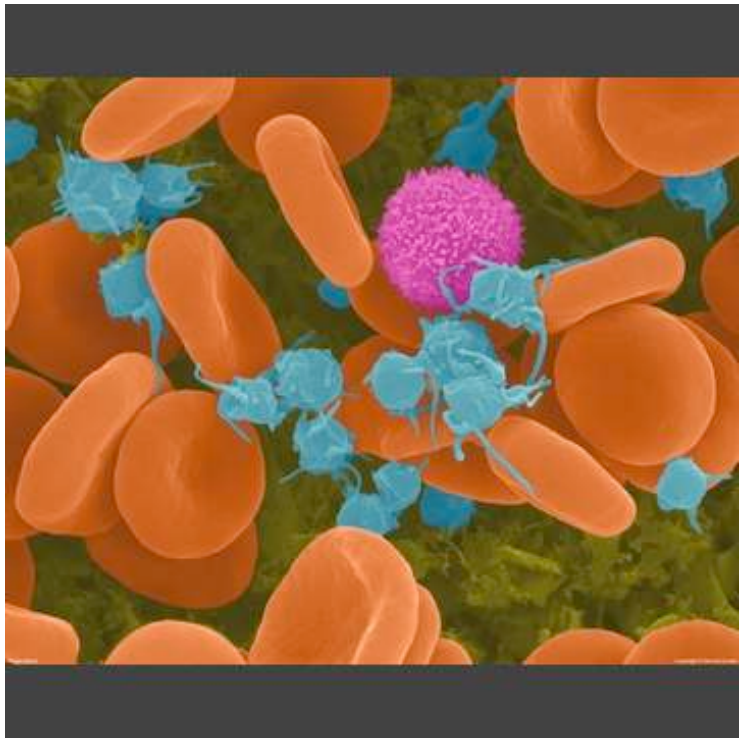
Lecture 1: Anatomy of a Blood Test - Window on the Cell Theory

Quantitative Models of Biological Function

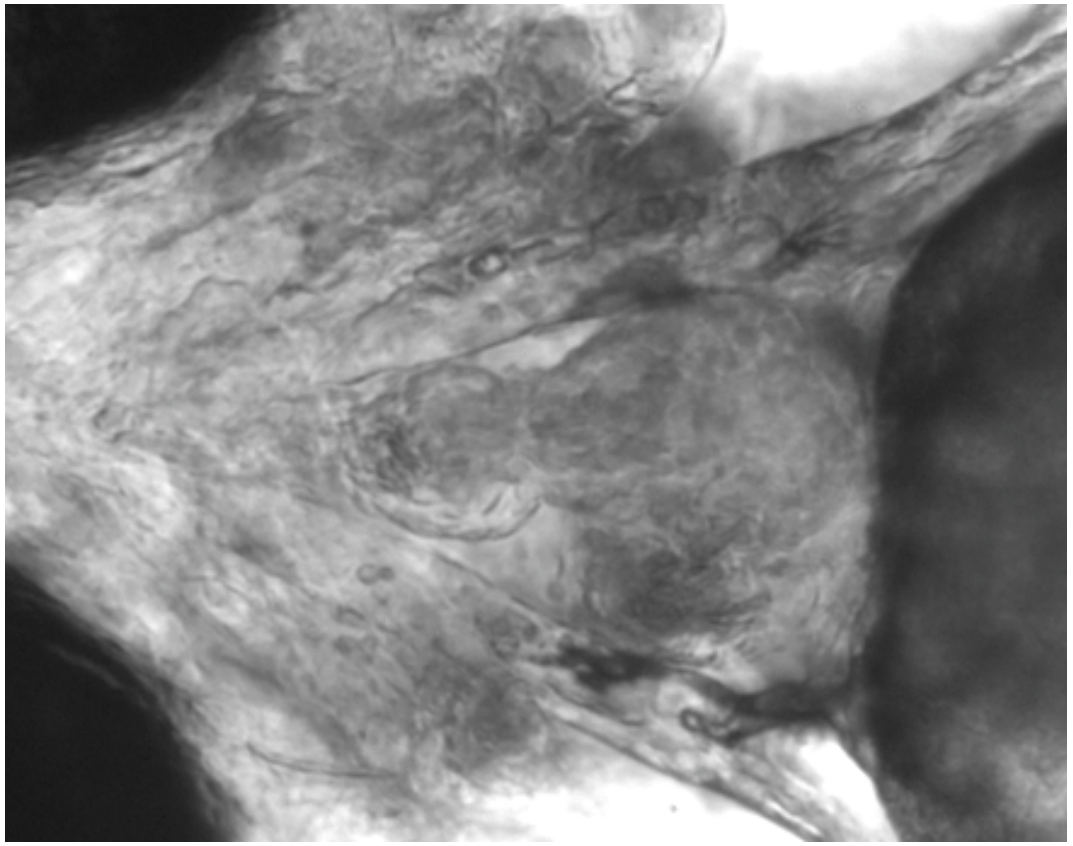


APh/BE161: Physical Biology of the Cell

The Beauty of the Beating Heart

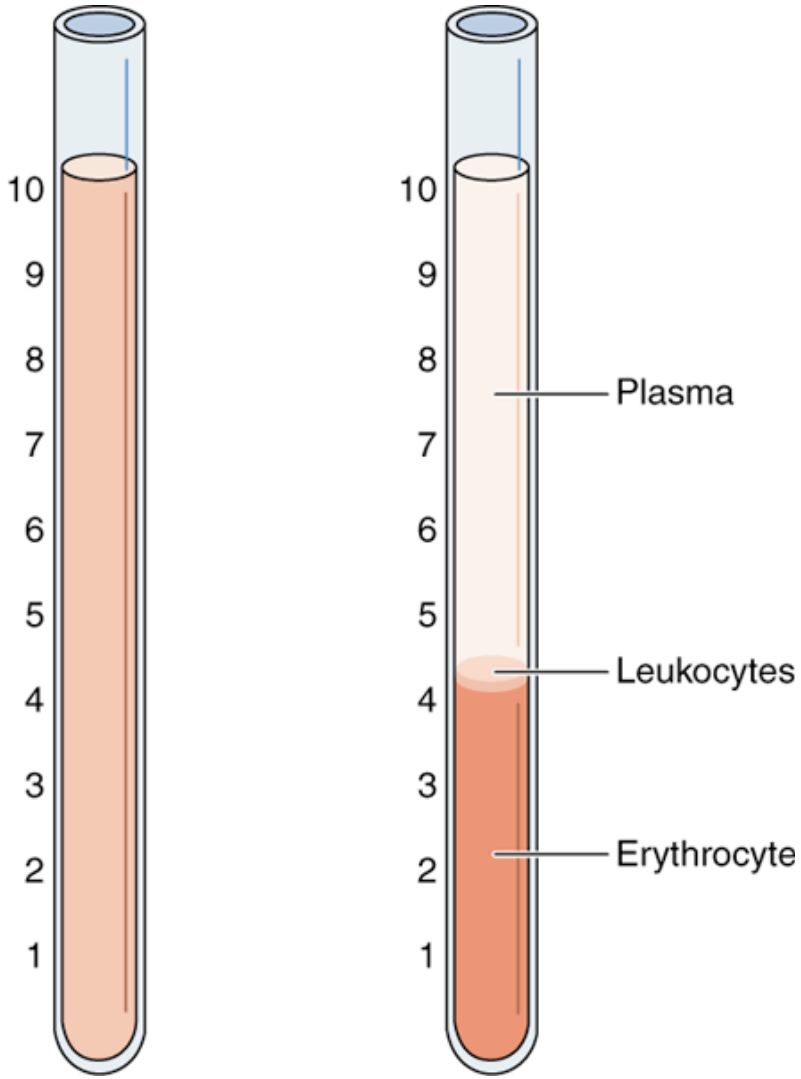
Art is long, and Time is fleeting,
And our hearts, though stout and brave,
Still, like muffled drums, are beating
Funeral marches to the grave.

Henry Wadsworth Longfellow,
``A Psalm of Life''



Spin it down baby!

- *After blood is extracted, anticoagulants such as heparin are added and then the suspension is spun in a centrifuge.*
- *The various interesting fractions are separated as a result of centrifugation and then they can be queried quantitatively resulting in the CBC.*
- *Figure from Junqueira and Carneiro, "Basic Histology"*



Results of a Complete Blood Count (CBC) Test

"I have your blood test results right here. It's bad news I'm afraid. It isn't blue."

