BME 42-620 Engineering Molecular Cell Biology

Lecture 01: Course Overview; Universal Properties of Cells

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Outline

- A definition of cell biology
- Course overview
- Learning objectives
- Course outlook
- Course organization
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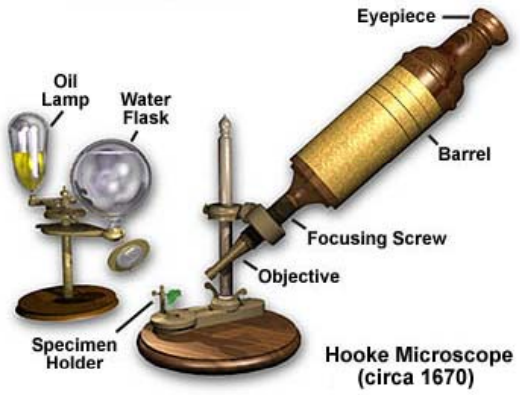
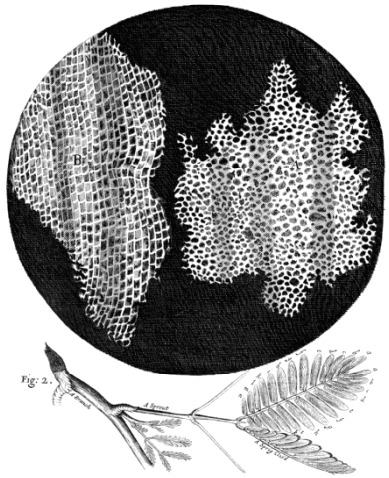
The Cell Theory: a Historical Perspective

- Cells were first discovered by Robert Hooke in 1665 using light microscopy. (*Micrographia*, 1665)
- The cell theory was proposed around the middle of 1800s. (Theodore Schwann, Matthias Schleiden, Rudolf Virchow)
- Some basic elements of the cell theory

  - Cells are basic units of structure, function, and organization of living organisms.
  - Cells come from pre-existing cells through division.
  - Cells store hereditary information that is passed from generation to generation in cell division.





1. Molecular expressions: microscopy world http://micro.magnet.fsu.edu/index.html
2. P. Mazzarello, A unified concept: the history of cell theory, *Nat. Cell. Biol.* 1:E13-E15, 1999.

A Definition of Cell Biology

- The meaning of cell biology is strongly dependent on the technology available at the time.

- Cell biology is an academic discipline that studies *at the molecular level* structure and function of cells.

- "Today, cell biology is a blend of advanced cytology, molecular biology, genetics, biochemistry, computation, and, engineering."

  - From T. Misteli, "The changing world of modern cell biology," J. Cell Biology, vol. 184, pp. 11-12, 2009.

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Course Overview (I)

- Cell biology courses at CMU
  - 03-240 Cell biology
  - 03-741 Advanced cell biology
  - 03-746 Core course in cell biology
  - 42-620 Engineering molecular cell biology

- Why another cell biology course?

- Prerequisites of a traditional cell biology course
  - Organic chemistry, biochemistry, molecular biology

- Perspectives of a traditional cell biology course
  - Emphasis is often placed on structure, biochemistry, molecular biology
  - Often qualitative rather than quantitative
  - Science rather than engineering

Course Overview (II)

- Cell biology training is essential to engineering students work on biomedical applications.
  - Biomolecules, biomaterials, biological processes
  - Biomedical devices

- Cells are extraordinary engineering systems at the micro- and nano-scale.

- Cell biology today offers many exciting and important applications for engineering strategies and techniques.

- Development of biology today has been making fundamental impacts on individuals and societies.

Course Overview (III)

- Prospective students for this course
  - Engineering students interested in biology
  - Biology students interested in quantitative and engineering perspectives of cell biology
  - Students who are curious about cells
- Expected background
  - ODE level mathematics
  - Computer programming (MATLAB will be covered in class)

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Learning Objectives

- Objective I: to understand basic concepts, facts, and principles of cell biology at the molecular level.
- Objective II: to develop basic skills to read current cell biology literature and to communicate biological information.
- Objective III: to develop basic understanding of the integration of engineering with biology.
- Overall, to start developing an in-depth appreciation of living organisms and biology.

