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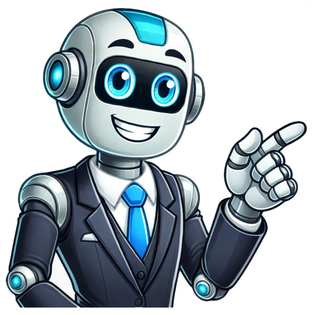

Structural Biochemistry is the field of biochemistry that focuses mainly on the components, functions, and structures of molecules of cells within living organisms. It helps us understand cells through the theories of Chemistry and the laws of Physics. Structural biochemistry concentrates on the study of macromolecules (such as carbohydrates, proteins, polysaccharides, lipids), their monomeric units (amino acids, nucleic acids, nucleotides) and important reactions involving them. Biochemistry is interlinked between Biology and Chemistry. Biology is the study of the cell's interaction within its environment. Chemistry takes these interactions and breaks it down to the molecular level and provides information on how these events occur. Structure is defined by how a system is composed. It is the way in which parts are arranged or put together to form the whole. As a result, when these two subjects are fused, Biochemistry and Structure, the subject known as Structural Biochemistry comes into being. Structural Biochemistry forms the basis of the molecular parts via interactions such hydrogen, ionic, and covalent bonding that form the cellular structure. Structural biochemistry is a study of various macromolecules and how their structure is appropriate to their functions. Macromolecules studied in structural biochemistry courses that consists of proteins, carbohydrates, lipids, and nucleotides. They cover everything from the multitude of functions that proteins participate in (such as transport of molecules, cytoskeleton formation, and cell growth) to the building blocks of DNA, and even to the catalytic mechanism of different enzyme. All macromolecules in general contribute to the survival of humans, as well as to the composition of inanimate objects. Another way to define structural biochemistry is by stating that it is the scientific study of the biochemical systems of life and living organisms; it is about biological molecules that construct chemical forms, and the close correlation between structure and function. Furthermore, biochemistry applies chemistry to biological studies at the cellular and molecular level. It surfaces as a distinct category at the turn of the 20th century, as scientists combined chemistry, physiology, and biology to explore the chemistry of living environments and systems. Using this field, biochemical scientists have been attempting to understand and explain the many chemical mechanisms and biological structures shared by living organisms, and to formulate some basic organizing principles shared by all forms of life as well. Today, biochemistry is considered as the study of life in its chemical processes; the study of both a life science and a chemical science. It investigates the chemistry of living organisms and the molecular basis for the alteration happening in the living cells. It uses the schemes of Chemistry, Physics, molecular biology and immunology to study the structure and behavior of the complex molecules found in biological material such as amino acids in a protein, a large organic compound. Along those lines, it also explores the ways these molecules interact to form cells, tissues, and whole organisms. The biochemist seeks to determine how specific molecules such as protein, nucleic acids , lipids, vitamins, and hormones function in such processes. Particular emphasis is placed on regulation of the chemical reactions in the living cells. Biochemistry has become the foundation for understanding all biological processes. It has presented explanations for the sources of many diseases in humans, animals, and plants alike through laboratory techniques such as chromatography, and spectroscopy. It can frequently propose ways by which such diseases may be treated or cured. Because biochemistry community is interested in unraveling the complex chemical reactions that occur in a wide variety of life forms, it offers the basis for practical advances in medicine, veterinary medicine, agriculture, and biotechnology. It also includes such exciting new fields as molecular genetics and bioengineering. The knowledge and methods developed by biochemists are applied to in all fields of medicine, for example, in agriculture and in many chemical and health related industries. The structural biochemistry helped to fight the AIDS epidemic because the structure of HIV protease, which should be blocked in order to prevent virus spreading, could be used as a reference to determine the types of molecules that might block the enzyme. Also, it helped patients with arthritis through the study of painkillers such as ibuprofen at the molecular level and by creating a new painkiller to shut down COX-2 so that ulcers would not form, and therefore prevent the side effects. Biochemistry is also unique in providing education and research in protein structure or function and genetic engineering, the two basic components of the rapidly expanding field of biotechnology. As the broadest of the basic sciences, biochemistry includes many subspecialties such as neurochemistry, bioorganic chemistry, clinical biochemistry, physical biochemistry, molecular genetics, biochemical pharmacology, and immunochemistry. Complex Internal Structures, there is a high degree of chemical complexity and microscopic organization. Thousands of molecules allow cells to maintain a very intricate internal structure, which include long polymers, each with characteristic sequences of subunits, its unique 3D structure and specific selection of binding sites. Systems are able to maintain equilibrium by extracting, transforming and using energy from the environment. This enables organisms to do mechanical, chemical and osmotic work. Reproduction, with defined function of organism's components, organisms are interacting with one another The interplay between organism have allowed changed in components that cause coordination and compensation to necessary adaptation to environment. Mechanisms for sensing and responding to alterations in organism environments A constant adjusting of internal chemistry in order to adapt to change in their local environment for better survival. Ability for precise self-replication and self-assemblyConstruction of entirely complete genetic material in each and every individual cell unique to the organism. A capability to evolve over time This fundamental unity of the living organism is reflected at the molecular level in similarities of gene sequences and protein structures. Structural biochemistry is a branch of the life sciences, specially biochemistry, that combines biology, physics, and chemistry to study living organisms and to summarize some mutual physicochemical underlying principles that all forms of life share. It is also referred to more generally as structural biology. Structural biochemists aim to describe, in atomic precision level, molecular terms of the structures, mechanisms, and chemical processes shared by all metabolism of all organisms, providing organizing principles that underlie life in all its diverse forms. Properties of Living Organisms Retinoid Analysis of Programmed Cell Death Unique Properties pH Buffer Osmosis Polarity Water Gas Reaction Vibrio fischeri: Let there be light Schizophrenia Autism Bipolar Huntington's Disease Biochemistry and Biophysics are the foundation of all cellular processes and systems. Biochemical processes account for the functions of cellular building blocks, from nucleic acids and proteins to lipids and metabolites, and the formation of complex networks that make a cell or system work. Biophysics explains the complexity of life with the simplicity of physical laws and math.The mission of our collaborative unit 'Biochemistry & Biophysics' is to train the next generation of scientists and to uncover how life works at the molecular level. Our scientists study macromolecular complexes and their specificity, protein design and evolution, and molecular networks. We illuminate how the cytoskeleton determines cell shape, how cells transduce signals, how membranes fuse, how chromatin organizes the genome, how metabolism is coordinated, how viruses hijack cells, how the immune response works, and how cells form patterns and communicate with each other.We are experts in bioengineering, structural