in Canal, T., and N. A. Peppas. "Correlation Between Mesh Size and Equilibrium Degree of Swelling of Polymeric Networks." *Journal of Biomedical Materials Research* 23 (1989): 1183-1193.

Mesh size of hydrogel networks

$\Delta S^* \sim k_b \ln P^*_{GEL,OPENING} \, P^*_{GEL,VOLUME}$



STATISTICAL SIZE OF POLYMER BETWEEN CROSSLINKS

END-TO-END DISTANCE

$$(\langle r_0^2 \rangle)^{1/2} = N_c^{1/2} a$$

statistical segment length

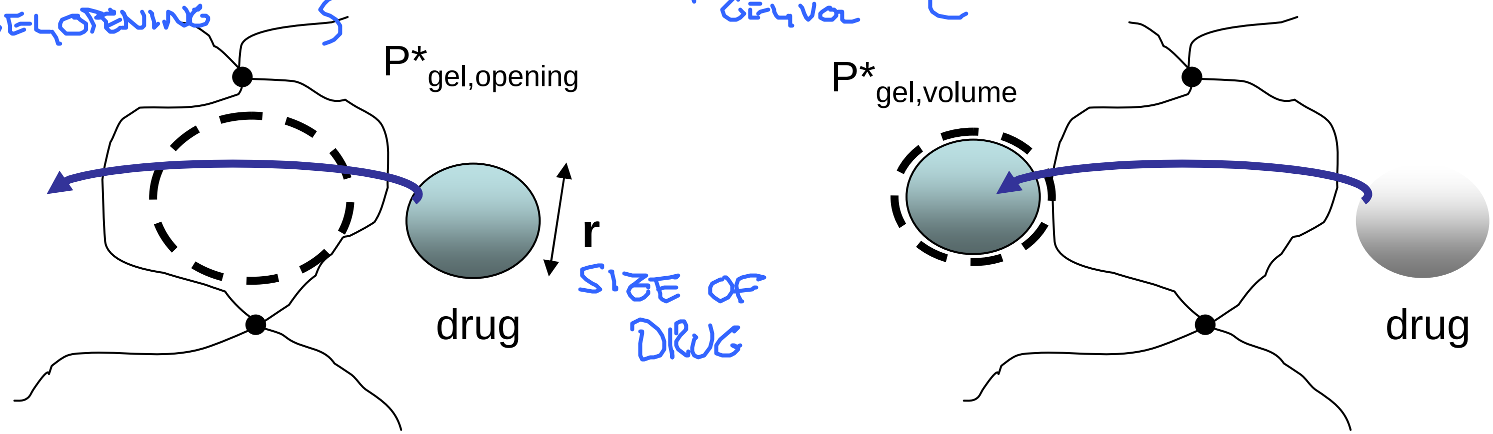
Number of segments between cross-links

SIZE OF COIL IN SOLID POLYMER GEL

↳ GAUSSIAN CHAIN DISTRIBUTION

$P^*_{GEL,OPENING} = \frac{\xi - r}{\xi}$

$P^*_{GEL,VOL} = e^{-\frac{1}{(Q-1)}}$



Connection between mesh size and diffusion coefficient of entrapped molecules

MESH SIZE: $\xi \sim \frac{\left(\overline{r_0^2}\right)^{1/2}}{\phi_{2,s}^{1/3}} \sim C\, N_c^{1/2}\, Q^{1/3}$

(C ← CONSTANT)

$\phi_{2,s} = \frac{1}{Q}$

$$\phi_{2,s}^{LOCAL} = \frac{\left(\left(\overline{r_0^2}\right)^{1/2}\right)^3}{\xi^3} = \frac{V_{DRY}^{SINGLE\ CHAIN}}{V_{SWOLLEN}^{SINGLE\ CHAIN}}$$