Example 1: **CBC WHL BLD***
(Complete Blood Count Whole Blood)

Lab Value		*Normal Range*
WBC	2.2 K/mm^3	3.4-9.6
RBC	3.6 m/mm^3	3.58-4.99
HGB	11.1 g/dL	11.1-15
HCT	32.6%	31.8-43.2
MCV	91 CU MICR	77-99
MCH	30.8 UUG	26-35
MCHC	34.0 g/dL	34-36
Platelets	8 K/mm^3	162-380

Differential

Lab Value			*Normal Range*
cell count	100		
NUC RBC	0		
polys	*14%*	*(0.14+0 = 0.14)*	38-78
bands	*0*		0-4
lymphocytes	79		14-51
monocytes	7		1-12
eosinophils	0		0-8
basophils	0		0-3
atyp lymph			

How to figure out the ANC
2200 (WBCs) x 0.14 (polys plus bands) = 308.00 = ANC

* *The abbreviations used are the ones you will see on your CBC lab report.*

Example 2: **CBC WHL BLD***
(Complete Blood Count Whole Bloo

Lab Value			*Normal Ra*
WBC	1.1 K/mm^3		3.4-9.6
RBC	2.41 m/mm^3		3.58-4.99
HGB	7.9 g/dL		11.1-15
HCT	23%		31.8-43.2
MCV	97 CU MICR		77-99
MCH	32.8 UUG		26-35
MCHC	33.8 g/dL		34-36
Platelets	16 K/mm^3		162-380

Differential

Lab Value			*Normal Ra*
cell count	50		
NUC RBC	0		
polys	*84%*	*(0.84+0.10 = 0.94)*	38-78
bands	*10%*		0-4
lymphocytes	6		14-51
monocytes	0		1-12
eosinophils	0		0-8
basophils	0		0-3
atyp lymph			

How to figure out the ANC
1100 (WBCs) x 0.94 (polys plus bands) = 1(= ANC

* *The abbreviations used are the ones you wi on your CBC lab report.*

A Blood Smear

- *The light microscope is one of the greatest inventions in the history of science.*
- *Different cell types in the blood are revealed by different morphology.*
- *The invention of new ways of staining cells and their internal features has been another of the most important journeys in the history of science. (Golgi found ways to stain neurons, green fluorescent protein (GFP) is a great modern "stain", etc. - really impressive.)*

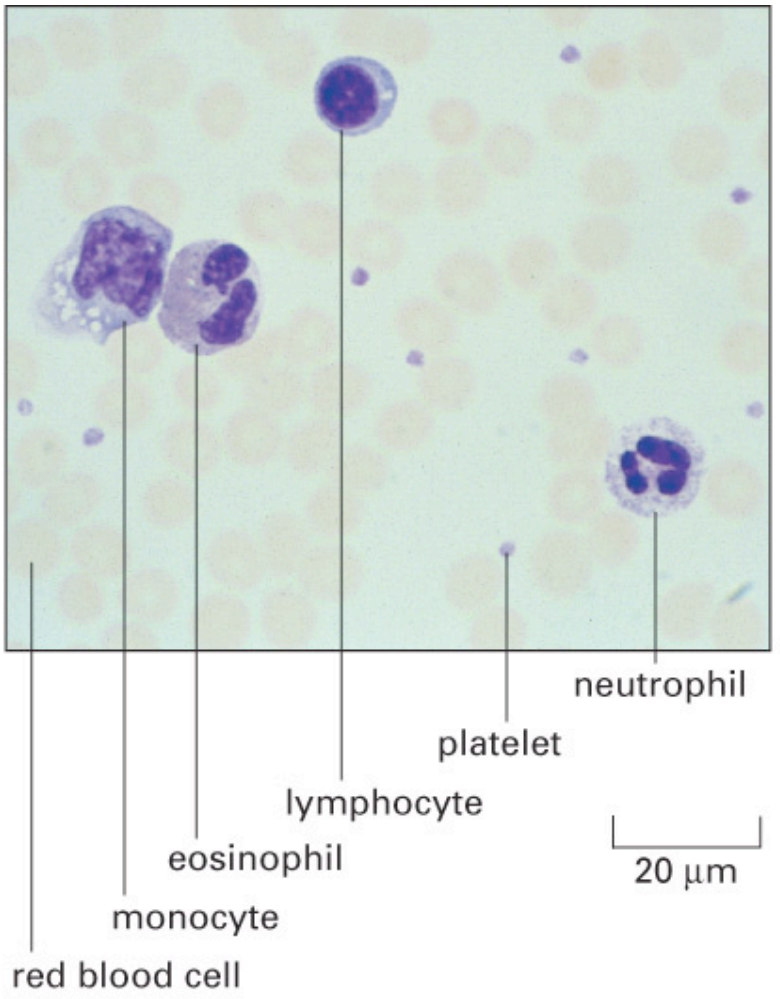
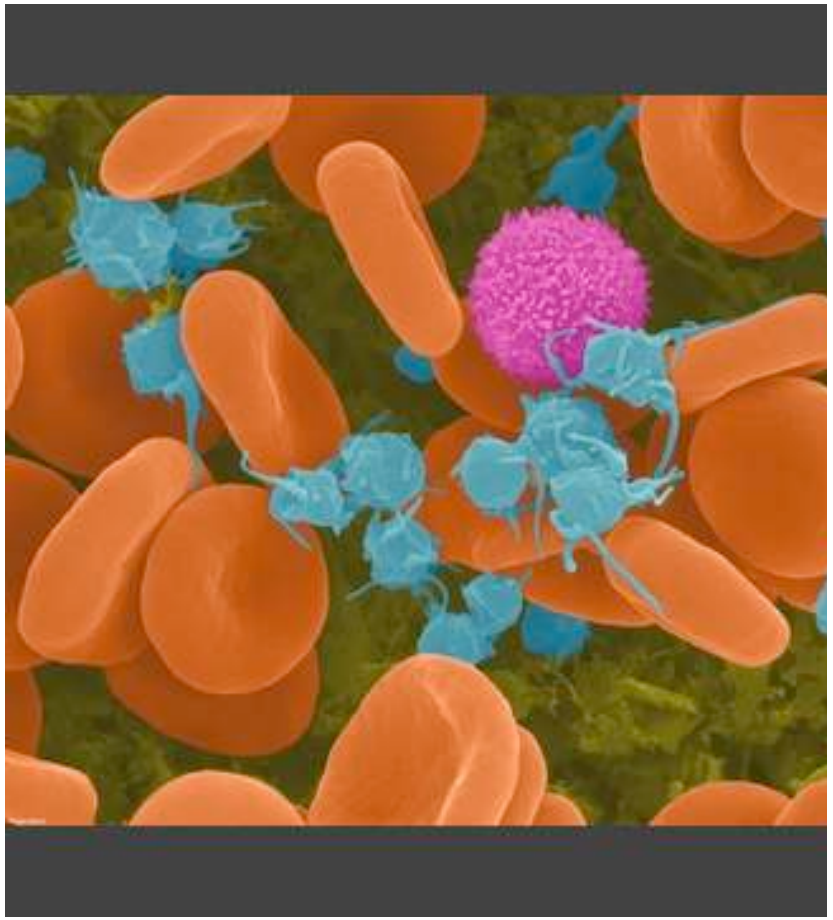


Figure 22–30 part 2 of 2. Molecular Biology of the Cell, 4th

Higher Resolution View of Blood Cells

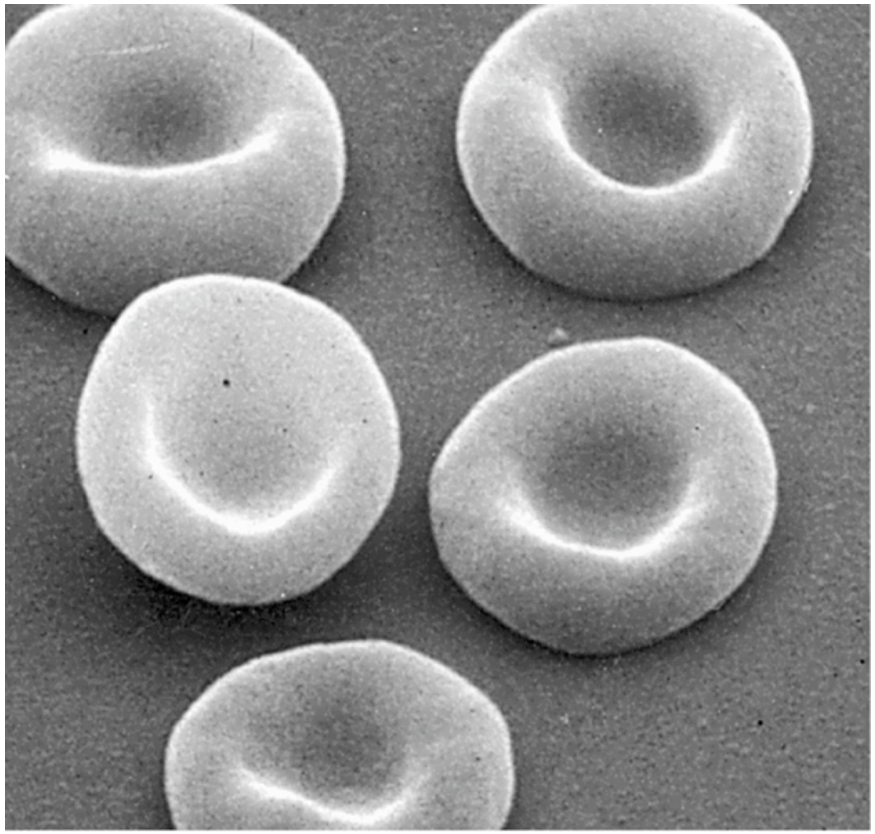
- *Scanning Electron microscope used to view blood cells.*
- *Do NOT take images like this for granted - this is an amazing technological feat!*
- *Image and text from Dennis Kunkel*
- *Note the annoying lack of scale bars.*