biology, computation and modeling, optics and microscopy, and microfluidics. Some examples of the approaches being used, and in some cases developed, at Princeton include X-ray crystallography, electron microscopy, mass spectrometry, NMR spectroscopy, super-resolution optical microscopy, single-molecule methods, and computational modeling. These tools are being applied to biological problems ranging from protein folding and design, to signal transduction, to intracellular trafficking.A long-standing tradition and strength of our University is that biologists, chemists and physicists work closely together in an interdisciplinary setting. It is also common to see computational biologists working together with wet-lab biologists to address problems that neither could tackle alone with spectacular results. This is facilitated by the intimate connection between the Department of Molecular Biology with the Departments of Chemistry, Physics and Chemical and Biological Engineering, as well as at the Lewis-Sigler Institute for Integrative Genomics Structural biology is the study of the three-dimensional structure of biological important molecules and macromolecules such as carbohydrates, proteins and nucleic acids. The 3D structure of these molecules generally defines their function. By determining their atomic structures, we can gain significant insights into how they function, and why mutations or deletions give rise to particular diseases. Analysis of the atomic-level structure of proteins also allows the rational design of small molecules that manipulates their function and therefore have powerful therapeutic potential. The two main techniques that are used to determine atomic level details of macromolecular structure are X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy. Within our department, these techniques are used to study the function of proteins involved in the mammalian immune response, retroviral assembly, and the structure of cell-surface carbohydrates. Within the last several years, other techniques such as electrospray ionization mass spectrometry (ESI-MS), have also been developed to study macromolecular structure that are not accessible by NMR or X-ray crystallography. This approach is being used within our department to probe nucleic acid and protein-nucleic acid structures in retroviruses. FACULTY WITH RESEARCH INTERESTS IN STRUCTURAL BIOLOGY Smith, Aaron Protein Translation, Posttranslational Modification, and Heme and Pathogenic Iron Uptake and Delivery Summers, Michael Application of nuclear magnetic resonance to studies of retrovirus structure and function. We're getting everything ready for you. The page is loading, and you'll be on your way in just a few moments. Thanks for your patience! Fact Checked Content Last Updated: 05.09.2024 10 min reading time Content creation process designed by Content cross-checked by Content quality checked by Save Article Save Article Structural biochemistry is a branch of biology that focuses on the molecular structures of biological macromolecules, particularly proteins and nucleic acids, and how changes in their structures affect their functions within the cell. It's a fascinating field that combines aspects of chemistry, biology, and physics to understand molecular functions in a detailed manner. Diving into structural biochemistry lays the groundwork for comprehending the complex architecture of life on a molecular level.The understanding of structural biochemistry is vital as it provides insights into how biomolecules like DNA, RNA, and proteins interact and function. These insights are crucial for a variety of reasons:Drug Design: Knowledge of protein structures can guide the design of drugs that fit like keys into molecular locks.Genetic Engineering: Understanding DNA structures allows for precise genetic modifications.Diagnosis of Diseases: Structural changes in proteins can indicate certain diseases.Evolution and Phylogenetics: Structures help trace evolutionary relationships among species. One striking example of structural biochemistry at work is the discovery of the double-helix structure of DNA by James Watson and Francis Crick. This discovery was pivotal in advancing genetic research and understanding inheritance patterns. Proteins are often referred to as the workhorses of the cell due to their vast array of functions, each dependent on their unique structures.Structural biochemists use a range of sophisticated tools and techniques to examine and manipulate biological molecules. These tools include:X-ray crystallography: Used to determine the three-dimensional structure of large biomolecules.Nuclear Magnetic Resonance (NMR) Spectroscopy: Allows researchers to study protein structures in solution.Cryo-electron Microscopy: Provides high-resolution images of biomolecular structures.These techniques help scientists visualize structures at the angstrom level, revealing essential details about molecular interactions and functions.X-ray crystallography has been instrumental in solving the structures of many important biomolecules. It involves diffracting X-rays through a crystallized sample of the protein or nucleic acid and analyzing the pattern to deduce its structure. However, not all molecules can be easily crystallized, posing a challenge. Cryo-electron microscopy overcomes some limitations of crystallography by allowing scientists to observe molecules in a near-native state without the need for crystallization. This advancement has been recognized with a Nobel Prize in Chemistry.In structural biochemistry, various advanced techniques are used to unravel the mysteries of biomolecular structures. These techniques enable scientists to observe, model, and manipulate biological macromolecules, facilitating the understanding of their diverse functions and interactions.X-ray crystallography is a pioneering method for determining the atomic and molecular structure of crystals, including proteins and nucleic acids. By measuring the angles and intensities of X-rays diffracted through a crystal, researchers can produce a three-dimensional image of electron densities, which helps in mapping out the precise structure of a molecule.Here is a basic equation involved in X-ray crystallography:Bragg's Law: $n\lambda = 2d\sin\theta$ where n is an integer, λ is the wavelength of the incident X-ray, d is the spacing between the crystal planes, and θ is the angle of incidence. A significant example of X-ray crystallography's impact is the determination of the structure of hemoglobin, which elucidated how it carries oxygen in the bloodstream. NMR spectroscopy is utilized to study the structure and dynamics of proteins and nucleic acids in solution. NMR provides information about the physical and chemical properties of atoms or the molecules in which they are contained, making it ideal for viewing biomolecules in their natural state.One of the limitations of X-ray crystallography is that it requires the biomolecule to be in a crystallized form, which is not always feasible. On the other hand, NMR spectroscopy does not require crystallization. It uses the magnetic properties of atomic nuclei and their interaction with magnetic fields to get high-resolution data, allowing researchers to analyze molecules in more physiologically relevant environments. The challenge with NMR lies in its difficulty to analyze very large biomolecules and the need for high concentrations of samples.Cryo-electron microscopy (Cryo-EM) is a state-of-the-art technique that has revolutionized the field of structural biochemistry. By flash-freezing aqueous samples of biomolecules, scientists can use electron beams to capture detailed images of biomolecular complexes without requiring crystallization.Cryo-EM is especially powerful for studying large complexes such as ribosomes. Using Cryo-EM, researchers were able to visualize the Zika virus at an unprecedented resolution, which was crucial for the development of vaccines and therapeutic strategies. For clarity and quick comparison, here's a chart comparing the various techniques:TechniqueRequires Crystallization?Sample StateBest forX-ray CrystallographyYesCrystallineSmall to Medium-sized proteinsNMR SpectroscopyNoSolutionSmall proteins and nucleic acidsCryo-EMNoFrozen HydratedLarge complexesStructural biochemistry plays a significant role in medical research by offering