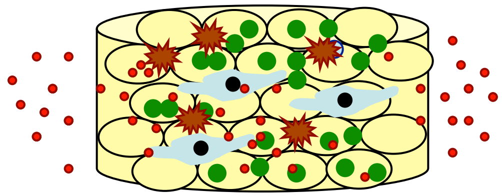
# Biomaterials and Cell-Biomaterial Interactions

## Module 3, Lecture 2

20.109 Spring 2010

# Lecture 1 review

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



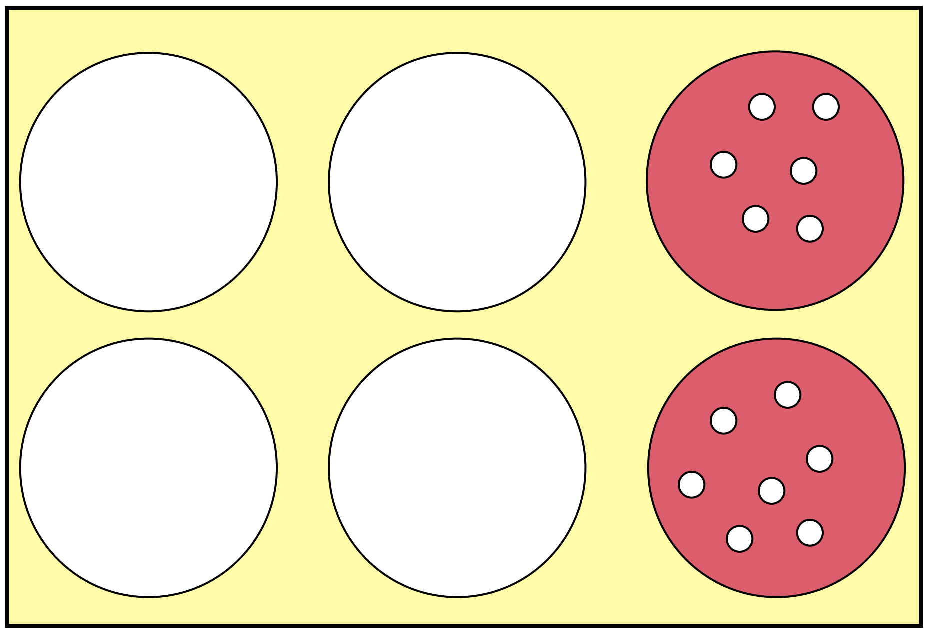
# Topics for Lecture 2

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

# Module 3 goals

- Lab concepts/techniques
  - Mammalian cell culture
  - Phenotypic assays
- Short informal report
  - Accountability to 20.109 community
- Discussions in lecture
  - Engage with meta-scientific issues, ethics, etc.
- Research idea presentation
  - Investigate literature independently
  - Exercise scientific creativity
  - Design experiments to address a specific question

# Today in Lab: M3D2



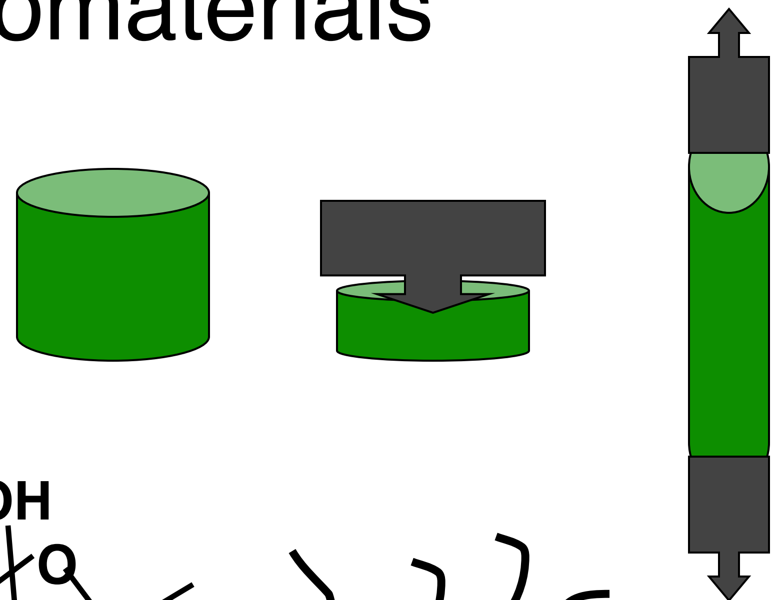
0.5 mL beads,
6 mL media

0.5 mL beads,
6 mL media

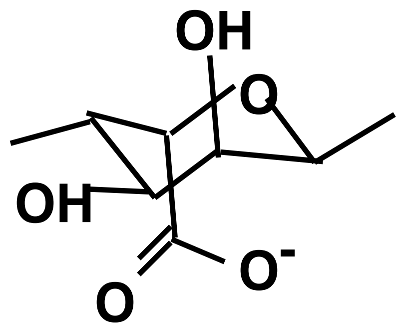
1 condition per plate (2 plates total).
2 wells per plate (split 1 mL of beads).
1 well for viability test, 1 for collagen tests.

