Bioimage Informatics

BME42-731/ECE18-795/CB02-740, Spring 2012

Lecture 1 Introduction

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Outline

- Introduction to biological imaging
- Overview of bioimage informatics
- Some historical perspectives
- Course objectives
- Course syllabus
- Discussions

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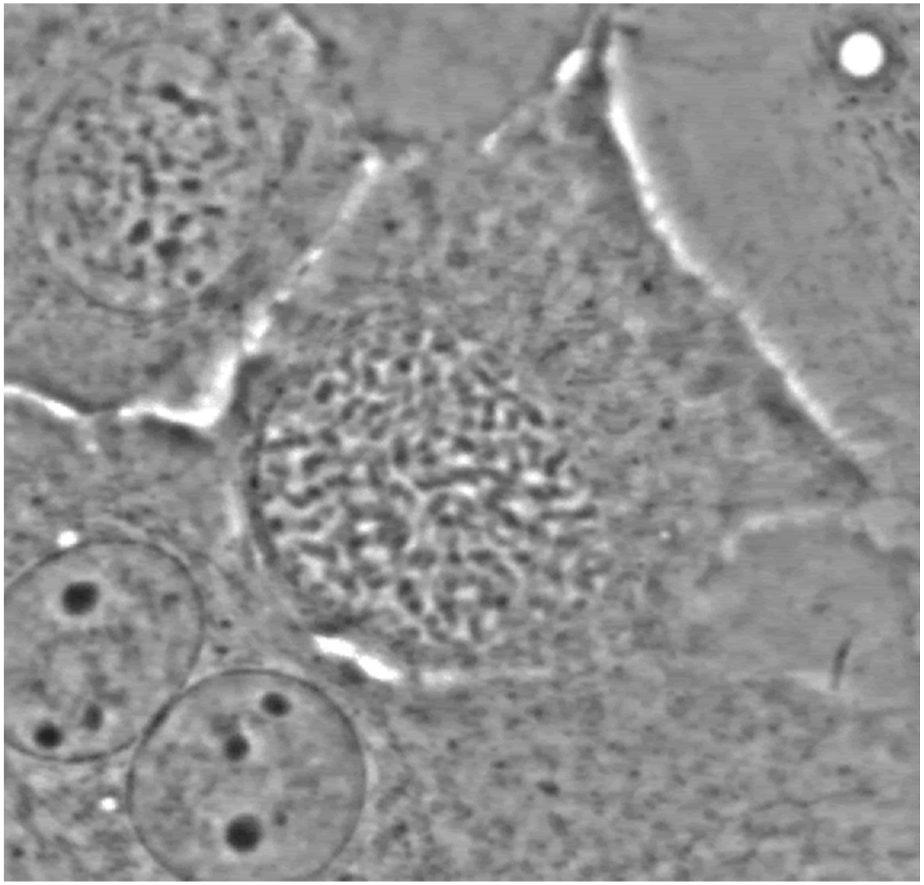
Introduction to Biological Imaging: Phase Contrast (I)



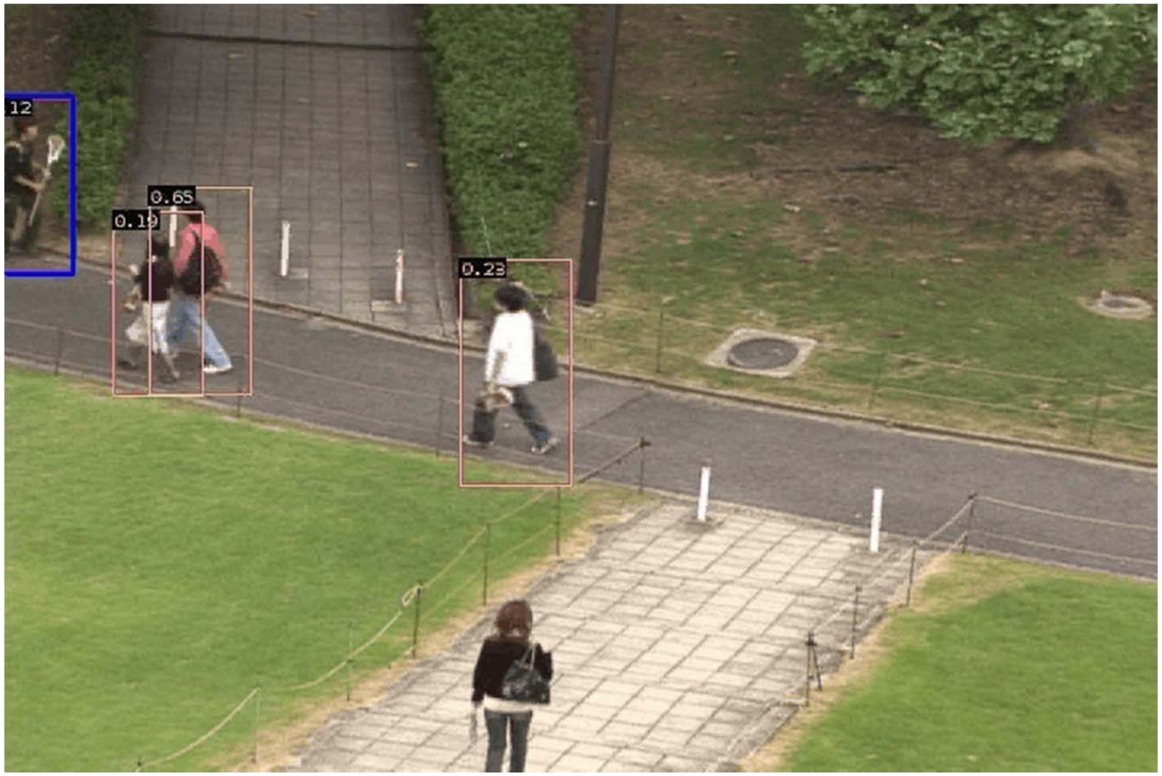
Introduction to Biological Imaging: Phase Contrast (II)

- A main goal of the biologists is to measure/quantify this process.
  - In an adult human, ~25 million cell divisions occur every second.