profound insights into the molecular structures of biological compounds. Understanding how these molecules function and interact provides a foundation for many medical breakthroughs.In drug discovery, structural biochemistry is essential for understanding the specific interactions between drug molecules and their biological targets. This understanding leads to the development of medications that can effectively combat diseases. By analyzing molecular structures, researchers can design drugs that fit precisely into the active sites of their target proteins.At the molecular level, the interaction between a drug and its target is often described through equations such as the binding affinity equation: $K_d = \frac{[D][T]}{[DT]}$ where K_d is the dissociation constant, $[D]$ represents the concentration of the drug, $[T]$ is the concentration of the target, $[DT]$ is the concentration of the drug-target complex.A lower K_d value indicates a higher affinity of the drug for its target, which is often desirable in therapeutic settings.By studying the structures of DNA and associated proteins, structural biochemists can identify mutations that lead to genetic disorders. These abnormalities in genetic material can cause conditions such as sickle cell anemia or cystic fibrosis. By mapping out these molecular structures, researchers can pinpoint exact locations of defects and understand their biochemical consequences, paving the way for potential therapies.Consider the case of cystic fibrosis, a genetic disorder caused by mutations in the CFTR gene. Structural biochemistry has enabled researchers to determine the precise configuration of the CFTR protein, shedding light on how specific mutations disrupt its function. This understanding has led to the development of targeted drugs that can correct these defects, providing significant relief to patients.Enzymes are proteins that catalyze biochemical reactions, and understanding their structure is key to manipulating their activity. Structural biochemistry helps explain how enzymes recognize their substrates and what structural features are critical for their function. This knowledge can be used to design inhibitors that prevent enzyme action, which is crucial in treating diseases where enzyme activity is detrimental, such as in cancer or bacterial infections. A classic example of enzyme inhibition is the drug penicillin, which inhibits the enzyme transpeptidase in bacteria, preventing them from forming cell walls and thereby killing them. Structural biology in biochemistry delves into the architecture of biomolecules, revealing how their form enables their function. This field is crucial for understanding the complex interactions that sustain life.Proteins are fundamental macromolecules with diverse roles in biological processes. They function as enzymes, structural components, signaling molecules, and transporters. Understanding protein structure is vital since it dictates how they interact with other molecules.The primary structure of proteins consists of a sequence of amino acids, held together by peptide bonds. This linear chain folds into secondary structures like alpha-helices and beta-sheets, stabilized by hydrogen bonds. Tertiary structure refers to the overall 3D shape of a single polypeptide, while quaternary structure involves multiple polypeptides assembling into a functional protein complex. Protein Structure Hierarchy:Primary: Amino acid sequenceSecondary: Alpha-helices and beta-sheetsTertiary: 3D conformation of a single polypeptideQuaternary: Assembly of multiple polypeptides For instance, hemoglobin has a quaternary structure comprising four polypeptide chains. Its ability to transport oxygen is directly linked to its structural configuration. Minor alterations in amino acid sequences can significantly impact protein function, which is why genetic mutations sometimes result in diseases.Various techniques are used to study protein structures, each offering unique insights:X-ray Crystallography: Provides high-resolution details of crystalline proteins.NMR Spectroscopy: Useful for examining proteins in solution.Cryo-electron Microscopy: Captures images of large protein complexes in their native state.Spectrophotometry: Measures absorption of light to study protein-ligand interactions.X-ray crystallography has been a cornerstone in structural biology, leading to breakthroughs in understanding biomolecular structures. It works by analyzing the pattern of X-ray beams diffracted through crystals of biomolecules. The famous equation used here is Bragg's Law: $n\lambda = 2d\sin\theta$ where n is an integer, λ is the wavelength of X-rays, d is the distance between crystal planes, and θ is the angle of incidence. These details collectively enable the creation of a 3D model that showcases the atomic positions within the crystal.Cryo-EM has gained prominence for visualizing large biomolecular complexes that cannot be crystallized easily, like viruses and ribosomes. Structural Biochemistry Definition: A branch of biology focusing on molecular structures of biological macromolecules, such as proteins and nucleic acids, assessing how structural changes affect their functions.Structural Biochemistry in Medical Research: Provides crucial insights into interactions and functions of biomolecules, aiding drug design, genetic engineering, disease diagnosis, and understanding evolutionary relationships.Biochemistry Protein Structure and Function: Proteins' diverse biological roles depend on their structure, which includes primary (amino acid sequence), secondary (alpha-helices and beta-sheets), tertiary (3D conformation), and quaternary (assembly of polypeptides) structures.Biochemistry Protein Structure Techniques: Techniques include X-ray crystallography, NMR spectroscopy, Cryo-electron Microscopy, and spectrophotometry, each providing unique insights into protein structures.Techniques in Structural Biochemistry: Tools such as X-ray crystallography, NMR spectroscopy, and Cryo-electron Microscopy are used to determine molecular structures of biomolecules, crucial for visualizing molecular interactions.Structural Biology in Biochemistry: It examines the architecture of biomolecules, essential for understanding biological processes through molecular interactions. What is the role of structural biochemistry in drug design and development? Structural biochemistry plays a crucial role in drug design and development by providing insights into the molecular structures of biological targets, which facilitates the identification of binding sites and the design of molecules with optimal interactions, increasing the efficacy and specificity of potential therapeutic agents. How does structural biochemistry contribute to understanding protein functions? Structural biochemistry elucidates protein functions by revealing their three-dimensional structures. This understanding allows scientists to identify active sites, binding interactions, and conformational changes, which are crucial for protein activity. By correlating structure with function, it aids in drug design and understanding disease mechanisms related to protein dysfunctions. How does structural biochemistry aid in disease diagnosis and treatment? Structural biochemistry aids in disease diagnosis and treatment by providing insights into the molecular structure of biomolecules, allowing for the identification of abnormalities or mutations associated with diseases. This understanding facilitates the development of targeted therapies and drugs by revealing specific binding sites and mechanisms of action, improving precision medicine. What are the primary techniques used in structural biochemistry to determine molecular structures? The primary techniques used in structural biochemistry to determine molecular structures are X-ray crystallography, nuclear magnetic resonance (NMR) spectroscopy, cryo-electron microscopy (cryo-EM), and mass spectrometry. How does structural biochemistry differ from traditional biochemistry? Structural biochemistry focuses on the three-dimensional structures of biomolecules and how these structures influence their functions. It uses techniques like X-ray crystallography and NMR spectroscopy. Traditional biochemistry, meanwhile, explores the chemical processes within biological systems, including reactions, metabolism, and the roles