Repair - Adhere - Heal

Understanding biological materials such as proteins, fats and polysaccharides is important for many reasons. Not least of all they are the materials of which we are made, which heal, protect and make use grow; but they are also molecules that make it possible to trace how residues, toxins and chemicals travel through an ecosystem, even to offspring and organisms on the other side of the planet.

Rachel Carson's 1962 publication Silent Spring illuminated for the first time to the general public the impact of certain toxins and residues in the ecosystem. Rachel Carson's research examined how one type of toxin could be ingested by an insect, which was eaten by a bird. Carson's study lead her to learn that chemicals traveling from prey to predator would interrupt normal biological processes. The name ***Silent Spring*** come from the 1961 event that she witnessed, where the impact of pesticides damaged reproductive biological functions in birds, leaving a generation of birds unable to produce offspring.

"Sprays, dusts and aerosols are now applied almost universally to farms, gardens, forests and homes – non-selective chemicals that have the power to kill every insect, the 'good' and the 'bad', to still the song of the birds and the leaping of fish in the streams, to coat the leaves with a deadly film and to linger on in the soil – all this though the intended target may be only a few weeds or insects," she wrote.

Her book spurred a reversal in national pesticide policy, leading to a nationwide ban on DDT for agricultural uses.

We can trace toxins such as DDT through an ecosystems as they bind within different types of animal and plant tissue and how they bind to water, travel across the world via rising up to the stratosphere and infest the soil and water table for generation.

Biomaterials

polysaccarides proteins and THE CENTRAL DOGMA OF MOLECULAR BIOLOGY

DDT molecule

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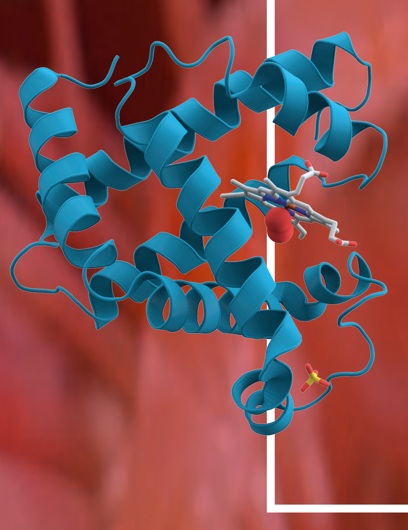
DDT is a persistent organic pollutant that is readily adsorbed to soils and sediments, which can act both as sinks and as long-term sources of exposure affecting organisms. DDT is lipophilic meaning that it will bond to fat and oil molecules in living creatures. It has been traced in the breast milk of mammals (including humans) and has been found in the fat depot of humans across the planet. DDT bioaccumulates in predatory birds and is toxic to marine animals too. Crayfish, daphnids, sea shrimp and many species of fish, will absorb it and thus it enters the food chain by this route. Despite being banned, DDT was detected in almost all human blood samples tested by the Centres for Disease Control in the USA 2005. While their levels have sharply declined since most uses were banned food tests commonly detect it.

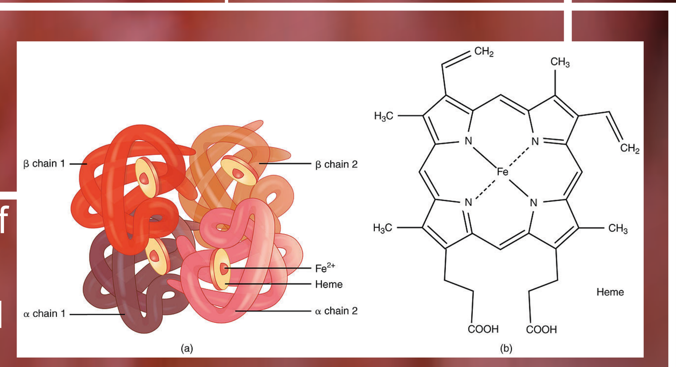
How DDT travels through the food chain

Atrazine is the common name for an herbicide that is widely used to kill weeds. It is used mostly on farms. Pure atrazine –an odourless, white powder –is not very volatile, reactive, or flammable. It will dissolve in water. Atrazine is made in the laboratory and does not occur naturally.

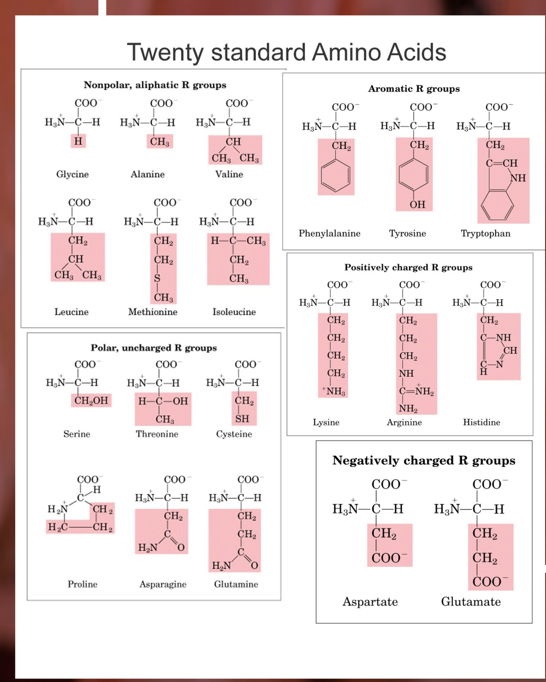


Proteins

Life depends on polysaccharides and sugars, but it also depends on proteins - large organic molecules composed of tens, hundreds or even thousands of amino acids bound together and folded into specifically shaped structures. Enzymatic, structural, and respiratory functions depend on them. Proteins are behind the workings of every biological function in your body and the body of every animal, bird, fish and plant on the planet. They are tiny molecular machines that make everything from respiration and the absorption of oxygen to the very mechanics of cell replication. Without proteins there is no DNA!



