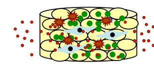
Biomaterials and Cell-Biomaterial Interactions

Module 3, Lecture 2

20.109 Spring 2009

Lecture 1 review

- What is tissue engineering?
- Why is tissue engineering?
- Why care about cartilage?
- What are we asking in Module 3?



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Topics for Lecture 2

- Introduction to biomaterials
  - properties
  - examples
- Cartilage composition
  - collagen
  - proteoglycans

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Module 3 goals

- Lab
  - Extend experience with mammalian cell culture
  - Phenotypic assays: concepts and experience
- Short informal report
  - Accountability to present/future 20.109 community
- Discussions in lecture
  - Engage with meta-scientific issues, ethics, etc.
- Presentation of novel research idea
  - Investigate literature independently
  - Exercise scientific creativity
  - Design experiments to address a specific question

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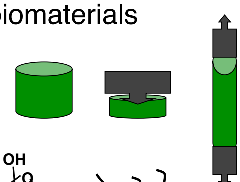
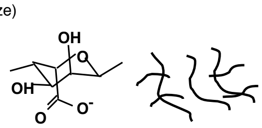
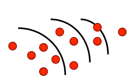
Properties of biomaterials

- Physical/mechanical
  - strength
  - elasticity
  - architecture (e.g., pore size)
- Chemical
  - degradability
  - water content
  - toxicity
- Biological
  - motifs that cells recognize
  - release of biological components
- Lifetime







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The right material for the job

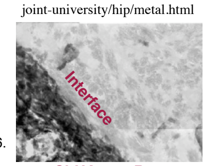
- Metals
  - types: Ti, Co, Mg alloys
  - pros: mechanically robust
  - applications: orthopedics, dentistry
- Ceramics
  - types: Al_2O_3, Ca-phosphates, sulfates
  - pros: strength, bonding to bone
  - applications: orthopedics, dentistry
- Polymers
  - diverse, tunable properties
  - applications: soft tissues

General: B. Ratner, ed. *Biomaterials Science*, 1996.

Image: Porter et al., *Biomaterials* **25**:3303 (2004).

Metal hip implant

http://www.weisshospital.com/joint-university/hip/metal.html



Si-HA Bone

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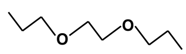
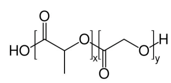
Polymers are diverse and tuneable

- Linear polymers
  - repeated chemical unit
- Co-polymers
  - heterogeneous repeats
- With increasing MW get
  - increased entanglements
  - increased strength
  - decreased processability
- Varying properties
  - hydrophilicity
  - gas permeability
  - stability
  - ease of chemical modification
  - mechanical properties



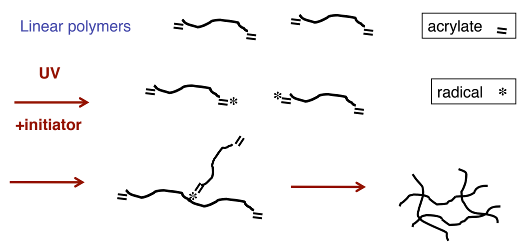
Poly(ethylene glycol)



Poly(lactic-co-glycolic acid)

[public domain image]

Free radical polymerization



Network polymer

- Network structure
  - covalently cross-linked chains
  - water-swollen (if hydrophilic)

Properties of hydrogels

- Mimic soft tissues
  - Water content
  - Elasticity
  - Diffusivity
- Synthesis at physiological conditions
  - Temperature
  - pH
  - UV light: spatio-temporal control; safe
- Injectability
- Chemical modification

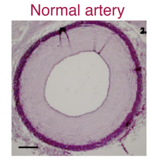
(Stachowiak & Irvine)

Review: Nguyen KT & West JL, *Biomaterials* **23**:4307 (2002)

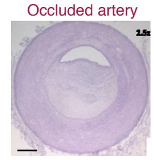
Materials must be biocompatible

- Avoid bio-incompatibility
  - immunogenicity
  - bacterial adhesion
  - clot formation
  - toxicity
- Material properties
  - sterility
  - resistance to protein adhesion
  - material *and* its degradation products non-toxic

Normal artery



Occluded artery

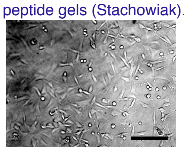


Data from: Zavan B, et al., *FASEB J* **22**:2853 (2008).

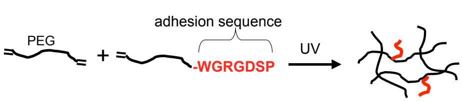
Beyond bioinert: bioactive materials

- Attach proteins/peptides for
  - adhesion
  - degradability
- Release cytokines for
  - proliferation
  - differentiation
  - attraction

Fibroblasts on polymer-peptide gels (Stachowiak).



- e.g., West JL and Hubbell JA *Macromolecules* **32**:241 (1999)



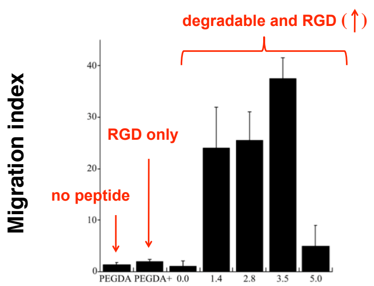
Interlude: mastery

1. Ricky Jay
   http://www.youtube.com/watch?v=OW9H4izfxqQ

2. What if you could be the Ricky Jay of science?
   "Towards responsible use of cognitive-enhancing drugs by the healthy" *Nature* ***456, 702-705***

   Ethical implications?