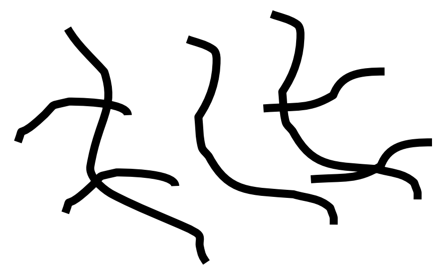
# Properties of biomaterials

- Physical/mechanical
  - strength
  - elasticity
  - architecture (e.g., pore size)

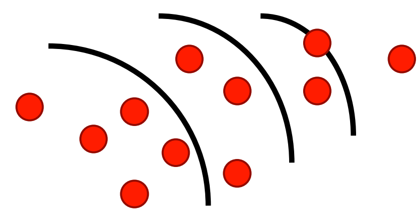


- Chemical
  - degradability
  - water content
  - toxicity



- Biological
  - motifs that cells recognize
  - release of biological components



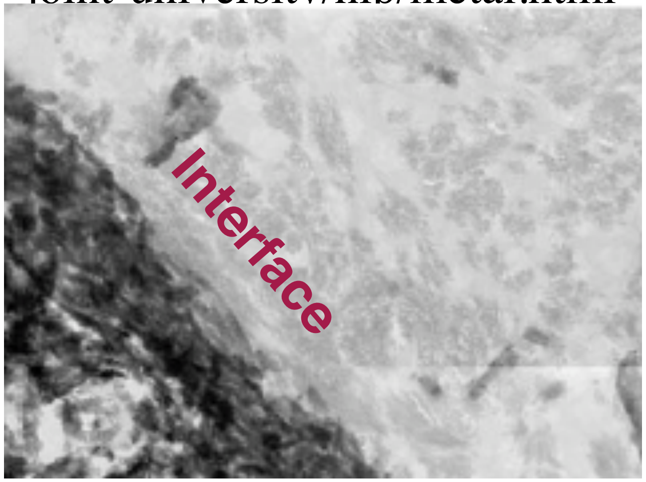
- Lifetime

# The right material for the job

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



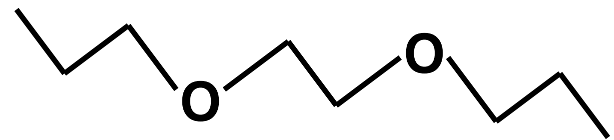

http://www.weisshospital.com/joint-university/hip/metal.html



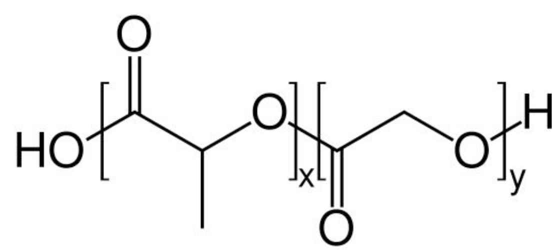

General: B. Ratner, ed. *Biomaterials Science*, 1996.
Image: Porter et al., *Biomaterials* **25**:3303 (2004).