- How do we do it?
  - For example, we can track the chromosome.
  - But this may be quite challenging.
    - e.g. noisy background; highly dynamic events
    - e.g. cell drift

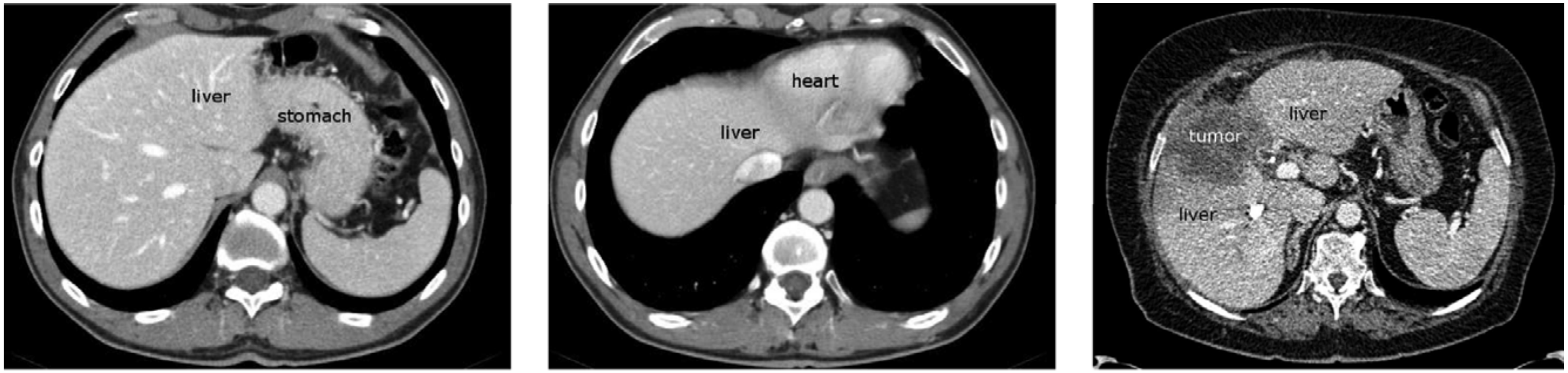
- Where do we get the techniques?
  - We can borrow techniques from computer vision and medical image analysis.
  - Some customization is likely needed (e.g. halo).

Example: An Application of Computer Vision Techniques

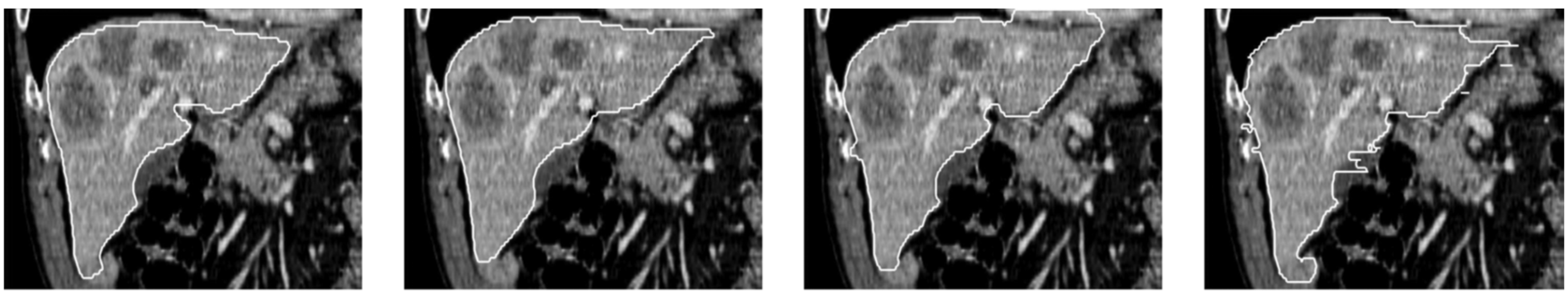


Kanade lab, CMU

Example: An Application of Medical Image Analysis Techniques



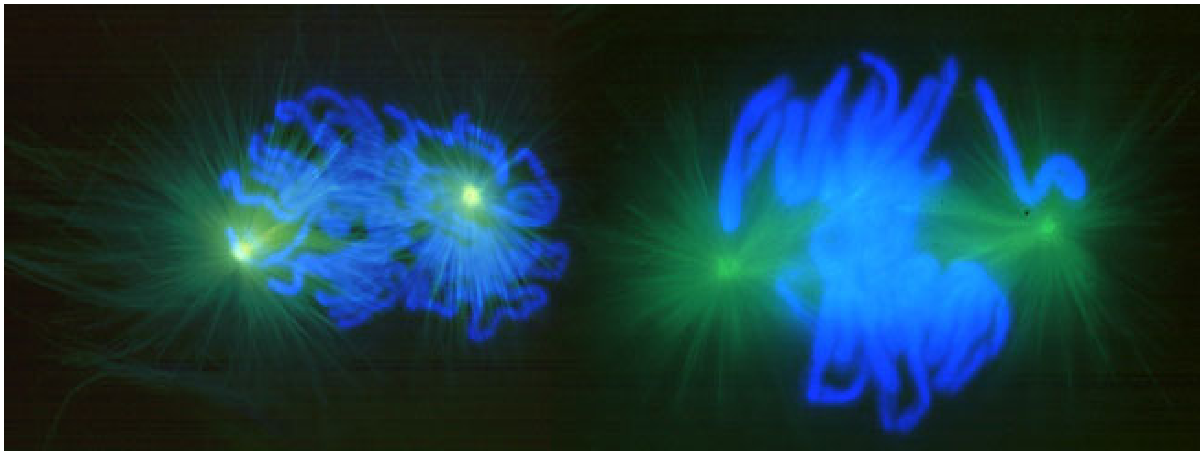
(a) (b) (c)

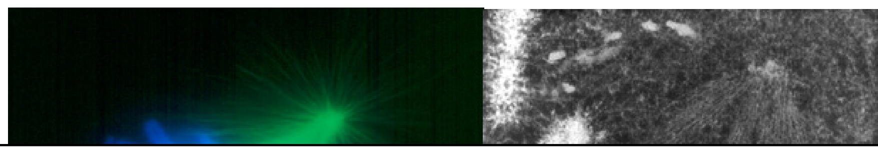


(a) (b) (c) (d)

Heimann et al, Comparison and Evaluation of Methods for Liver Segmentation From CT Datasets, *IEEE Trans. Medical Imaging*, vol. 28, no. 8, 1251-1265, 2009.

Fluorescence Imaging of Chromosomes





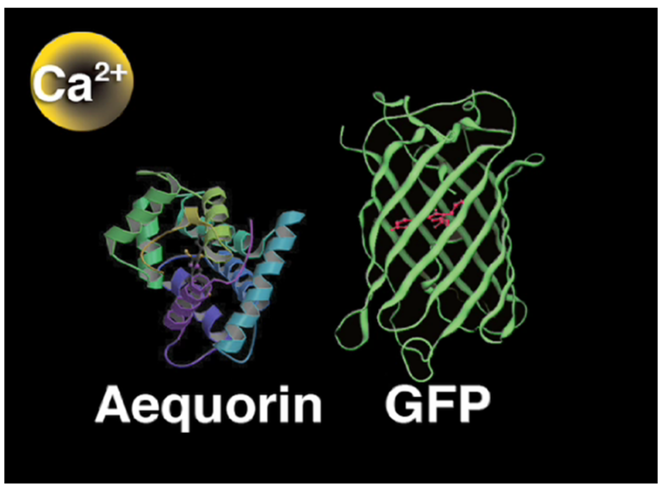
1) To analyze biological image data, we need to have at least some knowledge of the image formation process.