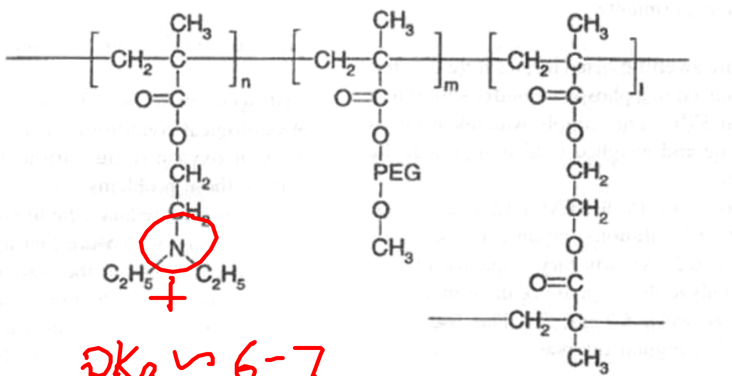
EYRING THEORY:

$$D_{GEL} = D_0\left(1 - \frac{r}{\xi}\right) e^{-\frac{1}{(Q-1)}}$$

D_0 ↑ DIFF COEFFICIENT OF SOLUTE IN PURE H_2O

Controlling diffusivity for responsive drug delivery: treatment of diabetes

GEL COMPOSITION



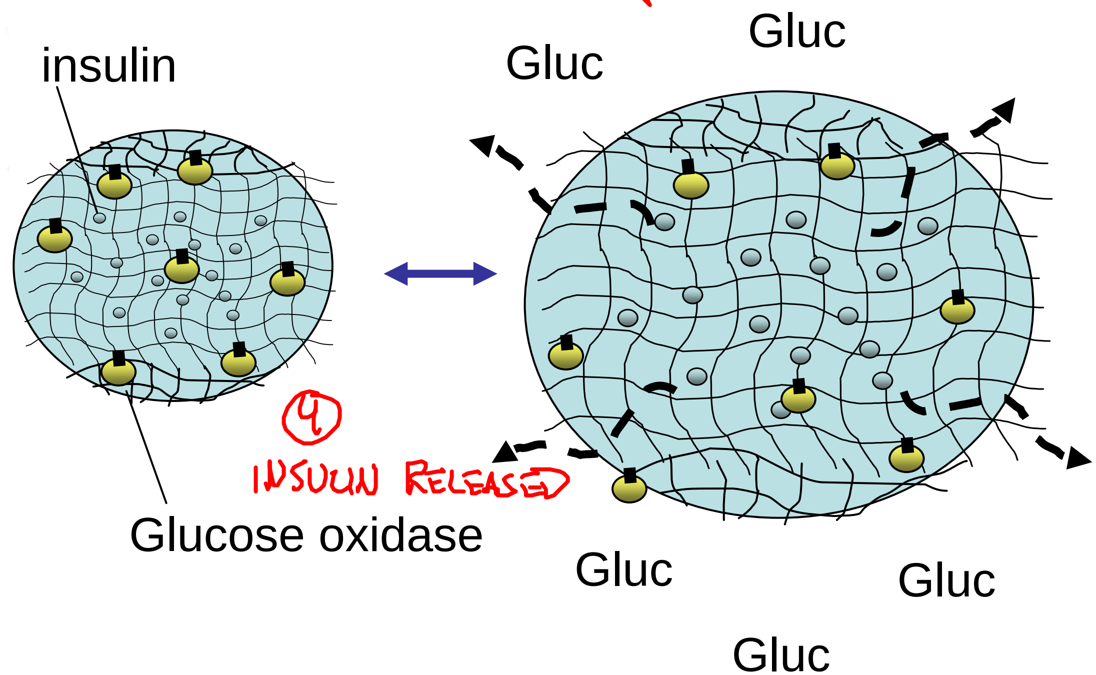
DEAEM PEGMA TEGDMA

pKa ~ 6-7

③ GEL IONIZES

① $$\text{Glucose} + O_2 \xrightarrow{\text{Glucose oxidase}} \text{Gluconic acid} + H_2O_2$$

② pH↓



④ INSULIN RELEASED

(PEPPAS GROUP)

Controlling diffusivity for responsive drug delivery: treatment of diabetes

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Please see:
Figure 3 in Podual, K., F. J. Doyle, and N. A. Peppas. “Dynamic Behavior of Glucose Oxidase-containing Microparticles of Poly(ethylene glycol)-grafted Cationic Hydrogels in an Environment of Changing pH.” *Biomaterials* 21 (2000): 1439-1450.

Response of gel microparticles

Graphs removed due to copyright reasons.
Please see:
Figures 8 and 9 in Podual, K., F. J. Doyle, and N. A. Peppas. "Dynamic Behavior of Glucose Oxidase-containing Microparticles of Poly(ethylene glycol)-grafted Cationic Hydrogels in an Environment of Changing pH." *Biomaterials* 21 (2000): 1439-1450.

