

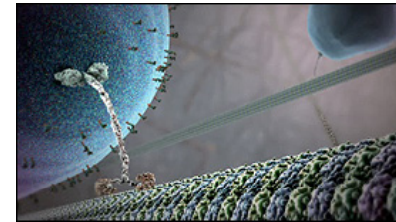
## Biochm 623

### Advanced General Biochemistry

<http://www-unix.oit.umass.edu/~bioch623/>

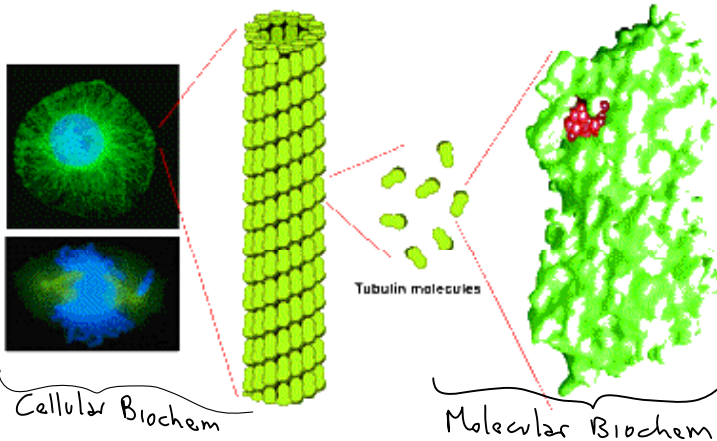
## Biochemistry

- Study the chemistry of life



Movie → check Web page

### Tubulin: From Cell Scaffold to Anti-Cancer Target



### Evolutionary and Genetic Origins of Protein Sequences

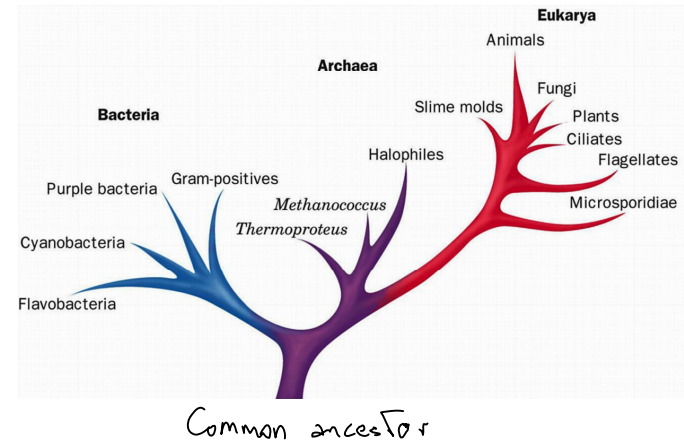
Voet-Voet Chapter 7.3A-7.3B  
Petsko-Ringe 4.0 to 4.3

} for reading

## A common ancestor

- All organisms are similar at the molecular level
- Why? →
  - same amino acids and nucleic acids
  - same metabolic pathways
  - all amino acids L-isomers
  - all DNA, RNA, riboses → D-isomers
- The higher the level of biochemical organization, the greater the molecular differences among species

## Phylogenetic tree



## Similar sequence imply descent from a common ancestor

- 1000 nucleotides (~333 aa)
  - $4^{1000}$  or  $10^{600}$  different sequences
  - $\sim 10^{79}$  atoms in the universe

100 amino acids

- $20^{100}$  or  $10^{130}$  different sequences

## Genes and proteins

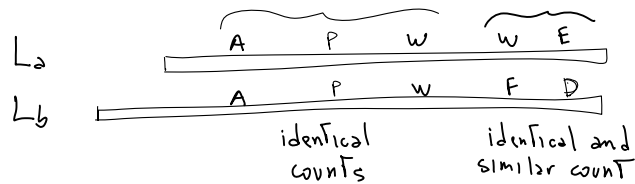
- When are they homologues?
- % similarity vs homology