# Polymers are diverse and tunable

- 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



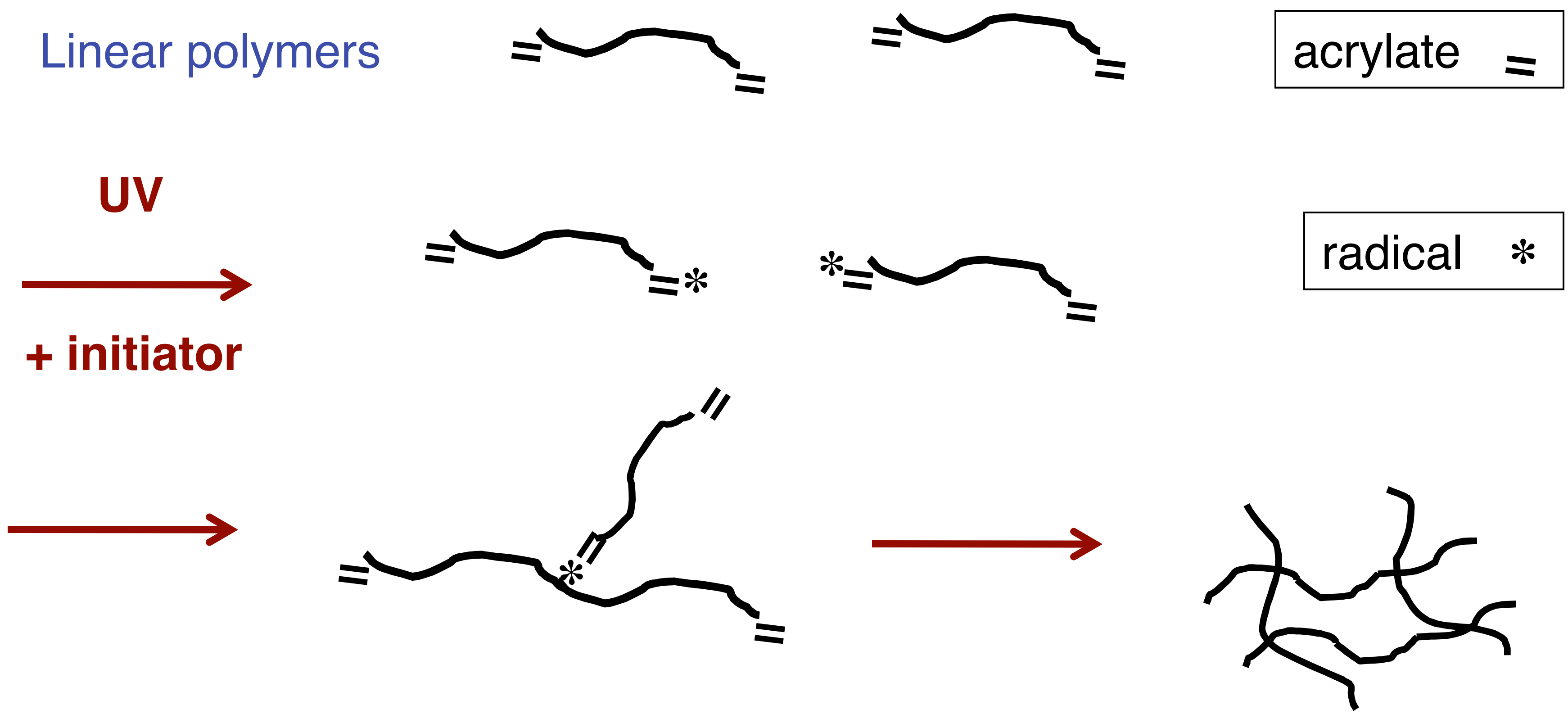
**Poly(ethylene glycol)**



**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)

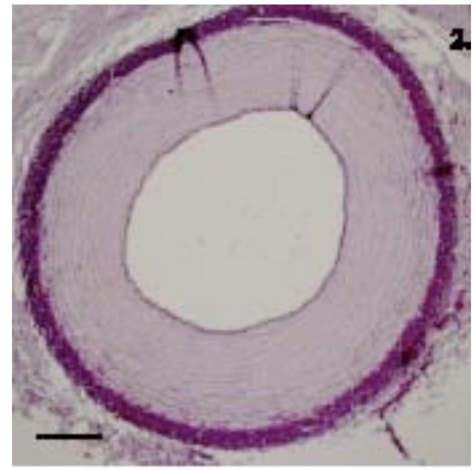
Review: Nguyen KT & West JL, *Biomaterials* **23**:4307 (2002)

# Materials must be biocompatible

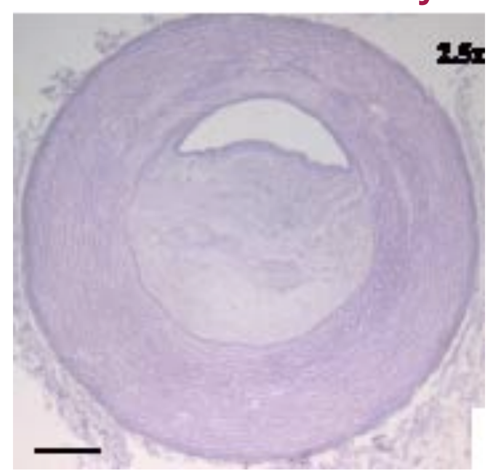
- Avoid bio-incompatibility
  - immunogenicity
  - bacterial adhesion
  - clot formation
  - toxicity
- Material properties
  - sterility
  - resistance to protein adhesion
  - material *and* its degradation products non-toxic