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Course Outlook (I)

- This is a graduate level course whose main goal is to provide classroom training of molecular cell biology.
- A main emphasis is placed on reading literature and communicating biological information.
- We will organize the class into multiple groups for various class activities.
- Integration of engineering strategies and techniques with cell biology is an active research area.
  - Research publications will be used frequently in this class.

Course Outlook (II)

- Molecular cell biology is an experimental science.
- Biological systems are often highly complex. Molecular details are important.
- Much of the text and papers reflects our current understanding.
  - Cell biology is a scientific discipline in rapid development.
- Engineering and cell biology communities have different cultures.

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Course Organization (I)

- Web page
  http://www.andrew.cmu.edu/course/42-620/

- Instructor information
  Office: Mellon Institute 403
  Email: geyang@andrew.cmu.edu
  Phone: 412-268-3186
  Web: www.andrew.cmu.edu/user/geyang
  Office hours: Friday 1-2PM in office or by appointment

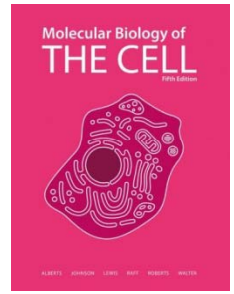
  Teaching Assistant: Yiyi Yu
  Office: Mellon Institute 401
  Email: yiyiy@andrew.cmu.edu

- Format
  - Lectures + literature reading & review
  - Assignments: projects + reading reports + problem sets

Course Organization (II)

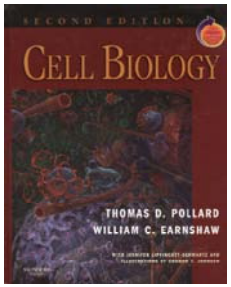
- Textbook

  - Molecular Biology of the Cell, 5/e, Bruce Alberts et al, Garland Science, 2007.



- The following reference is highly recommended.

  - Cell Biology 2/e, by Thomas Pollard & William Earnshaw, Saunders/Elsevier,2008



- Comments on the textbook

Course Organization (III)

- Lecture slides
  - All slides are posted on the class web site.
- There are many excellent online resources
  - Online seminars at http://www.ibioseminars.org/
  - Education resources at http://www.hhmi.org/coolscience/
  - Open courses

Assignments, Exams & Grading

Assignment	% of total grade
3 projects	30%
6-8 reading reports + problem sets	40%
2 exams/presentations	30% (15%+15%)

- Some minor adjustment may be made to this partition of grades.
- Exams are open-book.
- MATLAB basics will be covered in class.
- Active participation in class activities is factored into grades.
- Carnegie Mellon grading policy on undergraduate students taking a graduate level course