2) It is often feasible to significantly simplify image analysis tasks by choosing/developing a suitable imaging approach.

Rieder Lab, Wadsworth Center
http://www.wadsworth.org/bms/SCBlinks/web_mit2/res_mit.htm

Discovery of Green Fluorescence Protein

Jellyfish: *Aequorea victoria*



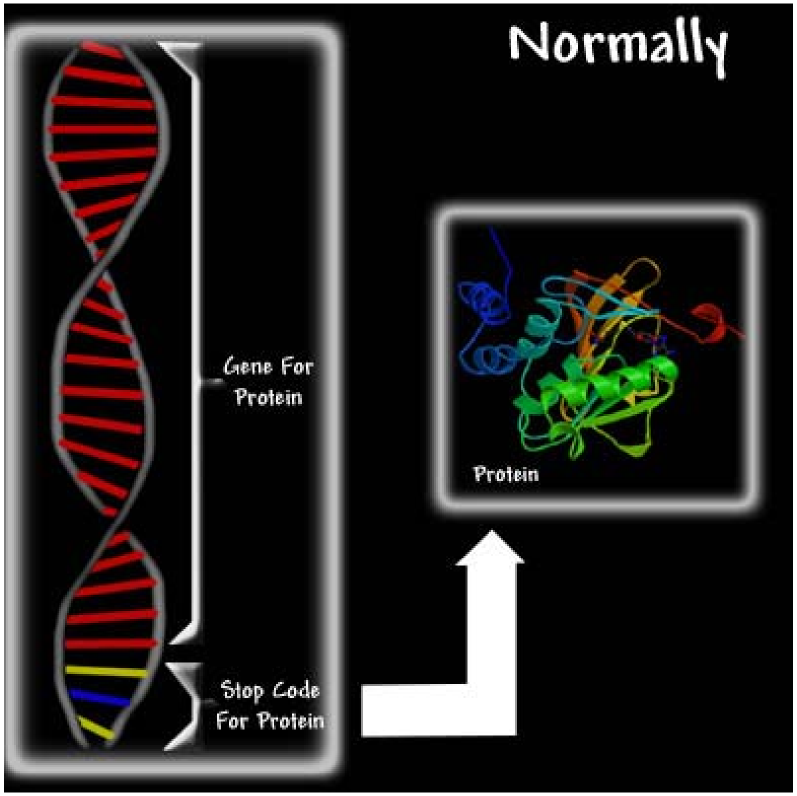
http://gfp.conncoll.edu/GFP-1.htm

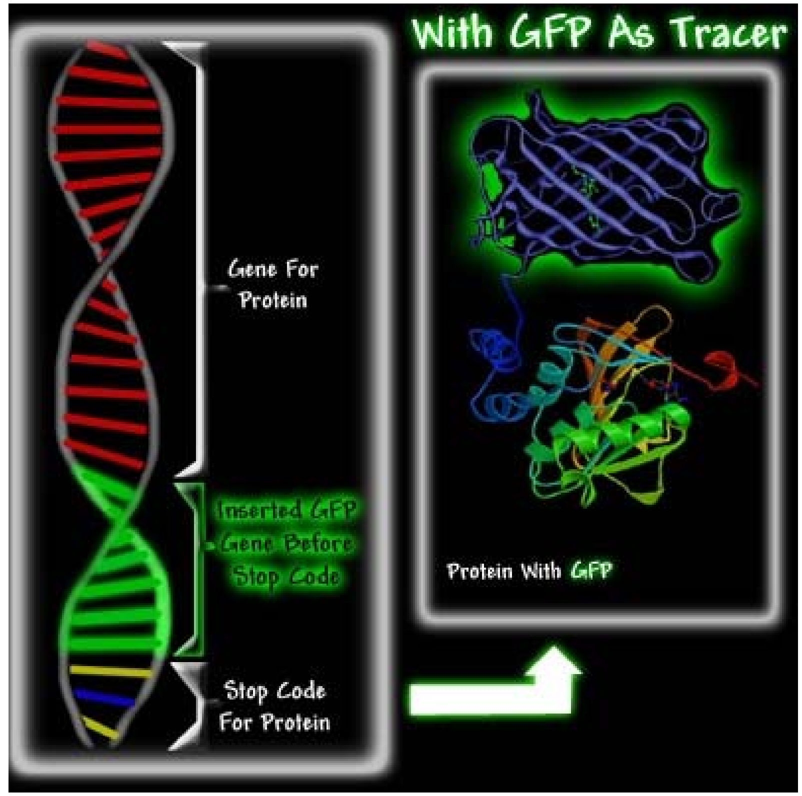
The Nobel Prize in Chemistry 2008

"for the discovery and development of the green fluorescent protein, GFP"

Osamu Shimomura	Martin Chalfie	Roger Y. Tsien
1/3 of the prize	1/3 of the prize	1/3 of the prize
USA	USA	USA
Marine Biological Laboratory (MBL) Woods Hole, MA, USA; Boston University Medical School Massachusetts, MA, USA	Columbia University New York, NY, USA	University of California San Diego, CA, USA; Howard Hughes Medical Institute
b. 1928 (in Kyoto, Japan)	b. 1947	b. 1952

