ME 411 / ME 511

Biological Frameworks for Engineers

Biological Frameworks for Engineers

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Class Organization

- Final Exam
  - Due on Wed 12/11
  - Turn in paper copy to Prof. Sniadecki's office (MEB 318)

ME 411 / ME 511

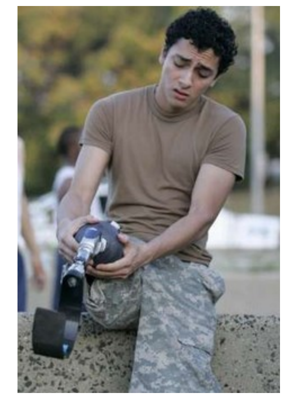
Tissue Replacement

Replacement Body Parts

We wear out – we are easily damaged

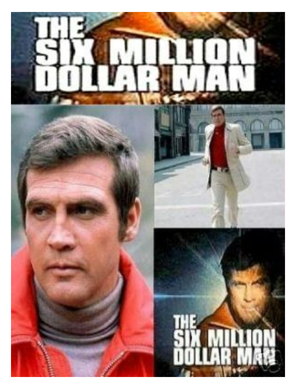
wear

tear



trauma

Can we build it?
Can we build it *better*?
Can we build it *stronger*?
Can we build it to *last*?



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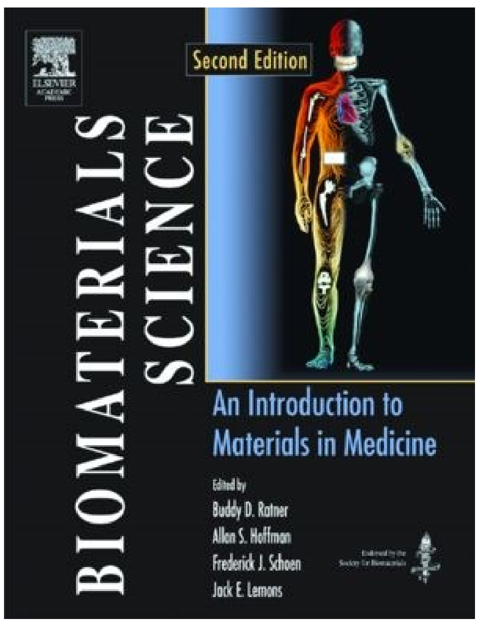
UWEB UNIVERSITY OF WASHINGTON ENGINEERED BIOMATERIALS

Buddy Ratner
(BIOE, ChemE)



http://www.uwtv.org/programs/displayevent.aspx?rID=20222

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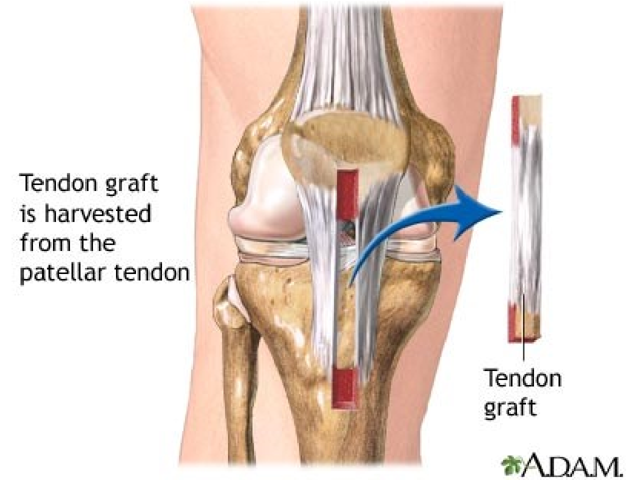
What do we need to know?

- Biomechanics :
  - How does the broken part work?
- Bioresponses :
  - Matrix protein
  - Cell
  - Tissue
- Healing:
  - Immune
  - Inflammation
  - Wound closure

Biologic or Synthetic?

- Autograft – same person
- Allograft – same species
- Xenograft – other species

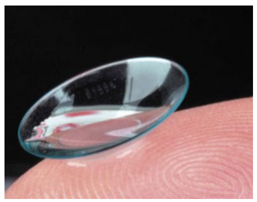


What is a Biomaterial?

- A material intended to interface with biological systems to evaluate, treat, and augment, or replace any tissue, organ, or function of the body.

Common Examples

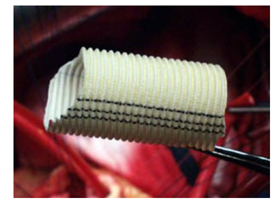
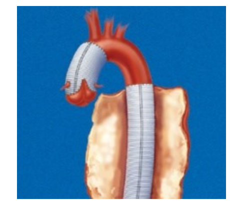
- Contact Lens…




