



BIOC 384: M01.T04-Miesfeld

Assigned Reading: “*Biochemistry*” Chapter 1.4





Biomolecular Structure and Function

M01.T04-Miesfeld

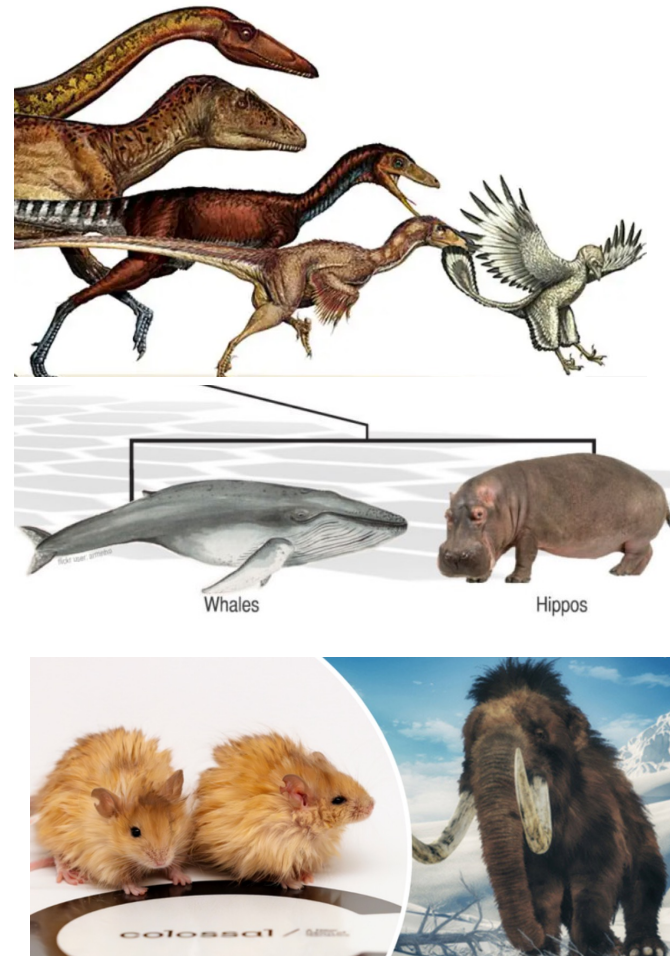


The Big Picture

- The intimate connection between molecular structure and function underlies all of biochemistry.
- While similar protein structures often have similar functions, this is not always the case as similar structures can have different functions and similar functions can have different structures.

Divergent evolution: two species with a common ancestor evolve specific traits to optimize life in their own unique environments which are very different; the whale in the ocean and the hippopotamus on land display divergent evolution.

Convergent evolution: two species that are unrelated or very distantly related evolve similar traits because they live in the same environment and natural selection drives adaptation; wings on bats and birds display convergent evolution.

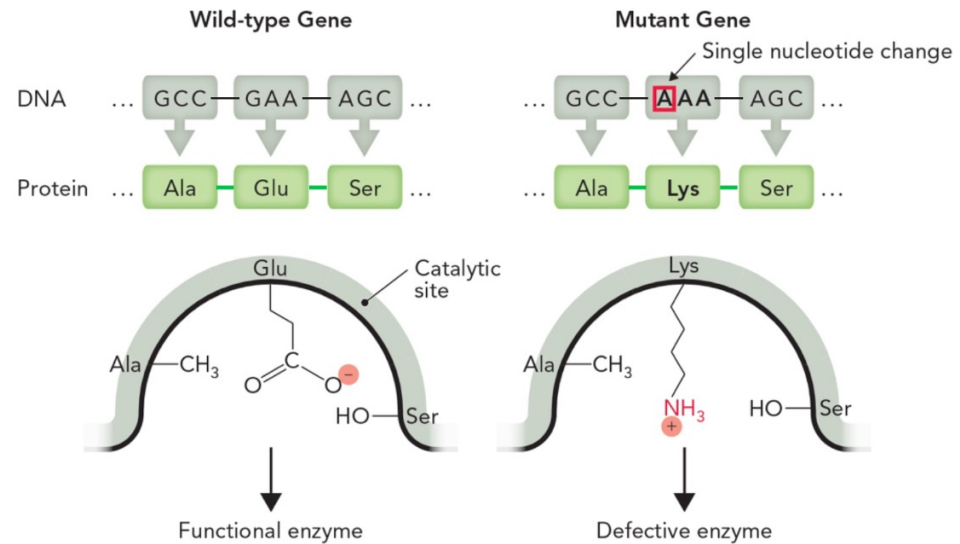


Divergent evolution; organisms with related common ancestors but adapted to unique environmental niches.