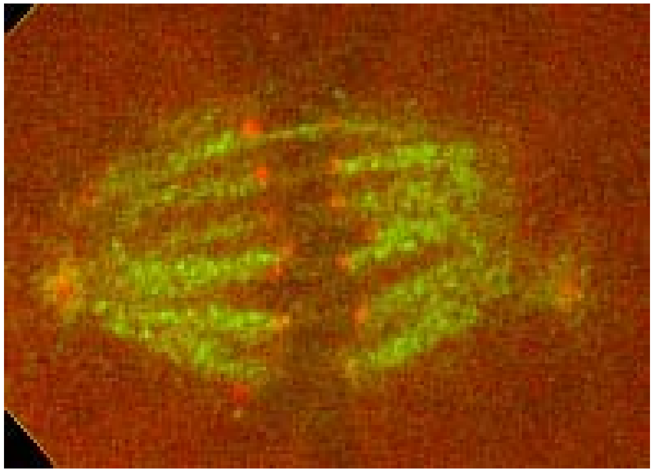
Labeling a Protein Using GFP





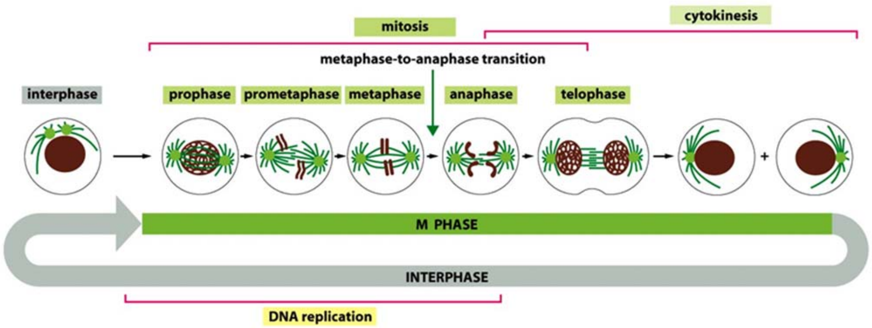
http://gfp.conncoll.edu/GFP-1.htm

Mitotic Spindle Visualized by Fluorescence Imaging



mitotic spindle

What has you noticed from this movie?



Biological Bioimaging

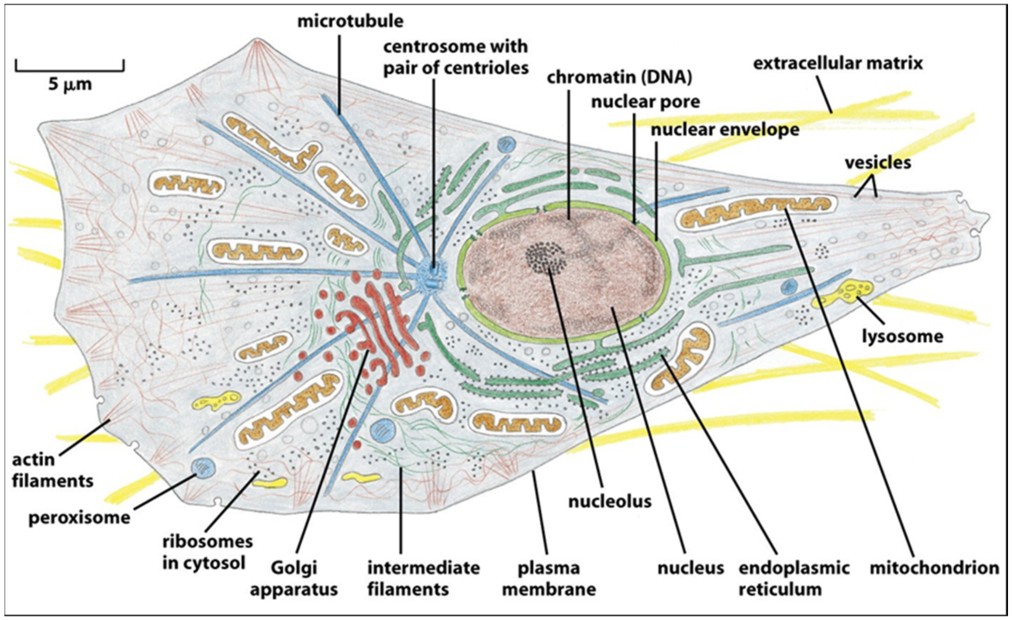
- Biological imaging (bioimaging) refers to the technology and/or process of visualizing biological processes, usually at the cellular and molecular level using microscopes and molecular probes.

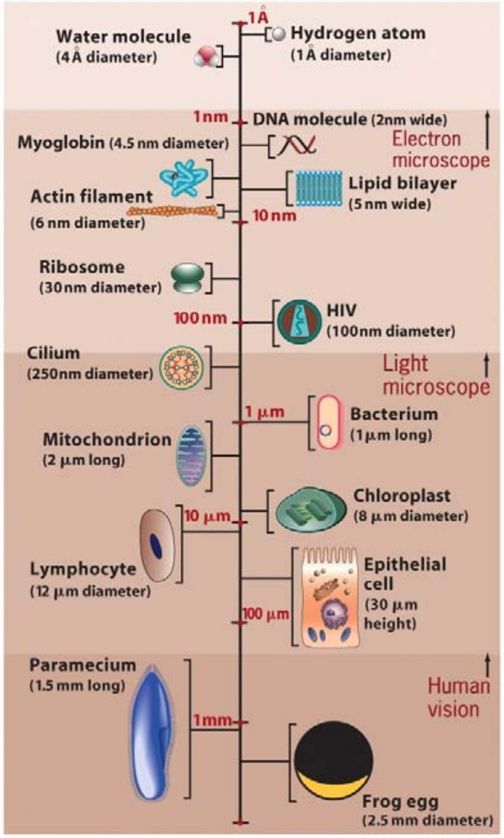
- Bioimaging makes it possible to follow spatiotemporal molecular activities with high specificity, high sensitivity, and high resolution.

- The basic paradigm is to label molecules of interests and then follow the labels.

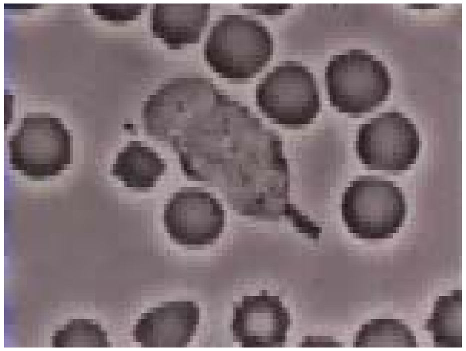
Light Microscopy vs Electron Microscopy

- Above 200nm, conventional light microscopy.
- Below 200nm, electron microscopy; assay must be fixed in preparation.