  http://www.cmu.edu/policies/documents/Grades.html

Outline

- What is cell biology?
- Course overview
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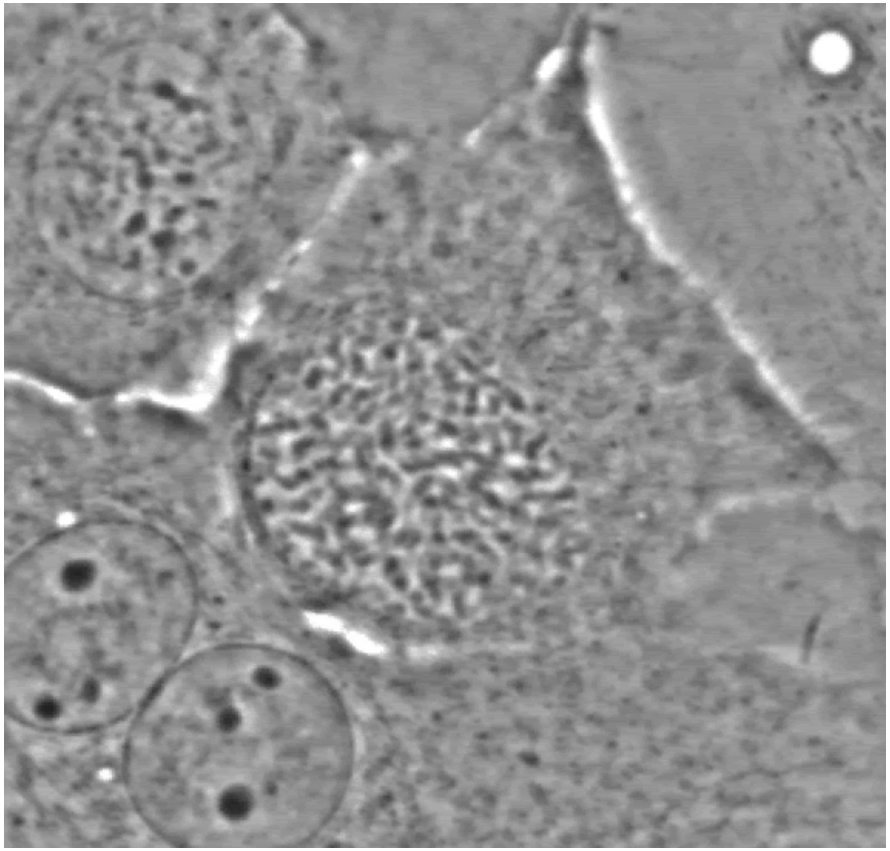
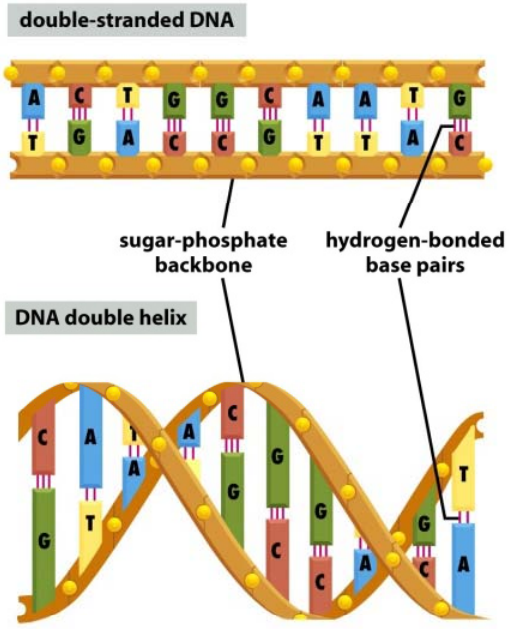
Cells Proliferate Through Division

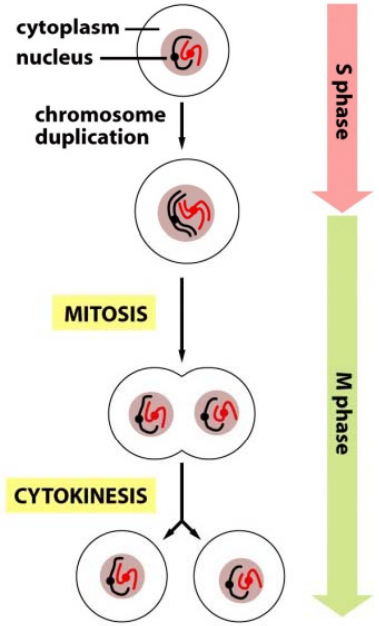
- In an adult human, ~25 million cell divisions per second.
- How do we make an engineering system?



Cells Transfer Hereditary Information in Division

- Hereditary information is stored in DNA and is transferred from the mother cell to daughter cells.

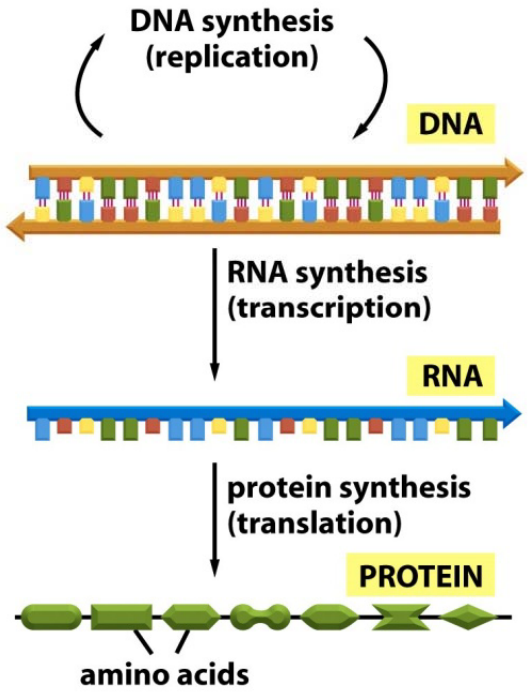




- In each human cell, ~3.2 billion nucleotide pairs get copied.
- All the cells in a living organism have the same genetic information.
- Does engineering systems contain instructions of self-replication?

