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A Review On Biophysic and Stractural Biology: (Chemistry and Its Stractural Properties)

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ABSTRACT: Different macromolecules in a biological system serve different purposes. The relationship between their structure and function is intimate. The surroundings also influence the structure. Hence, understanding the structure of macromolecules as well as details about their surroundings becomes crucial. Moreover, there are drugs that affect some of the most basic functions of living things, such as protein manufacturing, nucleic acid replication, and quality articulation, which are often referred to as antibiotics. Hence, understanding the structure and function of the molecules involved in the interaction of these medications at the molecular level is necessary. Spectroscopy, NMR, CD XRD, and other methods are used to make all of this research easier. This chapter provides in-depth information on the many facets of macromolecules as well as the methods used to investigate them.

KEYWORDS: Protein, DNA, RNA, NMR, XRD, CD, Alpha helix, Beta turn, DNA-drug interaction, DNA-protein interaction

Ⅰ. INTRODUCTION: - BIOPHYSICS OF TISSUES

Since the 1800s, scientists have been studying the electrical properties of biological tissues and cell suspensions. They are important for biological applications like functional electrical stimulation, weak electric current diagnostics and treatment, radio-frequency hyperthermia, electrocardiography, and body composition because they control how current flows through the body. These electrical properties give an explanation of the fundamental biological processes. In fact, studies of biological impedance have long been important in electrophysiology and biophysics, and dielectric experiments on cell suspensions provided evidence of the existence of the cell membrane [1]. We need relative permittivity and tissue conductivities to investigate the effects of electrical stimulation on various tissues. The variety of cell shapes, their distribution throughout the tissue, and the characteristics of the extracellular medium make a microscopic description of the reaction challenging. Thus, macroscopically descriptive descriptions of biological field distributions are common. Electrical properties are challenging at the macroscale. These may depend on the frequency of the applied field (the tissue is neither a perfect conductor nor a perfect dielectric), tissue orientation in relation to the applied field (directional anisotropy), or time- and space-dependent variables (e.g., variations in tissue conductivity during electro-permeabilization).

[Ⅱ]. BIOLOGICAL MATERIALS IN AN ELECTRIC FIELD

Conducting and insulating materials, including biological tissue, have electrical characteristics. An electric field moves electric charges easily in a conductor but not in a dielectric. Foster and Schwan explain tissue electrical characteristics in further depth [2]. Charges travel inside a conductor in an electric field until the interior field is zero. An insulator has no free charges; hence, no charge movement occurs. Polar materials have molecules with different positive and negative charge centers. Electric dipole moments do exist. An applied field, E0, orients the dipoles and creates a field within the dielectric, Ep, that opposes it. Polarization occurs. Most materials have orientable dipoles and relatively free charges, reducing the electric field compared to open space. The net field inside the material, E, is the

E= E0 – Ep

If the material is an insulator, the net field is much smaller than the applied field. For a strong conductor, it is almost nil. The relative permittivity or dielectric constant, er, characterizes this decrease, according to

E= Eo/Er

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Because dipoles and charges may flow in a constrained fashion, most materials, including biological tissue, exhibit some features of both insulators and conductors. Interfaces trap charges in heterogeneous materials. Under the applied field, positive and negative ions flow in opposing directions, creating internal charge separations that operate like a very big dipole [3]. Macroscopically, the material has permittivity (E) and conductivity (S). The material's conductivity transports charge, whereas its permittivity traps or stores charge or rotates molecular dipoles. The permittivity of free space is media: $e_0 = 8{:}85\ 10^{-12}$ F/m. For media

$E= e_r e_0$

The energy stored per unit volume in a material, u, is

$u= eE^2/2$

and the power dissipated per unit volume, p, is

$p= sE^2/2$

We can represent these tendencies by using a circuit model to describe the tissue (1,4). Consider a sample of material that has a thickness, d, and cross-sectional area, A. If the material is an insulator, then we treat the sample as a capacitor with capacitance [4].

C= e. A/d

[Ⅲ]. ELECTRIC PROPERTIES OF TISSUES

If it is a conductor, then we treat it as a conductor with conductance

$$G = \sigma A.\frac{}{d}$$

A simple model for a real material, such as tissue, would be a parallel combination of the capacitor and conductor. Such a model is referred to as ‘‘Debye-type.’’ Other, more complicated models are sometimes used, as will be described later [5]. If a constant (DC) voltage V is applied across this parallel combination, then a conduction current IC ¼ GV will flow and an amount of charge Q ¼ CV will be stored.

Suppose, instead, that an alternating (AC) voltage was applied to the combination:

$$V(t)= V0 \cos(\omega t)$$

Here, V0 is the amplitude of the voltage and $\omega = 2pf$, where f is the frequency of the applied signal. The charge on the capacitor plates now is changing with frequency f. This change is associated with a flow of charge or current in the circuit. We characterize this flow as a displacement current:

$$Id = dQ/dt = -\omega CV0 \sin(\omega t).$$

The total current flowing through the material is the sum of the conduction and displacement currents, which are 90 degrees apart in phase because of the difference in the trigonometric functions. This phase difference can be expressed conveniently by writing

$$V(t)= V_0 e^{iwt}$$ where $I =\sqrt{(-1}$

and taking its real part for physical significance. The total current is I= Ic + Id, hence

$I = GV + C.dV/dt = \sigma + i\omega\varepsilon$ A. v/d

The actual material, then, can be characterized as having an admittance,

$Y^* = G + I\omega c=(A/d)(\sigma + i\omega\varepsilon)$

Where * indicates a complex-valued quantity. In terms of material properties, we define a corresponding, complex valued conductivity.

$\sigma * = (\sigma + i\omega\varepsilon)$

Describing a material in terms of its admittance emphasizes its ability to transport current. Alternatively, we could emphasize its ability to restrict the flow of current by considering its impedance, Z* = 1/Y*, or, for a pure conductance, its resistance, R=1/G.

Factoring $I\omega\varepsilon°$ in Equation 11 yields

$I = (\varepsilon r - i\sigma/\omega\varepsilon o)A/d = c.\ dv/dt$

We can define a complex-valued, relative permittivity

$$\varepsilon * = \varepsilon r - \frac{i\sigma}{\omega\varepsilon o}$$
$$= \varepsilon r' - i\varepsilon''r$$

With $\varepsilon'r = \varepsilon r$ and $\varepsilon'' = \frac{\sigma}{\omega\varepsilon o}$. The complex conductivity and complex permittivity are related by

$$\sigma * = i\omega\varepsilon * = i\omega\epsilon o\epsilon r *.$$

The conductivity of a material is the rate at which an applied electric field will cause a charge to move through its volume. In a similar vein, permittivity is a metric for how easily its dipoles can spin or how much charge can be stored in response to an external field. It's important to keep in mind that although the conduction current remains constant regardless of frequency, the displacement current grows as a function of frequency even if the material's permittivity and conductivity do not. The material will act as a conductor at low frequencies, but at higher frequencies, the capacitive effects will dominate [6]. However, for the vast majority of materials, these qualities change depending on the signal's

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frequency. The orientation of the dipoles and the velocity of the charge carriers are key to making sense of dispersions. Dipoles are more amenable to reorienting in response to a change in the applied field at lower frequencies, whereas charge carriers traverse longer distances and are more likely to be trapped at a defect or interface. In this material, the permittivity is high but the conductivity is low. The polarization associated with dipoles is lost because they are less able to track the variations in the applied field at higher frequencies [7]. The charge carriers, on the other hand, travel shorter distances in a half-cycle and are therefore less likely to get stuck. The permittivity drops and the conductivity rises with increasing frequency because trapping plays a lesser role [8].