Glucose sensitivity

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Please see:
Figure 3 in Podual, K., F. J. Doyle, and N. A. Peppas. "Glucose-sensitivity of Glucose Oxidase-containing Cationic Copolymer Hydrogels Having Po y(ethylene glycol) Grafts." *Journal of Controlled Release* 67 (2000): 9-17.

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Please see:
Figure 6 in Podual, K., F. J. Doyle, and N. A. Peppas. "Glucose-sensitivity of Glucose Oxidase-containing Cationic Copolymer Hydrogels Having Poly(ethylene glycol) Grafts." *Journal of Controlled Release* 67 (2000): 9-17.

Diffusion rate changes in responsive microgels

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Please see:
Figures 5 and11 in Podual, K., F. J. Doyle, and N. A. Peppas. "Dynamic Behavior of Glucose Oxidase-containing Microparticles of Poly(ethylene glycol)-grafted Cationic Hydrogels in an Environment of Changing pH." *Biomaterials* 21 (2000): 1439-1450.

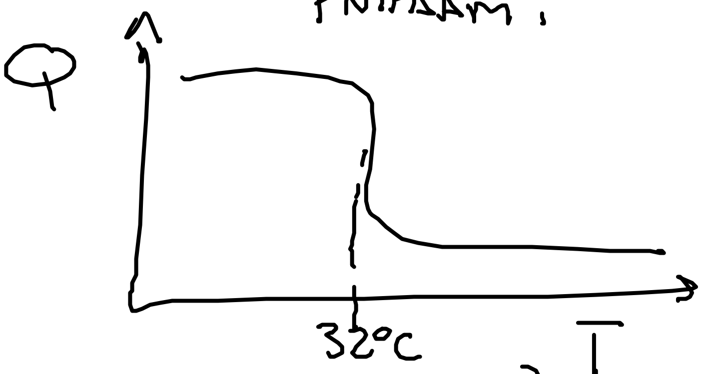
Chemical functionality in hydrogels can be utilized for responsive hydrogels

Mechanisms of environmental responsiveness in hydrogels:

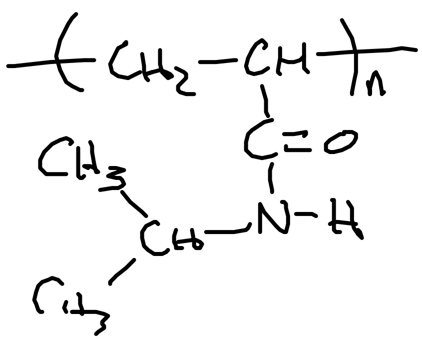
* LCST MATERIALS!

HYDROPHOBIC GROUPS THAT DEHYDRATE AT ELEVATED TEMP.

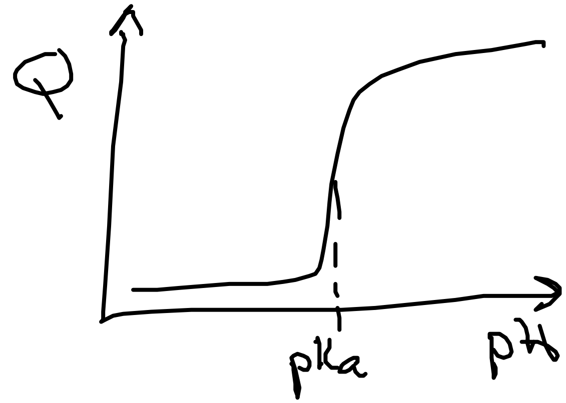
PNIPAAM:



POLY(N-ISOPROPYLACRYLAMIDE)



