

BME – 202

Molecular Biology and

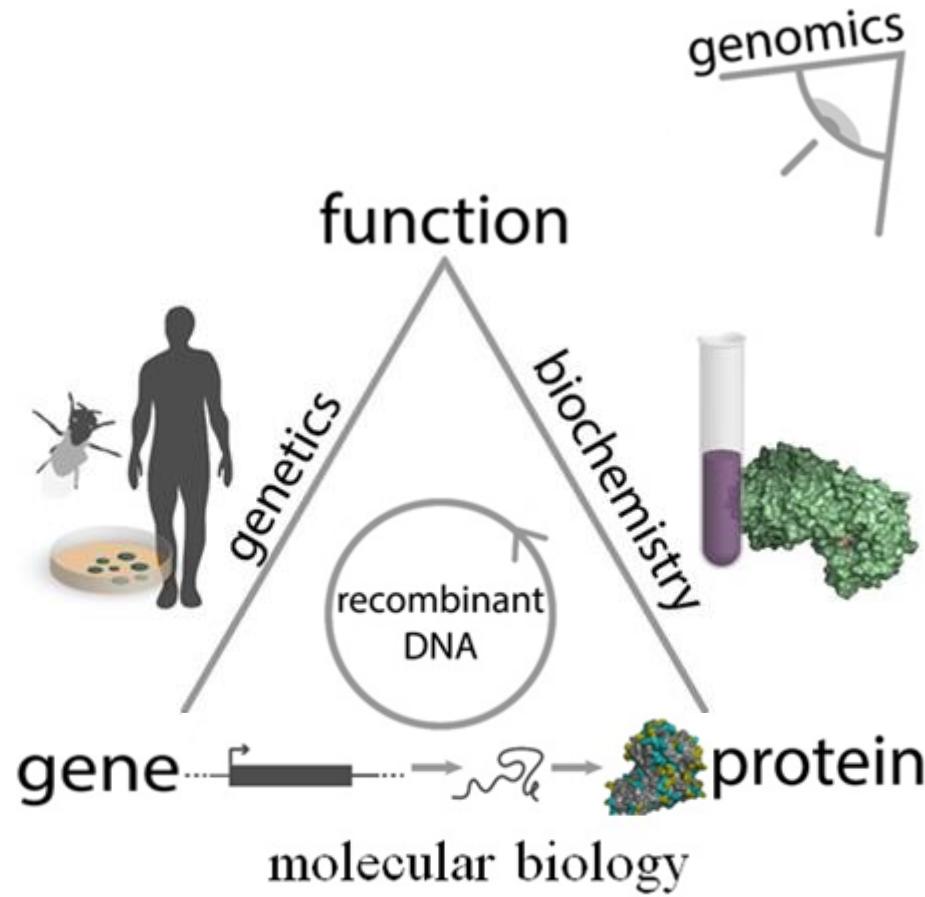
Genetics

Abeer Syed

Department of Biomedical Engineering
King Faisal University

- Proteins; Carbohydrates; Lipids; Nucleic acids – DNA and RNA.

Unit 3: Macromolecules



Introduction to Biochemistry

Sera Thornton, © 2013 Broad Institute

- **Unit 3: Macromolecules** – Proteins; Carbohydrates; Lipids; Nucleic acids – DNA and RNA.

Macromolecules



MinION

- Pocket-sized, portable device for biological analysis
- Up to 512 nanopore channels
- Simple 10-minute sample prep available
- Real-time analysis for rapid, efficient workflows
- Adaptable to direct DNA or RNA sequencing

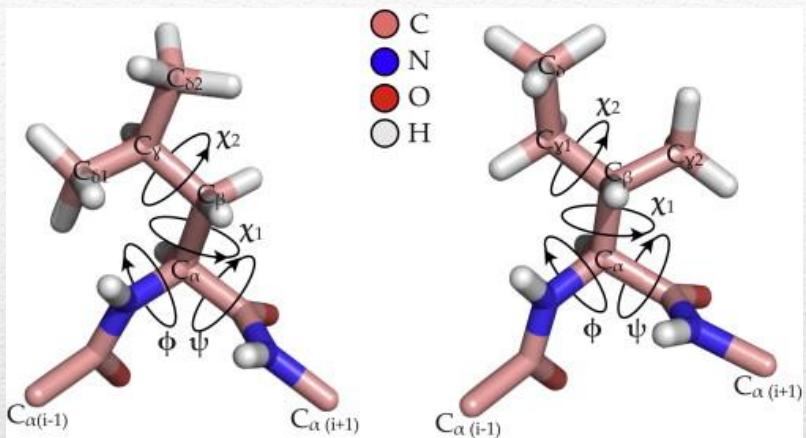
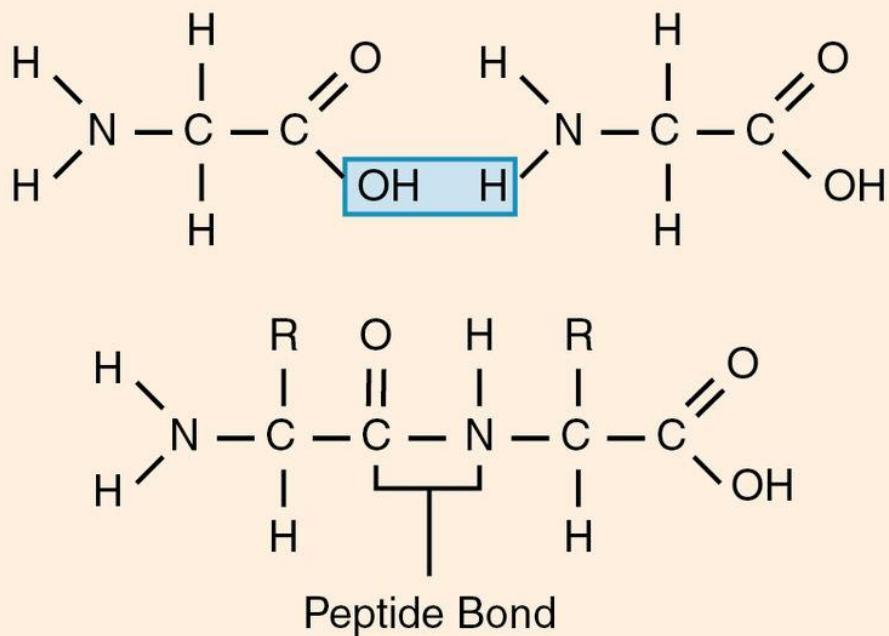
[About MinION](#)[Start using MinION](#)

Choose MinION if you:

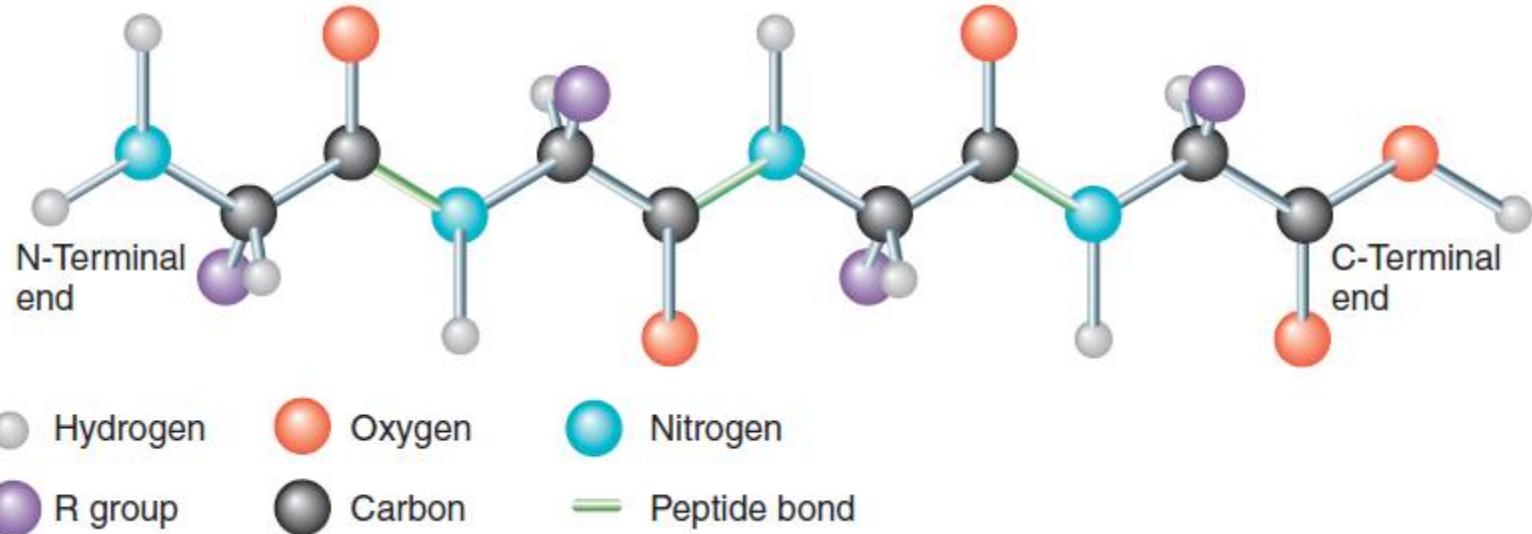
- would like access to sequencing for \$1,000
- want to sequence immediately, not wait
- want to sequence outside a lab
- need 10–20Gb per 48 hours
- want to avoid CapEx investments.

Nanopore sequencing and assembly of a human genome with ultra-long reads

Jain et al., (29 Jan 2018); Nature Biotechnology



Peptide Bond



Proteins – Primary Structure

hydrophobic



polar; uncharged



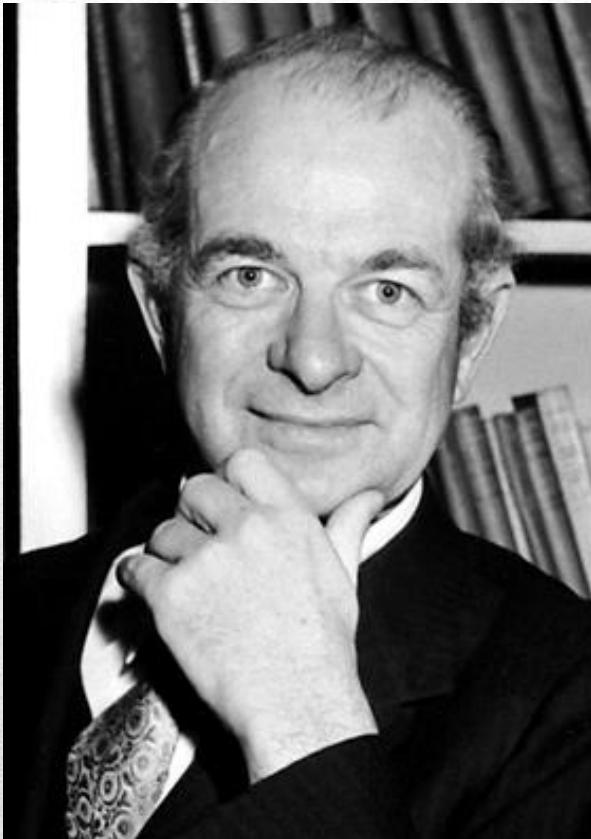
special



+ polar; charged



Amino Acids



Linus Carl Pauling

Born: 28 February 1901, Portland, OR, USA

Died: 19 August 1994, Big Sur, CA, USA

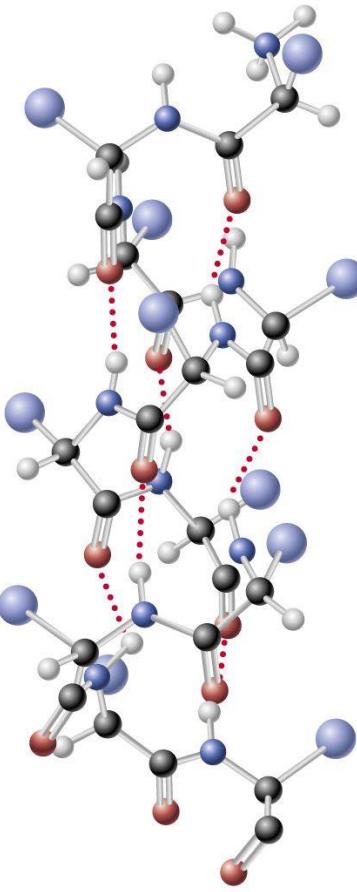
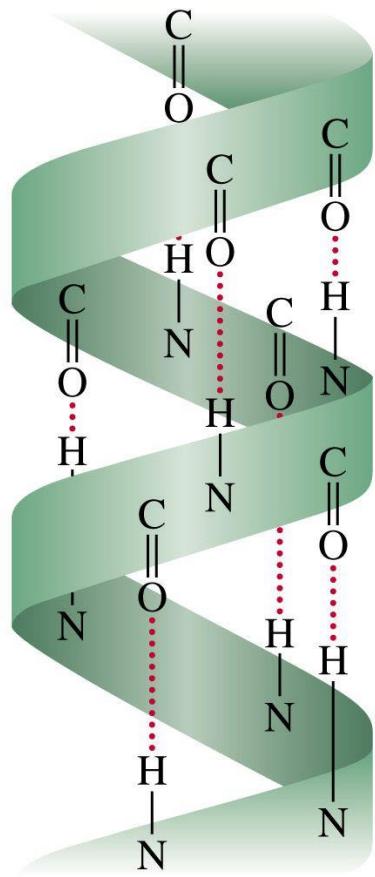
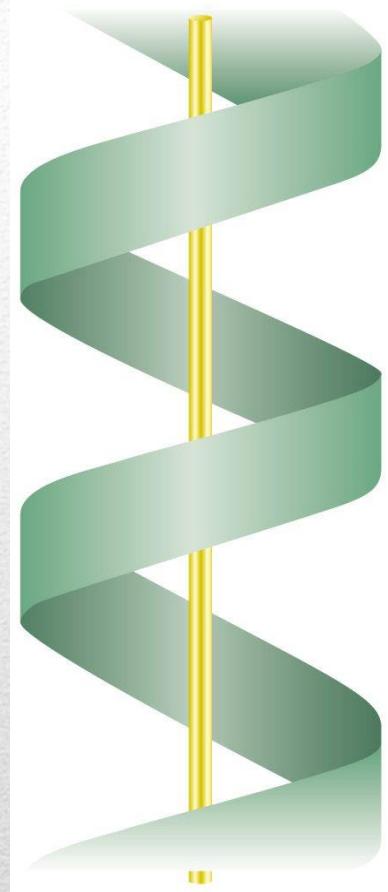
Affiliation at the time of the award: California Institute of Technology (Caltech), Pasadena, CA, USA