[Ⅳ] BRAGG'S LAW

As with all electromagnetic radiation waves, diffraction can cause interference between diffracted waves, which can either make the waves stronger or weaker depending on their relative phases. These behavior's, which are referred to as constructive and destructive interference, are typical of wave functions. Both of these processes coexist in a complex pattern of X-ray beam scattering that is detected in an X-ray diffraction experiment. The distribution of atoms in the sample through which X-rays flow determines the interference pattern. Systematic interference patterns emerge in crystals because they are highly ordered arrays of atoms, and these patterns may be thought of as 'encoding' information about relative three-dimensional atomic positions. Bragg suggested in 1913 that a crystal may be thought of as a collection of planes that act as "mirrors" to reflect X-rays. These lattice planes in a genuine crystal slash across the crystal lattice in three dimensions. In actuality, this means that the diffracted beams (also known as Bragg reflections) detected in an X-ray diffraction pattern are those coming from successive lattice planes that adhere to Bragg's law and reinforce one another through constructive interference, with a single reflection coming from each equivalent lattice plane in the crystal.

[Ⅴ]. CIRCULAR DICHORISM

In the early nineteenth century the French physicist Jean Baptiste Biot observed that solutions of some organic molecules appeared to rotate the plane of polarization of plane polarized light, a phenomenon referred to as optical rotatory dispersion. We now know that this is a consequence of the fact that each enantiomer of an optically active molecule interacts differently with left and right circularly polarized light. By convention, levorotation is designated as (–) while dextrorotation is denoted by (+). A 50: 50 mixtures of equal amounts of d and l-enantiomers does not rotate the plane of polarization nor does a solution of an achiral molecule such as glycine [9]. Light passing through a chromophore solution may interact with the sample in two main ways. The light may be refracted or delayed on passage through the solution or it may be absorbed. Refraction is quantified by the refractive index, n, of the solution while absorption is quantified by the molar extinction coefficient, ε. If the light is plane polarized and the sample is optically active, each enantiomer may interact differently with the left and right circularly polarized components of the light beam. ORD arises from the fact that there is a specific refractive index for left (nL) and right (nR) circularly polarized light [10].

$$nL = nR$$

The difference in refractive index at any wavelength may be expressed as an equation. Similarly, optically active samples have distinct molar extinction coefficients for left (εL) and right (εR) circularly polarized light. This is called circular dichroism (CD):

$$\varepsilon L = \varepsilon R$$

The difference between εL and εR may be expressed as ε. Combining equations with the Beer–Lambert law) means that there is a difference in the absorbance of left and right circularly polarized light.

$$A = \varepsilon \cdot c \cdot l$$

If ε or A or ellipticity is plotted against wavelength (λ), a CD spectrum is obtained. The CD spectrum of one enantiomer is a mirror image of that of the other and is related to the corresponding ORD spectrum (and vice versa) by a mathematical transformation called the general Kronig–Kramer transformation. Both ORD and CD spectra are evidence for optical activity in the sample and both reflect structure of molecules in the sample, especially of chiral biopolymers such as proteins and nucleic acids. In practice, ORD has now largely been superseded by CD spectroscopy.

[Ⅵ]. COMPLICATIONS IN DIELECTRIC MEASUREMENTS OF TISSUES:

Tissue inhomogeneity, anisotropy, and physiological condition may make tissue dielectric

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property measurement difficult. Heterogeneous material complicated permittivity frequency dependency. Thus, measuring process design must be cautious.

[Ⅵ. Ⅰ]. INHOMOGENEITY OF TISSUES

Heterogeneity exists within tissue. Cells include conductive cytosols that are encircled by insulating membranes. Insulating inclusions in conducting fluids are known as low-frequency cell suspensions. The lining of cells insulates. At MHz frequencies, capacitive interaction across this membrane becomes stronger. For a comprehensive description of how cell suspension dielectric properties vary with frequency, it is necessary to start in this range and take into account membrane and cytosolic dispersive features. A large extracellular matrix surrounds bone cells, whereas a smaller one is present around epithelial cells. Diverse tissue cells exist. In a collagen/hydroxyapatite matrix, bones include stromal cells, osteoblasts, osteocytes, and osteoclasts [11]. Blood-perfused tissue is connected to the central nervous system through neurons. Thus, extrapolating tissue-wide dielectric properties from cell suspensions is challenging. The literature has a broad range of electrical properties for biological materials. Different amounts of bodily fluids are present in excised samples, and the lack of measurement uniformity could result in a wider resistivity range. Additional variations include those caused by season, age, illness, and physiology [12].

[Ⅵ. Ⅱ]. ANISOTROPY OF TISSUES

Bone and muscle are anisotropic. Thus, when using published conductivity and permittivity values, we must evaluate electrode orientation relative to the tissue's main axis (e.g., longitudinal, transversal, or a combination of both). Tissue demands often cause electrical anisotropy. Leg bones and muscles create and sustain large longitudinal forces. Muscle fibers are big cells that contract in the same direction. Because the extracellular matrix is less conductive than the cell, electrical conduction along the fiber is much easier than between fibers. Muscle tissue has anisotropic electric characteristics. Even with charge transport channel variations, longitudinal conductivity is much greater than transverse conductivity, particularly in the low-frequency region [12]. Charge transmission is simpler along the longitudinal axis than transversely in long bones. Tissue anisotropy is frequency-dependent. Anisotropic features diminish at high current frequencies (specifically for muscle tissue, which happens in the MHz frequency range). At higher frequencies, charge transport occurs across shorter distances, making capacitive coupling across membranes more essential than large-scale structures. When evaluating the electrical characteristics of anisotropic materials, aligning the applied electric field and tissue fibers is a practical concern [13]. Thus, precise longitudinal and transverse values need perfect alignment. A 5-degree misalignment from real perpendicular or parallel orientations would result in an 18% exaggeration in the perpendicular direction and a 0.4% underestimate in the parallel direction when measuring specific conductivity in skeletal muscle tissue.

