Hydrogels for Medical Applications
Past, Present and Future

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Biological hydrogels

- Hydrogels are everywhere in nature
- Can be dynamic or permanent
- Diverse usage but mostly water

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Images: http://web.mechse.illinois.edu/research/ewoldt/research.html; www.scq.ubc.ca; www.naturalheightgrowth.com
**What are hydrogels?**

- **Ferry**
  - “…a substantially diluted system which exhibits no steady-state flow.”
  - Chemistry of the polymer, locked in place by “crosslinks” and supported by water

- **Stabilization (crosslinks)**
  - Electrostatic (clays)
  - Associative (mucins and consumer gels)
  - Hydrogen bonded “crystals” (gelatin and PVA)
  - Chemical crosslinks (contact lenses)
Why are they so important?

- Hydrogels are
  - Water filled (>80% in most cases)
  - Permeable
  - Viscoelastic
  - Lubricious
  - Hydrophilic
  - Chemically diverse
  - Environmentally sensitive
  - Allow solute transport
  - Multi-functional
Production of hydrogels

- Controlled by chemistry of chain and method of crosslinking
- Chemical crosslinker
- Self-assembly
  - Dynamic and labile gels generally
  - Usually pronounced yield stress
  - Triggered by temperature or environment
Common chemistries

- A snapshot of common biomedical systems
  - Poly(HEMA): poly(Hydroxyethyl methacrylate)
    - Contact lenses, dressings, drug release
  - PEG: poly(ethylene glycol)
    - Injectables, drug release, scaffolds
  - PVA: poly(vinyl alcohol)
    - Contact lenses, nerve guides cartilage, wound dressings, reconstructive
  - PVP: poly(vinyl pyrrolidone)
    - Wound dressings
  - Poly(acrylamide)
    - Water “solidifiers”, tissue bulking, soil conditioner

- Other common hydrogels
  - Starch, agarose, pectin, gelatin, and many others
Past & current uses

- **Industrial**
  - Bulkhead seals
  - Waste clean-up
- **Consumer**
  - Hair-gel
  - Cosmetics
- **Medical**
  - Contact lenses
  - Drug release
  - Nerve guides
  - Coatings
  - Tissue bulking
  - Nucleus replacement

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Images: [www.mide.com](http://www.mide.com); [www.chemicalengineering.byu.edu](http://www.chemicalengineering.byu.edu)
Where to next

• Current usage largely non-load bearing (even nucleus)
  – Drug release, scaffolds, guides, tissue bulking
• The body makes extensive use of hydrogels in the joint
  – Meniscus
  – Cartilage
  – Labrum
  – Intervertebral disc
• These joints readily compromised
  – Osteoarthritis
    • 27M people in US
  – Trauma
    • >800,000 meniscus surgeries annually
    • Accelerates degeneration
    • Associated with lesions
The trouble with the knee

• The human knee is a “simple” joint
  – Cylinder on flat
  – Contact forces 3-5x body weight
  – ~10 MPa normally
    • 30 MPa (stair) up to 50 MPa (lunge)
  – Kinematics
    • Rotation over 20°
    • Flexion up to 50°
    • Displacement 3-4 cm
  – Velocities up to 0.6 m/s
  – Coefficient of friction <0.04

• Soft-tissues allow it to function
  – Also represent its weakness

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Image: www.blenderartists.org, stemcelldoc.wordpress.com
**How to (re)build a knee**

- Soft-tissues have complex structure
  - Work as hybrid structures
- **Cartilage**
  - Properties change from surface to bulk to transition to boney substrate
  - Provides unique shear response
- **Meniscus**
  - Cartilagenous structure supported by radial hoops
**Engineered (and testing) soft-tissue repair**

- **Problem:**
  - Low friction
  - High load
  - Load distribution
  - Displacement/shear tolerant
  - Soft-tissue preserving

<table>
<thead>
<tr>
<th></th>
<th>Cartilage</th>
<th>Meniscus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water content</td>
<td>[%]</td>
<td>68-85</td>
</tr>
<tr>
<td>Collagen</td>
<td>%</td>
<td>10-20</td>
</tr>
<tr>
<td>Proteoglycan</td>
<td>[%]</td>
<td>5-10</td>
</tr>
<tr>
<td>Young’s modulus</td>
<td>[MPa]</td>
<td>5-10</td>
</tr>
<tr>
<td>Tensile modulus</td>
<td>[MPa]</td>
<td>~10</td>
</tr>
<tr>
<td>UTS</td>
<td>[MPa]</td>
<td>2/5</td>
</tr>
<tr>
<td>Aggregate modulus</td>
<td>[MPa]</td>
<td>~0.7</td>
</tr>
<tr>
<td>Permeability x 10^{15}</td>
<td>[m^4/N.s]</td>
<td>~4</td>
</tr>
<tr>
<td>Friction Coeff</td>
<td>[ ]</td>
<td>0.1</td>
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<tr>
<td>Thickness</td>
<td>[mm]</td>
<td>0.5-5</td>
</tr>
</tbody>
</table>
**Cartilage mimicking hydrogel**

- Cartilage properties in part due to PGs
- Mimic structure with hydrolyzed PVAc hydrogel with dangling chains

Polymerization with crosslinker (PEG-DMA) and chains (PEG-MA)

Hydrolysis in methanol and KOH

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Lubricity and Friction

- Low friction is a defining feature of cartilaginous joints
  - Impacted by disease level
  - Diseased synovial fluid loses lubricity

![Graph showing the relationship between COF and OA score](Image: Neu et al. 2010)

- Friction Coefficient
- Contact Pressure [MPa]
- OA Score

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Image: Neu et al. 2010
Lubricity and Friction

- Correct structure generates superb lubricity
Reinforcement

Simple compression (strain/strain)

Fiber wound
Mechanical properties

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**Issues**

- Use of polymers in soft-solids raises its own problems
- Permeability
  - Elutables major concern
  - Reaction biproducts
  - Access for media
- Mechanical testing complex
  - Viscoelastic solid implies rates critical
- Environment important
  - Humidity, salinity, pH
- Wear
  - How does one measure wear?
Thank you

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