Prize motivation: "for his research into the nature of the chemical bond and its application to the elucidation of the structure of complex substances"

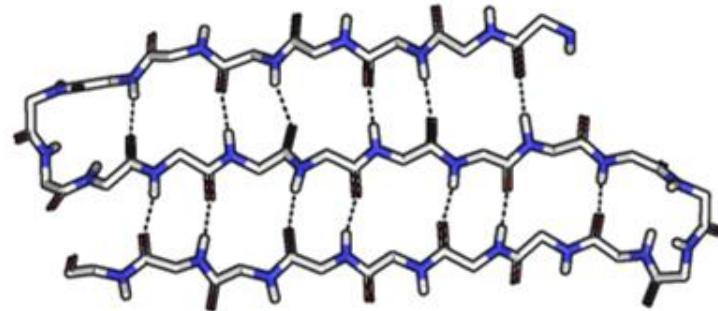
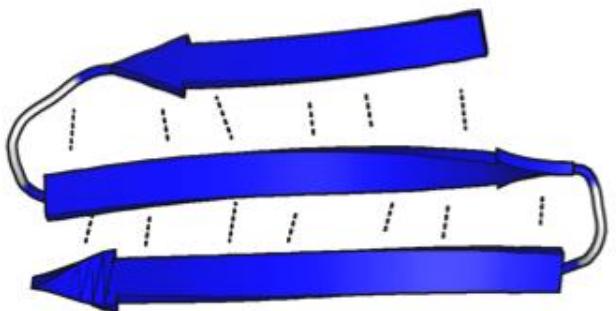
Field: chemical bonding, theoretical chemistry

Prize share: 1/1

Secondary Structure

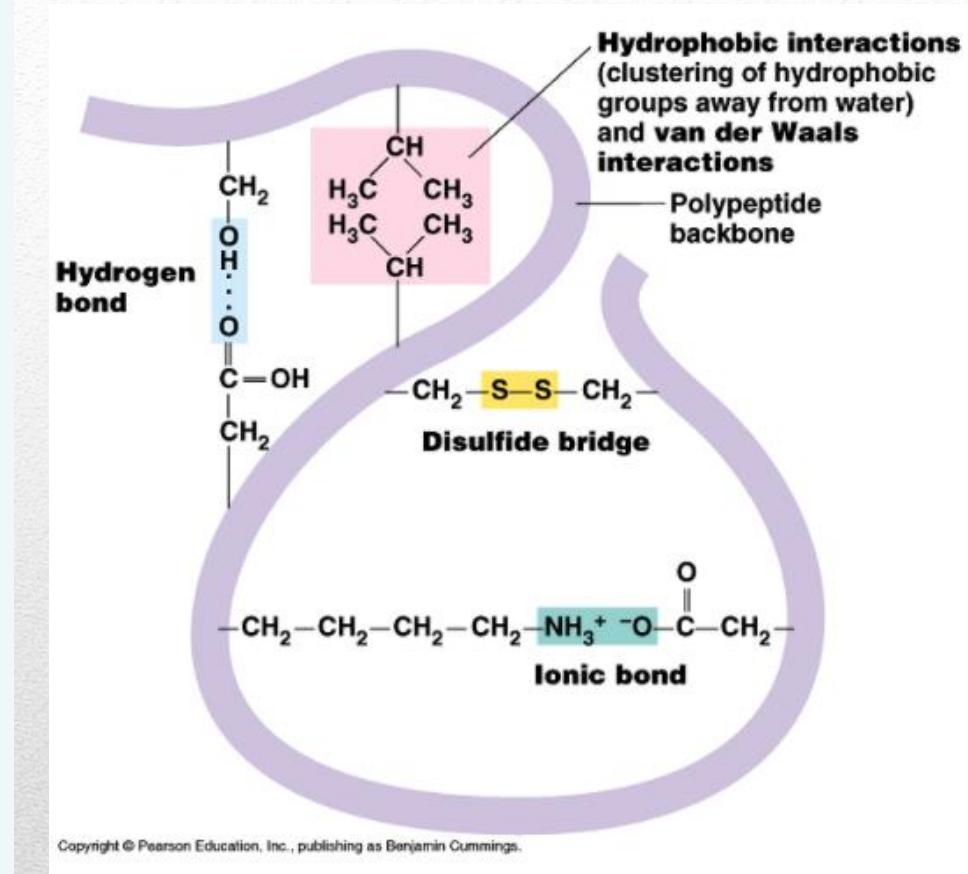
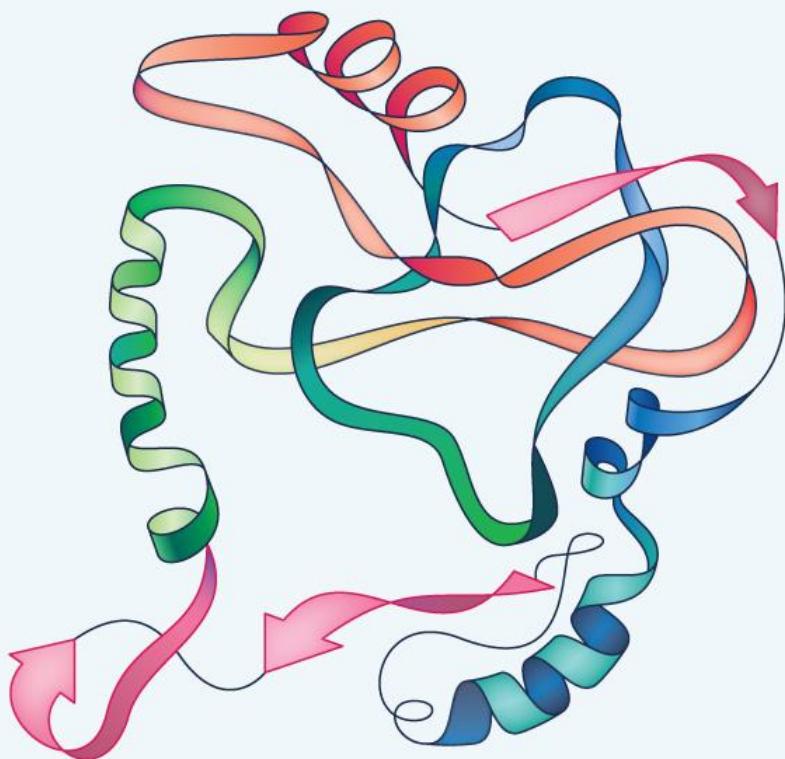