Proteins are Synthesized in Regulated Gene Expression

- DNA is transcribed into mRNA, which is then used as a template for protein synthesis.
- Gene expression involves multiple closely coupled and tightly regulated steps.
- How do we modify an engineering system while it is functioning?

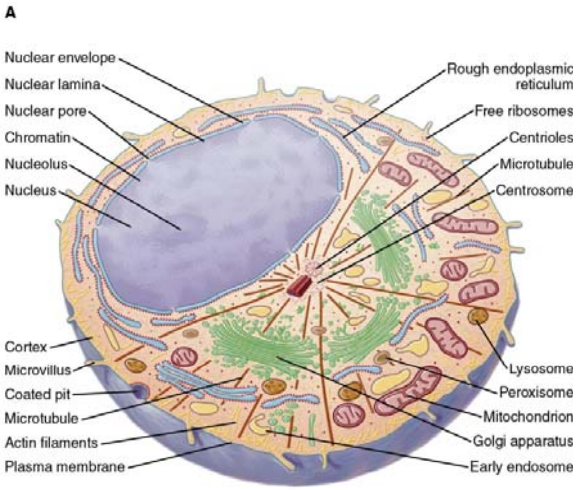


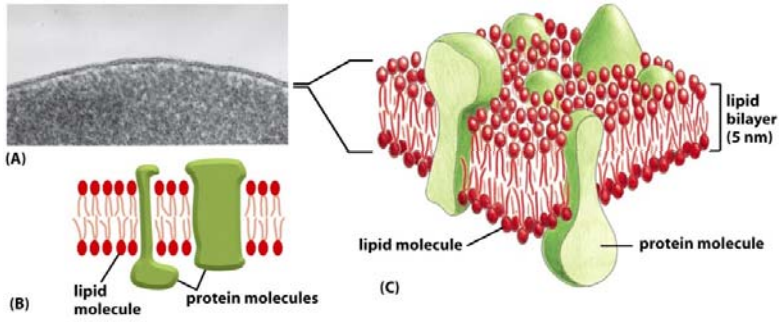
Central dogma of molecular biology

Cells are Structurally Organized

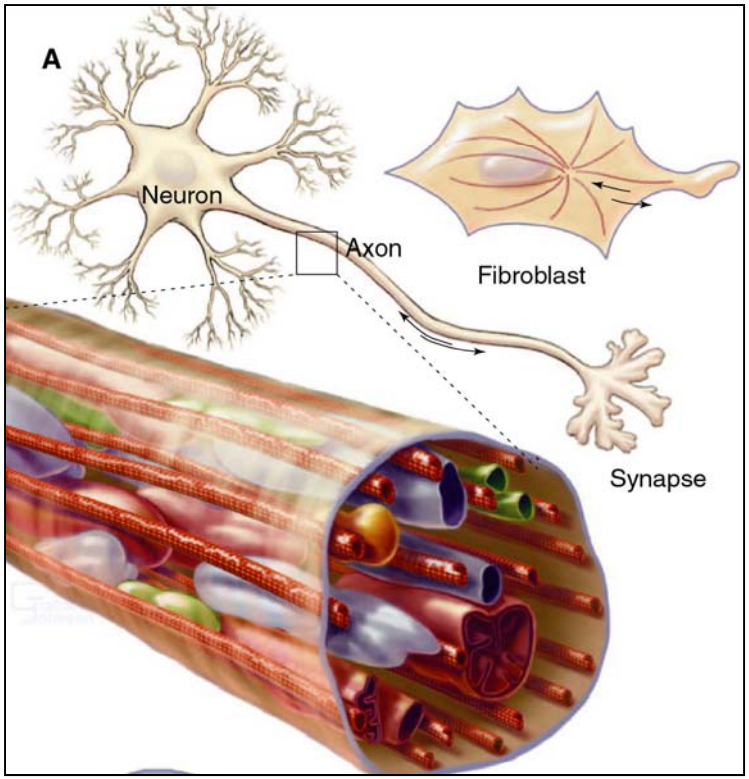
- Cells carry out a wide variety of biochemical reactions to produce, use, degrade, and recycle materials.

