BEH.410/2.798/6.524 Spring 2002 SYLLABUS

MOLECULAR, CELLULAR, & TISSUE BIOMECHANICS

2/6 L#1: Introduction: From Tissue biomechanics to Molecular Nanomechanics

I. TISSUE MECHANICS

2/11 L#2: Biomechanical Scaling Principles:
Bio-examples from nano- to micro- to milli- to m.
Readings: journal articles.

2/13 L#3: Stress Tensor; elastic strain tensor; stress-strain relations and the Generalized Hooke's Law:
Readings: Fung, Malvern

2/19 L#4: Composition and Nanomolecular Structure of Extracellular Matrix (ECM)
Collagens, proteoglycans, elastin; Cellular synthesis & secretion of ECM macromolecules; Cell-mediated assembly of ECM;
Readings: Lodish; Collagen superfamily, Proteoglycan superfamily, and Elastin: from *The Extracellular Matrix* by Comper + journal articles.

2/20 L#5: Elastic (Time-Independent) Behavior of Tissues:
Stress and strain in tissues modeled via Hookian constitutive law; Homogeneous/nonhomogeneous; isotropic/anisotropic; linear/nonlinear behavior of tissues and relation to the ECM. Relation between nano-molecular constituents and macroscopic tensile, compressive, and shear properties of connective tissues.

2/25 L#6: Examples: isotropic cross-linked gels compared to fibrous tissues such as meniscus, cornea (relevant to corneal dystrophy), tendon, ligament, cartilage, bone
Readings: Fung; Flory; Grodzinsky (Notes); journal articles.

2/27 L#7: Viscoelastic (Time Dependent) Behavior of Tissues:
Time-dependent viscoelastic behavior of tissues as single phase materials; Transient behavior (creep and stress relaxation); Dynamic behavior (storage and loss moduli). Lumped parameter models (advantages and limitations).
Examples: relevance of these models to behavior of tendon fibrils from fibromodulin knock-out mouse; corneal stroma, ligament, cartilage; gels
Readings: journal articles; Ferry; Fung; Grodzinsky (Notes)

3/4 L#8: Viscoelastic (Time Dependent) Behavior of Tissues (con't)

3/6 L#9: Poroelastic (Time-Dependent) Behavior of Tissues:

The role of fluid-matrix interactions in tissue biomechanics; Darcy's law and hydraulic permeability, continuity, conservation of momentum. Creep, stress relaxation, dynamic moduli revisited; poro-viscoelastic bahavior
Examples: muscle and soft tissues in health and disease; e.g., arthritis and joint degeneration
Readings: Journal articles; Grodzinsky (Notes)

3/11 L#10: Poroelastic (Time-Dependent) Behavior of Tissues (Con't)

3/13 L#11: Electromechanical and physicochemical properties of tissues:
Role of electrical and chemical phenomena in determining tissue biomechanical behavior. Fluid convection of ions during tissue deformation and electrokinetic phenomena; electrostatic interactions between charged ECM molecules: tissue swelling and Donnan osmotic swelling pressure.
Examples: bone, muscle, soft connective tissues; streaming potentials and electroosmosis; molecular electromechanical forces
Readings: Journal Articles; Grodzinsky (Notes)

3/18 L#12: Physical Regulation of Cellular Metabolism:
Effects of mechanical forces and deformations on cell and tissue responses at the levels of transcription, translation, and post-translational modifications; relation between macroscopic tissue deformation and cell, cell-matrix deformations: cellular metabolic and biosynthetic responses. Current understanding of mechano-signal transduction.
Examples: arterial endothelium, tendon, cartilage, bone,
Readings: Journal Articles

3/20 L#13: Molecular Mechanics and Electromechanics of the Extracellular Matrix:
Contribution of molecular level electrical interactions to tissue properties:
Relation between molecular structure of ECM macromolecules and resulting macroscopic tissue function; Feedback between molecular, cellular, and tissue mechanics in vivo.
Examples: Proteoglycans and tissue compressive stiffness; collagens and tissue tensile and shear behavior; effects of mechanical loading on deformation of intracellular organelles and the resulting changes in the molecular structure of ECM molecules via post-translational modifications.
Readings: Grodzinsky (Notes)

4/1 QUIZ #1

II. MOLECULAR MECHANICS

4/3 **L#15: Biomolecules and Intermolecular Forces:**
Some important biomolecules: Natural: DNA, proteins, Actin
Synthetic: Self-organizing peptides, artificial silk
Origins of forces
How big is kT; Entropy, Enthalpy, Free Energy

Single molecule force measurements: optical traps, magnetic beads, AFM, passive diffusion

Readings: Lodish, Israelachivili, Nelson manuscript

4/8 **L#16: Single Molecule Biopolymer Mechanics I:**

Introduction to classical polymer physics: gaussian chains.
Persistence length as measure of rigidity.
Elasticity and viscoeleslastic effects.
Experiments: Light scattering, fluorescence microscopy of DNA, actin, microrheology as a local probe.

Readings: Grosberg, LM notes.

4/10 **L#17: Single Molecule Biopolymer Mechanics II:**

DNA as an example
The worm-like chain model
Twist: modeling, importance and measurements
Assemblies with proteins: chromatin structure -entropy, enthalpy

Readings: Marko and Siggia, Bustamante.

4/17 **L#18: Formation and Dissolution of Bonds- Mechanochemistry:**

Unfolding a protein
Titin
Kramers theory of escape of a barrier/Eyring Rate Theory
Mechanochemistry of bond failure

Readings: Berg, Evans

4/22 **L#19: Motion at the Molecular/Macromolecular Level:**

Major Mechanisms:
I. Motor Proteins
II. Rectifying thermal motion by polymerization

Readings: Journal Articles

III. CELL MECHANICS

4/24 **L#20: Strucuture of the Cell:**

Qualitative description of cell
Effect of forces on a cell
Experiments
The cell as complex viscoelastic solid

Readings: Lodish

4/29 **L#21: Biomembranes:**

Importance
Stiffness & Role of transmembrane proteins
Equations for a 2-D elastic plate

How to measure viscoelasticity
Vesicles: model systems
Readings: RDK notes, Sackman

5/1 L#22: Guest Lecturer: Professor Christine Ortiz:
Pushing and pulling on molecules: Experimental aspects of high resolution force spectroscopy.

5/6 L#23: The Cytoskeleton:
Fiber microstructure;; models for cytoskeletal mechanics; actin and microtubule dynamics, methods of visualizing actin diffusion and polymerization. Rheology of the cytoskeleton. Active and passive measures of deformation. Storage and loss moduli and their measurements.
Readings: Lodish, Janmey, Maggs, Mackintosh.

5/8 L#24: Cell Adhesion and Aggregation:
Cell adhesion assays, cell-free adhesion assays. Receptor-ligand interactions mediated by the cytoskeleton and the cell membrane. Focal adhesions
Readings: Hammer, Bell, LM notes.

5/10 Term Paper Due

5/13 L#25: Cell Migration:
Measurement of cell motility (speed, persistence, "diffusivity"). Simple model for cell migration, environmental gradients. Actin filament assembly- crosslinking – disassembly.
Readings: Sheetz, Lauffenburger, notes.

5/15 L#26: Guest Lecturer: Peter So
Dynamics inside cells

TAKE HOME FINAL (Handed out during last week of class before finals period)