α Helix



β -Sheet (3 strands)

β - Sheets



Tertiary Structure

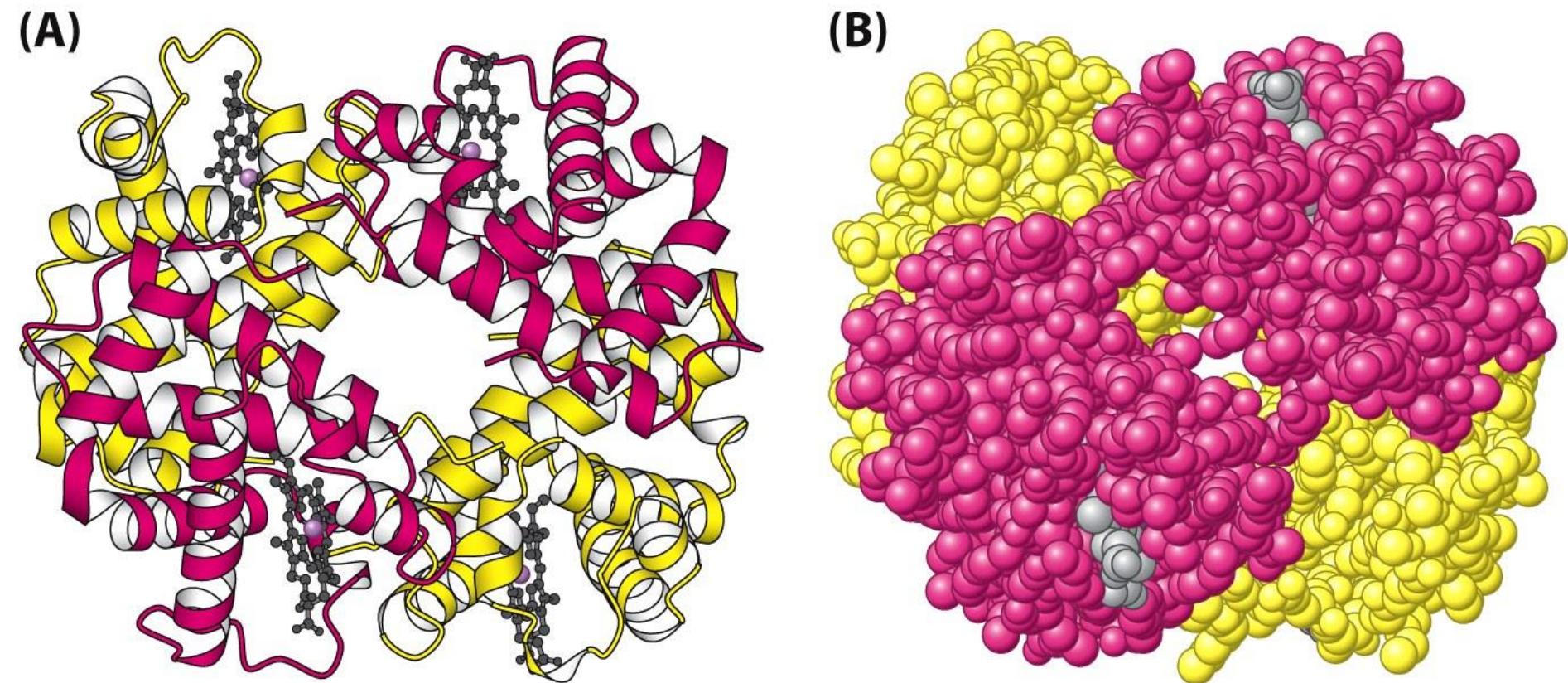
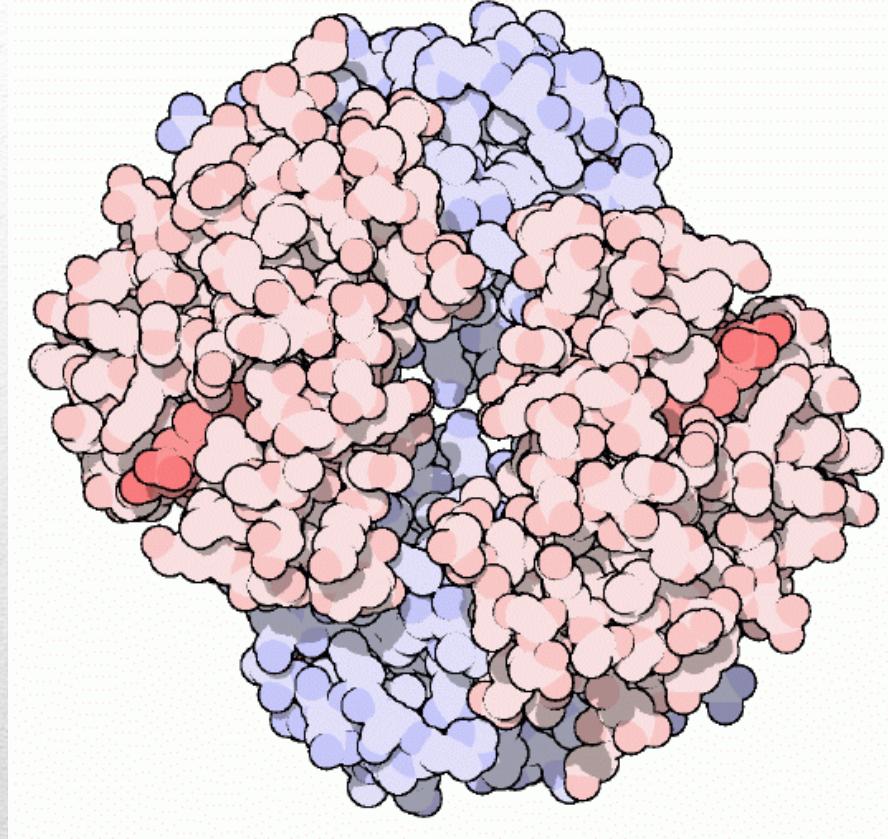


