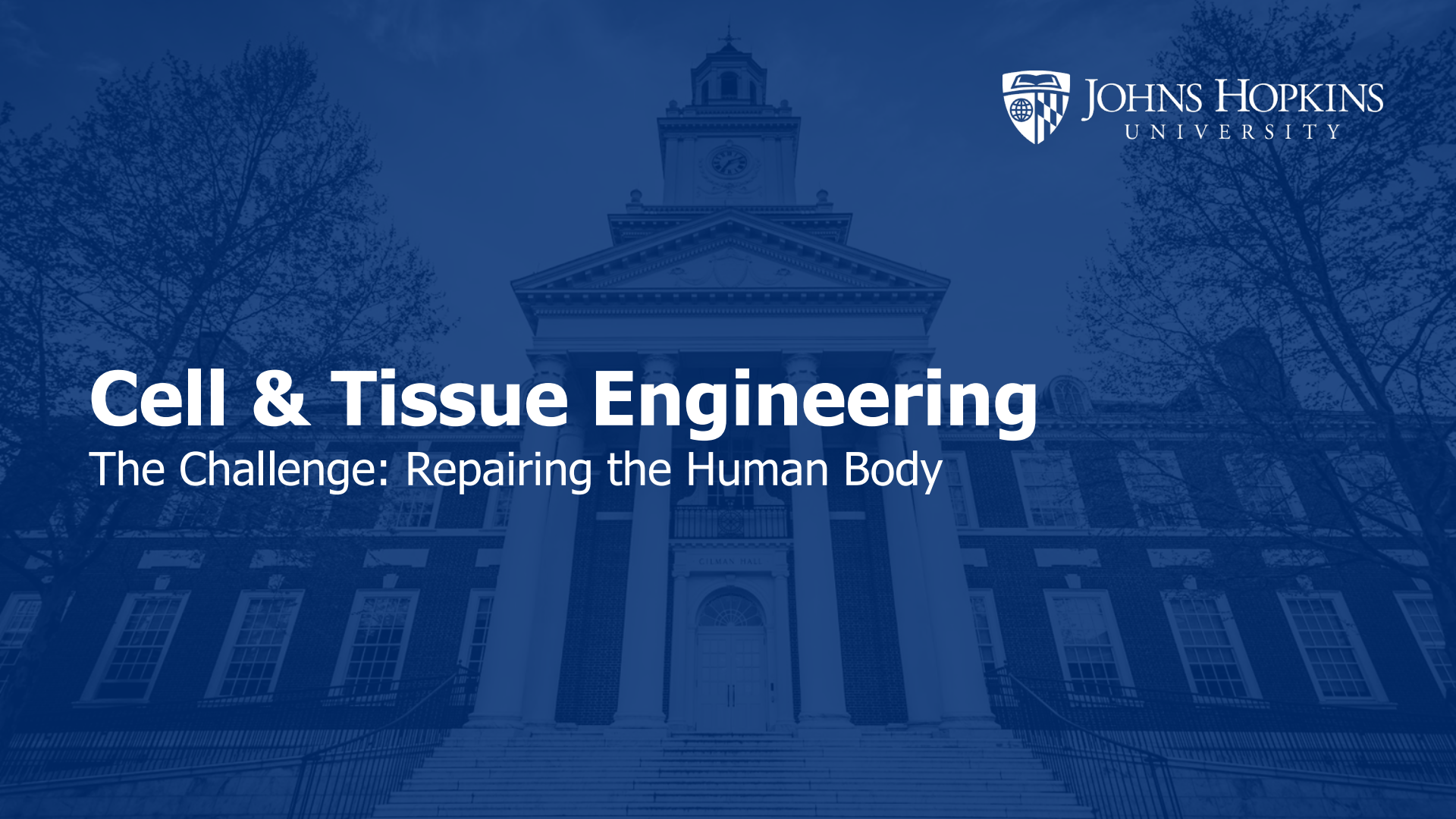


Cell & Tissue Engineering

The Challenge: Repairing the Human Body

Regenerative medicine

- Creating functional new tissues to repair or replace damaged or diseased tissues
  - Therapeutic agent = cell or a collection of cells (tissue)

Cell Engineering

- Manipulation of mammalian cell genome
  - Editing, reprogramming, resetting
    - Genetic and epigenetic level – gene expression, protein processing and ultimately cell behavior

Tissue engineering

- Development of biological substitutes to restore, maintain or improve tissue function (Y.C. Fung 1985)

