Fall 2013

Protein aggregation at solid/liquid interfaces: a Monte Carlo study with explicit and implicit solvent effects

Rehman Fazeem

Department:

PROTEIN AGGREGATION AT SOLID/LIQUID INTERFACES: A MONTE CARLO STUDY WITH EXPLICIT AND IMPLICIT SOLVENT EFFECTS

by

REHMAN FAZEEM

A THESIS

Presented to the Faculty of the Graduate School of the

MISSOURI UNIVERSITY OF SCIENCE AND TECHNOLOGY

In Partial Fulfillment of the Requirements for the Degree

MASTER OF SCIENCE IN CHEMICAL ENGINEERING

2013

Approved by

Daniel Forciniti, Advisor
Parthasakha Neogi
Jee-Ching Wang

ABSTRACT

Metropolis Monte Carlo (MC) simulations were performed with positively charged peptides in aqueous solution to study changes in peptide conformations at solid/liquid interface, and its effects on protein aggregation. Intermediate-resolution diblock model peptide, comprising of 10 units of ALA (non-polar) and LYS (polar) amino acid residues, was used for the simulations. In the first approach to modeling, solvent effects were considered explicitly. The explicit model was then used to study two peptide molecules, in helical structure, at solid/liquid interface. In order to increase the number of peptide molecules in the simulation box, with reduced computational cost, an implicit solvent model was developed with nonadditive hydrogen bonding and hydrophobic interaction potentials. The implicit model was used to simulate two peptides of helical structure at charged surfaces (to compare with the explicit model), and ten peptides of random coil structure with and without charged surfaces. The peptides were observed to always move towards the negatively charged surface and orient with residues of complimentary charge settling close to the surface, maximizing the electrostatic interactions. On reaching the surface, the peptides partially lose their secondary structure and clusters around the hydrophobic ends; this restructuring and dehydration of the peptides provides the entropic drive for adsorption and subsequent misfolding events. The 2- peptide-water-surface system in explicit model was also simulated with periodic switching of surface charge polarity, to induce a “shaking effect” in order to observe possible peptide configurational changes.

ACKNOWLEDGMENTS

I thank my advisor, Dr. Daniel Forciniti, for providing me with valuable guidance and insight into my thesis topic. He has been there always to assist me through building the potential model and analyzing the results.

This material is based upon work supported by the National Science Foundation under Grant No. 0933468.

I also thank my committee members, Dr. Parthasakha Neogi and Dr. Jee-Ching Wang, for reviewing my work and for providing their valuable input.

TABLE OF CONTENTS

LIST OF ILLUSTRATIONS

1. INTRODUCTION

Proteins are polymers of amino acids which are covalently linked through peptide bonds. Amino acids are small organic molecules that consist of an α-carbon atom linked to an amino and carboxylic acid functional groups, a hydrogen atom, and a variable group called a side chain. The linear sequence of amino acids within a protein forms its primary structure. The chemistry of each amino acid plays an important role in the 3D-stucture of proteins, as they can participate in non-covalent bonds, such as hydrogen bonds, which define the protein secondary structure. The tertiary structure of proteins is formed by the 3D arrangement of multiple secondary structures in single polypeptide chain. Quaternary protein structure refers to multiple polypeptide chains or subunits in a single protein molecule. Proteins are also prone to aggregation, where unfolded molecules associate and clump together. These aggregate structures may be fibrillar or amorphous.

Proteins support all vital functions of every cell and are often referred to as "biological workhorses". To carry out their functions, proteins assemble into complex three-dimensional structures through a mechanism called folding. When proteins do not fold correctly (misfolding) they lose their specific activities --adversely affecting various cellular functions. The self-templating ability of misfolded proteins leads to misfolding inheritance by the cell, and their aggregation and/or accumulation (called amyloid plaque) is a signature of several human diseases, such as Alzheimer's, Huntington's chorea, Parkinson's, type two diabetes, systemic amyloidosis, transmissible spongiform encephalopathy etc. These diseases are collectively known as protein misfolding or amyloid diseases. Amyloid diseases are apparently unconnected; however, intermolecular secondary structure (mostly β-sheets) is present in all amyloid aggregates. In spite of the large amount of published material, the effect of surfaces on the formation of the deposits remains obscure. The concentration of amyloid peptides in healthy or sick tissue is of the order of a few nano-moles. Therefore, the presence of a solid/liquid interface may serve as a crowding agent that "catalyses" the formation of the aggregates.

It is believed that virtually any protein may form amyloid fibrils, given appropriate conditions; this suggests that the amyloid fibril is the global free energy minimum assembly formed by polypeptide chains. The experimental pool suggests that

the fibrils minimize their energy by minimizing electrostatic repulsions and maximizing hydrophobic contacts. The current consensus is that all amyloid deposits consists of continuous β-sheets with β-strands oriented perpendicular to the fibril long axis. The remarkable stability and insolubility of the fibril structure poses greater threat for etiology and treatment of amyloid diseases. The aggregation process and the type of aggregate structure are largely dependent on the protein primary structure [1] and, sometimes, a minor change in amino acid sequence changes the aggregation phenomenon.

Protein aggregation may be desirable for situations such as in evolution [2] because it allows cells to acquire complex traits step wise, but is strongly undesirable in processes like protein crystallization, in vitro folding and formulation and delivery. Many vital protein functions, which depend on maintaining the protein native state, are lost as the protein aggregates. Recently it was found that these aggregate structures were not as non-specific as earlier believed [3]. Proteins form amorphous or ordered (fibril) aggregates structures depending on the polypeptide sequence, temperature, solution conditions and protein concentration.

Protein aggregation occurs readily in almost all biopharmaceutical processes and it is one of the top tumbling blocks in the rapid commercialization of protein drug candidates. Even though the protein preparation may have been aggregate-free, aggregates may form during storage. For over a 2 year shelf-life, build-up of aggregate levels as low as 1% can render a product clinically unsafe [4]. It is therefore important to understand the conditions at which protein stability is compromised. The main factors that affect protein stability in protein drug processing and delivery are shear/shaking (involves interaction with interfaces), temperature, pH and protein concentration. Irreversible aggregation, caused by disulfide shuffling or stable hydrophobic association, can have a direct impact on drug potency immunogenicity and unfolded protein response. The administration of a protein drug that aggregates reversibly could be also tricky if the disassociation is slow in the physiological time scale.

Some proteins in folded or unfolded state undergo non-specific self-association into disordered aggregates. When viewed in an electron microscope they look granular without any fibrils and they are called amorphous aggregates. Amorphous aggregation is usually an initial step in amyloid assembly before amyloid fibril formation proceeds.

Among the variety of aggregates formed, the aggregates with amyloid fibril structure are common. They have three characteristic features: (1) birefringent staining using congo red, (2) fibrous morphology observed by electron microscopy and (3) X-ray fiber diffraction pattern consistent with high cross-β structure [4]. However, debate still remains on the toxicity of these aggregates as few studies indicate that precursers to these aggregates are much more toxic than the mature fibrillar aggregates [5].

One of the least investigated areas in protein aggregation phenomena is the interface-induced aggregation at solid-liquid and air-liquid boundaries. Although there are some publications on this topic [6-9] there is not consensus among the scientific community about the actual mechanism of interface-induced aggregation. It has been suggested that since proteins are surface active, their structure gets perturbed by surface tension forces at interfaces. These perturbations restructure the protein folding energy landscape to energetically favor partially folded and structurally expanded transition states (which are aggregate prone) over the more compact native states [6]. However, it is found often that the structural conformational change alone cannot explain protein aggregation and hence there are no apparent reasons to believe that aggregation is preceded by a structural conformational change.

Some biopharmaceutical processing operations, like stirring, create air/liquid interfaces. At the interface, the hydrophobicity of air relative to water induces protein alignment, maximizing the exposure of the hydrophobic residues to the air and initiating aggregation. Many proteins aggregate at the air/liquid interface [10]. To suppress this in industrial processes surfactants are commonly used. Surfactants inhibit protein aggregation by competitively accumulating with proteins at hydrophobic surfaces/interfaces and/or by binding directly to proteins. Certain surfactants have the added advantage of increasing solution viscosity, which may limit the motion of the protein backbone and thus reduce aggregation.

Proteins adsorb at solid liquid interfaces. This process, which is driven by electrostatic and hydrophobic interactions, may alter the characteristics of the sorbent surface, and in many cases, of the protein molecules. Adsorption likely reduces the energy barrier for protein aggregation [10].

Adsorption of biopharmaceuticals at solid/liquid interfaces creates serious problems for their production, storage and delivery. For example, insulin gets destabilized by adsorption at hydrophobic surfaces like those formed by air-water or water-polymer. Nucleation precedes the process, followed by intermediate aggregation that serves as precursor for large insulin precipitates [11]. It is suggested that less stable insulin monomers undergo partial unfolding upon adsorption, and combine with neighboring unfolded species initiating nucleation. After reaching a critical size, the intermediate aggregates grow into larger aggregates [11]. Aggregation of insulin reduces its biological potency and obstructs continuous/controlled release pumps and polymeric devices, creating serious problems for drug delivery systems.

Experiments show that presence of negatively charged surfaces in beta amyloid peptide solutions shifts the random coil structure of beta amyloid peptide to a beta sheet conformation [12], under conditions that do not lead to aggregation in solution. This conformational change is triggered by adsorption of beta amyloid peptides, on both hydrophobic and hydrophilic surfaces, over a period of time [12]. After such conformational change, the process may follow two pathways: (1) The beta sheet form of the peptide may act as a template for other peptides to continue adsorbing at the surface, yielding surface-confined aggregates and (2) the peptide in beta sheet form diffuses back into solution to interact with other beta amyloid peptides to form aggregates. It is also observed that the amount of amyloid deposits in beta amyloid solution increases with exposure time to the surface. Following these observations it is suggested that surfaces have a seeding effect on beta amyloid peptides in solution, inducing their aggregation [12].

Kinetic experiments on protein folding indicate that, at least, for most proteins the folding event is spontaneous and reversible, usually occurring rapidly within few seconds. It is evident that considering the huge number of possible conformations, a protein molecule has to follow a specific path to fold into its native state in order to meet the biologically feasible time scale. It has been also suggested that metastable, partially folded, states of a protein exist and they could provide vital information on the folding mechanism [13]. For studying complex folding and aggregation mechanisms, occurring on very fast time scales, access to atomistic details of the process is needed. This has

been realized by combining experimental approaches with powerful theoretical models. Although modern experimental techniques can monitor folding events occurring at nanosecond to microsecond time scales, theoretical approaches facilitate harnessing information at atomic resolution, at least for small peptides [13]. Theoretical models should be robust and should be able to cover different scales (in space and time) for them help identifying the determinants of protein aggregation process and to direct experimental investigations.

In recent years, theoretical and experimental studies on protein folding have focused on characterizing the folding mechanism in detail. Experiments have shown that not all proteins follow specific pathways in the folding process. Search for the native conformation is driven by the bias towards the native state over much of the protein energy landscape. Thus proteins must have tilt, funnel-shaped energy landscape (meaning that many conformations have higher free energy and few have lower energy) to fold quickly and efficiently. Theoretically, an ideal protein landscape will be smooth funnel shaped, however, for real proteins the folding funnel should carry landscape features like kinetics, smoothness or barrier heights. This concept has replaced the random search concept of Levinthal paradox in protein folding problem, and thus the "golf course" model of the protein potential energy surface is no longer valid [14]. A number of experimental examples and theoretical models have shown that essentially any protein or polypeptide can form non-native aggregates in solution, if incubated for sufficient time without intervention of other processes such as chemical or proteolytic degradation. The unfolded/non-native monomeric state of proteins is often identified as the reactive pre-cursers that subsequently assemble to form ordered or disordered oligomers or higher molecular weight aggregates [15]. Studies have shown that a number of non-disease related proteins can also form amyloid fibrils. These studies also revealed that the process of destabilization of the native-structure is crucial in guiding normally soluble proteins into amyloid deposits [5]. This has led to the conclusion that fibril formation tendancy is a generic property of the peptide backbone, and thus a generic mechanism of aggregation should exist. Recent experiments show [16] that replacing leucine by isoleucine in a diblock peptide drastically change the amyloid forming properties of the peptides. Those experiments added to the undisputed importance of the solvent on protein conformation

suggest that solvent effects and the specifics of the aminoa acid side chain **cannot** be ignored.

Thus, understanding the physical-chemical factors shaping a protein folding energy landscape will provide an insight into its misfolding/aggregation process. Most of the theoretical and experimental studies on protein folding mechanism aim at dissecting the folding free energy landscape of interested proteins, particularly by studying the effect of perturbations on their populated folding routes [17].

In this thesis, Metropolis Monte Carlo (MC) simulations were performed with positively charged peptides in aqueous solution to study changes in peptide conformations at solid/liquid interface, and their effects on protein aggregation. An intermediate-resolution diblock model peptide, comprising of 10 units of ALA (non-polar) and LYS (polar) amino acid residues, was used for the simulations. In the first approach to modeling, solvent effects were considered explicitly. The explicit model was then used to study two peptide molecules, in helical structure, at solid/liquid interfaces. In order to increase the number of peptide molecules in the simulation box, with reduced computational cost, an implicit solvent model was developed with non-additive hydrogen bonding and hydrophobic interaction potentials. The implicit model was used to simulate two peptides of helical structure at charged surfaces (to compare with the explicit model), and ten peptides of random coil structure in bulk and at solid/liquid interfaces. The two-peptide-water-surface system using the explicit model was also simulated with periodic switching of surface charge polarity. This was done to simulate the effect of “shaking” on the conformation of short peptides.

2. MODEL DEVELOPMENT

Metropolis Markov Chain Monte Carlo (MCMC) Simulations, in the canonical ensemble, was chosen over Molecular Dynamics (MD), because of our own expertise [18-21] and because the focus of study was the final equilibrium state rather than the kinetics. Experiments show that helix formation takes place in a few hundred nanoseconds, while a small beta hairpin takes a microsecond to form. The fastest known time scale for complete folding of a small protein is of order of tens of microseconds. With current computing capabilities, the attainable time scale in MD is too short for studying protein folding with a reasonable model at atomistic resolution. Thus, MCMC simulations are a better choice for the present study.

The existing Monte Carlo code available in Dr. Forciniti's group [20,21] can simulate a peptide of arbitrary length dissolved at infinite dilution in explicit water. The Monte Carlo suite is able to handle peptides at infinite dilution in bulk as well as peptides at infinite dilution at solid/liquid interfaces (where the interface consists of a collection of Lennard Jones sites having a partial charge). This Monte Carlo suite was extended to handle multiple peptides. This extension is very important because a new model described later in this section needed to be benchmarked against the existing atomistic model.

2.1. EXTENSION OF EXISTING MODEL TO FINITE CONCENTRATIONS

The existing MCMC code simulates a single peptide molecule in explicit water. The peptide is generated by the molecular modeling software ALCHEMY and a simple point charge (SPC) model is used for water (the extension to other water models is straightforward). The GROMACS force field is used. The surfaces of same charge density were placed in the xy-plane at the two ends of the simulation box. The capability of the current MCMC simulator, limited to run models to study infinite dilution behavior only, was augmented to investigate protein aggregation process, involving multiple peptide molecules. A listing of the modified code is included in Appendix A. Appendix B includes instructions to run the program.

As a first step into handle multiple peptide molecules, it was decided to update the existing explicit model code to simulate a two-peptide-water-surface system. The peptides were identical and all program variables required to simulate a peptide model were duplicated. As part of system initialization, the ALCHEMY generated peptide coordinate file was modified to include the different z-coordinates of the two peptides, keeping the x and y coordinates the same. Thus, two identical peptides were placed in the box along the z-coordinate between the two charged surfaces. Water molecules were then positioned around the peptides in numbers to keep water density inside the simulation box equal to 1 g/cm^3. To the existing peptide-surface, peptide-water, water-surface and water-water inter-molecular interactions, peptide-peptide interactions were added. The intramolecular energy estimations for torsional and van der Waal's interactions were also extended for the second peptide molecule. Periodic boundary conditions were used in the x and y directions only, and the charged surfaces at the two ends of the box (in z-direction) ensured all molecules to stay inside the simulation box throughout the run. All the interactions were calculated by the minimum image (MI) convention, which is considered to be reliable for studying the structural features of protein aggregation at interfaces [18].

2.2. MIXING

A "mixing effect" was induced for the explicit 2-peptide(random coil)-water-surface model by continuously changing the polarity of the surfaces throughout the simulation run. It is believed that this will help in understanding, qualitatively, the effects of mixing on protein aggregation. A model diblock peptide, 5ALA-5LYS, was used for this experiment. In order for the peptides to have enough space for adsorption, the surfaces were extended along the y-axis and the peptides were initially arranged along y-axis equidistant from the surfaces. For every 20,000 MC steps the charges on the surfaces were switched and the simulation was continued.

2.3. DEVELOPMENT OF IMPLICIT WATER MODEL

It is evident that atomic-level simulations of the protein aggregation process are computationally uneconomical. To solve this problem, it was decided to use an implicit

model to account for solvent effects and thereby reducing the degrees of freedom introduced by the explicit treatment of water molecules. Takada et al. [22] performed MD simulations of a helical protein and a random hetero polymer to study their folding dynamics. They used a simplified description of the protein, which has a realistic backbone but single sphere side chains, to reduce the number of degrees of freedom. Solvent effects were captured by incorporating hydrogen bonds and hydrophobic interactions implicitly. Anisotropic hydrogen bonds (HB) were modeled by a particular combination of attractive and repulsive forces between donor and acceptor atoms; with the bond strength reflecting the local dielectric constant that is dependent on protein configuration. Hydrophobic (HP) interaction were modeled in terms of local density of the peptide atoms; this is similar (but computationally cheaper) to the nonadditive HP interaction model written in terms of accessible surface area (ASA) [22].

The HB/HP interaction model used by Takada's group [22] was extended to model the adsorption/aggregation of peptides at solvent-surface interfaces. By treating the solvent implicitly, finite peptide concentrations became manageable avoiding heavy computational load. In this new model, all peptide atoms (including the side chain groups) are treated explicitly except for the methyl groups, CHx (x=1-3), which are treated as united atoms. This is an advance to the model introduced by Takada's team [22] who oversimplified the side chains by modeling them as a united atom. The more detailed description of the peptide molecule and the extension to finite concentrations in this model call for some changes in HP/HB interaction relations as proposed by Takada et al. [22]. These modifications are described below.

The system potential term, V, is defined as,

$$V = V_{lc} + V_{nonlc} \tag{1}$$

where, V_{lc} and V_{nonlc} are the local potential and non-local potential terms, respectively. These terms are defined as,

$$V_{lc} = V_{tor} + V_{vdv-lc} \text{ and,} \quad (2)$$

$$V_{nonlc} = V_{vdw} + V_{HP} + V_{HB} \quad (3)$$

where, V_{tor} is the torsional potential, which was calculated the same as in our existing explicit model (Refer to Appendix A). The local van der Waals (vdW) potential (only for 1-4 pairs), V_{vdw-lc}, was estimated along with the non-local vdW potential, V_{vdw} , by LJ plus a Coulombic term following the approach used in our explicit model (Refer to Appendix A).

Following Takada et al.'s work [22], the hydrophobic interaction potential (V_{HP}) was incorporated in the model. It should be notice that the HP potential depends on the local density of the peptide atoms of **all** peptide molecules in the simulation box. For the HP interaction model (described in later section), only interactions among Cα and Cβ atoms were considered, where the interactions between Cβ atoms depend on the type of the amino acid.

