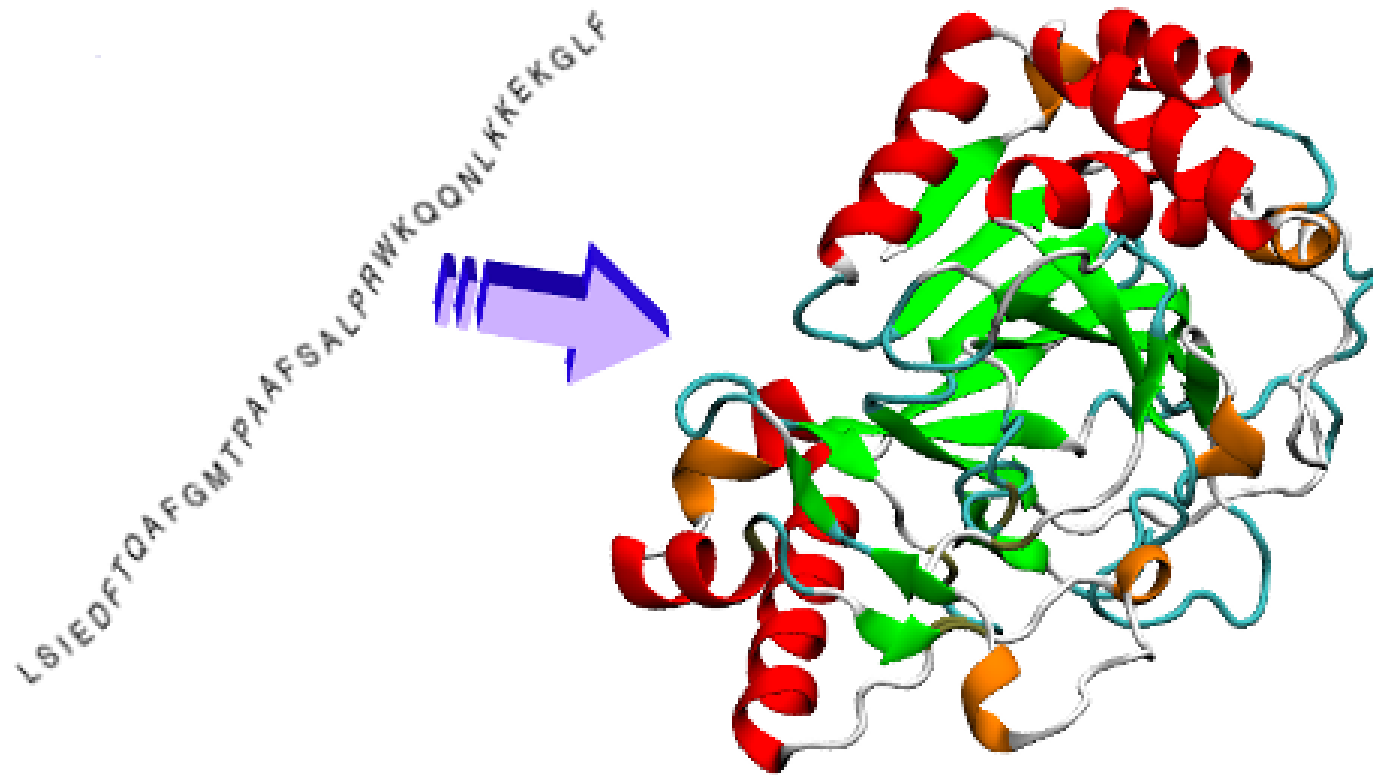


**Bioinformatics**  
**CS300**  
**Prediction and**  
**Modeling Protein Structure**

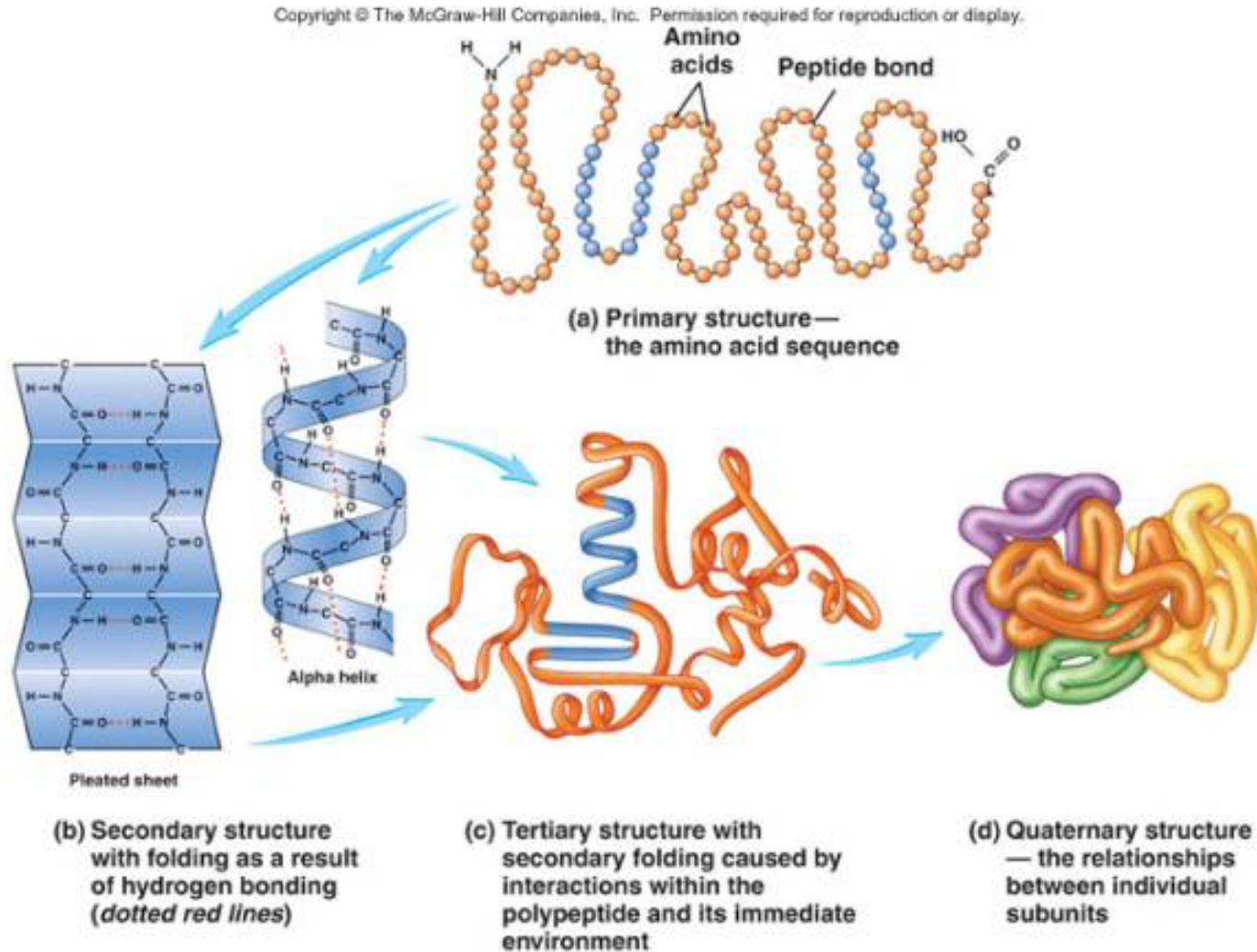
**Fall 2017**  
**Oliver Bonham-Carter**

# Protein Folding



- linear chain of amino acids produced by ribosome during translation
- folds into functional, 3D state based on properties of amino acids and structure

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# Supporting Videos

- Protein Folding (3 mins)
  - <https://www.youtube.com/watch?v=yZ2aY5lxEGE>
- What is a protein? (3D shape and function, 3 mins)
  - <https://www.youtube.com/watch?v=qBRFIMcxZNM>
- Protein folding simulation (3 mins)
  - <https://www.youtube.com/watch?v=meNEUTn9Atg>



# Protein Folding - Applications

- **Protein must fold correctly to function**
- Misfolded proteins
  - Accumulation – Huntington's and Parkinson's disease
  - Tagged for degradation – emphysema, cystic fibrosis
    - Pharmaceutical chaperones – fold mutated proteins to render them functional
- Antiviral drug development
  - Antibiotics vs antivirals
    - Bacteria – cells
    - Viruses – invade host's cells



