

Lecture #1

Administrative notes:

No required textbook, readings will come from the primary literature

Exams will be held Wednesday evenings from 7-9pm.

Material from “Techniques and Discussion” sections will be covered on exams.

Biochemistry inspires SHOCK and AWE!

Lecture 1

2/4/04

What is inside the cell?

- What are the concentrations of proteins and small molecules?
- What are the differences between eukaryotic and prokaryotic cells?
- How does studying something *in vitro* relate to reality inside a cell?

We need to know the sizes of cells and their constituents in order to understand the “jungle” of metabolism. How do these intracellular activities influence metabolic pathways and regulatory mechanisms by altering the thermodynamic and kinetic properties of macromolecular interactions?

Definition of BIOCHEMISTRY:

Understand in molecular detail (quantitatively) the function of some cellular machinery *in vitro* (under controlled conditions) AND to relate this information to what occurs in reality inside a living cell.

KEY: Take *in vitro* information and relate it back to *in situ*

Example: A Nobel Prize was awarded for the discovery of a DNA polymerase enzyme. However, further studies revealed that *in vitro*, the rate of polymerization with this enzyme was too slow to account for the doubling time of cells. This incongruence has at least two possible explanations:

1. they hadn't actually discovered the right enzyme and 2. the activity of the enzyme changed when studied outside the cell- perhaps interactions with other factors inside the cell, increased the rate inside the cell

In this case, the first explanation was correct, they had actually discovered a DNA repair enzyme, not the actual polymerase.

MORAL: always relate work back to cellular reality. Ask whether *in vitro* studies make sense within the context of the living cell.

Eukaryotes and Prokaryotes

Can we use the simpler prokaryotic system as a paradigm for thinking about machines in more complex eukaryotes? We think, Yes!

But, keep in mind basic differences, especially SIZES and TIMES.

Prokaryotes	versus	Eukaryotes
Inner membrane, cell wall, Outer membrane		Plasma membrane (no wall)
Smaller 1-2 μm (<i>E. coli</i>) (Implications for metabolism?)		10-100 μm –much larger
No organelles		Organelles- Cellular machinery in discrete compartments
Circular DNA		Nucleosomes- Protein/DNA complex, histones
Maybe?? Some cytoskeleton		Cytoskeleton- (Microtubules, actin, intermediate filaments...)
Larger surface to volume ratio therefore nutrients can enter cells rapidly		Much smaller surface to volume ratio and therefore mechanisms other than free diffusion required for nutrient movement within cell
Think about oxygen		