Proteins consist of one or more polypeptide chains, each of which is a linear polymer of amino acid residues. Twenty types of amino acid occur naturally in proteins. A polypeptide can be defined simply by its sequence of amino acids. These 20 alpha-amino acids each consist of a primary amino group, a carboxyl group, a hydrogen atom and an R group (side chain that gives each amino acid its individual properties). Amino acids are linked by peptide bonds to form polypeptide chains.



Atrazine

Human exposure to atrazine is linked to a number of serious health effects. A potent endocrine disruptor, atrazine interferes with hormonal activity of animals and humans at extremely low doses.

· Endocrine Disruption: The science on atrazine's effects on the hormone system continues to grow. It hormones in rats and can delay puberty. In male frogs, exposure to atrazine causes a kind of "chemical castration," causing them to develop female sex characteristics. Researchers hypothesize that atrazine signals the conversion of testosterone to oestrogen, demasculinizing the frogs.

· Reproductive Effects: Because atrazine disrupts hormones, it is not surprising that epidemiological studies find associations between exposure to the herbicide and reproductive effects including increased risk of miscarriage, fertility, weight, and higher incidence of abdominal defects;

· Cancer: Evidence for the carcinogenic potential of atrazine is growing — exposure has been linked to elevated risk of breast and prostate cancer. The recent President's Cancer Panel Report notes that atrazine has possible carcinogenic properties. In response to concerns, U.S. EPA is currently re-evaluating atrazine's carcinogenic potential.

Timing of exposure may be more important than exposure levels. Research shows that low levels of exposure during key periods of pregnancy may interfere with healthy foetal development. The third trimester of pregnancy appears to be most critical, says a recent epidemiological study. Synergistic effects between atrazine and other pesticides may also render health harms more severe.

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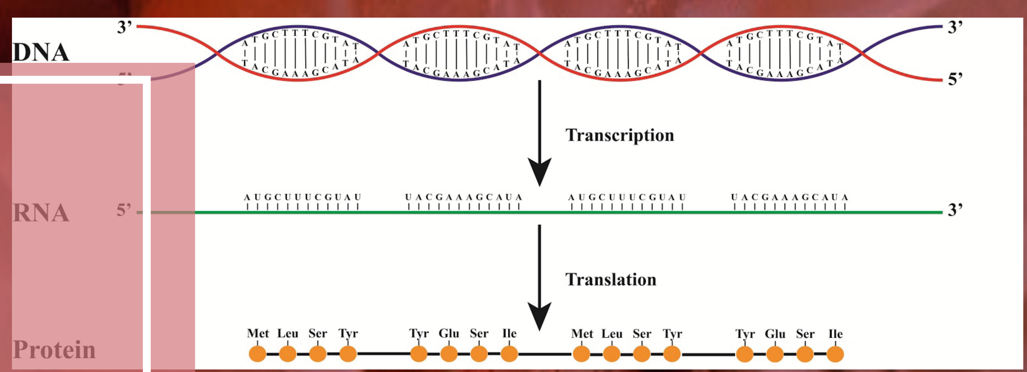
pregnancy may interfere with healthy foetal development. The third trimester of pregnancy appears to be most critical, says a recent epidemiological study. Synergistic effects between atrazine and other pesticides may also render health harms more severe.

Nuclear testing research carried out by the U.S. Department of Energy under the Atomic Energy Commission from 1946 onwards reveals the horrendous impact of nuclear tests carried out by the USA in great detail. In documents declassified under the Clinton administration we can learn about how radioactive nuclei passed into the food supply,how military personnel were harmed by experiments, the destruction of the Marshall Islands and devastation to its exiled inhabitants. From the Fukushima Daiichi nuclear disaster to Chernobyl and the bombing of Hiroshima and Nagasaki on August 6, 1945, we can trace radioactive isotopes binding to human, animal and vegetable tissue for decades following these events.

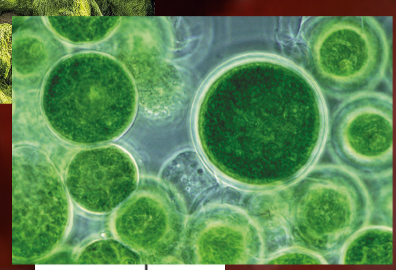
One of the impacts of strontium 90 is that it competes with calcium and is absorbed in the bones of young children.

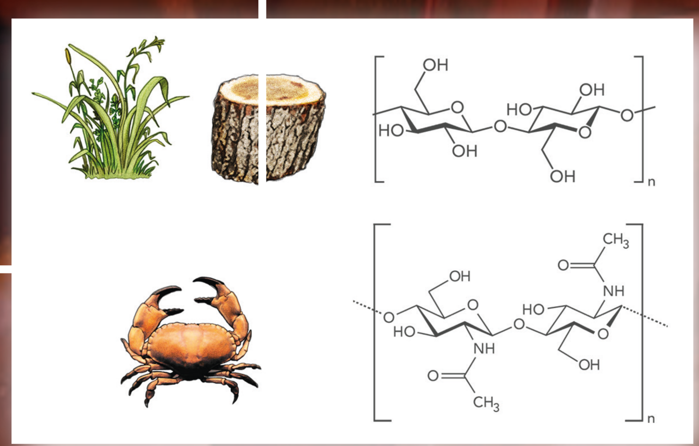
Let us turn now to biology, and focus on the nature of biological materials. Their role in our bodies and those of other living creatures and their potential applications in industry. This not only helps us to understand the diverse, overlapping roles of the biomaterials that constitute the different tissues in our bodies, but helps us to gain insight into the bioaccumulation of toxins and their extent.