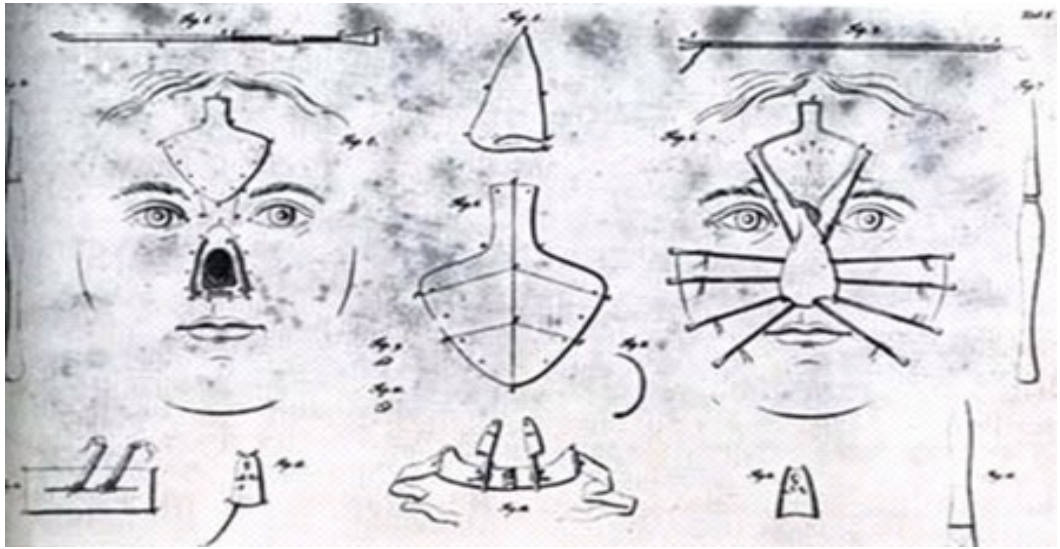
Tissue transplantation ancient history

Greek Mythology

Ancient Egypt

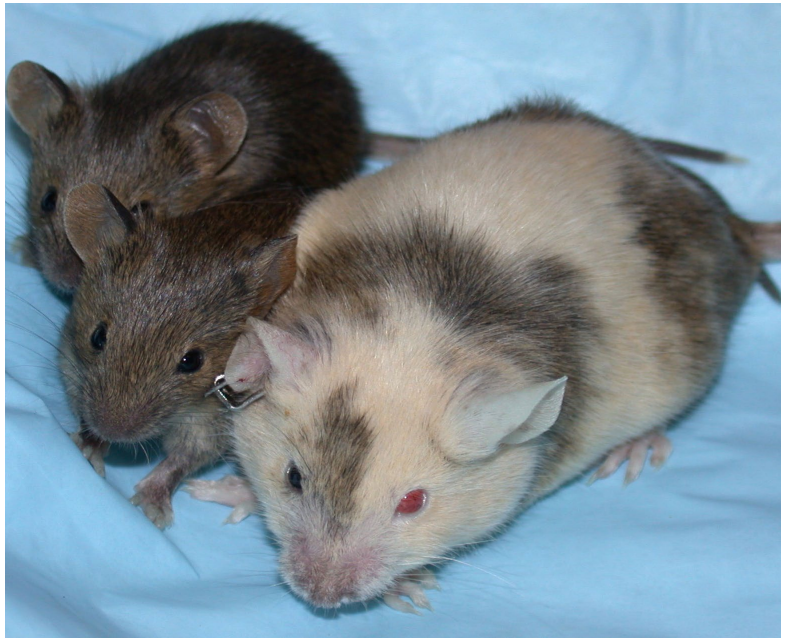
http://en.wikipedia.org/wiki/Chimera_(mythology)
http://en.wikipedia.org/wiki/Sphinx

1000 BC Nose Transplant



http://archive.ispub.com/journal/the-internet-journal-of-plastic-surgery/volume-3-number-2/sushruta-rhinoplasty-in-600-b-c.html#sthash.z69R07Cc.dpbs

Modern day



http://en.wikipedia.org/wiki/Chimera_(genetics)

Tissue transplantation in U.S.

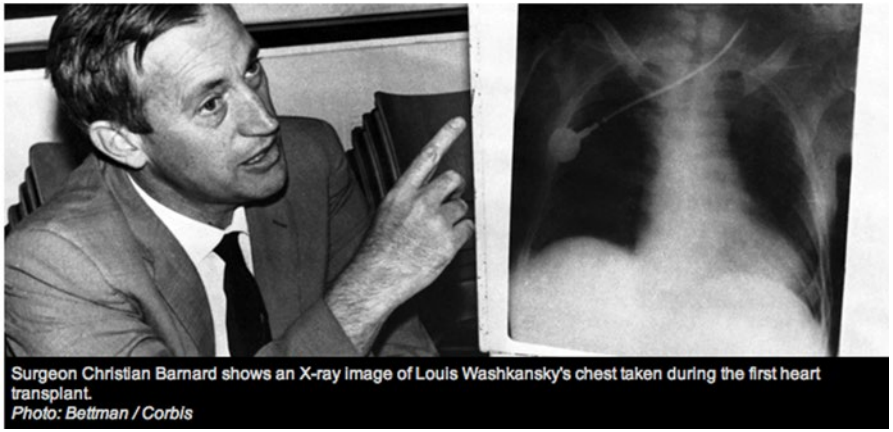
- Rate ~30,000 organ transplants per year in US
- Demand >110,000 people on waiting lists
- Lives lost ~19 people lost per day due to lack of organs

Tissue transplant history


MAN'S LIFE SAVED BY TWIN'S KIDNEY

Identical Brother Furnishes Organ in First Successful Transplanting Surgery

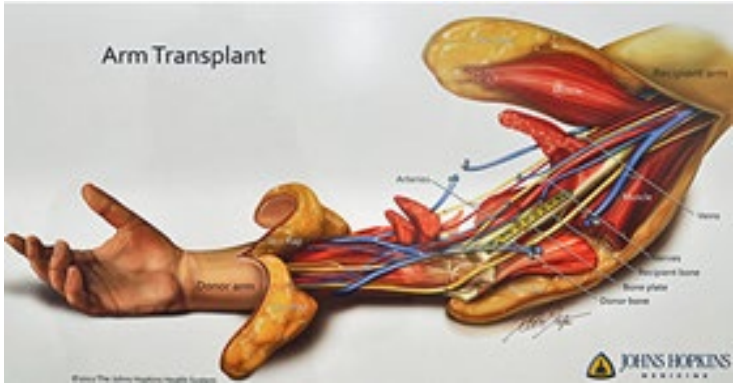
1954 – first successful kidney transplant (U.S)


Surgeon Christian Barnard shows an X-ray image of Louis Washkansky's chest taken during the first heart transplant.
Photo: Bettman / Corbis