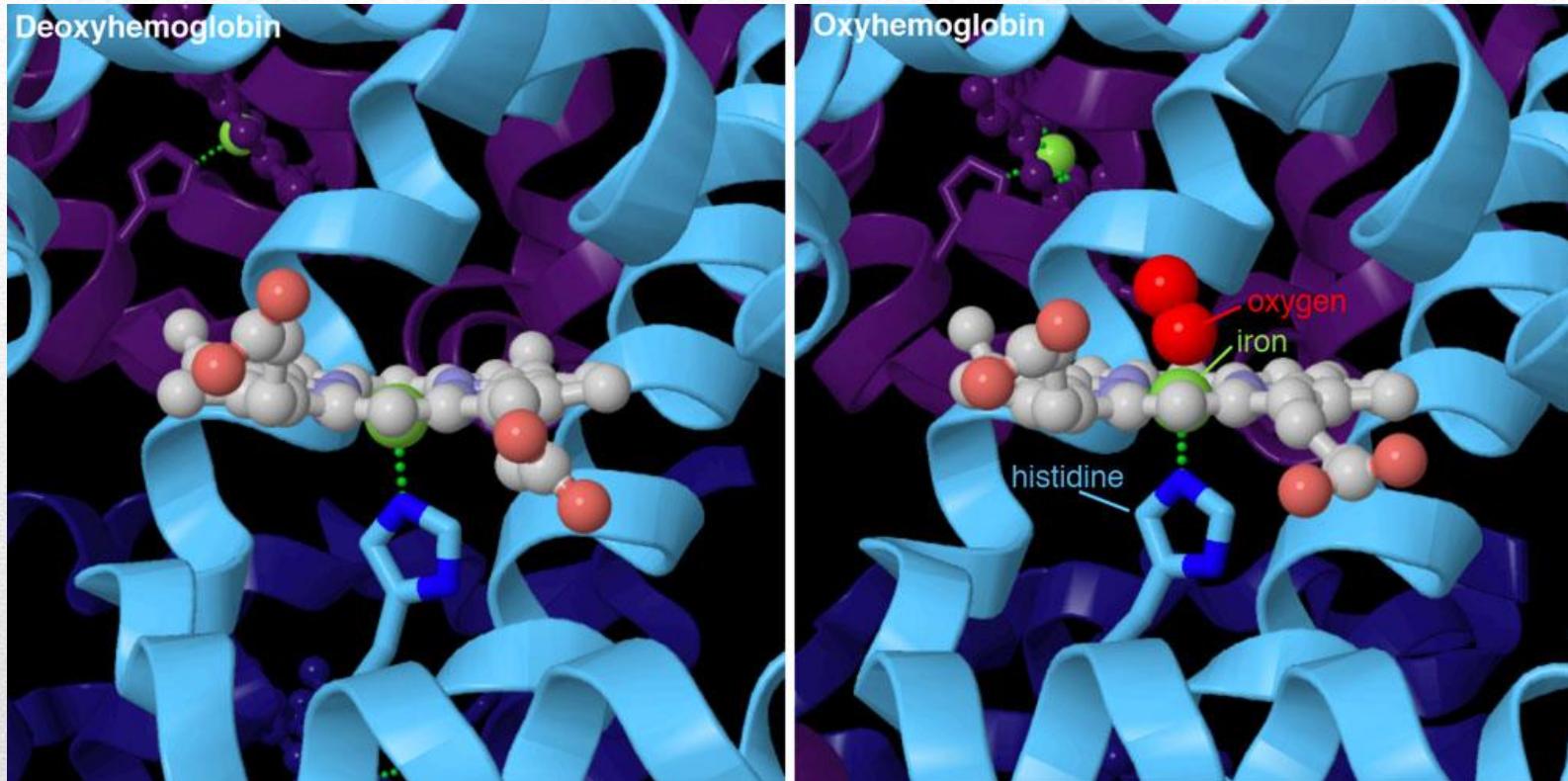
Figure 2.49
Biochemistry, Seventh Edition
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Quaternary Structure

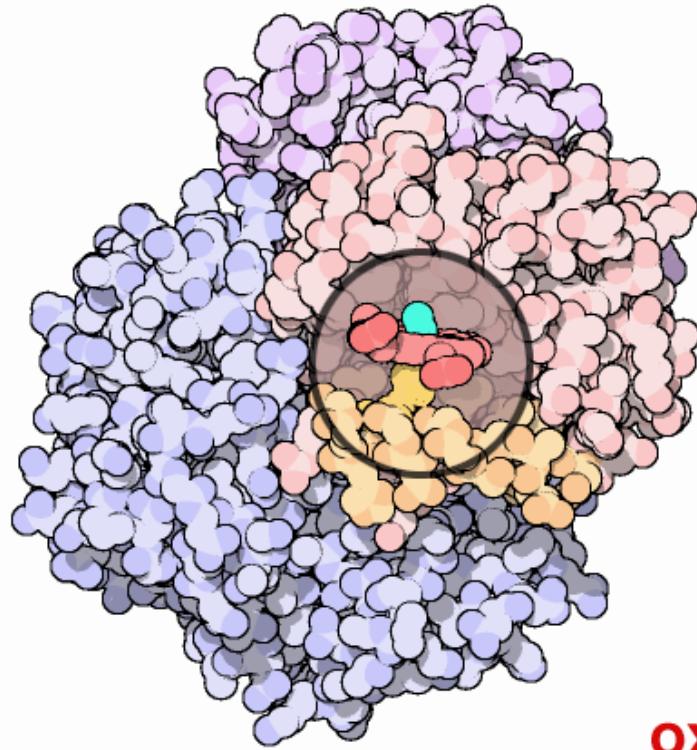


Hemoglobin, with hemes in red.

Hemoglobin



Deoxy and Oxy States of Hemoglobin



Deoxy and Oxy States of Hemoglobin

Porins are found in the outer membranes of Gram-negative bacteria, mitochondria and chloroplasts, where they form ion-selective channels for small hydrophilic molecules (up to ~600 D).

