2

Structure and Dynamics of Proteins

2.1 Introduction

Proteins are the most complex of biological molecules, composed of a large number of amino acid residues arranged in one or more polypeptide chain [145-148]. The structure of protein is related to its molecular size, relative proportions of various amino acids, their sequence and the arrangement of peptide chains in three dimensional shapes. They have a high molecular weight and their biological specificity is related to the number of amino acid residues and their sequence. Proteins are integral constituents of many structures in a living organism such as hair, skin, nails, horns, muscles, blood, membrane, etc. Some proteins function as enzymes to carry out biochemical reactions necessary for maintaining and building life. A few of them function as hormones that exert regulatory control over many
body functions. Besides they also play a role in immunological reactions and in transporting oxygen to the blood and muscles. Generally proteins are colorless and insoluble in water, alcohol and ether. They get easily denatured by heat or treatment with mineral acids. Proteins can be hydrolyzed by enzymic treatment or by mineral acids and the resultant products are the constituent amino acid residues. Globular proteins are essential components of all living organisms. These molecules are responsible for a remarkably wide range of biological functions, as may be seen by listing a few of the major groups within this vast family. Enzyme molecules are proteins that catalyze biochemical reactions. They act to build the structural elements of organisms and to provide the energy necessary for life processes. Familiar examples include the digestive enzymes that degrade foodstuffs to simple, assimilable compounds; the bio synthetic enzymes that build complex molecules from simpler compounds; and muscle proteins that produce mechanical work from chemical reactions. Transport proteins such as hemoglobin facilitate the movement of molecular oxygen and other essential compounds to their sites of utilization. Antibody molecules are proteins that bind to and neutralize foreign materials that may be harmful to an organism. Other globular proteins play essential roles in genetic expression, nerve conduction and all other biological processes. A number of physio-chemical techniques such as X-ray crystallography, NMR, etc., are used to study the structure and functions of proteins. However many of the properties of proteins and their biological functions
cannot be fully understood when their chemical structure alone is taken into consideration. But the physical and dynamical aspects are also found to be essential for understanding them. Hence in this thesis, we study the nonlinear dynamics of protein molecules. As a prelude to this in this chapter, we present details about the protein structure and dynamics from a physical point of view.

2.2 Protein Structure

Proteins are biopolymers of aminoacids. The spatial organization of proteins, their shape in three dimensions is a key to understanding how they work. The alpha - carbon atom ($C_\alpha$) of amino acids, which is adjacent to the carboxyl group is bonded to form different chemical groups: an amino ($NH_2$) group, a carboxyl ($COOH$) group, a hydrogen ($H$) atom and one variable group called a side chain or R- group which is shown in Figure 2.1. Nature has evolved a single chemical
linkage, the peptide bond to connect amino acids into a linear unbranched chain. The peptide bond is formed by a condensation reaction between the amino group of another which is depicted in the Figure 2.2a. The repeated amide $N$, $C_\alpha$ and carboxyl $C$ atoms of each amino acid residue form the backbone of a protein molecule from which the various side chain groups project. As a consequence of the peptide linkage the backbone has polarity, since all the amino groups lie to the same side of the $C_\alpha$ atoms. This leaves at opposite ends of the chain free (unlinked) amino group (the $N$-terminus) and a free carboxyl group (the $C$-terminus). A protein chain is conventionally depicted with $N$-terminal amino acid on the left and its $C$-terminal acid on the right which is shown in Figure 2.2b.

\section*{2.3 Four Levels of Proteins Structure}

The structure of proteins is commonly described in terms of four hierarchical levels of organization.

The \textbf{primary structure} of a protein is the linear arrangement or sequence of amino acid residues that constitute the polypeptide chain linked through covalent peptide bonds. The alpha-carboxyl group of one amino acid is covalently linked to the alpha-amino group of the next amino acid by an amide bond, commonly known as a \textbf{peptide bond} in proteins. The sequence of aminoacids from the N to the C terminus is the primary structure of the polypeptide.
2.3 Four Levels of Proteins Structure

Figure 2.2: The peptide bond

(a) A condensation reaction between two amino acids forms the peptide bond, which links all the adjacent residues in a protein chain.