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

Normal artery



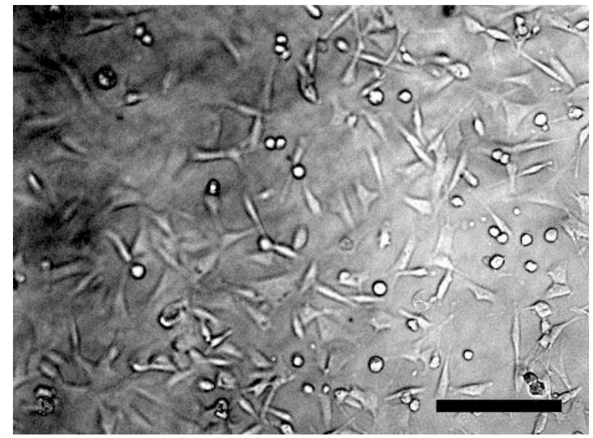
Occluded artery



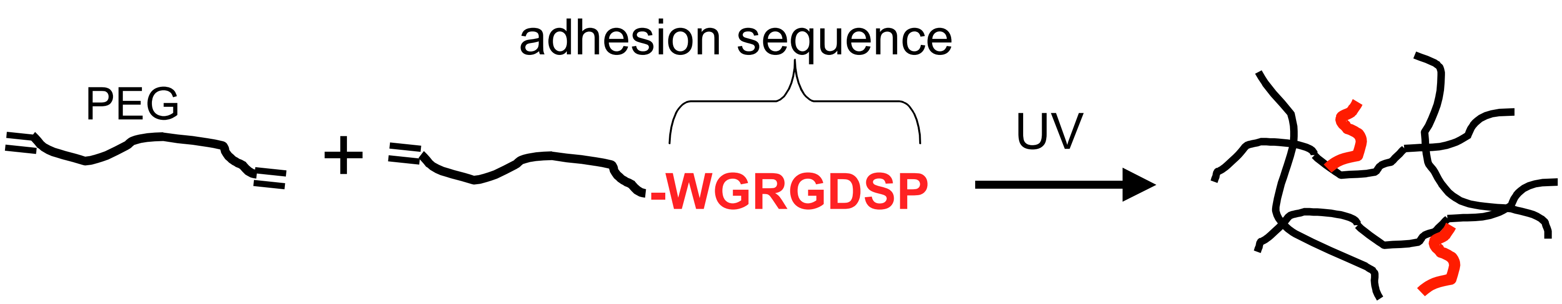
# Beyond bioinert: bioactive materials

- 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)