of different biomolecules. Save Article Access over 700 million learning materials Study more efficiently with flashcards Get better grades with AI Sign up for free Already have an account? Log in Good job! Keep learning, you are doing great. Don't give up! Next Open in our app At StudySmarter, we have created a learning platform that serves millions of students. Meet the people who work hard to deliver fact based content as well as making sure it is verified. Lily Hulatt is a Digital Content Specialist with over three years of experience in content strategy and curriculum design. She gained her PhD in English Literature from Durham University in 2022, taught in Durham University's English Studies Department, and has contributed to a number of publications. Lily specialises in English Literature, English Language, History, and Philosophy. Get to know Lily Gabriel Freitas is an AI Engineer with a solid experience in software development, machine learning algorithms, and generative AI, including large language models' (LLMs) applications. Graduated in Electrical Engineering at the University of São Paulo, he is currently pursuing an MSc in Computer Engineering at the University of Campinas, specializing in machine learning topics. Gabriel has a strong background in software engineering and has worked on projects involving computer vision, embedded AI, and LLM applications. Get to know Gabriel StudySmarter is a globally recognized educational technology company, offering a holistic learning platform designed for students of all ages and educational levels. Our platform provides learning support for a wide range of subjects, including STEM, Social Sciences, and Languages and also helps students to successfully master various tests and exams worldwide, such as GCSE, A Level, SAT, ACT, Abitur, and more. We offer an extensive library of learning materials, including interactive flashcards, comprehensive textbook solutions, and detailed explanations. The cutting-edge technology and tools we provide help students create their own learning materials. StudySmarter's content is not only expert-verified but also regularly updated to ensure accuracy and relevance. Learn more Read time: 32 minutes An Introduction to Structural Biology. Credit: Technology Networks via YouTube What is structural biology? Structural biology is a field dedicated to the study of the structure of molecules that form living matter, including proteins, nucleic acids, lipid membranes and carbohydrates. The information provided by structural biology is crucial to understand the function and dynamics of biomolecules, as well as the mechanisms of interaction among them.1 ContentsWhat can structural biology tell us? - Macromolecule structure - Primary structure, secondary structure, tertiary structure and quaternary structure - Structural domains - Structural motifs - Protein folding - Protein shape - Protein dynamicsCommon techniques in structural biologyIntegrative structural biologyIn-silico protein structure predictionsApplications of structural biology - Identifying drug targets - Studying host–pathogen interactions - Protein aggregation in health and disease - Determining virus structure - Making a molecular modelReferences The origins of modern structural biology date back to the 1910s, when the German physicist Max von Laue discovered that biological crystal samples irradiated with X-rays produced diffraction patterns that depended on their internal atomic organization.2 This discovery, together with the work of William and Lawrence Bragg, marked the beginning of the development of one of the main structural biology techniques: X-ray crystallography.3 These advances allowed the elucidation of a protein structure for the first time4 and the identification of the DNA double-helix in the 1950s.5 Nuclear magnetic resonance (NMR) spectroscopy contributed enormously to the development of structural biology from the 1980s, when scientists started to apply it extensively to the study of biomolecules.6 Finally, in the last decades, other techniques have gained prominence in structural biology, such as small-angle X-ray scattering (SAXS),7 electron paramagnetic resonance spectroscopy (EPR)8 and, especially, cryogenic electron microscopy (cryo-EM).9 Structural biology provides information about the organization of living matter, including the spatial disposition of atoms and molecules, the global folding of a biopolymer or even the association of biological macromolecules to form large, intricate complexes. Additionally, structural biology is capable of unveiling details about molecular interactions and dynamic parameters, such as molecular flexibility. Proteins and nucleic acids are the most studied biomolecules due to the large number of diverse functions they perform in living organisms. These functions are closely related to their structural organization. To address this relationship between structure and function, structural biology makes use of some fundamental concepts related to the hierarchical assembly of proteins and nucleic acids (such as macromolecule structure; primary, secondary, tertiary and quaternary structures; structural domains and motifs; protein shape), or to the process of structural organization itself from a thermodynamic point of view (protein folding and protein dynamics). These concepts are explained below. The tertiary structure of a protein is its overall shape, including the arrangement of its constituent polypeptide chains, in three-dimensional (3D) space. This 3D arrangement will be influenced by interactions between different parts of the chain(s), such as hydrogen and ionic bonds and hydrophobic interactions between nonpolar amino acid side chains. Macromolecule structure Macromolecules are usually considered to be biopolymers with a mass larger than 5,000 Da and are a central constituent of living matter.1 The disposition of the different atoms within the molecule and their connectivity determine the location of chemical groups able to establish interactions or to undergo chemical transformations. Their positionings are essential for the macromolecule to associate to other partners or to perform a biological activity. Primary structure, secondary structure, tertiary structure and quaternary structure Proteins are polymeric molecules consisting of monomers called amino acids, which are connected by peptide bonds. There are 20 different common amino acids in proteins that differ in their side chains and therefore show different physicochemical properties. The protein primary structure is defined by the distribution or sequence of amino acids in the polymer chain (Figure 1). Within the protein polymer, the angles formed by the bonds between an amino acid, the preceding one and the successive one, are called "dihedral angles" (represented as φ and ψ, respectively). These angles are defined by the non-covalent interactions established between different amino acids. When a polypeptide sequence contains a series of consecutive amino acids displaying the same dihedral angles, the polymeric chain forms regular structures known as protein secondary structures (Figure 1). The most common are α-helices (φ = -60°; ψ = -45°), β-strands (φ = -135°; ψ = 135°) and turns (variable φ and ψ values). The way in which the secondary structure elements of a protein, together with unstructured regions, fold to form a packed entity is known as the tertiary structure (Figure 1). To perform their function, many proteins need to form complexes by associating with other proteins. Each protein within the complex is a subunit and the way the different subunits associate to form a larger, organized, functional entity is known as the quaternary structure (Figure 1).1, 10, 11, 12 The structure of nucleic acids can be described following a similar scheme, as they are polymeric macromolecules composed by monomers (nucleotides) connected by phosphodiester bonds. There are five different types of nucleotides (adenine, cytosine, guanine, thymine – only in DNA – and uracil – only in RNA) and, as in the case of proteins, the specific sequence of the nucleotides defines the primary structure of nucleic acids (Figure 1). In both DNA and RNA, secondary structure elements are determined by the interactions between nucleotides, which can be sequential (stacking interactions) or non-sequential (hydrogen bonds) (Figure 1). Regarding DNA, hydrogen bonds between nucleotides from different chains generate helical structures. In the case of RNA, the most common elements of the secondary structure are helices (also called stems, formed by paired nucleotides) and loops (formed by unpaired nucleotides). DNA organizes at a higher level, forming double-helical structures, when two DNA molecules have their nucleotides paired through hydrogen bonds. This is the tertiary structure of DNA (Figure 1) and it can display diverse conformations, such as A-DNA, B-DNA (predominant in living cells) and Z-DNA. Other tertiary structures observed in DNA are triple and quadruple helices (triplexes and quadruplexes). In the case of RNA, the most common tertiary structure elements are the stem-loop (a base-paired helix that ends in a small loop) and the pseudoknot (a stem-loop in which the unpaired loop pairs with another region of the sequence). Quaternary structure (Figure 1) is the higher level of organization in nucleic acids. For DNA, it can be applied to the association with proteins (histones) to form chromatin. For RNA, a typical example is the association of various RNA molecules (subunits) to form larger entities, such as the ribosome.1, 10, 11, 12 Structural domains In proteins, a structural domain is defined as a region of the polypeptide chain composed by less than 200 amino acids and usually capable of maintaining their folding when isolated from the rest of the protein. Structural domains are very compact and often display a globular shape. Regarding their secondary structure elements, structural domains can be classified into five groups: α (only α-helices), β (only β-strands), α/β (β-strands connected by α-helices), α+β (separate helical and β-strand regions) and cross-linked (elements of secondary structure stabilized by metal ions or disulfide bonds).1, 10, 11, 12 Structural motifs In both proteins and nucleic acids, secondary structures can pack with each other, creating a more compact structural level (supersecondary structure) whose elements are known as structural motifs and that can be found in different molecules. In proteins, the most common structural motifs can be divided into α-packings (such as the helix-turn-helix motif), β-packings (such as the β-hairpin, β-meander, Greek key, β-barrel and β-helix) or αβ-packings (such as the αβ-barrel, Rossmann fold and βαβ motif). In the cases of nucleic acids, structural motifs are considered tertiary structure elements and some examples include the stem loops, quadruplexes, cruciform DNA and displacement loops (D-loops).1, 10, 11, 12, 13 Figure 1: Hierarchical organization of the structure of proteins and nucleic acids showing examples of the most common structural elements. Credit: Technology Networks. Protein folding Protein folding is a process in which a polypeptide chain adopts its functional three-dimensional (3D) molecular arrangement (called native conformation). This process takes place in a hierarchical manner, meaning that the simpler structural elements are formed first (secondary structure) and then they pack with each other to create a folding core. Once this core is constructed, global protein folding occurs in a cooperative manner. During the course of folding, many physicochemical interactions play key roles, such as hydrogen bonds, van der Waals forces and hydrophobic effects. Sometimes, special types of proteins called chaperones assist the process, ensuring correct protein folding .14 Due to the high complexity of polypeptides, the folding process could be expected to be slow, as there is a myriad of possible folding schemes. However, in reality, most proteins are able to acquire their functional structure within a time range in the order of milliseconds.15To explain this fact, protein folding is usually illustrated with an energy landscape funnel (Figure 2). Initially, the polypeptide folding is not energetically favored (it is high energy), but once some regions of the chain start to adopt regular conformations, the energy of the folding intermediate decreases. In this context, the polypeptide chain passes through a series of intermediate steps (molten globule) that gradually decrease its energy requirement, making the process more energetically favorable. In each folding step, only a certain number of energy states are accessible and this way, the folding process becomes more and more cooperative until reaching the final structure (native structure), which has the lowest energy.16, 17 Figure 2: Energy landscape funnel showing the protein folding process from the unfolded state to the native state (lowest energy). Credit: Thomas Splettstoesse, reproduced under the Creative Commons Attribution-Share Alike 3.0 Unported license. Protein shape The tertiary structure of a protein determines its global shape, which is strongly related to the protein function. Many scientists have tried to develop bioinformatics tools able to classify proteins according to their shape or global structure. These tools will enable a better understanding of protein functions and the design of new proteins with specific functions for clinical or biotechnological applications.18, 19, 20 Generally, proteins can be divided into four classes regarding their global shape: globular proteins, fibrous proteins, membrane proteins and intrinsically disordered proteins (IDPs), shown in Figure 3. Globular proteins display a spheroidal shape, they can show a high degree of structural complexity and perform diverse functions. On the other hand, fibrous proteins have elongated shapes, are relatively simple from a structural point of view and play structural roles, typically constituting fibrillar networks. Membrane proteins contain regions that are able to embed into the hydrophobic core of lipid bilayers and are specialized in signal transduction or membrane trafficking. Finally, IDPs are proteins with a very low level of structuration and thus very dynamic.12, 21, 22, 23, 24 Figure 3: Examples of the different protein shapes found in nature: A) Globular (human hemoglobin, PDB: 1SI4); B) Fibrous (human keratin, PDB: 6EC0); C) Membrane protein (human CCR5 chemokine receptor, PDB: 4MBS); D) Intrinsically disordered protein (human TDP43, PDB: 2N4P). Credit: All structures are from the RCSB Protein Data Bank, reproduced under the CC0 1.0 Universal (CC0 1.0) Public Domain Dedication. A) Sen U, Dasgupta J, Choudhury D, Datta P, Chakrabarti A, Chakrabarty SB, Chakrabarty A, Dattagupta JK, B) Eldirany SA, Lomakin IB, Bunick CG, C) Tan Q, Zhu Y, Han GW, Li J, Fenalti G, Liu H, Cherezov V, Stevens RC, GPCR Network (GPCR), Zhao Q, Wu B, altered to include parallel lines to indicate the position of the membrane, D) Mompean M, Romano V, Pantoja-Uceda D, Stuani C, Baralle F, Buratti E, Laurents DV. Protein dynamics Proteins are not rigid solids but very dynamic macromolecules with different degrees of freedom. At the local level, rotation around chemical bonds, especially in amino acid side chains, is common and hence many chemical groups are able to modify their orientation within the protein. At a higher level, the protein backbone is flexible in those regions that are not regularly structured, such as loops or disordered regions. Rearrangement of those regions often occurs upon binding of other molecules or changes in the environmental conditions. Sometimes, this kind of structural reorientation leads to more drastic changes in the whole protein shape, with notable displacement of protein domains.25, 26, 27 As a result of these dynamic features, a protein does not display a unique structure under physiological conditions, but rather fluctuates between many different conformations (conformers). Dynamic changes in proteins are essential for function because they allow them to adapt their shape to other binding partners or receptors, or switch between active and inactive forms.25, 26, 27 There are many techniques used to address structural biology questions. All these techniques possess strengths and limitations and thus, scientists usually combine some of them to achieve a more complete description of the studied system. The main techniques used in structural biology are: Cryo EMX ray crystallography (including serial femtosecond crystallography (SFX) and high-throughput (HT) crystallography)NMR