Bacteria

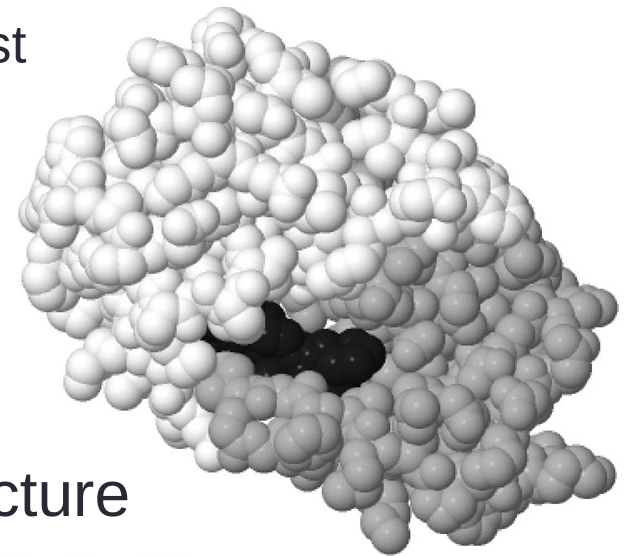
VS.



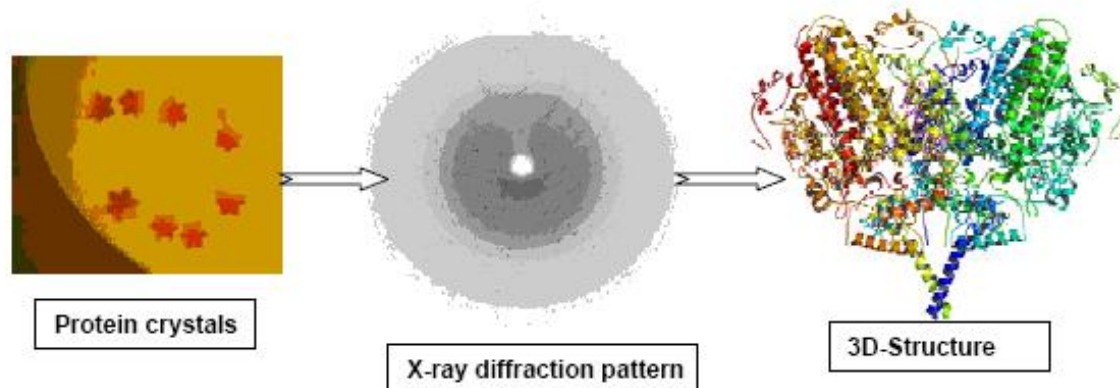
Virus

# Protein Folding - Applications

- Antimicrobial Drugs: helps to...
  1. Be effective against the disease-causing agent
  2. Be selectively toxic
    - kill or inhibit the microbe without harming the host
- Rational Drug Design: helps to...
  - Understand 3-D structure of viral proteins
  - Design drugs to fit protein and block function



Laboratory – challenging to predict 3-D structure





# Genomics & Computational Structural Biology

## Genomics

- Determines the ordered sequence of nucleotides in a genome
- Assigns predicted functions to regions of nucleotides via annotation

## Computational Structural Biology

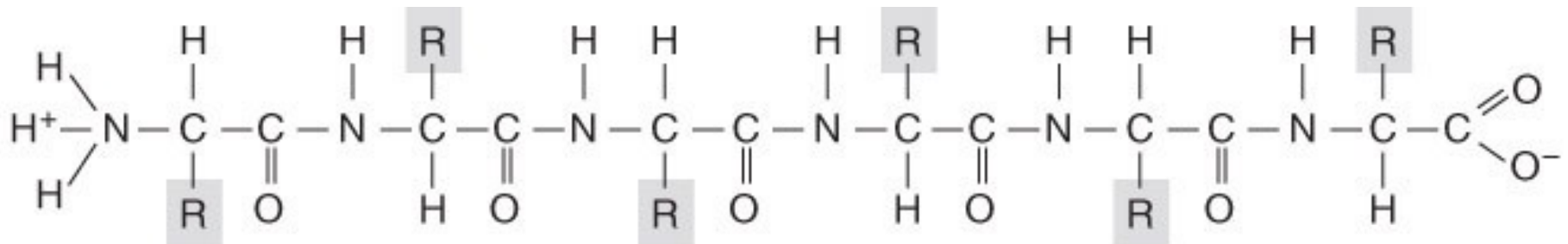
- Takes predicted gene sequence for translation into primary amino acid sequence
- Predicts 3-D protein structure based on primary amino acid sequence
- Note: this step is very difficult because the number of possible outcomes to process and consider is enormous
- The study of structural rules and their contribution to the final mature protein.