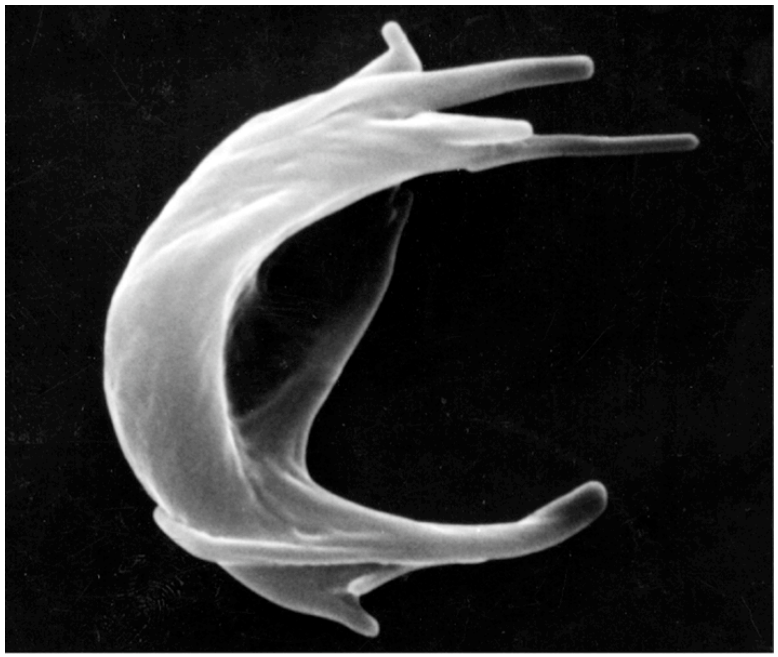


Human blood is the fluid circulated by the heart through the human vascular system. There are three cellular components of human blood: red blood cells, white blood cells, and platelets. Red blood cells transport oxygen to other cells of the body. Packed with hemoglobin (an iron-bearing protein) and shaped like plump disks with indented centers, red bloods cells are produced in bone marrow and have a life span of about 120 days. White blood cells (purple) protect the body from infection, attacking and destroying foreign particles like dust, pollen, and viruses. Platelets defend the body against excessive blood loss. Platelets (blue) flow freely in the blood in an inactive state; but when an injury is sustained, platelets become sticky to plug the injured area.

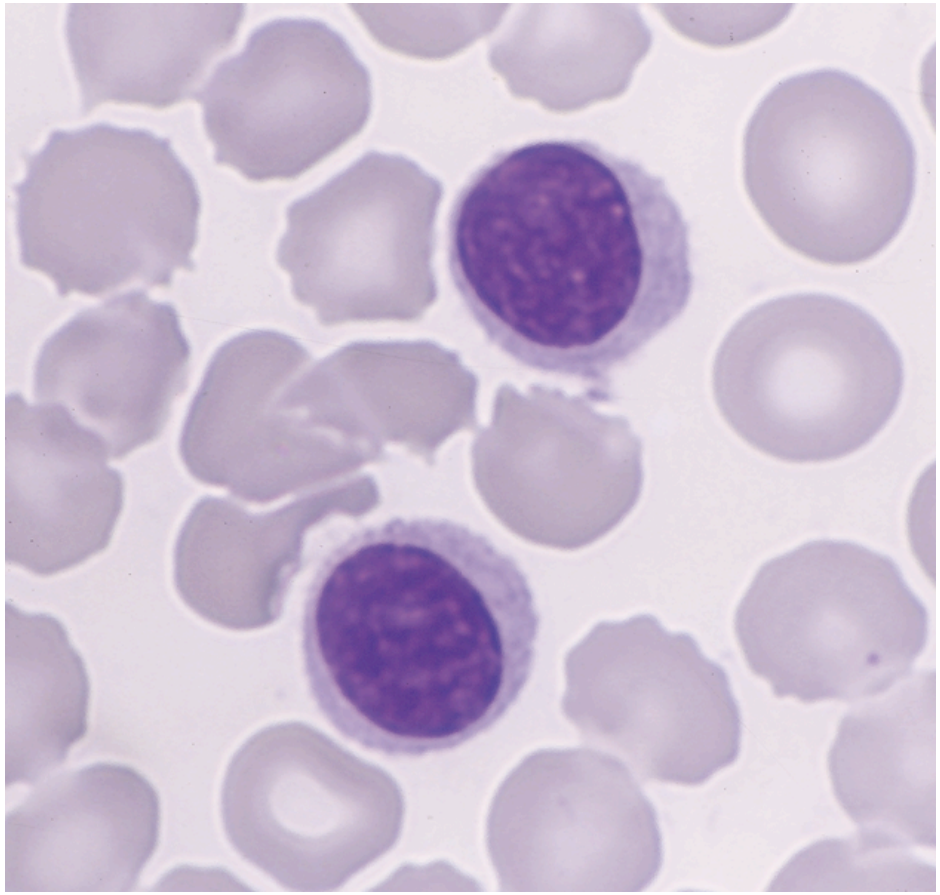
Red Blood Cells (Erythrocytes)

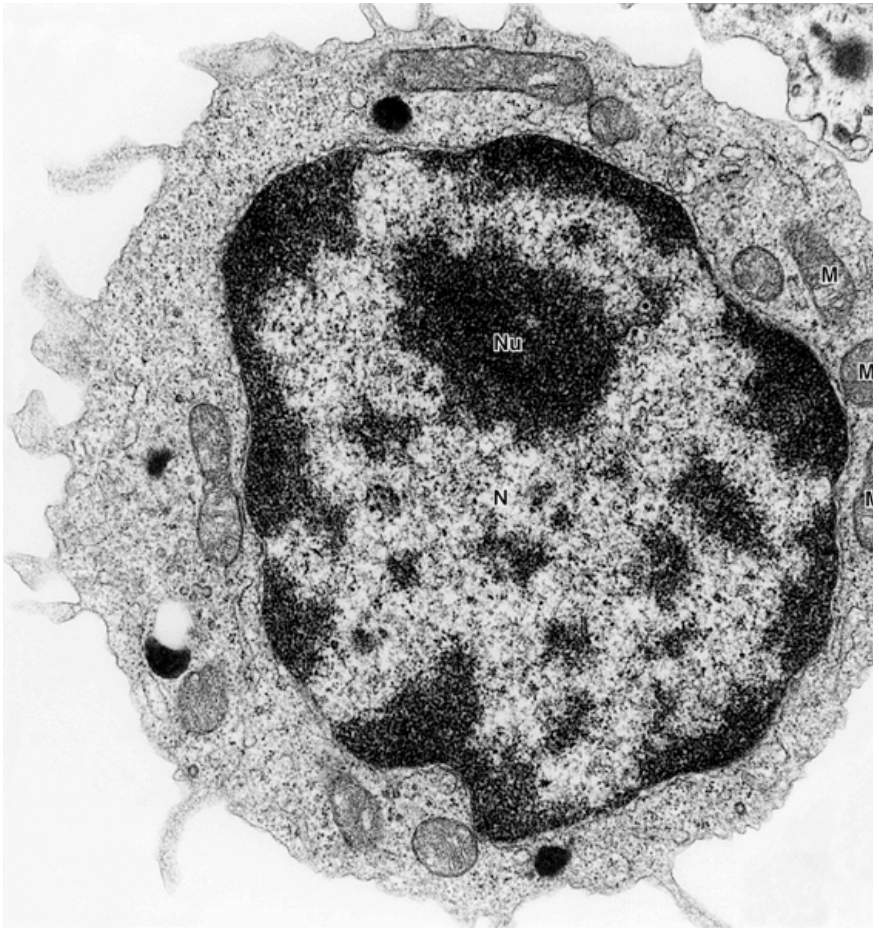
- *What confers shape? The sickle cell morphology is a symbol of the first mole understanding of disease (Pauling, here at Caltech).*
- *From Junqueira and Carneiro, "Basic Histology"*





