Harvard-MIT Division of Health Sciences and Technology
HST.523J: Cell-Matrix Mechanics
Prof. Myron Spector

CHAPTER 1

Clinical Examples of the Roles of Mechanical Forces in Tissue and Organ Development and Maintenance: The Working Paradigm

1.1 Introduction; Operational Definitions: Mechanics

1.2 Genotype/Phenotype (Fig. 1.1)

1.3 The Working Paradigm: The Unit Cell Process/The Control Volume (Fig. 1.2)

1.4 Importance of Matrix Properties/Mechanical Properties

1.5 Examples Showing the Effects of Mechanical Forces on Tissue and Effects of Forces Generated by Cells

1.1 OPERATIONAL DEFINITIONS: MECHANICS

A. Mechanics of Non-Deformable Bodies
(No deformation of the "body" on which the forces act.)

1. Statics

a. Forces and moments on body - no displacement or rotation of the body
b. Forces cause translation. Moments cause rotation.
c. Forces are "vectors" having magnitude and direction. Can "resolve" the force vector into "components" in any set of directions.
d. Moments cause rotation in clockwise or counterclockwise direction. Magnitude calculated by multiplying a force times the distance to the point of rotation (measured on a line perpendicular to the direction of force).
e. Problems: Given several forces acting on a body determine the magnitude and direction of unknown forces required to keep the body from translating or rotating.
Solution: Use the equations that state that the sum of all forces acting on the body equals zero and the sum of all moments equals zero.

2. Dynamics

a. Forces on body - body moves.
b. Problems: Given forces on a body determine how it moves.
Solution: Use the equations that state that force equals mass times acceleration and momentum equals mass times velocity.

3. Kinematics

a. No consideration of forces - characterize only how a body moves.
b. Problem: Describe knee rotation.
Solution: Use the graphical construction of the "instant centers of rotation."

B. Mechanics of Deformable Bodies (Strength of Materials)
(Force causes deformation of the body.)

1. Elasticity

a. Stress (force divided by area) is directly proportional to strain (deformation divided by original length).
b. No permanent deformation; material returns to original shape when force (stress) is removed.
c. The load (force)-deformation behavior of a material is generally presented as a stress-strain curve.

2. Plasticity

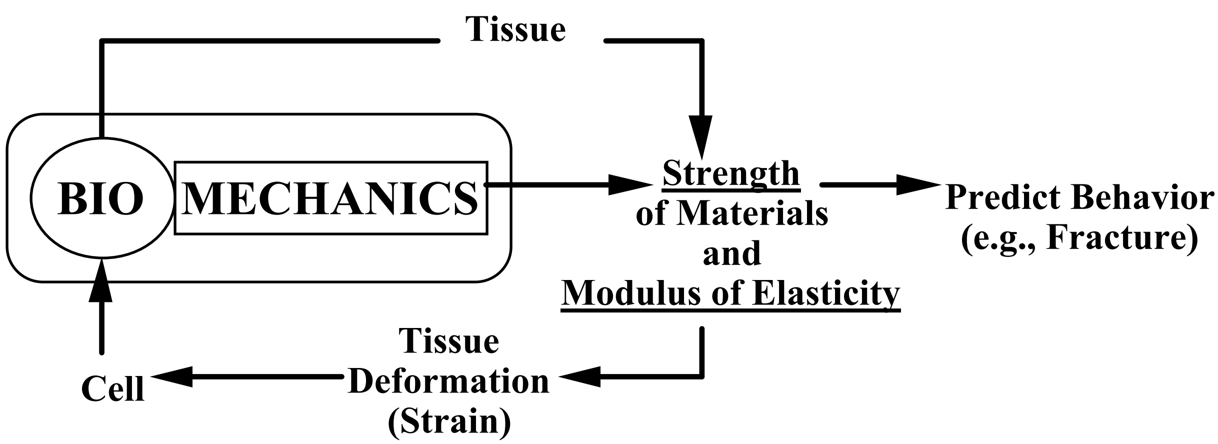
Permanent deformation when the stress is removed.

3. Viscoelasticity

a. Time-dependent stress-strain behavior. Some materials display fluid-like behavior under certain circumstances of loading and elastic behavior under other loading conditions. Stress is related to the rate of strain (i.e., how fast the body undergoes deformation).

b. Bone and most natural materials and polymers are viscoelastic materials.
c. Creep and stress relaxation.