Lys Arg  
 Asp Glu  
 Ser Thr  
 Tyr Phe Trp  
 Ala Val Leu Ile Met

## Similarity vs Identity

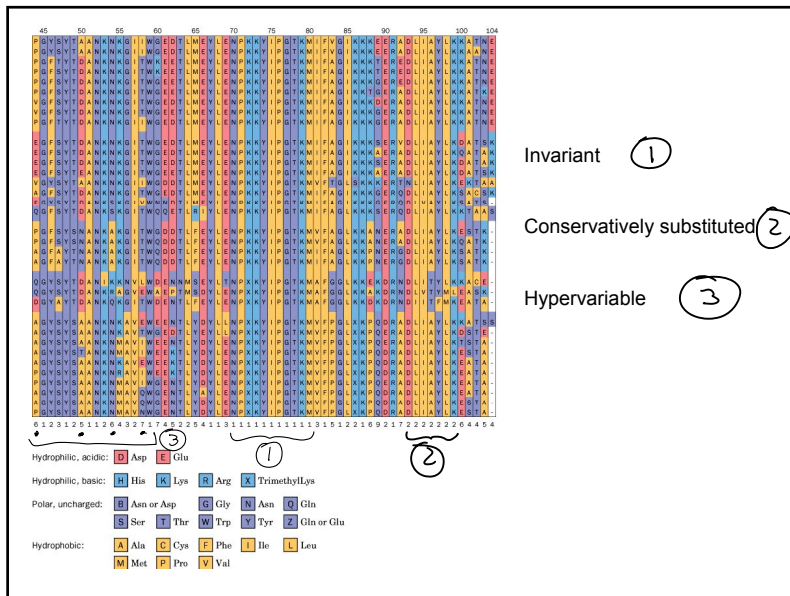
- % sequence similarity ( $L_a < L_b$ )  $L \equiv \text{length}$   
 $S = (L_s / L_a) \times 100$

- % sequence identity  
 $I = (L_i / L_a) \times 100$

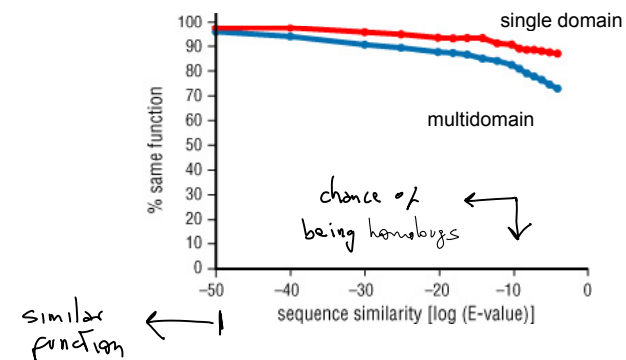


## Comparing homologous proteins

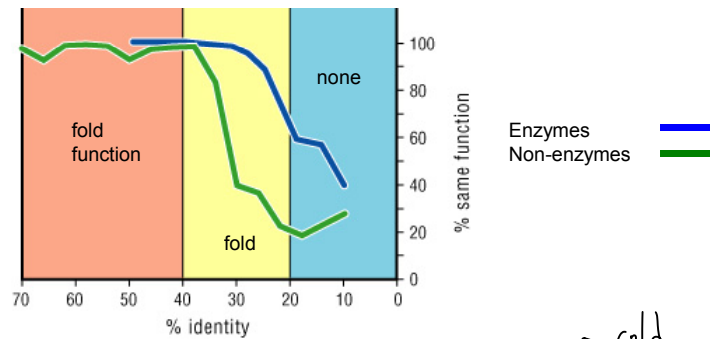
- Essential residues for its function  
*e.g. active sites of enzymes*
- Less significant  
*e.g. protein-membrane interaction*
- Little specific function  
*e.g. solvent-exposed loops*



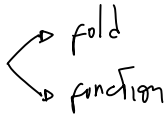
**E-values:** probability that the two sequences will have this degree of overall similarity by chance



## Functional assignment from sequence comparison



What can be predicted from sequence comparison?



## Genomics era

- Genomic analysis reveals a great number of proteins of unknown function
- Sequence and structural comparison provide useful, but limited information
- To fully characterize a protein function:
  - Purified protein *in vitro* <sup>1<sup>st</sup> part</sup>
  - Cell biological and mutational studies *in vivo* <sup>2<sup>nd</sup> part</sup>