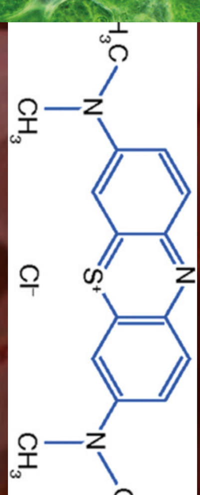


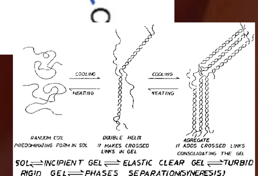
The Central Dogma of Molecular Biology "DNA makes RNA makes Protein...".

A wide range of important industrial molecules that we use in pharmaceuticals, the food industry and construction only exist because they originate from living creatures. A collection of these molecules, which only exist because they are coded for by the DNA of living creatures are explored briefly below:



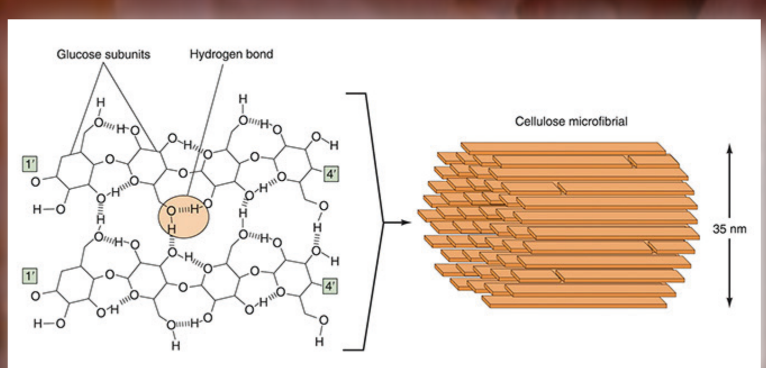






Cellulose and polysaccharides

Cellulose contains only glucose and is the major polysaccharide in woody and fibrous



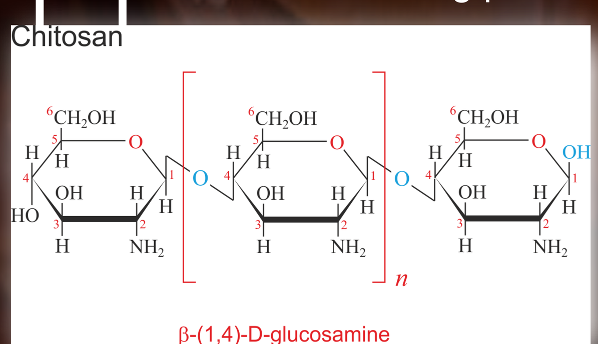
plants. It is the most abundant single polymer in the biosphere.

Polysaccharides more broadly referred to as carbohydrates. These are produced by plant seeds, tubers, fruits and vegetables as an energy source as well as for structural purposes. They come in many forms, including starch that can be found in corn, potatoes, rice and grain - bread, cereal and pasta also contain starch. Polysaccharides such as pectin, agar and chitosan can broaden our view of this wonderful natural group of molecules.

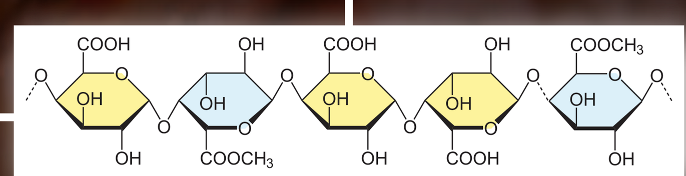
The diverse naturally obtained polysaccharide chitosan can supply a broad range of resources applicable in the biomedical field. It can be found in marine creatures such as crabs and shrimp.

As well as having potential to support development in the biomedical field it can be used to create biodegradable plastics (bioplastics) and with over 400 millions tonnes of waste from the food and fishing industry, it seems a shame to waste this wonderous material.

Chitosan



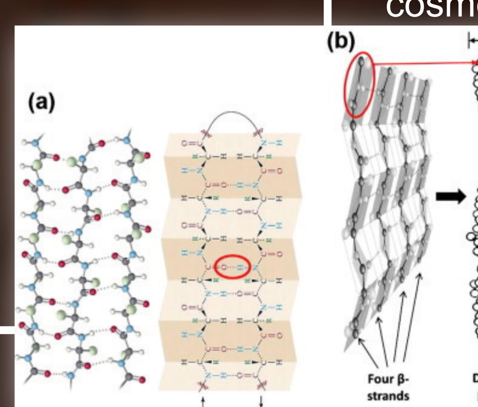
Chitosan is also used in the cosmetics and pharmaceutical industry and extracted from the shells of marine creatures by crushing them and dissolving the calcium carbonate and bicarbonate that also constitutes these shelly structures in hydrochloric acid.

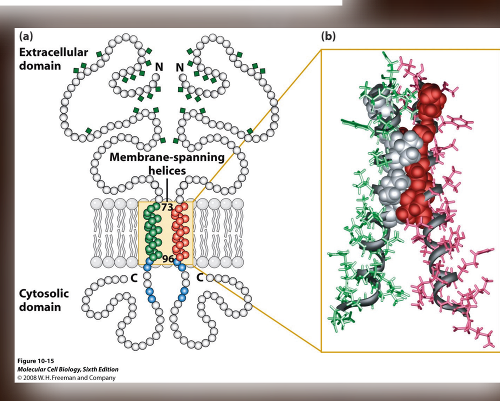


Pectin

Blueberries, pears, apples, guavas, quince, plums, gooseberries, orange peel and other citrus fruits contain a lot of pectin, while softer cherries, grapes, and strawberries contain small amounts.