- Dental Implants…


- Cosmetic…

- Vascular Grafts…

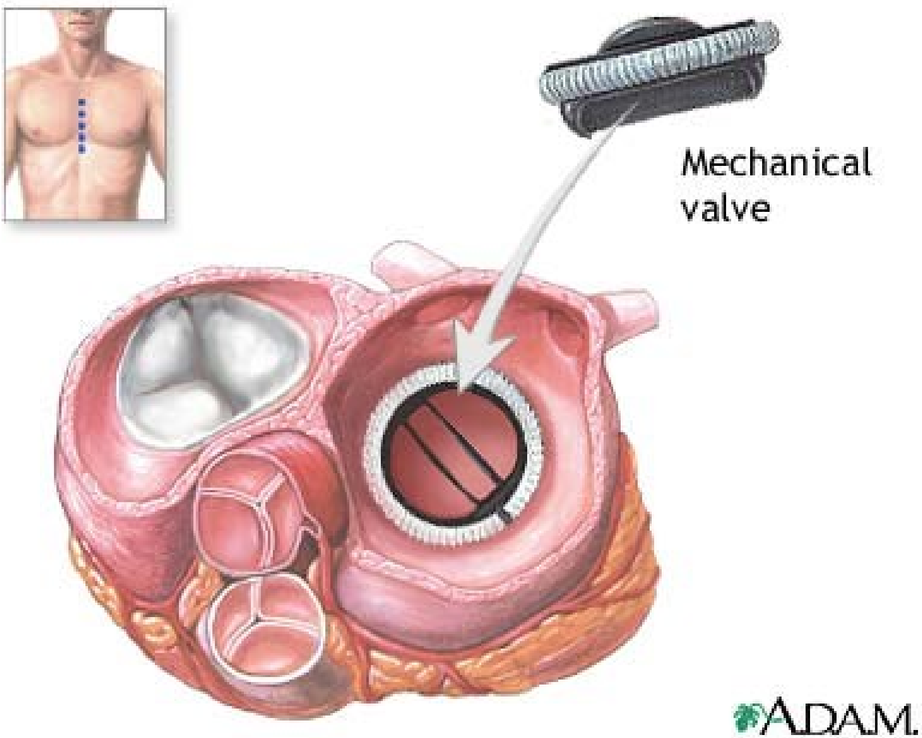



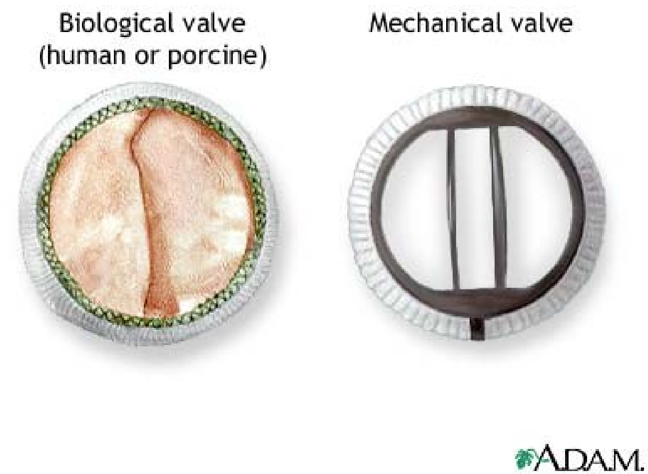
- Joint Replacement…


- Artificial Heart…


Biocompatibility

- Heart Valves – 100,000/yr





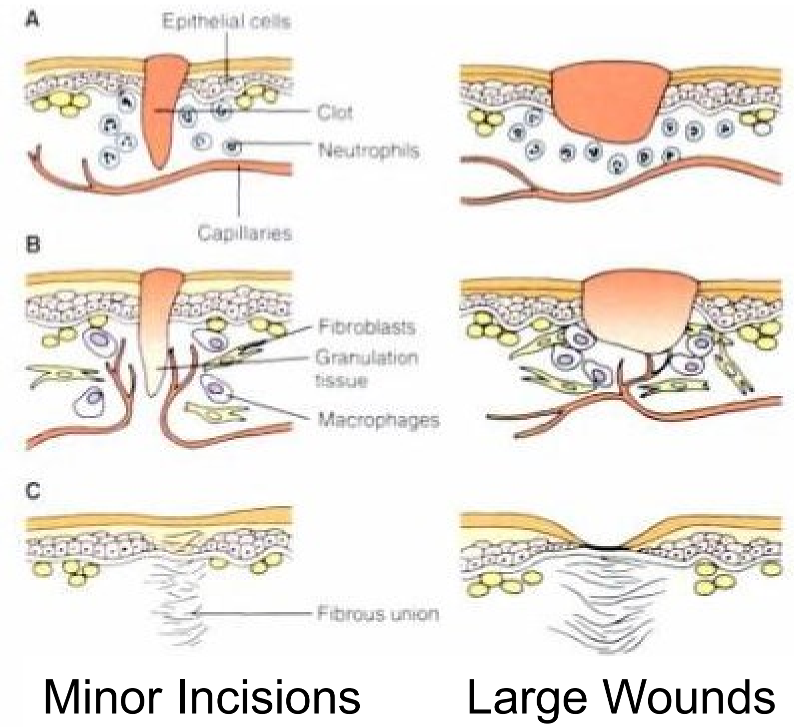
Correct Material Choices

- Inert (1960-1970)
  - Negative immune response
  - Artificial materials have few antigens
  - Nonspecific interactions
  - Hypersensitivity

- Bioactive (1990 – present)
  - Promote local healing
  - Smart/Instructive materials
  - Minimally invasive surgery
  - Nanomaterials

Integration with the Body

- After implantation
  - Integration into surrounding tissue
  - Isolation with fibrous encapsulation
- Wound Healing



Integration with the Body

- After implantation
  - Integration into surrounding tissue
  - Isolation with fibrous encapsulation
- Inflammation : angiogenesis and granulation tissue
- Immune response : antigen or nonspecific
- Blood clotting : platelets and thrombosis
- Infection : bacterial or viral invaders
- Tumor formation : excessive proliferation
- Calcification : deposition of $Ca_3(PO_4)_2$ nodules

Types of Biomaterials

- **<u>Metals</u>** (formable, strong)
  - Cobalt-chromium alloy
    - Heart valves, dental prostheses, orthopedic plates and joints, vascular stents
  - Gold, platinum
    - Dental fillings, electrodes for cochlear implants
  - Silver-tin-copper alloys
    - Dental amalgams
  - Stainless steel
    - Dental prothesis, orthopedic fixation plats, vascular stents
  - Titanium alloys
    - Heart valves, dental implants, orthopedic joints & screws, pacemakers, vascular stents

Types of Biomaterials

- **Ceramic** (hard, degradation resistant)
  - Aluminum oxides
    - Orthopedic joint components, load-bearing components, implant coatings, dental implants
  - Bioactive glasses
    - Orthopedic and dental coatings, dental implants, facial reconstruction components, bone graft substitute materials
  - Calcium phosphates
    - Orthopedic and dental coatings, dental implant materials, bone graft substitute materials, bone cement

Types of Biomaterials

- **<u>Polymers</u>** (natural vs. synthetic, elastomers, hydrogels, composites)
  - Synthetic (PMMA, PDMS, PE, PTFE, PLGA, etc.
    - Contact lenses, cosmetic implants, orthopedic wearing implants, vascular grafts, resorbable meshes and sutures
  - Natural (Collagen, Elastin, Fibrin, Hyaluronic Acid, GAGs, etc.)
    - Matrices: orthopedic repair, tissue engineered parts, skin repair, hemostatic sealants

Biomaterial Properties

- Degradable
  - pH resistant
  - Inflammation resistant
  - Biodegradable for cell/factor release
- Surface properties
  - Mechanical coatings
  - Hydrophobic/philic
  - Roughness or topology
- Bulk properties
  - Strength and stiffness
  - Anisotropy
  - Fatigue
  - Temperature
- Fabrication

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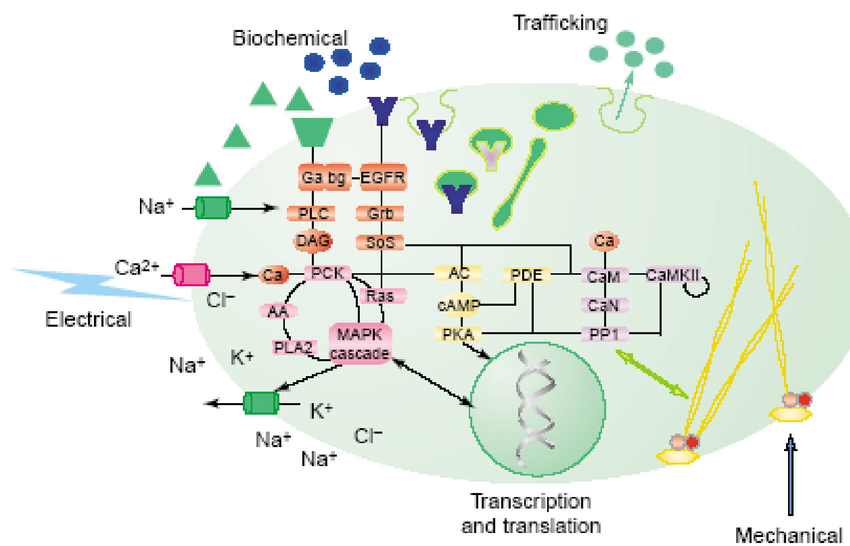
Tissue Engineering

Tissue Engineering

- A field that seeks to replace, repair or enhance biological function at the scale of a tissue or organ by manipulating cells via their extracellular environment.