(b) Side-chain groups (R) extend from the backbone of a protein chain, in which the amino N, α carbon, carbonyl carbon sequence is repeated throughout.
Secondary structure refers to the localized organization of parts of a polypeptide chain which can assume several different spatial arrangements. The highly polar nature of the C=O and N-H groups of the peptide bonds gives the C-N bond partial double bond character. This makes the peptide bond unit rigid and planar, though there is free rotation between adjacent peptide bonds. This polarity also favors hydrogen bond formation between appropriately spaced and oriented peptide bond units. Thus polypeptide chains are able to fold into a number of regular structures which are held together by these hydrogen bonds. The best known secondary structures is the alpha-helix. The polypeptide backbone forms a right-handed helix with 3.6 amino acid residues per turn such that each peptide N-H group is hydrogen bonded to the C=O group of the peptide bond three residues away. Sections of alpha helical secondary structure are often found in globular proteins and in some fibrous proteins. The beta-pleated sheet (beta-sheet) is formed by hydrogen bonding of the peptide bond N-H and C=O groups to the complementary groups of another section of the polypeptide chain. Several sections of polypeptide chain may be invoked side-by-side, giving a sheet structure with the side chains (R) projecting alternately above and below the sheet. If these sections run in parallel; if they alternate and $N \to C$ and $C \to N$, then the sheet is antiparallel. Beta-sheets are strong and rigid and are important in structural proteins.

Tertiary structure, the next higher level of structure refers to the overall
conformation of a polypeptide chain, i.e., the three dimensional arrangement of all the amino acids residues. The way in which the different sections of alpha-helix, beta-sheet, other minor secondary structures and connecting loops fold in three dimensions is a tertiary structure of the polypeptide. The nature of the tertiary structure is inherent in the primary structure and given the right conditions, most polypeptides will fold spontaneously into the correct tertiary structure as it is generally the lowest energy conformation for that sequence. Folding is such that amino acids with hydrophilic side chains locate mainly on the exterior of the protein where they can interact with water or solvent ions, while the hydrophobic amino acids become buried in the interior from which water is excluded. This gives overall stability to the structure. Various types of noncovalent interaction between side chains hold the tertiary structure together: van der Waals forces, hydrogen bonds, electrostatic salt bridges between oppositely charged groups and hydrophobic interactions between the nonpolar side chains of the aliphatic and aromatic amino acids. In addition, covalent disulfide bonds can form between two cysteine residues which may be far apart in the primary structure but close together in the folded tertiary structure. Disruption of secondary and tertiary structure by heat or extremes of pH leads to denaturation of the protein and formation of a random coil conformation.

Multimeric proteins contain two or more polypeptide chains or subunits held together by noncovalent bonds. Quaternary structure describes the num-
ber (stoichiometry) and relative positions of the subunits of multimeric protein. Hemogglutinin is a trimer of three identical subunits; other multimeric proteins can be composed of any number of identical or different sub units. Hemoglobin has two alpha-globin and two beta-globin chains. The same forces which stabilize tertiary structure hold these subunits together, including disulfide bonds between cysteines on separate polypeptides. This level of organization is known as quaternary structure and has certain consequences.

Among the four structural levels, it is easy to understand the dynamics associated with the energy transfer through polypeptide chains of proteins only with the help of the secondary structure of proteins. Hence we consider for our study the alpha - helical secondary structure of proteins.