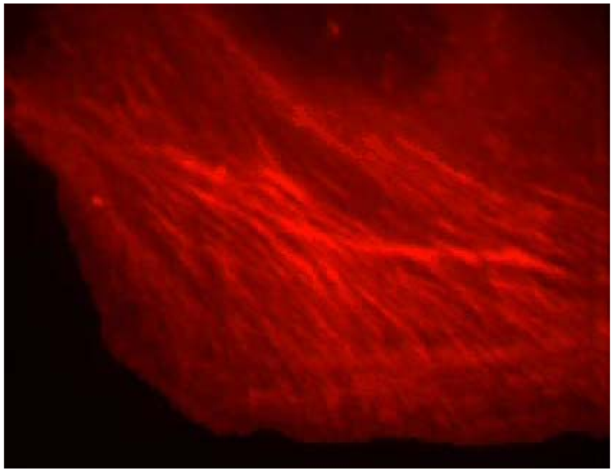




Example: Actin Network at Cell Leading Edge

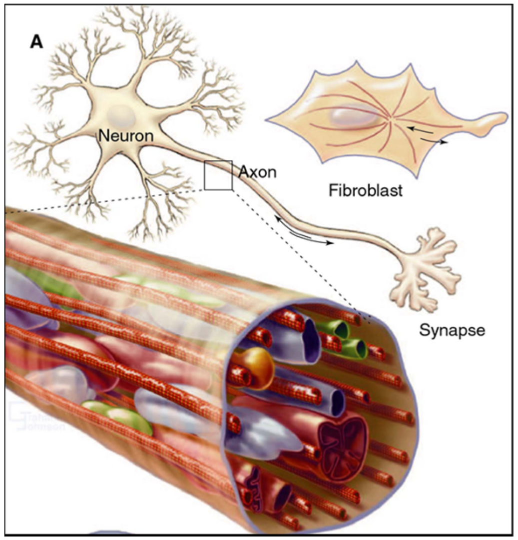


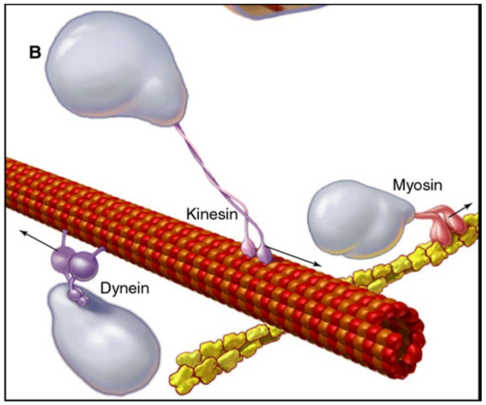
A neutrophil chasing a bacterium. ***Devreotes Lab, Johns Hopkins U.***

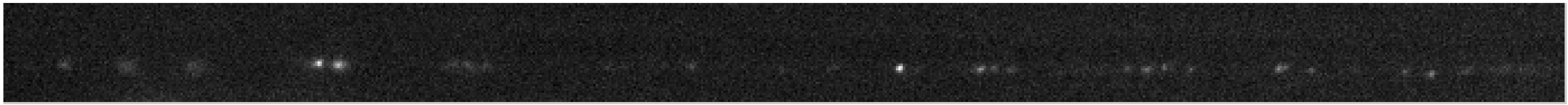


actin network

Example: Axonal Cargo Transport







Images must be transformed into <u>quantitative measurements</u>.

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What is Bioimage Informatics (I)

- The main goal of bioimage informatics is to use computational methods to analyze and understand images of biological processes.

- Bioimage informatics is often considered as a branch of bioinformatics and/or computational biology.

- Key components of bioimage informatics
  - low-level image analysis (e.g. feature detection)
  - high-level information extraction (e.g. pattern recognition)
  - image data management (database)
  - image visualization (graphics)

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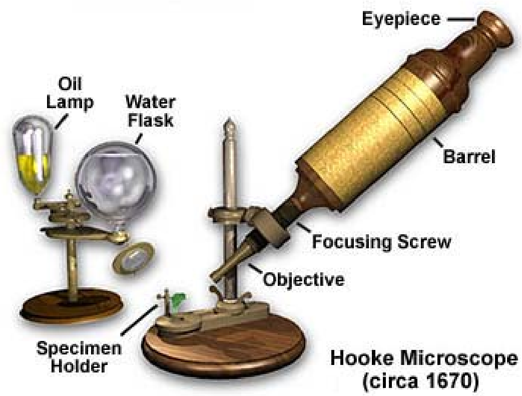
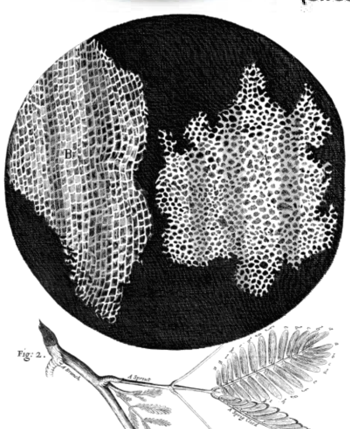
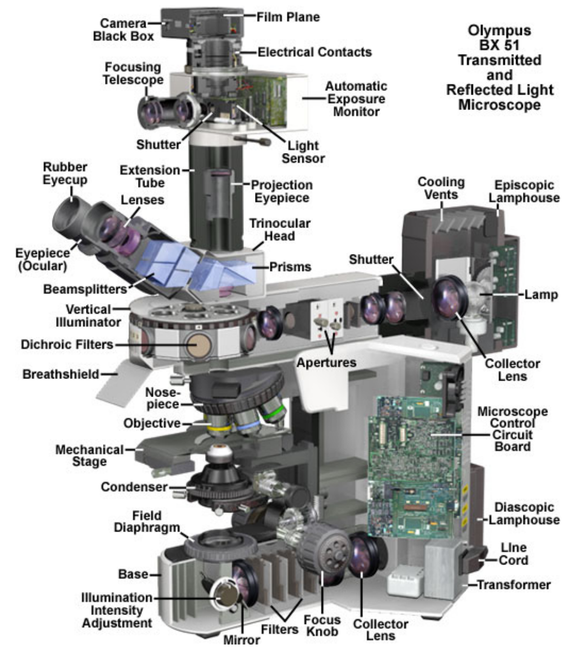
Development of Microscopy Techniques

- Microscope was invented more than 300 years ago.





http://micro.magnet.fsu.edu/index.html
Molecular expressions: microscopy world



Some Historical Perspectives (I)

- Digital image processing started to become widely applied to bioimage analysis in early 1980s.
  - Shinya Inoue pioneered the use of video devices and image processing in microscopy.

- Computational image analysis can improve image quality.