[Ⅵ. Ⅲ] PHYSIOLOGICAL FACTORS AND CHANGES OF TISSUE

With changes in tissue physiology, tissue electrical properties change [14]. The diagnosis or monitoring of body fluid shift, blood flow, cardiac output, and muscle dystrophy has been done using impedance plethysmography, rheoencephalography, and thoracic impedance cardiography. Tumours retain more water than normal cells due to cellular necrosis and irregular, fenestrated vascularization. Membrane architecture might differ. Increased conductivity could be a sign of cancer, but a circuit model that incorporates the dielectric spectrum might be more accurate [15]. In real life, skin may make it more difficult to detect impedance changes in tissues like the breast. Because of their increased MHz-frequency conductivity, tumours may be specifically targeted by radio-frequency hyperthermia. Compared to fat, water transmits electricity better. Body water and fat content are reflected in tissue impedance. Biggs et al. calculated the proportion of whole-body fat by measuring upper arm and leg resistance at 50 kHz. Van Kreel et al. determined the body water content by measuring body impedance at various frequencies. This method benefits certain organs. Cardiac tissue complex permittivity was linked to ischemia by Schaefer et al. Electrical properties may be drastically altered by tissue death or excision. Once tissue is removed, metabolism and temperature fall. For a brief period of time, temperature control and perfusion systems in vitro may keep tissue alive (ex vivo). Without intervention, however, permanent changes as well as cell and tissue death will occur. Anaerobic metabolism results from blood flow stoppage.

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Osmosis enlarges cells and harms tissues. Extracellular channels narrow as a result, increasing 10 kHz low-frequency impedance [16]. Various tissues develop at various periods. Reduced blood flow lowers tissue resistance since blood is such a good conductor. Researchers have studied changes in conductivity brought on by cell and tissue death. A 100-Hz change takes longer to occur. Because tissue impedance is mostly ohmic at low frequencies, permittivity errors are minimal [17]. Electrical readings on tissues that have been removed must thus be evaluated carefully. The electrical properties of tissue are influenced by temperature. The viscosity of extracellular fluid decreases with temperature, increasing the mobility of current-carrying ions. Under 1 GHz, tissue conductivity rises by 2% for every degree Celsius up to 401C. When the level is exceeded, the cell membrane deteriorates, allowing cytosol to flow outside the cell. Use the conductivity's rapid increase with temperature to track the progress of hyperthermia treatment.

[VI. IV]. ELECTRODE POLARIZATION

It is challenging to measure the electrical properties of living tissues. At low and high frequencies, respectively, electrode polarization and lead inductance result in systematic errors [18]. Water molecules and hydrated ions arrange molecular charge at the sample-electrode interface, leading to electrode polarization. A frequency-dependent capacitor connected in series with a resistor makes up the most basic form. In comparison to ionic solutions and biological samples, the influence is more pronounced and increases with sample conductivity. Counterion layers may form in cell suspensions as a result of electrodes. The electric field that may be used to drive charge transport in the bulk suspension is reduced by the potential drop in this layer, giving the suspension an apparent low conductivity [19]. The counterion layer's ability to follow the applied signal decreases with increasing frequency, and the potential drop at the suspension/electrode interface becomes smaller. Meanwhile, the apparent conductivity of the suspension increases [20]. The ions in the layer depend on the electrode material and suspension. The degree and frequency responsiveness of the electrode polarization will thus vary with a change in the electrode material or suspension. It's complicated by tissue. Electrodes may release electrolytes from the surrounding tissue and produce a wound area that is only faintly conductive. In comparison to an ionic solution that is similar to intracellular fluid, this region may shield a section of the electrode from the ionic current and lessen the effects of polarization. The polarization impedance of the electrode material decreases with frequency, much like a cell suspension. Tissue impedance has to be assessed in vivo once electrode polarization has stabilized. Waiting periods are influenced by tissue type and electrodes. Measure the impedance spectrum until no changes are seen, then calculate the waiting time [21]. Two- and four-electrode approaches are used to evaluate the electric properties of biological materials, and they typically take 30 minutes [22]

[VI. IV. I] TWO-ELECTRODE METHOD.

This technique measures alternating current. It cannot be used for direct current measurements due to the electrode polarization that incorrectly calculates sample conductivity between electrodes. The frequency range where electrode polarization matters for alternating current measurements varies with the system and electrode material. It matters up to approximately 100 kHz for cell suspensions but only up to 1 kHz for tissue measured in vivo. Electrode polarization may be identified and reduced by changing electrode separation [23].

[VI. IV. II] FOUR-ELECTRODE METHOD.

It measures direct and alternating current. Outer (current) and inner electrodes are inner (voltage) electrodes the samples transport the source current. The sample has known-separation voltage electrodes between the current electrodes. One may calculate the sample's inner electrode conductance by measuring the current as the voltage drop across a resistor in series with the sample and the voltage drop across the inner electrodes [24]. They feel the four-electrode technique does not reduce voltage electrode polarization. Some publications claim 20% greater muscular resistance measurements with the two-electrode approach without error correction [25]. In vivo direct current measurements must use very small currents to avoid electrochemical injection of ions at the electrodes and nerve activation. Lead inductance becomes critical above MHz because inductive connections between leads, measurement equipment, and surrounding metal surfaces cause extraneous voltage drops that rise with frequency. Replace the sample to be tested with a saline solution whose electrical characteristics should not change with frequency until the GHz range to detect and decrease the effects of electrode

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polarization at low frequencies and lead inductance at highfrequencies [26].

[Ⅶ]. STRACTURAL BIOLOGY:

Biomolecules, which are also called "organic atoms," are parts of animals that are needed for at least one organic cycle, such as cell division, morphogenesis, or development [27]. Proteins, carbohydrates, lipids, and nucleic acids are large biomolecules. Other essential, auxiliary, and unique chemicals are also large biomolecules. This category includes natural materials. In living cells, proteins, nucleic acids, carbohydrates, lipids, and low-atomic-weight ligands collaborate to carry out biochemical operations. It is essential to comprehend these interactions in order to understand how life develops, disease spreads, and host life forms are defenseless against infectious germs [28]. Planning for treatments is also aided. The biomolecules found in living things are often endogenous. Biomolecular interactions, such as those between proteins, proteins and nucleic acids, and proteins and ligands, are essential to natural chemistry. Studies in cell and molecular biology must comprehend how the fundamental characteristics of natural macromolecules influence their capabilities. Understanding biological cycle instruments requires an understanding of how protein interactions, interactions with other proteins, and complex formation are controlled at certain cell sites and periods. Data on macromolecule assembly and separation over time are required for biomolecular restricting. 2 Due to the pH, ionic strength, temperature, and natural or sub-molecular organization of the surrounding milieu, the successful surface charge, soundness, dissolvability, and hydration of nanoparticles may differ significantly from bulk material of comparable creation (e.g., proteins, lipids, sugars, surfactants) [29]. There are interactions between proteins, drugs, and DNA. Proteins and nucleic acids are given priority in biophysics and structural biology.

[Ⅶ. Ⅰ] PROTEIN

Proteins—amino acids linked by peptide bonds—make up a large amount of our DNA. One-carboxyl group an amino acid forms a peptide link with the -amino group of another amino acid [30].

