HFM Fabrication
-Fiber Spinning
Phase Inversion

- Controlled precipitation
- Solution --> porous solid that is interconnected and traversed by an interpenetrating pore structure which provides channels across the wall structure
Dry-Jet Wet Spinning

Spinnerette

Nonsolvent Stream

Polymer Solution Stream

Nonsolvent Bath

Note: Picture not drawn to scale
Anatomy of a Spinneret

Note: Picture not drawn to scale
Required Elements

- A polymer of sufficient Mw that is, enough length to provide inter chain entanglement following precipitation and adhesive force to provide the appropriate mechanical properties for a particular application.

- Polymer & solvent
- Miscible non-solvent
Anatomy of a Spinneret

Note: Picture not drawn to scale
The Addition of Non-solvent
Precipitation with Chain Entanglement
Anatomy of a Spinneret

- Spinneret
- Polymer Solution Stream
- Nonsolvent Stream
- Outflow Stream

Note: Picture not drawn to scale
Various Stages in the Early Life of a HFM
Polymer Rich Zone

Dense Skin

Lumen of Hollow Fiber
Topography of Selective Skin Layer

Photodiode

XYZ piezotranslator

Laser

Cantilever and Probe Tip
Inner Skin Ultra-topography
$4^\circ C - 100\% \text{ H}_2\text{O Quench}$

$22^\circ C - 100\% \text{ H}_2\text{O Quench}$

$54^\circ C - 100\% \text{ H}_2\text{O Quench}$

$54^\circ C - 50/50 \text{ DMF/H}_2\text{O Quench}$

$1000 \times 1000 \text{ nm}$
Production Spinning Line
On a Larger Scale Various Structures are Apparent and can be controlled by changing Fabrications conditions

A  PAN-PVC  Li et al. 1998
B  PAN-PVC  Li et al. 1998
C  Polyimide  Chung et al. 1992
D  Polysulfone  Valette et al. 1999
E  Cellulose acetate  Hao et al. 1996
F  PAN copolymer  Valette et al. 1999
G  AN69  Valette et al. 1999
H  PMMA  Valette et al. 1999
Nerve Track Repair: Bridging Substrates
Nerve Repair-Entubulation
Hydrogels
Definition

-water insoluble, three dimensional network of polymeric chains that are crosslinked;
-polymers capable of swelling substantially in aqueous conditions (e.g., hydrophilic)
-polymeric network in which water is dispersed throughout the structure
-typically in the swollen state the mass fraction of water is much higher than the mass fraction of polymer.
The Cross-links may be physical or chemical:

- by reaction of one or more monomers with pendant functional groups
- Electrostatic, hydrogen or van der Waals interactions (physical), heating creates a solution;
- Covalent bonds (chemical)
Hydrogels

- One or more highly electronegative atoms which results in charge asymmetry favoring hydrogen bonding with water;
- Hydrophilic nature - dry materials absorb water;
- By definition, water must constitute at least 10% of the total weight (or volume) for a material to be a hydrogel;
- When the content of water exceeds 95% of the total weight (or volume), the hydrogel is said to be superabsorbant;
Hydrogels: Swelling

Degree of swelling can be quantified by:

- ratio of sample volume in the dry state to sample volume in the swollen state;

- weight degree of swelling: ratio of the weight of swollen sample to that of the dry sample
Hydrogels:

- In a chemically cross-linked hydrogel, all of the polymer chains are connected by covalent bonds to form a network; and, thus
- The material can be viewed as one molecule of large size or supramacromolecule;
- The thermodynamically driven swelling force is counterbalanced by the retractive force of the crosslinked structure;
- The unique property of these gels is their ability to maintain their original shape during and after swelling;
- Two forces become equal at some point and equilibrium is reached
FIGURE 1

Swelling of a dried hydrogel (left) to a larger size of the same shape (right) in water.
Xerogels

- Dried hydrogels;
- Usually clear and swelling in water takes a long time;
- The swelling behavior is due to slow diffusion of water through the compact polymer chains;
- A useful property in controlled drug delivery;
Chitosan
Hydrogels: Swelling

- Why is the degree of swelling important?
  - solute diffusion coefficient through the hydrogel
  - surface properties and surface mobility
  - optical properties (particularly for contact lens applications)
  - mechanical properties
Hydrogel Forming Polymers

Natural

poly(hyaluronic acid)  poly(sodium alginate)

Synthetic

poly(lactic acid)  poly(N-isopropyl acrylamide)  poly(ethylene glycol)
Fibrin Hydrogel (Blood Clot)
Hydrogels

Highly swollen hydrogels:
- cellulose derivatives
- poly(vinyl alcohol)
- poly(N-vinyl 2-pyrrolidone), PNVP
- poly(ethyleneoxide)