Atala (WF)
[TED talk]

Langer (MIT)



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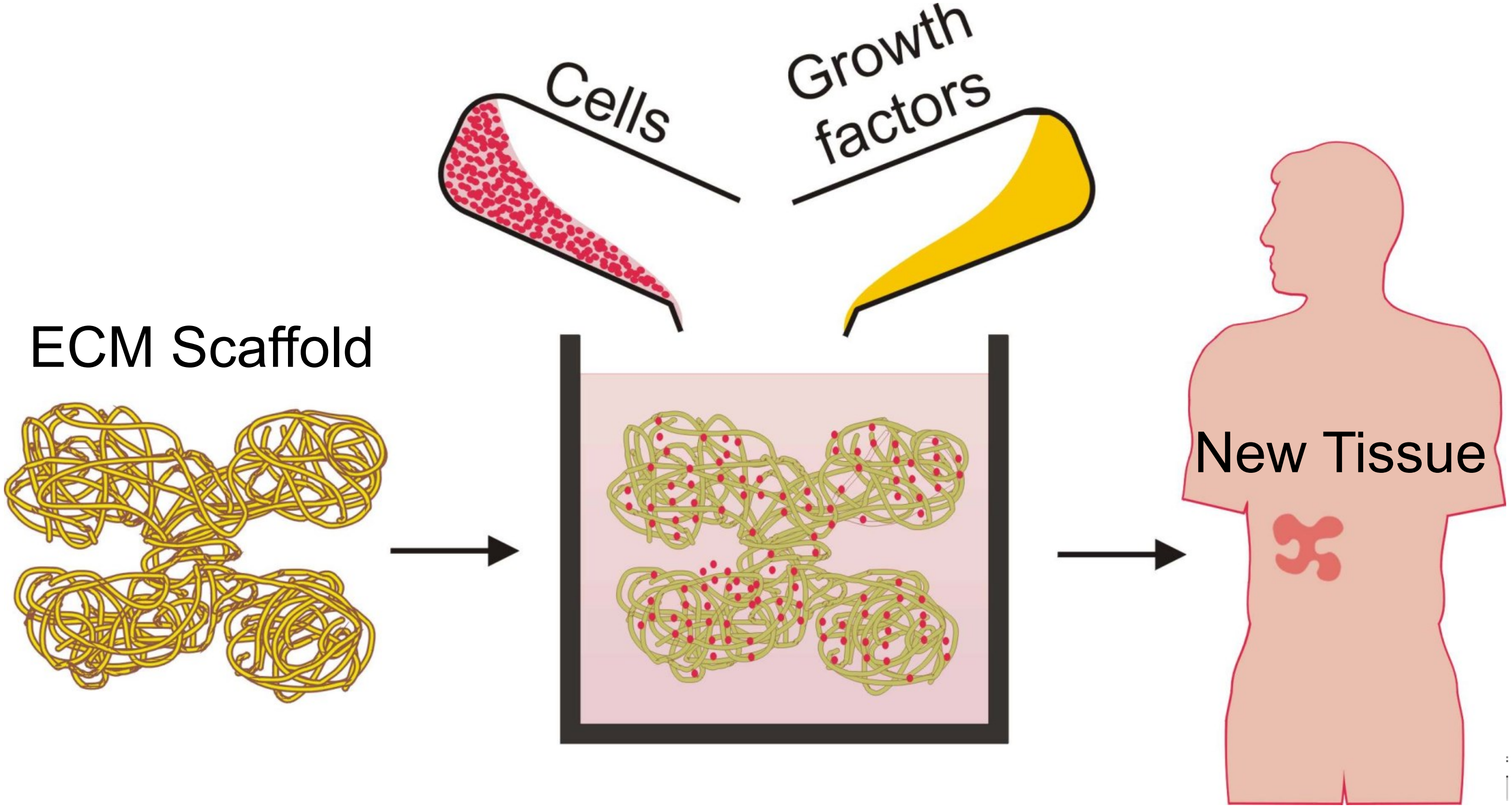
Central Hypothesis

Cells + ECM + GF = New Tissue



Defect Objectives

- Mechanical
  - Bone, cartilage, ligaments
- Metabolic
  - Replace physiological function (liver)
- Synthetic
  - Deliver secretory products (insulin production)
- Communication
  - Nervous system
- Any combination of the above

Success Stories

- Cornea
  - Corneal epithelial cells pre-seeded in hydrogels and transplanted into rabbit cornea, where remained adherent and proliferated up to 2 weeks
- Liver
  - Hepatocyte systems for extracorporeal and implantable applications
  - Implants offers the advantage of permanent liver replacement
- Pancreas
  - Destruction of pancreatic islets, leading to loss of glucose and insulin regulation
  - Transplant microencapsulated islets cells to avoid immune rejection
- Cartilage
  - collagen-glycosaminoglycan templates using chondrocytes
  - chondrocytes grown in agarose gel culture produce tissues with mechanical properties similar to articular cartilage
- Bone
  - synthetic and natural polymers should have optimal strength and degradation properties
  - use bone morphogenetic proteins (BMPs) and growth factors (e.g., TGF-b)
- Bladder
  - Seminal attempt in generation of complete organ
  - Collagen scaffolds seeded with autologous bladder epithelial cells on inside and smooth muscle cells on outside
- Skin (most successful application)
  - Implant a composite material of silicone upper layer and chondroitin-sulfate and collagen lower layer; prevents liquid loss and induce angiogenesis
  - in vitro culture of keratinocytes (epidermis) from burn patients and multiply 10,000-fold in laboratory; requires 4 weeks

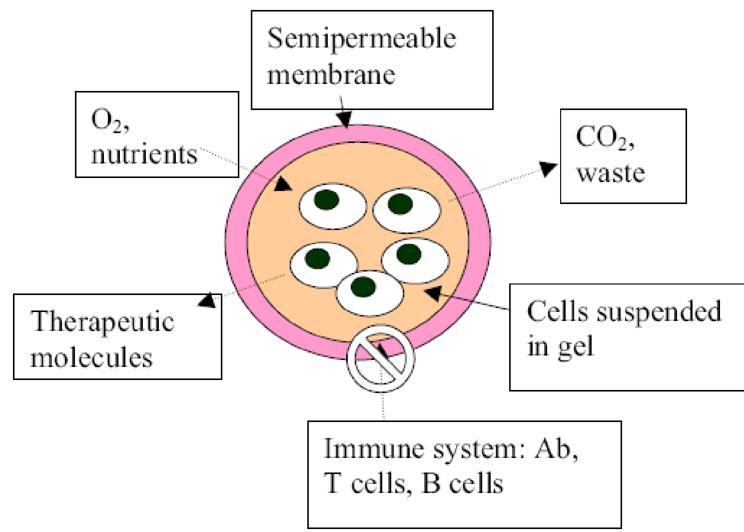
Next Frontier : Muscle and Blood Vessels

Extracorporeal Method

- "Microencapsulation"

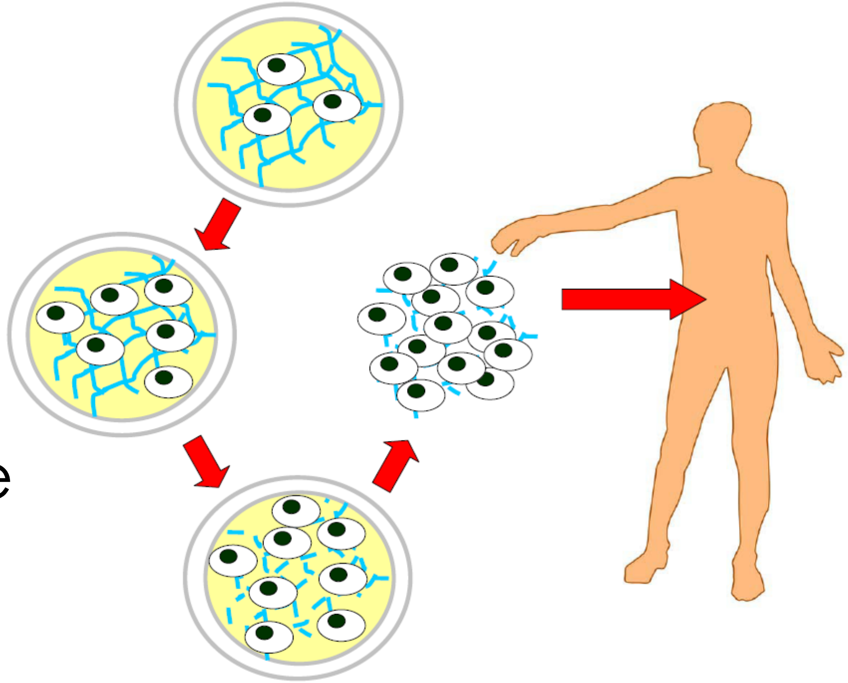
  Ex: insulin-secreting β-islet cells from pancreas of cadaver

