

## Molecular Biology

### 2.4- Proteins

Protein Thermal Irreversible Denaturation

Native albumen    Denaturation    Crosslinking

A    B    C

## Essential idea:

- Proteins have a very wide range of functions in living organisms.
  - Form muscle, skin, enzymes, and signals

## Nature of science:

- Looking for patterns, trends and discrepancies
  - most but not all organisms assemble proteins from the same 20 amino acids. (3.1)

## Amino Acids

- Amino acids are linked together by condensation to form polypeptides
- There are 20 different amino acids in polypeptides
- Polypeptides are synthesized on ribosomes (70s or 80s).

## Amino Acids

- Amino acids can be linked together in any sequence giving a huge range of possible polypeptides.
  - Polypeptide of 7 AA =  $20^7 = 1,280,000,000$
- The amino acid sequence of polypeptides is coded for by genes. (Central Dogma)

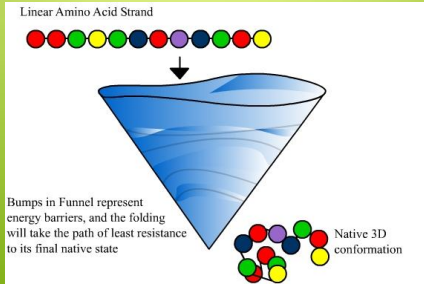
		Second Letter							
		U	C	A	G				
1st letter	U	Phe UUU UUC UUA UUG	Leu UCU UCC UCA UUG	Ser UAC UAA UAG UAG	Tyr UAU UAA UAG UAG	Stop UAG UAG UAG	Cys UGU UGC UGA UGG	Trp UGG UGG UGG UGG	U C A G
	C	Leu CUU CUC CUA CUG	Leu CCU CCC CCA CCG	Pro CAU CAC CAA CAG	His CAU CAC CAA CAG	Gln CAA CAG CAA CAG	Arg CGU CGC CGA CGG	Arg CGA CGG CGG CGG	U C A G
	A	Ile AUU AUC AUA AUG	Ile AUC ACC ACA ACG	Thr AUA AAC AAA AAG	Asn AAU AAC AAA AAG	Lys AAA AAG AAA AAG	Ser AGU AGC AGA AGG	Arg AGA AGG AGG AGG	U C A G
3rd letter	G	Val GUU GUC GUA GUG	Val GCU GCC GCA GCG	Ala GAU GAC GAA GAG	Asp GAU GAC GAA GAG	Glu GGU GGC GGA GGG	Gly GGU GGC GGA GGG	U C A G	

## Amino Acids

- Most organisms use the same 20 amino acids in the same genetic code although there are some exceptions.
  - 21<sup>st</sup>: Selenocysteine (derived from UGA stop codon)
  - 22<sup>nd</sup>: Pyrrolysine (from a methanogen)

# Amino Acids

- The amino acid sequence determines the three-dimensional **conformation of a protein**. (native conformation)



# Proteins

- Living organisms synthesize many different proteins with a wide range of functions. (**specific IB examples**)

Type of protein	Example	Function
Enzymes	Amylase	Digestion
Transport	Hemoglobin Myoglobin Albumin Lipoprotein	Transports O <sub>2</sub> in blood Transports O <sub>2</sub> in muscle Transports fatty acids Transports lipids
Storage	Ovalbumin Milk Ferritin	Egg-white protein Milk Iron storage in spleen
Contractile	Myosin, actin	Muscle movement
Protection	Antibodies Fibrinogen, thrombin	Fight infection Blood clotting
Hormones	Insulin Growth hormone	Carbohydrate metabolism Growth and regeneration
Structural	Glycoproteins Collagen Elastin	Cell walls, skin Tendons, bones, cartilage Ligaments
Toxins	Clostridium botulinum Ricin Snake venom	Botulism food poisoning Castor bean toxin Snake venom

# Genome

- Entire set of genes in a cell, tissue, or organism.
- Determines what proteins an organism can possibly produce.

From Genes to Proteins

# Proteome

- Entire set of proteins expressed by a cell, tissue, or organism.
- Every individual has a unique proteome.
- Function of both the genome and the environment.
- Varies over time.

Stem Cell

Environment

Genomics

Transcriptionomics

Proteomics

Phenotype

Proteome Complexity

# Proteome

- The environment influences what proteins an organism needs to produce and in what quantity.
- Example factors would be nutrition, temperature, activity levels and anything else that affects a cell's activities

Environment influences Phenotype  
"Nature vs Nurture"

- Siamese cats and Himalayan rabbits have dark colored fur on their extremities
- Allele that controls pigment production is only able to function at the lower temperatures of those extremities.