Lymphocytes





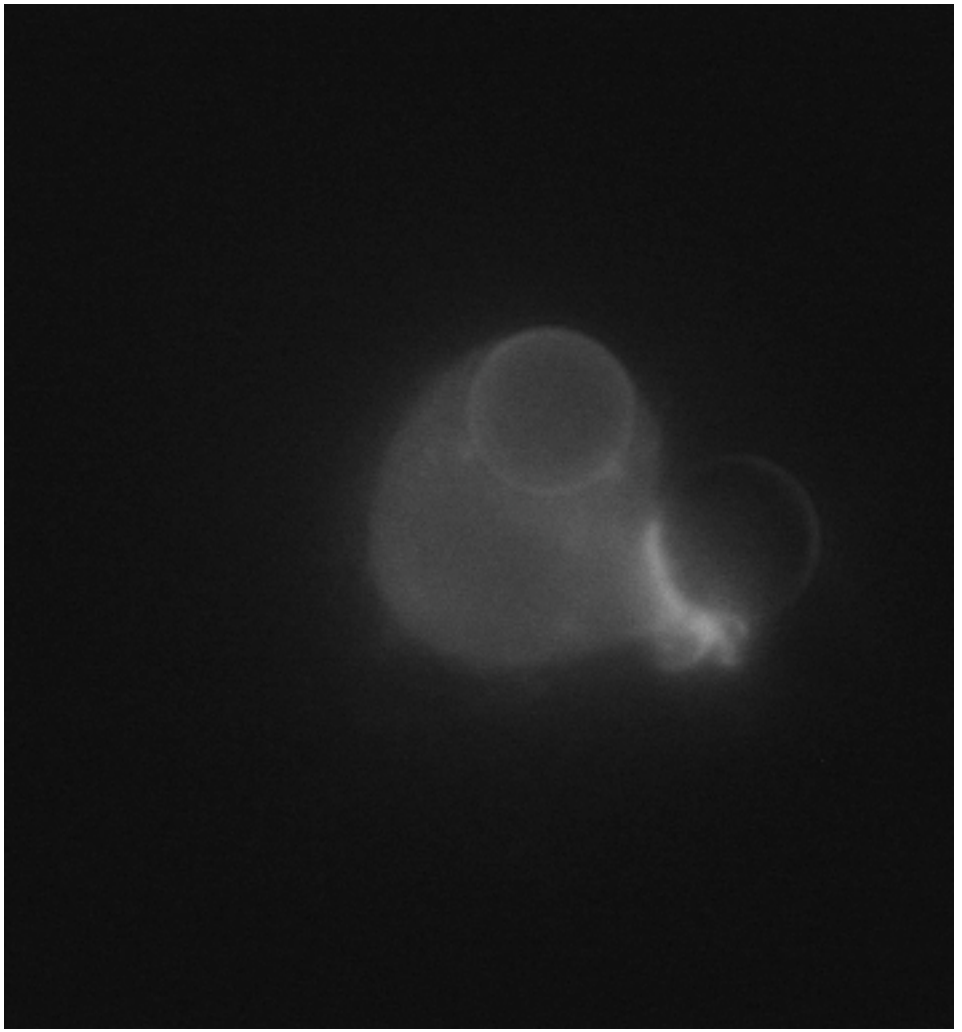
- *These are key cells in the immune system.*
- *From Junqueira and Carneiro, "Basic Histology"*
- *Note the annoying lack of scale bars.*
- *Cell morphology is quite different from other cell types - more later.*

Neutrophil Chasing a Bacterium: The Great Themes of Biology

- *How do cells decide?*
- *How do cells move?*
- *How do cells differentiate into different types?*

IMacrophage Performing Phagocytosis: More Great Themes of Biology

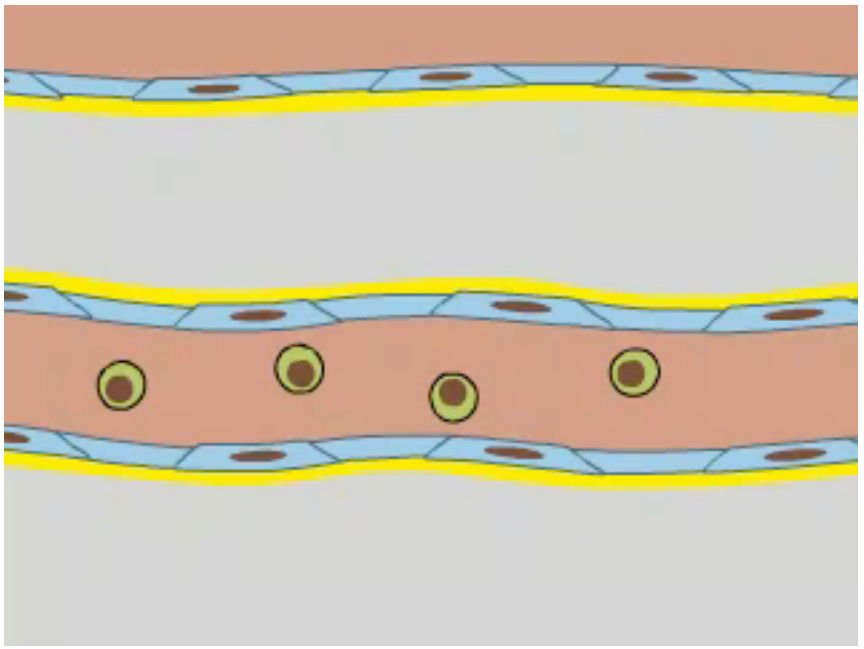
- *How do cells recognize other objects - molecular recognition?*
- *How do cells metabolize products from the external world?*



You can see fluorescent actin being recruited to (and presumably polymerized near) a 5 micron anti-body coated bead. The 1st step is the formation of a "phagosomal actin cup". That's the fluorescent blob at the base of the 5micron bead. The actin front then works around the perimeter of the bead, to pinch the membrane closed at the opposite end. After the bead is engulfed, the actin filaments then de-polymerize and redistributes through out the cell.

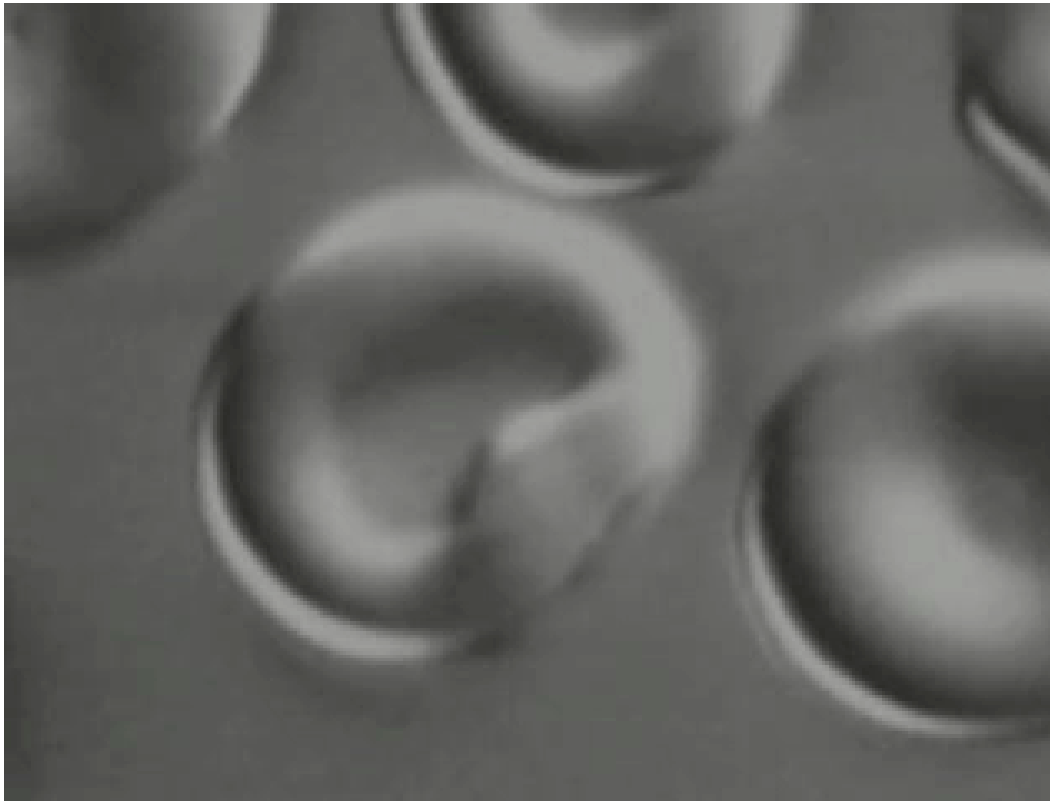
Leukocyte Rolling

- *The workings of the immune system.*
- *From Alberts et al., "Molecular Biology of the Cell"*
- *Once again, a microcosm of many of the great themes and questions in biology (and all of science, for that matter).*