The existing code was modified to include the hydrogen bond potential (V_{HB}). This potential was modeled anisotropic by considering attractive forces between CO and NH while a repulsive force is introduced between NH and NH, NH and CαH, between CαH and CO, and between CO and CO. Since all these groups are treated explicitly in the new model, interactions between particular atoms of the groups (as described in Figure 2.1) were selected. The interaction scheme in the HB model is amino acid type specific, as it consists of feasible pair-wise interactions among the backbone atoms and also among side chain atoms. In addition to the intra-molecular amino acid interactions for estimating V_{HB} as proposed by Takada et al. [19], the new model considered inter-molecular amino acid interactions also. The proposed HB interaction model can be represented as (for K^{th} peptide molecule),

$$V_{HB,\,intra,\,K} = \varepsilon_{HB} \sum_{\substack{ij\,(s.t\ I \geq J+3) \\ I,J \in K}} S_{HB,\,IJ}\, u_{HB}^{a,r}(r_{ij}) + \varepsilon_{HB}\, c_{HB,c} \sum_{I} S_{HB,c,I} \quad (4)$$

$$V_{HB,\,inter,\,K} = \varepsilon_{HB} \sum_{J \in K} \sum_{\substack{peptide\ Q \\ Q \neq K}} \sum_{I \in Q} S_{HB,IJ}\, u_{HB}^{a,r}(r_{ij}) \quad (5)$$

$$V_{HB,K} = V_{HB,intra,K} + \left(\frac{V_{HB,inter,K}}{NMOLP}\right) \quad (6)$$

where, I and J represent the amino acids to which the *i*th and *j*th atoms belong, respectively. The distance between those atoms (in Å units) is stored in the term r_{ij}. The variables K and Q represent any two peptide molecules in the system. The constant HB strength is represented by the variable ε_{HB}.

results in anisotropic HB interactions. These interactions may occur between intramolecular amino acids or between intermolecular amino acids.

The term $S_{HB,IJ}$ accounts for the local density dependence of actual hydrogen bonds, and is defined as,

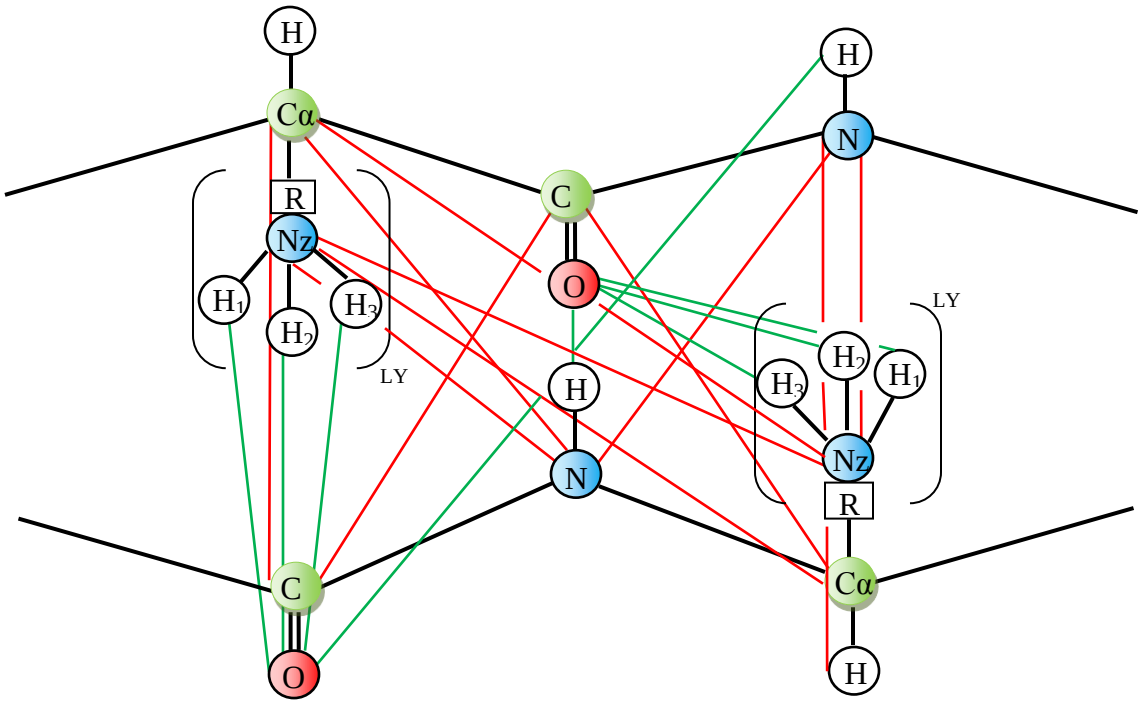
$$S_{HB,IJ} = \frac{S_{HB,I} + S_{HB,J}}{2} \quad (7)$$

$S_{HB,I}$ is a function of the term $\sum_K u_{HP}(r_{IK}), \eta_{HB,min}, \eta_{HB,max}$, where $\sum_K u_{HP}(r_{IK})$ monitors the local density on the I^{th} amino acid and r_{IK} is the distance between C^{α} of I^{th} and K^{th} residues. The functional form of $u_{HP}(r)$, which represents the distance dependent interaction (with pre-set parameters, η) as a smooth switching function, is

$$u_{HP} = \begin{cases} 1 & r < \sigma_{HP1} \\ \frac{1}{2}\left(1 + \cos\pi \frac{r - \sigma_{HP1}}{\sigma_{HP2} - \sigma_{HP1}}\right) & \sigma_{HP1} \leq r \leq \sigma_{HP2} \\ 0 & r > \sigma_{HP2} \end{cases}$$

The function S_{HB} is a smooth switching function and has the explicit form of,

$$S_{HB}(x, xmin, xmax) = \begin{cases} 1 & x > xmax \\ \frac{1}{2}\left(1 + cos\pi \frac{xmax - x}{xmax - xmin}\right) & xmin \leq x \leq xmax \\ 0 & x < xmin \end{cases} \quad (9)$$



Attractively interacting pairs

Repulsively interacting pairs

Rigidly bonded pairs

Figure 2.1 A schematic figure of the side-chain dependent HB interactions, between two selected lysine amino acid groups, as proposed in this model. The repulsive forces are half as strong as the attractive ones and the combination of attractive and repulsive forces

(8)

The terms $u_{\mathrm{HB}}^{a,r}(r_{ij})$ account for the distance dependent part of the potential, which based on the atom type of i, j may be either attractive or repulsive. (Refer to Figure 2.1 for details of attractive/repulsive interactions between atoms of two neighboring amino acid groups). The interaction has the form,

$$u_{\mathrm{HB}}^{a}(r_{ij}) = 60\left[\frac{1}{12}\left\{\frac{\sigma_{\mathrm{HB}}}{r_{ij}}\right\}^{12} - \frac{1}{10}\left\{\frac{\sigma_{\mathrm{HB}}}{r_{ij}}\right\}^{10}\right] \tag{10}$$

$$u_{HB^{r}}(\mathrm{r_{ij}}) = 30\left[\frac{1}{10}\left\{\frac{\sigma_{\mathrm{HB}}}{\mathrm{r_{ij}}}\right\}^{10}\right] \tag{11}$$

where, σ_{HB} represents the length scale for hydrogen bonding. The model for HP interaction potential for the K^{th} peptide is given by,

$$V_{HP,K} = \left[-\varepsilon_{HP^{\alpha}} \sum_{\mathrm{I,J}\,\epsilon\,\mathrm{K}} \mathrm{S_{HP,\,I}} \left(\sum_{\mathrm{J}\,\neq \mathrm{I}} u_{HP}(r_{ij}), \eta_{HP,\alpha} \right) \right] - \left[\sum_{\mathrm{L,M}\,\epsilon\,\mathrm{K}} \varepsilon_{HP,L^{\beta}}\, \mathrm{S_{HP,L}} \left(\sum_{\mathrm{M}\,\neq \mathrm{L}} u_{HP}(r_{LM}), \eta_{HP,\beta} \right) \right] \quad (12)$$

Where I and J represents α carbons, and L and M represents β carbons in peptide K. $\varepsilon_{HP}{}^{\alpha}$ and $\varepsilon_{HP,L}{}^{\beta}$ are, respectively, the HP energy parameters for α carbons and side chains. The function S_{HP} represents buriedness of the atom and is defined as,

$$\mathrm{S}_{HP}(\mathrm{x}, \mathrm{xmax}) = \begin{cases} 1 & \mathrm{x} > xmax \\ \cos\left(\frac{\pi}{2}\right) \frac{\mathrm{xmax} - \mathrm{x}}{\mathrm{xmax}} & \mathrm{x} \leq \mathrm{xmax} \end{cases} \quad (13)$$

The listing of the Fortran code that implements this implicit model is included in Appendix C. Appendix D includes detail instructions to run the code.

3. RESULTS

The explicit model was used to study the adsorption of multiple peptides and to study the effect of mixing on the their conformation. The explicit model extended to handle multiple peptides was used to simulate two peptides in a box. The purpose of this exercise was to benchmark the results obtained with the implicit model. Multiple peptides were "computationally shaken" by switching the polarity of the simulation box. For the sake of clarity the results of all the simulations done with the explicit model are presented in Appendix E.

To code the proposed implicit model in FORTRAN, the existing MC code for simulating a single-peptide-surface system in vacuum was modified. In the new code up to fifty identical peptide could be simulated in the user defined simulation box with/without charged surfaces. After extending the existing explicit model interaction subroutines for peptide-surface and intra-peptide interactions (of torsional and vdW forces) to handle multiple peptide system, a subroutine to estimate inter-peptide vdW interactions was coded. Then to calculate the implicit solvent interactions (of HB/HP forces) four different subroutines were coded for each of the following:

1. UHP_est(): This is used to calculate the distance dependent interaction term u_{HP} that monitors the local density of each amino acid sites of all the peptide molecules available in the simulation box. The two types of u_{HP} terms, one defined in terms of Cα-Cα and the other in terms of Cβ-Cβ distances between all pairs of amino acid residues, are determined by this subroutine. For this the Cα and Cβ atomic positions of the selected peptide molecular model should be provided in the input peptide configuration file (A5-L5.cod for our model).
2. HPenrg(): It is used to estimate the HP interaction energy of the selected peptide molecule.
3. HBenrg_intra(): It calculates the intramolecular HB interaction energy for the selected peptide molecule.
4. HBenrg_inter(): This subroutine determines the intermolecular HB interaction energy for a given peptide.

At first, a two-peptide(helix)-surface system was simulated using the newly coded implicit model program. This allows benchmarking the proposed implicit model using the results obtained from the existing explicit model simulation of the same system. The energy profile, end-to-end distance profile and COM z-location profile for this system were plotted vs. the number of Monte Carlo steps (NMCS) (refer to Figures 3.1, 3.2 and 3.3 respectively).

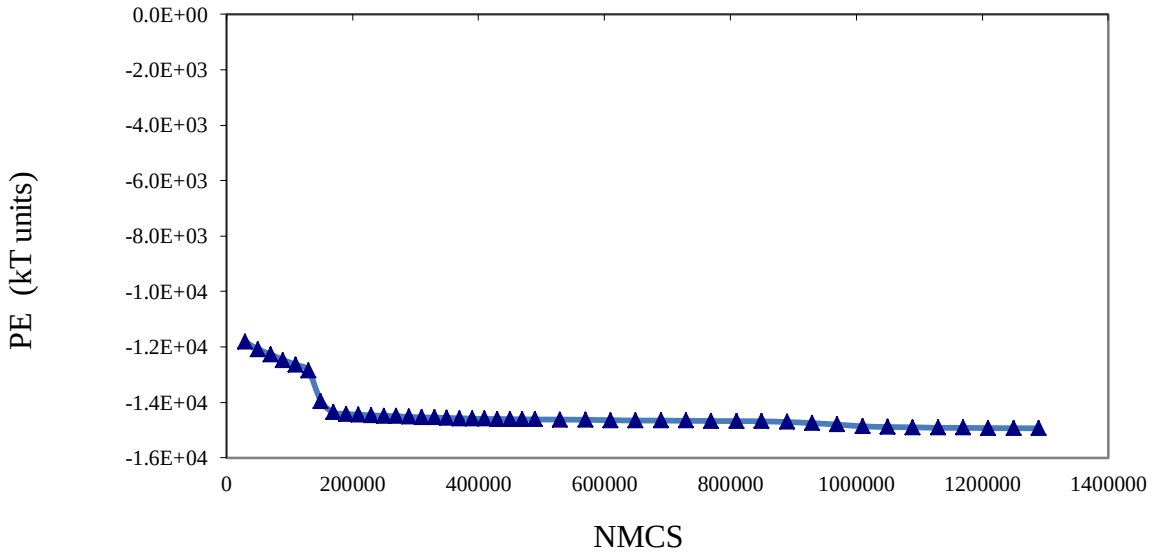


Figure 3.1 Total energy vs. NMCS for 2-peptide(helix)-surface system simulated using the implicit model.

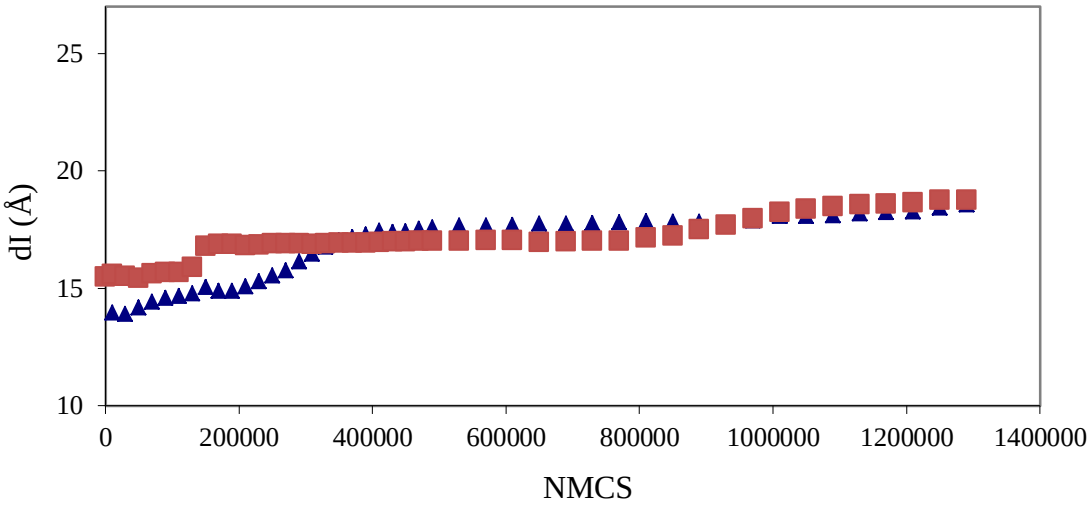


Figure 3.2 Peptide ETED profile for 2-peptide(helix)-surface system simulated using the implicit model.

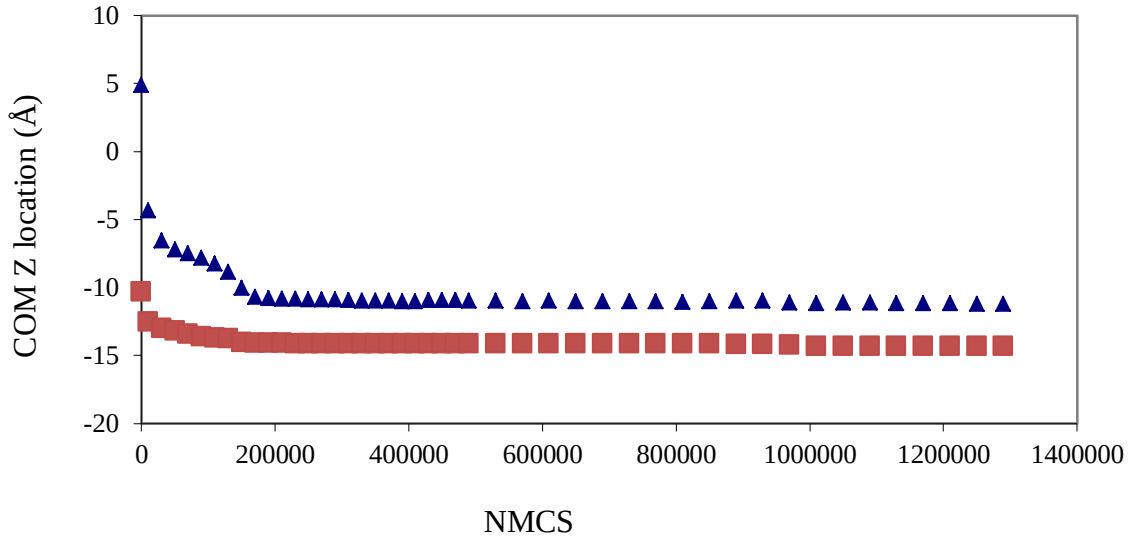
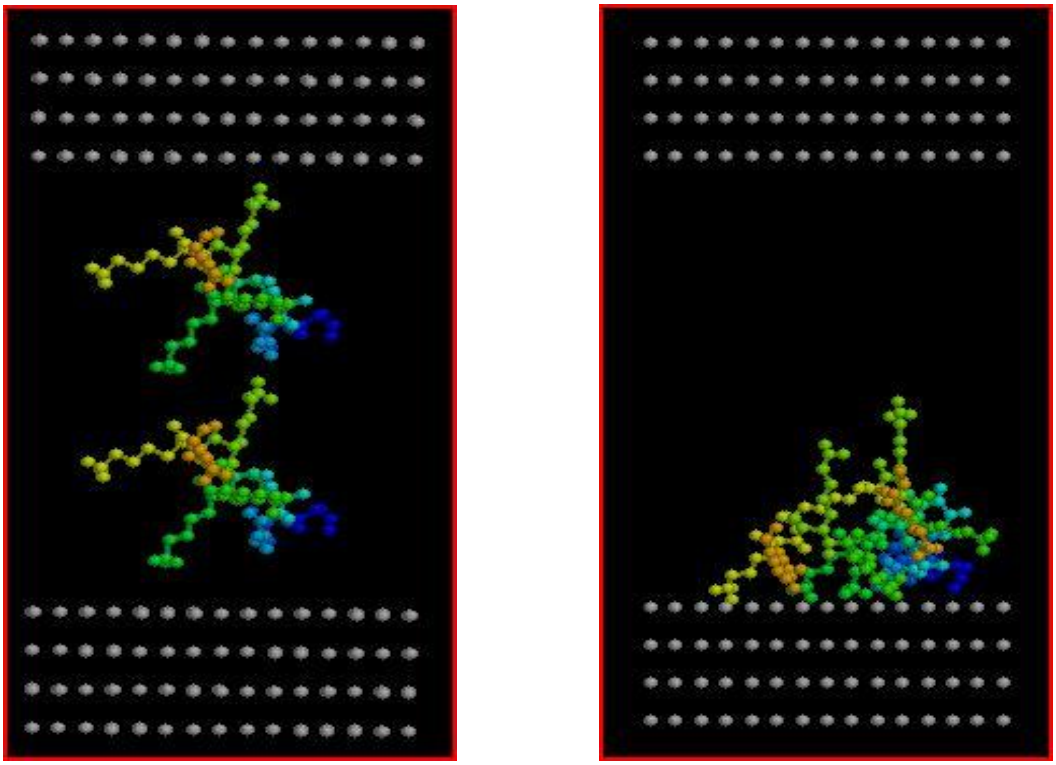


Figure 3.3 COM z-location profile for 2-peptide(helix)-surface system simulated using the implicit model.

Figure 3.4 shows snapshots of the initial and final system configurations. The two peptides move towards the surface and were adsorbed flat on the surface increasing the electrostatic contacts between the oppositely charged residues (LYS) and the surface. The

peptides orient parallel to each other, similar to what was observed in the explicit model run (refer to Appendix E).