spectroscopyCross-linking mass spectrometry (XL-MS)Small-angle X-ray scattering (SAXS)Neutron diffractionProteolysisCircular dichroism (CD)Electron paramagnetic resonance spectroscopy (EPR) To find out more about the techniques used in structural biology, their strengths and limitations, visit the article below. Structural characterization of biomolecules is frequently challenging. While sometimes it is possible to build high-resolution molecular models, many biological molecules display characteristic features that hamper structural analysis. For this reason, integrative structural biology has emerged as a clever approach to circumvent those difficulties. This field addresses the structural study of biomolecules by integrating information obtained through different experimental techniques combined with physical and statistical methodologies.28, 29, 30, 31, 32 Integrative structural biology provides a very complete description of biomolecular ensembles by combining information about aspects such as atomic spatial organization, relative disposition of subunits in complexes, molecular dynamics and flexibility and intra- and inter-molecular interactions, obtained by different techniques. This information is transformed into structural restraints that must be fulfilled with an acceptable tolerance by molecular models that are usually built and optimized by computational methods. This process is known as integrative/hybrid (I/H) modeling and is performed in a series of consecutive and iterative steps, including the retrieval of all the available data of the system, the use of that information to build models of the structural components, the scoring and filtering of those models and, finally, the validation of the whole model.28, 29, 30, 31, 32 Integrative structural biology is an advantageous approach to overcome the inherent limitations of using a sole technique to construct a detailed structural description of a biomolecule. In this regard, the approach is especially useful to tackle the study of large, intricate biomolecular ensembles. An emblematic example of the use of I/H modeling is the structural study of the nuclear pore complex of yeast (NPC). NPC is a huge ensemble of proteins (> 500 subunits) embedded in the nuclear envelope that is the main component responsible of the transport of proteins and nucleic acids between the nucleus and the cytoplasm. Due to its size and flexibility, it is impossible to elucidate its structure using uniquely atomic resolution techniques such as X-ray crystallography or NMR spectroscopy. Nonetheless, a precise model has been solved using an integrative approach that combines information from X-ray crystallography (isolated subunit structures), XL-MS (distance restraints), quantitative MS and in vivo calibrated imaging (stoichiometry) and cryo-EM (overall complex shape). By combining the information from all of these techniques, a series of molecular models that fulfilled the imposed restraints was built. These models were ranked by the value of a scoring function that quantifies how well the models fit to the restraints. The models with highest score were selected as they were the most consistent with the experimental data, and they were optimized by computational tools that introduced slight changes in the structure without violating any restraint in order to minimize the energy of the system. Finally, to validate the overall model, it is useful to keep some experimental data aside and, once the model is built, employ these data to check whether the model is consistent with them (Figure 4).28, 29, 30, 31, 32 Figure 4: Summary of the integrative approach for structure determination. Credit: Technology Networks, modified from Rout et al.29 Proteins play a central role in every biological process, performing a wide variety of functions. These functions are closely related to their native structure. For this reason, one of the purposes of structural biology is the elucidation of protein structures to understand how they work. As explained before, solving protein structures is a challenging process that can be expensive and time consuming. In this regard, the development of increasingly powerful informatics tools has led to the expansion of the field of in-silico protein structure prediction. This discipline is focused on the inference of the 3D organization of proteins from their amino acid sequence using computational methodologies. Since proteins display a hierarchical structural organization, in-silico approaches can be applied to predict secondary, tertiary or quaternary structures. As organization complexity increases, structural prediction becomes more arduous, and it is more difficult to get a high degree of accuracy. There are various in-silico approaches for protein structure prediction, such as secondary structure prediction, homology modeling, protein threading, ab initio methods and artificial intelligence (AI) methods. Secondary structure prediction (SSP): This method predicts secondary structure elements (α-helices, β-strands and turns) from the amino acid sequence by using algorithms based on machine learning, neural networks (NNs) and sequence alignments. Although SSP only gives information on the number, type and sequential position of secondary structure elements, it is a very useful and quick tool, able to reach an accuracy of around 90%.33 Some examples of software used for secondary structure prediction are PredictProtein,34 GOR35 and Jpred.Homology modeling: In this method, the structure of a protein is predicted from its amino acid sequence and the use of a template structure of a homologous protein to build the model. This method provides a good accuracy provided that the sequence identity is higher than 50%. Homology modeling is limited by the availability of solved structures of homologous proteins with a significant degree of sequence identity. Examples of homology modeling tools are SWISS-MODEL,37 IntFOLD38 and ESyPred3D.Protein threading: When the target protein has no homologous proteins with solved structures, its structure can be predicted using proteins with the same kinds of folds as templates. This methodology is carried out by selecting adequate protein structures as templates and aligning each amino acid of the protein with those templates. A scoring function allows evaluation of how well each amino acid fits to the template. By optimizing that scoring function, a model is constructed following statistical criteria. This methodology is able to generate good predictions when sequence identity between the target protein and template is low (< 25%). Some examples of protein threading software are Phyre240 and I-TASSER.Ab initio methods: These methods are designed to predict the tertiary structure of a protein using solely its amino acid sequence as a starting point. This complex task requires a great computational effort, and it has been used with proteins of relatively small size. The strategy consists of starting with some candidate conformations and filtering them based on thermodynamic and energetic criteria. To facilitate the prediction, the initial candidates are sometimes built according to previous secondary structure predictions. The most renowned tool used for ab initio protein predictions is Rosetta.AI methods: During the last decades, the increasing sophistication of computational technologies has permitted the implementation and optimization of AI approaches, especially those based on NNs and deep learning. From the amino acid sequence and without the need of templates, these methods are able of predict protein structures with a very high degree of accuracy.43, 44, 45 In 2018, the program AlphaFold was presented, a deep learning-based software to predict protein structures that allowed the elucidation of many challenging protein structures with a high degree of accuracy in a short period of time. Although it is considered a milestone in the field of protein structure prediction, it also has some limitations: it cannot reliably predict the structure of IDPs; it does not include predictions for post-translational modifications or co-factors and it describes only one conformation in proteins that can adopt multiple ones.46, 47 There is a plethora of applications and potential applications for structural biology studies, let us consider a few of key areas. Identifying