2.4 Alpha Helical Secondary Structure

Polypeptide segments can assume a regular spiral or helical conformation called the alpha helix. In this secondary structure, the carboxyl oxygen of each peptide bond is hydrogen bonded to the amide hydrogen of the amino acid four residues toward the C - terminus. This uniform arrangement of bonds confers a polarity on a helix because all the hydrogen bond donars have the same orientation. The peptide backbone twists into a helix having 3.6 amino acids per turn. The stable arrangement of aminoacids in the alpha helix holds the backbone as a rod like cylinder from which the side chains point outward.
As the name implies, the conformation of these proteins is a helix formed by the twisting of the protein backbone. In addition, hydrogen bonds link the peptide groups together to form three spines that span the length of the helix and stabilize it. To form the helix wind the backbone into a right hand spiral and attach the hydrogen of the first peptide group to the oxygen of the fourth group, the hydrogen of the second peptide group to the oxygen of the fifth and so on. The first spine consists of the first, fourth, seventh, tenth, etc., peptide groups. The second and third spines form similarly. The spines of an alpha helical protein are not exactly linear or parallel to the axis of the helix as given in Figure 2.3.

2.5 Energy Transport in Alpha Helical Proteins

The energy supply for most protein activities is provided by the hydrolysis of ATP (adenosine triphosphate) molecules [148]. An ATP molecule binds to a specific site on the protein reacts with water and under normal physiological conditions releases 0.49 electron volt (eV) of free energy. This is about twenty times greater than the average energy available from the thermal background at 300 Kelvin. Molecular dynamics calculations based on ball and spring models of proteins show that heat from a thermal bath induces a variety of motions in proteins. These equilibrium calculations show motions ranging from localized, high frequency vibrations of individual bonds to collective, low-frequency motions of the entire protein. One may question however whether such equilibrium dynamics could
2.5 Energy Transport in Alpha Helical Proteins

Figure 2.3: Model of the alpha helix.
account for the efficient transport or use of energy over the characteristics length of proteins, which range from tens to hundreds of Angstroms.

An alternative hypothesis is that the energy of ATP hydrolysis is converted through resonant coupling to a particular vibrational excitation within the protein. This coupling might proceed through an intermediate vibrational excitation of water. This vibration is primarily a stretching and contraction of the carbon-oxygen double bonds in the peptide groups of the protein. The energy of the amide-I vibration is about 0.21eV, which corresponds to about 1660 reciprocal centimeters ($cm^{-1}$). This energy is a little less than half the energy of ATP hydrolysis and is almost equal to the energy of the H-O-H bending mode of water at about 1646 $cm^{-1}$. The amide-I vibration is a prominent feature in the infrared absorption and Raman spectra of proteins. Moreover its energy remains almost constant from one protein conformation to another, indicating that it is rather isolated from other degrees of freedom. All these factors lead to the conjecture that the energy released by ATP hydrolysis might stay localized and stored in the amide-I vibration.

The objection was raised that the lifetimes of typical vibrational excitations in complex biological molecules are too short ($10^{-12}$ seconds) for them to be important in the storage and transfer of biological energy. In particular peptide groups have large electric dipole moments; therefore dipole-dipole interactions among peptide groups would cause the amide-I vibrational energy to spread to neighbouring
peptide groups. Thus the energy would not remain localized but instead would disperse throughout the protein and be lost as a source for biological processes.

The Soviet physicist A. S. Davydov countered this objection with an argument from nonlinear physics. He suggested that the energy of ATP hydrolysis can be stored in the amide - I vibration through a nonlinear interaction that self focuses or traps, the energy in a soliton [149-157]. The soliton results from a nonlinear coupling between the vibrational excitation and deformation in the protein structure caused by the presence of the excitation. The excitation and deformation balance each other and the resulting excitations move through the proteins uninhibited much the way electrons move in the superconducting state of a metal.

Davydov worked out these ideas for one particular protein conformation. He introduced a simple mathematical model to show how solitons could travel along the three spines or hydrogen bonded chains of the protein.