1967 – first successful heart transplant (South Africa)

Recent advances- transplantation

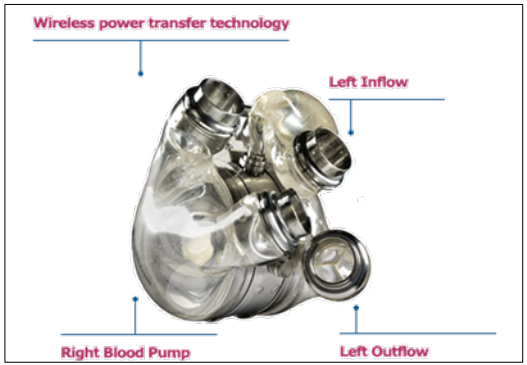
Replacement of soldier's arms



Alternatives to tissue transplantation

- Medicine

- Artificial or synthetic organs

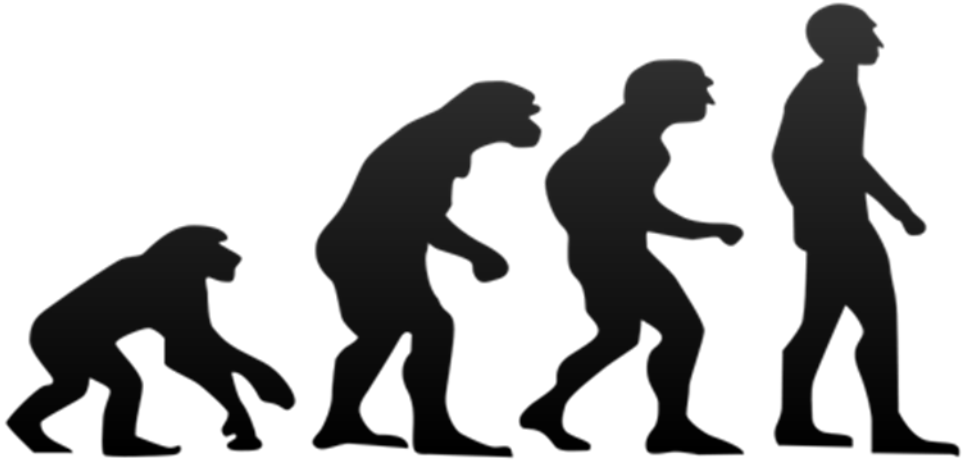


- Cell & tissue engineering

commons.wikimedia.org, http://www.abiomed.com/products/heart-replacement/, http://en.wikipedia.org/wiki/Vacanti_mouse, http://www.sciencedaily.com/releases/2013/06/130606110026.htm

Difficulties of cell & tissue engineering

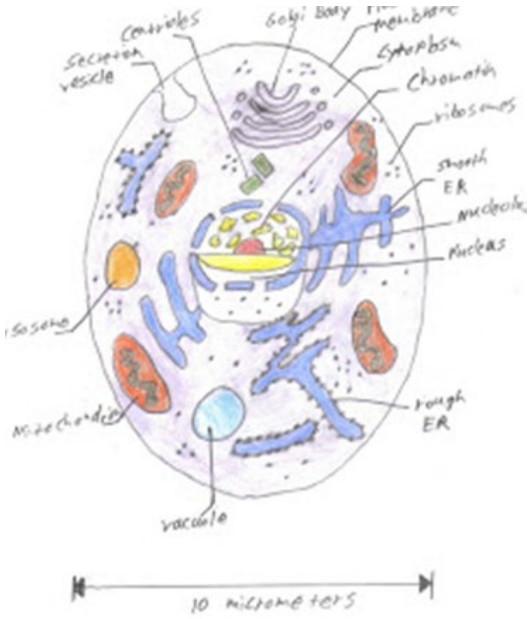
- Time



http://en.wikipedia.org/wiki/Human_evolution

Difficulties of cell & tissue engineering (cont.)

- Function
  + self-renewable
  + self-rechargeable
  + self-repairable



http://beautifulgrace2008.blogspot.com/2008/12/plant-and-animal-cell-drawings-by-fire.html

Difficulties of cell & tissue engineering (cont.)

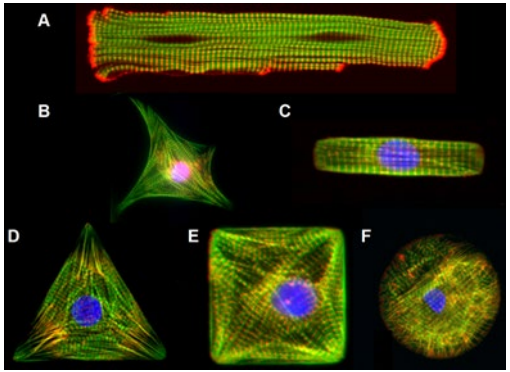
- Dynamic range
- Unknown Functions
- Risks
- Scaling-up

Advances in cell & tissue engineering

- Cells
- Matrices/scaffolds
- Signals

Advances – cell engineering

- **Cell Engineering (Autologous, Allogeneic, or Xenogenic)**
  1. Differentiated cells of same type as tissue
  2. Stem cells (e.g., bone marrow-derived)
  3. Other cell types (e.g., dermal cells)



http://www.corning.com/lifesciences/us_canada/en/about_us/cell_culture_history_1907.aspx
diseasebiophysics.seas.harvard.edu

Advances – cell engineering (cont.)