Porin

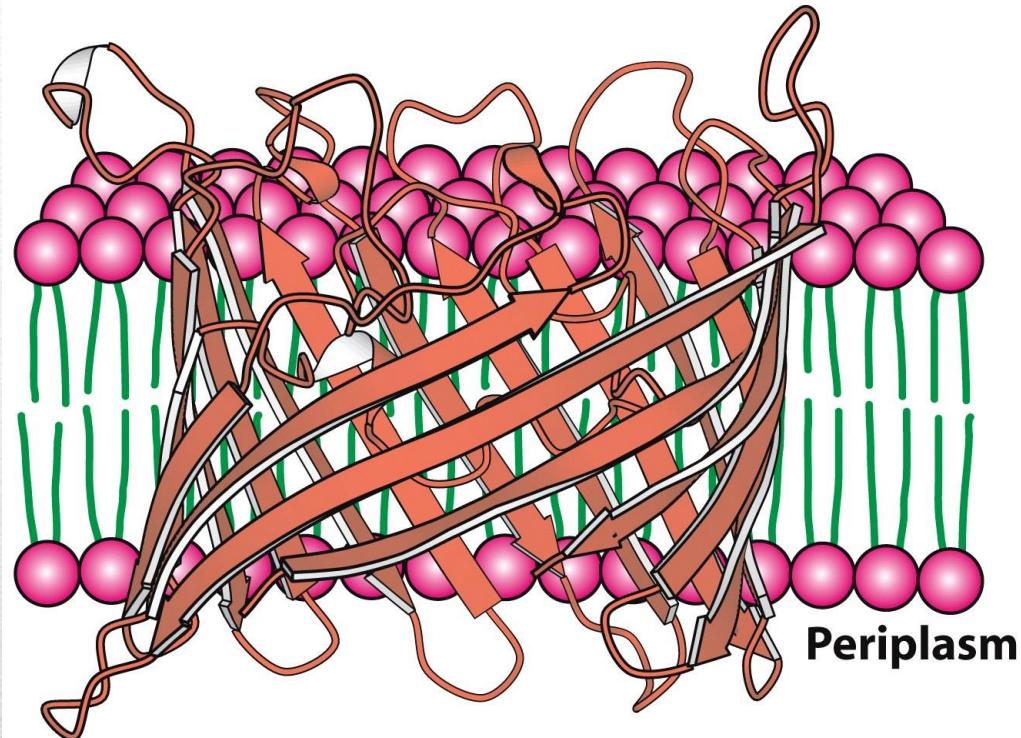
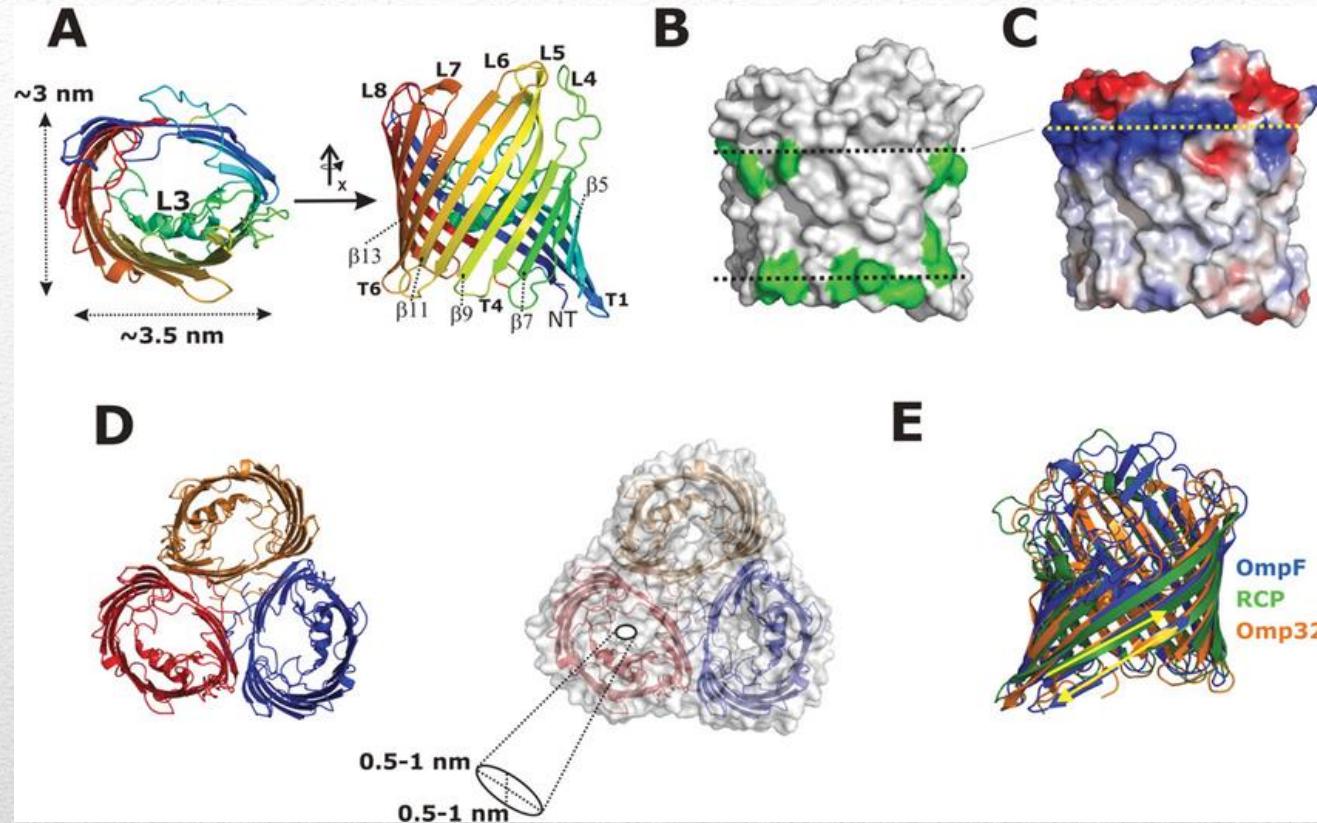
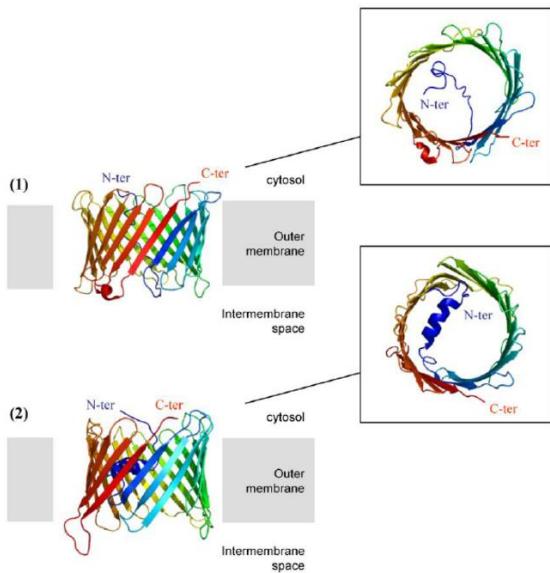


Figure 12.20a
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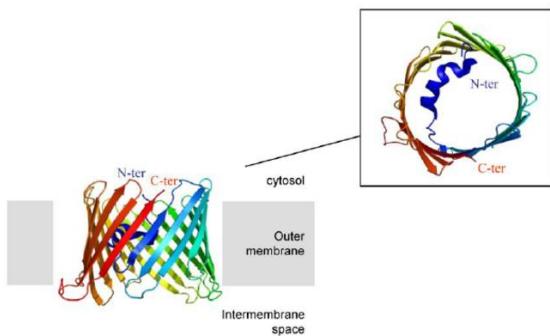


Bacterial Porin

(a)