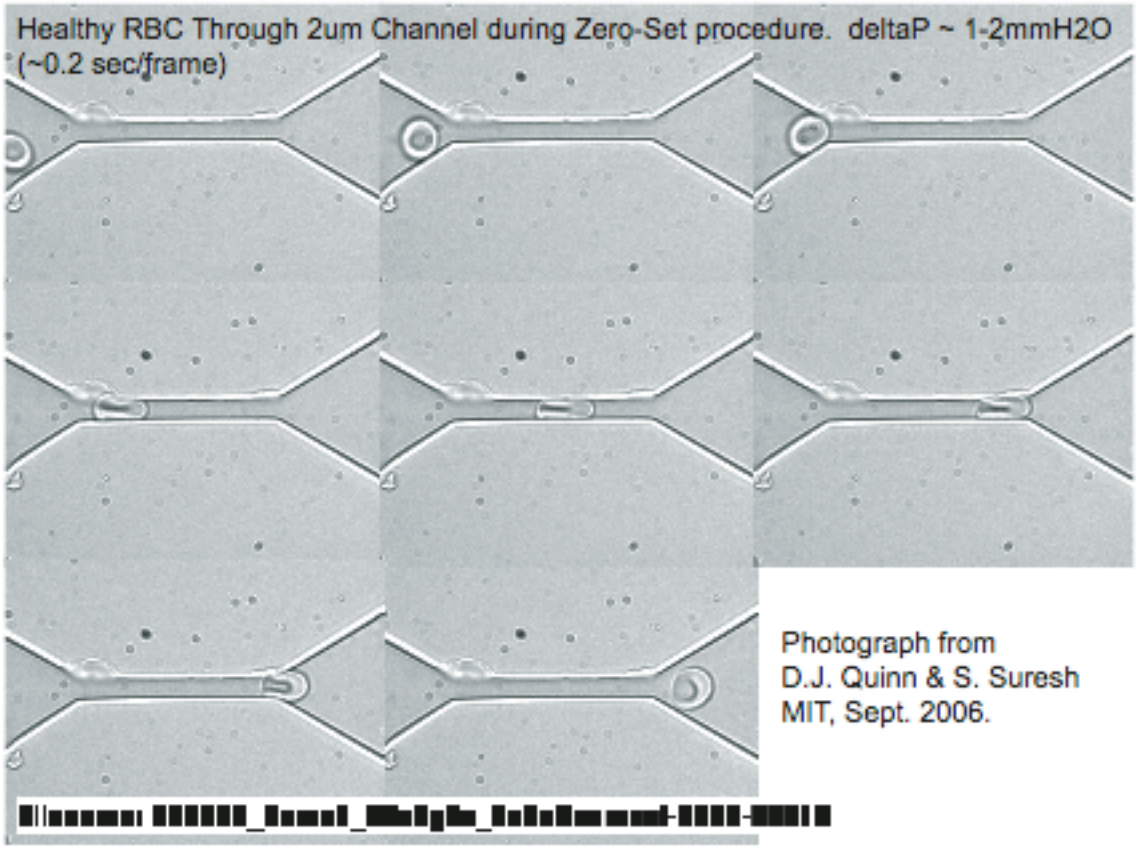


Shape and Function of Red Blood Cells

- *Physical question: how do cells that are larger than 5 microns pass through capillaries that have characteristic dimensions of a micron?*
- *Mechanical properties of cells crucial to their function.*



Mechanical and Medical Consequences of Disease



Photograph from
D.J. Quinn & S. Suresh
MIT, Sept. 2006.

Cool Things Done By Red Blood Cells

- *Study of blood cells: a prism through which to see almost all of biology.*
- *Fantastic process of shedding of the nucleus.*

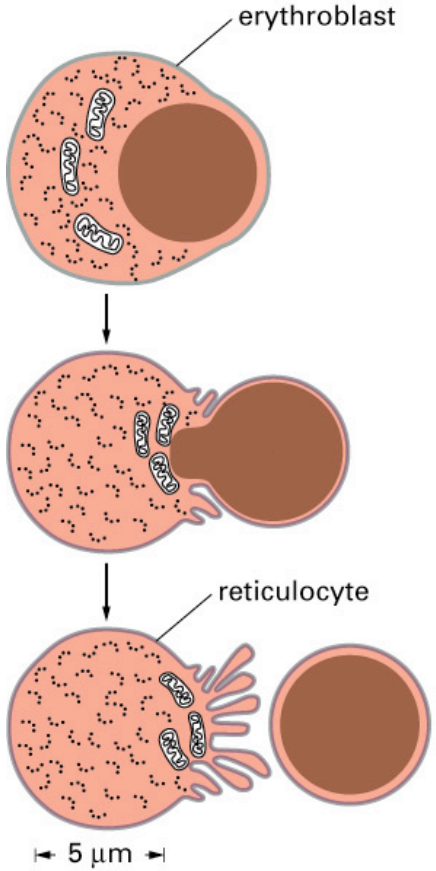
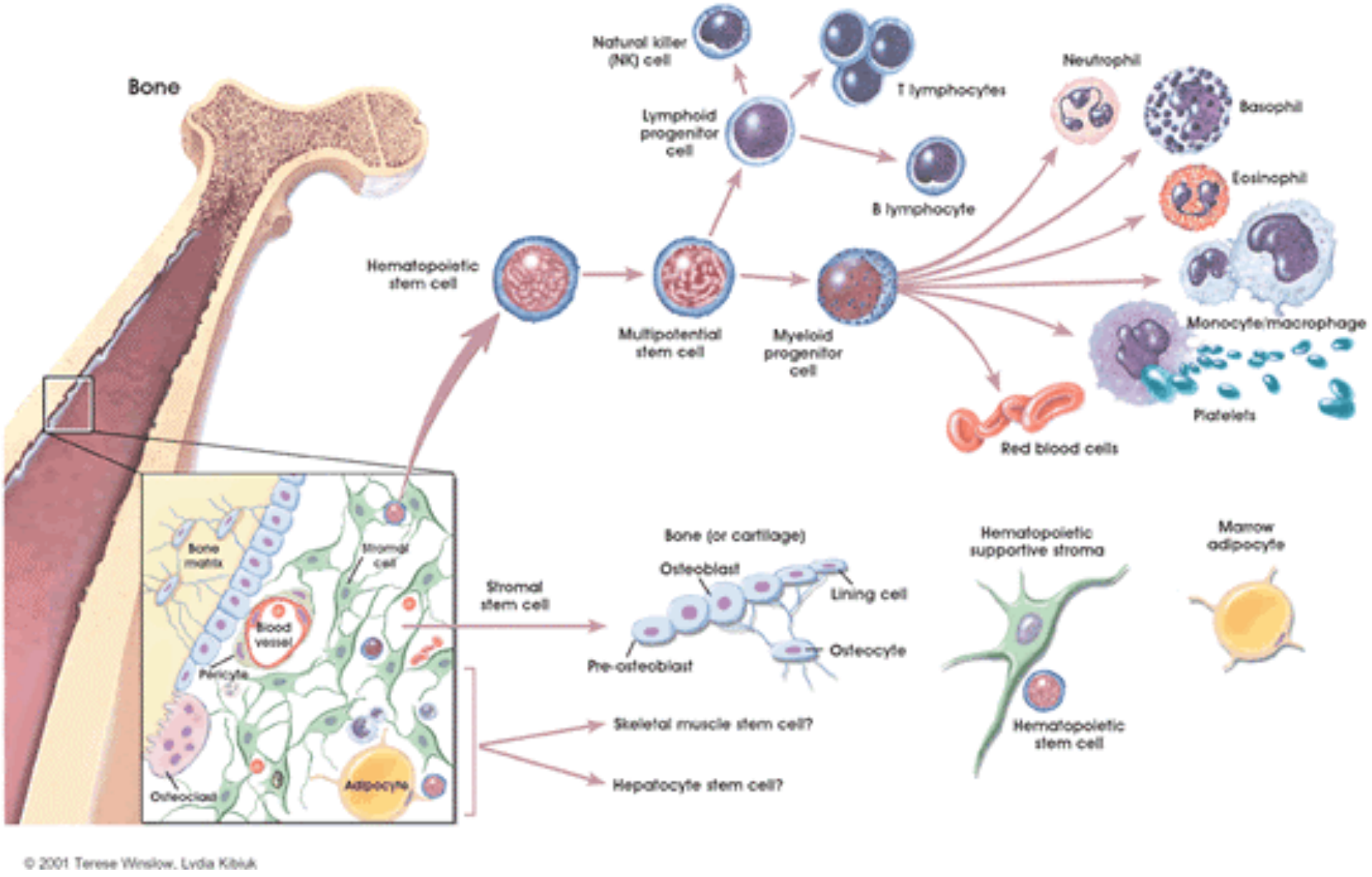


Figure 22–37. Molecular Biology of the Cell, 4th Edition.

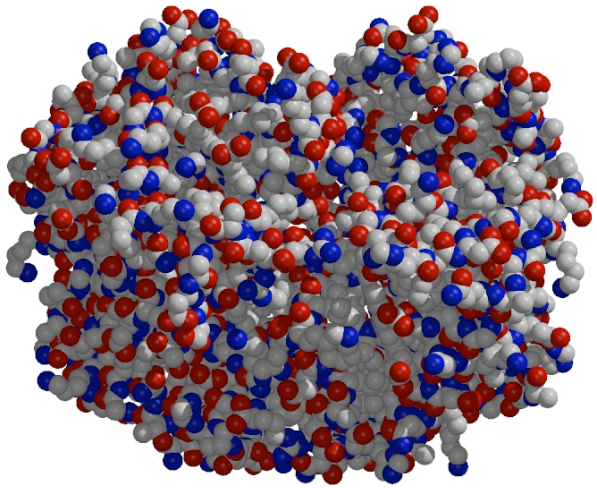
Stem Cells and the Development of Blood Cells: More Great Themes

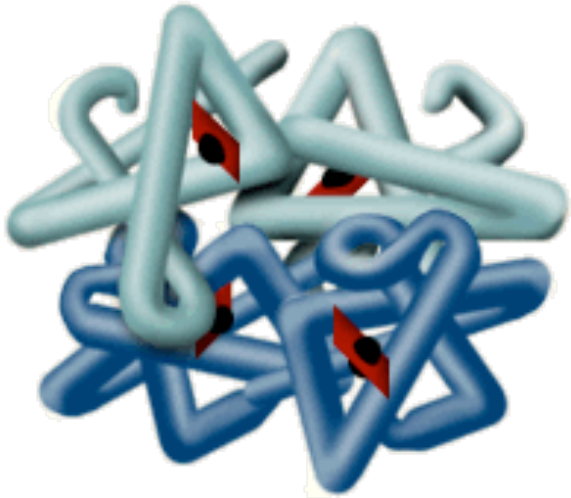


http://people.hofstra.edu/faculty/Sina_Y_Rabbany/Bonemarrow/Diagram7small.gif

What is Hemoglobin?