  - Encapsulate cells within membrane construct
  - Immunoisolate from antibodies and leukocytes
  - Implant construct
  - Cells secrete product
  - Remove when concluded



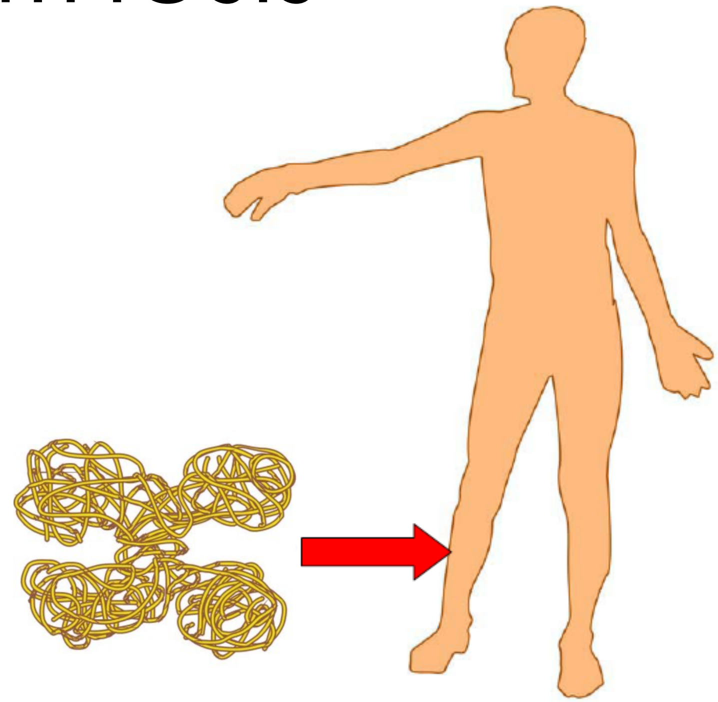
In Vitro Synthesis

- Cultured Scaffolds
  - Cells seeded onto scaffold in vitro
  - Cells maintained in culture to expand population and organize
  - Device implanted once colony established
  - Device degrades and replaced by remodeled tissue



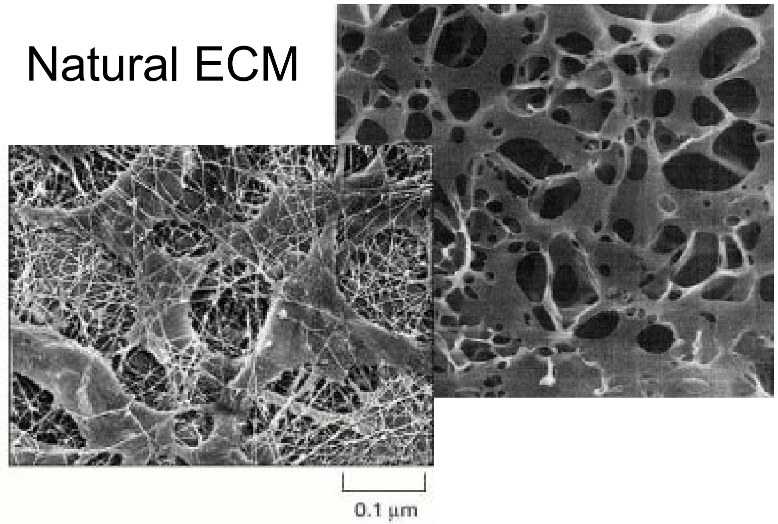
In Vivo Synthesis

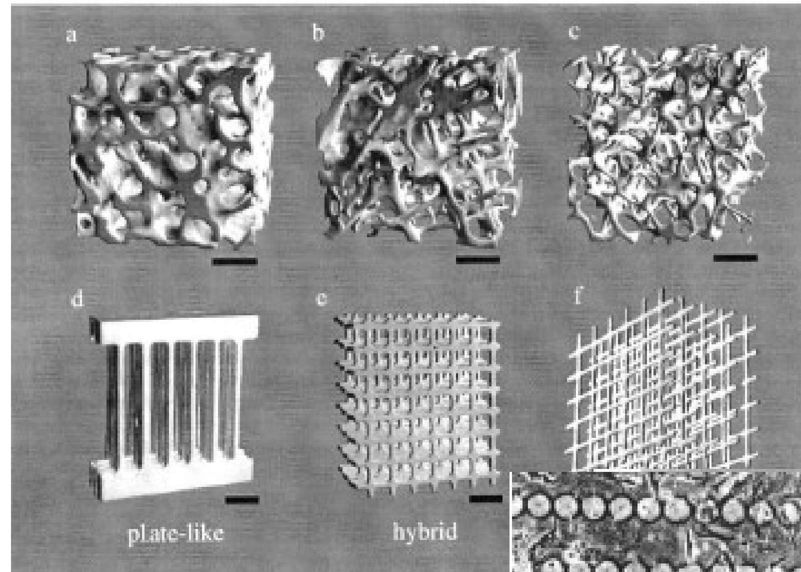
- Implanted Scaffold
  - Constructed bioactive scaffold (ECM, GFs, topology)
  - Implant porous scaffold device
  - Cellular in-growth in vivo (integration and vascularization)
  - Scaffold replace by remodeled tissue