1907
First cell culture at Johns Hopkins

1990
First genetically engineered cells put into a patient

1991
Therapeutic gene transfer

Adult and embryonic stem cell engineering

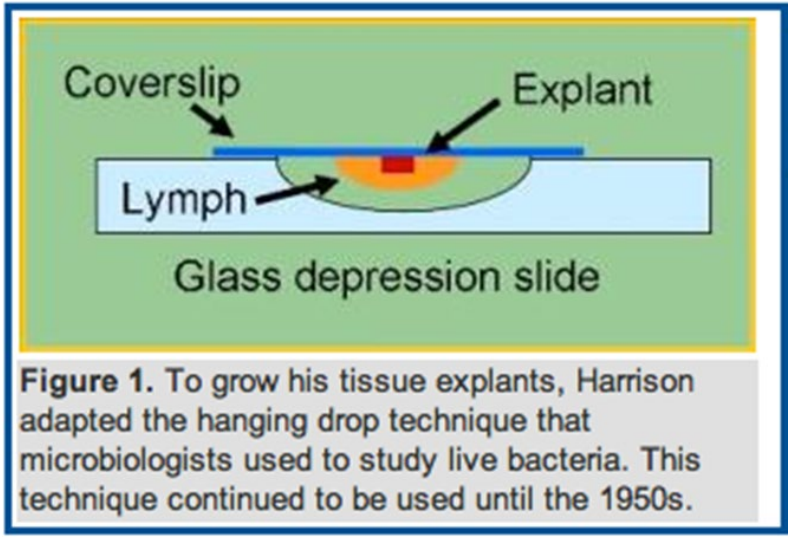
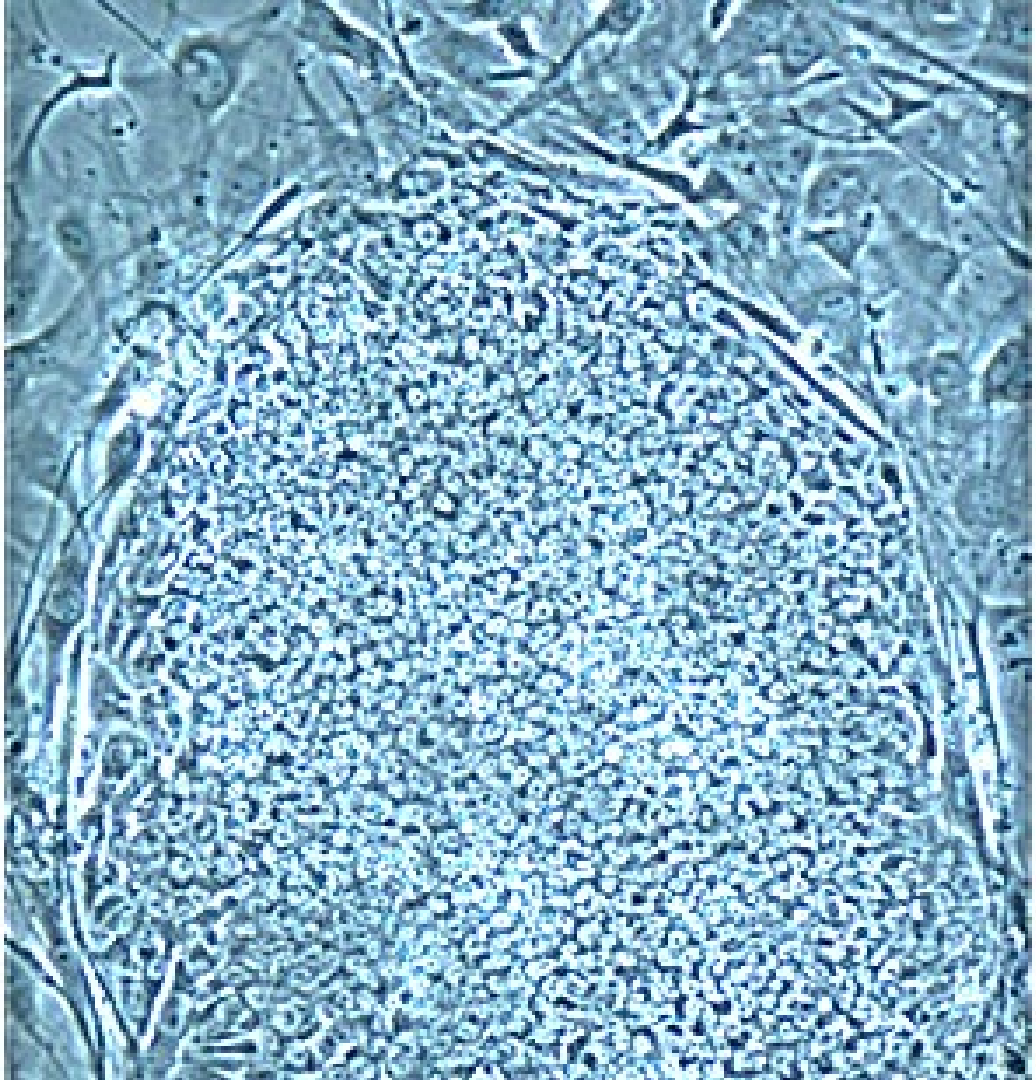


Figure 1. To grow his tissue explants, Harrison adapted the hanging drop technique that microbiologists used to study live bacteria. This technique continued to be used until the 1950s.

http://www.corning.com/lifesciences/us_canada/en/about_us/cell_culture_history_1907.aspx