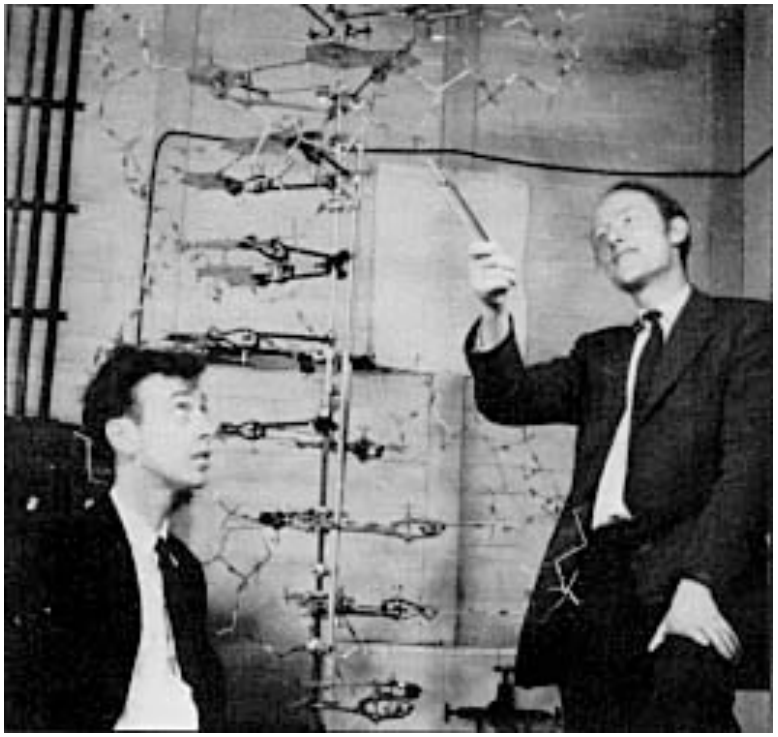
- *Roughly 66 kDa protein, 4 subunits with heme group that binds oxygen.*
- *All-atom picture is a bit hard to interpret, need some sort of ``coarse-grained'' description.*

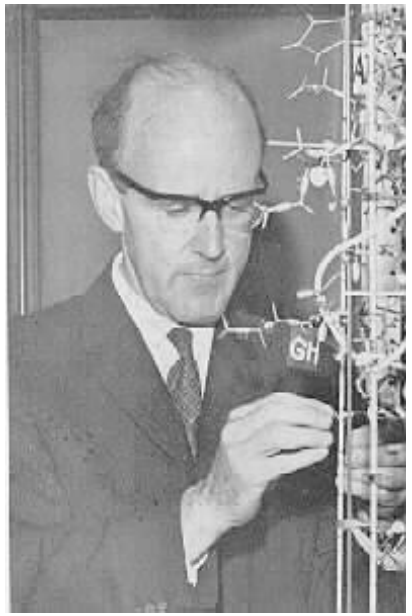


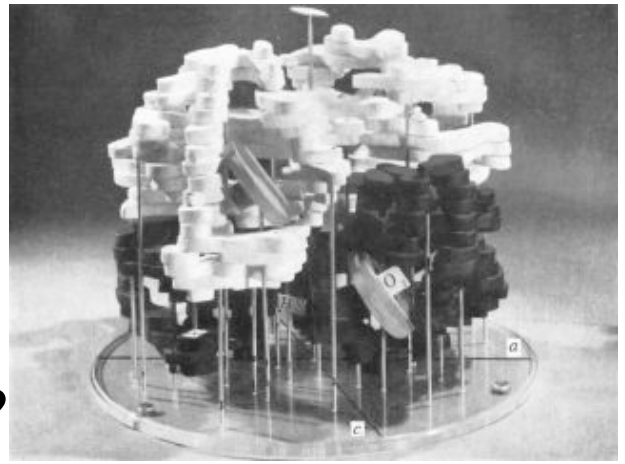


hemoglobin

The Experimental Transformation of Biology: Molecular Structures



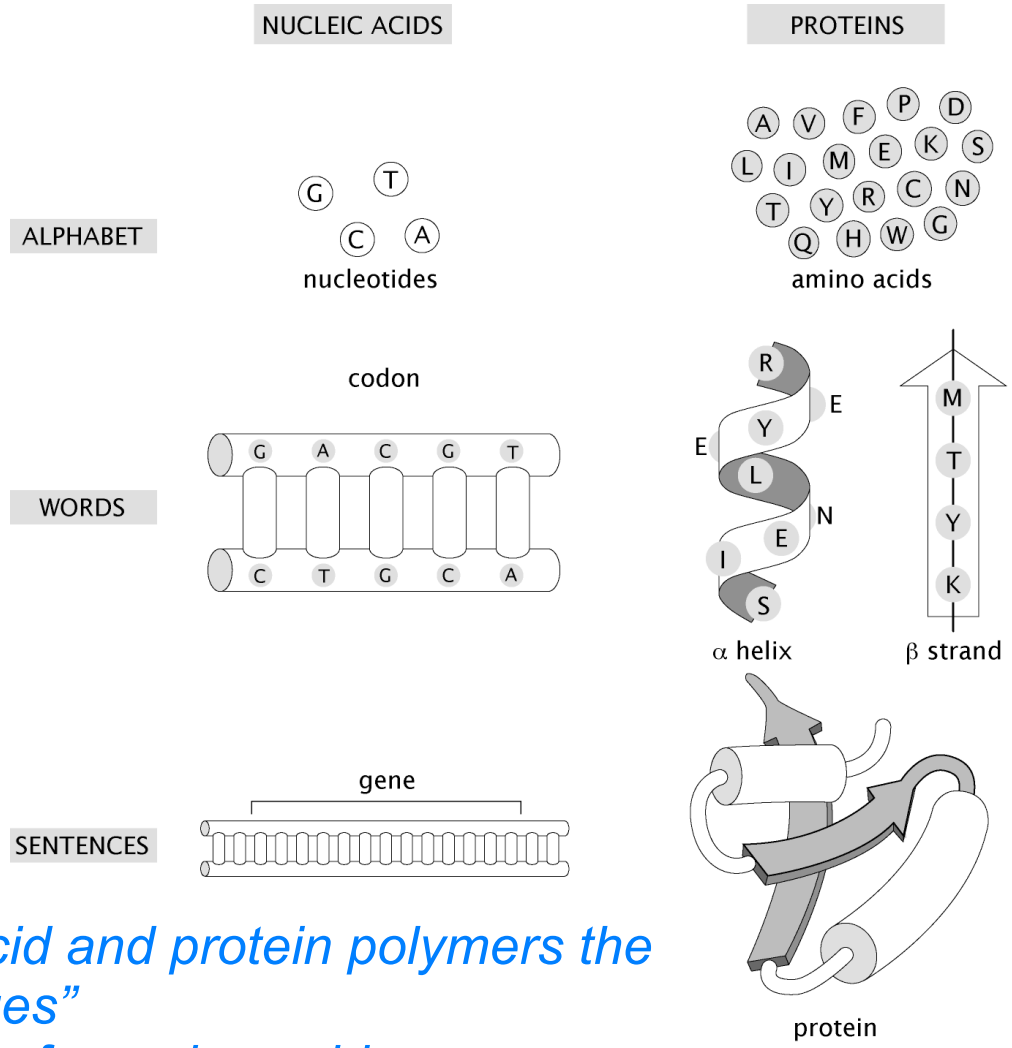




How do we know what we know about structures?

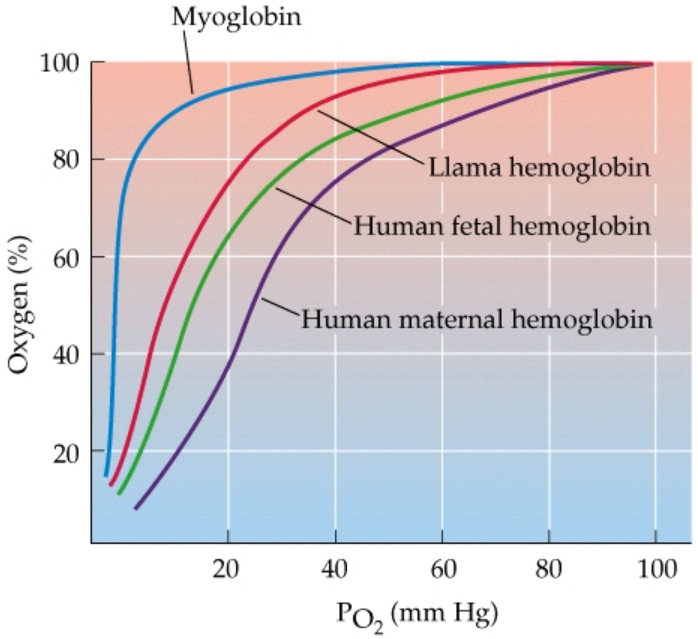
A Single Molecule Census of the Cell: The Parts List - Crick's Great Polymer Languages

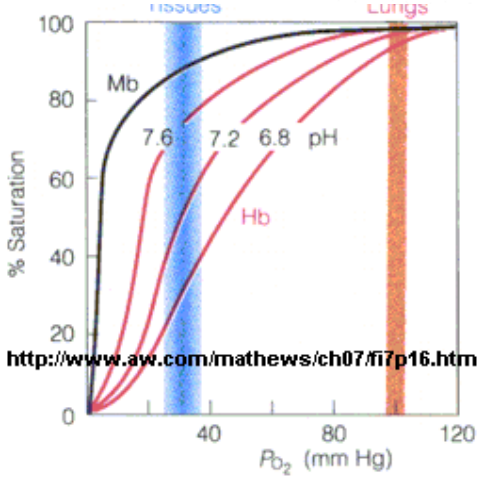
Two great classes of biological polymers of the Central Dogma.