TE constructs to study cell migration



Gobin AS & West J, *J Biomed Mater Res* **67**:255 (2003)

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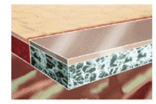
Natural vs. synthetic polymers

- Natural pros/cons
  - built-in bioactivity
  - poor mechanical strength
  - immunogenicity (xenologous sources)
  - lot-to-lot variation, unpredictable



- Synthetic pros/cons
  - biocompatibility may be difficult to predict, must be tested
  - mechanical and chemical properties readily altered
  - minimal lot-to-lot variation
- Synthetic advantages: tuneable and reproducible

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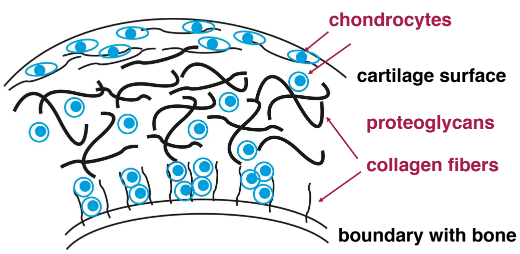
Revisiting cartilage structure



Avascular, highly water-swollen, heterogeneous tissue.

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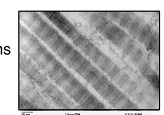
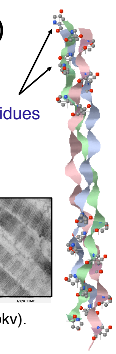
Structure of collagen(s)

- Primary structure:
  - Gly-X-Y repeats
  - proline, hydroxyproline
- Tertiary structure: triple helix
  - Gly: flexibility
  - Hyp: H-bonding
- Quaternary structure: fibrils
  - many (incl. I & II) but not all collagens
  - cross-links via lysine, hydroxylysine
  - periodic banding structure observed





Molecular image made using *Protein Explorer* (PDB ID: 1bkv).
Fibril image from public domain.

E. Vuorio & B. de Crombrugghe *Annu Rev Biochem* 59:837 (1990)

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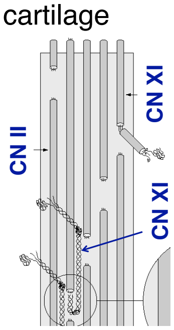
Collagen composition in cartilage

- Collagen type variation
  - location
  - glycoslyation
  - higher-order structure
  - homo- (II) or hetero- (I) trimers
- Collagen composition in cartilage
  - Type II with IX and XI
  - exact roles of IX and XI unknown
    - inter-fibrillar cross-links
    - modulate fibril diameter
    - mutations to IX, XI, II cause disease
  - Others(III, VI, X, XII, XIV)
- Little collagen turnover in adult cartilage



D.J. Prockop *Annu Rev Biochemritis Res* 64:403 (1995)
D. Eyre *Arthritis Res* 4:30 (2002)

D. Eyre (2002)

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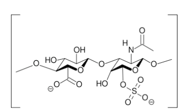
Proteoglycans are bulky and charged

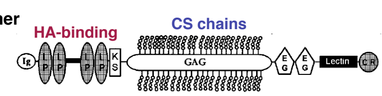
- Proteins with GAG side chains
  - GAG is glycosaminoglycan
  - many charged groups: COO^- SO_3^-
- Predominant PG in cartilage is aggrecan
  - GAG is primarily chondroitin sulfate (CS)
  - aggrecans polymerize via hyaluronin (HA)



Chondroitin sulfate
(public domain image)

Aggrecan monomer

R.V. Iozzo *Annu Rev Biochem* 67:609 (1998)



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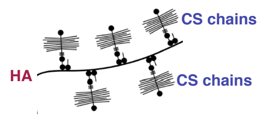
PG form heterogeneous aggregates

- Monomer > 1M, aggregates > 100M Da
- Average size decreases
  - with age
  - with osteoarthritis
- Aggrecenase inhibitors may be a target
- Under compression: water exuded, osmotic resistance

Aggrecan aggregate

C.B & W. Knudson
Cell & Dev Bio
12:69 (2001)



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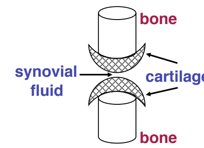
Cartilage structure and function

- Composition of cartilage
  - dry weight: CN 50-75% ; PG 15-30%
  - water: 60-80%
  - cells: 5-10% by volume
- Requirements of a joint
  - load transfer (bone/bone, bone/muscle)
  - flexibility, lubrication
- Role of PG
  - high compressive strength (osmotic swelling)
  - low permeability, friction coefficient reduces wear and tear
- Role of CN
  - high tensile strength (~GPa)
  - contain swelling forces of PG



V.C. Mow, A. Ratcliffe, and S.LY. Woo, eds. *Biomechanics of Diarthrodial Joints* (Vol. I) Springer-Verlag New York Inc. 1990

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Lecture 2: conclusions

- A variety of biomaterials are used in TE.
- Cell-material interactions can be (+), (-), or neutral.
- Hydrogels are useful for soft tissue engineering, due to their similarity to tissue and ease of modification.
- The composition of cartilage supports its functions.

Next time… standards in tissue engineering and other scientific communities.

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