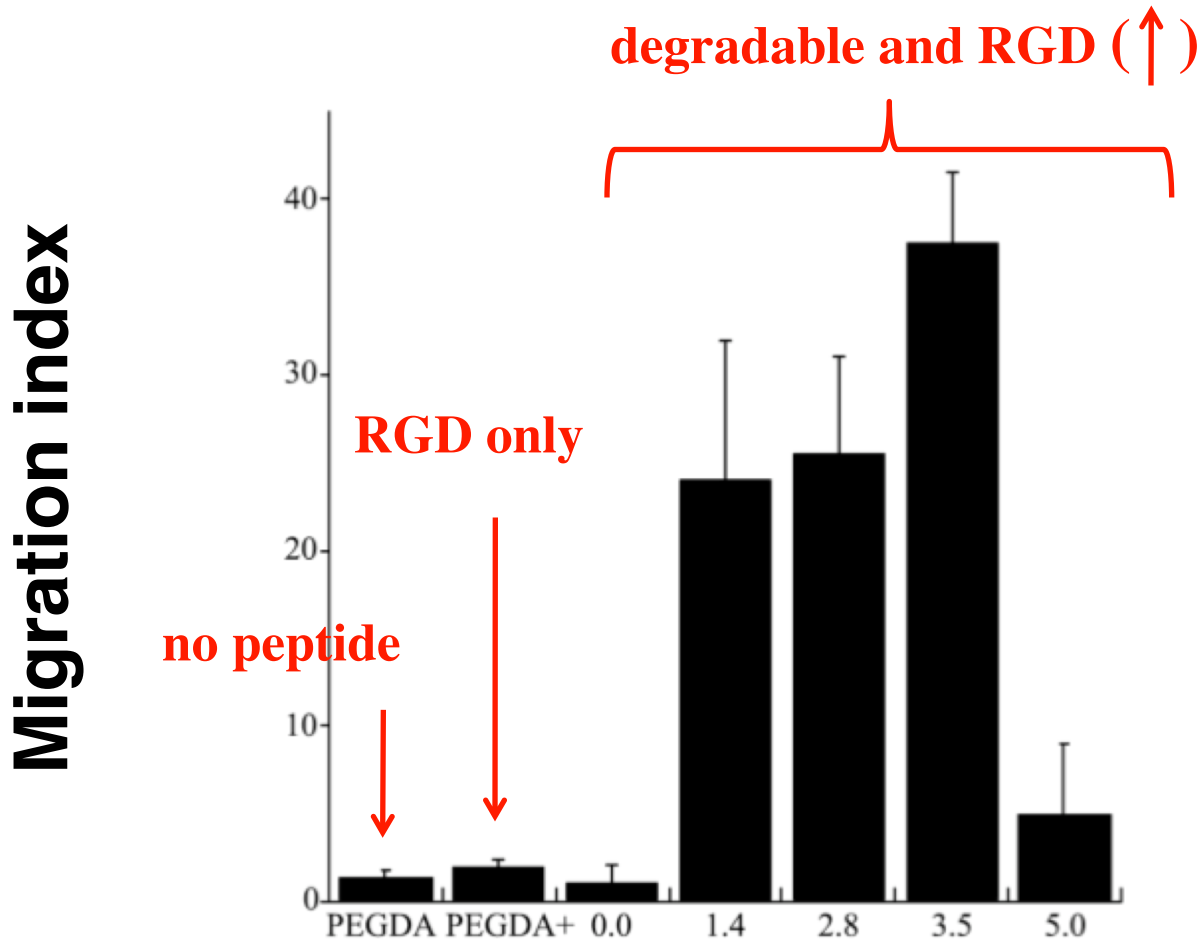
# Interlude: what (if any) should be off-limits to science?

1. "Hallucinogens have doctors tuning in again"
   *NY Times* April 2010

"Researchers from around the world are gathering this week in San Jose, Calif., for the largest conference on psychedelic science held in the United States in four decades. They plan to discuss studies of psilocybin and other psychedelics for treating depression in cancer patients, obsessive-compulsive disorder, end-of-life anxiety, post-traumatic stress disorder and addiction to drugs or alcohol."

2. "Towards responsible use of cognitive-enhancing drugs by the healthy" *Nature* ***456, 702-705***

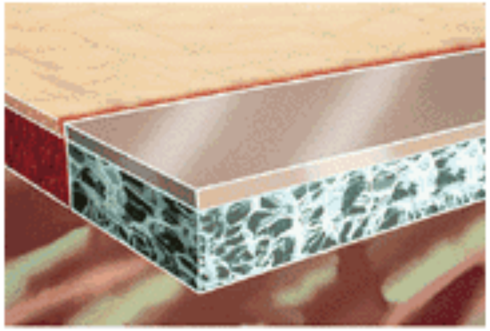
# TE constructs to study cell migration




Gobin, A. S., and J. L. West. *FASEB J* 16 (2002): 751.