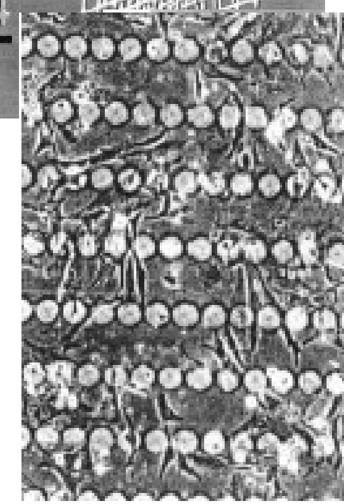


Scaffolds

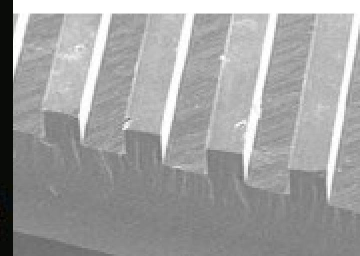
Natural ECM

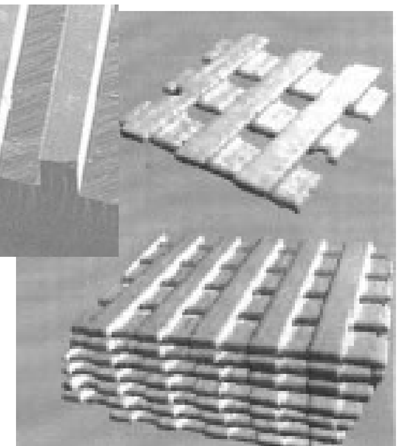






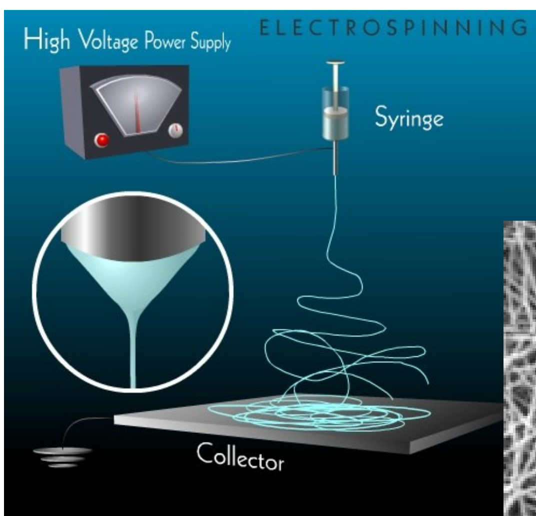
Synthetic ECM

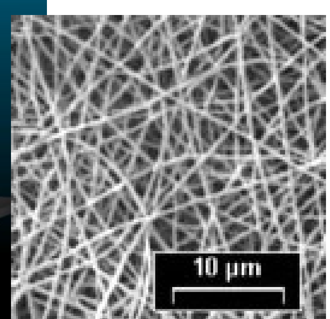


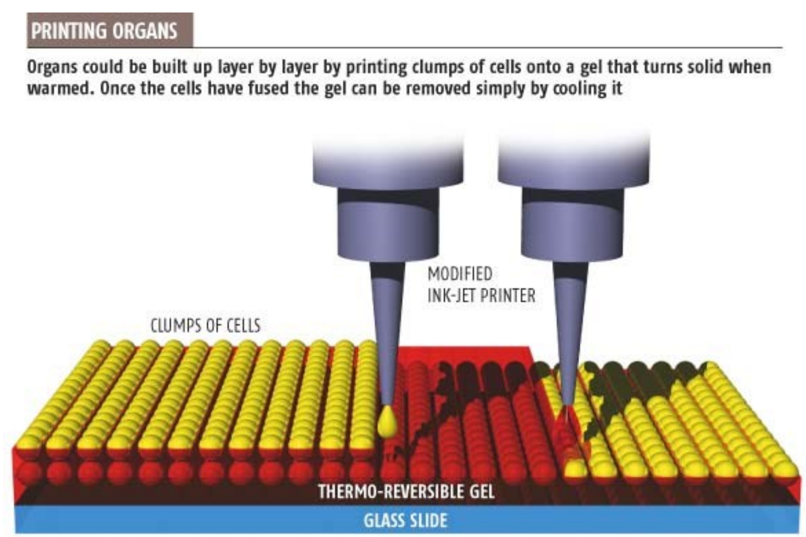


Fabrication

- Biological
  - Decellularization Collagen
  - Hydrogels
- Textile Fibers
  - Weaving/Braiding
  - Electrospinning
- Particles
  - Colloidal Sintering
  - Nanoparticle Condensation
- 3D fabrication
  - Stereolithography
  - “Ink” printing

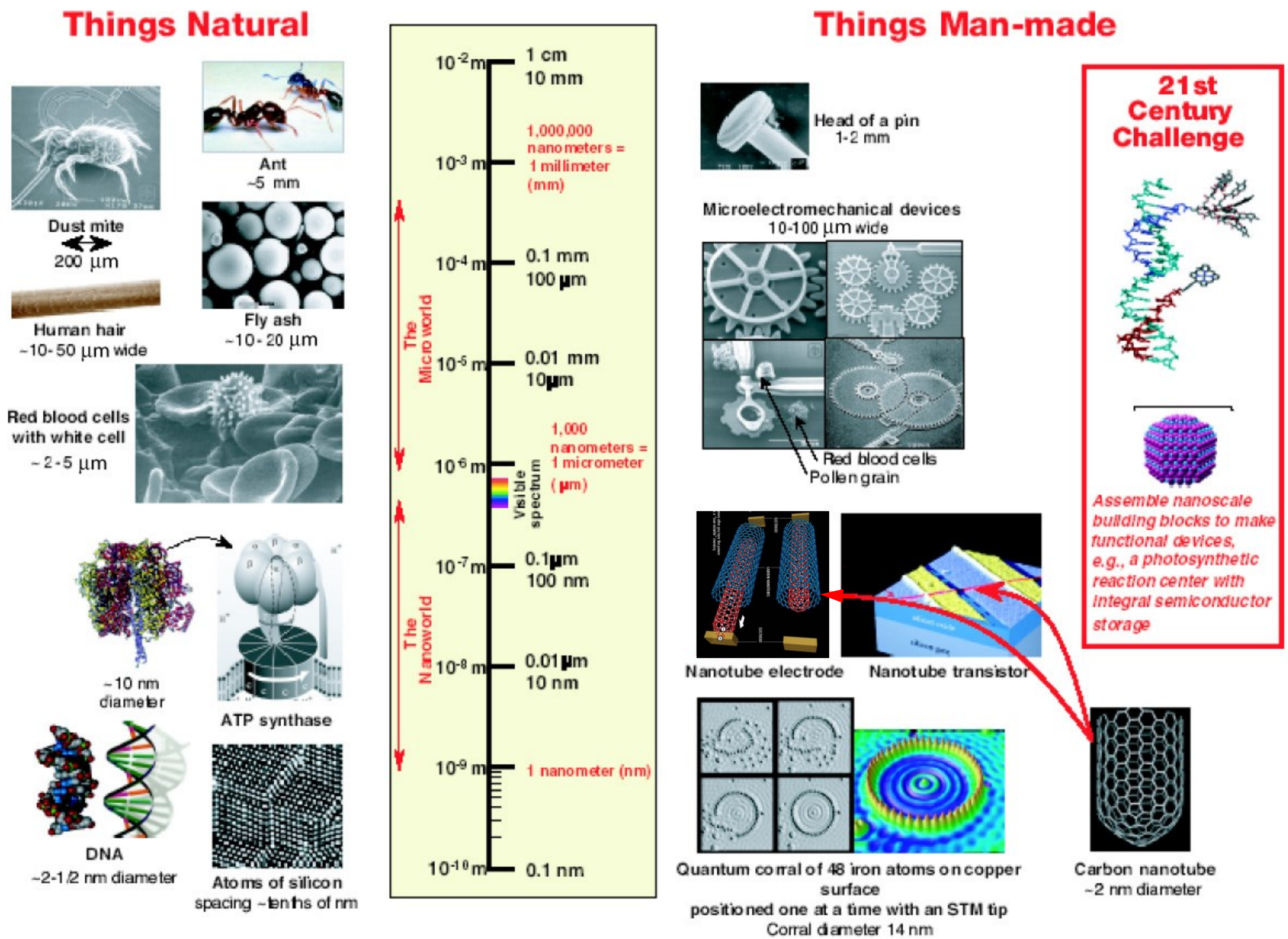


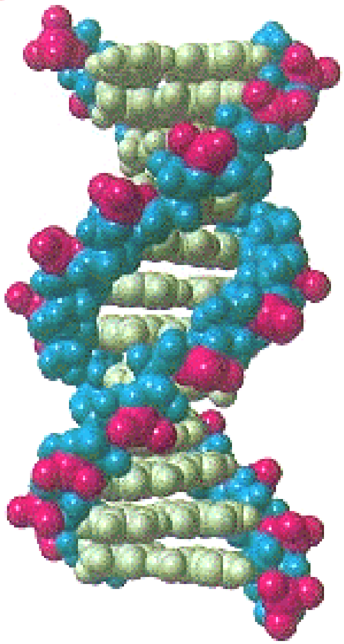




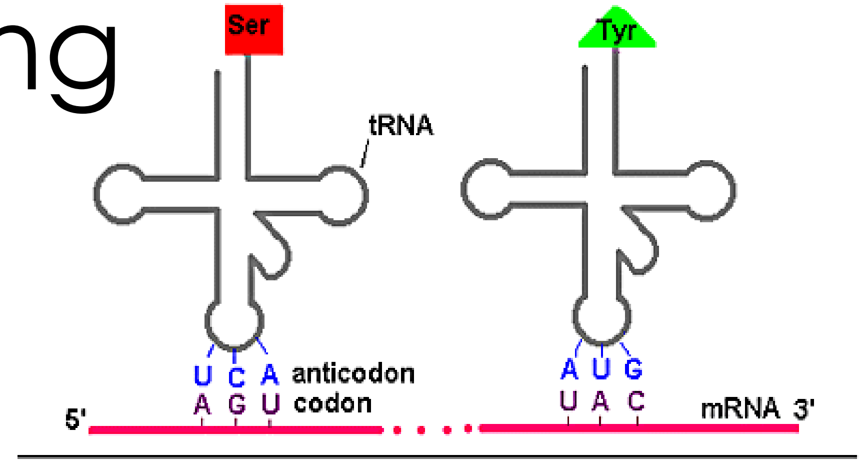
Big Picture [nm-m]