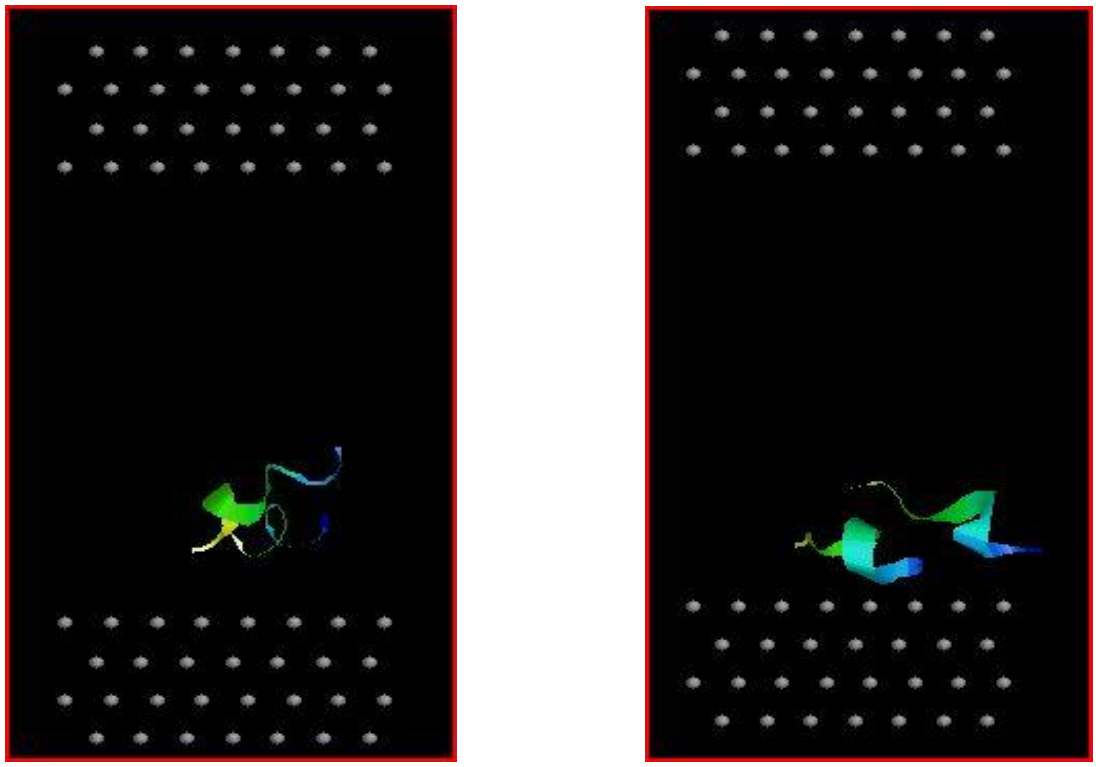


(a) (b)

Figure 3.4 Snapshots of initial (a) and final (b) configurations of 2-peptide(helix)-surface system simulated using the implicit model.

The end-to-end distance profiles suggest some re-structuring of the peptide molecules, with both peptides partially losing their secondary helical structure. This change in the secondary structure could be also viewed in the snapshots shown in Figure 3.5. Unlike the explicit model, the peptides in the implicit model follow matching end-to-end distances after reaching equilibrium. The COM z-location profiles and the snapshots indicate that the two peptides lie closer and parallel on the surface than in the explicit model. This could be due to two reasons. First, the water molecules trapped between the surface and the peptides, in the explicit model, affect the interaction between the surface

and the peptide .[19] The second possible reason is the larger peptide structural re-arrangement observed in the implicit model; this is evident from longer end-to-end distances for both peptides (18.56 Å and 18.75 Å) compared to those for the explicit model (15 Å and 17.04 Å).



(a) (b)

Figure 3.5 “Ribbon” graphic snapshots of final configurations of 2-peptide(helix)-surface system simulated using the explicit (a) and the implicit models (b).

In the second simulation a 10-peptide (5ALA-5LYS) system in bulk and in between two charged surfaces was used. The selected simulation box dimensions (27.748 X 48.061 X 85 Å) were unchanged for both model systems, thus they differ only in the presence of charged surfaces. After placing the peptides in the box, their initial position in the box was randomized by “computational shaking”. Every 20,000 MC steps the polarity of the surfaces was switched generating a random configuration after 0.1 million MC steps. Refer to Figure 3.6 for a snapshot of the final distribution of the peptides after

initial shaking. This configuration was then used as the initial configuration for simulating the 10-peptide system with and without surfaces.

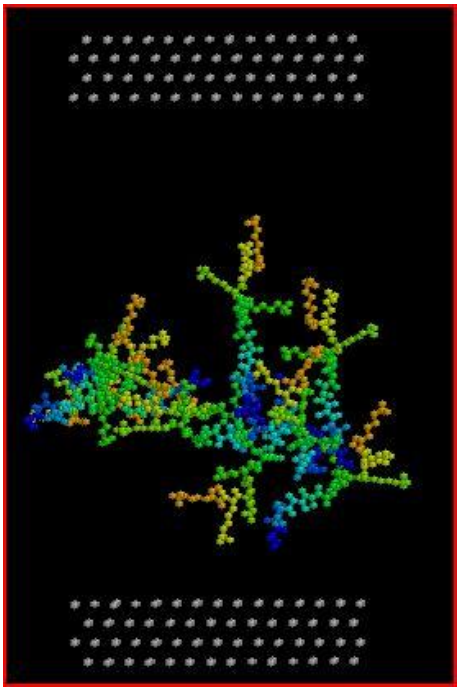


Figure 3.6 Initial configuration obtained by computational "shaking" for 10-peptide(random coil) simulations.

For the 10-peptide system without surfaces, the energy of the box is minimized after completing 0.4 million MC steps. The simulation was continued to complete a total of 0.722 million steps, while the system energy remained at the minimum value corresponding to the equilibrium configuration. Figure 3.7 shows the energy profile curve, and Figures 3.8 and 3.9 show the end-to-end distance profiles and COM z-location profiles for all the 10 peptide molecules inside the simulation box. Figures 3.10 and 3.11 are snapshots of the simulation box after equilibration. After equilibrium, the peptides orient in clusters with their hydrophobic ends forming the inner core. The COM z-location profile also indicates this clustering effect with respect to the z-axis.

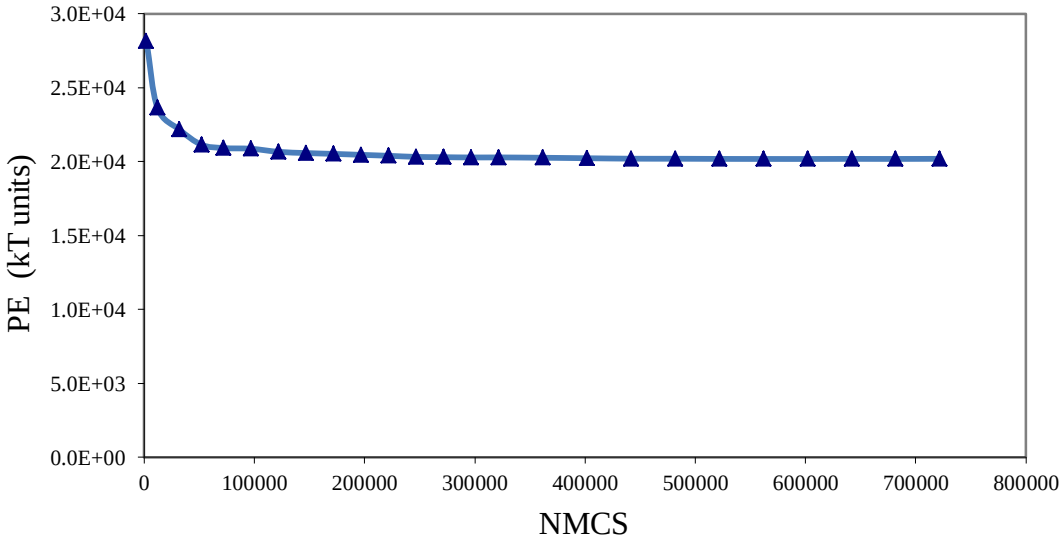


Figure 3.7 Energy profile for 10-peptide(random coil) system simulated using the implicit model.

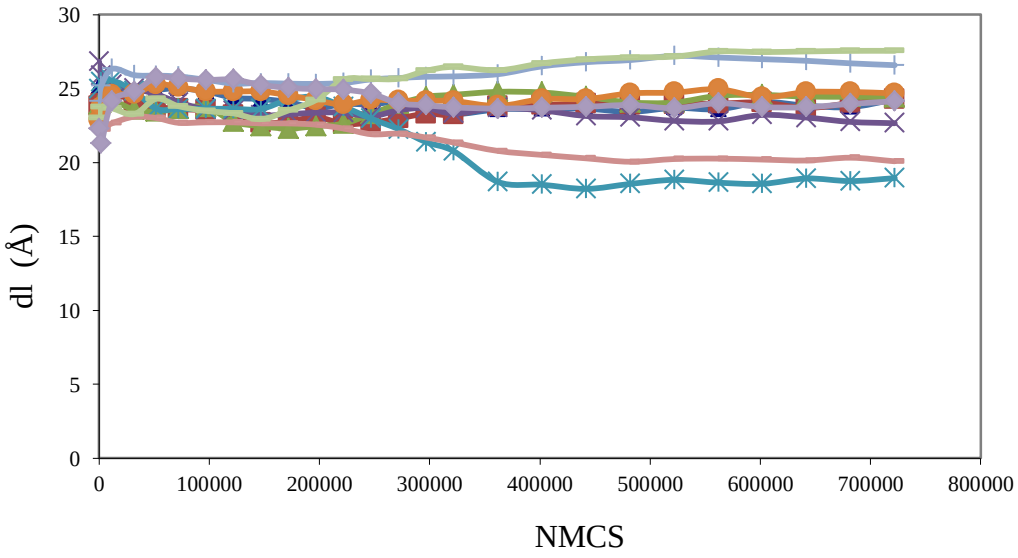


Figure 3.8 Peptide ETED profile for 10-peptide(random coil) system simulated using the implicit model.

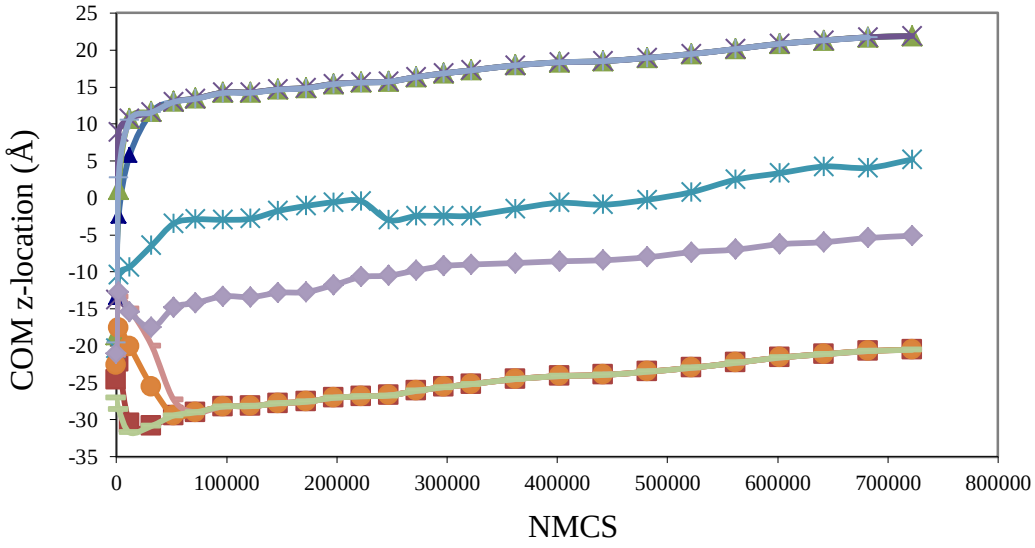


Figure 3.9 COM z-location profile for 10-peptide(random coil) system simulated using the implicit model.

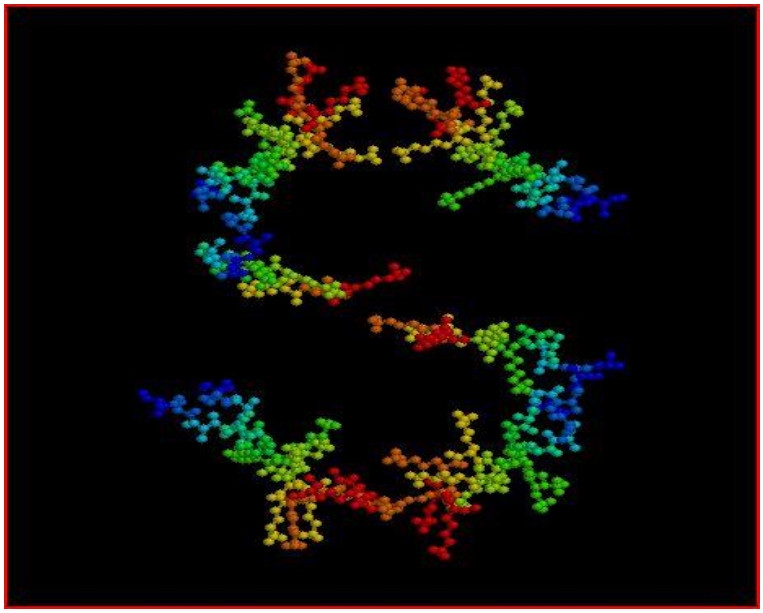


Figure 3.10 “Ball & Stick” snapshot of the final configuration for 10-peptide(random coil) system simulated using the implicit model.

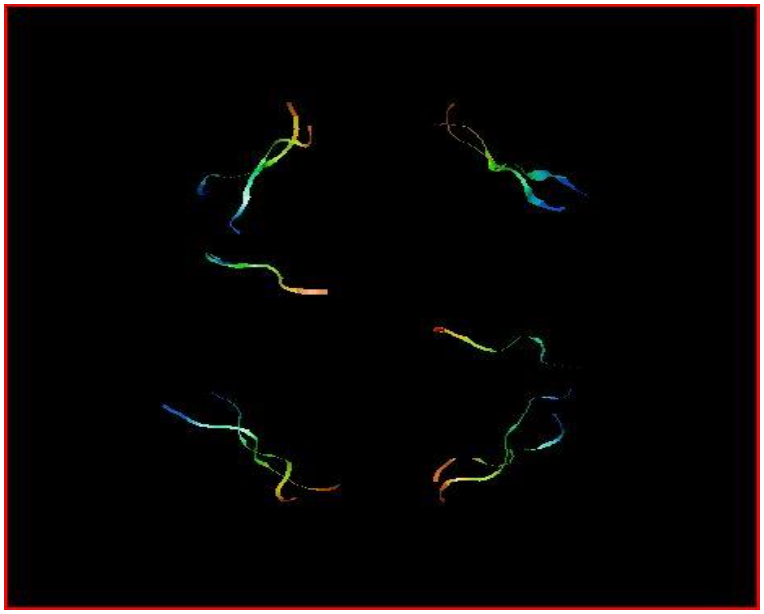


Figure 3.11 “Ribbon” snapshot of the final configuration for 10-peptide(random coil) system simulated using the implicit model.

The system energy, end-to-end distance of all peptides, and the COM z-location of all peptides vs. the number of Monte Carlo stepes for the 10-peptide-surface system, simulated using the implicit model and in the presence of charge surfaces are shown in Figures 3.12, 3.13 and 3.14, respectively. The energy reaches its minimum value after 0.7 million MC steps. All peptides moved towards the negatively charged surface, and each of them oriented perpendicular to the surface. The positively charged LYS ends of the peptides are in contact with the surface thereby maximizing electrostatic interactions. The hydrophobic ends, extending out from the surface, clustered together and sink-in closer to the surface. This effect is further evident from the negative slope of the end-to-end distance profile (Figure 3.13) for the peptides. Figure 3.15 is a snapshot of the simulation box during the production run. A close-up view of the snapshot near the negatively charged surface is displayed in Figure 3.16. For the implicit model simulations of 2-peptide and 10-peptide systems with charged surfaces, the change in peptide end-to-end distances depends on their orientation with respect to the surface. The ETED decreased for peptides oriented normal to the surface and it increased for peptides parallel to the surface.

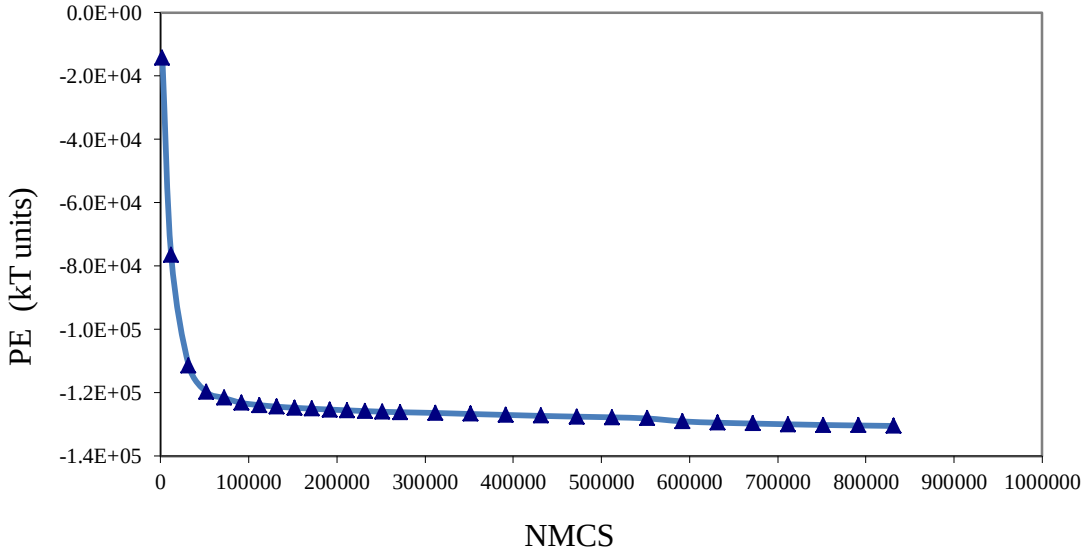


Figure 3.12 Energy profile for 10-peptide(random coil)-surface system simulated using the implicit model.

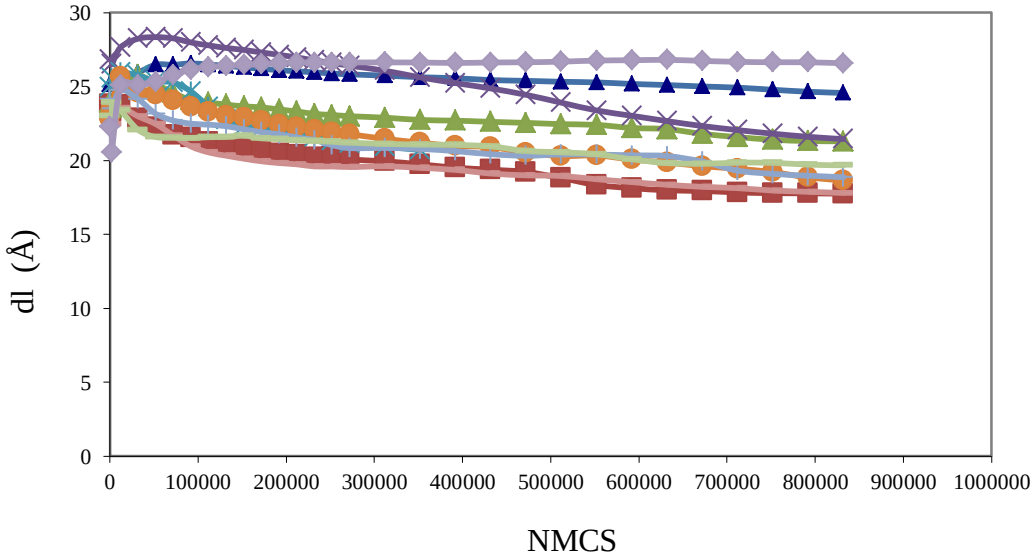


Figure 3.13 Peptide ETED profile for 10-peptide(random coil)-surface system simulated using the implicit model.

