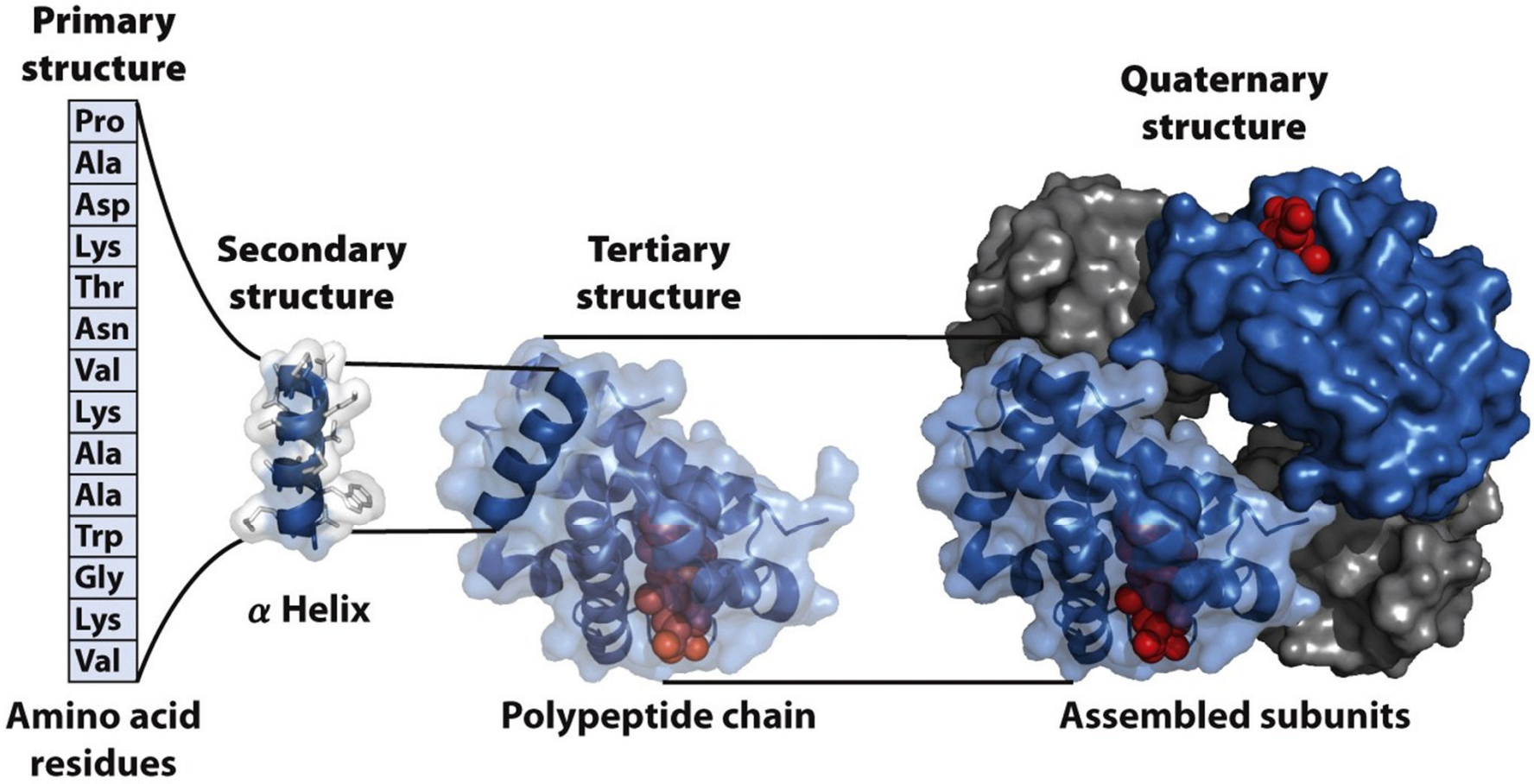
There are four levels of structure in proteins