This has jellifying properties, as does agar which is found in seaweed and algae. Making bioplastics from agar and algae more generally hold much promise for sustainability… and of course, other biomolecules also include gelatin, collagen and other proteins.





Keratin

Keratin is a fibrous structural protein found in hair, nails, horn, hoofs, wool, feathers, and of the epithelial cells in the outermost layers of the skin. Keratin serves important structural and protective functions, particularly in the epithelium. Much like collagen and chitosan, keratin is also used in cosmetics

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Biomaterials

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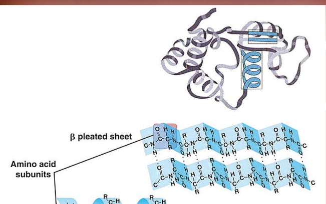
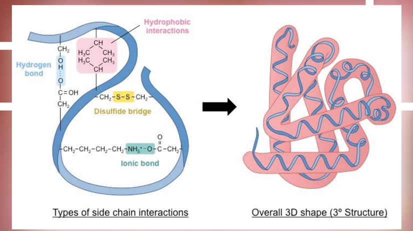
Tertiary structures

Tertiary structures are the level of structure created when further hydrogen bond interactions cause the secondary structures to folds and twist upon themselves resulting in complex three-dimensional forms.

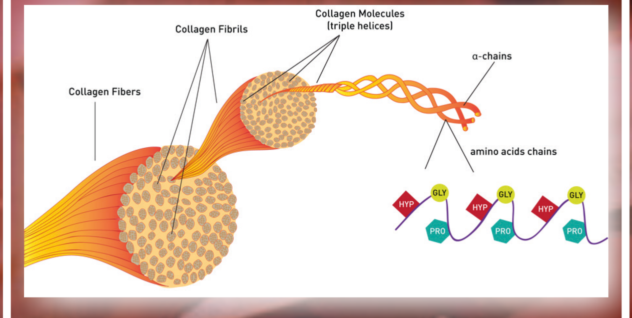




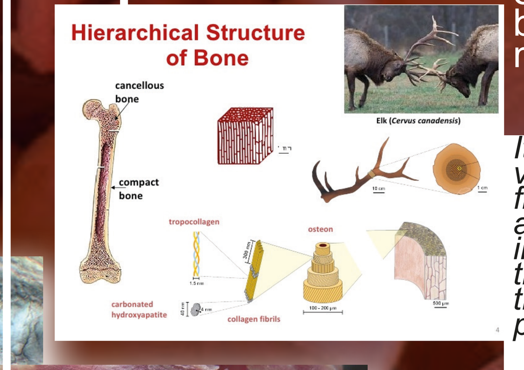
The form of a tertiary structure depends on 'distant group interaction' between the R-groups of the amino acids in the primary structure. Again the hydrogen bonds are responsible for stabilising the tertiary structure although other bonds such as hydrophobic packing, Van Der Waals forces and disulphide bridges also play a role in the resulting shape of a protein's tertiary structure. A tertiary structure's form will be partially dependant on the environment in which it usually forms, for example in water (which is polar) all the polar molecules of the protein will interact with the polar H_2O molecules, creating a non-polar internal space, this is what hydrophobic packing entails. Disulphide bridges happen only between cysteines – amino acids with a thiol side chain that contains sulphur – and are essentially covalent bonds between the sulphur groups resulting from oxidation. Because of the oxidizing environment necessary for the formation of disulphide bridges they tend to form in extracellular space.

Collagen

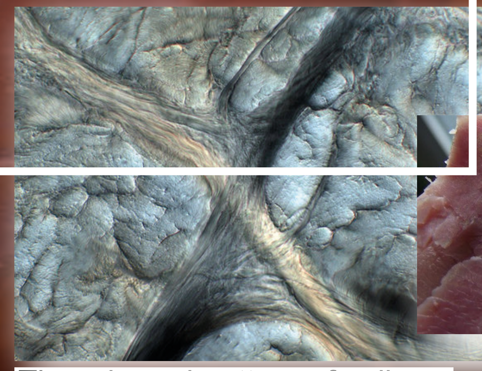
Collagen is a ubiquitous protein. It is an important component of connective tissue, skin, bone, cartilage, and tendons and is the single most abundant protein in the animal kingdom.



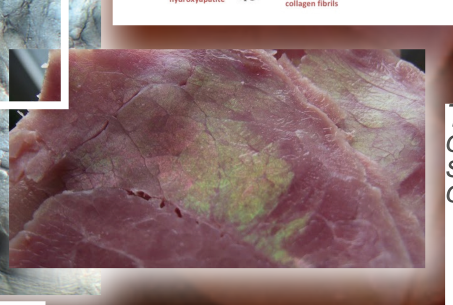
Its biological function is to provide support, structure and flexibility to living creatures, organs, bone and muscles.



It is also very reflective and has interesting optical properties



The crimped pattern of collagen fibrils, showing their reflective optical properties



The crimped pattern of collagen fibrils results in interesting optical properties.

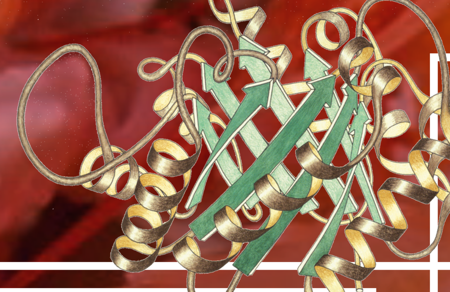
PROTEIN STRUCTURE BACKGROUND

There are four levels of protein structure: the primary, secondary, tertiary and quaternary structure. A polypeptide is a polymer of amino acids linked together by peptide bonds. Each amino acid is termed a residue and all amino acids have the same basic structure. Amino acids are individual molecules consisting of carbon atoms bonded with carboxyl (COOH) and amino functional groups (NH_2), as well as a hydrogen atom bonded to one of the carbon atoms in the molecule. Amino acids also contain a variable group that is termed the R group. The R group provides each amino acid its characteristic chemical properties. A protein is one or more polypeptides, and a

primary structure

is simply the linear sequence of amino acids. There are just twenty amino acids but by varying the number and order of these amino acids, has the possibility to generate a vast number of different polypeptides and resulting proteins.