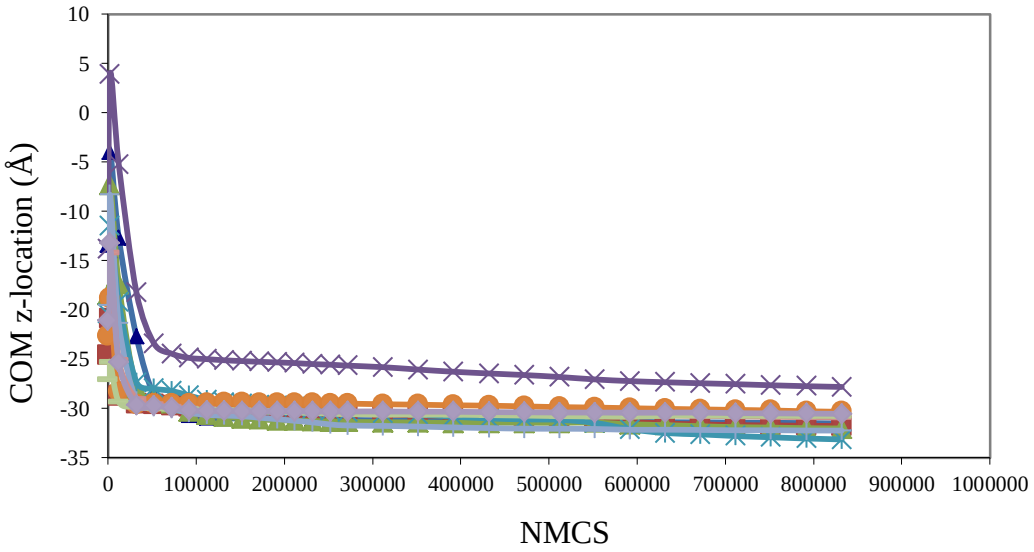


Figure 3.14 COM z-location profile for 10-peptide(random coil)-surface system simulated using the implicit model.

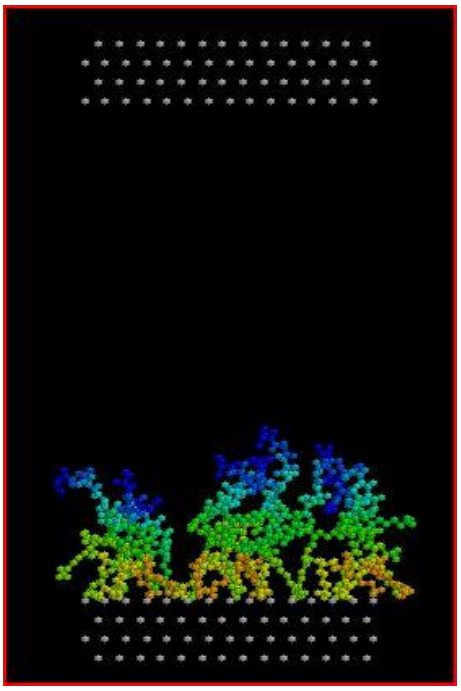


Figure 3.15 Snapshot for 10-peptide(random coil)-surface system simulated using the implicit model.

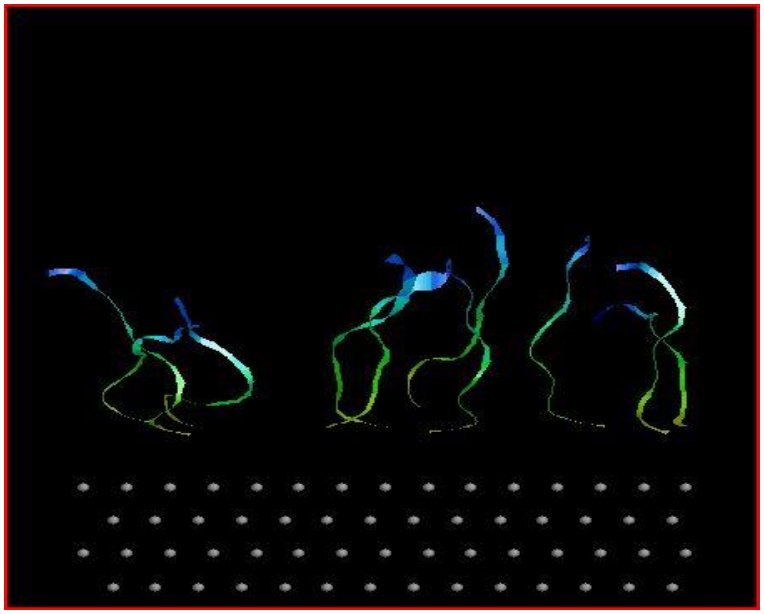


Figure 3.16 A close-up view near the negatively charged surface of the final configuration of 10-peptide(random coil)-surface system using the implicit model.

The implicit model was successfully used to simulate a multi-peptide system in a reasonable computational time. The results for 10-peptide (random coil) systems shows peptide restructuring at the surface and clustering of hydrophobic ends, which may be seen as a hydrophobic collapse effect. These effects are consistent with current knowledge of protein behavior near solid/liquid interfaces [8]. However, the local density dependent HB model did not seem to induce any secondary structure formation in random coil peptide structures. This may be due to the shortness of the model peptides (only 10 residues) used in our simulation. Short peptides are not expected to easily fold into secondary structures [22].

The 2-peptide (helix) simulation in implicit model showed structural changes similar to those observed with the explicit system. However there is a considerable mismatch in the ETED profiles. This could be due to the lack of tuning of HB model parameters and the short peptide size selected for the system model. Although the implicit model may not be able to capture all the solvent effects (like dehydration effect around the peptide and at the surface interface), it could qualitatively capture (with proper tuning) conformational changes which may induce the formation of aggregates.