drug targets Structural biology is essential in the field of drug discovery in which the main goal is to find new chemical compounds targeting biomolecules as treatments for disease. The process of drug discovery based on structural information is known as structure-based drug discovery (SBDD). The SBDD workflow generally starts by identifying those proteins that are involved in the development of any disease. Then, the proteins are expressed, extracted and purified to be analyzed by different physicochemical techniques, such as X-ray crystallography, cryo-EM and NMR spectroscopy. Following an integrative structural biology approach, the 3D structure of the target protein is solved. Next, screening is performed on an active compounds database, including the computational docking of the compounds into the binding site of the target protein. Finally, the compounds that bind more favorably to the protein binding site are selected as hits. These hits will be evaluated experimentally to check their capacity to bind to the protein in vitro and in vivo (and eventually block its functionality) in order to select the best candidates (leads) to follow the drug development process. Those lead compounds will be slightly modified to create variants that potentially display better therapeutic properties (such as improved action, lower toxicity and better absorption).48, 49, 50, 51, 52, 53, 54, 55 Some examples of drugs discovered by using an SBDD approach are raltitrexed (treatment of HIV infection), isoniazid (treatment of tuberculosis) and STX-0119 (treatment of lymphoma). The use of structural biology is enormously advantageous because a structural model of the target proteins allows extensive screenings to be carried out by computational methods, considerably reducing experimental costs and time.48, 49, 50, 51, 52, 53, 54, 55 Studying host–pathogen interactions Pathogens (viruses, bacteria and parasites) are capable of establishing interactions with the host, which help them to infect, multiply and survive within the host organism. The identification and characterization of host–pathogen interactions at the molecular level is crucial to understand how many diseases are transmitted and developed and, eventually, how they can be treated. In this regard, structural biology is a very powerful tool to predict and study host–pathogen interactions (as they usually involve protein–protein interactions) and characterize the structure of the biomolecules involved in those interactions.56, 57, 58 There are various approaches to address the prediction of host–pathogen interactions that can be classified into two categories: based on sequence and domain information and based on 3D structural information. Some of the methods based on sequence and domain information are:56, 57, 58 Homology-based methods: They are based on the search of known interacting sequences in homologous proteins of different organisms. Since pathogens' interacting proteins can undergo rapid variations to adapt to the host defenses, these methods are prone to generate a lot of false positives.Domain-based methods: As sequences can be variable, some methods use higher order structural data, such as protein domain structure. These structures are preserved in homologous proteins, even if the sequence changes.Motif and integration-based methods: Motifs are structural features simpler than domains and have been proven to be essential in host–pathogen interactions. Sometimes this structural information is combined with the sequence data in an integrative way to improve the predictions. With regard to the approaches based on 3D structural information, the workflow includes the search of the genome of both host and pathogen to find proteins similar to known complexes and the use of available 3D structural data to assess the potential interactions.56, 57, 58. From a general perspective, all these approaches use the available information provided by structural biology about structure and interactions as input data for AI tools, such as machine learning. These AI methodologies employ the data, together with a series of training sets (information given to the AI tool to improve its capacity to make good predictions), to predict networks of potential host–pathogen interactions that should be validated by experimental assays.56, 57, 58 Protein aggregation in health and disease Protein aggregation is a process that takes place under certain circumstances in which IDPs or misfolded proteins accumulate and stack together, generating deposits inside the cell or in the extracellular medium. The product of protein aggregation can be amorphous aggregates, oligomers or amyloids, the last ones being the most clinically relevant. Amyloids are protein structures made up of two tightly packed long β-sheets forming long fibers. In humans, the presence of amyloid fibers is associated with the development of many diseases, some of them serious neurodegenerative conditions, such as Alzheimer's, Parkinson's, Huntington's diseases and amyotrophic lateral sclerosis (ALS).59, 60 At present, there is no cure for these diseases and, unfortunately, they are fatal in the long term. For this reason, the structure of amyloids and their mechanism of formation and elongation have been the focus of many structural biology research projects during the last decades. The amyloid fiber structures have been analyzed by low- and high-resolution techniques, including CD spectroscopy, Förster resonance energy transfer (FRET), atomic force microscopy (AFM), dynamic light scattering (DLS), surface plasmon resonance (SPR), X-ray crystallography, cryo-EM and NMR spectroscopy.61, 62, 63, 64 All the structural information available on amyloid fibrils has allowed the characterization of its mechanism of aggregation and suggestion of different therapeutic structure-based strategies. Some of the therapeutic approaches are focused on the inhibition of the aggregation by using denaturants, chaperones, organic compounds or peptides. Other approaches are oriented to block the pathways that amyloids follow to cause pathogenicity.61, 62, 63, 64 Determining virus structure Viruses are molecular assemblies with infectious capacity that are responsible for a myriad of diseases affecting humans, animals and plants. With a genome encoding very few proteins, viruses are able to infect and replicate inside living cells using a very simple machinery. Their simplicity is precisely one of their strengths, as it makes them difficult to target with drugs. Viral capsids are made up of proteins and can display a great variety of shapes and sizes. Understanding how viruses assemble and interact with the host cells and their machinery is essential to develop effective treatments. In this context, different structural biology techniques have been used to gain structural information about viruses. On one hand, some low-resolution techniques provide data about secondary structural elements and folding/unfolding dynamics, for instance CD spectroscopy65, 66 or fluorescence spectroscopy;65 or about subunit assembly and complex formation, like SAXS.67 On the other hand, high-resolution techniques are able to provide further structural details at the atomic level. For instance, MS can be used to identify protein subunits and their post-translational modifications, as well as the stoichiometry of the viral capsid.68 Alternatively the complete structure of viral capsids can be elucidated by solid-state NMR spectroscopy,69, 70 X-ray crystallography71 and, especially, cryo-EM.72 Structural information about viruses and their components has been used for the discovery of new antiviral drugs and for the search of potential repurposing opportunities of pre-existing drugs. The strategy followed for antiviral drug discovery is the classic SBDD approach but, in this case, the target proteins are those expressed by the viruses.73, 74, 75 Making a molecular model Structural biology is concerned with the search for information about the structural features of biomolecules by using a plethora of physicochemical techniques. The use of experimental data from different techniques in an integrative way enables the construction of molecular models. These models are structures whose atomic organization matches with the experimental results within a tolerance range. The physicochemical techniques