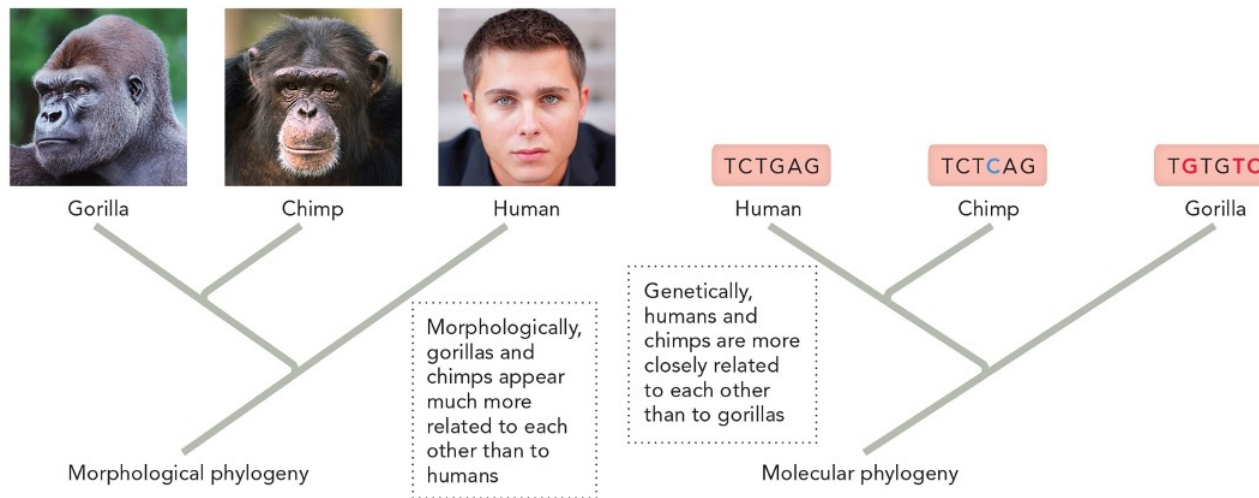
Evolution as a Molecular Experiment

- Evolutionary driving forces that create diverse protein structures result from nucleotide changes in the coding sequences of genes.
- Random mutations are “tested” by natural selection to determine fitness; beneficial mutations are retained whereas deleterious mutations are lost.



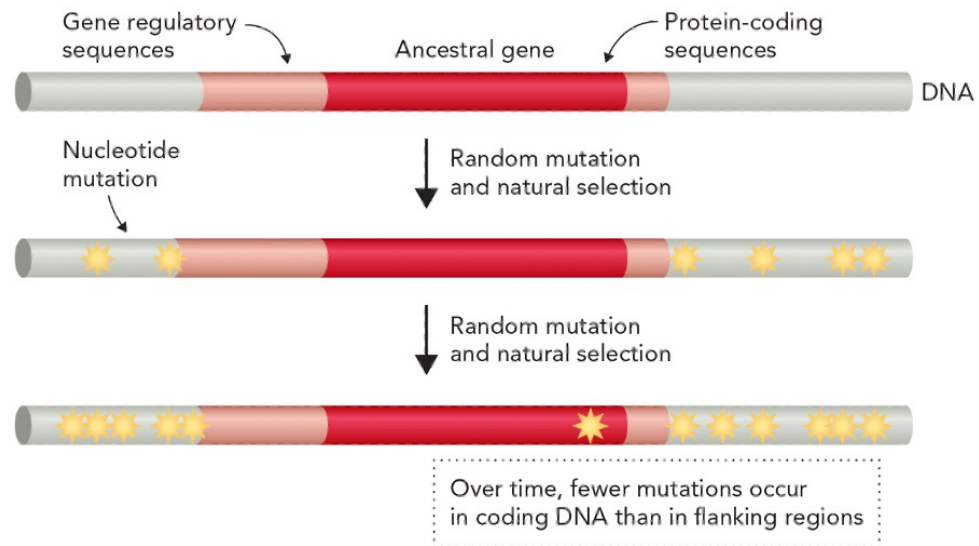
Bioinformatics: Evolutionary Relationships

- Bioinformatics uses computational analyses to compare nucleotide sequences that can reveal conserved and divergent amino acid sequences.
- On the basis of morphologies alone, it was thought that chimpanzees and gorillas were more closely related to each other than they were to humans.