APPENDIX A

EXPLICIT MODEL SIMULATION PROGRAM CODE

```
C**EXPLICIT SOLVENT MODEL FOR 2-PEP-WATER-SURFACE SYSTEM.  EXISTING CODE BY AMOL IS
JUST REPLICATED TO ACCOUNT FOR THE ADDITIONAL PEPTIDE MOLECULE. CORRECTION MADE
FOR THE INITIAL SYSTEM ENERGY (V) CALCULATION. LIMITS ARE: NATOM=200, RESNUM=20,
NMOLW=2000, NSURF=600, NMCS=50000. PEPTIDES ARE ARRANGED ALONG THE Z-AXIS. THE
SURFINP FILE STAYS THE SAME AND A5-L5 FILE IS MODIFIED TO INCLUDE. Z-COORDINATES FOR
BOTH PEPTIDES. MAKE CHANGES IN VARIABLE INITIALIZATION FOR PRODUCTION RUN**
      program  main
      implicit NONE
      external INCONFIG,NRGTOT,RNDMOVE
      external SUMBINW,RANDOM
      external PDBOUT,DISTPP,NRGPP
      external DISTW,NRGW
      external DISTWMSURF
      external DISTWMPEP,DISTPEPSF
      external NRGWMPEP,NRGPEPSF
      external MOVEPEP,pepenrg
      external SUMBINPEP,TORSION
*************************************************************************
      integer ACCMOVEW,ACCMOVEWACC,ACCMOVEWTMP,C,I,ISEED,J,M,K,N
      integer NADJUST,NBIN,NMCS,NMCSACC,NMCSOLD
      integer NMCSTMP,NMOLW,NPTS,NSAVE,RUNSTAT,STEP
      integer GSUM(600,3),NMOL,NSURF
      integer ZWSUM(2000,2),NBINZ
      integer NATOM,NHB,HB(100),NEND,CEND
      integer ATOM(200),AA(200),GROUP(200)
      integer ACCTOR,ACCPEP
      integer ZPEP1SUM(2000,3),ZPEP2SUM(2000,3)
      integer NEIBOURWSUM1(100),NEIBOURWSUM2(100)
      integer GRPWSUM1(600,2,100),GRPWSUM2(600,2,100)
      integer RESNUM
      double precision ACCPEPACC,ACCPEPTMP,AVGACCPEP
      double precision AVGACCTOR,ACCTORACC,ACCTORTMP
      double precision DELZ,UPPOLD,UPPNEW
      double precision GOFZW(2000,2),AW(200)
      double precision VOLUMEZ,TMP2
      double precision AVGNRG,AVGVW
      double precision DELR,DELV,DENS,ESUM,ESUMACC,ESUMACCTMP,LOHW
      double precision LMIN,MAXROTW,MAXTRNW,PI
      double precision LX,LY,LZ
      double precision QFACT,RANDOM,RMIN,RMAX,RXMAX,RXMAX2,TEMP
      double precision THHOH,AVGACCW
      double precision V,VERR
```

```
double precision VERRSUM
double precision VWNEW,VWOLD,VOLUME,VWATER,VWERR
double precision VWERRSUM,VWINI,VWSUM,VWSUMACC,VWSUMACCTMP
double precision QSURF,RSURF(600,3)
double precision AIIW(3),A12W(3,3),CIIW(3),C6W(3,3)
double precision AII(2),CII(2),Q(2)
double precision A12WS(3,2),C6WS(3,2),QCONWS(3,2)
double precision D2WNEW(3,2000,3),D2WOLD(3,2000,3)
double precision GOFR(600,3)
double precision QW(3),QCONW(3,3)
double precision RW(2000,3,3),RWMNEW(3,3),RWMOLD(3,3)
double precision VTOT(0:50001),VTOTPT(100),VW(0:50001)
double precision VWPT(100)
double precision VWMSURFNEW,VWMSURFOLD
double precision D2WSURF1OLD(3,600),D2WSURF1NEW(3,600)
double precision D2WSURF2OLD(3,600),D2WSURF2NEW(3,600)
double precision PEPCORD1(200,3),PEPCORD2(200,3)
double precision QPEP(200),APEP(200),A12PP(200,200),CPEP(200)
double precision phi1(20),psi1(20),phi2(20),psi2(20)
double precision COM1(3),COM2(3),C6PP(200,200)
double precision v1,v2,v3,v4,v5,v6,QCONPP(200,200)
double precision A12WP(200,3),C6WP(200,3),QCONWP(200,3)
double precision A12PS(200,2),C6PS(200,2),QCONPS(200,2)
double precision D2WPEP1OLD(200,2000,3),D2WPEP2OLD(200,2000,3)
double precision D2WPEP1NEW(200,2000,3),D2WPEP2NEW(200,2000,3)
double precision UWMPEP(2000,2)
double precision UPEP1SFNEW,UPEP2SFNEW,UPEP1SFOLD,UPEP2SFOLD
double precision D2WMPEP1NEW(200,3),D2WMPEP1OLD(200,3)
double precision D2WMPEP2NEW(200,3),D2WMPEP2OLD(200,3)
double precision UPEP1WM,UPEP2WM,COM1OLD(3),COM2OLD(3)
double precision UPEP1WNEW,UPEP1WOLD,UPEP2WNEW,UPEP2WOLD
double precision UWMPEPOLD(2000,2)
double precision PEPCORD1OLD(200,3),PEPCORD2OLD(200,3)
double precision phi1old(20),psi1old(20),phi2old(20),psi2old(20)
double precision MXTPEP,MXRPEP,maxpsi,maxphi
double precision D2PEP1SF1NEW(200,600),D2PEP1SF2NEW(200,600)
double precision D2PEP2SF1NEW(200,600),D2PEP2SF2NEW(200,600)
double precision D2PPOLD(200,200),D2PPNEW(200,200)
double precision NEWP1ENRG,OLDP1ENRG,NEWP2ENRG,OLDP2ENRG
double precision RWM(3,3)
double precision UPEP1WMOLD,UPEP1WMNEW,UPEP2WMOLD,UPEP2WMNEW
double precision VPEP,PE1,PE2
```

```
      double precision NEIBOURW1(100),NEIBOURW2(100)
      double precision GOFRWP1(600,2,100),GOFRWP2(600,2,100)
      double precision COSAVG1,COSSQAVG1,COSAVG2,COSSQAVG2
      double precision ZPEP1(2000,3),ZPEP2(2000,3)
      double precision COSSQSUM1,COSSUM1,COSSQSUM2,COSSUM2
      double precision ETED1(50000),ETED2(50000),ETEDP1(100),ETEDP2(100)
      double precision ETED1T,ETED2T,ETED1AVG,ETED2AVG
      double precision CMP1T,CMP2T,CMP1AVG,CMP2AVG
      double precision CM1(50000),CMP1(100),CM2(50000),CMP2(100)
      double precision VSUS(50000),VSOP(50000)
      double precision VPS(50000)
      double precision VSUSPT(100)
      double precision VPSPT(100),VSOPPT(100)
      double precision VSUSS,VSOPS
      double precision VPSS,VSURSOLI,VRESTI
      double precision VSURSOL,VREST,UPEPWI
      character CFGINP*15,CFGOUT*15,OUTPUT*15
      character TITLE*50,PDB*15
      character SURFINP*15,SURFNAME*15
      character PEP*15
      parameter (PI=3.14159265d+0)
C *****************************************************
C ** INPUT DATA.                          **
C *****************************************************
      open(unit=5,file='input1.inp',status='unknown',
     & form='formatted')
      rewind(5)
      read(5,*)
      read(5,*)
      read(5,*) TITLE
      read(5,100) RUNSTAT
      read(5,*) CFGINP
      read(5,*) CFGOUT
      read(5,*) OUTPUT
      read(5,*) PDB
      read(5,110) NMOLW
      if(NMOLW.GT.2000) STOP 'Matrix size too small'
      read(5,120) NMCS
      if(NMCS.GT.50000) STOP 'Matrix size too small'
      read(5,140) TEMP
      read(5,*) NSAVE
      read(5,*) NADJUST
```

```
      read(5,*) SURFINP
      read(5,*) QSURF
      read(5,*) PEP
      read(5,*) VPEP
      read(5,*) RESNUM
100   format(i1)
110   format(i4)
120   format(i6)
140   format(f6.2)
      open(unit=88,file='phipsi1',status='unknown')
      open(unit=89,file='phipsi2',status='unknown')
      open(unit=7,file=SURFINP,status='unknown',form='formatted')
      read(7,*) NSURF
      if(NSURF.GT.600) STOP 'Matrix size too small'
      do 105 N=1,NSURF
        read(7,222) (RSURF(N,I),I=1,3)
105   continue
222   format(f17.13,2x,f17.13,2x,f17.13)
      read(7,*) SURFNAME
      read(7,*) LX
      read(7,*) LY
      open(unit=9,file=OUTPUT,status='unknown',form='formatted')
C *****************************************************
C ** BOX DIMENSIONS & CONSTANTS FOR PCFs.        **
C *****************************************************
      LZ=38.00D+0
      NMOL=NMOLW
      DENS=NMOL/(LX*LY*LZ - VPEP)
      write(*,*)LZ,NMOL,NMOLW,DENS
      NPTS=1
      if(NMCS.gt.100) then
        NPTS=NMCS/100
      end if
      MAXTRNW=0.20
      MAXROTW=0.30
      MXTPEP=0.005
      MXRPEP=0.008
      maxpsi=0.002
      maxphi=0.004
      QFACT=1.671d+5/TEMP
      NMCSTMP=0
      ACCMOVEWTMP=0
```

```
      ESUMACCTMP=0.d+0
      VWSUMACCTMP=0.d+0
      NMCSACC=0
      ACCMOVEWACC=0
      ESUMACC=0.d+0
      VWSUMACC=0.d+0
      ESUM=0.d+0
      VWSUM=0.d+0
      UPEPWI=0.0D+0
      LMIN=LX
      if(LY.LT.LMIN) then
        LMIN=LY
      end if
      if(LZ.LT.LMIN) then
        LMIN=LZ
      end if
      RXMAX=LMIN/2.0d+0
      RXMAX2=RXMAX*RXMAX
      DELR=0.05d+0
      DELZ=DELR
      NBIN=idint(RXMAX/DELR-0.5d+0)
      NBINZ=idint(LZ/DELZ)
      ACCMOVEW=0
      ACCPEP=0
      ACCTOR=0
      open(unit=2,file=CFGOUT,status='unknown',form='formatted')
C ***************************************************
C ** WATER MODEL PARAMETERS.                  **
C ** current model = SPC.                    **
C ***************************************************
      LOHW=1.0d+0
      THHOH=109.47d+0*PI/180.0d+0
      AIIW(1)=5.110d+0
      CIIW(1)=8.248d+0
      AIIW(2)=0.d+0
      CIIW(2)=0.d+0
      AIIW(3)=AIIW(2)
      CIIW(3)=CIIW(2)
      QW(1)=-0.82d+0
      QW(2)=+0.41d+0
      QW(3)=QW(2)
```

```
*********************************************
** Surface Parameters ***********************
*********************************************
     AII(1)=6.344d+0
     CII(1)=10.152d+0
     AII(2)=AII(1)
     CII(2)=CII(1)
     Q(1)=QSURF
     Q(2)=-QSURF
*********************************************
     do 1100 I=1,3
       do 1110 J=1,3
         A12W(I,J)=(AIIW(I)*AIIW(J))**6/TEMP
         C6W(I,J)=(CIIW(I)*CIIW(J))**3/TEMP
         QCONW(I,J)=QFACT*QW(I)*QW(J)
1110     continue
1100  continue

     do 1581 I=1,3
       do 1481 J=1,2
         A12WS(I,J)=(AIIW(I)*AII(J))**6/TEMP
         C6WS(I,J)=(CIIW(I)*CII(J))**3/TEMP
         QCONWS(I,J)=QFACT*QW(I)*Q(J)
1481     continue
1581  continue

C *****************************************************************
C ** INITIAL CONFIGURATION AND ENERGY.                        **
C ** RUNSTAT=0...cold start, call INCONFIG.                  **
C ** RUNSTAT=1...warm start, before equilibrium, read in coords.**
C ** RUNSTAT=2...1st data collecting run                     **
C ** RUNSTAT=3...collecting data (after 1st collecting run)    **
C *****************************************************************
     if(RUNSTAT.eq.0)then
       call INCONFIG(NMOL,NMOLW,LX,LY,LZ,LOHW,
    &         THHOH,RW,NATOM,PEPCORD1,PEPCORD2,APEP,
    &  CPEP,QPEP,AW,AA,ATOM,GROUP,NHB,HB,NEND,CEND,phi1,phi2,psi1,
    &  psi2,v1,v2,v3,v4,v5,v6,PEP,RESNUM)
       do 1032 I=1,3
         COM1(I)=0.d+0
         COM2(I)=0.d+0
1032     continue
```

```
      do 1006 K=1,NBIN
        do 1016 I=1,3
          GSUM(K,I)=0
1016      continue
        do 1026 I=1,2
          do 1014 N=1,NHB
            GRPWSUM1(K,I,N)=0
            GRPWSUM2(K,I,N)=0
            NEIBOURWSUM1(N)=0
            NEIBOURWSUM2(N)=0
1014        continue
1026      continue
1006    continue

      do 8027 N=1,NBINZ
       do I=1,2
        ZWSUM(N,I)=0
       ENDDO
        do 3026 I=1,3
          ZPEP1SUM(N,I)=0
          ZPEP2SUM(N,I)=0
3026      continue
8027      continue
    else
      open(unit=1,file=CFGINP,status='unknown',form='formatted')
      read(1,*) NATOM
      do 35500 M=1,NATOM
        read(1,889) AA(M),ATOM(M),GROUP(M),PEPCORD1(M,1),
     &    PEPCORD1(M,2),PEPCORD1(M,3),PEPCORD2(M,1),PEPCORD2(M,2),
     &    PEPCORD2(M,3),APEP(M),CPEP(M),QPEP(M),AW(M)
35500   continue
889     format(5x,I3,1x,I3,1x,I4,1x,f8.3,f8.3,f8.3,f8.3,f8.3,f8.3,
     1       f8.3,f8.3,f8.3,f8.3)
      read(1,*) NHB
      do 35020 M=1,NHB
        read(1,*) HB(M)
35020   continue
      do 1208 I=1,3
       read(1,778)COM1(I),COM2(I)
1208    continue
      read(1,*) NEND
      read(1,*) CEND
```

```
      do 1200 M=1,NMOLW
        read(1,*)
      do 1210 I=1,3
        read(1,777) (RW(M,C,I),C=1,3)
1210    continue
1200    continue
      do I=1,RESNUM
      read(1,1523)phi1(I),phi2(I),psi1(I),psi2(I)
      enddo
      read(1,1524)v1,v2,v3,v4,v5,v6
1523   format(5x,f8.3,5x,f8.3,5x,f8.3,5x,f8.3)
1524   format(f8.3,f8.3,f8.3,f8.3,f8.3,f8.3)
      read(1,*) MAXTRNW
      read(1,*) MAXROTW
      read(1,*) MXTPEP
      read(1,*) MXRPEP
      read(1,*) maxpsi
      read(1,*) maxphi
      if(RUNSTAT.ne.3)then
        do 1005 K=1,NBIN
          do 1015 I=1,3
            GSUM(K,I)=0
1015        continue
          do 1027 I=1,2
            do 8028 N=1,NHB
              GRPWSUM1(K,I,N)=0
              GRPWSUM2(K,I,N)=0
              NEIBOURWSUM1(N)=0
              NEIBOURWSUM1(N)=0
8028          continue
1027        continue
1005      continue
        COSSUM1=0.d+0
        COSSQSUM1=0.d+0
        COSSUM2=0.d+0
        COSSQSUM2=0.d+0
        do 1001 K=1,NBINZ
          DO I=1,2
           ZWSUM(K,I)=0
          ENDDO
          do 1011 I=1,3
            ZPEP1SUM(K,I)=0
```

```
            ZPEP2SUM(K,I)=0
1011         continue
1001       continue
       else
         read(1,*) NMCSACC
         read(1,*) ACCMOVEWACC
         read(1,*) ESUMACC
         read(1,*) VWSUMACC
         read(1,*) ACCPEPACC
         read(1,*) ACCTORACC
         read(1,*)
         do 1003 K=1,NBIN
           read(1,333) (GSUM(K,I),I=1,3)
1003       continue
         read(1,*)
         do 1028 K=1,NBIN
             do 1029 N=1,NHB
               read(1,334) (GRPWSUM1(K,I,N),I=1,2)
1029           continue
1028       continue
         read(1,*)
         do 10266 K=1,NBIN
             do 1030 N=1,NHB
               read(1,334) (GRPWSUM2(K,I,N),I=1,2)
1030           continue
10266      continue
         read(1,*)
         do 1031 N=1,NHB
           read(1,*) NEIBOURWSUM1(N)
1031       continue
         read(1,*)
         do 1033 N=1,NHB
           read(1,*) NEIBOURWSUM2(N)
1033       continue
         read(1,*)
         do K=1,NBINZ
           read(1,338) (ZWSUM(K,I),I=1,2)
         enddo
         read(1,*)
         do 1004 K=1,NBINZ
           do 2478 I=1,3
             read(1,*) ZPEP1SUM(K,I)
```

```
2478          continue
1004        continue
          do 1007 K=1,NBINZ
            do 2480 I=1,3
              read(1,*) ZPEP2SUM(K,I)
2480          continue
1007        continue
          read(1,*)
          read(1,339) COSSUM1,COSSUM2
          read(1,339) COSSQSUM1,COSSQSUM2
        end if
        close(1)
      endif
333   format(i12,2x,i12,2x,i12,2x,i12,2x,i12,
     &      2x,i12,2x,i12,2x,i12,2x,i12,2x,i12)
334   format(i12,2x,i12,2x,i12)
338   format(i12,2x,i12,2x,i12)
339   format(f8.3,2x,f8.3)

C ***************************************************
C ** PEPTIDE-WATER MODEL PARAMETERS.            **
C ***************************************************

      do 30107 M=1,NATOM
        do 30108 I=1,3
          A12WP(M,I)=(APEP(M)*AIIW(I))**6/TEMP
          C6WP(M,I)=(CPEP(M)*CIIW(I))**3/TEMP
          QCONWP(M,I)=QFACT*QPEP(M)*QW(I)
30108     continue
30107 continue

      do 30172 M=1,NATOM
        do 30182 I=1,2
          A12PS(M,I)=(APEP(M)*AII(I))**6/TEMP
          C6PS(M,I)=(CPEP(M)*CII(I))**3/TEMP
          QCONPS(M,I)=QFACT*QPEP(M)*Q(I)
30182     continue
30172 continue

C ***************************************************
C ** PEPTIDE-PEPTIDE MODEL PARAMETERS.          **
C ***************************************************
```

```
      do 30173 M=1,NATOM
        do 30183 N=1,NATOM
          A12PP(M,N)=(APEP(M)*APEP(N))**6/TEMP
          C6PP(M,N)=(CPEP(M)*CPEP(N))**3/TEMP
          QCONPP(M,N)=QFACT*QPEP(M)*QPEP(N)
30183    continue
30173 continue

C**INITIAL ENERGY ESTIMATION*****************************
      call NRGTOT(V,NMOLW,LX,LY,LZ,RW,A12W,C6W,QCONW,
     & A12WS,C6WS,QCONWS,A12WP,C6WP,QCONWP,A12PS,C6PS,QCONPS,
     & A12PP,C6PP,QCONPP,NSURF,RSURF,NATOM,PEPCORD1,PEPCORD2,
     & D2WPEP1OLD,D2WPEP2OLD,COM1,COM2,UWMPEP,UPEP1SFOLD,UPEP2SFOLD,
     & VWINI,VSURSOLI,VRESTI,UPPOLD,UPEP1WOLD,UPEP2WOLD,D2PPOLD)

      call pepenrg(OLDP1ENRG,APEP,CPEP,QPEP,PEPCORD1,NATOM,
     1   phi1,psi1,v1,v2,v3,v4,v5,v6,RESNUM)
      call pepenrg(OLDP2ENRG,APEP,CPEP,QPEP,PEPCORD2,NATOM,
     1   phi2,psi2,v1,v2,v3,v4,v5,v6,RESNUM)
      write(*,*)'V,OLDP1ENRG,OLDP2ENRG'
      write(*,*)V,OLDP1ENRG,OLDP2ENRG
      VTOT(0)=V+OLDP1ENRG+OLDP2ENRG
      V=VTOT(0)
      VWATER=VWINI
      VSUSS=VSURSOLI
      do M=1,NMOLW
          UPEPWI=UPEPWI+UWMPEP(M,1)+UWMPEP(M,2)
      enddo
      VSOPS=UPEPWI
      VPSS=UPEP1SFOLD+UPEP2SFOLD
      VWINI=VWINI/dble(NMOLW)
      AVGACCW=0.5d+0
      AVGACCPEP=0.5d+0
      AVGACCTOR=0.5d+0
      call PDBOUT(RSURF,RW,PEPCORD1,PEPCORD2,'SYSTEM0.pdb',NATOM,NMOLW,
     & NSURF,AA,ATOM,GROUP)
C ************************************************************
C ** MC STEPS.                                  **
C ** each MC step consists of an attempted move for each and every molecule in the system.  Every NADJUST steps,
maximum movements are adjusted for an acceptance rate of 0.50.  Every NSAVE steps, configurations and results are
saved for recovery in case the job is killed.              **
```

```
C ************************************************************
      do 10000 STEP=1,NMCS
        if(mod(STEP,NADJUST).eq.0) then
          AVGACCW=dble(ACCMOVEW)/dble(NMOLW*(STEP-1))
          AVGACCPEP=dble(ACCPEP)/dble(2*(STEP-1))