Davydov first applied this idea to the problem of muscle contraction. He proposed that myosin, a major contractile protein in striated muscle that has an alpha helical tail approximately 1500 angstroms long, propagates a soliton that squeezes and pulls on the actin filaments around it. This action serves to slide the actin and myosin filaments together and thereby results in muscle contraction. In addition Davydov and his coworkers have considered the idea that alpha helical proteins may facilitate electron transport through a soliton mechanism. In this
2.5 Energy Transport in Alpha Helical Proteins

case an extra electron causes a lattice distortion in the protein that stabilizes the electron’s motion. Thus it may be reasonable to consider charge transfer across membranes, energy coupling across membranes and energy transport along filamentous cytokeletal proteins in terms of a soliton mechanism.

Figure 2.4 shows three interactions that occur when an amide-I vibration in a particular peptide group is excited, by the hydrolysis of ATP. First there will be resonant interactions with neighbouring peptide groups due to electromagnetic dipole-dipole interactions much like the interaction between transmitting and receiving antennae of a radio system. This interaction alone would lead to dispersion of amide-I energy as given in Figure 2.4a. Second (Figure 2.4b), due to changes in static forces (hydrogen bonds, Van der Waals forces etc.), the excited peptide group will tend to move from its equilibrium position, causing a local deformation of the hydrogen bond in the region of excitation. In alpha helical proteins the largest displacement will also be along the hydrogen bonds because hydrogen bonds are weaker than the covalent bonds along the helix. Since the hydrogen bond behaves like a weak spring, this movement of the peptide group away from equilibrium will set up a longitudinal sound wave or phonon along the chain as the peptide groups oscillate above their equilibrium positions. These two dynamical effects are displayed in the above Figure as if they were uncoupled; i.e., dispersion of amide-I bond energy is independent of the propagation of longitudinal sound waves. Davydov however pointed out that these two effects
2.5 Energy Transport in Alpha Helical Proteins

are coupled by a nonlinear interaction that arises from the change in amide - I vibrational energy caused by a change in the distance $R$ between peptide groups along the chain (hydrogen - bond stretching). The strength of this coupling is proportional to the nonlinear parameter

$$\chi = \frac{dE}{dR},$$

(2.1)

which can be expressed in unit of joules per meter or newtons. The effect of this nonlinear coupling is displayed graphically in Figure 2.4c. Localized amide - I vibrational energy acts as a source of longitudinal sound and this longitudinal sound reacts as a potential well that traps the amide - I vibrational energy and prevents its dispersion coupled together the localized amide - I vibrational energy and the longitudinal deformation can travel along the chain as a soliton with no energy loss. The strength of the nonlinear effect is proportional to $\chi$. It is also inversely proportional to $K$, the spring constant of the hydrogen bonds connecting the peptide groups. If the linear chain were absolutely rigid, $K$ would equal infinity, there would be no nonlinear interaction and amide - I energy would disperse. In alpha helical proteins, the three spines are coupled to each other by additional transverse dipole - dipole interactions. The solutions to these equations yield two types of solitons, a symmetric one in which the energy of the amide - I excitation is shared equally by all three chains and an asymmetric one in which the amide - I energy and the accompanying deformation are shared unequally and the molecule bends which is given in Figure 2.5. The antisymmetric soliton
2.5 Energy Transport in Alpha Helical Proteins

![Diagram of hydrogen bonded peptide groups showing the three interactions that combine CO trap amide - I vibrational energy in a stable solitary wave or soliton. Peptide groups with electric dipole moment $d$ are separated by a distance $R$ from each other.]

**Figure 2.4:** Linear chain of hydrogen bonded peptide groups showing the three interactions that combine CO trap amide - I vibrational energy in a stable solitary wave or soliton. Peptide groups with electric dipole moment $d$ are separated by a distance $R$ from each other.
2.6 The Davydov Model

The mathematical model first developed by Davydov is a semi classical approximation in which the amide-I excitations are treated quantum mechanically and the displacements of the peptide groups or longitudinal sound wave along the hydrogen bonded chain are treated classically [149-157]. We present in this section the Davydov model for collective excitations along a single chain of hydrogen bonded peptide groups [158] and show how the continuum approximation of this model leads to the NLS equation and its well known soliton solutions.