[Ⅶ. Ⅰ. Ⅰ] PROTEIN STRUCTURE

1.The primary structure specifies polypeptide chain amino acid order and disulfide bond locations
2. Secondary structure results from stable amino acid residue groupings.
3. Polypeptides have three-dimensional tertiary structures.
4. Proteins with two or more polypeptide chains have a quaternary structure

[Ⅶ. Ⅰ. Ⅱ] FUNDAMENTALS OF THE PEPTIDE BOND

Linus Pauling and Robert Corey pioneered peptide bond research. Their comprehensive investigation of X-ray diffraction data from simple dipeptides and tripeptides showed that the peptide C–N bond is considerably weaker. Second, peptide bond atoms are coplanar. The carbonyl oxygen and amide nitrogen share two electrons. Thus, oxygen and nitrogen have partial negative and positive charges, creating a dipole. The carbonyl group's oxygen atom and the amide nitrogen's hydrogen atom are trans. Due to incomplete double-bonding, C–N bonds cannot spin freely. N–C and C–C bonds may rotate. The N–C bond angle and the C–C bond angle come from C rotations. Peptide bonds have torsion and dihedral angles. Due to steric interference between polypeptide backbone atoms and amino acid side chains, many values of and are disallowed.

[Ⅷ] DIFFERENT PROTEIN SECONDARY STRUCTURES

[Ⅷ. Ⅰ] *α*-helix:Typically, polypeptides fold into helices. It contains 32–38% of the residues in globular proteins. The electronegative carbonyl oxygen atom of the fourth amino acid on the amino-terminal side and the hydrogen atom attached to the electronegative nitrogen atom of a peptide bond serve to maintain the structure. Except for those at the helix, every peptide bond terminates hydrogen bonding in this way. There are 3.6 residues per helix turn, and 3–4 hydrogen bonds hold each helix turn together. 6 The helical structure is stabilized by hydrogen bonds throughout. The peptide amino and carbonyl groups, which are close to the carboxyl- and amino-terminal ends of the helix, respectively, exhibit partial positive and negative charges because of hydrogen bonding. Positively charged amino acids are often found towards the carboxyl-terminal end of the helix, whereas negatively charged amino acids are usually found at the amino terminus [31].

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[Ⅷ.Ⅱ]FIVE RESTRICTIONS AFFECT ALPHA HELIX FORMATION AND STABILITY:

[Ⅰ] Electrostatic repulsion or attraction between consecutive amino acid residues with charged R groups Continuous blocks of similarly charged amino acids in polypeptides frequently prevent alpha helix formation [32].

[Ⅱ]. Adjacent R-group bulkiness When near each other, cysteine, asparagine, serine, and threonine might destabilize.

[Ⅲ]. Three- or four-residue R group interactions An -helix twist keeps important connections between amino acid side chains that are 3-4 residues apart. A positively charged amino acid often forms an ion pair with a negatively charged amino acid three residues away

[Ⅳ]. proline/glycine presence This functionality is crucial. The tight ring around proline's nitrogen atom prevents rotation around the N–C bond. helix kinks or breaks. Proline is an amino acid, not an amino acid; hence, its nitrogen atom, which participates in the peptide bond, has no hydrogen to form hydrogen bonds with other residues. These factors make proline in alpha-helixes uncommon. Glycine blocks, on the other hand, frequently form coiled structures other than alpha helices [33].

[Ⅴ]. The electric dipole of the helix interacts with amino acid residues at the ends of the helical segment. Peptide bonds have tiny electric dipoles. Hydrogen bonds join these dipoles, creating a net dipole along the helix. Since the amino acids at the endpoints do not fully engage in the helix hydrogen bonding, the peptide amino and carbonyl groups near the amino- and carboxyl-terminal ends of the helix, respectively, have partial positive and negative charges [34].

[Ⅸ] B-CONFORMATION

Conformation transforms the peptide backbone into a zigzag rather than a helix. A-sheets are pleated structures made of zigzag polypeptide chains. Unlike an -helix, hydrogen bonds form between polypeptide chain segments. -sheet segments can be derived from the same or different polypeptide chains [35]. Segments from the same polypeptide chain may be close or far apart. -Pleats have an alternating pattern because the R groups of neighboring amino acids protrude in different directions from the zigzag structure. In proteins with two or more sheets, bulky R groups on amino acid residues on interacting surfaces may cause steric clashes. The chains of -sheet polypeptides can be parallel or antiparallel (opposite amino-to-carboxyl orientation). Parallel conformations have 6.5 repetition periods, whereas antiparallel conformations have [36].

[Ⅹ]. B-TURNS

Two antiparallel -sheet segments are joined by -turns. The first residue's carbonyl oxygen forms a hydrogen connection with the fourth residue's amino-group hydrogen. The center two residues' peptide groups don't hydrogen bond. -turns include glycine and proline residues [37]. Glycine can readily turn because of its tiny side chain. 11 Proline's amino nitrogen peptide link may create a tight turn in cis. There are type I and type II -turns. Type II A-turns are rarer than type I. Gly is always the third residue in Type II -turns. Both varieties have different hydrogen bonding geometries.

[Ⅹ Ⅰ]. TERTIARY STRUCTURE

Protein tertiary structure depicts the three-dimensional arrangement of all atoms. This divides proteins into two main categories: [1] filamentous and globular proteins, which are formed by folding polypeptide chains into spherical or globular shapes. Unlike fibrous proteins, globular proteins have several secondary structures. [2] Fibrous proteins give structure and form. Enzymes are globular proteins.

[Ⅺ Ⅰ]. STRUCTURAL MOTIFS:

Understand the distinction between a motif and a domain before learning about structural motifs [38].

Sl. No.	Motif	Domain
1	A super secondary structure of a protein	Tertiary structure of the protein 17
2	Not stable independently	Stable independently
3	Made of secondary structural elements and their connection in between19	Independently folding unit of the 3D structure

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4	Mainly have structural function	Mainly have functional importance 18

[XIⅠ. Ⅰ] SOME BASIC TYPES OF STRUCTURAL MOTIFS COMMONLY SEEN IN THE PROTEINS INCLUDE [39].

[Ⅰ] β-α-β motif: These motifs are common in parallel beta sheets; wherein parallel beta strands are often connected by small alpha helical segments.

[Ⅱ] β-hairpin motif: These are one of the simplest structural motifs and are often present in globular proteins. They are present as short loop regions between antiparallel hydrogen bonded beta-strands.

[Ⅲ]α-α motif: It is made of two alpha helices connected by a short loop.

[Ⅳ] Greek key motif: It is made up of four adjacent antiparallel beta strands folded upon itself to give appearance of a Greek key, hence the name.

Besides some of the basic structural motif types, certain structural motifs are essentially seen in the DNA binding or regulatory proteins. All these motifs have distinct signatures which are relevant for specific interactions with the DNA molecule. These motifs recognize specific DNA sequence because their surface is extensively complementary to the special surface features of the double helix in that region [40].A significant number of number of contacts with the DNA, involving hydrogen bonds, ionic bonds, and hydrophobic interactions are usually established. With several such contacts at the protein-DNA interface, both specific and very strong interactions are conferred. Some common examples are highlighted below [41].