Sequence Conservation Indicates Function

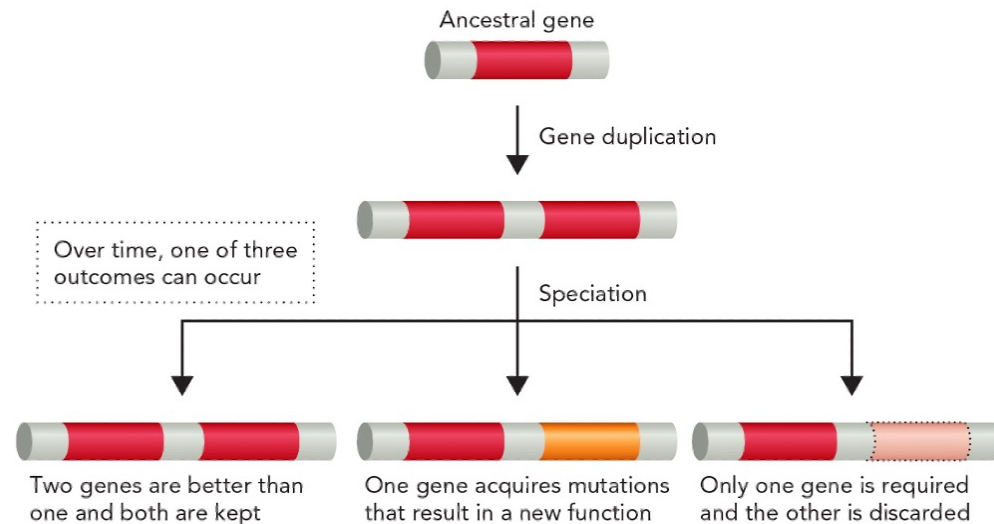
- Highly conserved regions often indicate structural or catalytic importance, especially within enzyme active sites.
- Random nucleotide mutations without an effect on gene expression accumulate in flanking DNA at higher rates than deleterious mutations that accumulate within genes.



Gene Duplication Drives Protein Evolution

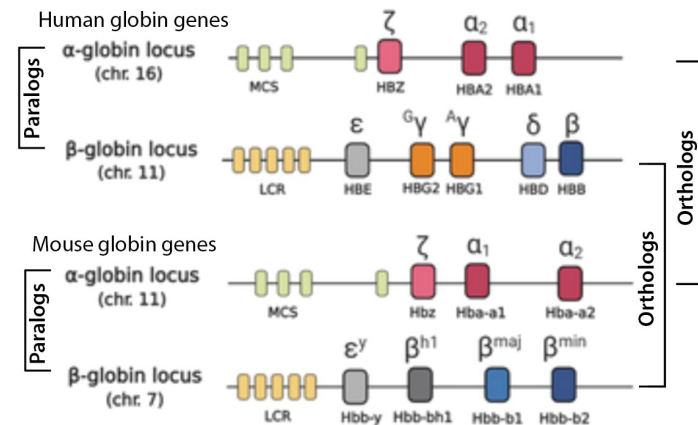
Duplication of an ancestral gene leads to three distinct outcomes.

- 1) The 2nd gene provides an evolutionary advantage.
- 2) The 2nd gene diverges and acquires a new beneficial function.
- 3) The 2nd gene diverges and acquires deleterious mutations.



Paralogous and Orthologous Genes

- Genes that share similar sequences within a species are paralogous genes such as the human α -globin and a β -globin cluster.
- Genes conserved across species such as the human and mouse α -globin and β -globin gene clusters are orthologous genes.