Proteins fulfil a number of functions in the cell including: catalysis; defence; transport (i.e. haemoglobin transporting oxygen; support (actin fibres; motion; regulation (hormones) and energy storage. The R-groups in their amino acids must be sequenced properly in order for them to fold in the correct final structure, as it is the proteins structure that makes it function properly and carry out its role without damaging the organism.

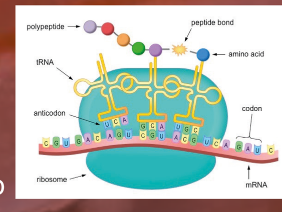


Triose phosphate isomerase is a protein found in both prokaryotic and eukaryotic cells. According to UNIPROT, it is an enzyme that is involved in the pathway gluconeogenesis, which is part of Carbohydrate biosynthesis'. This subpathway is part of the pathway glycolysis, which is itself part of Carbohydrate degradation. Its primary structure will influence how its secondary and subsequent structures are folded.

Process of Translation

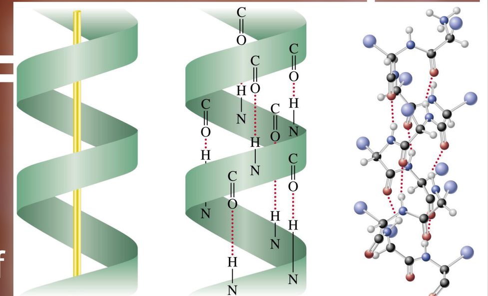
DNA Polymerase is also an important protein in the process as it unzips the DNA molecule in order for the mRNA to copy the appropriate sequence of nucleotides in the first place. This enables the process of transcription to occur. DNA Polymerase is a DNA-binding protein with helix-turn-helix motifs, containing both alpha-helices and beta sheets.

Proteins with a similar structure resulting from a common ancestor are called homologous. The human cyclophilin family is one example of such a family group of proteins. The structure of this family contains both alpha helices and beta pleats.

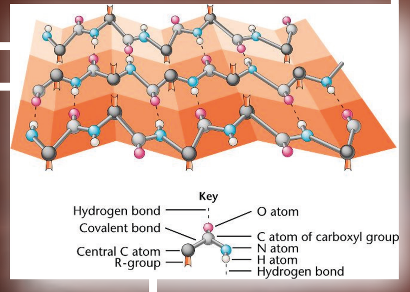


Secondary structure

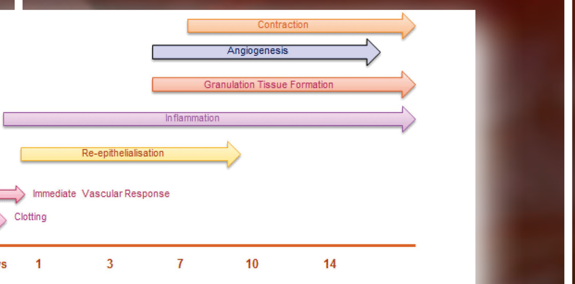
Secondary structure refers to the way in which primary structures fold over themselves. The form that the secondary structure of a linear polypeptide sequence will take is primarily dependant on hydrogen bonds although other intramolecular interactions also play a role. Secondary structures can be understood as being determined by 'backbone interactions' and may result in any number of folded forms or motifs. In an alpha helix for instance the polypeptide will twist into a coil that is stabilised by hydrogen bonds acting between each coil – the resulting from is that of a spiral staircase.

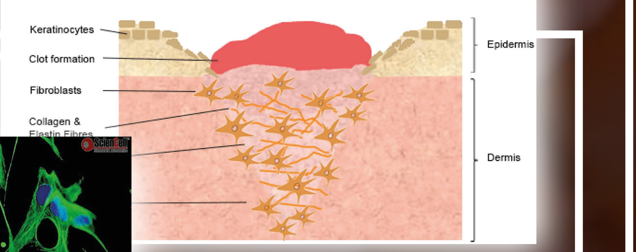


Another secondary structure motif is a beta pleated sheet that looks much like a zigzag whereby the point of each zigzag is stabilised by a hydrogen bond.



If the resulting motif is such that the amino ends and the carboxyl ends of the pleated sheet are lined up, then it is described as parallel pleated sheets. An alternative manifestation of a beta sheet is an anti-parallel beta sheet where by the zigzagging pattern of linear amino acids folds over itself, resulting in amides lining up with carboxyls, and alternating in how the carboxyls and amines line up as illustrated in the image below





The Central Dogma of Molecular Biology

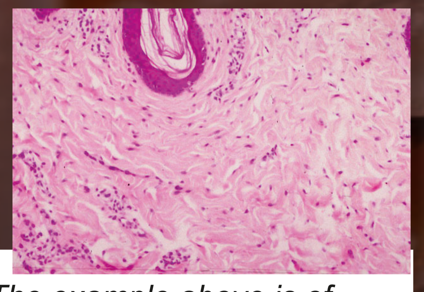
The Central Dogma of Molecular Biology is "DNA makes RNA makes Protein...". RNA is short for Ribonucleic acid, RNA is a polymeric molecule essential in various biological roles in coding, decoding, regulation, and expression of genes. RNA has a ribose sugar in its chain of molecules while in DNA a deoxyribose sugar exists in the polymer. RNA nucleotides have a uracil base instead of thymine (see R-groups above).