          AVGACCTOR=dble(ACCTOR)/dble(2*(STEP-1))
          if (AVGACCW.gt.0.50) then
            MAXTRNW = MAXTRNW * 1.03d+0
            MAXROTW = MAXROTW * 1.03d+0
          else
            MAXTRNW = MAXTRNW / 1.03d+0
            MAXROTW = MAXROTW / 1.03d+0
          end if
          if (AVGACCPEP.gt.0.50) then
            MXTPEP = MXTPEP * 1.1d+0
            MXRPEP = MXRPEP * 1.1d+0
          else
            MXTPEP = MXTPEP / 1.1d+0
            MXRPEP = MXRPEP / 1.1d+0
          end if
          if (AVGACCTOR.gt.0.50) then
            maxpsi = maxpsi * 1.1d+0
            maxphi = maxphi * 1.1d+0
          else
            maxpsi = maxpsi / 1.1d+0
            maxphi = maxphi / 1.1d+0
          end if
          if(mod(STEP,NSAVE).eq.0) then
            NMCSTMP=STEP-1
            ACCMOVEWTMP=ACCMOVEW
            ESUMACCTMP=ESUM
            VWSUMACCTMP=VWSUM
            ACCPEPTMP=ACCPEP
            ACCTORTMP=ACCTOR
            if(RUNSTAT.GE.2) then
              NMCSTMP=NMCSACC+STEP-1
              ACCMOVEWTMP=ACCMOVEWACC+ACCMOVEW
              ESUMACCTMP=ESUMACC+ESUM
              VWSUMACCTMP=VWSUMACC+VWSUM
              ACCPEPTMP=ACCPEPACC+ACCPEP
              ACCTORTMP=ACCTORACC+ACCTOR
            end if
```

```
      open(unit=3,file='CFG.TMP',status='unknown',form=
     &     'formatted')
      rewind(3)
      do 34000 M=1,NATOM
       write(3,889)AA(M),ATOM(M),GROUP(M),PEPCORD1(M,1),
     &   PEPCORD1(M,2),PEPCORD1(M,3),PEPCORD2(M,1),PEPCORD2(M,2),
     &   PEPCORD2(M,3),APEP(M),CPEP(M),QPEP(M),AW(M)
34000   continue
      write(3,*) NHB
      do 35030 M=1,NHB
        write(3,*) HB(M)
35030   continue
      do 35031 I=1,3
        write(3,778)COM1(I),COM2(I)
35031   continue
      write(3,*) NEND
      write(3,*) CEND
      do 2105 M=1,NMOLW
        write(3,*)
        do 2115 I=1,3
          write(3,777) (RW(M,C,I),C=1,3)
2115      continue
2105    continue
      do I=1,RESNUM
      write(3,1522)phi1(I),phi2(I),psi1(I),psi2(I)
      enddo
      write(3,1525)v1,v2,v3,v4,v5,v6
1522    format(5x,f8.3,5x,f8.3,5x,f8.3,5x,f8.3)
1525    format(f8.3,f8.3,f8.3,f8.3,f8.3,f8.3)
      write(3,*) MAXTRNW
      write(3,*) MAXROTW
      write(3,*) MXTPEP
      write(3,*) MXRPEP
      write(3,*) maxpsi
      write(3,*) maxphi
      write(3,*) NMCSTMP
      write(3,*) ACCMOVEWTMP
      write(3,*) ESUMACCTMP
      write(3,*) VWSUMACCTMP
      write(3,*) ACCPEPTMP
      write(3,*) ACCTORTMP
      write(3,*) 'GSUM'
```

```
      do 1108 K=1,NBIN
        write(3,333) (GSUM(K,I),I=1,3)
1108    continue
      write(3,*) 'GRPSUM-Peptide 1'
      do 41000 K=1,NBIN
        do 41100 N=1,NHB
          write(3,334) (GRPWSUM1(K,I,N),I=1,2)
41100     continue
41000   continue
      write(3,*) 'GRPSUM-Peptide 2'
      do 41001 K=1,NBIN
        do 41101 N=1,NHB
          write(3,334) (GRPWSUM2(K,I,N),I=1,2)
41101     continue
41001   continue
      write(3,*) 'NEIBOURSUM-Peptide 1'
      do 41200 N=1,NHB
        write(3,*) NEIBOURWSUM1(N)
41200   continue
      write(3,*) 'NEIBOURSUM-Peptide 2'
      do 41201 N=1,NHB
        write(3,*) NEIBOURWSUM2(N)
41201   continue
      write(3,*) 'ZWSUM'
      do K=1,NBINZ
        write(3,338) (ZWSUM(K,I),I=1,2)
      enddo
      write(3,*) 'ZPEPSUM-Peptide 1'
      do 1107 K=1,NBINZ
        do 41800 I=1,3
          write(3,*) ZPEP1SUM(K,I)
41800     continue
1107    continue
      write(3,*) 'ZPEPSUM-Peptide 1'
      do 1109 K=1,NBINZ
        do 41802 I=1,3
          write(3,*) ZPEP2SUM(K,I)
41802     continue
1109    continue
      write(3,339) COSSUM1,COSSUM2
      write(3,339) COSSQSUM1,COSSQSUM2
      write(3,*) 'STEP= ',STEP
```

```
          close(3)
         end if
        end if
        UPEP1WOLD=0.0D+0
        UPEP2WOLD=0.0D+0
        do 50010 M=1,NMOLW
          UPEP1WOLD=UPEP1WOLD+UWMPEP(M,1)
          UPEP2WOLD=UPEP2WOLD+UWMPEP(M,2)
          UWMPEPOLD(M,1)=UWMPEP(M,1)
          UWMPEPOLD(M,2)=UWMPEP(M,2)
50010    continue
        do 50000 M=1,NATOM
          do 51000 I=1,3
            PEPCORD1OLD(M,I)=PEPCORD1(M,I)
            PEPCORD2OLD(M,I)=PEPCORD2(M,I)
51000       continue
50000    continue
       do I=1,RESNUM
       phi1old(i)=phi1(i)
       phi2old(i)=phi2(i)
       psi1old(i)=psi1(i)
       psi2old(i)=psi2(i)
       enddo
        do 54000 I=1,3
          COM1OLD(I)=COM1(I)
          COM2OLD(I)=COM2(I)
54000    continue
********************* peptide movement ************************
**peptide-1**

        call MOVEPEP(NATOM,PEPCORD1,COM1,MXTPEP,MXRPEP,
     &               LX,LY,LZ,ISEED)
        call DISTPEPSF(D2PEP1SF1NEW,D2PEP1SF2NEW,RSURF,NSURF,
     &                PEPCORD1,NATOM,LX,LY,COM1)
        call NRGPEPSF(A12PS,C6PS,QCONPS,UPEP1SFNEW,D2PEP1SF1NEW,
     &               D2PEP1SF2NEW,NSURF,NATOM)
        call DISTPP(D2PPNEW,PEPCORD1,PEPCORD2,NATOM,LX,LY,COM1,COM2)
        call NRGPP(D2PPNEW,A12PP,C6PP,QCONPP,UPPNEW,NATOM)
        call pepenrg(NEWP1ENRG,APEP,CPEP,QPEP,PEPCORD1,NATOM,
     &   phi1,psi1,v1,v2,v3,v4,v5,v6,RESNUM)

        UPEP1WNEW=0.0D+0
```

```
      do 51100 M=1,NMOLW
        do 51200 I=1,3
          do 51300 C=1,3
            RWM(C,I)=RW(M,C,I)
51300       continue
51200     continue
      call DISTWMPEP(D2WMPEP1NEW,PEPCORD1,NATOM,RWM,LX,LY,COM1)
      call NRGWMPEP(D2WMPEP1NEW,A12WP,C6WP,QCONWP,UPEP1WM,NATOM)
        do 51210 N=1,NATOM
          do 51220 I=1,3
            D2WPEP1NEW(N,M,I)=D2WMPEP1NEW(N,I)
51220       continue
51210     continue
        UWMPEP(M,1)=UPEP1WM
        UPEP1WNEW=UPEP1WNEW+UPEP1WM
51100   continue
      DELV=UPEP1WNEW+UPEP1SFNEW+NEWP1ENRG+UPPNEW
     &      -UPEP1WOLD-UPEP1SFOLD-OLDP1ENRG-UPPOLD

      if((DELV.ge.0.0d+0).and.(dexp(-DELV).lt.RANDOM(ISEED)))then
      do 52000 N=1,NATOM
        do 53000 I=1,3
          PEPCORD1(N,I)=PEPCORD1OLD(N,I)
          do 53100 M=1,NMOLW
            D2WPEP1NEW(N,M,I)=D2WPEP1OLD(N,M,I)
53100       continue
53000     continue
52000   continue
      do 54200 N=1,NMOLW
        UWMPEP(N,1)=UWMPEPOLD(N,1)
54200   continue
      do 54100 I=1,3
        COM1(I)=COM1OLD(I)
54100   continue
      call SUMBINPEP(PEPCORD1,LZ,NMOLW,NATOM,
     1    RXMAX2,DELR,DELZ,D2WPEP1NEW,COSSUM1,COSSQSUM1,
     1    ZPEP1SUM,NEND,CEND,GRPWSUM1,NEIBOURWSUM1,
     1    HB,NHB,COM1)
      else
      V=V+DELV
      VPSS=VPSS+UPEP1SFNEW-UPEP1SFOLD
      VSOPS=VSOPS+UPEP1WNEW-UPEP1WOLD
```

```
      ACCPEP=ACCPEP+1
      OLDP1ENRG=NEWP1ENRG
      do 54110 N=1,NATOM
       do 54120 I=1,NATOM
        D2PPOLD(I,N)=D2PPNEW(I,N)
54120     continue
54110   continue
      call SUMBINPEP(PEPCORD1,LZ,NMOLW,NATOM,
     1    RXMAX2,DELR,DELZ,D2WPEP1NEW,COSSUM1,COSSQSUM1,
     1    ZPEP1SUM,NEND,CEND,GRPWSUM1,NEIBOURWSUM1,
     1    HB,NHB,COM1)
      UPEP1SFOLD=UPEP1SFNEW
      UPPOLD=UPPNEW
     end if
**peptide-2**
      call MOVEPEP(NATOM,PEPCORD2,COM2,MXTPEP,MXRPEP,
     &             LX,LY,LZ,ISEED)
      call DISTPEPSF(D2PEP2SF1NEW,D2PEP2SF2NEW,RSURF,NSURF,
     &              PEPCORD2,NATOM,LX,LY,COM2)
      call NRGPEPSF(A12PS,C6PS,QCONPS,UPEP2SFNEW,D2PEP2SF1NEW,
     &             D2PEP2SF2NEW,NSURF,NATOM)
      call DISTPP(D2PPNEW,PEPCORD1,PEPCORD2,NATOM,LX,LY,COM1,COM2)
      call NRGPP(D2PPNEW,A12PP,C6PP,QCONPP,UPPNEW,NATOM)
      call pepenrg(NEWP2ENRG,APEP,CPEP,QPEP,PEPCORD2,NATOM,
     &  phi2,psi2,v1,v2,v3,v4,v5,v6,RESNUM)

      UPEP2WNEW=0.0D+0
      do 54111 M=1,NMOLW
       do 54114 I=1,3
        do 54112 C=1,3
         RWM(C,I)=RW(M,C,I)
54112     continue
54114    continue
      call DISTWMPEP(D2WMPEP2NEW,PEPCORD2,NATOM,RWM,LX,LY,COM2)
      call NRGWMPEP(D2WMPEP2NEW,A12WP,C6WP,QCONWP,UPEP2WM,NATOM)
       do 54130 N=1,NATOM
        do 54132 I=1,3
         D2WPEP2NEW(N,M,I)=D2WMPEP2NEW(N,I)
54132     continue
54130    continue
       UWMPEP(M,2)=UPEP2WM
       UPEP2WNEW=UPEP2WNEW+UPEP2WM
```

```
54111    continue
       DELV=UPEP2WNEW+UPEP2SFNEW+NEWP2ENRG+UPPNEW
     &       -UPEP2WOLD-UPEP2SFOLD-OLDP2ENRG-UPPOLD
       if((DELV.ge.0.0d+0).and.(dexp(-DELV).lt.RANDOM(ISEED)))then
        do 54140 N=1,NATOM
          do 54142 I=1,3
            PEPCORD2(N,I)=PEPCORD2OLD(N,I)
            do 54144 M=1,NMOLW
              D2WPEP2NEW(N,M,I)=D2WPEP2OLD(N,M,I)
54144         continue
54142       continue
54140    continue
        do 54150 N=1,NMOLW
          UWMPEP(N,2)=UWMPEPOLD(N,2)
54150    continue
        do 54152 I=1,3
          COM2(I)=COM2OLD(I)
54152    continue
        call SUMBINPEP(PEPCORD2,LZ,NMOLW,NATOM,
     1    RXMAX2,DELR,DELZ,D2WPEP2NEW,COSSUM2,COSSQSUM2,
     1    ZPEP2SUM,NEND,CEND,GRPWSUM2,NEIBOURWSUM2,
     1    HB,NHB,COM2)
       else
        V=V+DELV
        VPSS=VPSS+UPEP2SFNEW-UPEP2SFOLD
        VSOPS=VSOPS+UPEP2WNEW-UPEP2WOLD
        ACCPEP=ACCPEP+1
        OLDP2ENRG=NEWP2ENRG
        do 54154 N=1,NATOM
          do 54156 I=1,NATOM
            D2PPOLD(I,N)=D2PPNEW(I,N)
54156       continue
54154    continue
        call SUMBINPEP(PEPCORD2,LZ,NMOLW,NATOM,
     1    RXMAX2,DELR,DELZ,D2WPEP2NEW,COSSUM2,COSSQSUM2,
     1    ZPEP2SUM,NEND,CEND,GRPWSUM2,NEIBOURWSUM2,
     1    HB,NHB,COM2)
       UPEP2SFOLD=UPEP2SFNEW
       UPPOLD=UPPNEW
       end if

*****************TORSION MOVEMENT*******************************
```

```
      do I=1,3
        COM1OLD(I)=COM1(I)
        COM2OLD(I)=COM2(I)
      enddo
      do M=1,NATOM
        do I=1,3
         PEPCORD1OLD(M,I)=PEPCORD1(M,I)
         PEPCORD2OLD(M,I)=PEPCORD2(M,I)
        enddo
      enddo
      do N=1,NATOM
      do I=1,3
      do M=1,NMOLW
        D2WPEP1OLD(N,M,I)=D2WPEP1NEW(N,M,I)
        D2WPEP2OLD(N,M,I)=D2WPEP2NEW(N,M,I)
      enddo
      enddo
      enddo
      UPEP1WOLD=0.0D+0
      UPEP2WOLD=0.0D+0
      do 50017 M=1,NMOLW
        UPEP1WOLD=UPEP1WOLD+UWMPEP(M,1)
        UPEP2WOLD=UPEP2WOLD+UWMPEP(M,2)
        UWMPEPOLD(M,1)=UWMPEP(M,1)
        UWMPEPOLD(M,2)=UWMPEP(M,2)
50017   continue

**TORSIONAL MOVEMENT PEPTIDE-1**
      call TORSION(NATOM,PEPCORD1,maxpsi,maxphi,phi1,psi1,
     &    COM1,AW,RESNUM,ISEED)
      call DISTPEPSF(D2PEP1SF1NEW,D2PEP1SF2NEW,RSURF,NSURF,
     1              PEPCORD1,NATOM,LX,LY,COM1)
      call NRGPEPSF(A12PS,C6PS,QCONPS,UPEP1SFNEW,D2PEP1SF1NEW,
     1             D2PEP1SF2NEW,NSURF,NATOM)
      call DISTPP(D2PPNEW,PEPCORD1,PEPCORD2,NATOM,LX,LY,COM1,COM2)
      call NRGPP(D2PPNEW,A12PP,C6PP,QCONPP,UPPNEW,NATOM)
      call pepenrg(NEWP1ENRG,APEP,CPEP,QPEP,PEPCORD1,NATOM,
     1  phi1,psi1,v1,v2,v3,v4,v5,v6,RESNUM)

      UPEP1WNEW=0.0d+0
      do 51103 M=1,NMOLW
        do 51203 I=1,3
```

```
          do 51303 C=1,3
           RWM(C,I)=RW(M,C,I)
51303       continue
51203     continue
      call DISTWMPEP(D2WMPEP1NEW,PEPCORD1,NATOM,RWM,LX,LY,COM1)
      call NRGWMPEP(D2WMPEP1NEW,A12WP,C6WP,QCONWP,UPEP1WM,NATOM)
       do 51213 N=1,NATOM
          do 51223 I=1,3
           D2WPEP1NEW(N,M,I)=D2WMPEP1NEW(N,I)
51223       continue
51213     continue
        UWMPEP(M,1)=UPEP1WM
        UPEP1WNEW=UPEP1WNEW+UPEP1WM
51103   continue
      DELV=UPEP1WNEW+UPEP1SFNEW+NEWP1ENRG+UPPNEW
   &       -UPEP1WOLD-UPEP1SFOLD-OLDP1ENRG-UPPOLD
      if((DELV.ge.0.0d+0).and.(dexp(-DELV).lt.RANDOM(ISEED)))then
       do 52111 N=1,NATOM
        do 53111 I=1,3
          PEPCORD1(N,I)=PEPCORD1OLD(N,I)
          do 53112 M=1,NMOLW
           D2WPEP1NEW(N,M,I)=D2WPEP1OLD(N,M,I)
53112       continue
53111     continue
52111    continue
       do I=1,3
        COM1(I)=COM1OLD(I)
       enddo
       do i=1,RESNUM
       phi1(i)=phi1old(i)
       psi1(i)=psi1old(i)
       enddo
       do 54211 N=1,NMOLW
        UWMPEP(N,1)=UWMPEPOLD(N,1)
54211    continue
       call SUMBINPEP(PEPCORD1,LZ,NMOLW,NATOM,RXMAX2,
   1    DELR,DELZ,D2WPEP1NEW,COSSUM1,COSSQSUM1,
   1    ZPEP1SUM,NEND,CEND,GRPWSUM1,NEIBOURWSUM1,
   1    HB,NHB,COM1)
      else
       do i=1,RESNUM
       write(88,*)phi1(i),psi1(i)
```

```
        enddo
        V=V+DELV
        VPSS=VPSS+UPEP1SFNEW-UPEP1SFOLD
        VSOPS=VSOPS+UPEP1WNEW-UPEP1WOLD
        ACCTOR=ACCTOR+1
        call SUMBINPEP(PEPCORD1,LZ,NMOLW,NATOM,RXMAX2,
     1    DELR,DELZ,D2WPEP1NEW,COSSUM1,COSSQSUM1,
     1    ZPEP1SUM,NEND,CEND,GRPWSUM1,NEIBOURWSUM1,
     1    HB,NHB,COM1)
        UPEP1SFOLD=UPEP1SFNEW
        UPPOLD=UPPNEW
                        OLDP1ENRG=NEWP1ENRG
       end if
**TORSIONAL MOVEMENT PEPTIDE-2**
       call TORSION(NATOM,PEPCORD2,maxpsi,maxphi,phi2,psi2,
     &    COM2,AW,RESNUM,ISEED)
       call DISTPEPSF(D2PEP2SF1NEW,D2PEP2SF2NEW,RSURF,NSURF,
     1              PEPCORD2,NATOM,LX,LY,COM2)
       call NRGPEPSF(A12PS,C6PS,QCONPS,UPEP2SFNEW,D2PEP2SF1NEW,
     1             D2PEP2SF2NEW,NSURF,NATOM)
       call DISTPP(D2PPNEW,PEPCORD1,PEPCORD2,NATOM,LX,LY,COM1,COM2)
       call NRGPP(D2PPNEW,A12PP,C6PP,QCONPP,UPPNEW,NATOM)
       call pepenrg(NEWP2ENRG,APEP,CPEP,QPEP,PEPCORD2,NATOM,
     1  phi2,psi2,v1,v2,v3,v4,v5,v6,RESNUM)

       UPEP2WNEW=0.0d+0
       do 51105 M=1,NMOLW
         do 51205 I=1,3
           do 51305 C=1,3
             RWM(C,I)=RW(M,C,I)
51305        continue
51205      continue
       call DISTWMPEP(D2WMPEP2NEW,PEPCORD2,NATOM,RWM,LX,LY,COM2)
       call NRGWMPEP(D2WMPEP2NEW,A12WP,C6WP,QCONWP,UPEP2WM,NATOM)
        do 51215 N=1,NATOM
           do 51225 I=1,3
             D2WPEP2NEW(N,M,I)=D2WMPEP2NEW(N,I)
51225         continue
51215      continue
        UWMPEP(M,2)=UPEP2WM
        UPEP2WNEW=UPEP2WNEW+UPEP2WM
51105   continue
```

```
      DELV=UPEP2WNEW+UPEP2SFNEW+NEWP2ENRG+UPPNEW
     &       -UPEP2WOLD-UPEP2SFOLD-OLDP2ENRG-UPPOLD
      if((DELV.ge.0.0d+0).and.(dexp(-DELV).lt.RANDOM(ISEED)))then
       do 52113 N=1,NATOM
        do 53113 I=1,3
          PEPCORD2(N,I)=PEPCORD2OLD(N,I)
          do 53115 M=1,NMOLW
            D2WPEP2NEW(N,M,I)=D2WPEP2OLD(N,M,I)
53115       continue
53113     continue
52113    continue
       do I=1,3
        COM2(I)=COM2OLD(I)
       enddo
       do i=1,RESNUM
       phi2(i)=phi2old(i)
       psi2(i)=psi2old(i)
       enddo
       do 54213 N=1,NMOLW
        UWMPEP(N,2)=UWMPEPOLD(N,2)
54213    continue
       call SUMBINPEP(PEPCORD2,LZ,NMOLW,NATOM,RXMAX2,
     1   DELR,DELZ,D2WPEP2NEW,COSSUM2,COSSQSUM2,
     1   ZPEP2SUM,NEND,CEND,GRPWSUM2,NEIBOURWSUM2,
     1   HB,NHB,COM2)
      else
       do i=1,RESNUM
       write(89,*)phi2(i),psi2(i)
       enddo
       V=V+DELV
       VPSS=VPSS+UPEP2SFNEW-UPEP2SFOLD
       VSOPS=VSOPS+UPEP2WNEW-UPEP2WOLD
       ACCTOR=ACCTOR+1
       call SUMBINPEP(PEPCORD2,LZ,NMOLW,NATOM,RXMAX2,
     1   DELR,DELZ,D2WPEP2NEW,COSSUM2,COSSQSUM2,
     1   ZPEP2SUM,NEND,CEND,GRPWSUM2,NEIBOURWSUM2,
     1   HB,NHB,COM2)
        UPEP2SFOLD=UPEP2SFNEW
        UPPOLD=UPPNEW
                    OLDP2ENRG=NEWP2ENRG
      end if
********************* Water Movement ****************************
```

```
      do 10100 M=1,NMOLW
        do 11000 I=1,3
          do 11100 C=1,3
            RWMOLD(C,I)=RW(M,C,I)
11100         continue
11000     continue
        call DISTW(D2WOLD,RWMOLD,RW,M,NMOLW,LX,LY,LZ)
        call DISTWMSURF(D2WSURF1OLD,D2WSURF2OLD,RSURF,RWMOLD,
     1        NSURF,LX,LY)
        UPEP1WMOLD=UWMPEP(M,1)
        UPEP2WMOLD=UWMPEP(M,2)
        do 55400 N=1,NATOM
         do 55410 I=1,3
           D2WMPEP1OLD(N,I)=D2WPEP1NEW(N,M,I)
           D2WMPEP2OLD(N,I)=D2WPEP2NEW(N,M,I)
55410      continue
55400     continue
        call NRGW(RWMOLD,M,NMOLW,D2WOLD,A12W,C6W,QCONW,
     1    A12WS,C6WS,QCONWS,VWOLD,VWMSURFOLD,D2WSURF1OLD,
     1    D2WSURF2OLD,NSURF,LX,LY,LZ)
        call RNDMOVE(RWMOLD,RWMNEW,MAXTRNW,MAXROTW,LX,LY,LZ,ISEED)
        do 11200 I=1,3
          do 11300 C=1,3
            RW(M,C,I)=RWMNEW(C,I)
11300       continue
11200     continue
        call DISTW(D2WNEW,RWMNEW,RW,M,NMOLW,LX,LY,LZ)
        call DISTWMSURF(D2WSURF1NEW,D2WSURF2NEW,RSURF,RWMNEW,
     1        NSURF,LX,LY)
        call DISTWMPEP(D2WMPEP1NEW,PEPCORD1,NATOM,RWMNEW,LX,LY,COM1)
        call DISTWMPEP(D2WMPEP2NEW,PEPCORD2,NATOM,RWMNEW,LX,LY,COM2)
        call NRGWMPEP(D2WMPEP1NEW,A12WP,C6WP,QCONWP,UPEP1WMNEW,NATOM)
        call NRGWMPEP(D2WMPEP2NEW,A12WP,C6WP,QCONWP,UPEP2WMNEW,NATOM)
        call NRGW(RWMNEW,M,NMOLW,D2WNEW,A12W,C6W,QCONW,