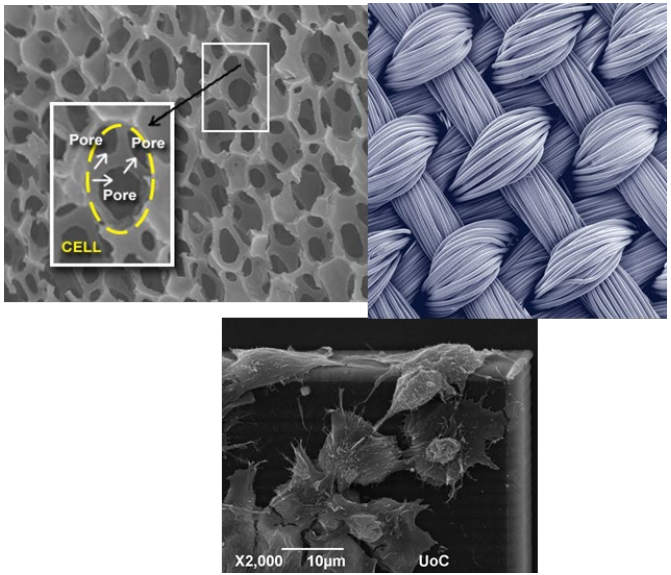
Embryotic stem cells

http://www.cbsnews.com/8301-204_162-57584654/scientists-successfully-clone-human-stem-cells-via-skin-cells/

http://www.corning.com/lifesciences/us_canada/en/about_us/cell_culture_history_1907.aspx

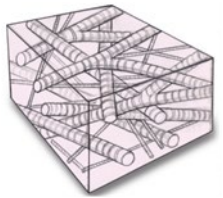
Advances – matrices and scaffolds

1. Biomaterials
2. Synthetics



www.biomatrix.com; www.faseb.org

Biomaterial advances



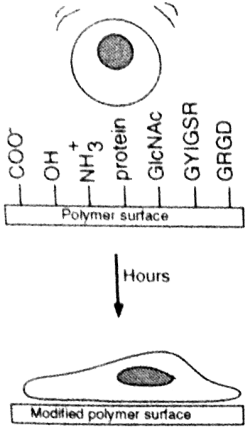
- Polymers – since 1800
- Polyamides, polyesters, polyethylene – since 1930s

Polymer	Application
Poly(methyl methacrylate)	Intraocular lens, bone cement, dentures
Poly (ethylene terephthalate)	Vascular graft
Poly (dimethylsiloxane)	Breast prostheses
Poly (tetraflouroethylene)	Vascular graft, facial prostheses
Polyethylene	Hip joint replacement
Polyurethane	Facial prostheses, blood/device interfaces

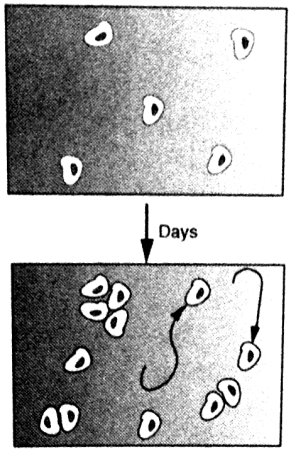
http://biomed.tamu.edu/biomaterials/bmen482/7_Biodegradable_Polymers_in_TE_and_DD.pdf

Biomaterial advances (cont.)

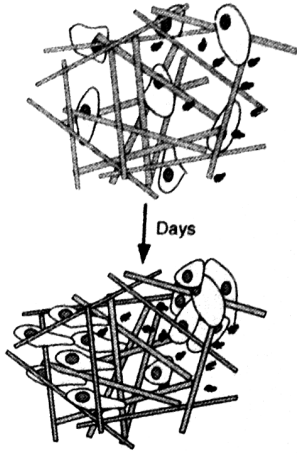
- **Development**



Adhesion
spreading
function



Growth
motility
orientation



Aggregation
orientation

Biomaterial uses

- Artificial hip, heart, skin
- Prosthetics
- Catheters
- Coating pacemaker leads
- Contact lens
- Drug delivery
- Dentures
- Sutures

http://biomed.tamu.edu/biomaterials/bmen482/7_Biodegradable_Polymers_in_TE_and_DD.pdf