* POLYELECTROLYTE GELS



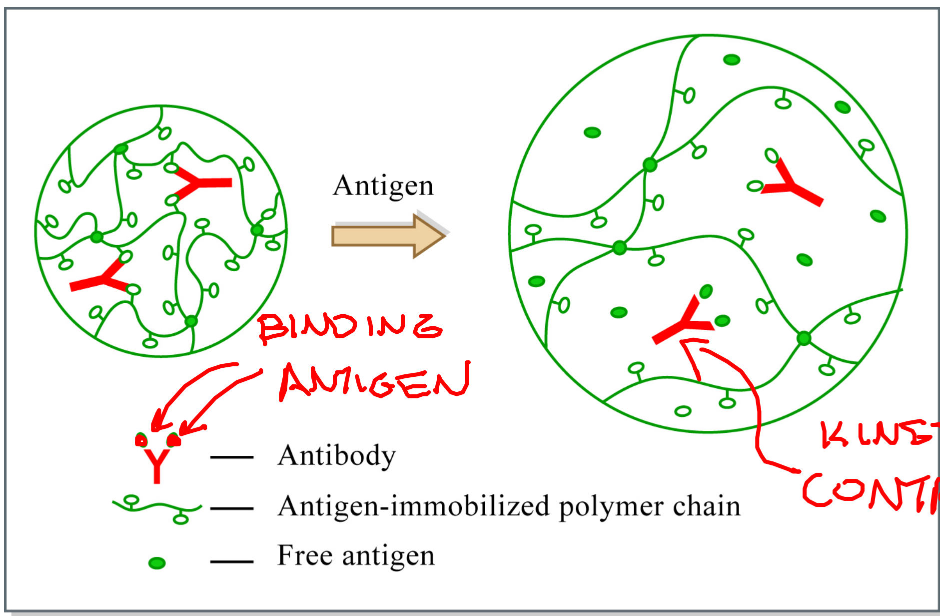
* LIGHT, CHEMICAL REACTIONS

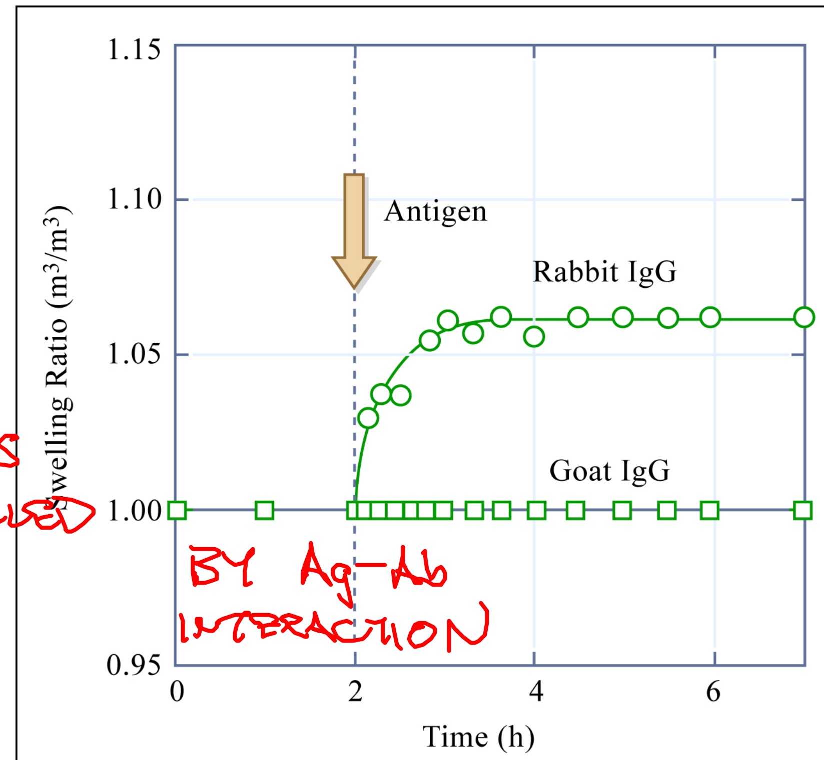
Chemical functionality in hydrogels can be utilized for responsive hydrogels

REACTIONS / PRESENCE OF SPECIFIC SPECIES CAN REGULATE GEL SWELLING

↓

APPLICATIONS: CAPTURE / RELEASE MOLECULES | CLOSE/OPEN PORES TO CONTROL TRANSPORT "GATING" | DETECT MOLECULES VIA PHYSICAL VOLUME CHANGES