The process by which an RNA sequence complementary to the DNA sequence of the gene to be expressed is synthesised is termed transcription; the process by which a protein is synthesised, with its sequence determined by the RNA sequence, is termed translation. Besides the protein-coding genes, there are also sequences in the human genome (as in all genomes) that are transcribed into functional RNA molecules, and these are sometimes termed RNA genes. Without proteins in the first place however these is not DNA.

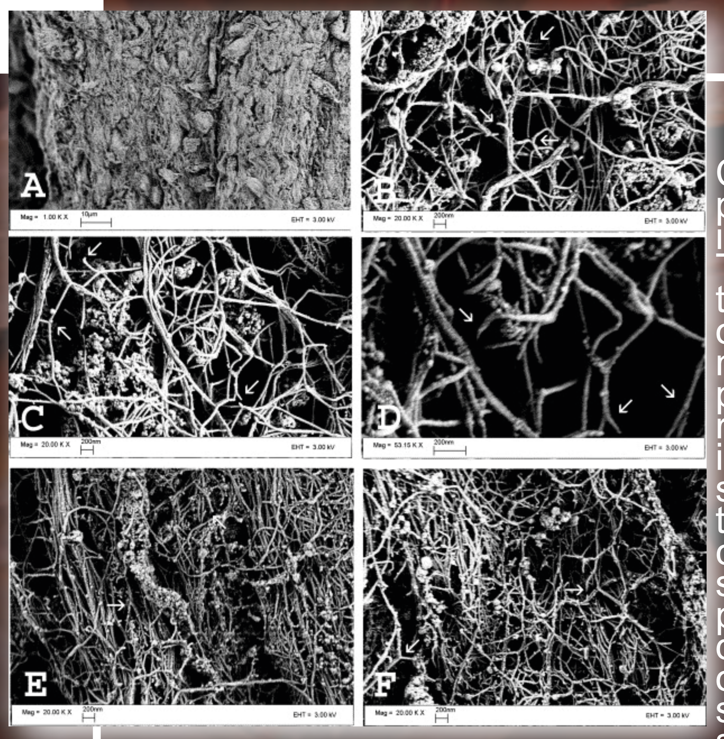
The quaternary structure

The quaternary structure of a protein describes the bonding between multiple polypeptides.

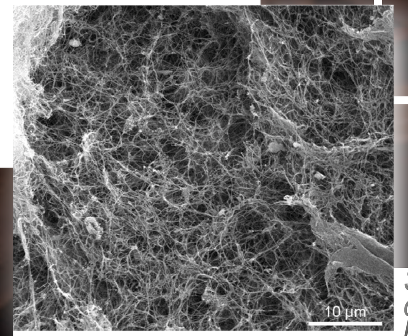
The same interactions of hydrogen, Van Der Waals, hydrophobic packing and disulphide bridges are involved in the formation of the quaternary structure. Within the resolved protein, each individual polypeptide is called a subunit. If there are two subunits interacting then you have a quaternary structure called a dimer. For three subunits the term 'trimer' is used, for you tetramer and more that four produces a multimer. The term for a completely, properly folded protein is the proper confirmation of a protein. Triose phosphate isomerase, is a dimer – or dimeric enzyme. The word dimer refers to the two subunits present in the enzyme. Haemoglobin on the other hand is a quaternary structure.



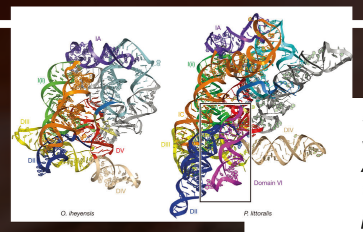
The example above is of dense irregular collagenous connective tissue in skin from a pig. The dark purple U-shaped band at the top of the field is the epithelium of the skin, and the rest is the connective tissue. Connective tissues as a group of tissues categorically have protective or supportive functions.

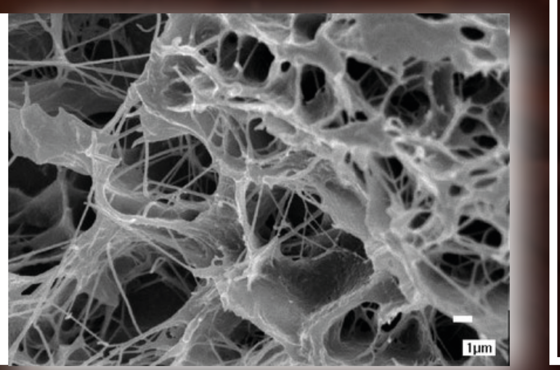


Collagen is produced in our cells. The skin is the largest organ of the human body and plays a major role in maintaining homeostasis and protection. As the main component of skin, animal cells produce many different kinds of collagen, resulting in larger scale structures that resemble long rope-like structures and tough sheets. These are used for structural support.

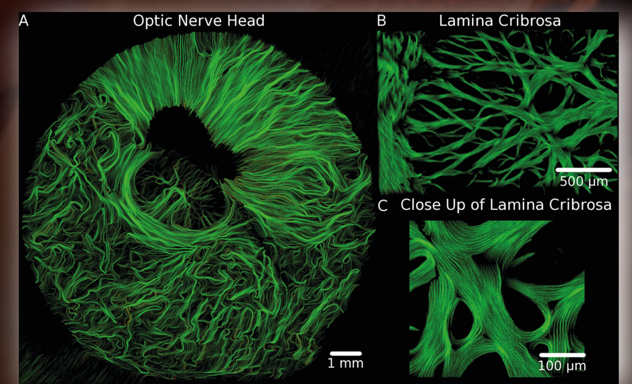


Scanning Electron Microscopy (SEM) of a fibrin-collagen blend hydrogel. The aqueous part of the hydrogel is evaporated after critical point drying and fibrillar structures of fibrin and collagen is left behind. The random architecture of the hydrogel is clearly visible.