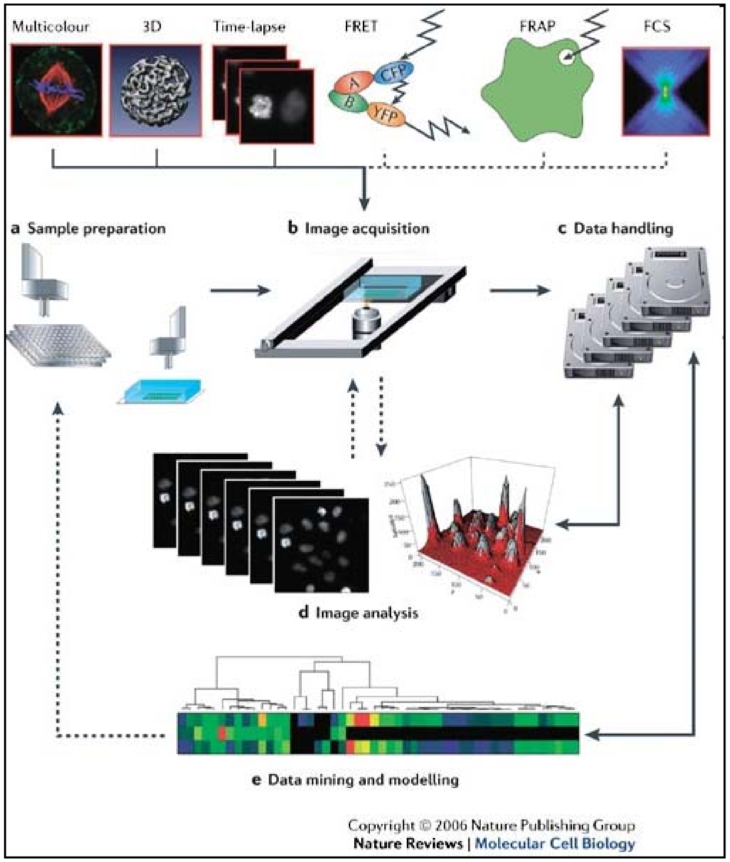
- Computational image analysis is essential to <u>understand</u> images.

Shinya Inoue,
Marine Biology Lab, Woods Hole, MA

Some Historical Perspectives (II)

- Several critical developments in contemporary biology fundamentally changes the nature of bioimage analysis and lead to the origination of bioimage informatics
  - Genomics & proteomics; bioinformatics
  - System biology
  - High throughput screening

- Main challenges
  - Complex image data
  - Very high data volume
  - Complex events



Pepperkok & Ellenberg, *Nat. Rev. Mol. Cell Biol*., 7:690-696, 2006

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Course Objectives

- Aim I: To understand fundamentals of biological imaging techniques, especially fluorescence imaging techniques.
- Aim 2: To understand basic concepts and principles of bioimage informatics.
- Aim 3: To be able to use basic computational image analysis techniques to analyze biological image data.
- Aim 4: To understand basic statistical analysis and informatics techniques that are commonly used to analyze biological data.

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Course Overview

- The course is organized into multiple modules
  - Fundamentals of microscopy techniques
  - Super-resolution microscopy
  - Bioimage data analysis
  - Special topics: informatics techniques
  - Other molecular-level imaging modalities
- Format
  - Lectures
  - Literature reading + discussion; Reading assignments
  - Lab visit
  - Projects; presentations

Course Organization (I)

- My contact 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 @ Mellon Institute 403

- Teaching assistant contact information

  Ms. Anupama Kuruvilla, BME PhD student
  Email: anupamak@andrew.cmu.edu
  Office: Center for bioimage informatics, C119-122 Hamerschlag Hall

- Class web page
  http://www.andrew.cmu.edu/course/42-731/

Course Organization (II)

- Grading

Category	% of final grade
5 reading reports	40%
4-5 projects	50%
Class participation	10%

- There will be no mid-term or final exams.
- A note to undergraduate students taking this class.

Course Organization (III)

- Students are expected to attend lectures. Repetitive (>3) absences without instructor approval will result in up to 10% deduction of final grade.

- Policy regarding absence from <u>your group presentations</u> without approval by the instructor <u>before</u> the class.
  - First time: warning; 10% deduction from final grade
  - Second time: warning; final grade lowered by one tier (i.e. A→B; B→C)
  - Third time: automatic failure

Comments (I): What to Expect

- Bioimage informatics is interdisciplinary.
  - Patience, openness, & inquisitiveness expected

- We will focus on the engineering aspects of bioimage informatics: microscopy, image analysis, and computer vision.

- Required biological background will be introduced.

- This is a research-oriented course. We will read research articles. Often there are no standard solutions.

Comments (II): What to Expect

- All slides will be posted online
  - No need to copy slides in notebooks.
  - Slides from previous semesters are available before class. Revisions are likely as the class proceeds.
  - Revised lecture notes will be posted after classes.

- The list of lectures is for reference only. Adjustments are likely as the class proceeds.

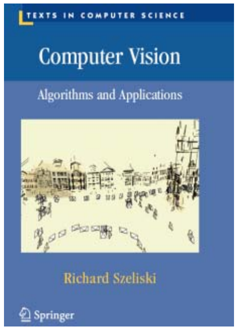
Prerequisites & Textbook (I)

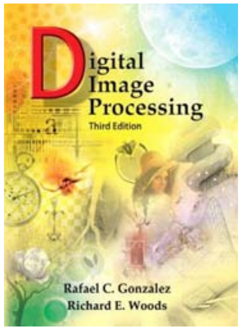
- Image processing

- Proficiency in programming
  - MATLAB is the required implementation language for projects.

- Suggested references

  - Gonzalez & Woods, *Digital image processing*, 3rd ed., Prentice Hall, 2007.
  - Szeliski, *Computer Vision*, Springer, 2009.





Prerequisites & Textbook (II)

- This class cannot substitute for courses on imaging processing, computer vision, or medical image analysis.

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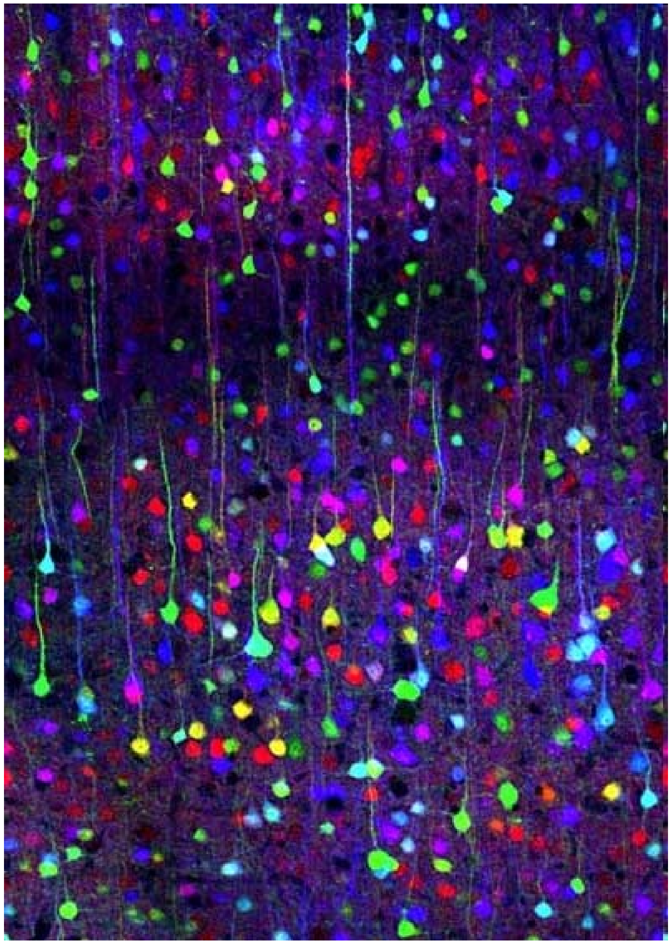
Bioimaging vs Medical Imaging