Moderately or poorly swollen hydrogels:
- poly(hydroxyethyl methacrylate), PHEMA and derivatives

One may copolymerize a highly hydrophilic monomer with other less hydrophilic monomers to achieve desired swelling properties
Examples of biological hydrogels:

- Jello (a collagen gel ~ 97% water)
- Extracellular matrix components
- Polysaccharides
- DNA/RNA
- Blood clot
- Mucin - lining the stomach, bronchial tubes, intestines
- Gycocalyx - lining epithelial cells of blood vessels
- Sinus secretions
Function of a biological hydrogel

- Decreased permeability to large molecules
- Structural strength (for epithelial cell walls)
- Capture and clearance of foreign substances
- Decreased resistance to sliding/gliding
- High internal viscosity (low washout)
Hyaluronic Acid

D-Glucuronic acid
N-Acetyl D-Glucosamine

principal targets for chemical modification
Polyelectrolyte Hydrogels

- Polyelectrolytes studied as coacervates for biomaterials:
  - Polyanions
    - Carboxymethylcellulose
    - Alginate
    - Dextran sulfate
    - Carboxymethyl dextran
    - Heparin
    - Carrageenan
    - Pectin
    - xanthan
  - Polycations
    - Chitosan (derived from crab shells)
    - Polyethyleneimine
    - Poly(4-vinyl-N-butylpyridinium) bromide
    - Quartenized polycations
    - Poly(vinylbenzyltrimethyl)ammonium hydroxide
Polyelectrolyte Multilayers

Layer by layer deposition

1) Polyanion
2) Wash
3) Polycation
4) Wash
Alginate gels

M-rich network

G-rich network

represents M-fractions
represents cross-linked G-fractions
Alginate gels

e.g. chitosan (cationic polysaccharide), polylysine

+ cationic polymer

+ divalent cations

Salt bridge
Divalent cations
Enzyme Immobilization

Enzyme + alginate

CaCl₂

Calcium alginate beads with entrapped enzyme
Cell Encapsulation
Microencapsulation Method

1. Cells in Alginate Beads
2. Poly-L-Lysine layer Added
3. Second Layer of Alginate Added

APA CAPSULES

Encapsulated Cells maintained in regular tissue culture
Applications

Pharmaceutical applications

- monomer composition and relative amounts of multi-polymer hydrogels can be varied to alter the diffusion characteristics; and
- permeability of the gel containing pharmaceutical agents

Delivery

- drug gets trapped in the hydrogel during polymerization
- drug introduced during swelling in water
- Release occurs by outflow of drug from the gel and inflow of water to the gel
Drug delivery
Applications in Biomaterials and Tissue Engineering

- Cell Encapsulation
- Drug delivery
- Surface modification
- Enzyme Immobilization
- Biosensors
- Lab on a chip
Hydrogels: Applications

- Biomedical use due to bio- and blood-compatibility
- Pharmaceutical use due to hydrophilicity (controlled/sustained drug release)
- Earliest biomedical application contact lenses
  - good mechanical stability
  - favorable refractive index
  - high oxygen permeability
  - needs hygienic maintenance
  - unable to correct for astigmatism
- lubricating surface coating
  - used with catheters, drainage tubes and gloves
  - non-toxic
Corning® Ultra Low Attachment Products
Unique hydrogel surface inhibits cell attachment
Important features of hydrogels

- Usually comprised of highly polyionic polymers
- Often exhibit large volumetric changes eg. Highly compressed in secretory vesicle and expand rapidly and dramatically on release
- Can undergo volumetric phase transitions in response to ionic concentrations (Ca++, H+), temperature, ..
- Volume is determined by combination of attractive and repulsive forces:
  - repulsive electrostatic, hydrophobic
  - attractive, hydrogen binding, cross-linking
Hydrogel Forming Polymers

Natural

 poly(hyaluronic acid)  poly(sodium alginate)

Synthetic

 poly(lactic acid)  poly(N-isopropyl acrylamide)  poly(ethylene glycol)
Hydrogels / Applications in Opthamology
Hydrogels: Applications

Earliest biomedical application contact lenses

- good mechanical stability
- favorable refractive index
- high oxygen permeability
- needs hygienic maintenance
- unable to correct for astigmatism
Acrylates
Methacrylates

\[
\begin{align*}
\text{H} & \quad \text{C} \equiv \text{C} \quad \text{CH}_3 \\
\text{H} & \quad \text{C} \equiv \text{C} \quad \text{C} = \text{O} \\
\text{H} & \quad \text{C} \equiv \text{C} \quad \text{C} = \text{O} \\
\text{O} & \quad \text{R} \\
\end{align*}
\]

a methacrylate

3/30/2006
Poly(methyl methacrylate)

methyl methacrylate

poly(methyl methacrylate)

free radical vinyl polymerization
Table 1.—Summary of the Historical Development of Contact Lenses