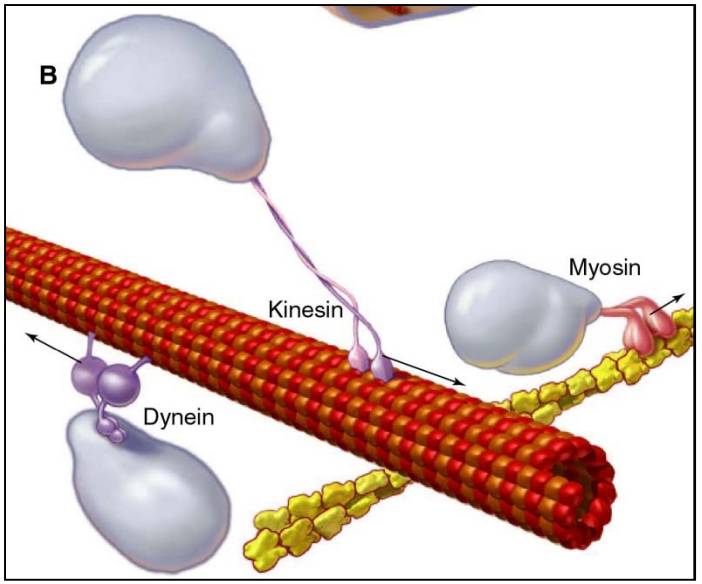
- For functional organization and interference avoidance, cells use a variety of strategies, especially by forming membranous organelles.





Cells Utilize an Internal Transport System



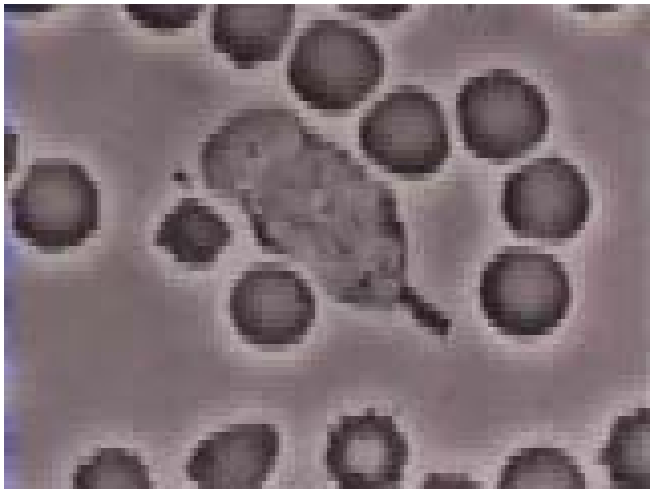


Vesicle transport in *Drosophila* nerve axons

Cells Actively Interact with Environment

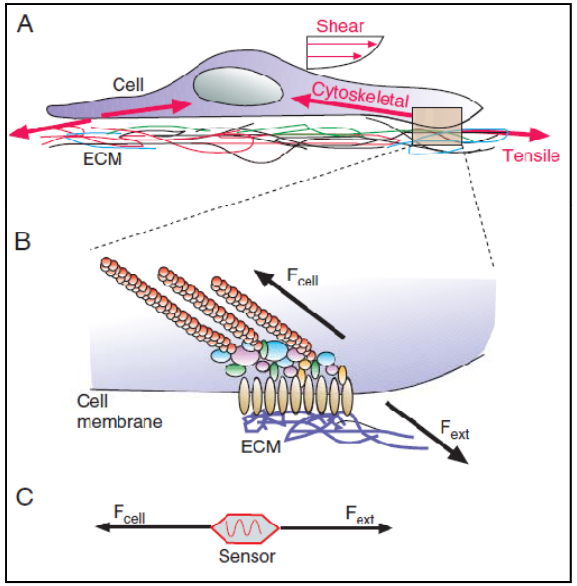
- Cells are active and autonomous molecular machines.
  - Cells acquire and utilize material and energy
  - Cells sense its environment
  - Cells make decisions
  - Cells engage in mechanical activities

Single dictyostelium cell exposed to cAMP gradient. *Devreotes Lab, Johns Hopkins*