# Natural vs. synthetic polymers

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

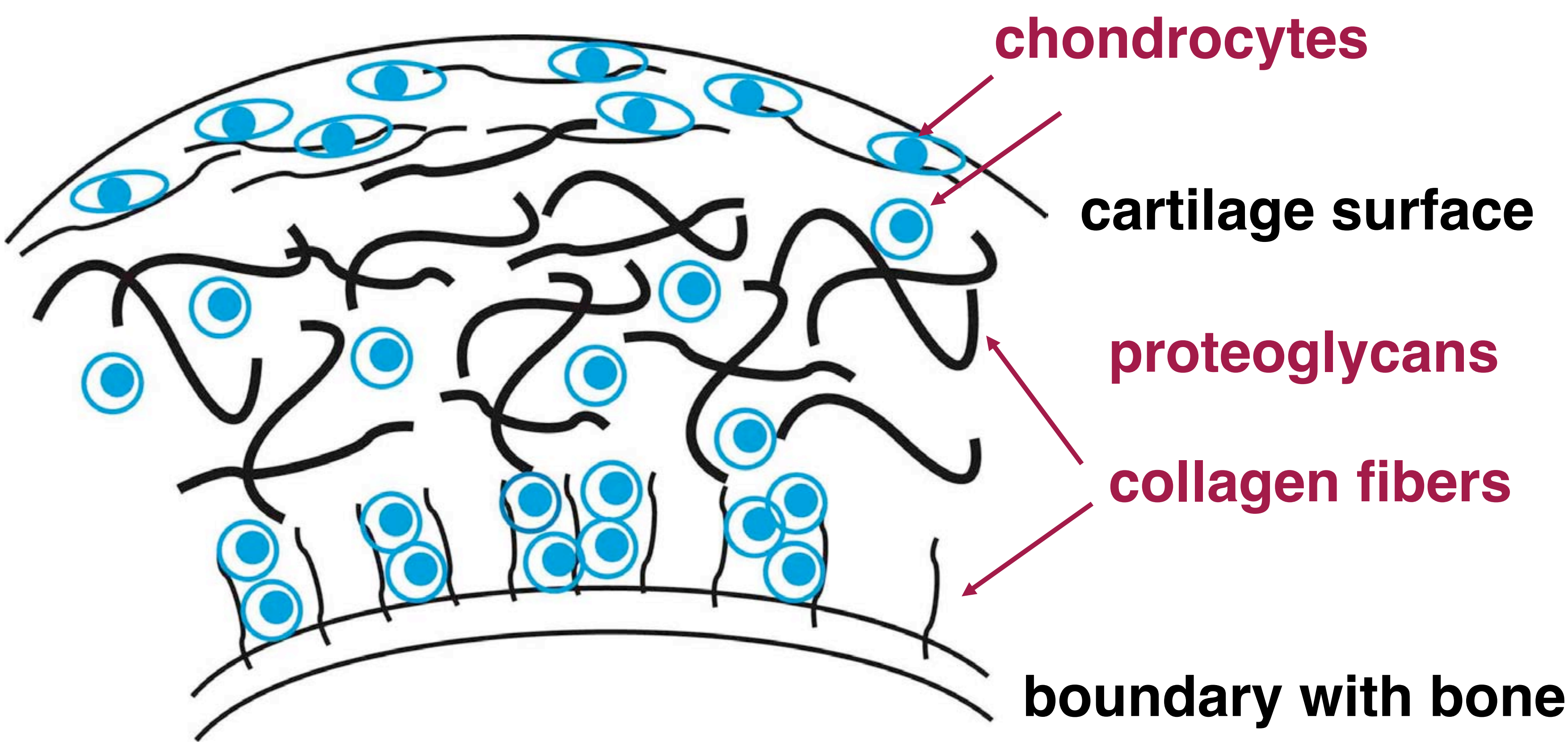


Courtesy of Integra LifeSciences Corporation, Plainsboro NJ. Used with permission.

- Synthetic pros/cons
  - predicting biocompatibility is tough
  - mechanical and chemical properties readily altered
  - minimal lot-to-lot variation

- Synthetic advantages: tunable and reproducible

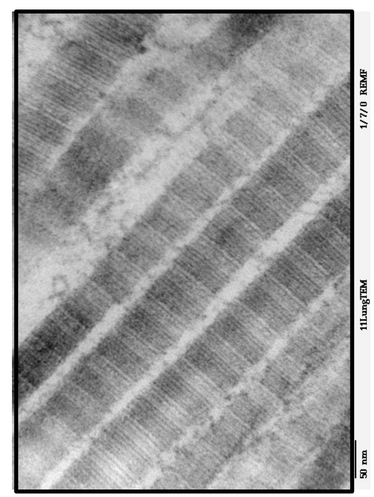
# Revisiting cartilage structure




Water-swollen, heterogeneous, avascular tissue.