Scale of Life

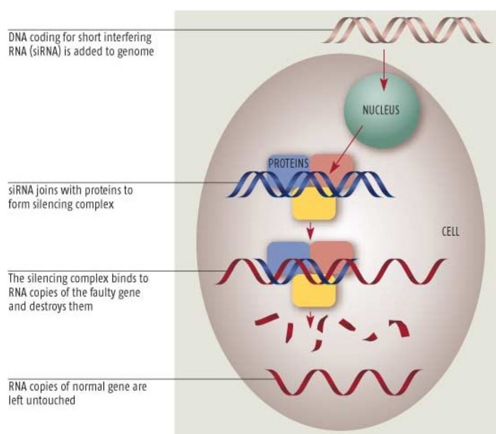




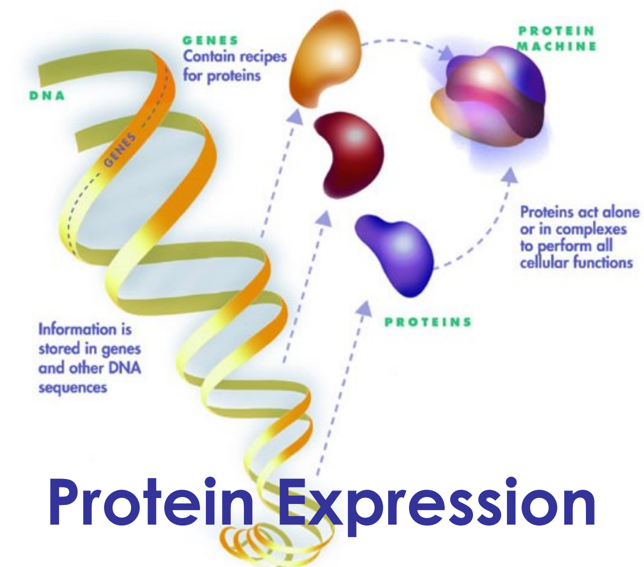
Coding



(5')G G A T A G C A T G A A A C C A G C A T A A (3')