<table>
<thead>
<tr>
<th>Year</th>
<th>Individual(s)</th>
<th>Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>1508</td>
<td>Leonardo da Vinci</td>
<td>Described glass contact lens</td>
</tr>
<tr>
<td>1636</td>
<td>René Descartes</td>
<td>Tube of water used to neutralize the cornea</td>
</tr>
<tr>
<td>1801</td>
<td>Thomas Young</td>
<td>Used Descartes' principle to study the eye</td>
</tr>
<tr>
<td>1827</td>
<td>John Herschel</td>
<td>Described how a contact lens could be ground; concept of molding the eye</td>
</tr>
<tr>
<td>1887</td>
<td>F. A. Muller</td>
<td>Fitted a glass blown lens for a patient to protect the eye</td>
</tr>
<tr>
<td>1888</td>
<td>A. E. Fick</td>
<td>Described first glass lens to be worn to correct vision</td>
</tr>
<tr>
<td>1888</td>
<td>E. Kalt</td>
<td>Designed and fitted glass corneal lenses; Used ophthalmometer to fit lenses</td>
</tr>
<tr>
<td>1936</td>
<td>W. Feinbloom</td>
<td>Made lens with glass central optic and plastic surround (first plastic used in contact lens)</td>
</tr>
<tr>
<td>1938</td>
<td>Mullen and Obrig</td>
<td>First all-plastic (PMMA) contact lens</td>
</tr>
<tr>
<td>1947</td>
<td>N. Bier</td>
<td>Fenestrated minimum-clearance haptic lens</td>
</tr>
<tr>
<td>1947</td>
<td>K. Tuohy</td>
<td>All-plastic corneal lens</td>
</tr>
<tr>
<td>1950</td>
<td>Butterfield</td>
<td>Designed corneal lens to parallel the cornea; used peripheral curves</td>
</tr>
<tr>
<td>1960</td>
<td>Wichterle and Lim</td>
<td>Hydrogel polymers for contact lenses</td>
</tr>
<tr>
<td>1968</td>
<td></td>
<td>U.S. FDA became involved in regulating contact lenses</td>
</tr>
<tr>
<td>1971</td>
<td>Bausch &amp; Lomb</td>
<td>First hydrogel lens approved in United States</td>
</tr>
<tr>
<td>1970s</td>
<td>J. DeCarle</td>
<td>Extended wear with high water content hydrogel lenses</td>
</tr>
<tr>
<td>1970s</td>
<td>Rynco Scientific</td>
<td>Use of CAB polymer for contact lenses</td>
</tr>
<tr>
<td>1970s</td>
<td></td>
<td>First clinical marketing of soft silicone lenses</td>
</tr>
<tr>
<td>1978</td>
<td>Danner Laboratories</td>
<td>U.S. FDA approval of CAB lenses</td>
</tr>
<tr>
<td>1979</td>
<td>Syntex Ophthalmic</td>
<td>U.S. FDA approval of a PMMA-silicone copolymer lens</td>
</tr>
</tbody>
</table>

Poly(2-hydroxyethylmethacrylate) 

pHEMA
Hydrogels: PHEMA

- The most widely used hydrogel
- Water content similar to living tissues
- Inert to biological processes
- Shows resistance to degradation
- Permeable to metabolites
- Not absorbed by the body
- Withstands sterilization by heat
- Prepared in various shaped and forms
Contact lens

- PMMA
- HEMA
- Fabrication methods
  - Computer assisted cutting (lathe)-PMMA rods
  - Spin casting-polymerization
  - Molding-polymerization
Intraocular lens

- PMMA
- HEMA
- Polymer backbone - mixture of PMMA and PHEMA
- Varying water contents
- Additives such as UV blockers
Foldable IOL complications/explantations -

Survey Lens Totals 2001

- Multifocal, Silicone: 25%
- One Piece (plate), Silicone: 8%
- One Piece with Haptics, Acrylic: 16%
- Three Piece, Acrylic: 14%
- Three Piece, Hydrogel: 16%
- Three Piece, Silicone: 9%

3/30/2006
Reasons for Revision Surgery

- Incorrect lens power seen most commonly
- Glare/optical aberrations
- Dislocation/decentration
- Late postoperative opacification
IOL Optic Opacification

- Surface opacification
- Opacification within the substance of the optic
- Analysis of opacifications reveals presence of calcium
- Calcium staining
- Scanning electron microscopic analysis
Accommodative IOL: 1CU (HumanOptics)

Total
diameter:
9.7 mm