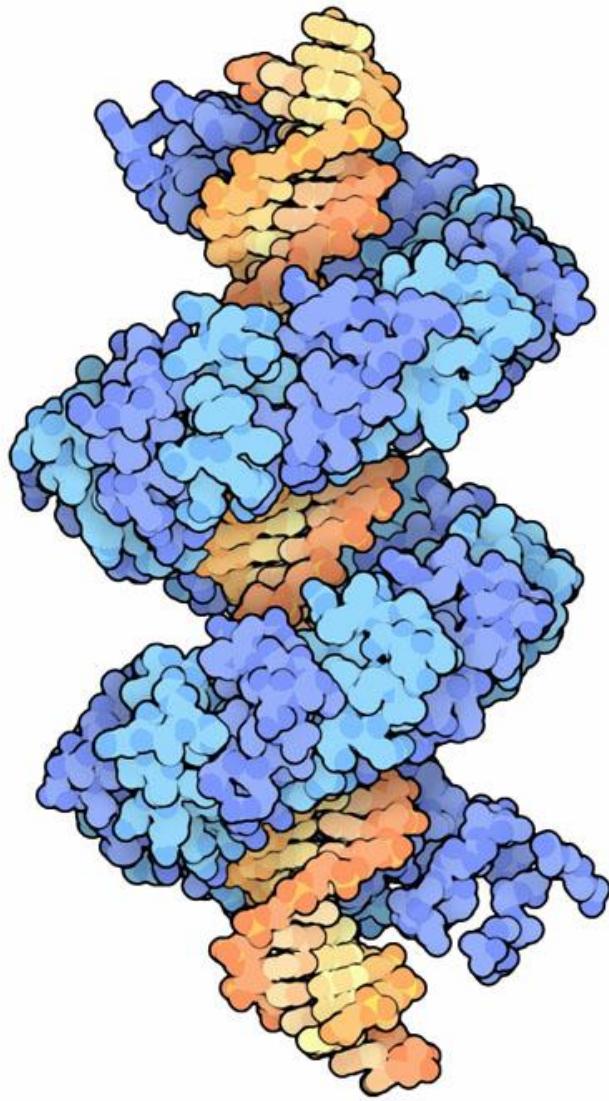
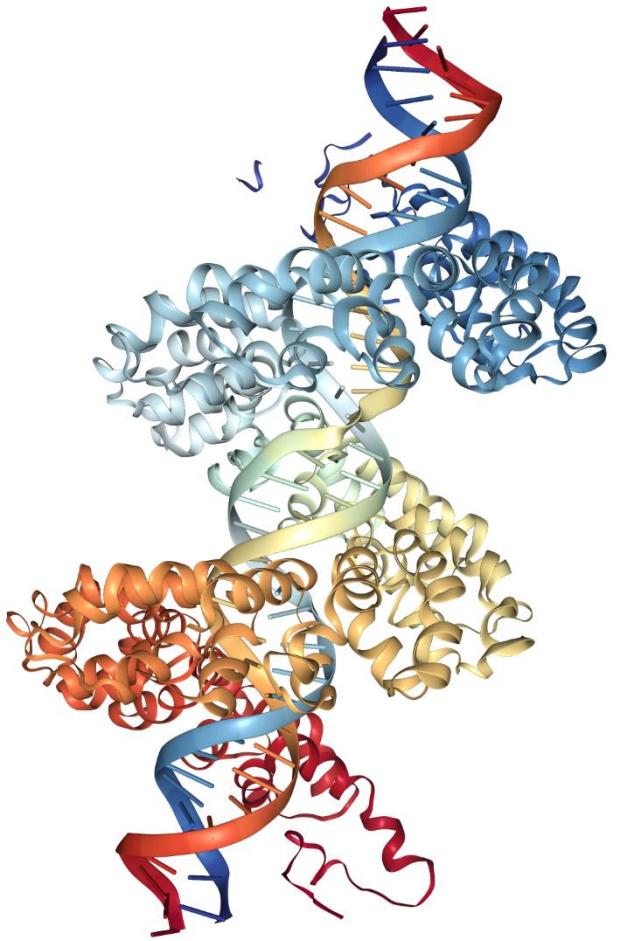
(b)



Mitochondrial Porin

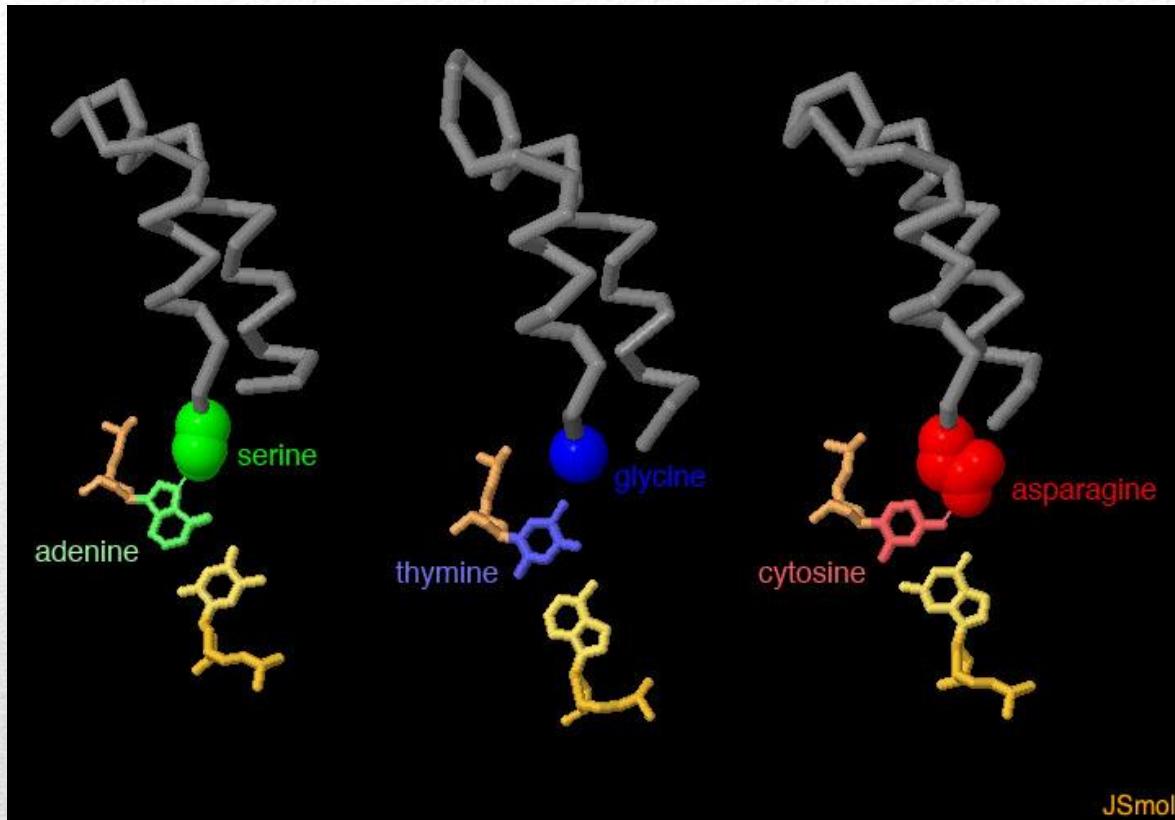
- TAL (transcription activator like) effector is a modular protein that can read the sequence of nucleotides in DNA. Structural understanding of this protein opens the door to all manner of applications in medicine and biotechnology.
- We can now customize a protein to read any DNA sequence that we desire, and thus target the protein to specific places in a genome. Already, these sequence-reading proteins are being used to create the tools for genome editing, as a possible way to correct genetic diseases.