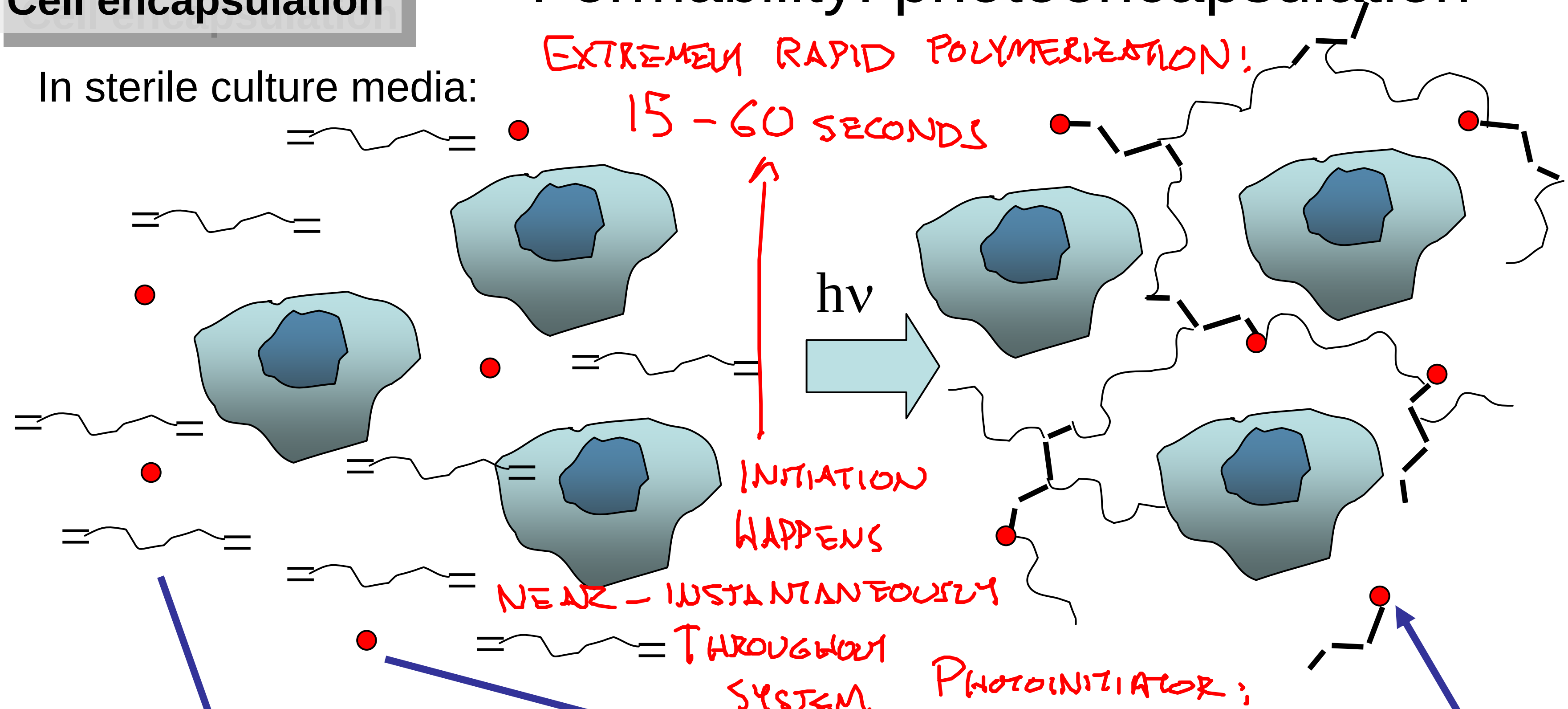
KINETICS CONTROLLED BY Ag-Ab INTERACTION

(Takahashi et al. *Macromol* **32**, 2082-2084 (1999)

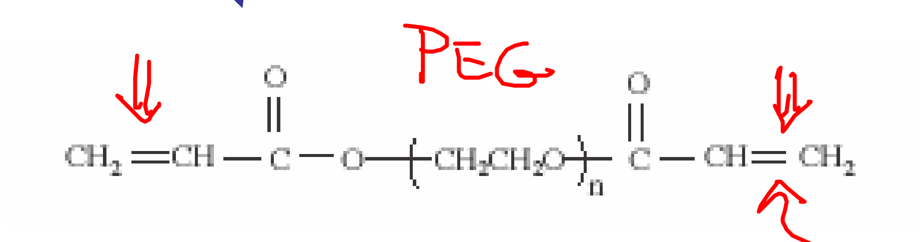
Immunoisolation/encapsulation of living cells

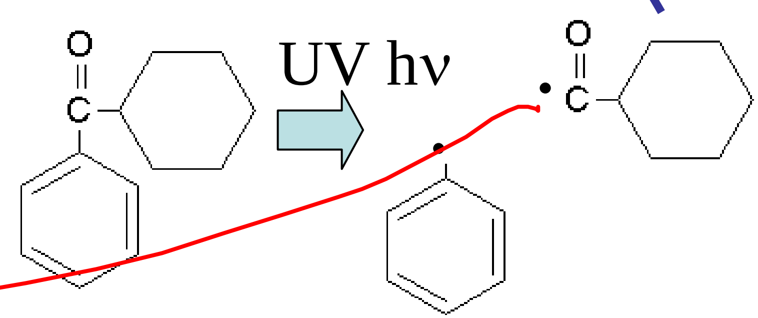
Formability: photoencapsulation

In sterile culture media:

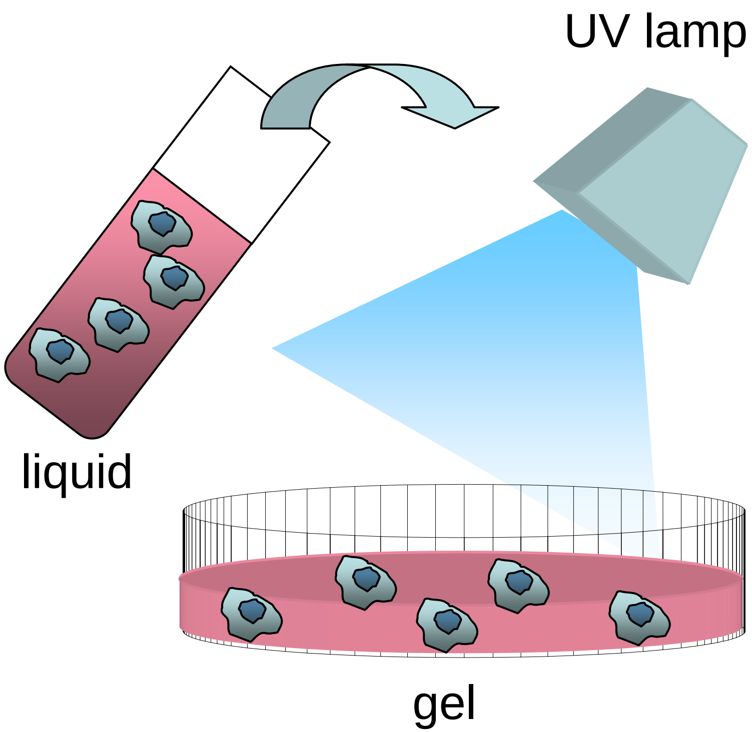


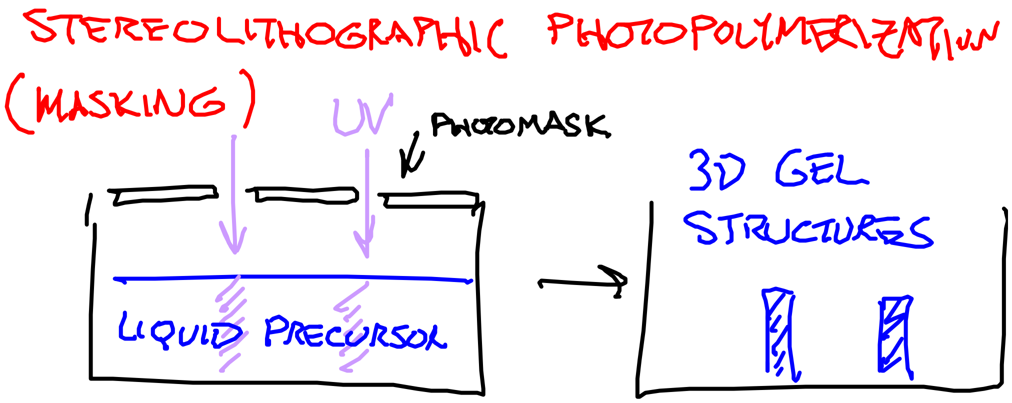
Cyclohexyl phenyl ketone:





Formability: photoencapsulation





Graph of Biochemical Analysis removed due to copyright restrictions.

immunoisolation

Images removed due to copyright restrictions,
Please see:
Lee, et al. *Adv. Drug Deliv Rev* 42 (2000): 103-120.

Hydrogels for tissue engineering

Motivation for hydrogels as tissue scaffolds:

1) READILY FUNCTIONALIZED FOR BIOLOGICAL RECOGNITION

2) PROCESS COMPLEX STRUCTURES UNDER MILD CONDITIONS

3) MATCH MECH. PROPERTIES OF SOFT TISSUES

COMPRESSIVE MODULI: ~1-10 KPa TYPICAL OF SOFT TISSUES

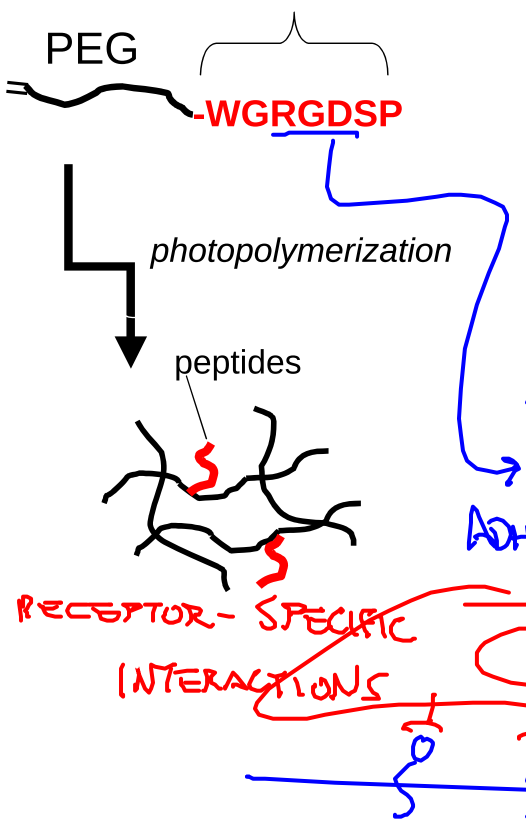
4) EFFICIENT TRANSPORT OF O_2, NUTRIENTS, WASTE DIRECTLY THROUGH THE STRUCTURE

5) RAPID TRANSPORT MITIGATES BUILDUP OF ACID PRODUCTS IN DEGRADABLE GELS

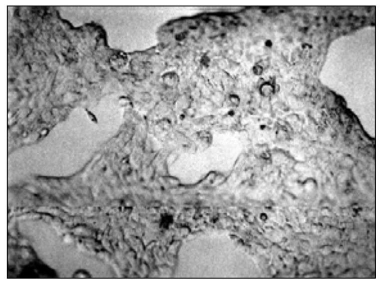
Hydrogels are readily modified with biological recognition sites

EXPLOIT FLEXIBLE CHEMISTRY: -NH2 -COOH -SH -OH

Incorporating biological recognition:



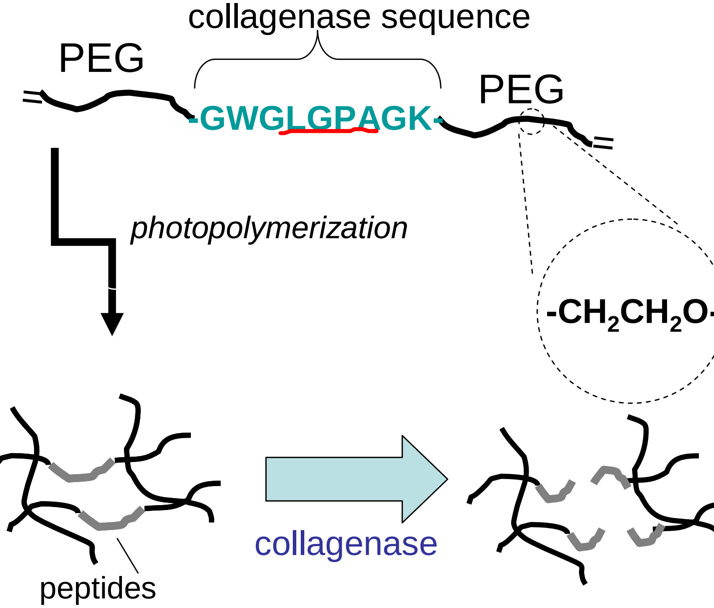
NR6 fibroblast adhesion on PEG-RGD hydrogel



(no cell adhesion on ligand-free hydrogels)

DERIVED FROM FIBRONECTIN, AN ADHESION PROTEIN

ENZYME THAT DEGRADES COLLAGEN



B.K. Mann, A.S. Gobin, A.T. Tsai, R.H. Schmedlen, J.L. West, *Biomaterials* **22**, 3045 (2001)

... MIMIC PROPERTIES OF ECM

In situ formability: strategies for macroporous structures

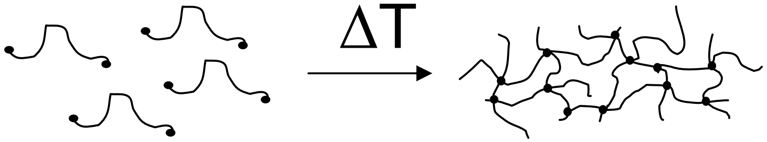
Images removed for copyright reasons.
Please see:
Ford, Lavik, et al. *PNAS* 103 no. 8 (2006): 2512-2517.