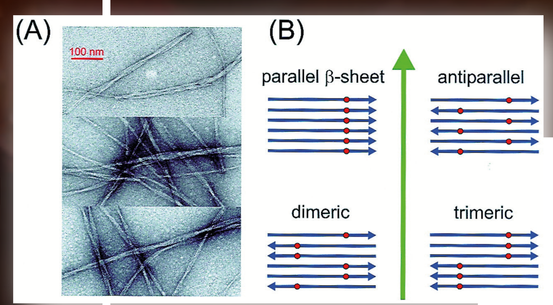
Research team from Purdue University-based startup GeniPhys led by Associate Professor Sherry Harbin is commercialising a synthetic collagen polymer known as Collymers. It exhibits uncommon self-assembly properties not seen in conventional collagen. These collagens work in a similar way as those in the body's tissues – they polymerise to form fibrils. As such, they can be used to customise 3D collagen-fibril matrices and materials for cell and tissue research, in vitro drug discovery and toxicity testing as well as 3D bioprinting.

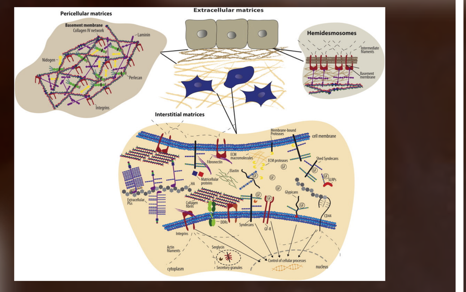


polarized light microscopy (PLM) image showing collagen fiber architecture of posterior pole and optic nerve.

Collagen's role in wound healing is fascinating and it also has a role in the bodies other defense processes. Inflammation plays a role in collagen degradation to prevent the toughening of tissue.

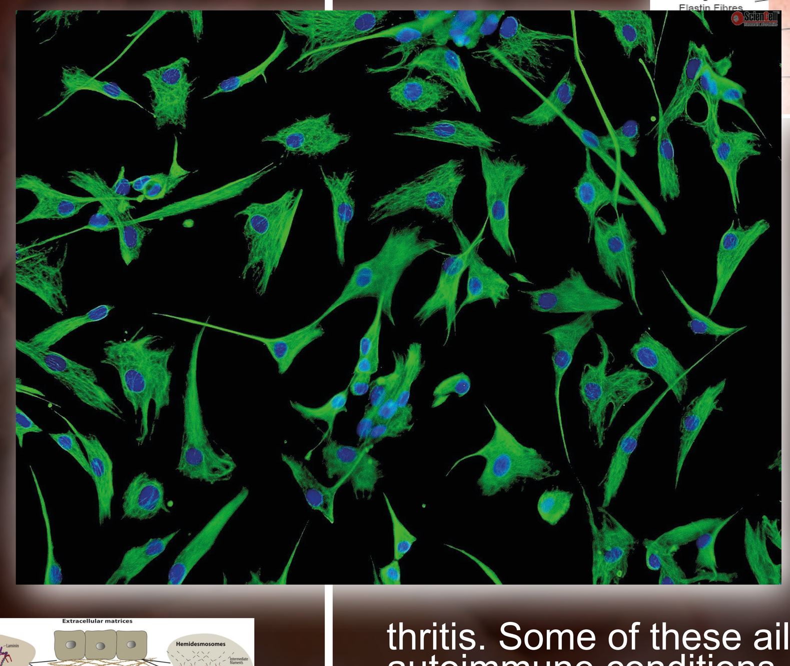
Proteins are formed by chains of nucleotides which as they are formed fold and twist into different and more complex three dimensional forms. Some of the shapes proteins can take as they form are helices and folded sheets and the basic structural unit of collagen is a triple helix. From the microscopic view of the helix to macroscopic structure of collagen fibres, its mechanical properties make it strong and flexible and during the wound-healing process, collagen fibres with grow across a wound and begin to stabilise.





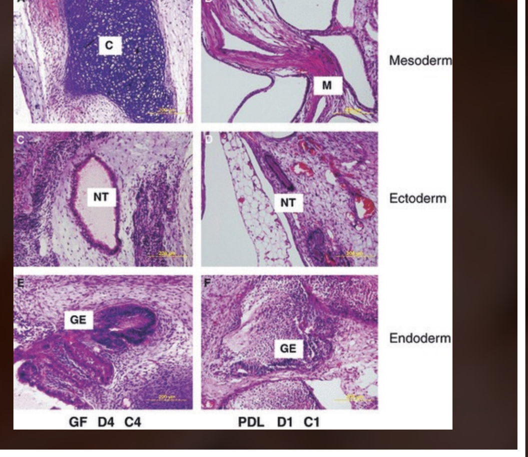
(A)Anti-parallel (B) Parallel

Triose phosphate isomerase contains both beta-pleated sheets and alpha-helices.



Inflammation is one of many biological responses within the body's tissues to harmful stimuli, protecting us from pathogens, damaged cells and irritants. Inflammation appears to be connected to a wide range of chronic diseases such as heart disease, cancer, diabetes, obesity, allergies, asthma and arthritis. Some of these ailments can be called autoimmune conditions, whereby the immune system responds inappropriately to stimuli, and results in the body attacking its own tissues. It is s an ongoing internal barrel that is directly related to either an external irritant or an epigenetic malfunction.

A variety of diseases that are characterized by fibrosis share common features including the proliferation of fibroblasts and the deposition of excess collagen in the extracellular matrix of our cells.