# Structure of collagen(s)

- 1° structure:
  - Gly-X-Y repeats
  - proline, hydroxyproline
- 3° structure: triple helix
  - Gly: flexibility
  - Hyp: H-bonding
- 4° structure: fibrils
  - many but not all collagens
  - cross-links via lysine, hydroxylysine
  - periodic banding observable

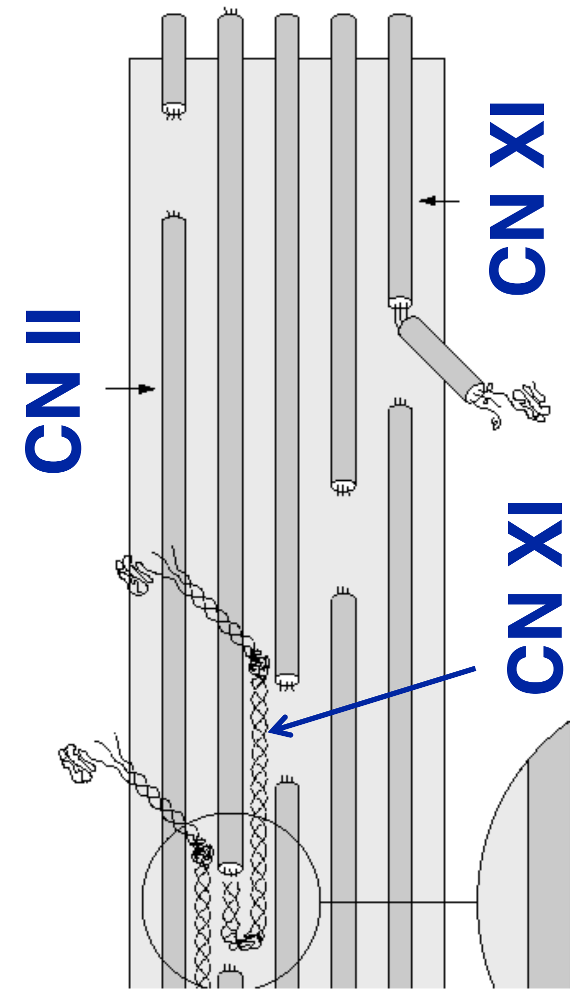



Molecular image made using *Protein Explorer* (PDB ID: 1bkv).
Fibril image from public domain.

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

# Collagen composition in cartilage

- Collagen types vary in
  - location
  - glycoslyation
  - higher-order structure
  - homo- (II) or hetero- (I) trimers
- Cartilage collagens
  - 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



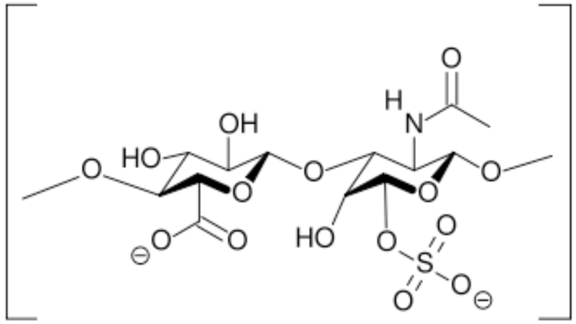

D.J. Prockop *Annu Rev Biochem* 64:403 (1995)
D. Eyre *Arthritis Res* 4:30 (2002)




Source: Eyre, D. "Articular Cartilage and Changes in Arthritis: Collagen of Articular Cartilage." *Arthritis Res* 4, 30 (2002).

# Proteoglycans are bulky and charged

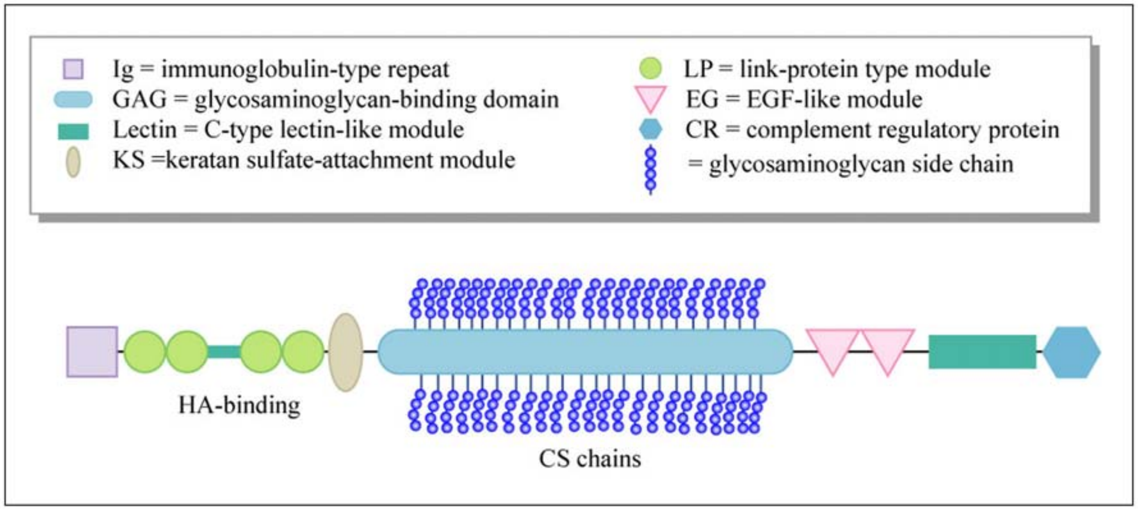
- Proteins with GAG side chains
  - GAG is glycosaminoglycan
  - many charged groups: $COO^-$ , $SO_3^-$
- Main cartilage PG is aggrecan
  - GAG is primarily chondroitin sulfate (CS)
  - aggrecans polymerize via hyaluronin (HA)



