Biomaterials & Tissue Engineering

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Explore how **combination of physical and biochemical cues** influence cell behavior and tissue function.

Design **versatile building blocks** to create **multicomponent, biomimetic materials**.
What are biomaterials?

“any substance or combination of substances, other than drugs, synthetic or natural in origin, which can be used for any period of time, which augments or replaces partially or totally any tissue, organ, or function of the body, in order to maintain or improve the quality of life of the individual”

*official definition from the National Institutes of Health*
What are biomaterials?

a natural or synthetic material that is suitable for introduction into living tissue to augment or replace any tissue, organ, or function in the body
What are biomaterials?

*a natural or synthetic material* that is suitable for introduction into living tissue to augment or replace any tissue, organ, or function in the body

- metals
- ceramics
- polymers
What are biomaterials?

A natural or synthetic material that is suitable for introduction into living tissue to augment or replace any tissue, organ, or function in the body.

- Metals
- Ceramics
- Polymers
  - Bioinert
  - Biocompatible
  - Bioactive
  - Regenerative
What are biomaterials?

A natural or synthetic material that is suitable for introduction into living tissue to augment or replace any tissue, organ, or function in the body.

- Metals
- Ceramics
- Polymers
- Bioinert
- Biocompatible
- Bioactive
- Regenerative
- Mechanical
- Chemical
- Biological
- Electrical
History of biomaterials

**Gold** used in dentistry thousands of years ago by Romans, Chinese, and Aztecs

**Glass** used as artificial eyes in the early 20th century

images: Science Museum, London
Plants, animal hair/tendons/arteries/muscles/nerves/intestines, **silk** all used as sutures (earliest reported suture in 3000 B.C.)

Poly(methyl methacrylate) aka PMMA used for intraocular lens after WWII
Biomaterial design criteria

- tissue or organ type
- functions
- size and scale of defect
- age of the patient
- disease conditions
- etc...

image adapted from Stupp, *MRS Bulletin* 2005
### Table 1: Key Applications of Synthetic Materials and Modified Natural Materials in Medicine

<table>
<thead>
<tr>
<th>Application</th>
<th>Biomaterials Used</th>
<th>Number/Year – World (or World Market in US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skeletal system</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint replacements (hip, knee, shoulder)</td>
<td>Titanium, stainless steel, polyethylene</td>
<td>2,500,000</td>
</tr>
<tr>
<td>Bone fixation plates and screws</td>
<td>Metals, poly(lactic acid) (PLA)</td>
<td>1,500,000</td>
</tr>
<tr>
<td>Spine disks and fusion hardware</td>
<td></td>
<td>800,000</td>
</tr>
<tr>
<td>Bone cement</td>
<td>Poly(methyl methacrylate)</td>
<td>($600M)</td>
</tr>
<tr>
<td>Bone defect repair</td>
<td>Calcium phosphates</td>
<td>--</td>
</tr>
<tr>
<td>Artificial tendon or ligament</td>
<td>Polyester fibers</td>
<td>--</td>
</tr>
<tr>
<td>Dental implant-tooth fixation</td>
<td>Titanium</td>
<td>($4B)</td>
</tr>
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<td><strong>Cardiovascular system</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood vessel prosthesis</td>
<td>Dacron, expanded Teflon</td>
<td>200,000</td>
</tr>
<tr>
<td>Heart valve</td>
<td>Dacron, carbon, metal, treated natural tissue</td>
<td>400,000</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>Titanium, polyurethane</td>
<td>600,000</td>
</tr>
<tr>
<td>Implantable defibrillator</td>
<td>Titanium, polyurethane</td>
<td>300,000</td>
</tr>
<tr>
<td>Stent</td>
<td>Stainless steel, other metals, PLA</td>
<td>1,500,000</td>
</tr>
<tr>
<td>Catheter</td>
<td>Teflon, silicone, polyurethane</td>
<td>$1B ($20B)</td>
</tr>
<tr>
<td><strong>Organs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart assist device</td>
<td>Polyurethane, titanium, stainless steel</td>
<td>4000</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Polysulfone, silicone</td>
<td>1,800,000 patients ($70B)</td>
</tr>
<tr>
<td>Blood oxygenator</td>
<td>silicone</td>
<td>1,000,000</td>
</tr>
<tr>
<td>Skin substitute</td>
<td>Collagen, cadaver skin, nylon, silicone</td>
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<td><strong>Ophthalmologic</strong></td>
<td></td>
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<tr>
<td>Contact lens</td>
<td>Acrylate/methacrylate/silicone polymers</td>
<td>150,000,000</td>
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<tr>
<td>Intraocular lens</td>
<td>Acrylate/methacrylate polymers</td>
<td>7,000,000</td>
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<td>Corneal bandage lens</td>
<td>hydrogel</td>
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<tr>
<td>Glaucoma drain</td>
<td>Silicone, polypropylene</td>
<td>($200M)</td>
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<td><strong>Other</strong></td>
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<tr>
<td>Cochlear prosthesis</td>
<td>Platinum, platinum-iridium, silicone</td>
<td>250,000 total users</td>
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<td>Breast implant</td>
<td>Silicone</td>
<td>700,000</td>
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<tr>
<td>Hernia mesh</td>
<td>Silicone, polypropylene, Teflon</td>
<td>200,000 ($4B)</td>
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<tr>
<td>Sutures</td>
<td>PLA, polydioxanone, polypropylene, stainless steel</td>
<td>($2B)</td>
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<td>Blood bags</td>
<td>Poly(vinyl chloride)</td>
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<tr>
<td>Ear tubes (Tympanostomy)</td>
<td>Silicone, Teflon</td>
<td>1,500,000</td>
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<td>Intrauterine device (IUD)</td>
<td>Silicone, copper</td>
<td>1,000,000</td>
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**Blood vessel prosthesis**