that supply the experimental data for molecular modeling are just as important as the computational tools (including AI resources) that help to integrate all the information and optimize models to achieve the highest accuracy.76, 77, 78, 79 The importance of molecular models stems from the fact that they are very useful to understand how biomolecules organize, their dynamics and their ability to interact with other molecules. This information is not only relevant for basic science, but also for its applications in the field of medicine, pharmacology or biotechnology.76, 77, 78, 79 Building accurate molecular models of biomolecules is a grueling task, costly and time-consuming. For this reason, scientists have created specialized public databases that are accessible on the internet where they deposit the solved structures. In this regard, the most important database is the Protein Data Bank (PDB),80 where thousands of peptide and protein structures elucidated by different techniques can be found and downloaded, as well as all the information available. There are similar databases for nucleic acids (NDB)81 and carbohydrates (CSDB).82 (Click to expand)References1. Nelson DL, Cox MM. Lehninger Principles of Biochemistry. New York: WH Freeman; 2021. ISBN:9781319322342.2. Von Laue M, van der Lingen JS. Beobachtungen über Röntgenstrahlinterferenzen. Naturwissenschaften. 1914; 2(13):328-329. doi:10.1007/BF014957123. Bragg WH. The analysis of crystal structure by X-rays. Science. 1924; 60(1546):139-149. doi:10.1126/science.60.1546.1394. Kendrew JC, Bodo G, Dintzis HM, Parrish RG, Wyckoff H, Phillips DC. A three-dimensional model of the myoglobin molecule obtained by X-ray analysis. Nature. 1958; 181(4610):662-666. doi:10.1038/181662a05. Watson JD, Crick FHC. 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Tokyo, Springer. 2017:75-113. doi:10.1007/978-4-431-56454-6_5 Structural Biochemistry is the field of biochemistry that focuses mainly on the components, functions, and structures of molecules of cells within living organisms. It helps us understand cells through the theories of Chemistry and the laws of Physics. Structural biochemistry concentrates on the study of macromolecules (such as carbohydrates, proteins, polysaccharides, lipids), their monomeric units (amino acids, nucleic acids, nucleotides) and important reactions involving them. Biochemistry is interlinked between Biology and Chemistry. Biology is the study of the cell's interaction within its environment. Chemistry takes these interactions and breaks it down to the molecular level and provides information on how these events occur. Structure is defined by how a system is composed. It is the way in which parts are arranged or put together to form the whole. As a result, when these two subjects are fused, Biochemistry and Structure, the subject known as Structural Biochemistry comes into being. Structural Biochemistry forms the basis of the molecular parts via interactions such hydrogen, ionic, and covalent bonding that form the cellular structure. Structural biochemistry is a study of various macromolecules and how their structure is appropriate to their functions. Macromolecules studied in structural biochemistry courses that consists of proteins, carbohydrates, lipids, and nucleotides. They cover everything from the multitude of functions that proteins participate in (such as transport of molecules, cytoskeleton formation, and cell growth) to the building blocks of DNA, and even to the catalytic mechanism of different enzyme. All macromolecules in general contribute to the survival of humans, as well as to the composition of inanimate objects. Another way to define structural biochemistry is by stating that it is the scientific study of the biochemical systems of life and living organisms; it is about biological molecules that construct chemical forms, and the close correlation between structure and function. Furthermore, biochemistry applies chemistry to biological studies at the cellular and molecular level. It surfaces as a distinct category at the turn of the 20th century, as scientists combined chemistry, physiology, and biology to explore the chemistry of living environments and systems. Using this field, biochemical scientists have been attempting to understand and explain the many chemical mechanisms and biological structures shared by living organisms, and to formulate some basic organizing principles shared by all forms of life as well. Today, biochemistry is considered as the study of life in its chemical processes; the study of both a life science and a chemical science. It investigates the chemistry of living organisms and the molecular basis for the alteration happening in the living cells. It uses the schemes of Chemistry, Physics, molecular biology and immunology to study the structure and behavior of the complex molecules found in biological material such as amino acids in a protein, a large organic compound. Along those lines, it also explores the ways these molecules interact to form cells, tissues, and whole organisms. The biochemist seeks to determine how specific molecules such as protein, nucleic acids , lipids, vitamins, and hormones function in such processes. Particular emphasis is placed on regulation of the chemical reactions in the living cells. Biochemistry has become the foundation for understanding all biological processes. It has presented explanations for the sources of many diseases in humans, animals, and plants alike through laboratory techniques such as chromatography, and spectroscopy. It can frequently propose ways by which such diseases may be treated or cured. Because biochemistry community is interested in unraveling the complex chemical reactions that occur in a wide variety of life forms, it offers the basis for practical advances in medicine, veterinary medicine, agriculture, and biotechnology. It also includes such exciting new fields as molecular genetics and bioengineering. The knowledge and methods developed by biochemists are applied to in all fields of medicine, for example, in agriculture and in many chemical and health related industries. The structural biochemistry helped to fight the AIDS epidemic because the structure of HIV protease, which should be blocked in order to prevent virus spreading, could be used as a reference to determine the types of molecules that might block the enzyme. Also, it helped patients with arthritis through the study of painkillers such as ibuprofen at the molecular level and by creating a new painkiller to shut down COX-2 so that ulcers would not form, and therefore prevent the side effects. Biochemistry is also unique in providing education and research in protein structure or function and genetic engineering, the two basic components of the rapidly expanding field of biotechnology. As the broadest of the basic sciences, biochemistry includes many subspecialties such as neurochemistry, bioorganic chemistry, clinical biochemistry, physical biochemistry, molecular genetics, biochemical pharmacology, and immunochemistry. Complex Internal Structures, there is a high degree of chemical complexity and microscopic organization. Thousands of molecules allow cells to maintain a very intricate internal structure, which include long polymers, each with characteristic sequences of subunits, its unique 3D structure and specific selection of binding sites. Systems are able to maintain equilibrium by extracting, transforming and using energy from the environment. This enables organisms to do mechanical, chemical and osmotic work. Reproduction, with defined function of organism's components, organisms are interacting with one another The interplay between organism have allowed changed in components that cause coordination and compensation to necessary adaptation to environment. Mechanisms for sensing and responding to alterations in organism environments A constant adjusting of internal chemistry in order to adapt to change in their local environment for better survival. Ability for precise self-replication and self-assemblyConstruction of entirely complete genetic material in each and every individual cell unique to the organism. A capability to evolve over time This fundamental unity of the living organism is reflected at the molecular level in similarities of gene sequences and protein structures.