Hypothermia causes normal pigmentation. Melanin is black in cooler soil and pink in warmer.

# Proteomics

- The production of proteins by cells cultured in fermenters.
- Offer many opportunities for the food, pharmaceutical and other industries.
- To analyze a proteome mixtures of proteins are extracted from a sample and are then separated by gel electrophoresis

Human Insulin Production

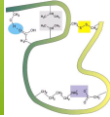
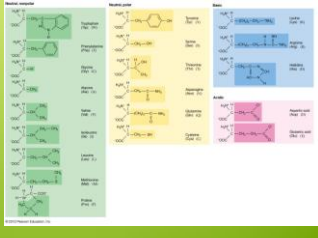
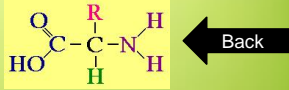
Human insulin production process:

- Isolation of insulin gene
- Insertion of insulin gene into a bacterium
- Recombinant DNA
- Production of insulin in a fermenter
- Purification of insulin
- Formulation of insulin

Final step: End

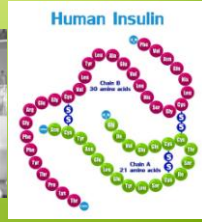
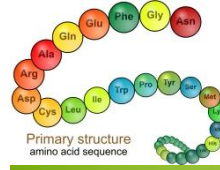
## Amino Acid Structure

- Carboxyl (-COOH) group
- Amino group (NH<sub>2</sub>)
- H atom
- Variable group (R)
  - categorized by chemical properties
  - Interactions of R groups determine structure and function of that region of the protein



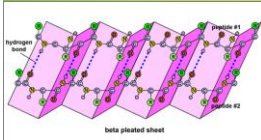
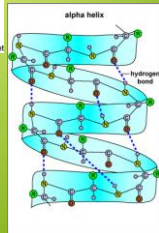
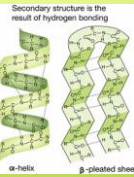
## Protein Structure

- Primary Structure
  - The AA sequence
  - Coded by genes
  - Frederick Sanger
    - Pioneered work on AA sequence of insulin
    - late 1940s-early 1950s



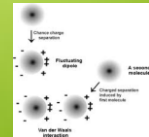
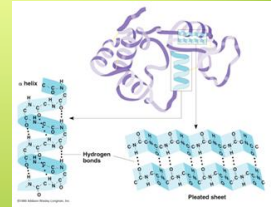
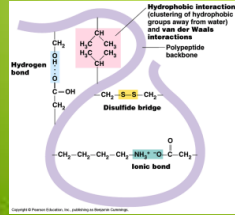
## Protein Structure

- Secondary Structure
  - Folding due to "R" interactions
  - Stabilized by H-bonds
  - α Helix
  - β Pleated Sheet



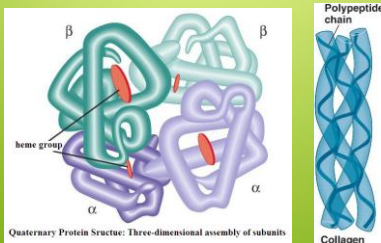
## Protein Structure

- Tertiary Structure
  - H-bonds
  - Disulfide bridges
  - Ionic bonds
  - van der Waals



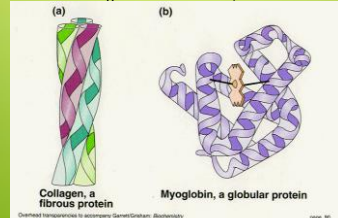
## Protein Structure

- Quaternary Structure
  - Two or more polypeptides
  - Proteins are commonly described as either being fibrous or globular in nature.



## Protein Structure

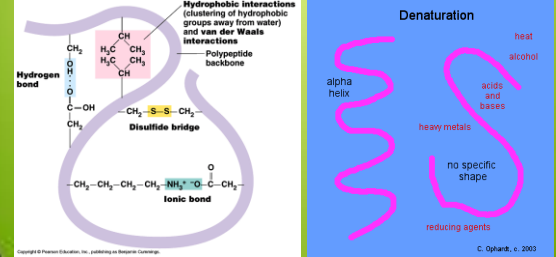
- Fibrous proteins have structural roles
  - o Hydrophobic R groups are exposed and therefore the molecule is insoluble
- Globular proteins are functional (catalytic, transport)
  - o Hydrophobic R groups are folded into the core of the molecule, away from the surrounding water molecules, this makes them soluble.