**Chondroitin sulfate**
(public domain image)

**Aggrecan monomer**

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

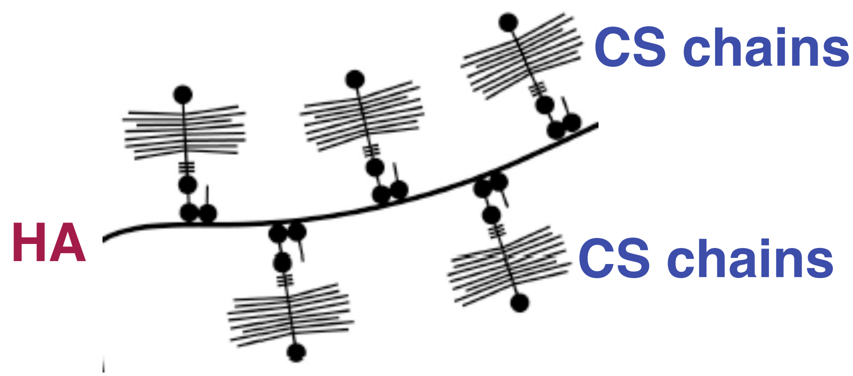


# PG form heterogeneous aggregates

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

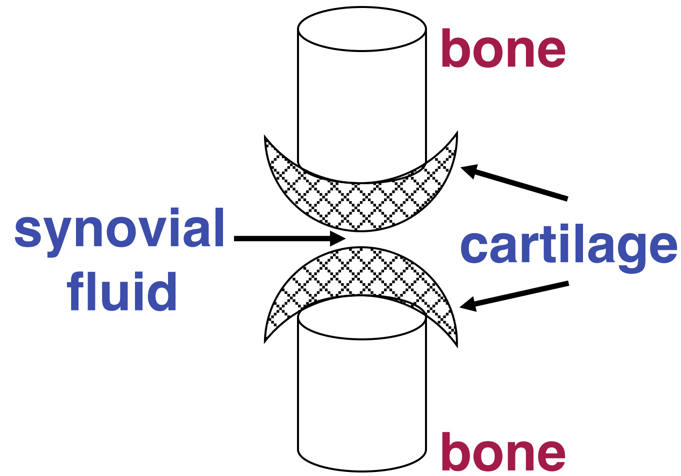
**Aggrecan aggregate**

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



# Cartilage structure and function

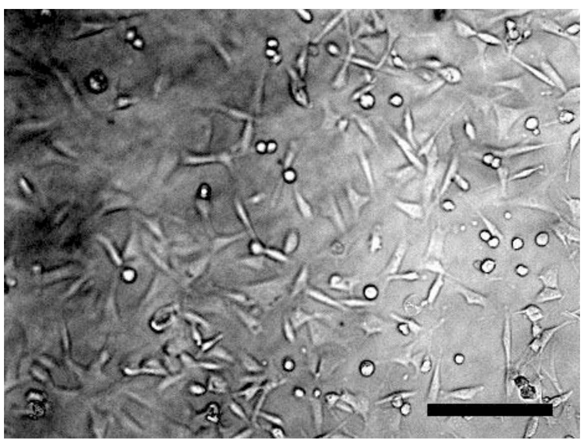
- Cartilage composition
  - dry weight: CN 50-75% ; PG 15-30%
  - water: 60-80%
  - cells: 5-10% by volume
- Requirements of a joint
  - load transfer (bone/bone, bone/muscle)
  - flexibility, lubrication
- Role of PG
  - high compressive strength (osmotic swelling)
  - low permeability, friction coefficient 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

# 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: they mimic such tissue and are easy to modify.
- The composition of cartilage supports its functions.



Next time… intro to statistics, and to standards in scientific communities.

20.109 Laboratory Fundamentals in Biological Engineering
Spring 2010