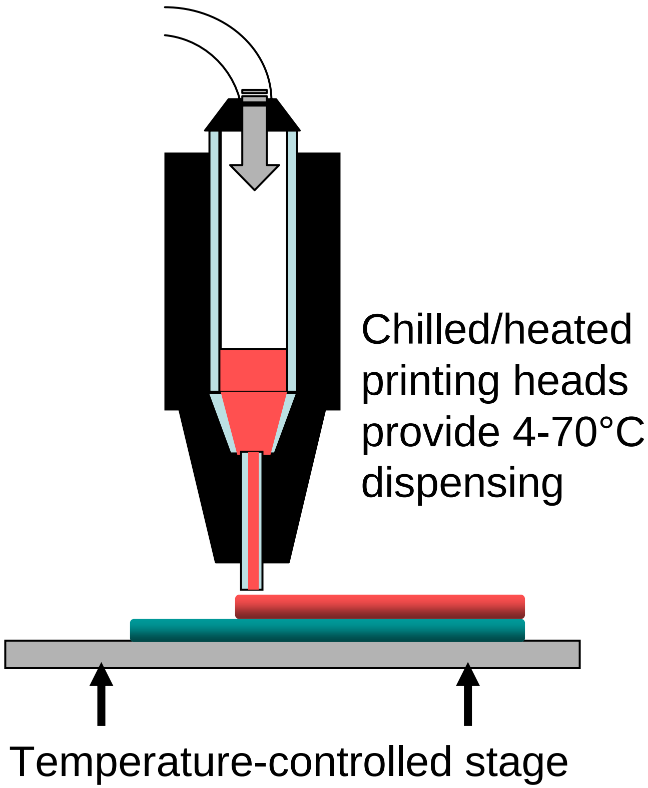
In situ formability: example: 'printable' gels

DEPOSIT TEMP-SENSITIVE MATERIALS:

PLURONICS (GEL AS T↑)

POLY(VINYL ALCOHOL) (GEL AS T↓)





Images removed for copyright reasons.
Please see:
Landers, et al. 2002.

Further Reading

1. Byrne, M. E., Oral, E., Hilt, J. Z. & Peppas, N. A. Networks for recognition of biomolecules: Molecular imprinting and micropatterning poly(ethylene glycol)-containing films. *Polymers for Advanced Technologies* **13**, 798-816 (2002).
2. Hart, B. R. & Shea, K. J. Molecular imprinting for the recognition of N-terminal histidine peptides in aqueous solution. *Macromolecules* **35**, 6192-6201 (2002).
3. Tan, Y. Y. & Vanekenstein, G. O. R. A. A Generalized Kinetic-Model for Radical-Initiated Template Polymerizations in Dilute Template Systems. *Macromolecules* **24**, 1641-1647 (1991).
4. Shi, H. Q., Tsai, W. B., Garrison, M. D., Ferrari, S. & Ratner, B. D. Template-imprinted nanostructured surfaces for protein recognition. *Nature* **398**, 593-597 (1999).
5. Shi, H. Q. & Ratner, B. D. Template recognition of protein-imprinted polymer surfaces. *Journal of Biomedical Materials Research* **49**, 1-11 (2000).
6. Lustig, S. R. & Peppas, N. A. Solute Diffusion in Swollen Membranes .9. Scaling Laws for Solute Diffusion in Gels. *Journal of Applied Polymer Science* **36**, 735-747 (1988).
7. Canal, T. & Peppas, N. A. Correlation between Mesh Size and Equilibrium Degree of Swelling of Polymeric Networks. *Journal of Biomedical Materials Research* **23**, 1183-1193 (1989).
8. Podual, K., Doyle, F. J. & Peppas, N. A. Dynamic behavior of glucose oxidase-containing microparticles of poly(ethylene glycol)-grafted cationic hydrogels in an environment of changing pH. *Biomaterials* **21**, 1439-1450 (2000).
9. Podual, K., Doyle, F. J. & Peppas, N. A. Preparation and dynamic response of cationic copolymer hydrogels containing glucose oxidase. *Polymer* **41**, 3975-3983 (2000).
10. Podual, K., Doyle, F. J. & Peppas, N. A. Glucose-sensitivity of glucose oxidase-containing cationic copolymer hydrogels having poly(ethylene glycol) grafts. *Journal of Controlled Release* **67**, 9-17 (2000).