Biomaterial example

Polymer	Application
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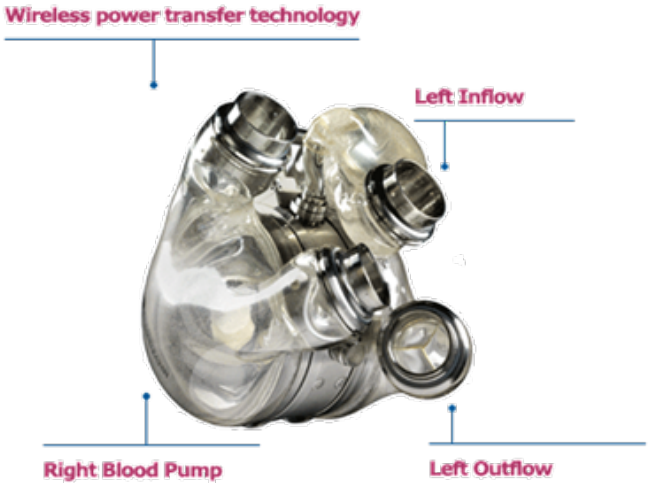
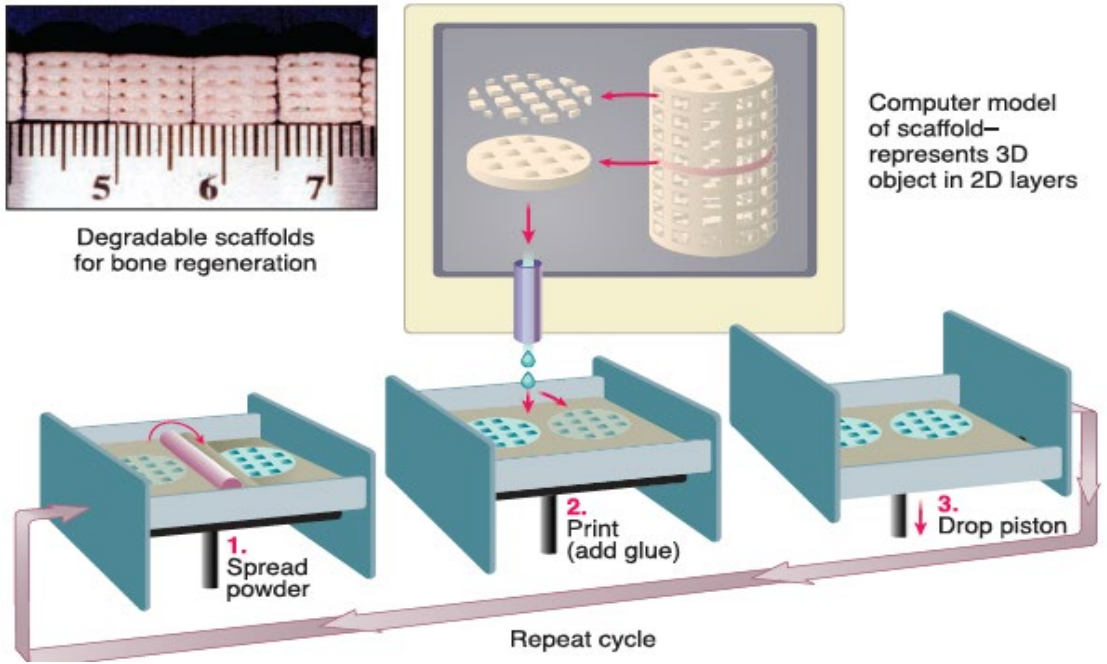


http://biomed.tamu.edu/biomaterials/bmen482/7_Biodegradable_Polymers_in_TE_and_DD.pdf;
http://www.abiomed.com/products/heart-replacement/

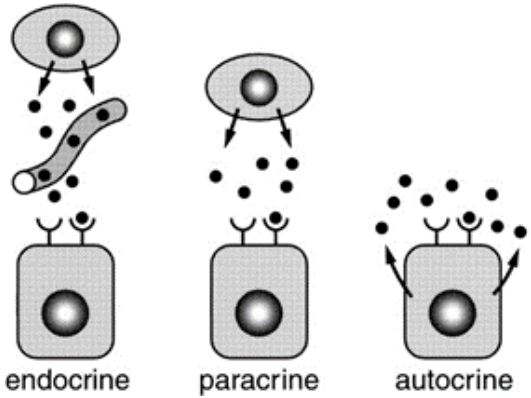
Biomaterial (cont.)

- **3D Printing**



Advances - signals

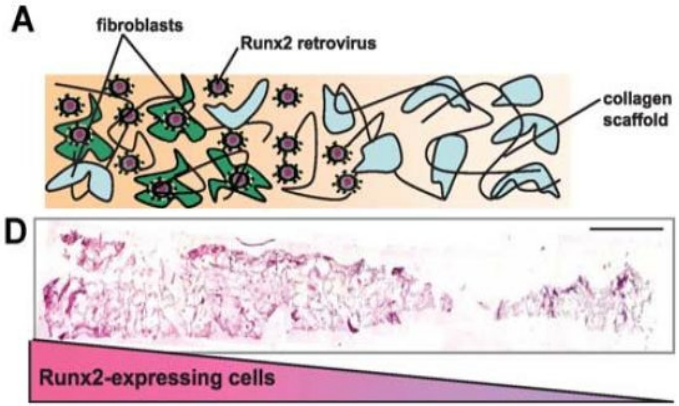
1. Biochemical
   - Growth factors, hormones, etc.
2. Physical
   - Stretch, electrical impulses, pH, etc.



http://alevelnotes.com/Cell-Signalling/131

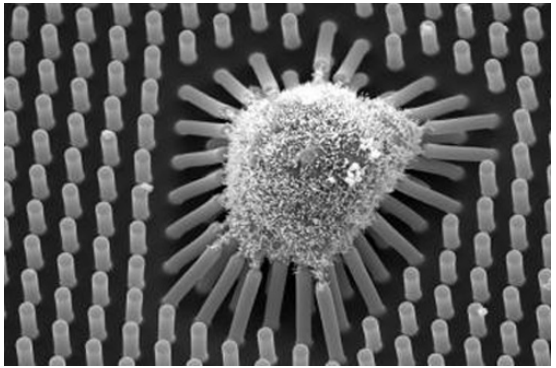
Advances – signals (cont.)