The energy operator $H$ or Hamiltonian for the collective excitation along the chain is a sum of three operators:

$$H = H_1 + H_2 + H_3.$$  \hspace{1cm} (2.2)
In Eq. (2.2), $H_1$ stands for the exciton Hamiltonian representing internal molecular excitations. If $E_0$ is the amide - I excitation energy and $B_n^\dagger$ is an operator for creation of this excitation on the $n$th peptide group, then $H_1$ is given by

$$H_1 = \sum_n B_n^\dagger [E_0 B_n - J_0 (B_{n+1} + B_{n-1})],$$

(2.3)

where the summation is carried out over all N peptide groups. The first term $E_0 B_n^\dagger B_n$ defines the amide-I excitation energy and the second term describes the resonance dipole - dipole interaction between nearest neighbours. The operator $B_{n+1}^\dagger B_{n+1}$ and $B_n^\dagger B_{n-1}$ represent the transfer of amide - I energy from peptide group $n$ to $n \pm 1$ due to the dipole - dipole interaction. The dipole - dipole interaction energy $J_0$ is given by $2|d|^2/R^3$, which is the usual electrostatic energy associated with two collinear dipoles of moment $d$ (0.3 Debye) separated by the distance $R$ (2.8 Å).

The energy $H_2$ associated with displacing the peptide groups away from their equilibrium positions is given in the harmonic approximation by

$$H_2 = \frac{1}{2m} \left( \frac{p_n^2}{m} + K(u_n - u_{n-1})^2 \right),$$

(2.4)

where $u_n$ is the operator for the longitudinal displacement of peptide group parallel to the helical axis from its equilibrium position, $p_n$ is the momentum operator conjugate to $u_n$, $m$ is the mass of the peptide group, $K$ is the spring constant or elasticity coefficient of the hydrogen bonds associated with the nearest neighbours. The first term is the kinetic energy, the second term represents the potential energy due to the nearest neighbour interactions. $H_3$ is the Hamiltonian.
2.6 The Davydov Model

for the interaction between the amide-I excitation and the displacements of the peptide groups which takes the form

\[ H_3 = \chi B_n^\dagger B_n (u_n+1 - u_{n-1}), \] (2.5)

where the coupling constant \( \chi \) is the nonlinear coupling coefficient representing the change in energy of the amide-I bond caused by the stretching of the helix between two neighbouring unit cells.

The total Hamiltonian \( H \) of the system must satisfy the Schrödinger equation:

\[ i\hbar \frac{\partial}{\partial t} |\psi\rangle = H |\psi\rangle. \] (2.6)

The wave function for collective excitations of the chain may be sought in the form [149]

\[ \psi(t) = \sum_n a_n(t) \exp[\sigma(t)] B_n^\dagger |0\rangle, \] (2.7)

where \(|0\rangle\) is the vacuum state wave function and

\[ \sigma(t) = -\frac{i}{\hbar} \sum_n \{ b_n(t) p_n - \phi_n(t) u_n \}. \] (2.8)

Here \( a_n(a_n^\dagger) \) is the coherent state representation of the operator \( B_n(B_n^\dagger) \) and the function \(|a_n|^2\) characterizes the probability of excitation of the \( n \)-th peptide group in the spine. Introducing \( b_n \) as the coherent state representation for the displacement \( u_n \) and \( \phi_n \) for their conjugate momenta \( p_n \) respectively, we can write the coherent state operators \( B_n, B_n^\dagger, u_n \) and \( p_n \) as

\[ a_n(t) = \langle \psi(t) | B_n |\psi(t)\rangle, \quad a_n^\dagger(t) = \langle \psi(t) | B_n^\dagger |\psi(t)\rangle, \]

\[ b_n(t) = \langle \psi(t) | u_n |\psi(t)\rangle, \quad \phi_n(t) = \langle \psi(t) | p_n |\psi(t)\rangle. \] (2.9)
The Hamiltonian for the collective excitation can be written as

$$\langle H \rangle = \sum_n \{ a_n^*(E_0 + W)a_n - J_0(a_{n+1} + a_{n-1}) + \chi(b_{n+1} - b_{n-1})a_n \},$$