[XIⅠ. Ⅱ] HELIX-TURN-HELIX MOTIF

This motif is one of the most common motifs seen in gene regulatory proteins. The basic structure comprises of two helices connected by a turn. The C-terminal α-helix is called the recognition helix and it participates in sequence-specific interaction with the DNA. The recognition helix recognizes and fits into the major groove of DNA, wherein it interacts with the edges of the base pairs. The N-terminal α-helix essentially acts as a structural component that helps position the recognition helix for its interaction with the major groove. In most of the cases, these motifs function as dimers. For instance, the λ repressor of lambda-phage utilizes two helix-turn-helix motifs to interact with DNA [42].

[XIⅠ.Ⅲ] ZINC-FINGER MOTIF

One common form of zinc-finger is present in the Cyst-Cyst-His-His family of zinc finger proteins. The three-dimensional structure of this type of zinc finger is comprised of an antiparallel β-sheet followed by an α-helix. Four amino acids, namely two cysteine and two histidine residues coordinate with a zinc atom and hold one end of the α-helix firmly to one end of the β-sheet [43]. Like the helix-turn-helix motif, zinc-fingers also participate as multimers while interacting with DNA, thus increasing the strength and specificity of the interactions. Another form of zinc finger is present in the family of certain intracellular receptor proteins, wherein instead of one β-sheet and oneα-helix, two alpha helices coordinate with the zinc atom [43]. Although structurally distinct, both use zinc as a structural element, and both use an α-helix to recognize the major groove of the DNA.

[XIⅠ.Ⅳ] HELIX-LOOP-HELIX MOTIF

This type of DNA-binding motif has an overall structural resemblance to the leucine zipper. The motif consists of 2 alpha helices, a short one connected by a loop to a second, longer one. The flexibility of this loop allows one helix to fold back and pack against the other. This two-helix structure binds both to DNA as well as to another helix-loop-helix motif from a second protein. This second helix-loop-helix containing protein can be the same (a homodimer) or different (a heterodimer). The two longer alpha- helices extending from the dimerization interface make specific contacts with the major groove of the DNA [44].

[XIIⅠ] NUCLEIC ACIDS

Nucleic acids are built from nucleotides which essentially contain three components: a nitrogenous base, a pentose sugar, and a phosphate. The molecule without the phosphate group is called a nucleoside. The nitrogenous bases are of further two types, the pyrimidine and purine. Nucleic acids contain two types of pentose sugars. While the DNA contains nucleotide units with 2'-deoxy-D-ribose, the nucleotide units of RNA contain D-ribose. The pentose sugars are also in their β-furanose form. Both DNA and RNA contain two major purines, adenine and guanine and two major pyrimidines. Out of the two pyrimidines, one is cytosine, but the second one is different in both

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types of nucleic acids. Thymine present in DNA is replaced by an uracil in RNA. The phosphate groups play an important role in connecting the successive nucleotides of DNA and RNA. The 5'-phosphate group of one nucleotide unit is linked to the 3'-OH group of the next nucleotide creating via a phosphodiester linkage.

[XIII. I] STRUCTURE OF DNA

It was Rosalind Franklin and Maurice Wilkins who laid the foundation for solving the structure of DNA. They utilized X-ray diffraction studies to reveal the typical diffraction pattern of a DNA molecule. It was clear from the pattern that that DNA molecules are helical in shape and possess two periodicities along their long axis, a primary one of 3.4 Å and a secondary one of 34 Å. Watson and Crick utilized this knowledge as a template and exploited other already available information like the Chargaff's rule (no. of A=T and G=C in a DNA molecule) to propose the 3D-model of DNA [45]. As per the model, two helical strands are wound around the same axis to form a right-handed double helical structure of DNA. The sugar-phosphate backbone faces the exterior of the double helix and contacts the surrounding water. Nitrogenous bases from both strands are stacked inside the double helix. The offset pairing of the two strands creates a major groove and minor groove on the surface of the duplex. Nitrogenous base of one nucleotide from one strand pairs with a base of the other strand within the same plane. To take Chargaff's rule into account, Watson and Crick proposed that a G always should pair with C and A should always pair with T, better known as the complimentary pairing [46]. Notably, three hydrogen bonds form between G and C, and two can form between A and T. They also arrived at a conclusion after extensive analysis that the proposed model appears conclusive when the strands of DNA run antiparallel to each other. In other words, 5,3-phosphodiester bonds of the two strands run in the opposite directions.

[XIII. II] OTHER FORMS OF DNA

The Watson-Crick structure described above is referred to as the B form of DNA, or B-DNA. The B form is the most stable form for a DNA molecule under physiological conditions and is used as the standard point of reference for studying the structural features. However, two other structural variants are also known for DNA and have been well studies with the help of crystal structures. These forms are denoted as the A and Z forms.

Table 15.3 summarizes its features and contrasts them with features of the B form [47].

S.NO		A Form	B Form	Z Form
01	Helical sense	Right-handed	Right-handed	Left-handed
02	Diameter	~26 Å	~20 Å	~18 Å
03	Base pairs per helical turn	11	10.5	12
04	Helix rises per base pair	2.6 Å	3.4 Å	3.7 Å
05	Sugar pucker conformation	C-3'	C-2' endo	endo C - 2' e n d o f o r pyrimidines; C-3' endo for purines
06	Glycosyl bond conformation	Anti	Anti	Anti for pyrimidines, syn for purines

[XIII.III]. UNUSUAL STRUCTURES OF DNA

Under many conditions, some unusual structures of DNA that involve three to four strands can develop. Besides the usual base pairing seen in DNA structures, better known as Watson-Crick base pair, a few additional hydrogen bonds can be formed by the nucleotides. For example, a cytidine residue (if protonated) can pair with the guanosine residue of a Ga"C nucleotide pair, and a thymidine can pair with the adenosine of an A=T pair. Three atoms of the purines, namely, N-7, O6, and N6 of purines, participate in the hydrogen bonding and result in the formation of triplex DNA [48]. These atoms are referred to as Hoogsteen positions, and the resultant non-Watson-Crick type pairing is regarded as Hoogsteen pairing. One example, Ca" G^{a0}%C+ typically forms under low pH conditions, because there is requirement of a protonated cytosine. Four DNA strands can also pair to form a special type of tetraplex/quadruplex structure, when the DNA sequences are richly populated with guanosine residues. This G quadruplex is relatively much more stable than other unusual structures that are known. The G-quadruplex can also be

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intramolecular as well as intermolecular. Another kind of unusual structure is called as the I-motif. I-motifs are four stranded DNA structures held together by hemi-protonated and intercalated cytosine base pairs (C:C+) [49]. Initially it was thought that i-motif structures can only develop at acidic pH values due to the requirement of hemi-protonated base pairs. However, recent studies have shown that phenomenon such as molecular crowding favors G quadruplex and I- motif formation. I-motif structures are usually located in the regulatory regions of the genome and both G4 and I-motif structures play complementary roles in the regulation of gene expression [50].

[XIII.IV] STRUCTURE OF RNA

The single-stranded RNA which is product of transcription assumes a righthanded helical conformation which primarily is stabilized by base stacking which are stronger between two purines than between a purine and pyrimidine or between two pyrimidines. Any self-complementary sequences in the molecule produce more complex structures [51].