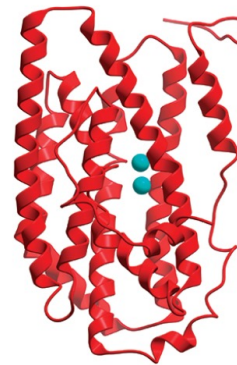
<https://doi.org/10.3389/fcell.2021.640060>



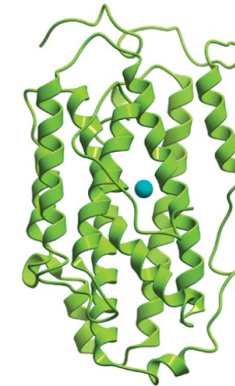
Similar Structure, Similar Function

- Protein structure of the enzyme ribonucleotide reductase has remained remarkably similar over the several billion years of evolutionary time separating bacteria and mammals.
- These two proteins consist of bundled α helices that have metal ions in the catalytic site of the enzyme.

a. Similar structure and function



Ribonucleotide reductase (bacteria)



Ribonucleotide reductase (mouse)



Chocolate donut

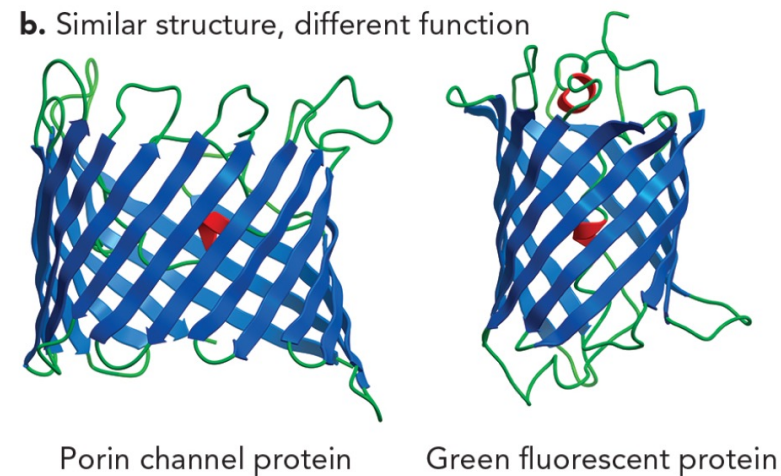


Everything bagel



Similar Structure, Different Function

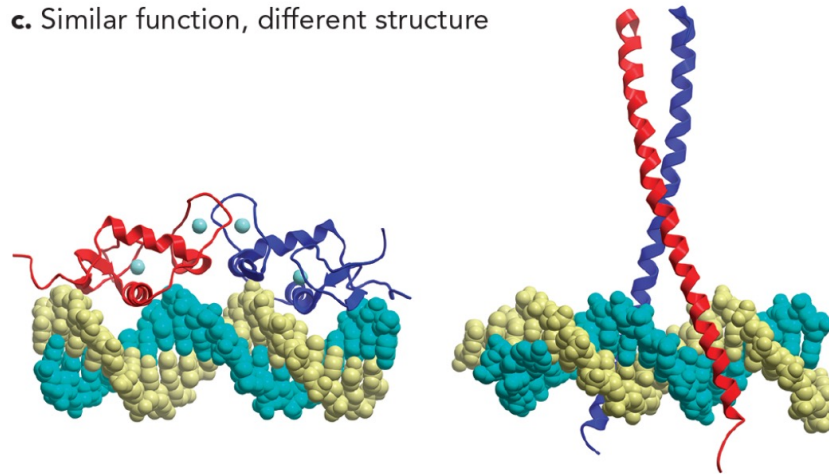
- The bacterial porin channel protein has a β barrel structure that forms a water-filled pore in the outer bacterial membrane.
- The green fluorescent protein also contains a β barrel but it functions as a scaffold to position the intrinsic chromophore.



Similar Function, Different Structure

- The glucocorticoid receptor is a transcription factor that uses short α helices to form high-affinity contacts with nucleotide bases in target.
- The GCN4 transcription factor protein also binds DNA with high specificity and affinity but uses two α helices to bind into the DNA major groove.

c. Similar function, different structure



GR transcription factor

GCN4 transcription factor



A motorcycle



An automobile

Key Concepts to Guide Your Learning

- Structure determines function in chemistry and biology.
- Evolution through natural selection influences macromolecular structure and function.
- DNA mutations in protein coding genes can alter protein structure and function depending on the type of mutation.
- Gene duplications lead to the evolution of paralogous (within species) and orthologous (between species) genes.
- Protein structure–function relationships are of three types: same structure and function, similar structure and different function, and similar function, different structure.