(2.10)

where

$$W = \frac{1}{2} \sum_n \left( \frac{\phi_n^2}{m} + K(b_n - b_{n-1})^2 \right)$$

(2.11)

is the deformation energy of the chains. Having written down the Hamiltonian in the semi classical description, the dynamics of the protein molecular system is understood by constructing the Heisenberg’s equation of motion

$$i\hbar \frac{d\langle A_n \rangle}{dt} = \langle [A_n, H] \rangle,$$

(2.12)

where $A$ represents the dynamic variables $a_n, b_n,$ and $\phi_n$ satisfying the commutation relations

$$[A, A^\dagger] = 1$$

(2.13)

and

$$[u_n, p_n] = [b_n, \phi_n] = i\hbar.$$  

(2.14)

Substituting Eq. (2.10) in Eq. (2.12) we get the following set of differential equations:

$$i\hbar \frac{da_n}{dt} = [E_0 + W + \chi(u_{n+1} - u_{n-1})]a_n - J_0(a_{n-1} + a_{n+1})$$

(2.15)

and

$$m \frac{d^2u_n}{dt^2} = K(u_{n+1} + u_{n-1} - 2u_n) + \chi(|a_{n+1}|^2 - |a_{n-1}|^2).$$

(2.16)
Eqs. (2.15) and (2.16) describe the time evolution of amide-I vibrational energy coupled to displacements of the hydrogen bonded chain of peptide groups. When the function $a_n$ and $b_n$ change smoothly over one link of the chain, it is appropriate to make a continuum approximation for $a_{n\pm 1}$ and $b_{n\pm 1}$ using the Taylor expansion

$$
\begin{align*}
a_{n\pm 1} &= a \pm \epsilon a_x + \frac{\epsilon^2}{2} a_{xx} + \frac{\epsilon^3}{6} a_{xxx} + \frac{\epsilon^4}{24} a_{xxxx} + \ldots, \\
b_{n\pm 1} &= b \pm \epsilon b_x + \frac{\epsilon^2}{2} b_{xx} + \frac{\epsilon^3}{6} b_{xxx} + \frac{\epsilon^4}{24} b_{xxxx} + \ldots
\end{align*}
$$

which is a valid approximation in the long wavelength, low temperature limit. Here $\epsilon$ is the lattice parameter and suffix $x$ represents partial derivative with respect to $x$.

Substituting Eqs. (2.17) in Eqs. (2.15) and (2.16) and rescaling gives

$$
iha_t = (E_0 + 2\chi u_x)a - J u_{xx}
$$

and

$$
u_{tt} - \frac{K}{m} u_{xx} = \frac{2\chi}{m}(|a|^2)_x.
$$

The left side of Eq. (2.19) is essentially a wave equation for longitudinal sound in the system of coupled peptide groups. The right side acts as a source term for generation of sound.

We shall seek traveling wave solutions to Eqs. (2.18) and (2.19) in the form of excitations that propagate along the chain with a velocity $v_1$, i.e.,

$$
u(x, t) = u(x - v_1 t).
$$
Inserting Eq. (2.20) into Eq. (2.19) we get

\[ u_x = \frac{-2\chi}{K(1 - s^2)} |a(x,t)|^2, \quad (2.21) \]

where \( s \) is the ratio of the propagation velocity to the velocity of sound which takes the form \( s^2 = \frac{v^2}{v_0^2} \) where \( v_0^2 = \frac{K}{m} \).