# Structural Rules for Protein Folding

- Linus Pauling – Studied the limitations on protein folding
  - Nature of chemical bonds between amino acids
  - Bond angles
  - Rotation of atoms
  - Flexibility of side chains

Christian B. Anfisen – Studied the influence of thermodynamics of cellular environment



**(A) Primary (1°) structure**





# Protein folding : an idea of structure

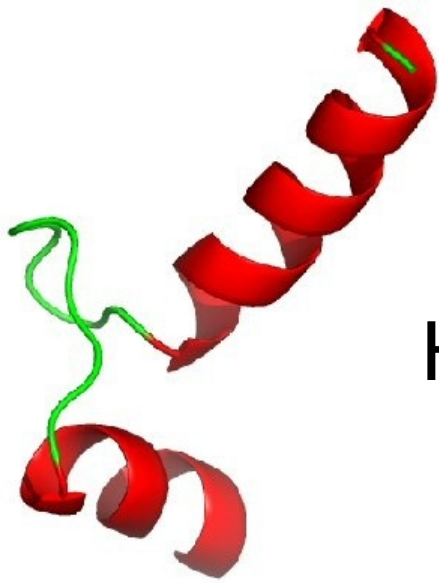
- Garnier (a text-based, command-line tool)
  - Inputs protein sequence in fasta format
  - Outputs a model of folding in text base
  - **Usage: garnier file.fasta**

```
      .   10   .   20   .   30   .   40   .   50
      MQIFVKLTGKTTITLEVEPSDTIENVKAKIQDKEGIPPDQQLIFAGKQL
helix  HH                      HHHHHHHHHHHH                      H
sheet  EEEE          EEEEE                                     EEEEE
turns  T                                     TTTT  TT
coil   CCC CC          CCC                                     CC          CCCCC
      .   60   .   70
      EDGRTLSDYNIQKESVNHLVLRRLGG
helix  HHH HHH
sheet  EEEEE
turns  TTTT  TT          TTT
coil   CCC  CC  C

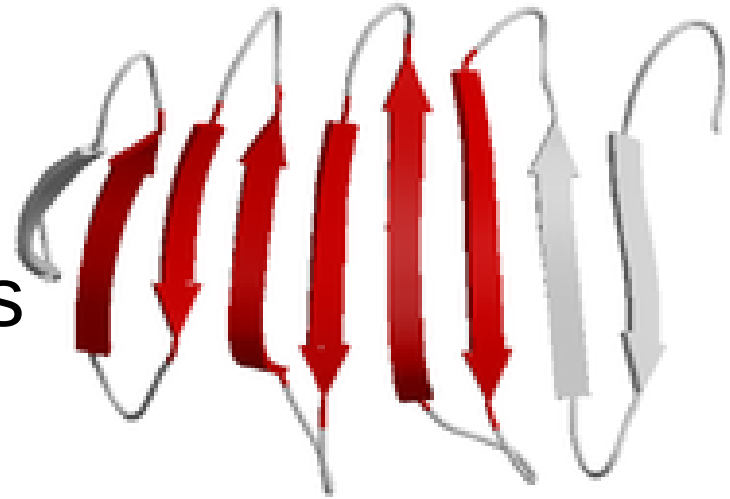
#-----
#
#  Residue totals: H: 20   E: 19   T: 16   C: 21
#                   percent: H: 33.3 E: 31.7 T: 26.7 C: 35.0
#-----
#
```

**H: Helices**  
**E: Sheets**  
**T: Turns**  
**C: Coils**

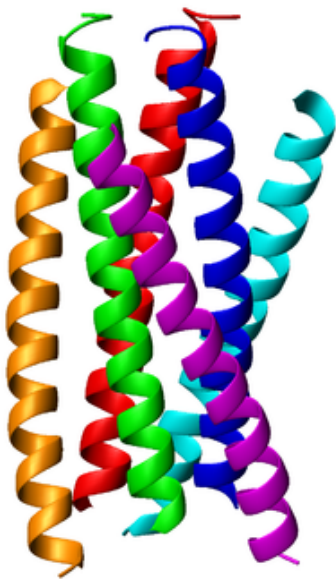
# Parts of Protein (Structures)