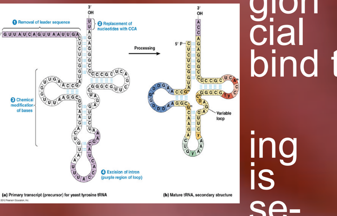


DNA makes RNA makes Protein - CONNECTS US TOGETHER

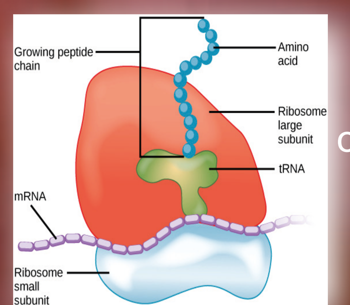
RNA is a single stranded molecule similar to DNA with some key differences. It contains ribose as part of its sugar backbone and contains uracil instead of thymine. RNA is necessary in protein synthesis.

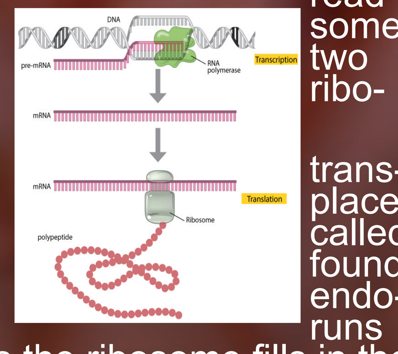
A piece of Messenger RNA (mRNA) must be copied – or transcribed – from DNA, in order to make proteins. The information held by the mRNA is encoded in its nucleotides.

More precisely, each group of three nucleotides (called a codon) is used to construct each amino acid needed to make a specific protein. An mRNA molecule begins with a 5 prime non-reading end (made of five nucleotides) known as the 5' untranslated region (UTR). This is followed by a special sequence of nucleotides which bind to the ribosome.

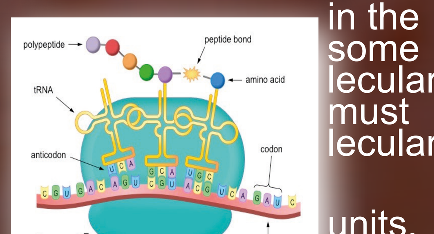


This binding section is next (reading linearly from left to right), and is called the Shine-Dalgarno (SD) sequence. The SD section if followed by another non coding region which is followed by the start codon – commonly with the indicator nucleotide sequence of AUG – which always codes for methionine, until it reaches the stop codon (usually UAA, UAG or UGA) which is followed by another non-coding region. mRNA resembles a sequence of nucleotides, much like the primary structure of a protein (polypeptide) this structure allows it to be read and transcribed by the ribosome, as it must slide between the two component molecules of the ribosome to be useful.

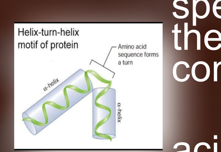




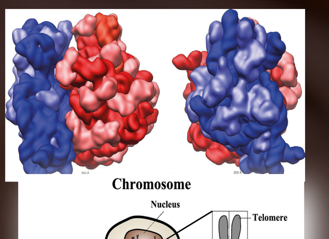
Protein synthesis is called translation. Protein translation takes place within an organelle in our cells called the ribosome, which can be found in the cell cytoplasm and rough endoplasmic reticulum. The mRNA runs through the ribosome, as it does the ribosome fills in the corresponding nucleic acids in the correct sequence. The ribosome itself is made from two molecular components, and the mRNA must run between these two molecular components to be translated.

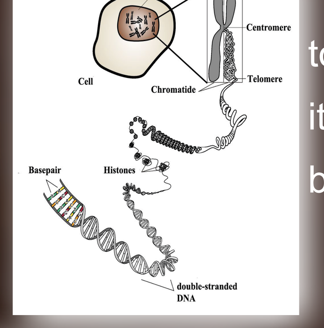


These are referred to as subunits, called the large subunit and small subunit. They are each composed of Ribosomal RNA (rRNA) and proteins, which are both structured to form each subunit. The ribosome subunits usually exist separately in the cytoplasm. Once the smaller subunit finds, and binds to a specific site on the mRNA (the start codon) then the large subunit is toed in and forms the complete ribosome.

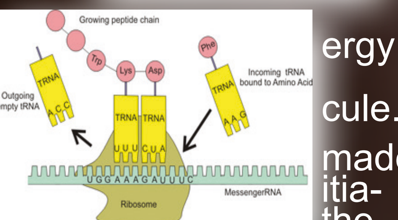


In order to get the necessary amino acids to carry out translation the ribosome needs a protein called Transfer RNA (tRNA), which brings (or transfers) the different amino acids to the ribosome. The tRNA is much smaller than the ribosome and has a clover-like structure. If you imagine a clover shape, with three leaves and a stem, and imagine that there are three nucleotides along the edge of the leaf in the middle of the clover. These three nucleotides that are found at this point in the tRNA structure are what determines the amino acid is has to collect.





This part of tRNA's structure is called the anticodon. The anticodon will collect an amino acid, made from the complementary sequence of nucleotides, which is the codon. So UUU (which happens to codes for phenylalanine) will in fact collect AAA (lysine) and bring it to the ribosome to build into a required protein, as requested by the mRNA. Other proteins and enzymes are involved throughout the entire process, one example is aminoacyl-tRNA synthetases, which consists of an amino acid which makes us of a high energy ester bond to bind to the 3′-hydroxyl group of a tRNA molecule.



The process of translation is made up of different steps. First initiation: where the SD section of the mRNA is detected by the ribosome, and read until it gets to the start codon AUG. At this point a tRNA molecule will bring (transfer) the amino acid UAC (formyl-etheline in eukaryotes) to the ribosome. The second phase is called elongation: where the mRNA, ribosome and tRNA start to build the polypeptides. The final phase is termination where the end codon goes through the ribosome.

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