Substituting Eq. (2.21) in Eq. (2.18), we get

\[ i\hbar a_t + J a_{xx} - E_0 a + \kappa |a|^2 a = 0, \quad (2.22) \]

where

\[ \kappa = \frac{4\chi^2}{K(1 - s^2)}. \quad (2.23) \]

Eq. (2.22) is the perturbed NLS equation, which has soliton solutions. Upon making the transformations \( a \to a \sqrt{\frac{K(1-s^2)}{2\chi^2}}, \quad t \to \frac{J}{\hbar} t, \) Eq. (2.22) becomes the completely integrable NLS equation

\[ ia_t + a_{xx} + 2|a|^2 a = 0. \quad (2.24) \]

Also the stationary solution of Eq. (2.22) is given by

\[ a(x,t) = \frac{\chi}{(2KJ)^{1/2}} \text{sech} \frac{\chi^2}{KJ}(x-x_0) \text{exp}[-\frac{i}{\hbar}(E_0 - \frac{\chi^2}{K^2J})t]. \quad (2.25) \]

The constant \( x_0 \) is the position of maximum probability of amide-I excitation along the chain and the pulse shaped form given by Eq. (2.25) falls off rapidly when one moves away from \( x_0 \). Eq. (2.25) represents a soliton and thus Davydov proved that the energy released during the hydrolysis of ATP molecules is propagated through proteins in the form of solitons without any loss.
2.7 Experimental Evidence for Davydov Solitons

(a) Muscle Contraction

In 1979, Davydov proposed that his soliton may be the key element in the contraction of striated muscle. His basic notion is that the longitudinal displacement of "thick" with respect to "thin" fibers is effected by a "lump" of solitons propagating more or less together toward the Sacromere center. As a variation on this theme, one might consider the model for contraction suggested by Jarosch [159]. Although Jarosch provides structural arguments for the pitch of the screw a soliton on one alpha helix of the coiled - coil structure might do as well. Following this line of thought the coiled coil with one soliton might provide an explanation for a wide range of mechanical motions in living organisms.

(b) Sensitivity of living organisms to low intensity nonionizing electromagnetic radiation

Over the past decade a rather impressive amount of experimental evidence has been accumulating to indicate that living organisms are behaviorally sensitive to low-intensity e.m. radiation which raises tissue temperature only by "orders of magnitude less than" 0.1°C. Proteinaceous material on cell membrane surfaces appears to be the site of detection and it is clear that nonlinear mechanisms must be invoked to explain the extraordinary sensitivity observed. One such nonlinear mechanism is the influence of e.m. fields on the dynamics of Davydov solitons.
that play functional roles in vital processes of energy transport.

(c) Rupturing of a helix by tuberculosis and its effect on soliton dynamics

It has been suggested that the additional lines appearing in spectrofluorometric analysis of blood from tubercular patients is related to a change in the dynamics of Davydov solitons when alpha helix protein molecules are ruptured by microbacterium tuberculosis.

(d) Raman spectra shift in green algae

Davydov solitons have been invoked to explain the temperature-dependent Raman spectrum of a green alga (chlorella pyrenoidosa). In this the solitons are supposed to be excited by phase transitions that appear between 230 and 260 K and to spread the scattered energy over a larger number of vibrational modes.

(e) The Laser - Raman spectra of metabolically active cells

The Laser Raman measurements on living cells reports (i) at 300K a Raman spectrum is observed only when cells are metabolically active; (ii) the intensity ratios of Stokes to anti-Stokes lines indicate that the Raman active states are produced by nonthermal means; and (iii) spectral lines below 200 cm$^{-1}$ shift to lower wave numbers as the cells progress through their life cycles. Although broad Laser-Raman spectra have been observed on alpha helical proteins in aqueous solution and in crystalline form and assigned to various linear modes of mechanical vibration, such an explanation is unlikely for the lines. As noted above, these
lines appear only when an intact cell is metabolically active and move to lower wave numbers as the cell ages. Interpretation as the internal vibrational spectrum of Davydov solitons, however, is straightforward. The vibration spectrum of the soliton corresponds to the two energies between two levels and their sums and differences. Furthermore, the tendency of the measured lines to shift toward lower wave numbers as cells progress through their life cycles is gracefully explained by assuming that solitons receive less input energy and therefore move more slowly as a cell ages. Thus there is experimental evidence to suggest that Davydov solitons play a functional role in metabolic processes.