[XIV.] DENATURATION OF PROTEINS AND NUCLEIC ACIDS:

Effects of Temperature, pH etc. Denaturation of proteins involves the disruption of the secondary and tertiary structures. Since the effect of denaturants are not strong enough to break peptide bonds, the primary structure remains intact after the denaturation process. However, denaturation can disrupt the secondary structure elements like the alpha-helices and beta sheets and result in a more random shape. Some of the common denaturants and their effects are summarized below [52].

S.NO		Effect on Protein Structure
01	Temperatures above 50o C or ultraviolet (UV) radiation.	Heat or UV radiation supplies kinetic energy which cause the atoms to vibrate more rapidly and disrupting the relatively weak hydrogen bonding and dispersion forces
02	Use of organic compounds, such as ethyl alcohol.	These compounds can engage in hydrogen bonding with protein molecules, disrupting intramolecular hydrogen bonding within the protein [53].
03	Salts of heavy metal ions, such as mercury, silver, and lead.	These ions can form strong bonds with the carboxyl groups and SH groups of the negatively charged amino acids and cysteine, respectively, disrupting the native linkages [54].
04	Urea	Urea causes protein denaturation in multiple ways. One primary mechanism involves hydrogen bonding of urea to polarized areas of charge, like the peptide groups. This results in weakening of the intermolecular bonds and interactions, thus altering the overall secondary and tertiary structure [55].

Native DNA solutions are highly viscous at room temperature and neutral pH conditions. When such a solution is subjected to extremes of pH or to temperatures above 80 to 90o C, the DNA undergone a physical change and the viscosity of the solution changes drastically. Much similar to proteins, heat and extremes of pH also result in denaturation or melting of double helical DNA. This phenomenon includes loss of the hydrogen bonds between the base pairs as well as the hydrophobic interactions between the stacked bases [56]. As a result, the double helical structure unwinds to form two single strands, which can be completely or partially separated from each other. Like the protein denaturation process, covalent bonds in the DNA remain intact. Thermal denaturation studies provide crucial insights into the secondary structure of DNA molecules. Since G and C base pairs are held together by three hydrogen bonds compared to A and T, which are

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only held together by two hydrogen bonds, a DNA sample with a high GC content will require much more energy to separate the strands, leading to a higher DNA melting temperature. UVvis Spectrophotometry is generally used to monitor the thermal denaturation of wherein the sample is heated to allow the determination of the DNA melting temperature [57].

[ⅩⅤ] BIOMOLECULAR INTERACTIONS

[ⅩⅤ. Ⅰ] DNA-PROTEIN INTERACTION

Among proteins and nucleic acids interaction controls the controlled and coordinated articulation of the genome in cell metabolism, replication, and improvement functional classes of DNA-associating proteins can be partitioned further into those which communicate with explicit nucleotide successions or locales and those which connect with the DNA non-arrangement explicitly. we should be worried about both the chemical types sorts of functional groups accessible on every macromolecule and the overall demeanor of these groups in space. From this viewpoint similar sorts of configurational and compound thinking should be applied to the DNA-protein interaction issue as have generally been utilized in thinking about the particularity of the communication among proteins and their substrates and inhibitors [58]. The prospects inborn in the tertiary structure and subunit communications of globular proteins are basically boundless, and along these lines we will move toward the issue by considering the varieties conceivable in the more mentally manageable accomplice: the DNA. We should briefly understand the structure of DNA that characterize the conformational, chemical, and thermodynamic features in solution. There are few structural aspects in DNAPROTEIN interaction process by inspecting the DNA molecule as it might appear to a protein (e.g., repressor) in search of a specific sequence of bases (e.g., an operator site) with which to interact. Pathway is used by proteins in searching for the interaction site Most biologically critical connections among protein and DNA happen under conditions in which the local, twofold helical structure addresses the thermodynamically preferred DNA structure [59].]However, proteins exist that tight spot explicitly to one or the other local or random coil (single-stranded) DNA districts under these conditions. The last sort, which we call liquefying ‘proteins, promptly approach a degree of grouping explicitness controlled by contrasts in the neighborhood solidness of the local DNA twofold helix. Accordingly, the free energy of restricting of a protein to a single strand of DNA in an area ordinarily twofold abandoned under the predominant natural conditions should at any rate balance the free energy preferring the local over the arbitrary curl conformity at that locus. Inorganic ions, dyes, etc. illustrate interaction modes available with DNA for ligands these might serve as models for certain types of functional groups found in proteins, these also defines other interactive specificities of which DNA is capable.

[ⅩⅤ. Ⅱ] ANALYSIS OF DNA-PROTEIN INTERACTION

Electromobility shift measure is a basic, proficient, and quick strategy for the investigation of explicit DNA–protein associations. It depends on the decrease in the electrophoretic versatility gave to a DNA part by a cooperating protein. The procedure is reasonable to subjective, quantitative, and dynamic examinations. It can additionally be utilized to dissect conformational changes. This is based on the basic reasoning that particles of varying size, sub-atomic weight, and charge will have diverse electrophoretic mobilities in a non-denaturing gel lattice. On account of a DNA–protein complex, the presence of a DNA-binding protein will cause the complex to relocate in an unexpected way (generally more gradually) comparative with the free DNA, and will subsequently cause a shift apparent upon identification [60].

[ⅩⅤ. Ⅲ] DNA-DRUG INTERACTIONS

The DNA- Drug interaction has been to designed specifically for rare diseases and to target their action at the DNA level. Uncommon strategies have now been created to give exact record of the exact area of ligand-DNA adducts on DNA that is target. The acknowledgment of one sort of molecule by another is key also, a typical component of every single living life form. The replication of DNA and its record to RNA, which gives the format to protein amalgamation, is maybe extraordinary compared to other known illustration of molecular recognition. These nonprotein molecules that are known to tie DNA atoms incorporates common items like antimicrobials, antitumor etc. what’s more, other optional metabolites from microbes and growths and plants, manufactured mixtures, viz.; CC 1065, copper phenanthroline complex, Alkyl nitroso-urea and homopyrimidine oligonucleotides. The cooperation

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of generally little particles of this kind with DNA may prompt a "valuable" results like antibacterial and anticancer action, yet may likewise include unfortunate natural reactions, for example, carcinogenesis or mutagenesis [61].