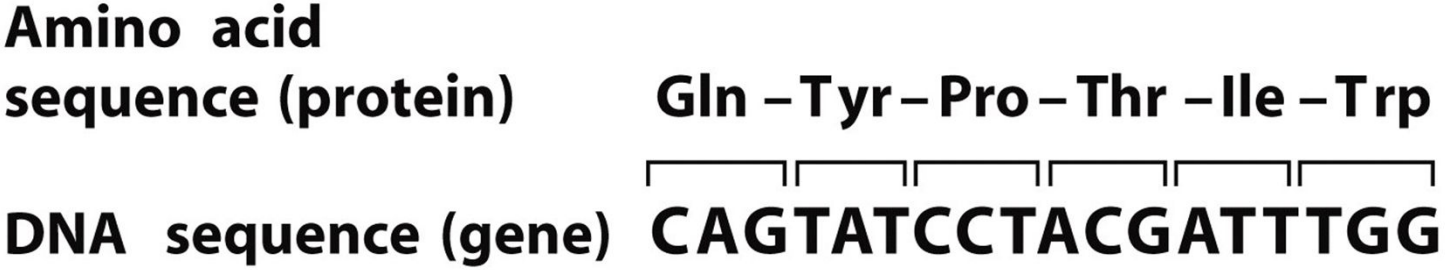
We know that sequence → structure, but we can't (yet) predict a structure from a sequence. So what good is knowing the sequence?

We can learn about proteins by *comparing* their sequences:

- **Structure** – similar sequences form similar structures
- **Function** – motifs (sequence patterns) can indicate particular functions
- **Location** – signal sequences (at the protein's N-terminus) direct proteins to specific locations in the cell, or to be excreted
- **Modification** – signal sequences or motifs can indicate sites for modification
- **Evolution** – differences in related sequences reflect evolutionary distance
- **Dysfunction** – changes in sequence can lead to disease

How do we determine a protein's sequence?

- Directly from the protein
  - Chemical sequencing
  - Physical methods for analyzing structure
- From the gene sequence

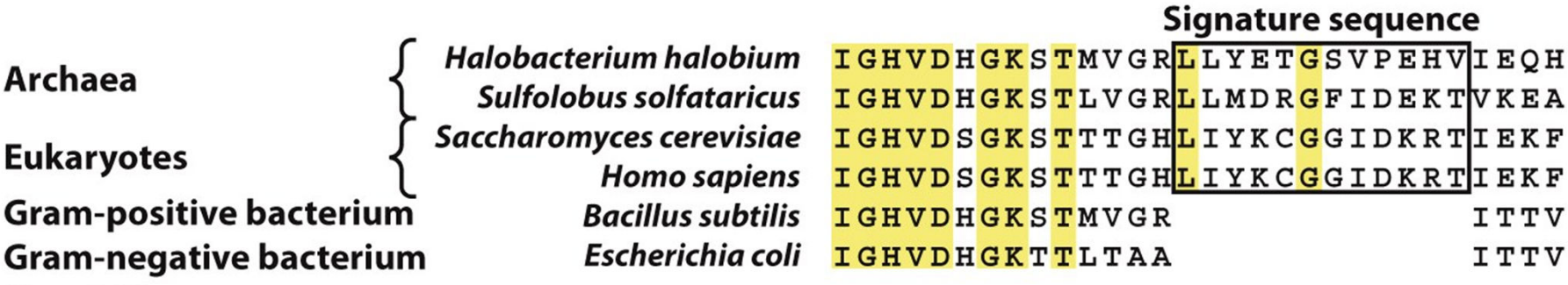


Important protein sequence databases

- RefSeq (NCBI) – “Reference Sequence”
  - Non-redundant database of well-annotated sequences (gene, transcript, protein)
  - http://www.ncbi.nlm.nih.gov/projects/RefSeq/
  - Can also use ‘Entrez’ at NCBI site to search multiple sequence databases
- UniProt (EBI) – “Universal Protein Resource”
  - Protein sequences and annotations, plus links to other databases
  - http://www.uniprot.org/

Proteins are aligned for comparison

Sequence alignments:



Consensus sequences, showing conserved sites, may be represented in different ways