2.8 Recent Progress: A Review

The transparency and seminal properties of Davydov’s model continues to encourage intense work regarding the research of the nonlinear treatment of alpha helical proteins [160-246]. These works include both analytical and numerical studies based on the simplest nonlinear model of Davydov incorporating energies corresponding to the internal molecular excitations, displacement of unit cells and interactions between the two. For the first time, the effect of discreteness and higher order molecular excitations and interactions on the soliton dynamics of alpha helical proteins was investigated [247] and the results were found to be again in favour of soliton propagation through the chains. A more generalized model [248] described by internal molecular excitations of different orders and
nonlinear couplings with nearest and next nearest neighbouring peptide units was studied assuming that the left and right interactions with the nearest neighbouring peptide units are unequal in general. At different orders of continuum approximation, the generalized model describing molecular excitations reduces to completely integrable models of the NLS family for specific parametric choices. Discrete model supporting soliton excitations was also proposed in recent times both in the lower and higher order cases of molecular interactions and excitations [249]. Analytical studies were carried out in this case and the governing dynamical equations appear as completely integrable soliton possessing discrete NLS equations of lower and higher order respectively. On the other hand, in addition to considering the structure of the alpha helix, particular attention has been paid to the existence of the soliton at the biologically relevant temperature (300K) and the solitonic properties in the protein with the structural disorders and non uniformity [250-266]. However, in all these models only a single channel or spine is considered as it was assumed that the study of the dynamics of a single molecular chain along the hydrogen bonding spine will reproduce the dynamics of the full alpha helical protein molecular chain. The effect of interspine coupling was first studied by Scott [267] by constructing a model to represent the change in amide - I bond energy caused by changing the length of an adjacent hydrogen bond which is slightly different from that of Davydov [149] because it represents the observation [268] that only the hydrogen bond which is on the C=O side of a
peptide unit will influence amide - I energy and he obtained the dynamical equations in the form of 3-dimensional vector NLS equation. Earlier, Davydov [269] also studied the collective excitations of the alpha helical proteins restricting the calculations by including only the resonance interactions and two types of peptide group displacements provided by changes of the helix pitch and its radius and derived a set of equations which represent three types of solitons and calculated the soliton energy. A detailed analytical study on the dynamics of a slightly modified Davydov’s model of alpha helical proteins was also made both at the discrete and continuum levels giving consideration to the interspine coupling and the excitations were found to be governed by soliton modes [270-273]. Recently applying ultrafast infrared pumb-probe spectroscopy, a N-H stretching mode self-trapping in the poly-γ-benzyl-L-glutamate helix has been observed [274-276]. Two positive bands in the transient absorption spectrum have been assigned to self-trapped two exciton states [277-282]. An analytical study on two exciton states in alpha helical proteins has also been reported very recently [283].

2.9 Present Work

Inspired by the considerations put forth earlier, in this thesis we investigate the nonlinear excitations in an alpha helical protein chain with intra- and inter-spine coupling including different molecular excitations and interactions both at the discrete and continuum levels. Specifically, we analyze the higher order and
discreteness effects in an alpha helical protein chain with intra-spine and inter-spine coupling. The systems which we wish to analyze are the framework of a certain generalization of the Davydov’s model by incorporating dipole-dipole and quadrupole-quadrupole type molecular excitations and interactions considering both the single spine and three spine structure of alpha helical proteins. To understand the dynamics of proposed models, we present the soliton solutions and interactions using the well known techniques such as Hirota’s bilinearization, Darboux transformation, Sine-Cosine Function Method, Tanh function Method and Extended tanh method. We also investigate the effect of inhomogeneities due to the presence of drug molecules in an alpha helical protein chain with intra- and inter-spine coupling. In addition, we analyze the stability of soliton propagating through alpha helical proteins by considering models with intra- and inter-spine couplings.