     1    A12WS,C6WS,QCONWS,VWNEW,VWMSURFNEW,D2WSURF1NEW,
     1    D2WSURF2NEW,NSURF,LX,LY,LZ)
        DELV=VWNEW+VWMSURFNEW+UPEP1WMNEW+UPEP2WMNEW
     &    -VWOLD-VWMSURFOLD-UPEP1WMOLD-UPEP2WMOLD
       if((DELV.ge.0.0d+0).and.(dexp(-DELV).lt.RANDOM(ISEED)))then
        do 11400 I=1,3
          do 11500 C=1,3
            RW(M,C,I)=RWMOLD(C,I)
```

```
11500       continue
11400     continue
        do 53131 N=1,NATOM
          do 53141 I=1,3
            D2WPEP1NEW(N,M,I)=D2WPEP1OLD(N,M,I)
            D2WPEP2NEW(N,M,I)=D2WPEP2OLD(N,M,I)
53141       continue
53131     continue
        call SUMBINW(M,NMOLW,PEPCORD1,RXMAX2,GSUM,DELR,D2WOLD,
    &     D2WMPEP1OLD,GRPWSUM1,NEIBOURWSUM1,HB,NHB,LX,LY,LZ,
    &     RW,DELZ,ZWSUM)
        call SUMBINW(M,NMOLW,PEPCORD2,RXMAX2,GSUM,DELR,D2WOLD,
    &     D2WMPEP2OLD,GRPWSUM2,NEIBOURWSUM2,HB,NHB,LX,LY,LZ,
    &     RW,DELZ,ZWSUM)
       else
        do 53130 N=1,NATOM
          do 53140 I=1,3
            D2WPEP1OLD(N,M,I)=D2WMPEP1NEW(N,I)
            D2WPEP2OLD(N,M,I)=D2WMPEP2NEW(N,I)
53140       continue
53130     continue
        UWMPEP(M,1)=UPEP1WMNEW
        UWMPEP(M,2)=UPEP2WMNEW
        V=V+DELV
        VWATER=VWATER+VWNEW-VWOLD
        VSUSS=VSUSS+VWMSURFNEW-VWMSURFOLD
        VSOPS=VSOPS+UPEP1WMNEW+UPEP2WMNEW-UPEP1WMOLD-UPEP2WMOLD
        ACCMOVEW=ACCMOVEW+1
        call SUMBINW(M,NMOLW,PEPCORD1,RXMAX2,GSUM,DELR,D2WNEW,
    &     D2WMPEP1NEW,GRPWSUM1,NEIBOURWSUM1,HB,NHB,LX,LY,LZ,
    &     RW,DELZ,ZWSUM)
        call SUMBINW(M,NMOLW,PEPCORD2,RXMAX2,GSUM,DELR,D2WNEW,
    &     D2WMPEP2NEW,GRPWSUM2,NEIBOURWSUM2,HB,NHB,LX,LY,LZ,
    &     RW,DELZ,ZWSUM)
       end if
10100 continue
*********************************************************************

      VTOT(STEP)=V
      VW(STEP)=VWATER/dble(NMOLW)
      VSUS(STEP)=VSUSS
      VSOP(STEP)=VSOPS
```

```
      VPS(STEP)=VPSS
      ESUM=ESUM+VTOT(STEP)
      VWSUM=VWSUM+VW(STEP)
      ETED1(STEP)=
     &    ( (PEPCORD1(94,1)-PEPCORD1(1,1))**2 +
     &    (PEPCORD1(94,2)-PEPCORD1(1,2))**2 +
     &    (PEPCORD1(94,3)-PEPCORD1(1,3))**2 )**0.5
      ETED2(STEP)=
     &    ( (PEPCORD2(94,1)-PEPCORD2(1,1))**2 +
     &    (PEPCORD2(94,2)-PEPCORD2(1,2))**2 +
     &    (PEPCORD2(94,3)-PEPCORD2(1,3))**2 )**0.5

      CM1(STEP)=COM1(3)
      CM2(STEP)=COM2(3)
10000 continue
      call NRGTOT(V,NMOLW,LX,LY,LZ,RW,A12W,C6W,QCONW,
     & A12WS,C6WS,QCONWS,A12WP,C6WP,QCONWP,A12PS,C6PS,QCONPS,
     & A12PP,C6PP,QCONPP,NSURF,RSURF,NATOM,PEPCORD1,PEPCORD2,
     & D2WPEP1NEW,D2WPEP2NEW,COM1,COM2,UWMPEP,UPEP1SFNEW,UPEP2SFNEW,
     & VWATER,VSURSOL,VREST,UPPNEW,UPEP1WNEW,UPEP2WNEW,D2PPNEW)
       call pepenrg(PE1,APEP,CPEP,QPEP,PEPCORD1,NATOM
     1  ,phi1,psi1,v1,v2,v3,v4,v5,v6,RESNUM)
       call pepenrg(PE2,APEP,CPEP,QPEP,PEPCORD2,NATOM
     1  ,phi2,psi2,v1,v2,v3,v4,v5,v6,RESNUM)
      VTOT(NMCS+1)=V+PE1+PE2
      VWATER=VWATER/dble(NMOLW)
      NMCSOLD=NMCS
      if(RUNSTAT.GE.2) then
        NMCSACC=NMCSACC+NMCS
        ACCMOVEWACC=ACCMOVEWACC+ACCMOVEW
        ACCPEPACC=ACCPEPACC+ACCPEP
        ACCTORACC=ACCTORACC+ACCTOR
        NMCS=NMCSACC
        ACCMOVEW=ACCMOVEWACC
      end if
C ***************************************************
C ** AVERAGES.                          **
C ** acceptance ratio. energy. pair correlation functions.          **
C ***************************************************
      AVGACCW=dble(ACCMOVEW)/dble(NMOLW*NMCS)
      AVGACCPEP=dble(ACCPEP)/dble(NMCS)
      AVGACCTOR=dble(ACCTOR)/dble(NMCS)
```

```
      if(RUNSTAT.GE.2)then
        ESUMACC=ESUMACC+ESUM
        VWSUMACC=VWSUMACC+VWSUM
        ESUM=ESUMACC
        VWSUM=VWSUMACC
      end if
      AVGNRG=ESUM/dble(NMCS)
      AVGVW=VWSUM/dble(NMCS)
      do 13100 K=1,NBIN
      RMIN=DELR*(dble(K)-0.5d+0)
      RMAX=RMIN+DELR
      VOLUME=4.0d+0/3.0d+0*PI*(RMAX*RMAX*RMAX-RMIN*RMIN*RMIN)
      VOLUME=VOLUME*DENS*dble(NMCS)
      GOFR(K,1)=(dble(GSUM(K,1)))/(VOLUME*dble(NMOLW))
      GOFR(K,2)=(dble(GSUM(K,2)))/(4.0d+0*VOLUME*dble(NMOLW))
      GOFR(K,3)=(dble(GSUM(K,3)))/(4.0D+0*VOLUME*dble(NMOLW))
      do 13110 N=1,NHB
        NEIBOURW1(N)=dble(NEIBOURWSUM1(N))/dble(NMCS*2)
        NEIBOURW2(N)=dble(NEIBOURWSUM2(N))/dble(NMCS*2)
        GOFRWP1(K,1,N)=(dble(GRPWSUM1(K,1,N)))/(VOLUME*2.d+0)
        GOFRWP1(K,2,N)=(dble(GRPWSUM1(K,2,N)))/(VOLUME*4.d+0)
        GOFRWP2(K,1,N)=(dble(GRPWSUM2(K,1,N)))/(VOLUME*2.d+0)
        GOFRWP2(K,2,N)=(dble(GRPWSUM2(K,2,N)))/(VOLUME*4.d+0)
13110 continue
13100 continue
      VOLUMEZ=LX*LY*DELZ
      TMP2= VOLUMEZ*DENS*NMCS
      do 83 K=1,NBINZ
        GOFZW(K,1)=ZWSUM(K,1)/TMP2
        GOFZW(K,2)=ZWSUM(K,2)/(TMP2*2.d+0)
83    continue
      do 13101 K=1,NBINZ
        do 13102 I=1,3
          ZPEP1(K,I)=dble(ZPEP1SUM(K,I))/dble(NMCS)
          ZPEP2(K,I)=dble(ZPEP2SUM(K,I))/dble(NMCS)
13102    continue
13101 continue
      COSAVG1=COSSUM1/NMCS
      COSSQAVG1=(COSSQSUM1*3.d+0-dble(NMCS))/(2.d+0*NMCS)
      COSAVG2=COSSUM2/NMCS
      COSSQAVG2=(COSSQSUM2*3.d+0-dble(NMCS))/(2.d+0*NMCS)
C ***************************************************
```

```
C ** OUTPUT DATA. final configuration. acceptance ratios. energies. pair correlation functions.  **
C ***************************************************
      write(9,*)
      write(9,*) '***********************************'
      write(9,*)
      write(9,*) 'GENERAL OUTPUT DATA'
      write(9,*)
      write(9,*) TITLE
      write(9,100) RUNSTAT
      write(9,*) CFGINP
      write(9,*) CFGOUT
      write(9,*) OUTPUT
      write(9,*) PDB
      write(9,110) NMOLW
      write(9,120) NMCS
      write(9,140) TEMP
      write(9,*) NSAVE
      write(9,*) NADJUST
      write(9,*) SURFINP
      write(9,*) QSURF
      write(9,*) PEP
      write(9,*) VPEP
      write(9,*) NSURF
      write(9,*) SURFNAME
      write(9,*) LX,LY,LZ
      write(9,*)
      write(9,*) 'AVERAGE WATER ACCEPTANCE RATIO'
      write(9,*) AVGACCW
      write(9,*) 'Maximum WATER Translational Movement'
      write(9,*) MAXTRNW
      write(9,*) 'Maximum WATER Rotational Movement'
      write(9,*) MAXROTW
      write(9,*) 'AVERAGE PEPTIDE MOVEMENT ACCEPTANCE RATIO'
      write(9,*) AVGACCPEP
      write(9,*) 'AVERAGE PEPTIDE TORSIONAL ACCEPTANCE RATIO'
      write(9,*) AVGACCTOR
      write(9,*) 'Maximum psi Movement of Peptide'
      write(9,*) maxpsi
      write(9,*) 'Maximum phi Movement of Peptide'
      write(9,*) maxphi
      write(9,*)
      write(9,*) 'INITIAL ENERGY'
```

```
      write(9,*) VTOT(0)
      write(9,*) 'Initial Water Energy'
      write(9,*) VWINI
      write(9,*)
      write(9,*) 'ENERGIES (system and water)'
      do 3111 STEP=1,NMCSOLD
        if(mod(STEP,NPTS).eq.0)then
          N=STEP/NPTS
          VTOTPT(N)=VTOT(STEP)
          VWPT(N)=VW(STEP)
          ETEDP1(N)=ETED1(STEP)
          ETEDP2(N)=ETED2(STEP)
          CMP1(N)=CM1(STEP)
          CMP2(N)=CM2(STEP)
          VSUSPT(N)=VSUS(STEP)
          VSOPPT(N)=VSOP(STEP)
          VPSPT=VPS(STEP)
        end if
3111  continue
      VERRSUM=0.d+0
      VWERRSUM=0.d+0
      do 3000 N=1,100
        write(9,888) N*NPTS,VTOTPT(N),VWPT(N)
        VERRSUM=VERRSUM+dabs(VTOTPT(N)-AVGNRG)
        VWERRSUM=VWERRSUM+dabs(VWPT(N)-AVGVW)
3000  continue
888   format('step=',I6,'<E>=',D18.10,'<VW>=',D18.10)
C     do 30005 N=1,100
C       write(9,8885) N*NPTS,VSUSPT(N),VSOPPT(N),VPSPT(N)
C30005 continue
C8885  format('step=',I6,'<VSUS>=',D18.10,
C     &       '<VSOP>=',D18.10,'<VPS>=',D18.10)
      VERR=VERRSUM/100.0d+0
      VWERR=VWERRSUM/100.0d+0
      write(9,*)
      write(9,*) 'FINAL ENERGY'
      write(9,*) VTOT(NMCSOLD+1)
      write(9,*) 'Final Water Energy'
      write(9,*) VWATER
      write(9,*) 'AVERAGE ENERGY & UNCERTAINTY'
      write(9,*) AVGNRG,VERR
      write(9,*) 'AVERAGE WATER ENERGY & UNCERTAINTY'
```

```
      write(9,*) AVGVW,VWERR
      write(9,*)

      do N=1,100
        ETED1T=ETED1T+ETEDP1(N)
        ETED2T=ETED2T+ETEDP2(N)
        CMP1T=CMP1T+CMP1(N)
        CMP2T=CMP2T+CMP2(N)
      end do
      ETED1AVG=ETED1T/100D+0
      ETED2AVG=ETED2T/100D+0
      CMP1AVG=CMP1T/100D+0
      CMP2AVG=CMP2T/100D+0
C       write(9,890) N*NPTS,ETEDP1(N),ETEDP2(N),CMP1(N),CMP2(N)
C       end do
C890   format('STEP=',I6,'<ETEDP1>=',D18.10,'<ETEDP2>=',D18.10,
C     &       '<CMP1>=',D18.10,'<CMP2>=',D18.10)
      write(9,895) ETED1AVG,CMP1AVG,ETED2AVG,CMP2AVG
895   format('<ETEDP1AVG>=',D18.10,'<CMP1AVG>=',D18.10,
     &       '<ETEDP2AVG>=',D18.10,'<CMP2AVG>=',D18.10)
      write(9,*)
      write(9,*) 'COSAVG1= ',COSAVG1,'COSAVG2= ',COSAVG2
      write(9,*) 'COSSQAVG1= ',COSSQAVG1,'COSSQAVG2= ',COSSQAVG2
      write(9,*)

      if(RUNSTAT.gt.1) then
        Write(9,*) 'Closest neighbour number peptide 1'
        do 55110 N=1,NHB
          write(9,*) 'NW(',HB(N),')= ',NEIBOURW1(N)
55110   continue
        Write(9,*) 'Closest neighbour number peptide 2'
        do 55112 N=1,NHB
          write(9,*) 'NW(',HB(N),')= ',NEIBOURW2(N)
55112   continue
        write(9,*) 'WATER DENSITY PROFILE'
        do 92 I=1,2
          write(9,*) 'ZW(',I,' )'
          do 91 K=1,NBINZ
            write(9,999) GOFZW(K,I)
 91       continue
 92     continue
        write(9,*) 'PEPTIDE-1 Z position'
```

```
      do 5001 I=1,3
       write(9,*) 'ZPEP(',I,' )'
       do 5011 K=1,NBINZ
        write(9,999) ZPEP1(K,I)
5011     continue
5001   continue
      write(9,*) 'PEPTIDE-2 Z position'
      do 5003 I=1,3
       write(9,*) 'ZPEP(',I,' )'
       do 5013 K=1,NBINZ
        write(9,999) ZPEP2(K,I)
5013     continue
5003   continue
      write(9,*) 'WATER-WATER PAIR CORRELATION FUNCTIONS'
      write(9,*) '(from r = DELR to RXMAX)'
      do 5000 I=1,3
       write(9,*) 'g(',I,' )'
       do 5010 K=1,NBIN
        write(9,999) GOFR(K,I)
5010     continue
5000   continue
999    format(f8.4)
      write(9,*) 'PEPTIDE 1 - WATER PAIR CORRELATION FUNCTIONS'
      write(9,*) '(from r = DELR to RXMAX)'
      do 55000 N=1,NHB
       do 55100 I=1,2
        write(9,*) 'g(',HB(N),'-',I,')'
        do 55010 K=1,NBIN
          write(9,999) GOFRWP1(K,I,N)
55010     continue
55100    continue
55000  continue
      write(9,*) 'PEPTIDE 2 - WATER PAIR CORRELATION FUNCTIONS'
      write(9,*) '(from r = DELR to RXMAX)'
      do 55002 N=1,NHB
       do 55102 I=1,2
        write(9,*) 'g(',HB(N),'-',I,')'
        do 55012 K=1,NBIN
         write(9,999) GOFRWP2(K,I,N)
55012     continue
55102    continue
55002  continue
```

```
      end if
      close(9)
*************************************************************************
      write(2,*) NATOM
      do 33000 M=1,NATOM
        write(2,889) AA(M),ATOM(M),GROUP(M),PEPCORD1(M,1),
     1   PEPCORD1(M,2),PEPCORD1(M,3),PEPCORD2(M,1),PEPCORD2(M,2),
     1   PEPCORD2(M,3),APEP(M),CPEP(M),QPEP(M),AW(M)
33000 continue
      write(2,*) NHB
      do 35040 M=1,NHB
        write(2,*) HB(M)
35040 continue
      do 35041 I=1,3
       write(2,778)COM1(I),COM2(I)
35041 continue
      write(2,*) NEND
      write(2,*) CEND
      do 2000 M=1,NMOLW
        write(2,*)
      do 2010 I=1,3
        write(2,777) (RW(M,C,I),C=1,3)
2010  continue
2000  continue
      do I=1,RESNUM
      write(2,1528)phi1(I),phi2(I),psi1(I),psi2(I)
      enddo
      write(2,1529)v1,v2,v3,v4,v5,v6
 1528 format(5x,f8.3,5x,f8.3,5x,f8.3,5x,f8.3)
 1529 format(f8.3,f8.3,f8.3,f8.3,f8.3,f8.3)
      write(2,*) MAXTRNW
      write(2,*) MAXROTW
      write(2,*) MXTPEP
      write(2,*) MXRPEP
      write(2,*) maxpsi
      write(2,*) maxphi
      if(RUNSTAT.gt.1) then
        write(2,*) NMCSACC
        write(2,*) ACCMOVEWACC
        write(2,*) ESUMACC
        write(2,*) VWSUMACC
        write(2,*) ACCPEPACC
```

```
      write(2,*) ACCTORACC
      write(2,*) 'GSUM'
      do 1008 K=1,NBIN
       write(2,333) (GSUM(K,I),I=1,3)
1008   continue
      write(2,*) 'GRPSUM Peptide 1'
      do 41500 K=1,NBIN
       do 41600 N=1,NHB
        write(2,334) (GRPWSUM1(K,I,N),I=1,2)
41600    continue
41500  continue
      write(2,*) 'GRPSUM Peptide 2'
      do 41502 K=1,NBIN
       do 41602 N=1,NHB
        write(2,334) (GRPWSUM2(K,I,N),I=1,2)
41602    continue
41502  continue
      write(2,*) 'NEIBOURWSUM Peptide 1'
      do 41700 N=1,NHB
       write(2,*) NEIBOURWSUM1(N)
41700  continue
      write(2,*) 'NEIBOURWSUM Peptide 2'
      do 41702 N=1,NHB
       write(2,*) NEIBOURWSUM2(N)
41702  continue
      write(2,*) 'ZWSUM'
      do K=1,NBINZ
       write(2,338) (ZWSUM(K,I),I=1,2)
      enddo
      write(2,*) 'ZPEPSUM Peptide 1'
      do 10077 K=1,NBINZ
       do 41710 I=1,3
        write(2,*) ZPEP1SUM(K,I)
41710    continue
10077   continue
      write(2,*) 'ZPEPSUM Peptide 2'
      do 1009 K=1,NBINZ
       do 41712 I=1,3
        write(2,*) ZPEP2SUM(K,I)
41712    continue
1009   continue
      write(2,*)
```

```
      write(2,339) COSSUM1,COSSUM2
      write(2,339) COSSQSUM1,COSSQSUM2
      write(2,*) 'STEP= ',NMCSOLD
    end if
    close(2)

    close(7)
    close(88)
777  format(f17.13,2x,f17.13,2x,f17.13)
778  format(f17.13,2x,f17.13)
    call PDBOUT(RSURF,RW,PEPCORD1,PEPCORD2,PDB,NATOM,NMOLW,
   &    NSURF,AA,ATOM,GROUP)
    close(7)
    stop
    end
************************************************************************
** RNDMOVE.....subroutine which randomly displaces a molecule.       **
** the displacement is performed as a translational displacement of   **
** the molecule coupled with a rotational displacement about the      **
** position of the oxygen atom.                                       **
************************************************************************
    subroutine RNDMOVE(RMOLD,RMNEW,MAXTRN,MAXROT,LX,LY,LZ,ISEED)
    implicit  NONE
    external  MULTMAT,RANDOM
************************************************************************
    integer        I,C,ISEED
    double precision LX,LY,LZ,DELC,MAXTRN,MAXROT,THX,THY,THZ
    double precision COSX,SINX,COSY,SINY,COSZ,SINZ
    double precision ROTX(3,3),ROTY(3,3),ROTZ(3,3),TMP1(3,3)
    double precision TMP2(3,3)
    double precision RMOLD(3,3),RMNEW(3,3),RHYOLD(3,2),RHYNEW(3,2)
    double precision RANDOM
C ***************************************************
C ** HYDROGEN COORDINATE MATRIX.                   **
C ** the positions of the hydrogen atoms are       **
C ** defined relative to the oxygen atom.          **
C ***************************************************
    do 1000 I=1,2
    do 1010 C=1,3
      RHYOLD(C,I)=RMOLD(C,I+1)-RMOLD(C,1)
1010  continue
1000  continue
```

```
C ************************************************
C ** RANDOM ROTATION.                    **
C ************************************************
      THX=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MAXROT
      THY=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MAXROT
      THZ=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MAXROT
      COSX=dcos(THX)
      SINX=dsin(THX)
      COSY=dcos(THY)
      SINY=dsin(THY)
      COSZ=dcos(THZ)
      SINZ=dsin(THZ)
      ROTX(1,1)=1.0d+0
      ROTX(1,2)=0.0d+0
      ROTX(1,3)=0.0d+0
      ROTX(2,1)=0.0d+0
      ROTX(2,2)=COSX
      ROTX(2,3)=-SINX
      ROTX(3,1)=0.0d+0
      ROTX(3,2)=SINX
      ROTX(3,3)=COSX
      ROTY(1,1)=COSY
      ROTY(1,2)=0.0d+0
      ROTY(1,3)=-SINY
      ROTY(2,1)=0.0d+0
      ROTY(2,2)=1.0d+0
      ROTY(2,3)=0.0d+0
      ROTY(3,1)=SINY
      ROTY(3,2)=0.0d+0
      ROTY(3,3)=COSY
      ROTZ(1,1)=COSZ
      ROTZ(1,2)=-SINZ
      ROTZ(1,3)=0.0d+0
      ROTZ(2,1)=SINZ
      ROTZ(2,2)=COSZ
      ROTZ(2,3)=0.0d+0
      ROTZ(3,1)=0.0d+0
      ROTZ(3,2)=0.0d+0
      ROTZ(3,3)=1.0d+0
      call MULTMAT(ROTX,ROTY,3,3,3,TMP1)
      call MULTMAT(TMP1,ROTZ,3,3,3,TMP2)
```

```
      call MULTMAT(TMP2,RHYOLD,3,3,2,RHYNEW)
C ***************************************************
C ** RANDOM TRANSLATION.                    **
C ***************************************************
      DELC=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MAXTRN
      RMNEW(1,1)=DELC+RMOLD(1,1)
      RMNEW(1,1)=RMNEW(1,1)-LX*dnint(RMNEW(1,1)/LX)
      RMNEW(1,2)=RMNEW(1,1)+RHYNEW(1,1)
      RMNEW(1,3)=RMNEW(1,1)+RHYNEW(1,2)