[XV. IV] PROTEIN- PROTEIN INTERACTIONS

To control various biological phenomena which includes cell to cell interactions and metabolic process proteins undergo Protein to protein interactions (PPI). In humans, disturbances of the normal patterns of PPIs and protein complexes can be causative or demonstrative of a disease state. PPIs incorporate heterogeneous strategies generally and the chance of their guideline is colossal. Different communications and the result of these connections are expected to recognize the better comprehension of PPIs inside the cell. Test judgments of connections between proteins are done at either an enormous or limited scope with two primary innovations that produce various kinds of PPI information [62]. The procedures that action direct actual collaborations between protein sets are "binary" strategies, while the strategies that action actual communications among gatherings of proteins, without pairwise assurance of protein accomplices, are "co-complex" techniques. The frequently utilized parallel and co-complex systems are, separately, yeast two-mixture (Y2H) and pair partiality refinement coupled to mass spectrometry (TAP-MS). Both are broadly applied in huge scope examinations. Co-complex techniques measure both immediate and roundabout connections between proteins. The most well-known methodology depends on the pre-choice of one protein labeled with a sub-atomic marker (the trap protein), which is utilized to catch or "fish out" a gathering of proteins (prey proteins) trailed by a biochemical strategy to "pull-down" and separate them from a blend [63]. Along these lines, what happens is a co-purging of protein gatherings. Another regular co-complex methodology, in light of protein counter acting agent acknowledgment, is co-immunoprecipitation (CoIP). The trial results got with co-complex techniques are unique in relation to those got with parallel strategies. Information got from co-complex examinations can't be straightforwardly allocated a twofold translation. A calculation or model is expected to make an interpretation of gathering based perceptions into pairwise collaborations. The spoke model is most regularly utilized, as it delivers the insignificant number of bogus positives. An illustration of organizations got from Y2H versus TAP-MS outlines the distinctions that must be surely known by any analyst delivering or breaking down PPI information.

[XVI] DIFFERENT LEVEL OF SPECIFICITY FOR DNA-PROTEIN INTERACTION

In Binding site specification, we first consider the framework in quite a while of supreme particularity; i.e., we expect a protein that can totally (and as it were) segregate between the four data components of DNA. There are four authoritative nucleotide deposits (A, T, G, and C) in single-abandoned DNA and four kinds of base sets (APT, T-A, G-C, and C(G) in twofold abandoned DNA [64]. The last will be our essential concentration here. A particular restricting site is perceived as far as explicit arrangements of base sets. A contingent likelihood approach10 can be utilized to decide the negligible length (n) of an arrangement of acknowledgment components (base sets) needed to determine a site, with the goal that the normal recurrence with which that site returns indiscriminately inside the genome is not as much as solidarity. For E. coli DNA this negligible length is - 12 base sets, expecting a twofold abandoned succession inside a genome of generally speaking creation A = T = G = C. This methodology accepts that the general grouping of the genome can be treated as synthetically (however clearly not hereditarily) arbitrary and that each base pair is completely indicated (as far as base-pair type). Unknown loci can, obviously, intrude on the general succession in characterized positions, however these loci won't check toward n. Essentially, determination just at the degree of R-Y (purine-pyrimidine) (versus Y-R) base sets can happen; such loci are weighted less in setting up [65]. After the binding site specification now, the sequence should be recognized there are two mechanism primary and secondary sequence recognition mechanism. In primary sequence recognition mechanism, the molecular mechanism that can unambiguously perceive and segregate singular base sets in twofold abandoned DNA is complementary hydrogen-holding through the major or minor scores of the twofold helix. These acknowledgment examples of hydrogen-bond donors and acceptors on DNA have been unequivocally recorded by Seeman et al., and have been introduced in an especially basic and valuable "stick-figure" portrayal. Such acknowledgment

relies upon the cooperation of the pertinent hydrogen bond donor and acceptor gatherings of the DNA base pair with a complementary matrix of hydrogen bond acceptor and donor bunches gave by suitably situated amino corrosive and peptide utilitarian gatherings in the restricting site of the administrative protein [66]. This hydrogen-reinforced acknowledgment matrix approach has all the more as of late been utilized by crystallographers in finding cooperation in explicit protein nucleic corrosive association buildings.

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REFERENCES

[1]. Bunge, M. (1979). Treatise on Basic Philosophy, vol. 4. Ontology II: A World of Systems, p. 61-2.
[2]. Voon, C. H.; Sam, S. T. (2019). "2.1 Biosensors". Nano biosensors for Biomolecular Targeting. Elsevier. ISBN 978-0-12-813900-4.
[3]. Piehler J. New methodologies for measuring protein interactions in vivo and in vitro. Cur Opin Struct Biol 2005;15(1): 4-14.
[4]. von Hippel PH, McGhee JD. DNA-protein interactions. Annual review of biochemistry. 1972 Jul;41(1): 231-300.
[5]. Prabhakar P, Kayastha AM. Mechanism of DNA-drug interactions. Applied biochemistry and biotechnology. 1994 Apr;47(1): 39-55.
[6]. Kuzmanov, U., Emili, A. Protein-protein interaction networks: probing disease mechanisms using model systems. Genome Med 5, 37 (2013). https: //Doi. org/10.1186/gm441
[7]. Garner, M.M.and Revzin, A. (1981). A gel electrophoresis method for quantifying the binding of proteins to specific DNA regions: application to components of the Escherichia coli lactose operon regulatory system. Nucleic Acids Res. 9, 3047 – 3060.
[8]. Gaudreault M, Gingras ME, Lessard M, Leclerc S, Guérin SL. Electrophoretic mobility shift assays for the analysis of DNA-protein interactions. InDNA Protein Interactions 2009 (pp. 15-35). Humana Press.
[9]. von Hippel, P. H. 1969. 1. Cell. Physiol. 74: Suppl. 1, 235
[10]. von Hippel, P. H. (1979) in Biological Regulation and Development, ed. Goldberger, R. F. (Plenum, New York), Vol. 1, pp. 279-347.
[11]. Von Hippel PH, Berg OG. On the specificity of DNA-protein interactions. Proceedings of the National Academy of Sciences. 1986 Mar 1;83(6): 1608-12.
[12]. Yarn, M. (1969) Annu. Rev. Biochem. 38, 841-880. 416 | Handbook of Biotechnology
[13]. von Hippel, P. H. and McGhee, J. D. (1972) Annu. Rev. Biochem. 41, 231-300.
[14]. Seeman, N. C., Rosenberg, J. M. and Rich, A. (1976) Proc. Natd. Acad. Sci. USA 73, 804-808.
[15]. [15]. Woodbury, C. P., Jr., and von Hippel, P. H. (1981) in The Restriction Enzymes, ed. Chirikjian, J. (Elsevier, Amsterdam), Vol. 1, pp. 181-207.
[16]. Melchior, W. B., Jr., and von Hippel, P. H. (1973) Proc. Natl. Acad. Sci. USA 70, 298-302.
[17]. Kopka, M. L., Yoon, C., Godsell, D., Pjura, P. and Dickerson, R. E. (1985) Proc. Natd. Acad. Sci. USA 82, 1376-1380.
[18]. deHaseth, P. L., Lohman, T. M. and Record, M. T., Jr. (1977) Biochemistry 16, 4783-4790.
[19]. Revzin, A. and von Hippel, P. H. (1977) Biochemistry 16, 4769-4776.
[20]. Kowalczykowski, S. C., Lonberg, N., Newport, J. W. and von Hippel, P. H. (1981) J. Mol. Biol. 145, 75-104.
[21]. Weintraub, H. and Groudine, M. (1976) Science 193, 848-856.
[22]. Thurston, D. E. and Thompson, A. S. (1990), Chem. Britain 8, 767.
[23]. Rawn, D. (1989), Text-Book of Biochemistry, Neff Patterson, Burlington, p. 829.
[24]. Zubay, G. (1989), Text-Book of Biochemistry, Macmillen, New York, pp. 792 and 924.
[25]. Fok, J. and Waring, M. J. (1972), Mol. Pharmacal. 8, 65.