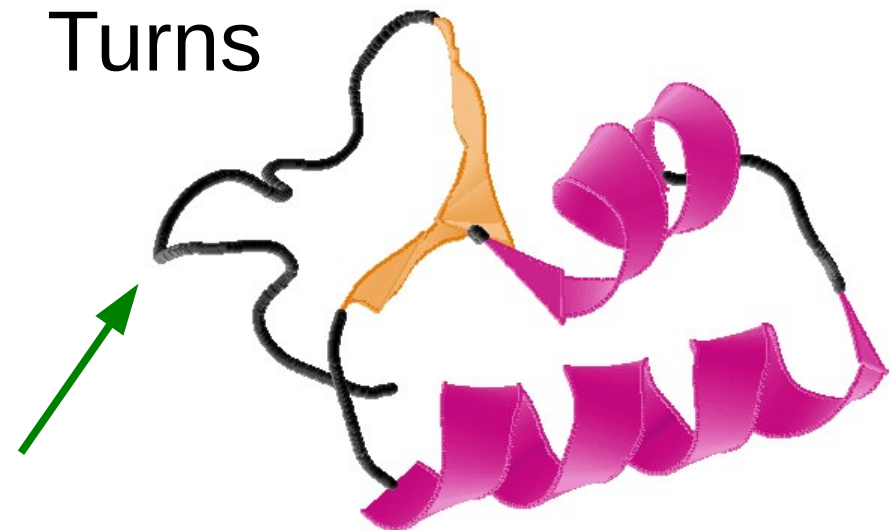
Helices



Sheets

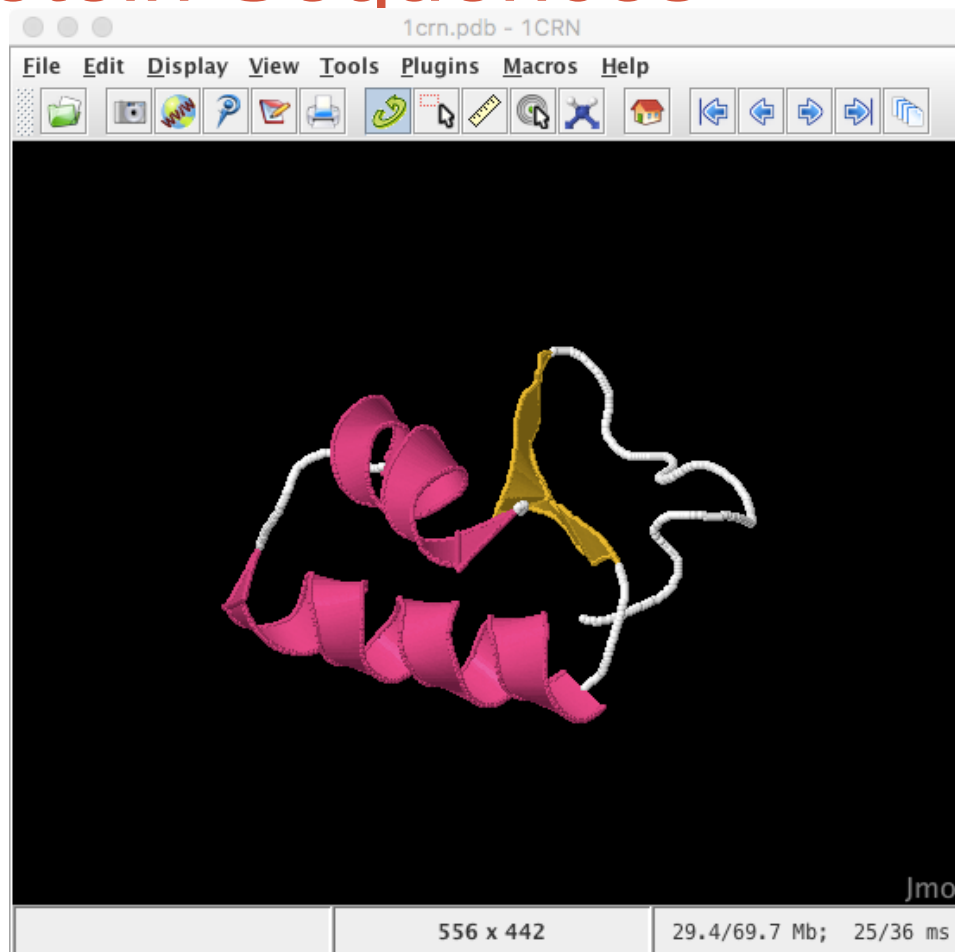


Coils



Turns

# Jmol: A Graphical Viewer For Protein Sequences



- <http://jmol.sourceforge.net/>
- [http://wiki.jmol.org/index.php/Jmol\\_Application#Installing\\_Jmol\\_Application](http://wiki.jmol.org/index.php/Jmol_Application#Installing_Jmol_Application)

# Protein DataBase (PDB)

- Database for 3-D structural data of large biological molecules
- <https://www.rcsb.org/>
- Data is viewable using jmol.