4. Viscosity
a. Behavior of fluids.
b. Shear stress is related to shear strain rate.



Conventional mechanics deals with the load-deformation behavior of materials. This subject matter is also referred to as "strength of materials." The focus of conventional mechanics is often on issues related to strength because the objective is to predict, or design for, load-carrying capacity. The "bio" of biomechanics is associated a) with the study of material that has been synthesized by cells (i.e., extracellular matrix, ECM), and b) the effects of mechanical strain on cell behavior. Relative to cell behavior, it is the modulus of elasticity of the material that is the determinant of the strains experienced by the cells as a result of the loads imparted to the tissue (i.e., the ECM) as a result of the activities of daily living, or the abnormal conditions associated with exertion or disuse.

1.2 GENOTYPE AND PHENOTYPE

$$\underset{\text{(genetic make-up)}}{\textbf{Genotype}} \xrightarrow{\substack{\textbf{Development}\\ \textbf{Wound Healing}\\ \textbf{Remodeling}}} \underset{\text{(expressed genes)}}{\textbf{Phenotype}}$$

$$\textbf{Genotype} \xrightarrow[\textbf{soluble regulators}]{\textbf{soluble regulators}} \textbf{Phenotype}$$

Fig. 1.1

1.3 THE WORKING PARADIGM: THE UNIT CELL PROCESS

1.3.1 Describes a specific cell-matrix interaction. Usually it describes the induction of a specific phenotype of the protagonist cell by an insoluble substrate.

1.3.2 Confined conceptually in a control volume dV (Fig/. 1.2). Order of magnitude: 10 μm^3.

1.3.3 Regulated by diffusible substances which enter into and exit from control volume. These substances regulate the cell-matrix interaction. Also regulated by mechanical forces which act by deforming the matrix, thereby modulating the cell-matrix interaction.

1.3.4 The cell-matrix interaction is a highly specific process: the cooperative configurational interaction between ligand and receptor. Usually both ligand and receptor are macromolecules, each with a highly specific configuration.

1.3.5 Can be reproducibly demonstrated (or rejected) *in vitro*. Falsifiability of each model of cell-matrix interaction.

1.3.6 Scale: small enough to be reproduced *in vitro* and large enough to have significant physiological content.

1.3.7 Forms a conceptual bridge between *in vitro and in vivo* phenomena.

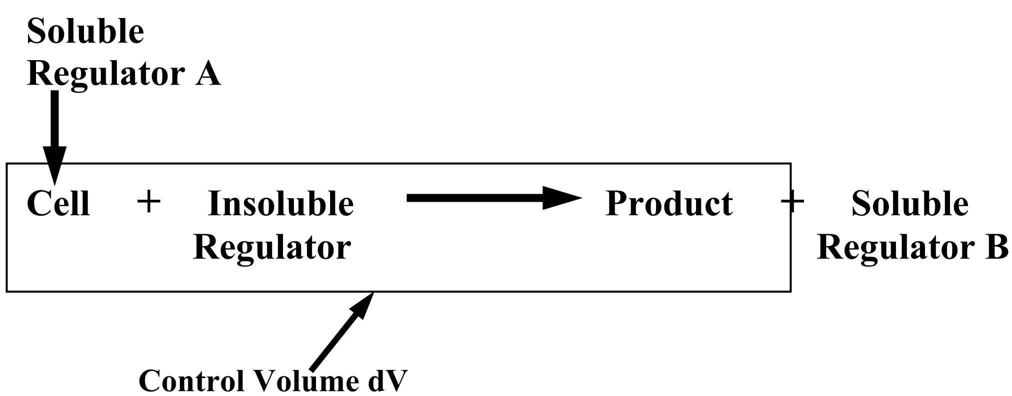


Fig. 1.2 Unit cell process confined conceptually in a control volume, dV. It describes the induction of a particular phenotype of a cell by a soluble regulator and a substrate (acting as an insoluble regulator).

1.4 IMPORTANCE OF MATRIX PROPERTIES/MECHANICAL PROPERTIES

Issues Related to the Mechanics of Nonliving and Living Materials
(to the Molecular Structure - Mechanical Properties Relationships)

	Nonliving Materials	**Living Materials**
Cells (no. cells/vol., size, shape) - Inclusions in material - Agents of formation and degradation of ECM - Cell type: connective tissue, muscle, nerve, epithelia	No	Yes
Time constant for change in molecular structure	Years	Days, months, years
Number of different molecules comprising materials (insoluble)	Many	Few
Types of primary bonds	Metal, covalent, ionic	Covalent (only 2 ionic)
Multiphase	Many (multi-phase alloys, composites)	Always (water as a phase)
Scale over which the molecular structure is uniform	some μm, most mm	μm, mm
Degree of hierarchical molecular structure	Low	High
Role of architecture (*e.g.*, pore characteristics, fiber orientation)	Generally minor	Major
Governing mechanical property	Yield strength-fatigue	Modulus of elasticity
Determination of molecular structure	Easy	Difficult
Mechanical testing	Easy	Difficult
Mathematical; models	Many	Few (including remodeling algorithm)