## Altering Protein Structure

- Most bonds and interactions of protein structure are relatively weak can be disrupted or broken.
- This results in a change to the conformation of the protein, which is called denaturation.



## Altering Protein Structure

- Denaturation is permanent in most cases.
- Soluble proteins often become insoluble and form a precipitate.

Albumen

Casein

Native albumen

Denaturation

Crosslinking

**A      B      C**

**Protein Thermal Irreversible Denaturation**

Water-soluble

Native albumen    Denaturation    Crosslinking

## Altering Protein Structure

- Extremes of pH can cause denaturation
  - charges on R groups are changed
  - breaks ionic bonds within the protein or causes new ionic bonds to form.
- Heat can cause denaturation
  - vibrations within the molecule breaks intermolecular bonds or interactions.

proteins (fish muscle)

protons (from acid)

denatured proteins

**TOO COLD**      e.g. 98.6      **TOO HOT**

Rate of chemical reaction

Temperature

Back

## Rubisco

- Ribulose Biphosphate Carboxylase
  - Enzyme
    - Catalyses carbon dioxide fixation from the atmosphere
    - Thus provides the source of carbon required by living organisms
  - Found in high concentrations in leaves and algal cells
  - The most plentiful single enzyme on the Earth

Calvin Cycle

## Insulin

- Hormone
- Secreted by  $\beta$  cells in the pancreas and transported by the blood.
- Signals cells to absorb glucose.
  - Cells have receptor (proteins) on their surface to which insulin can (reversibly) bind to.
  - Reduces the glucose concentration of the blood.
- Type 1 diabetics don't produce sufficient insulin
- Type 2 diabetics have defective receptor proteins

Insulin

C254H377N65O76S6

Insulin is Made in the Pancreas

glucose

glucose utilisation

glucagon / insulin / protein synthesis

## Immunoglobulins

- Antibodies
  - Two antigen binding sites.
    - Antigens are a molecule on the pathogen which provokes an immune response.
  - Binding sites vary greatly between immunoglobulins (hypervariable).
  - Enables them to respond a huge range of pathogens.
  - Other parts of the immunoglobulin molecule cause a response, e.g. acting as a marker to phagocytes (which engulf the pathogen)

Ag binding

Light chain

Disulfide bridge

Heavy chain

Hypervariable (CDR) regions

Variable regions

Constant regions

Monomer IgD, IgE, IgG

Dimer IgA

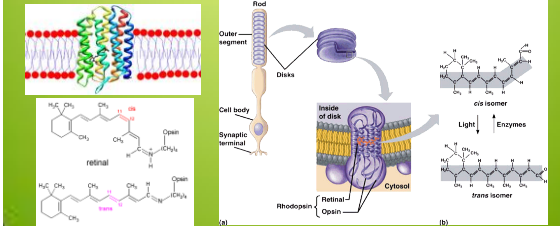
Pentamer IgM

antibodies

antigen

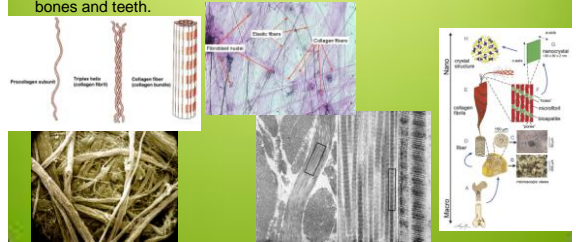
## Rhodopsin

- Pigment that absorbs light.
- Membrane protein of rod cells in the retina.
- Consists of the opsin polypeptide surrounding a retinal molecule.
- Retinal molecule absorbs a single photon of light -> changes shape -> change to the opsin -> the rod cell sends a nerve impulse to the brain.
- Even very low light intensities can be detected.



## Collagen

- Rope-like proteins made of three polypeptides wound together.
- About a quarter of all protein in the human body is collagen.
- Forms a mesh of fibers in skin and in blood vessel walls that resists tearing.
- Gives strength to tendons, ligaments, skin and blood vessel walls.
- Forms part of teeth and bones, helps to prevent cracks and fractures to bones and teeth.



## Spider Silk

- Different types of silk with different functions
- Dragline silk is stronger than steel and tougher than Kevlar
  - When first made it contains regions where the polypeptide forms parallel arrays .
  - Some regions seem like a disordered tangle (middle)
  - When the stretched the polypeptide gradually extends, making the silk extensible and very resistant to breaking.