- Bio *chemical*



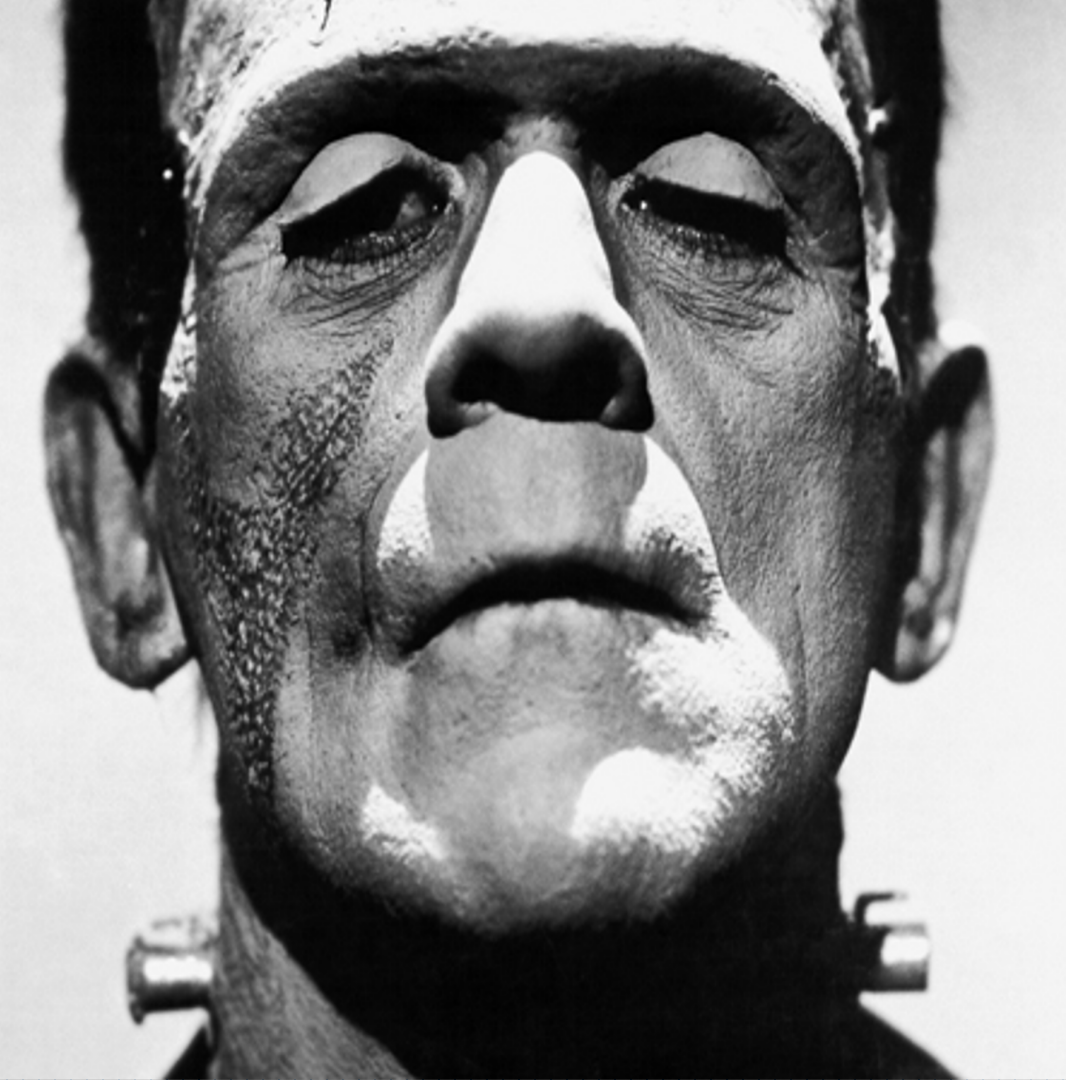
Spatially regulated gene modification

- Bio *mechanical*



Mechanically regulation of stem cell fate

Philips et al 208 Fu et al. 2011

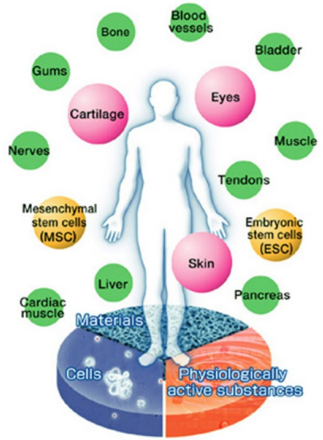


What have we done so far?

- We can outlive our organs
- Our bodies live with organs, cells, and genes of another
- We manipulate protein function, cell function and fate
- Safety? Efficiency?

What have we accomplished?

- 96 case studies for tissue engineering
- 120 case studies for cell engineering



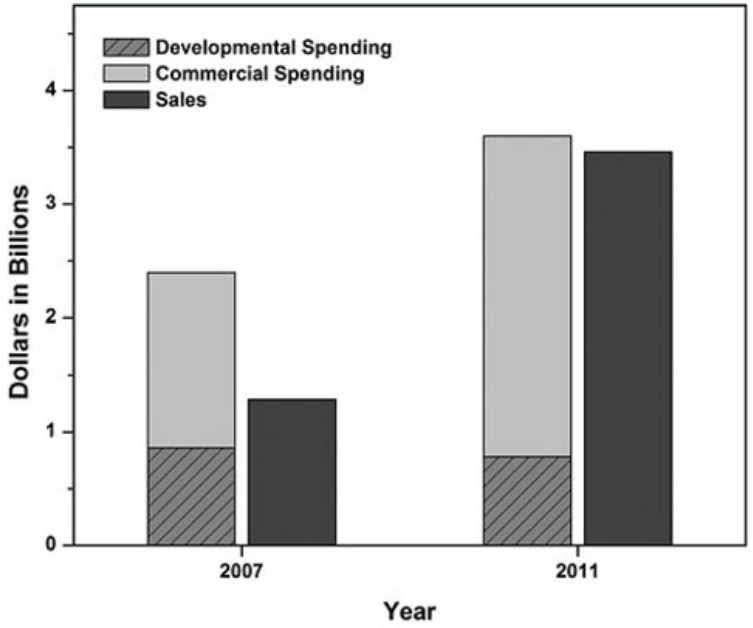
Examples	
Hair follicle regeneration	Rheumatoid arthritis
Spinal fusion	A-V shunt
Bone, cartilage, ligament reconstruction (face, knee, leg..)	Leukemia
Liver regeneration	Parkinson's Disease
Multiple sclerosis	Renal Failure
Diabetic ulcers	Stroke
Respiratory defects	Heart failure
Glaucoma	Brain lesion
Sickle cell anemia	Marfan Syndrome

http://www.jpte.co.jp/english/intro/index.html

What's next?