[26]. Goldberg, I. H. and Friedman, P. A. (1971), Ann. Rev. Biochem. 40, 772.
[27]. Warpehoski, M. A. and Hurley, L. H. (1988), Chem. Res. Toxicol. 1, 315.
[28]. Barton, J. K. (1986), Science 233, 727.
[29]. Taylor, J. S., Schultz, P. G., and Dervan, P. B. (1984), Tetrahedron 40, 457.
[30]. Denny, W. A., Baguley, B. C., and Cain, B. F. (1983), in Molecular Aspects of Anticancer Drug Action, Neidle, S. and Waring, M. J., eds., Macmillian, London, p. 1.
[31]. Pullman, B. (1989), in Advances in Drug Research, vol. 18, Academic, New York, p. 1.
[32]. Ward, D. C., Reich, E., and Goldberg, I. G. (1965), Science 149, 1259.
[33]. Behr, W., Honikel, K., and Hertmann, G. (1969), Eur. J. Biochem. 9, 82.
[34]. Kamiyama, M. (1968),]. Biochem. 63, 563.
[35]. Umezawa, H. (1978), in Bleomycin: Current Status and New Developments, Carter, S. K., Crooke, S. T., and Umezawa, H., eds., Academic Press, New York, p. 15.
[36]. Goldberg, I. H. and Friedman, P. A. (1971), Ann. Rev. Biochem. 40, 772.
[37]. Moffat, A. S. (1991), Science 252, 1374. Biophysics and Structural Biology | 417
[38]. Hurley, L. H. (1989), J. Med. Chem. 32, 2027.
[39]. Dervan, P. B. (1986), Science 232, 464.
[40]. Braun P, Gingras AC. History of protein-protein interactions: From egg-white to complex networks. Proteomics. 2012;12(10): 1478-1498. DOI: 10.1002/ pmic.201100563
[41]. Zhang A. Protein Interaction Networks: Computational Analysis. New York, NY: Cambridge University Press; 2009
[42]. Yu H, Braun P, Yildirim MA, Lemmens I, Venkatesan K, et al., High-quality binary protein interaction map of the yeast interactome network. Science. 2008;322: 104–110
[43]. Suter B, Kittanakom S, Stagljar I. Two-hybrid technologies in proteomics research. CurrOpinBiotechnol. 2008;19: 316–323.
[44]. Berggard T, Linse S, James P. Methods for the detection and analysis of proteinprotein interactions. Proteomics. 2007;7: 2833–2842.
[45]. Mackay JP, Sunde M, Lowry JA, Crossley M, Matthews JM. Protein interactions: is seeing believing? Trends Biochem Sci. 2007;32: 530–531.
[46]. Hakes L, Robertson DL, Oliver SG, Lovell SC. Protein interactions from complexes: a structural perspective. Comp Funct Genomics. 2007: 49356.
[47]. Dickerson, R. E.; Geis, I. Hemoglobin: Structure, Function, Evolution, and Pathology; The Benjamin/Cummings Publishing Company, Inc.: Menlo Park, CA, 1983.
[48]. Antonini, E.; Brunori, M. Hemoglobin and Myoglobin in Their Reactions With Ligands; North-Holland Publishing Company: Amsterdam, The Netherlands, 1971.
[49]. Degtyarenko, I.; Biarnes, X.; Nieminen, R. M.; Rovira, C. Coord. Chem. Rev. 2008, 252, 1497–1513.
[50]. Sigfridsson, E.; Ryde, U. JBIC, J. Biol. Inorg. Chem. 1999, 4, 99– 110.
[51]. Olson, J. S.; Phillips, G. N., Jr. JBIC, J. Biol. Inorg. Chem. 1997, 2, 544–552.
[52]. Ackers, G. K.; Doyle, M. L.; Myers, D.; Daugherty, M. A. Science 1992, 255, 54–63.
[53]. Arcovito, A.; Benfatto, M.; Cianci, M.; Hasnain, S. S.; Nienhaus, K.; Nienhaus, G. U.; Savino, C.; Strange, R. W.; Vallone, B.; Della Longa, S. Proc. Natl. Acad. Sci. U. S. A. 2007, 104, 6211–6216.
[54]. Maurus, R.; Overall, C. M.; Bogumil, R.; Luo, Y.; Mauk, A. G.; Smith, M.; Brayer, G. D. Biochim. Biophys. Acta, Protein Struct. Mol. Enzymol. 1997, 1341, 1–13.
[55]. McLendon, G.; Sandberg, K. J. Biol. Chem. 1978, 253, 3913– 3917.
[56]. Fersht, A. R. Structure and Mechanism in Protein Science; W. H. Freeman and Co.: New York, 1999. 418 | Handbook of Biotechnology
[57]. Foord, S. M. (2002). Receptor classification: post genome. Curr. Opin. Pharmacol. 2, 561–566. doi: 10.1016/S1471-4892(02)00214-X
[58]. Tuteja, N. (2009). Signaling through G protein coupled receptors. Plant Signal. Behav. 4, 942–947. doi: 10.4161/psb.4.10.9530
[59]. Schonenbach, N. S., Hussain, S., and O'Malley, M. A. (2015). Structure and function of G protein-coupled receptor

oligomers: implications for drug discovery. Wiley Interdiscip. Rev. Nanomed. Nanobiotechnol. 7, 408–427. doi: 10.1002/wnan.1319

[60]. Stockert, J. A., and Devi, L. A. (2015). Advancements in therapeutically targeting orphan GPCRs. Front. Pharmacol. 6: 100. doi: 10.3389/fphar.2015.00100

[61]. Bayburt, T. H., Leitz, A. J., Xie, G., Oprian, D. D., and Sligar, S. G. (2007). Transducin activation by nanoscale lipid bilayers containing one and two rhodopsins. J. Biol. Chem. 282, 14875–14881. doi: 10.1074/jbc.M701433200.

[62]. Pauling L, Corey RB. A proposed structure for the nucleic acids. Proceedings of the National Academy of Sciences of the United States of America. 1953 Feb;39(2): 84.

[63]. Rook MS, Treiber DK, Williamson JR. An optimal Mg2+ concentration for kinetic folding of the Tetrahymena ribozyme. Proceedings of the National Academy of Sciences. 1999 Oct 26;96(22): 12471-6.

[64]. Varani G. Exceptionally stable nucleic acid hairpins. Annual review of biophysics and biomolecular structure. 1995 Jun;24(1): 379-404.

[65]. Driessen RP, Sitters G, Laurens N, Moolenaar GF, Wuite GJ, Goosen N, Dame RT. Effect of temperature on the intrinsic flexibility of DNA and its interaction with architectural proteins. Biochemistry. 2014 Oct 21;53(41): 6430-8.

[66]. S. E. Wolkenberg, D. L. Boger, Chem. Rev. 2002, 102, 2477. 67. Wu P, Nakano SI, Sugimoto N. Temperature dependence of thermodynamic properties for DNA/DNA and RNA/DNA duplex formation. European journ