- Different modalities
  - Bioimaging $\rightarrow$ mostly cellular and molecular level.
  - Medical imaging $\rightarrow$ mostly tissue and organ level
- Different techniques & objectives; Some shared principles
  - Medical image analysis is technically more mature.
- There is a significant trend of convergence
  - E.g. molecular imaging

Fluorescence Imaging of Neurons in Cerebral Cortex Sections

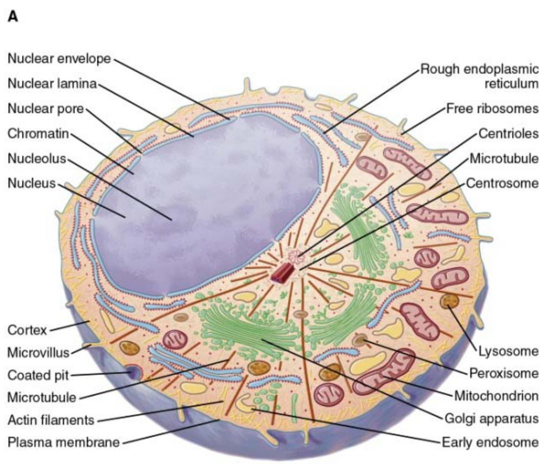


Livet J, Weissman TA, Kang H, *et al. Nature* **450**: 56–62, 2007

Questions?

Cells are Extraordinary Engineering Systems

- Structurally, each cell is organized into various subunits that serve different functions
  - material
  - energy
  - motion
  - information



Pollard & Earnshaw, Cell Biology, 2/e

- Each cell is made of a wide variety of molecules, mostly proteins.

Table 2–2 **The Approximate Chemical Composition of a Bacterial Cell**

	PERCENT OF TOTAL CELL WEIGHT	NUMBER OF TYPES OF EACH MOLECULE
Water	70	1
Inorganic ions	1	20
Sugars and precursors	1	250
Amino acids and precursors	0.4	100
Nucleotides and precursors	0.4	100
Fatty acids and precursors	1	50
Other small molecules	0.2	~300
Macromolecules (proteins, nucleic acids, and polysaccharides)	26	~3000

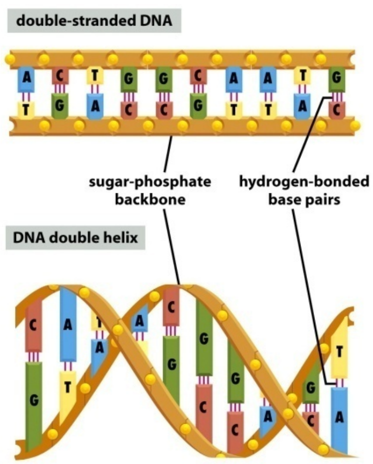
Alberts et al, Mol. Biol. Cell, 5/e

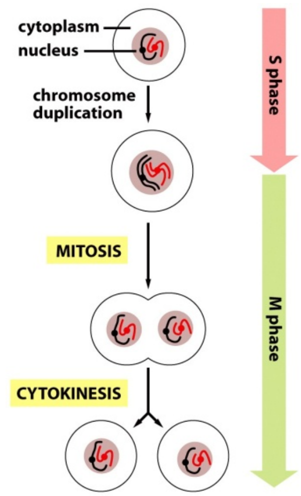
- The complex interactions between these molecules define life.
  - e.g. human cognitive processes

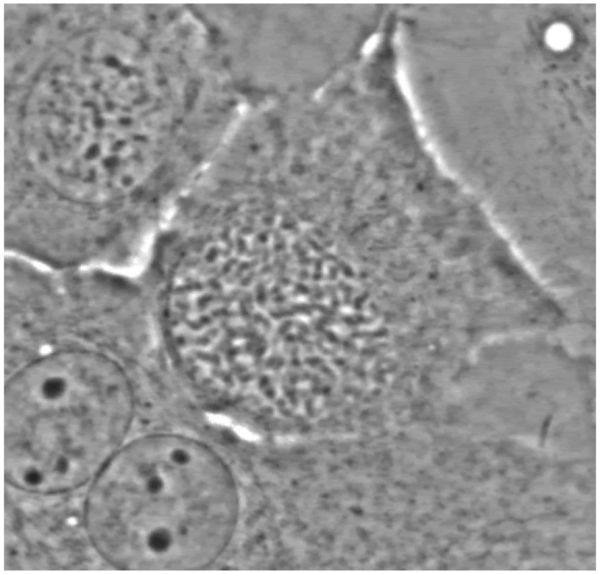
- The purpose of bioimage informatics is to use imaging and computation to understand cellular processes.