- Move cell and tissue engineered products out of the lab and into the patient
- Scale it up!

Sales for Commercial Products or Services		
Commercial products (# of companies)	**2011 sales (in millions)**	**%**
Orthopedic (19)	$1713	50
Wound healing (15)	$738	21
Multiple (16)	$554	16
Stem cell banking	$312	9
Other (5)	$144	4
Total	$3461	



Langer et al, 2013

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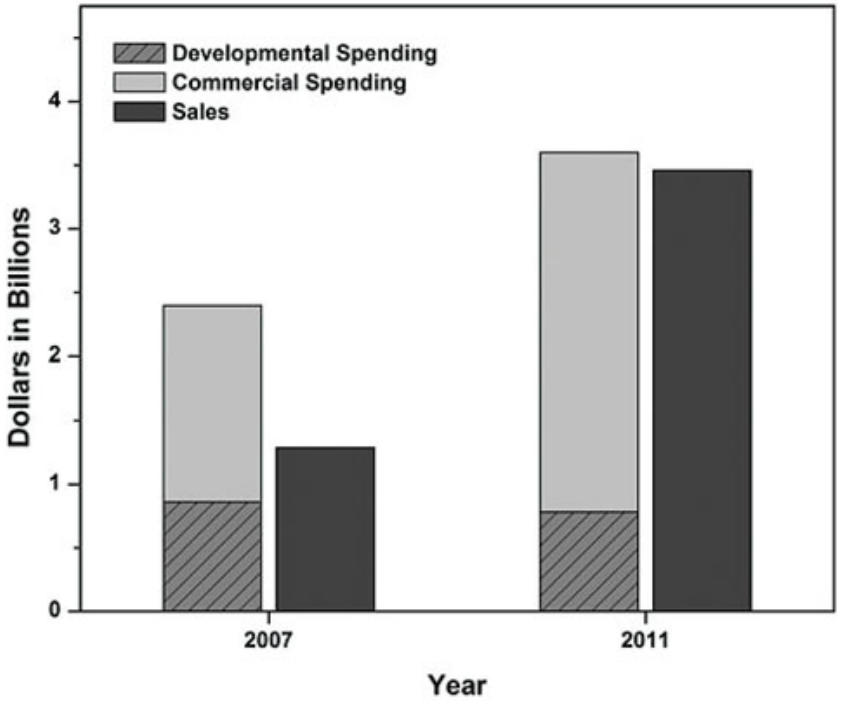
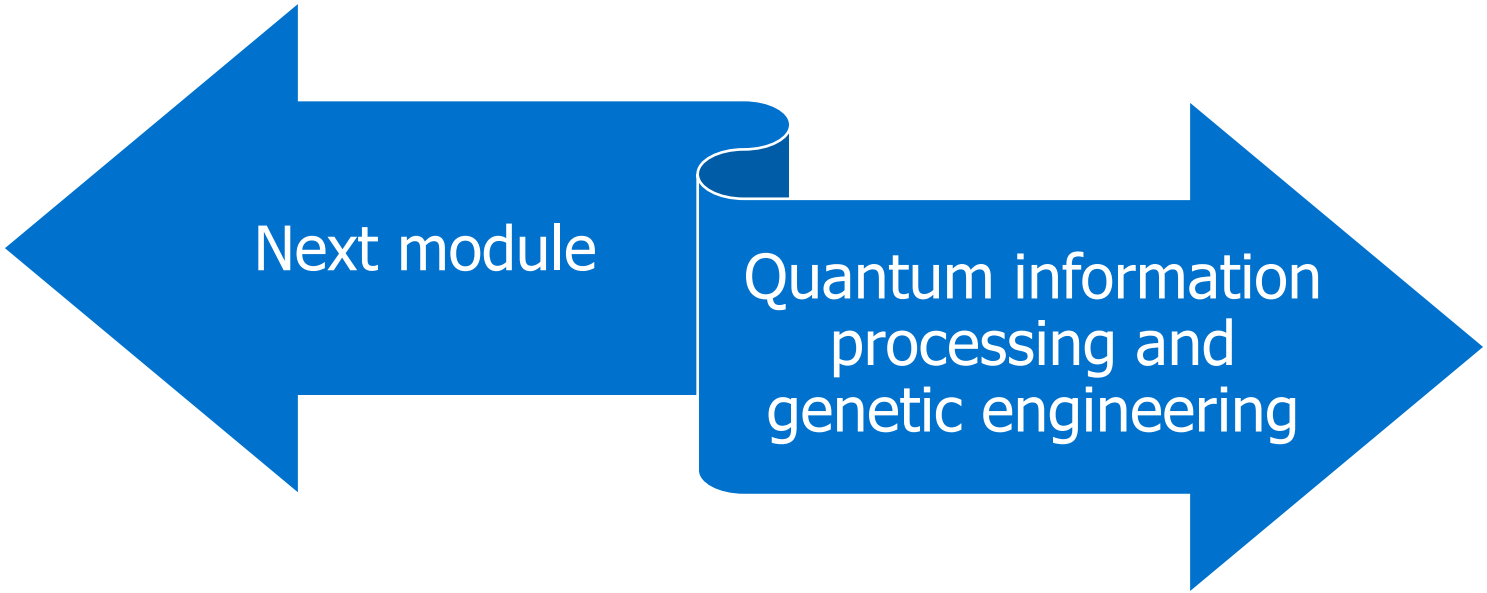


Langer et al, 2013


Next module
Quantum information processing and genetic engineering