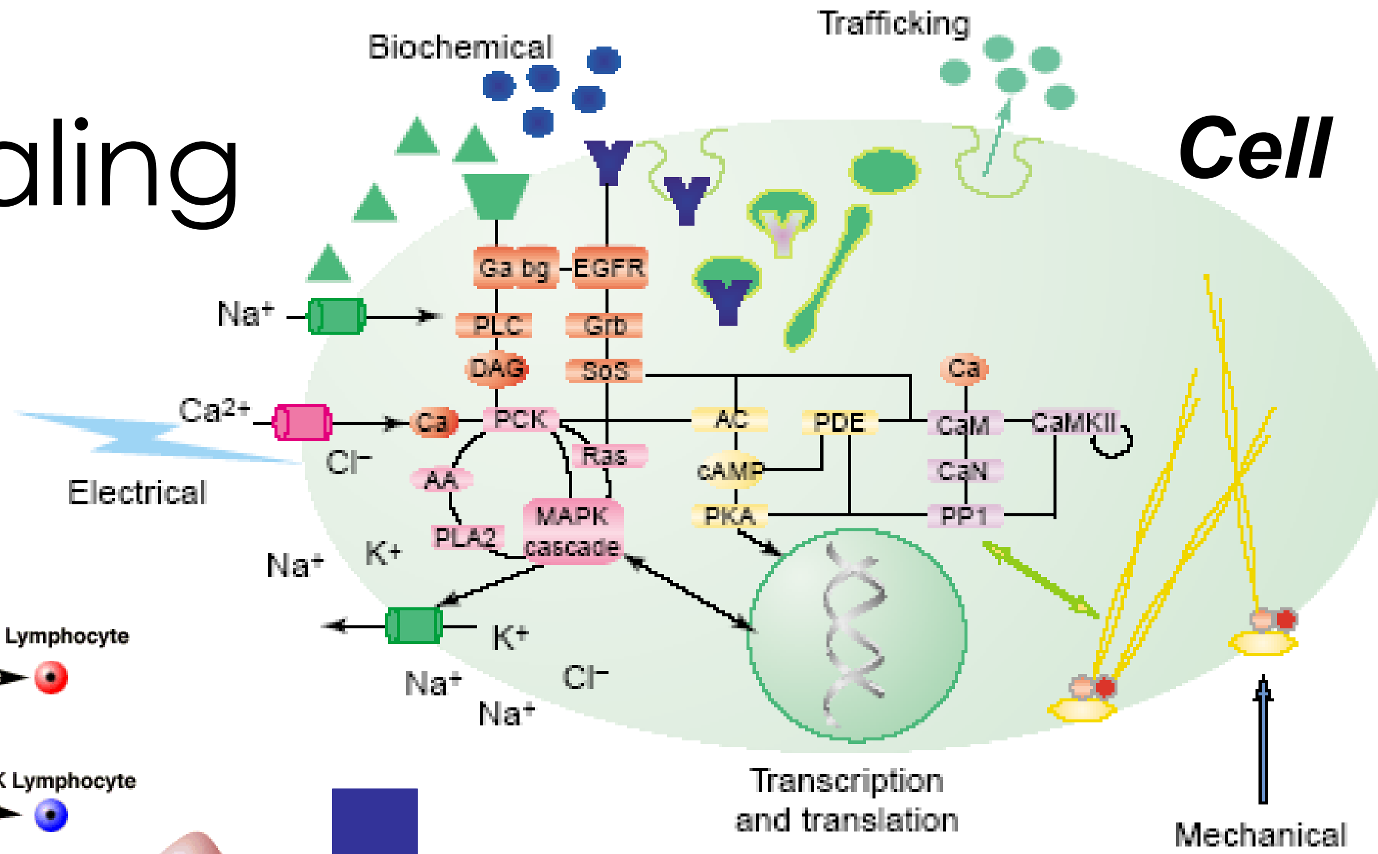


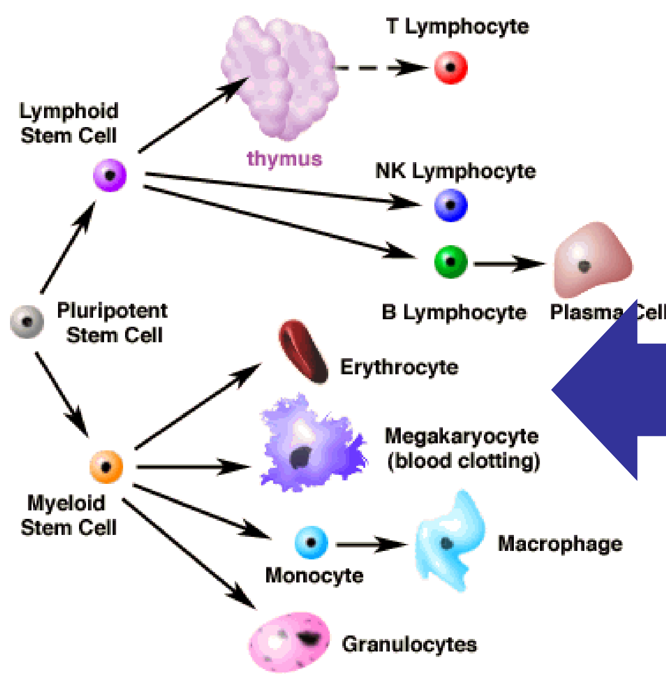
Gene Therapy



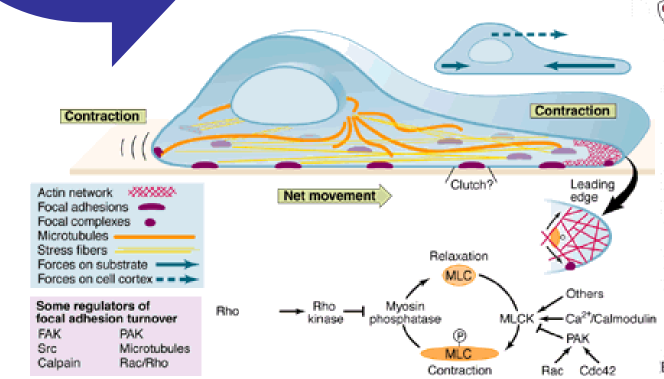
Protein Expression

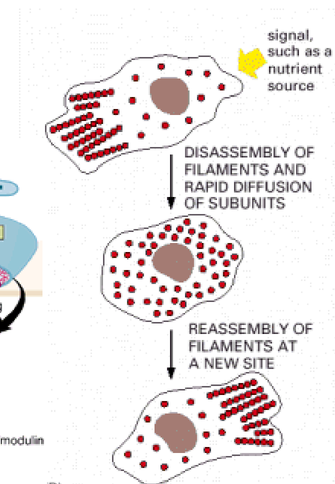
Signaling





Migration





Stem Cells

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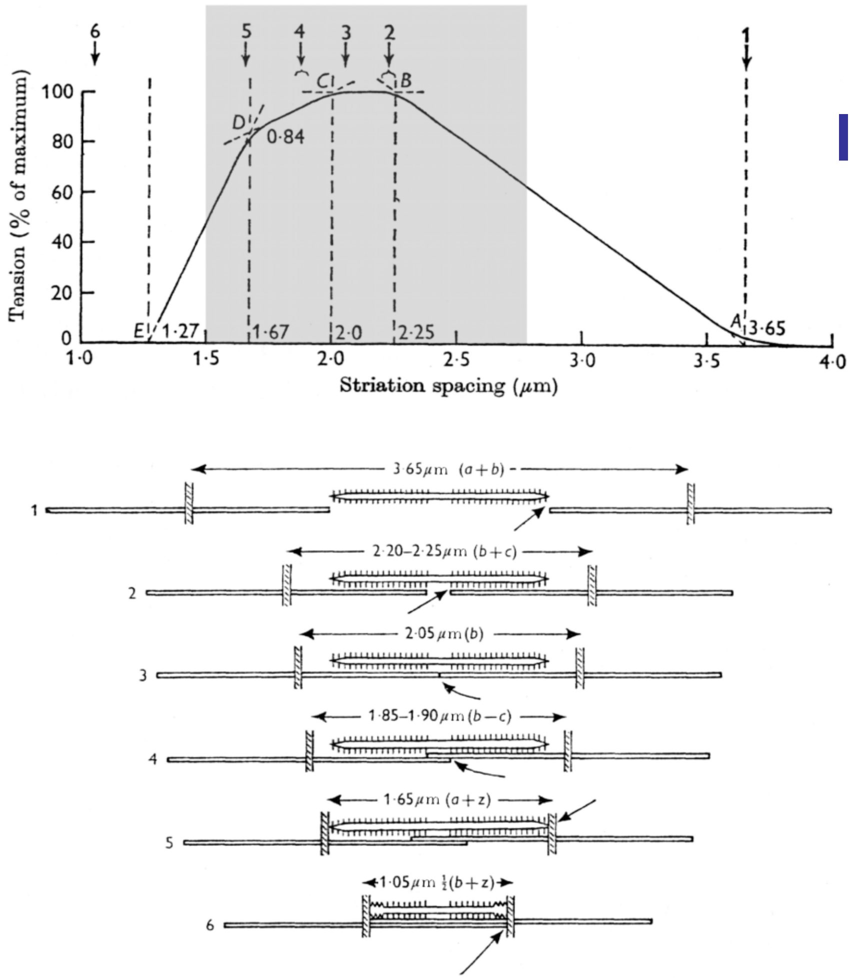
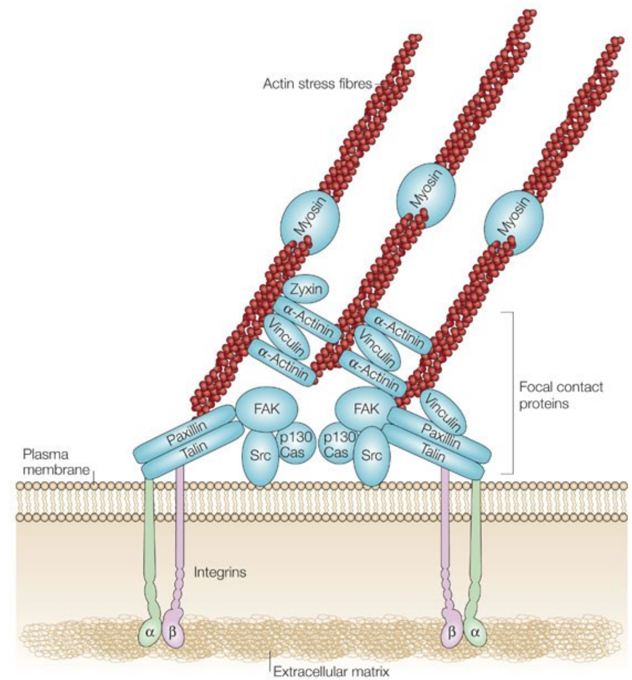
Structure-Function