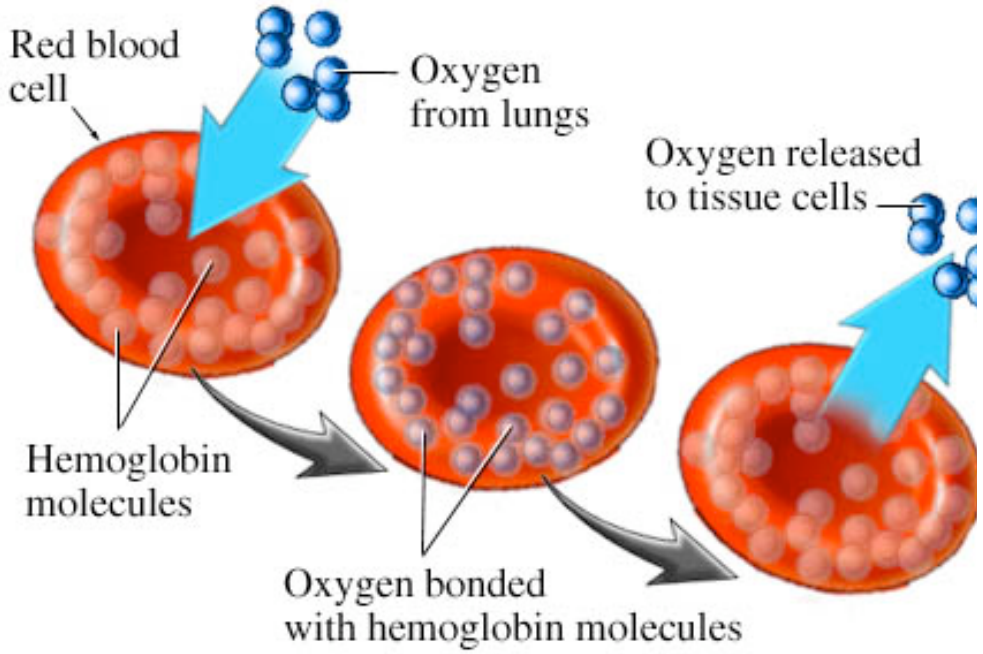
- *Crick dubbed the nucleic acid and protein polymers the "two great polymer languages"*
- *Nucleic acid alphabet codes for amino acids.*

Hemoglobin Binding Curves and the Quantitative Demands in Biology





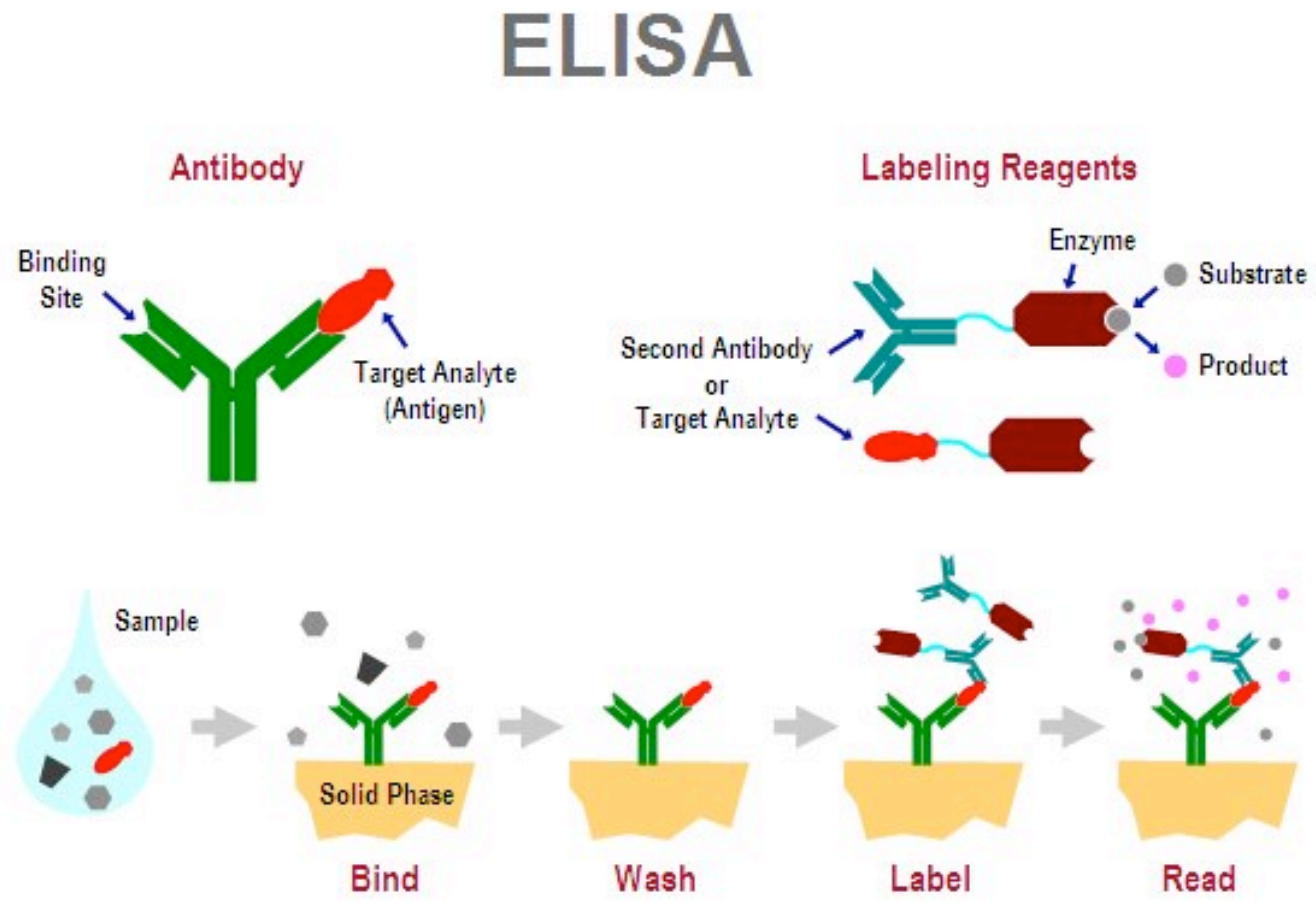
http://www.aw.com/mathews/ch07/fi7p16.htm



- *More of the great themes: DIFFUSION!!, when i equilibrium an appropriate notion, molecule thec disease, …*
- *``Corpora non agunt nisi ligata'' - ``A substance not effective unless it is linked to another.'' - Pau Ehrlich*