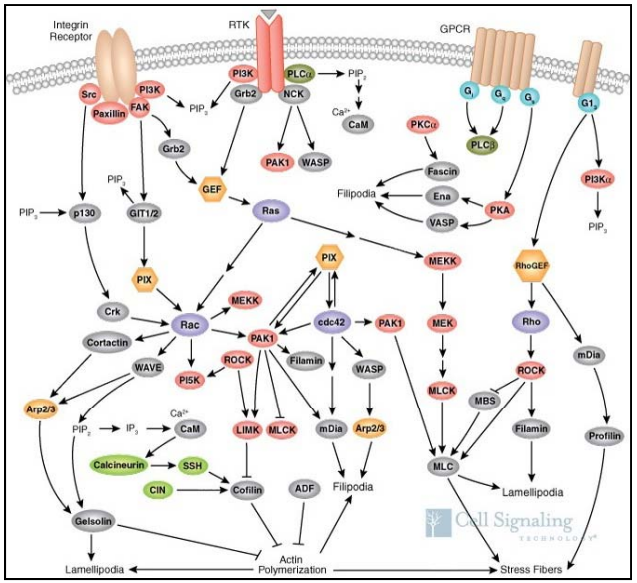


A neutrophil chasing a bacterium. *Devreotes Lab, Johns Hopkins*

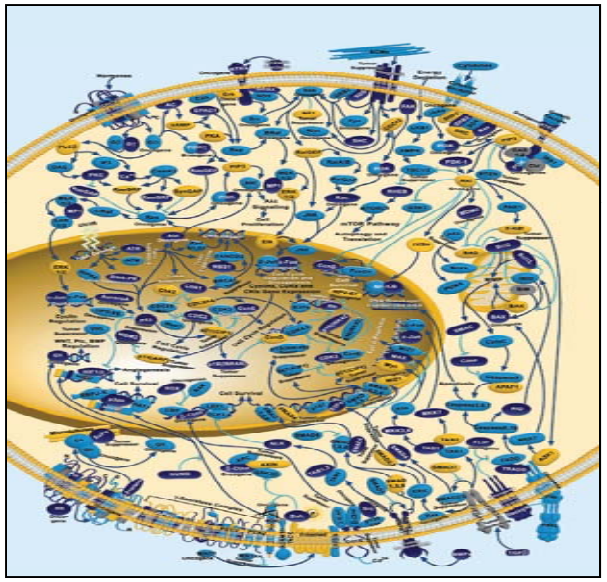
Cells Process Information Using Complex Signaling Pathways



Environment sensing



Actin regulation pathway



Human cancer pathways

Impact of Genomics on Cell Biology

- We now have a rather complete list of the molecular components, the challenge is to understand how they interact and function?

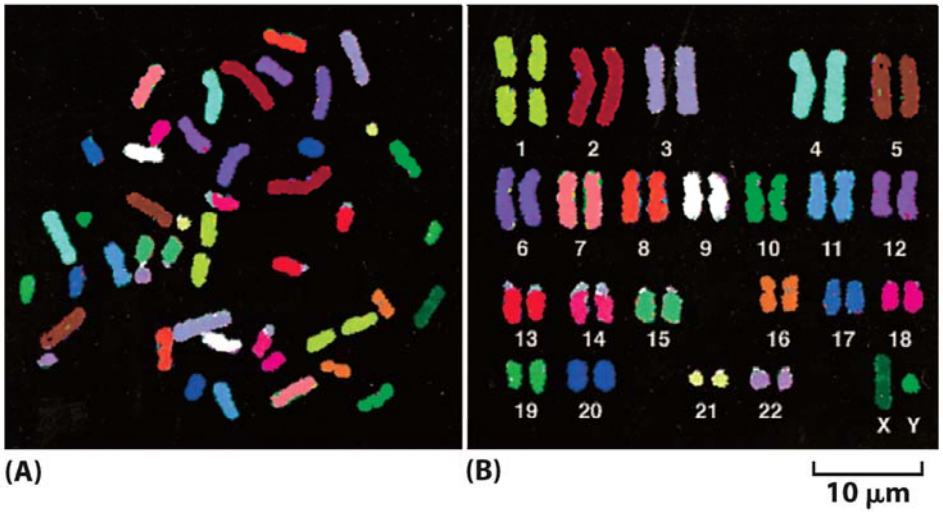


Table 4–1 Some Vital Statistics for the Human Genome

	HUMAN GENOME
DNA length	3.2×10^9 nucleotide pairs*
Number of genes	approximately 25,000
Largest gene	2.4×10^6 nucleotide pairs
Mean gene size	27,000 nucleotide pairs
Smallest number of exons per gene	1
Largest number of exons per gene	178
Mean number of exons per gene	10.4
Largest exon size	17,106 nucleotide pairs
Mean exon size	145 nucleotide pairs
Number of pseudogenes**	more than 20,000
Percentage of DNA sequence in exons (protein coding sequences)	1.5%
Percentage of DNA in other highly conserved sequences***	3.5%
Percentage of DNA in high-copy repetitive elements	approximately 50%

- Initial sequencing and analysis of the human genome, *Nature*, 409:860-921, 2001.
- The sequence of the human genome, *Science*, 291:1304-1351, 2001.