Actin-Myosin Crossbridge



Integrins… Focal Adhesion



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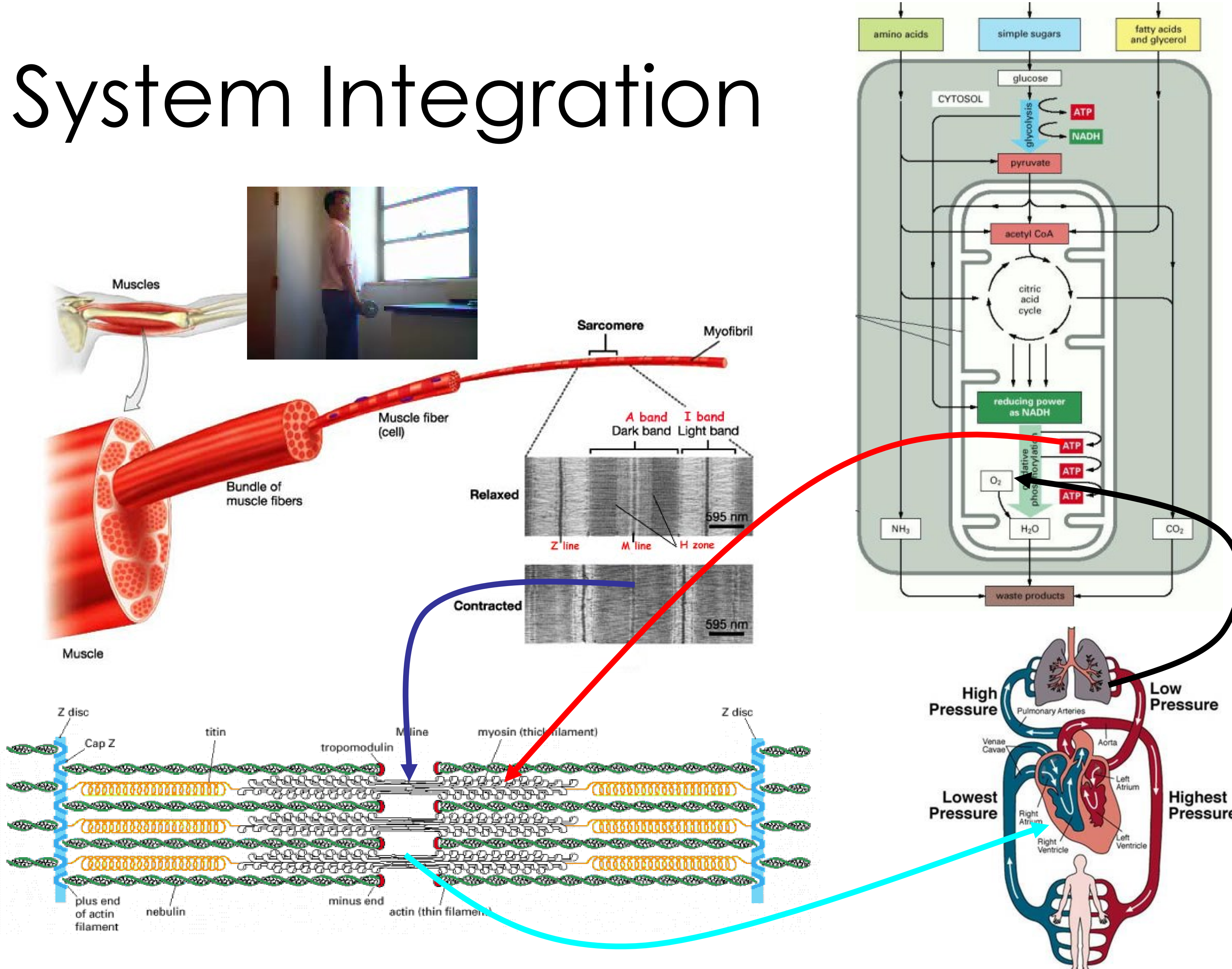
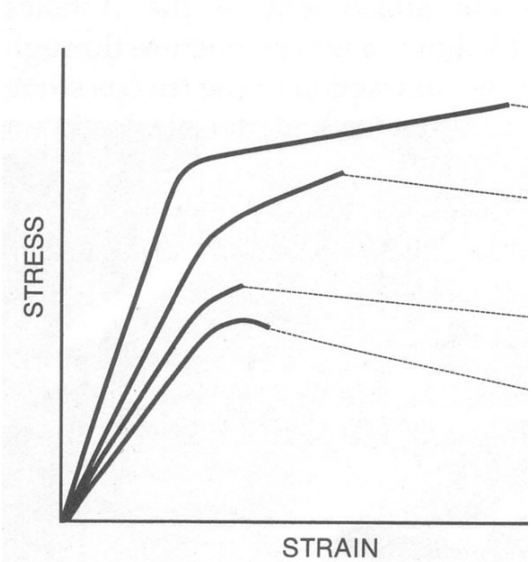
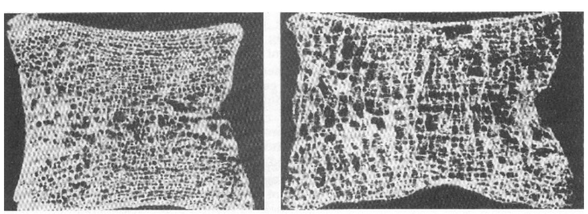
System Integration

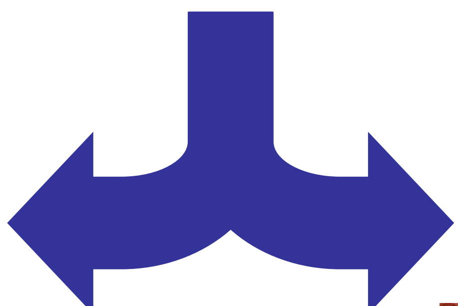


Structural Integration

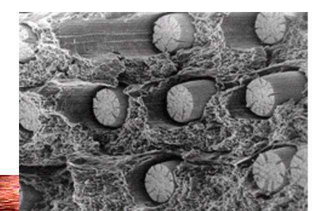


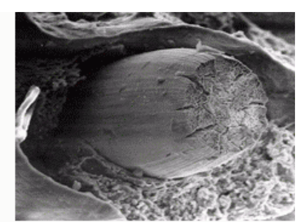


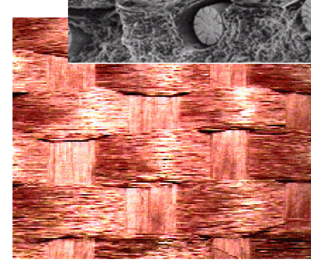
Osteoporosis Prevention



Composite Design







Biological Frameworks for Engineers

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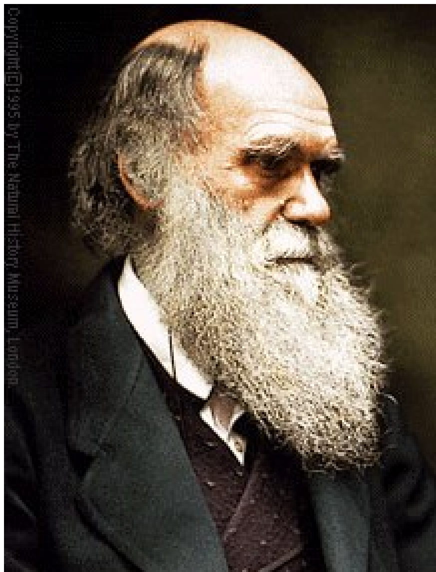
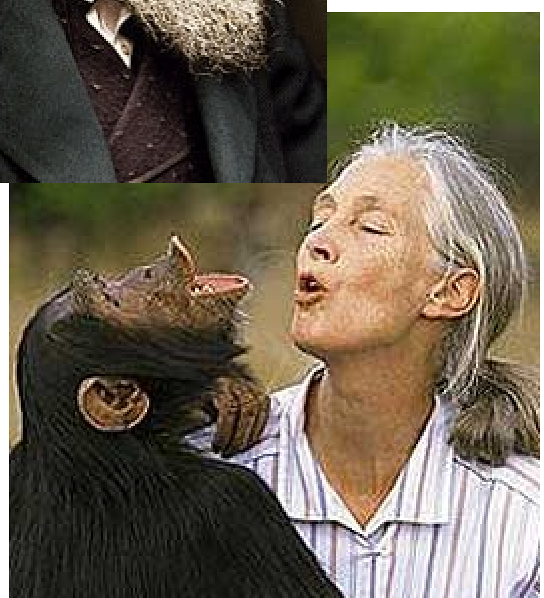
Biology vs. Engineering





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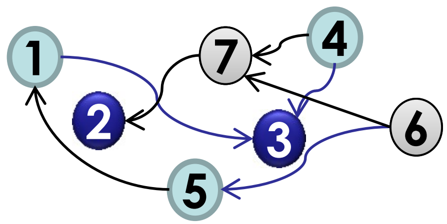
Stereotypes

- What words you think describe:

Biology *Engineering*

Biologists vs. Engineers

- Approach 1



- Observe a system in all its complexity
- Identify known features and classify new systems
- Compare new systems with known systems
- Keeps us on track toward a proper understanding of a biosystem

Knows nothing about REAL biology!

- Approach 2

$$\vec{F} = m\vec{a}$$

- Measure as many features as possible
- Fit features into physical laws, e.g. Newton's law, Hooke's law, Conservation Laws
- Compare properties with nonliving or similar biosystems
- Creates models to explain observations

Understands nothing at all!

Engineering Contributions

- How has engineering made biology better?

Biology Contributions

- How has biology made engineering better?

Suppose you have to work with a biologist…

- Tips to work effectively on a team

The Future

Search for solutions already worked out in nature to advance both traditional engineering and medicine