TAL Effector



TAL Effector

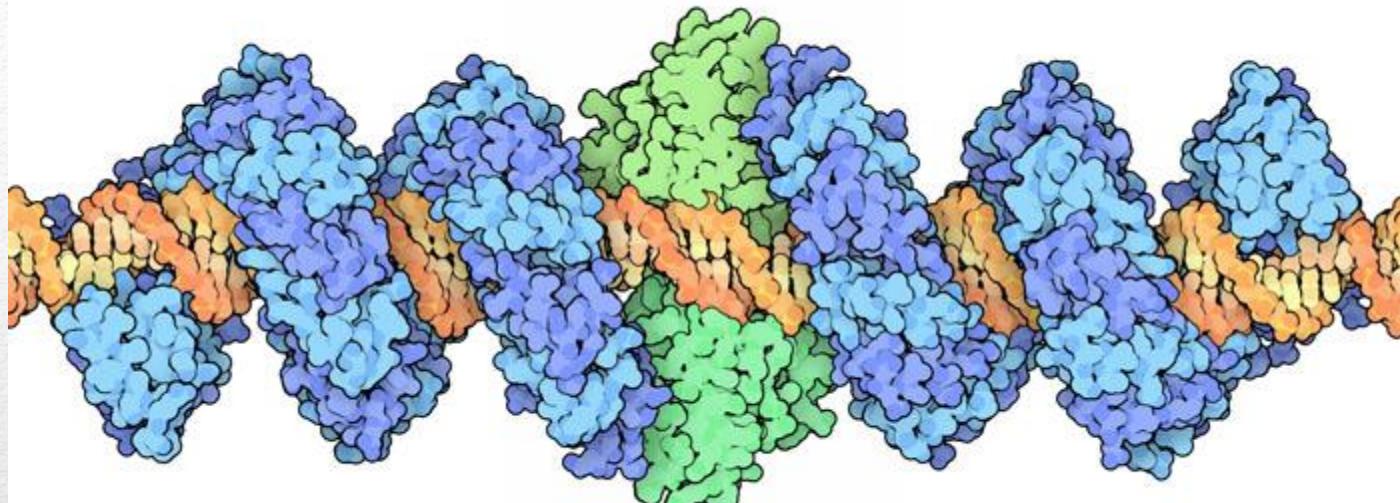
DNA-reading domains of a TAL effector (blue) wrapped around DNA (orange).



TAL Effector

- In the few short years since their discovery, researchers have put these DNA-reading proteins to good use. For instance, they have engineered TALE nucleases (TALEN) by attaching the DNA-cutting domain of FokI nuclease to one end of a TAL effector.
- This can be used to knock out a specific gene, or to stimulate the natural DNA repair methods that are present in cells, which may be coaxed into inserting a new engineered gene while they are making the repair.

TALENs



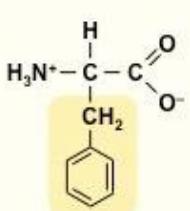
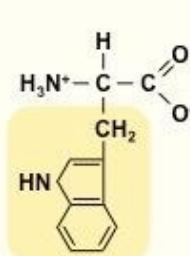
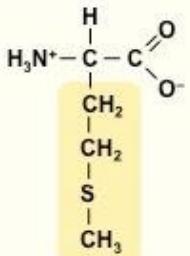
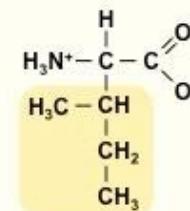
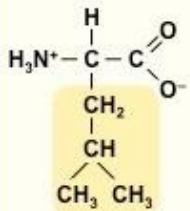
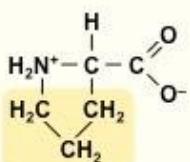
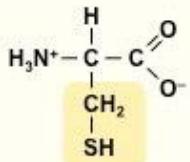
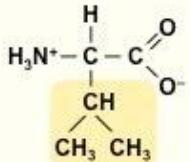
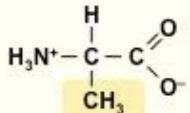
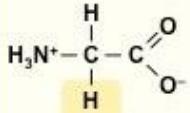
Model of an engineered TALE nuclease with the nuclease domain in green and the DNA-reading domains in blue.

TALENs

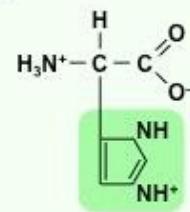
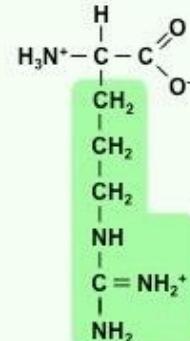
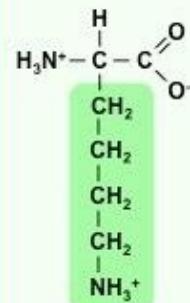
- Beta sheets – 2JOX
- Hemoglobin – 2DHB
- Porin - 1PHO
- TAL Protein – 3UGM

PDBs Visualized

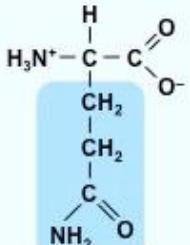
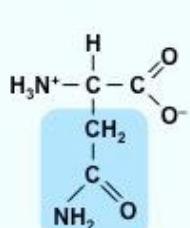
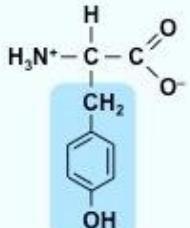
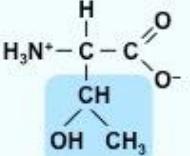
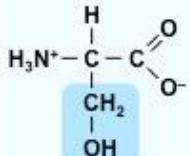
NON-POLAR



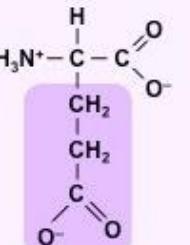
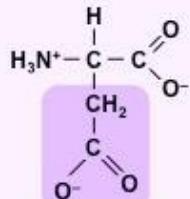
+ CHARGE



POLAR



- CHARGE



Serine
(Ser / S)

Threonine
(Thr / T)

Tyrosine
(Tyr / Y)

Asparagine
(Asn / N)

Glutamine
(Gln / Q)

Aspartic Acid
(Asp / D)

Glutamic Acid
(Glu / E)

- <http://www.ncbi.nlm.nih.gov/books/NBK26883/>
- <http://www.ncbi.nlm.nih.gov/books/NBK26911/>

Suggested Reading