**Heart valve**

**St. Jude’s Medical**

**Dacron, expanded Teflon**

**Dacron, carbon, metal, treated natural tissue**

**Perouse Medical**

**Ophthalmologic**

Contact lens
Intraocular lens
Corneal bandage lens
Glaucoma drain

**Skin substitute**
Collagen, cadaver skin, nylon, silicone ($1B)

**Other**
Cochlear prosthesis
Breast implant
Hernia mesh
Sutures
Blood bags
Ear tubes (Tympanostomy)
Intrauterine device (IUD)
Biomaterials for hip replacement

What properties would we want in our biomaterial?

What are the limitations?

titanium

polyethylene
Common problems with hip implants

- stress shielding = reduction in bone density due to removal of stress
- bones need stress/loading to be healthy and remodel
- bone-material integration critical for implant success
How materials science can help

Porosity to encourage bone ingrowth and bone-material integration

Biomaterials for vascular applications

What properties would we want in our biomaterial?

- suturable and works immediately
- no leaking
- flexible
- compatible with blood
- avoids clots/blockages
- resist bursting and repeated stress

poly(ethylene terephthalate) aka Dacron aka PET
Traditional biomaterials

- Stryker hip implants
- St. Jude’s Medical heart valve
- Perouse Medical vascular grafts
- Rayner intraocular lens
Traditional biomaterials

- traditional engineering solutions
- inert
- long-lasting, non-biodegradable
- acellular
- require replacement after 10-20 years
The evolution of biomaterials

First generation
- BIOINERT
  minimal reaction/interaction

Second generation
- BIOACTIVE
  controlled reaction with tissue, bioresorbable

Third generation
- REGENERATIVE
  biointeractive, integrative, resorbable, stimulates specific cell response, etc.

1940
now/future
Bioglass to promote bonding to bone

- ceramic composed of SiO$_2$, Na$_2$O, CaO, P$_2$O$_5$ that interacts with soft tissues and bone
- enhances strong bond to bone and can induce new bone formation
Coat metal implants with bioglass to improve bonding

Qiu et al., *Regenerative Biomaterials* 2014.
The evolution of biomaterials

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Timeline:
- 1940
- Now/future
What about the body’s ability to heal itself?
Salamander can fully regenerate their limbs and tail!
Human body has capacity to repair and regenerate

- skin
- bone
- intestine
- liver

Image adapted from Stupp, *MRS Bulletin* 2005
Repair vs regeneration

**Repair** = reestablishing lost or damaged tissue to *retain continuity*
Repair vs regeneration

**Repair** = reestablishing lost or damaged tissue to *retain continuity*

**Regeneration** = replacement of lost or damaged tissue with an exact copy so that *morphology and function are restored*
Biomaterials for regenerative tissue engineering

1. Isolate cells from patient
2. Expand cells in the lab
3. Seed cells on biomaterials
4. Grow engineered tissue
5. Implant engineered tissue into patient
Can we create biomaterials to stimulate regeneration?

Cells harvested from patient

Expanding cells

Cells seeded on scaffold

Construct with cells in scaffold cultured

Construct implanted in patient

Mechanical and/or molecular signalling

image adapted from van Blitterswijk et al., *Tissue Engineering* 2008
Decellularized heart maintains tissue architecture

- composed of *native ECM molecules*
- *biodegradable* and *biocompatible* after decellularization

Decellularized heart can be recellularized

Recellularized heart beats again!

- composed of *native ECM molecules*
- *biodegradable* and *biocompatible* after decellularization
- *requires donor...*
look at biological tissues as materials
tissue composition and organization linked to biological function
Perspective from a materials scientist

Can we design biomaterials that generate functional native-like tissues?


tissue composition and organization linked to biological function
**Injectable hydrogels for wound healing**


**Biodegradable scaffolds for tissue engineering**


**Biodegradable scaffolds for regenerative medicine**

Explore how **combination of physical and biochemical cues** influence cell behavior and tissue function.

Design **versatile building blocks** to create multicomponent, biomimetic materials.
3D printing peptide-functionalized biodegradable polymers

peptide exposed on fiber surface

poly(caprolactone) (PCL)

peptide exposed on fiber surface

ink: peptide-PCL conjugate mixed with unmodified PCL in volatile solvent prior to printing

as ink extrudes, solvent evaporates, polymer solidifies, and peptide emerges on surface

peptide-functionalized 3D-printed scaffold

Exploit 3D printing to spatially control multiple peptides

Print with multiple inks to control spatial organization of multiple peptides in a continuous scaffold
3D print biomaterials to mimic bone-cartilage interface


**osteochondral (bone-cartilage) interface**

osteochondral interface critical for load transfer between bone and cartilage and normal joint mechanics
Spatially organize bone and cartilage-promoting peptides

peptides promote spatially organized tissue formation
Change print pattern to control scaffold architecture
Independent control of architecture and biochemistry

Print with multiple peptide-PCL conjugates to control porosity and peptide functionalization in a single scaffold
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