Applications of hydrogels

ANNOUNCEMENTS:

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:

FRIDAY

ANNOUNCEMENTS: PS 4 DUE THURSDAY 5PM

- FIRST EXAM NEXT TUESDAY (IN CLASS)
- COVERAGE: LECTURES 1-10
- CLOSED BOOK
- EQUATIONS WILL BE PROVIDED

Lecture 10 Spring 2006
Last time

POLYELECTROLYTE HYDROGELS

COACERVATES

MULTILAYERS

UNPAIRED POLYELECTROLYTE GELS

DRIVEN BY OSMOTIC PRESSURE

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Applications of hydrogels in bioengineering

- CONTROLLED RELEASE

- IMMUNOISOLATION
  - TRANSPANTING CELLS
    - ISOLATION FROM IMMUNE SYSTEM
  - XENOGENIC (ANOTHER SPECIES)
    - ALLOGENIC (ANOTHER HUMAN)

- 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:
Drug delivery

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

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Please see:
Mesh size of hydrogel networks

\[(<r_0^2>)^{1/2} = N_c^{1/2}a\]

\[\Delta S^* = k_b \ln \frac{P_{gel,opening}}{P_{gel,volume}}\]

Statistical segment length

Number of segments between cross-links

\[P_{gel,opening}^* = \frac{\xi - 1}{\xi}\]

\[P_{gel,volume}^* = \frac{1}{(Q-1)}\]

Drug delivery
Connection between mesh size and diffusion coefficient of entrapped molecules

\[ \phi_{2,15}^{\text{local}} = \left( \frac{\bar{r}_0}{\xi} \right)^3 \]

Eyring Theory:

\[ D_{\text{gel}} = D_0 \left( 1 - \frac{r}{\xi} \right)^{-\frac{1}{(\Phi - 1)}} \]

Diff coefficient of solute in pure H_2O
Controlling diffusivity for responsive drug delivery: treatment of diabetes

1. Glucose + O₂ → Gluconic acid + H₂O₂

2. pH

3. Gel ionizes

4. Insulin released

(Drug delivery)

Glucose oxidase

(PEPPAS GROUP)

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Controlling diffusivity for responsive drug delivery: treatment of diabetes

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Please see:
Drug delivery

Response of gel microparticles

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Please see:
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 Poly(ethylene glycol) Grafts.”

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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.”
Diffusion rate changes in responsive microgels

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Please see:

Chemical functionality in hydrogels can be utilized for responsive hydrogels.

Mechanisms of environmental responsiveness in hydrogels:

- LCFM MATERIALS!
  - HYDROPHOBIC GROUPS THAT DEHYDRATE AT ELEVATED TEMP.
  - PNIPAAm:

- LCE GELS

- LIGHT, CHEMICAL REACTIONS

\[
P_{\text{CH}_2-\text{CH}} (\text{CH}_3-\text{C}=\text{O})
\]

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Chemical functionality in hydrogels can be utilized for responsive hydrogels.

REATIONS PRESENCE OF SPECIFIC SPECIES CAN REGULATE GEL SWELLING

CLOSE/OPEN CAPTURE/PORES TO CONTROL TRANSPORT "GATING"

APPLICATIONS: RELEASE MOLECULES DETECT MOLECULES VIA PHYSICAL VOLUME CHANGES

(Takahashi et al. *Macromol* 32, 2082-2084 (1999))
Immunoisolation/encapsulation of living cells
In sterile culture media:

Formability: photoencapsulation

**EXTREMELY RAPID POLYMERIZATION!**

15 - 60 SECONDS

**INITIATION HAPPENS**

NEAR-INSTANTANEOUSLY THROUGHOUT SYSTEM

**PHOTOINITIATOR:** Cyclohexyl phenyl ketone:

#17
Formability: photoencapsulation

STEREOLITHOGRAPHIC PHOTOPOLYMERIZATION

(MASKING) UV

PHOTOMASK

LIQUID PRECURSOR

3D GEL STRUCTURES

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Please see:
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 mechanical properties of soft tissues**
   - Compressive moduli: ~1-10 kPa, typical of soft tissues

4. **Efficient transport of O₂, 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.

**Incorporating biological recognition:**

- **PEG**
  - WGRGDSP
  - Photopolymerization
  - Peptides

**NR6 fibroblast adhesion on PEG-RGD hydrogel**

(no cell adhesion on ligand-free hydrogels)

**Peptides**

**Collagenase sequence**

- GWGLGPAGK
- Photopolymerization
- Collagenase

**Ernozyme that degrades collagen**

**Derived from fibronectin, an adhesion protein**

**Receptor-specific interactions**


...Mimic properties of ECM

Tissue engineering
In situ formability: strategies for macroporous structures

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Please see:
In situ formability: example: ‘printable’ gels

Depositing temp-sensitive materials:
- Pluronics (gel as T^↑)
- Poly(vinyl alcohol) (gel as T^↓)

Chilled/heated printing heads provide 4-70°C dispensing

Temperature-controlled stage

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Please see:
Further Reading