Example I: Information Replication and Transfer

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



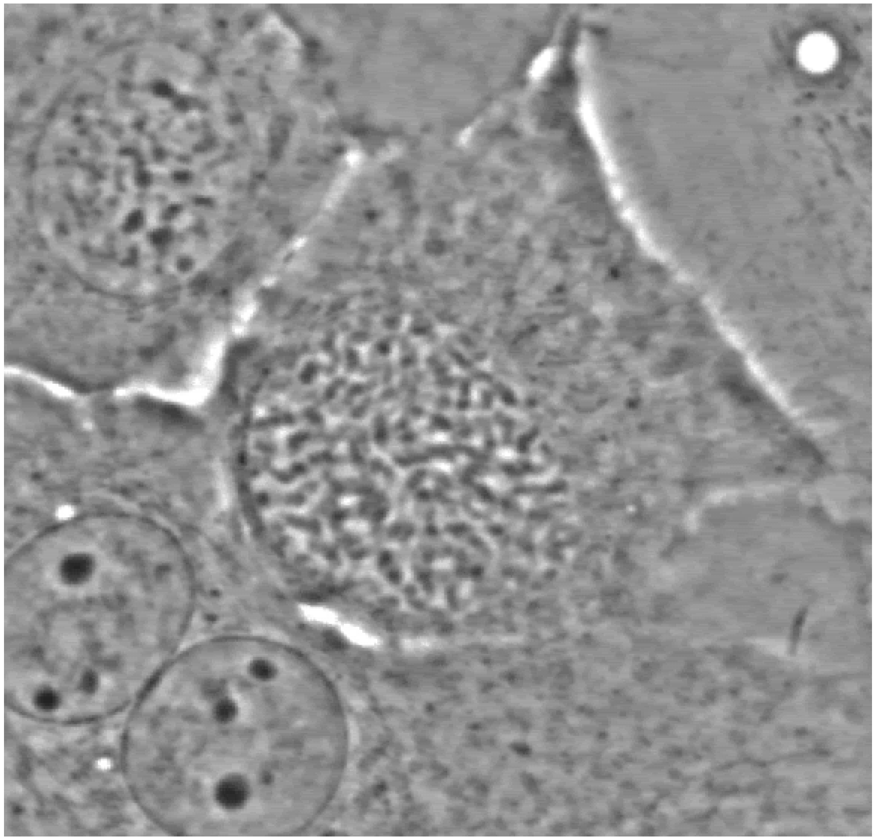




- <u>In an adult human, ~25 million cell divisions happen every second.</u>
- <u>In each human cell, ~3.2 billion nucleotide base pairs get copied.</u>
- Highly complex mechanisms of regulation, quality control, and error-correction.

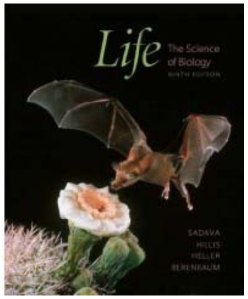
Discussion

- Cellular processes are highly complex.
- Cellular processes are highly dynamic.
- Understanding cellular processes depends critically on understanding the activities and interactions of the related molecules in space and time.
- Imaging provides a powerful noncontact approach to follow such activities and interactions.



General Biology & Cell Biology References

- General biology
  - Life: the science of biology, Savada et al, W. H. Freeman, 2009.



- Cell biology
  - Molecular Biology of the Cell, 4e/5e, Bruce Alberts et al, Garland Science, 2008

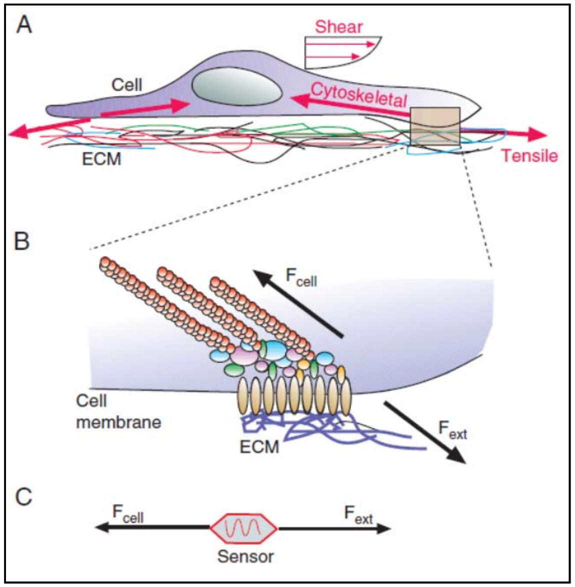
What is Bioimage Informatics (II)

- Interdisciplinary
  - Microcopy (especially fluorescence microscopy)
  - Image processing & computer vision
  - Statistical analysis, pattern recognition, machine learning

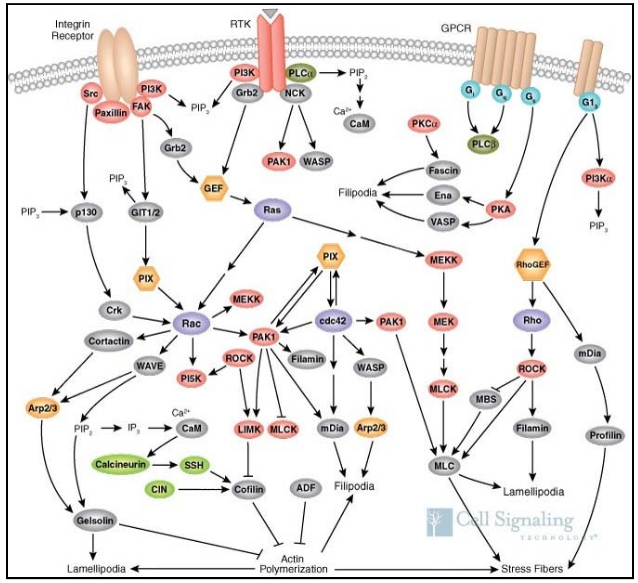
  - Molecular biology, biochemistry, genetics
  - Biophysics

- Bioimage data poses fundamental challenges to image analysis and computer vision; e.g.
  - Very large volume of data
  - Highly dynamic and complex events in images
  - Robustness and efficiency requirements for algorithms

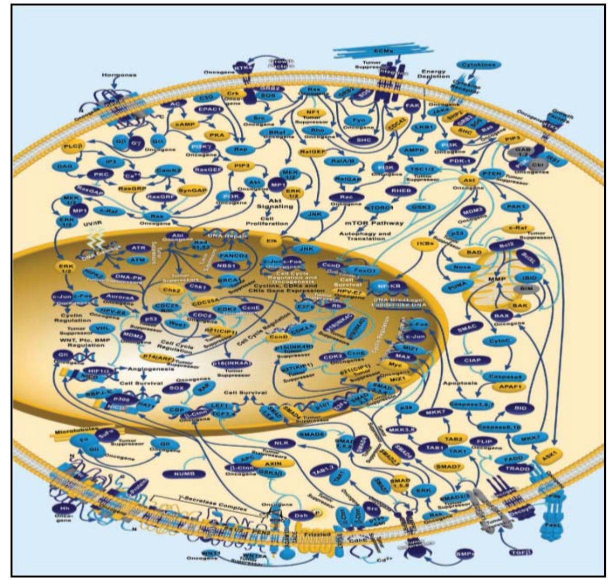
Example III: Information Processing and Decision Making



Environment sensing

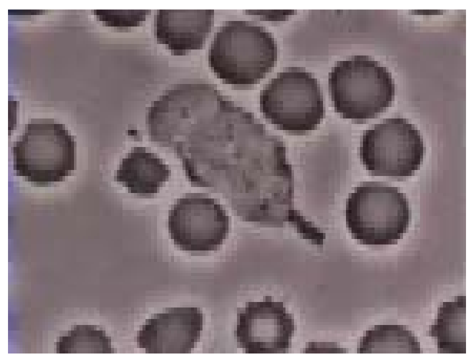


Actin regulation pathway



Human cancer pathways

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



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