Examples of Complex Engineering Systems

BOEING

747 Celebrating the Past, Building the Future

Boeing 747-400, by the Numbers

- 150: the length, in feet, of the 747 economy section -- long enough to contain the Wright brothers' first flight at Kitty Hawk, N.C. (45 meters)
- 171: the length, in miles, of wiring. (274 kilometers)
- 5,156: the area, in square feet, of the 747 postage stamp on the Everett, Wash., factory doors. (479.5 square meters)
- 5,600: the area, in square feet, of the wing -- large enough to hold 45 medium-sized automobiles. (521.9 square meters)
- 31,285: the volume, in cubic feet, of the passenger interior -- equivalent to more than three 1,500 square-foot houses. (876 cubic meters)
- 50,000: the number of in-flight service items used for a typical international flight.
- 147,000: the weight, in pounds, of high-strength aluminum. (66,150 kilograms)
- Six million: the number of parts, half of which are fasteners.
- 472 million: the volume, in cubic feet, of the largest building in the world -- where the 747 is assembled. (13.3 million cubic meters)

The space shuttle is one of the most complex machines ever devised. Its main elements – the orbiter, Space Shuttle Main Engines (SSME), external tank (ET), and Solid Rocket Boosters (SRB) – are assembled from more than 2.5 million parts, 230 miles of wire, 1,060 valves, and 1,440 circuit breakers. Weighing approximately 4.5 million-pounds at launch, the space shuttle accelerates to an orbital velocity of 17,500 miles per hour – 25 times faster than the speed of sound – in just over eight minutes. Once on orbit, the orbiter must

Cells vs Human-Made Engineering Systems

- Structure
  - Cell structure is highly dynamic and adaptive.
- Function
  - Cells are functionally autonomous.
- Scale
  - Microscale to nanoscale
- Complexity
  - Substantially higher than human-made systems
- Design
  - Cell designs are determined by evolution in addition to physics, chemistry, and engineering.

Integrating Engineering with Biology (I)

- Historical perspectives
  - Discovery of cells: 1665
  - Discovery of DNA structure: 1953 A Structure for Deoxyribose Nucleic Acid, Watson J. and Crick F., *Nature* 171, 737 (1953)
  - First raw draft of human genome: 2000

- Advances in physics and chemistry were critical to the development of molecular biology.
  - Francis Crick, Max Delbruck

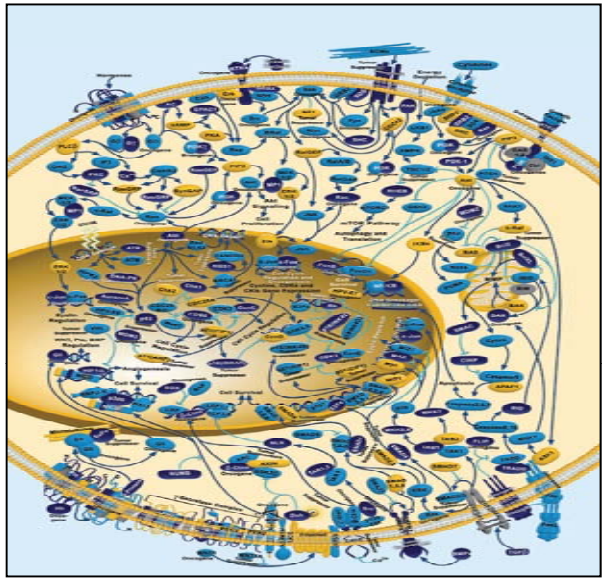
- Integration of engineering with physics was key to the 20th century innovation revolution.

- Integrating engineering with biology is likely key to innovation revoluaton of this century.

  - S. Hockfield, The next innovation revolution, 323-1147, *Science*, 2009.

Integrating Engineering with Biology (II)

- Cell biology relies on engineering strategies and technologies for understanding and control of complex cellular processes.
- Understanding of cellular processes will drive the development of engineering techniques, especially micro- and nano-technology.
- System-level understanding of cell systems → systems biology
- Computational analysis of cell systems → computational biology
- Design and build cell systems
  → synthetic biology



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Required Reading

- MBoC 5/e chapter 1

Questions?