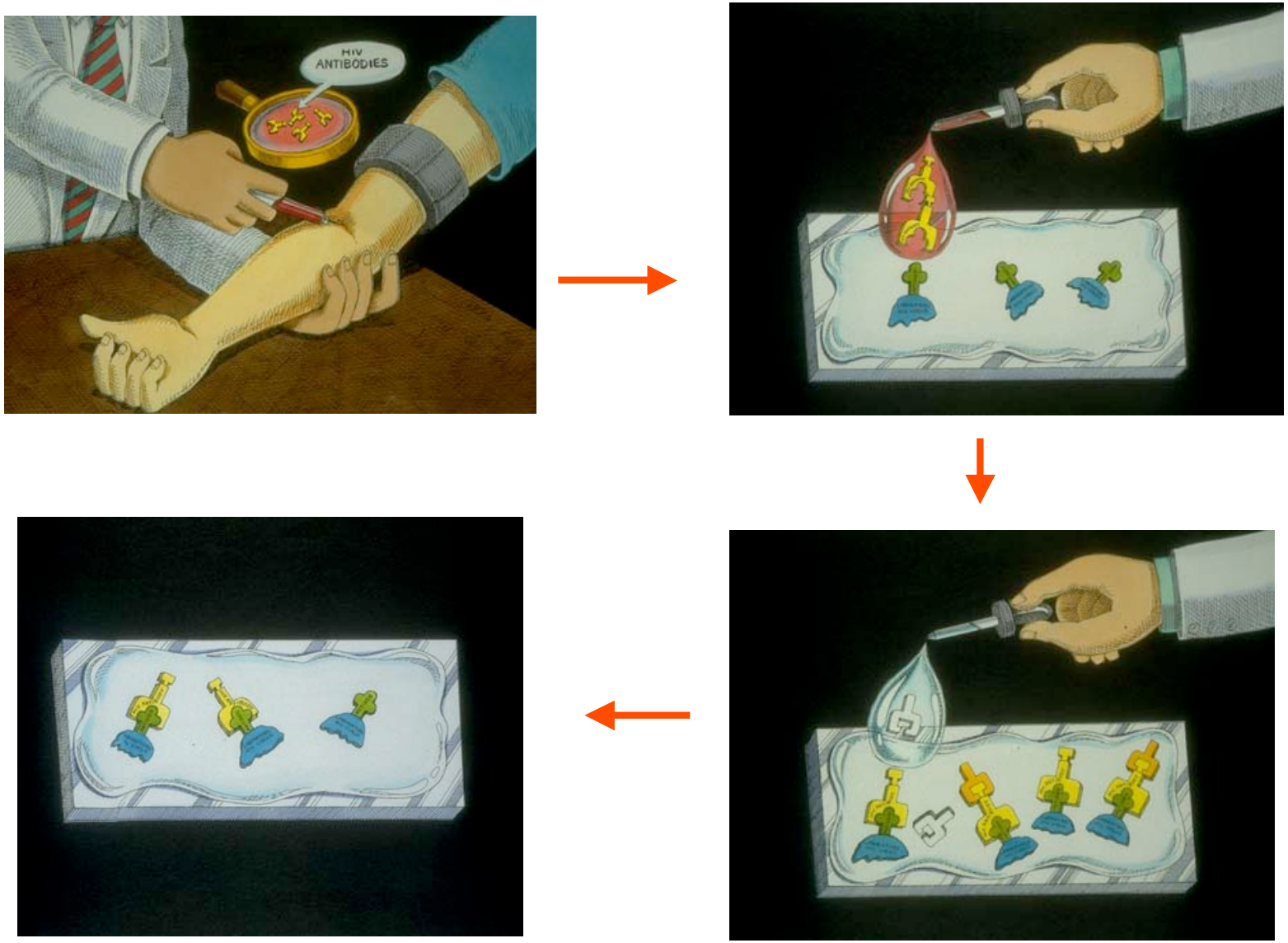
Other Outcomes of Blood Test: ELISA and Pathogens

Enzyme-Linked ImmunoSorbant Ass

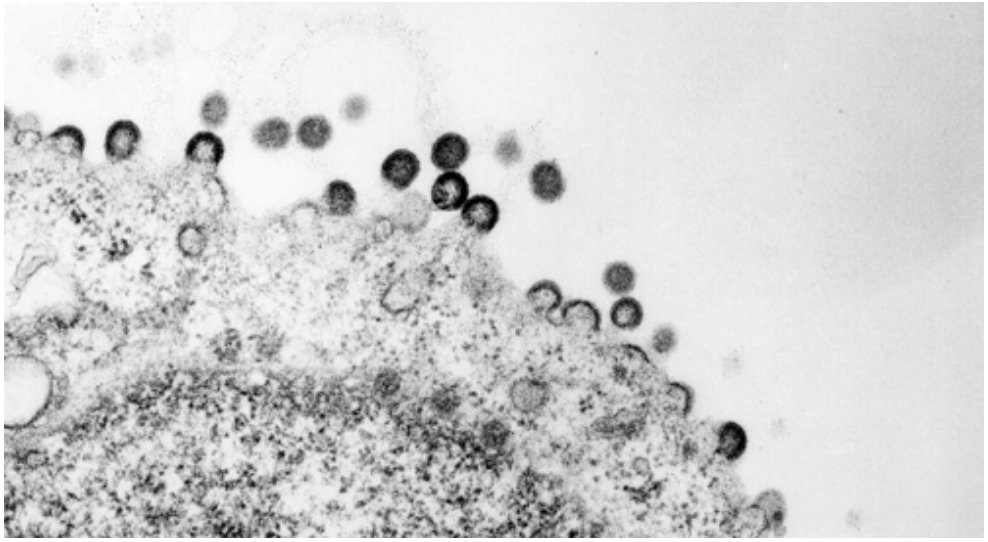


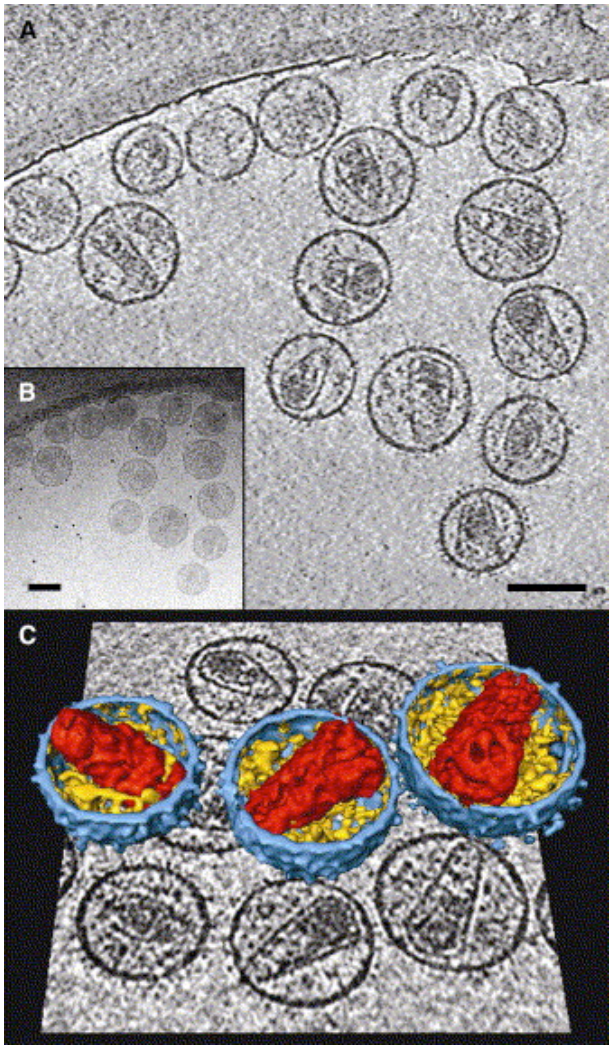
http://www.biosystemdevelopment.com/site graphics/elisa.jpg

Elisa and HIV



The Scourge of HIV: A Plague in our Own Time





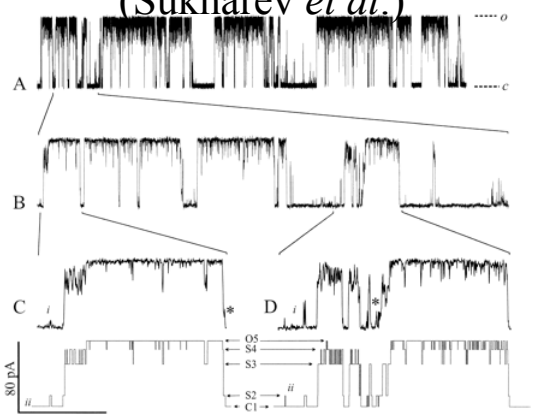
Fuller et al

The Quantitative Imperative

Quantitative Data Demands Quantitative Models and Quantitative Models Demand Quantitative Experimentation

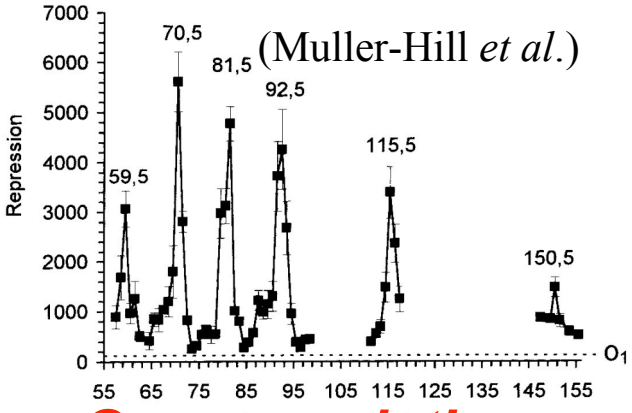
"I often say that when you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely, in your thoughts, advanced to the stage of Science, whatever the matter may be."
Lord Kelvin

(Sukharev *et al.*)



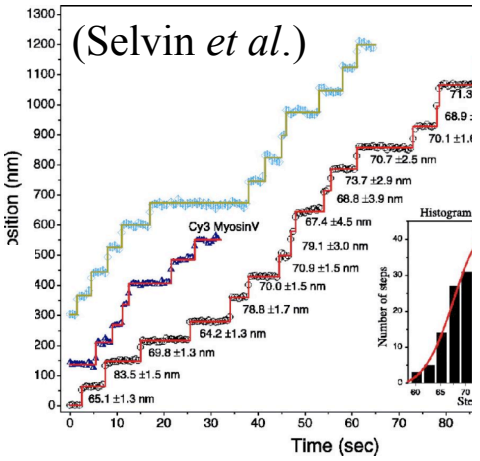
Ion channel dynamics

(Muller-Hill *et al.*)



Gene regulation

(Selvin *et al.*)



Motor dynam