      DELC=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MAXTRN*LY/LX
      RMNEW(2,1)=DELC+RMOLD(2,1)
      RMNEW(2,1)=RMNEW(2,1)-LY*dnint(RMNEW(2,1)/LY)
      RMNEW(2,2)=RMNEW(2,1)+RHYNEW(2,1)
      RMNEW(2,3)=RMNEW(2,1)+RHYNEW(2,2)
      DELC=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MAXTRN*LZ/LX
      RMNEW(3,1)=DELC+RMOLD(3,1)
      RMNEW(3,2)=RMNEW(3,1)+RHYNEW(3,1)
      RMNEW(3,3)=RMNEW(3,1)+RHYNEW(3,2)
      return
      end
*************************************************************************
** NRGTOT.....subroutine which calculates the total potential energy for any given configuration.  for programming simplicity, the code is written to sum up the potential energies felt by each molecule and then divide this sum by a factor of 2 since each pair interaction is counted twice.                    **
*************************************************************************
      subroutine NRGTOT(V,NMOLW,LX,LY,LZ,RW,A12W,C6W,
     & QCONW,A12WS,C6WS,QCONWS,A12WP,C6WP,QCONWP,
     & A12PS,C6PS,QCONPS,A12PP,C6PP,QCONPP,NSURF,RSURF,NATOM,PEPCORD1,
     & PEPCORD2,D2WPEP1,D2WPEP2,COM1,COM2,VWMPEP,VPEP1SF,VPEP2SF,VWATER,
     & VSURSOL,VREST,VPP,VWPEP1,VWPEP2,D2PP)
      implicit   NONE
      external   DISTW,NRGW
      external   DISTWMSURF
      external   DISTWMPEP,DISTPEPSF
      external   NRGWMPEP
*************************************************************************
      integer        M,I,C,NMOLW,NSURF,N,K,NATOM
      double precision V,VW,VREST,LX,LY,LZ,VWATER
      double precision D2W(3,2000,3),RW(2000,3,3),RWM(3,3)
      double precision A12W(3,3),C6W(3,3),A12PP,C6PP,QCONPP
      double precision QCONW(3,3)
      double precision A12WS(3,2),C6WS(3,2)
```

```
      double precision QCONWS(3,2)
      double precision RSURF(600,3),D2PP(200,200)
      double precision D2WSURF1(3,600),D2WSURF2(3,600)
      double precision VWMSURF,VWSURF
      double precision A12WP(200,3),C6WP(200,3),QCONWP(200,3)
      double precision A12PS(200,2),C6PS(200,2),QCONPS(200,2)
      double precision PEPCORD1(200,3),PEPCORD2(200,3),COM1(3),COM2(3)
      double precision D2WPEP1(200,2000,3),D2WPEP2(200,2000,3)
      double precision VWMPEP(2000,2),VPEP1SF,VPEP2SF,VPP
      double precision D2WMPEP1(200,3),D2WMPEP2(200,3)
      double precision D2PEP1SF1(200,600),D2PEP2SF1(200,600)
      double precision D2PEP1SF2(200,600),D2PEP2SF2(200,600)
      double precision VPEP1WM,VPEP2WM,VWPEP1,VWPEP2,VSURSOL
C ***************************************************
C ** TOTAL ENERGY. the calculation includes all pair interactions between a given molecule and the closest images of the remaining molecules. **
C ***************************************************
      V=0.0d+0
      VWATER=0.0d+0
      VREST=0.0d+0
      VWSURF=0.0D+0
      VWPEP1=0.0D+0
      VWPEP2=0.0D+0
      VSURSOL=0.0D+0
**WATER-WATER,WATER-SURFACE AND WATER PEPTIDE
      do 1000 M=1,NMOLW
        do 1010 I=1,3
        do 1020 C=1,3
        RWM(C,I)=RW(M,C,I)
1020  continue
1010  continue
        call DISTW(D2W,RWM,RW,M,NMOLW,LX,LY,LZ)
        call DISTWMSURF(D2WSURF1,D2WSURF2,RSURF,RWM,NSURF,LX,LY)
        call DISTWMPEP(D2WMPEP1,PEPCORD1,NATOM,RWM,LX,LY,COM1)
        call DISTWMPEP(D2WMPEP2,PEPCORD2,NATOM,RWM,LX,LY,COM2)
        call NRGWMPEP(D2WMPEP1,A12WP,C6WP,QCONWP,VPEP1WM,NATOM)
        call NRGWMPEP(D2WMPEP2,A12WP,C6WP,QCONWP,VPEP2WM,NATOM)
        call NRGW(RWM,M,NMOLW,D2W,A12W,C6W,QCONW,A12WS,C6WS,
     1   QCONWS,VW,VWMSURF,D2WSURF1,D2WSURF2,NSURF,LX,LY,LZ)
        VWATER=VWATER+VW
        VWSURF=VWSURF+VWMSURF
        VWPEP1=VWPEP1+VPEP1WM
```

```
      VWPEP2=VWPEP2+VPEP2WM
      VWMPEP(M,1)=VPEP1WM
      VWMPEP(M,2)=VPEP2WM
      do 2000 N=1,NATOM
        do 2010 K=1,3
          D2WPEP1(N,M,K)=D2WMPEP1(N,K)
          D2WPEP2(N,M,K)=D2WMPEP2(N,K)
2010      continue
2000    continue
1000  continue
     VWATER=VWATER/2.d+0
**PEPTIDE-PEPTIDE
     call DISTPP(D2PP,PEPCORD1,PEPCORD2,NATOM,LX,LY,COM1,COM2)
     call NRGPP(D2PP,A12PP,C6PP,QCONPP,VPP,NATOM)
**PEPTIDE-SURFACE
     call DISTPEPSF(D2PEP1SF1,D2PEP1SF2,RSURF,NSURF,PEPCORD1,
    1              NATOM,LX,LY,COM1)
     call DISTPEPSF(D2PEP2SF1,D2PEP2SF2,RSURF,NSURF,PEPCORD2,
    1              NATOM,LX,LY,COM2)
     call NRGPEPSF(A12PS,C6PS,QCONPS,VPEP1SF,D2PEP1SF1,
    1             D2PEP1SF2,NSURF,NATOM)
     call NRGPEPSF(A12PS,C6PS,QCONPS,VPEP2SF,D2PEP2SF1,
    1             D2PEP2SF2,NSURF,NATOM)
     V=VWATER+VWSURF+VWPEP1+VWPEP2+VPP+VPEP1SF+VPEP2SF
     VREST=VWATER
     VSURSOL=VWSURF
     return
     end
*************************************************************************
** DISTW.....subroutine which calculates the squared distances between the atoms of the chosen molecule and the
atoms of the closest images of the remaining molecules in the system.          **
*************************************************************************
     subroutine DISTW(D2,RM,R,M,NMOL,LX,LY,LZ)
     implicit   NONE
     integer    M,N,I,J,NMOL
     double precision LX,LY,LZ,CORX,CORY
     double precision DELX,DELY,DELZ
     double precision D2(3,2000,3),R(2000,3,3),RM(3,3)
C ************************************************
C ** SQUARED DISTANCES.                    **
C ** note that the minimum image convention is    **
C ** applied only to oxygen pairs.              **
```

```
C ************************************************
      do 1000 N=1,M-1
        DELX=R(N,1,1)-RM(1,1)
        CORX=LX*dnint(DELX/LX)
        DELY=R(N,2,1)-RM(2,1)
        CORY=LY*dnint(DELY/LY)
      do 1010 I=1,3
       do 1020 J=1,3
        DELX=R(N,1,J)-RM(1,I)-CORX
        DELY=R(N,2,J)-RM(2,I)-CORY
        DELZ=R(N,3,J)-RM(3,I)
        D2(I,N,J)=DELX*DELX+DELY*DELY+DELZ*DELZ
1020    continue
1010   continue
1000  continue
.     do 2000 N=M+1,NMOL
        DELX=R(N,1,1)-RM(1,1)
        CORX=LX*dnint(DELX/LX)
        DELY=R(N,2,1)-RM(2,1)
        CORY=LY*dnint(DELY/LY)
       do 2010 I=1,3
        do 2020 J=1,3
        DELX=R(N,1,J)-RM(1,I)-CORX
        DELY=R(N,2,J)-RM(2,I)-CORY
        DELZ=R(N,3,J)-RM(3,I)
        D2(I,N,J)=DELX*DELX+DELY*DELY+DELZ*DELZ
2020    continue
2010   continue
2000  continue
      return
      end
*************************************************************************
** NRGW.....subroutine which calculates the potential energy "felt" by a chosen molecule.
*************************************************************************
      subroutine NRGW(RM,M,NMOL,D2,A12,C6,QCON,A12WS,C6WS,QCONWS,
     &      VM,VMSURF,D2SURF1,D2SURF2,NSURF,LX,LY,LZ)
      implicit   NONE
*************************************************************************
      integer         M,N,I,J,NMOL,NSURF
      double precision VM,D,D6,D12,LX,LY,LZ
      double precision D2(3,2000,3),A12(3,3),C6(3,3),QCON(3,3),RM(3,3)
      double precision A12WS(3,2),C6WS(3,2),QCONWS(3,2)
```

```
      double precision D2SURF1(3,600),D2SURF2(3,600)
      double precision VMSURF,DSURF
C ***************************************************
C ** ENERGY CALCULATION. the calculation includes all pairs of atoms in the chosen molecule and the closest images of the remaining molecules.**
C ***************************************************
      VM=0.0d+0
      VMSURF=0.0D+0
      do 1000 I=1,3
      do 1010 J=1,3
      do 1100 N=1,M-1
        D=dsqrt(D2(I,N,J))
        D6=D2(I,N,J)*D2(I,N,J)*D2(I,N,J)
        D12=D6*D6
        VM=VM+A12(I,J)/D12-C6(I,J)/D6+QCON(I,J)/D
1100  continue
      do 1110 N=M+1,NMOL
        D=dsqrt(D2(I,N,J))
        D6=D2(I,N,J)*D2(I,N,J)*D2(I,N,J)
        D12=D6*D6
        VM=VM+A12(I,J)/D12-C6(I,J)/D6+QCON(I,J)/D
1110  continue
1010  continue
1000  continue
      VMSURF=0.0
      do 2000 I=1,3
        do 2100 N=1,NSURF
        DSURF=dsqrt(D2SURF1(I,N))
        D6=D2SURF1(I,N)*D2SURF1(I,N)*D2SURF1(I,N)
        D12=D6*D6
        VMSURF=VMSURF+A12WS(I,1)/D12-C6WS(I,1)/D6
     1       +QCONWS(I,1)/DSURF
        DSURF=dsqrt(D2SURF2(I,N))
        D6=D2SURF2(I,N)*D2SURF2(I,N)*D2SURF2(I,N)
        D12=D6*D6
        VMSURF=VMSURF+A12WS(I,2)/D12-C6WS(I,2)/D6
     1       +QCONWS(I,2)/DSURF
2100     continue
2000  continue
      return
      end
*************************************************************************
```

```
** MULTMAT.....subroutine which multiplies two matrices.            **
************************************************************************
      subroutine MULTMAT(A,B,ROW,MID,COL,AB)
      implicit   NONE
************************************************************************
      integer         I,J,K,ROW,MID,COL
      double precision A(ROW,MID),B(MID,COL),AB(ROW,COL)
C *************************************************
      do 1000 I=1,ROW
      do 1010 J=1,COL
        AB(I,J)=0.0d+0
      do 1020 K=1,MID
        AB(I,J)=AB(I,J)+A(I,K)*B(K,J)
1020  continue
1010  continue
1000  continue
      return
      end
************************************************************************
** SUMBINW.....subroutine which collects the data for the number of atoms in each bin.**
************************************************************************
      subroutine SUMBINW(M,NMOLW,PEPCORD1,RXMAX2,GSUM,DELR,
     1    D2,D2MPEP,GRPSUM,NEIBOURSUM,HB,NHB,LX,LY,LZ,
     1    RW,DELZ,ZSUM)
      implicit   NONE
      integer I,J,M,N,BIN,NMOLW,GSUM(600,3)
      integer ZSUM(2000,2),C,BINZ,NHB
      integer GRPSUM(600,2,100),HB(100),NEIBOURSUM(100)
      double precision D,DSQ,RXMAX2,DELR,DISTMIN
      double precision D2(3,2000,3)
      double precision HALFLZ,LX,LY,LZ
      double precision RW(2000,3,3),DELZ,RWM(3,3)
      double precision PEPCORD1(200,3),D2MPEP(200,3)
C *************************************************
C ** COLLECTION OF DATA.                  **
C *************************************************
      DISTMIN=3.3d+0
      HALFLZ=LZ/2.d+0
** Density profile
      do 2100 I=1,3
        do 2200 C=1,3
          RWM(C,I)=RW(M,C,I)
```

```
2200    continue
2100  continue
** Oxygen
      BINZ=idint((RWM(3,1)+HALFLZ)/DELZ)+1
      ZSUM(BINZ,1)=ZSUM(BINZ,1)+1
** Hydrogen
      BINZ=idint((RWM(3,2)+HALFLZ)/DELZ)+1
      ZSUM(BINZ,2)=ZSUM(BINZ,2)+1
      BINZ=idint((RWM(3,3)+HALFLZ)/DELZ)+1
      ZSUM(BINZ,2)=ZSUM(BINZ,2)+1
**PEPTIDE-WATER PCF and nearest neighbour
     do 1400 N=1,NHB
       DSQ=D2MPEP(HB(N),1)
       if(DSQ.LE.RXMAX2) then
         D=dsqrt(DSQ)
         if(D.LE.DISTMIN) then
           NEIBOURSUM(N)=NEIBOURSUM(N)+1
         end if
         BIN=idint(D/DELR-0.5d+0)+1
         GRPSUM(BIN,1,N)=GRPSUM(BIN,1,N)+1
       end if
       do 1410 J=2,3
         DSQ=D2MPEP(HB(N),J)
         if(DSQ.LE.RXMAX2) then
           D=dsqrt(DSQ)
           BIN=idint(D/DELR-0.5d+0)+1
           GRPSUM(BIN,2,N)=GRPSUM(BIN,2,N)+1
         end if
1410    continue
1400  continue
**Water-Water PCF
     do 1100 N=1,M-1
       DSQ=D2(1,N,1)
       if(DSQ.le.RXMAX2)then
         D=dsqrt(DSQ)
         BIN=idint(D/DELR-0.5d+0)+1
         GSUM(BIN,1)=GSUM(BIN,1)+1
       endif
       do 1110 J=2,3
         DSQ=D2(1,N,J)
         if(DSQ.le.RXMAX2)then
           D=dsqrt(DSQ)
```

```
          BIN=idint(D/DELR-0.5d+0)+1
          GSUM(BIN,2)=GSUM(BIN,2)+1
        endif
1110    continue
      do 1120 I=2,3
        DSQ=D2(I,N,1)
        if(DSQ.le.RXMAX2)then
          D=dsqrt(DSQ)
          BIN=idint(D/DELR-0.5d+0)+1
          GSUM(BIN,2)=GSUM(BIN,2)+1
        endif
1120    continue
      do 1130 I=2,3
      do 1140 J=2,3
        DSQ=D2(I,N,J)
        if(DSQ.le.RXMAX2)then
          D=dsqrt(DSQ)
          BIN=idint(D/DELR-0.5d+0)+1
          GSUM(BIN,3)=GSUM(BIN,3)+1
        endif
1140    continue
1130    continue
1100  continue
    do 1200 N=M+1,NMOLW
      DSQ=D2(1,N,1)
      if(DSQ.le.RXMAX2)then
        D=dsqrt(DSQ)
        BIN=idint(D/DELR-0.5d+0)+1
        GSUM(BIN,1)=GSUM(BIN,1)+1
      endif
      do 1210 J=2,3
        DSQ=D2(1,N,J)
        if(DSQ.le.RXMAX2)then
          D=dsqrt(DSQ)
          BIN=idint(D/DELR-0.5d+0)+1
          GSUM(BIN,2)=GSUM(BIN,2)+1
        endif
1210    continue
      do 1220 I=2,3
        DSQ=D2(I,N,1)
        if(DSQ.le.RXMAX2)then
          D=dsqrt(DSQ)
```

```
            BIN=idint(D/DELR-0.5d+0)+1
            GSUM(BIN,2)=GSUM(BIN,2)+1
          endif
1220     continue
        do 1230 I=2,3
        do 1240 J=2,3
          DSQ=D2(I,N,J)
          if(DSQ.le.RXMAX2)then
            D=dsqrt(DSQ)
            BIN=idint(D/DELR-0.5d+0)+1
            GSUM(BIN,3)=GSUM(BIN,3)+1
          endif
1240     continue
1230     continue
1200  continue
      return
      end
*************************************************************************
** INCONFIG.....subroutine which sets up the initial configuration of water molecules for a cold start**
*************************************************************************
      subroutine INCONFIG(NMOL,NMOLW,LX,LY,LZ,LOHW,
     &  THHOH,RW,NATOM,PEPCORD1,PEPCORD2,APEP,
     &  CPEP,QPEP,AW,AA,ATOM,GROUP,NHB,HB,NEND,CEND,phi1,phi2,psi1,psi2,
     &  v1,v2,v3,v4,v5,v6,PEP,RESNUM)
      implicit   NONE
*************************************************************************
      integer I,IX,IY,IZ,N,NMOL,NMOLW,M
      integer FLAGX,FLAGY,FLAGZ,RESNUM
      integer NATOM,NHB,HB(100),NEND,CEND
      integer ATOM(200),AA(200),GROUP(200)
      double precision DL,LX,LY,LZ,DXHY,DYHY,LOHW,THHOH
      double precision TMP1,TMP2,TMP3, MAX2(3),MIN2(3)
      double precision VMAX,VWATER,MAX1(3),MIN1(3)
      double precision RW(2000,3,3),PEPCORD1(200,3)
      double precision PEPCORD2(200,3),APEP(200),CPEP(200),QPEP(200)
      double precision phi1(20),psi1(20),phi2(20),psi2(20)
      double precision v1,v2,v3,v4,v5,v6
      double precision AW(200)
      character PEP*15
      open(unit=10,file=PEP,status='unknown',form='formatted')
      read(10,*)
      read(10,*) NATOM
```

```
      if(NATOM.GT.200) STOP 'Matrix size too small'
      do 35000 M=1,NATOM
       read(10,889) AA(M),ATOM(M),GROUP(M),PEPCORD1(M,1),PEPCORD1(M,2),
     1              APEP(M),CPEP(M),QPEP(M),AW(M)
                    PEPCORD2(M,1)=PEPCORD1(M,1)
                    PEPCORD2(M,2)=PEPCORD1(M,2)
35000 continue
      read(10,*)
      read(10,*) NHB
      do 35010 M=1,NHB
       read(10,*) HB(M)
35010 continue
889   format(5x,I3,1x,I3,1x,I4,1x,f8.3,f8.3,8X,f8.3,f8.3,f8.3,f8.3)
      read(10,*) NEND
      read(10,*) CEND
      read(10,*)
      do 34700 I=1,2
       read(10,222) MAX1(I),MIN1(I)
       MAX1(I)=MAX1(I)+1.1d+0
       MIN1(I)=MIN1(I)-1.1d+0
               MAX2(I)=MAX1(I)
               MIN2(I)=MIN1(I)
34700 continue
             read(10,222) MAX1(3),MIN1(3)
             read(10,222) MAX2(3),MIN2(3)
      MAX1(3)=MAX1(3)+1.1d+0
      MIN1(3)=MIN1(3)-1.1d+0
      MAX2(3)=MAX2(3)+1.1d+0
      MIN2(3)=MIN2(3)-1.1d+0
222   format(f8.3,1x,f8.3)
      do I=1,RESNUM
       read(10,21)phi1(I),psi1(I)
       phi2(I)=phi1(I)
       psi2(I)=psi1(I)
      enddo
 21   format(5x,f8.3,5x,f8.3)
      read(10,22)v1,v2,v3,v4,v5,v6
 22   format(f8.3,f8.3,f8.3,f8.3,f8.3,f8.3)
             read(10,*)
             do M=1,NATOM
       read(10,23) PEPCORD1(M,3),PEPCORD2(M,3)
      enddo
```

```
 23   format(f8.3,f8.3)
      close(10)
      VMAX=1.d+0
      do 3000 I=1,3
        VMAX=dabs(MAX1(I)-MIN1(I))*VMAX
3000  continue
              VMAX=VMAX+VMAX
      VWATER=LX*LY*LZ-VMAX
      DL=(VWATER/NMOL)**(1.d+0/3.d+0)
C ****************************************************
C ** constants and stuff                        **
C ****************************************************
      DXHY=LOHW*dsin(THHOH/2.0d+0)
      DYHY=LOHW*dcos(THHOH/2.0d+0)
77777 IX=1
      IY=1
      IZ=1
      do 1000 N=1,NMOL
9999     TMP1=(dble(IX)-0.5d+0)*DL-LX/2.0d+0
        if(dabs(TMP1).LT.LX/2.d+0) then
          FLAGX=0
          TMP2=(dble(IY)-0.5d+0)*DL-LY/2.0d+0
          if(dabs(TMP2).LT.LY/2.d+0) then
            FLAGY=0
            TMP3=(dble(IZ)-0.5d+0)*DL-LZ/2.0d+0+1.5d+0
            if(dabs(TMP3).LT.LZ/2.d+0) then
              FLAGZ=0
            else
              write(6,*) 'Wait,configure fails,trying smaller DL'
              DL=DL*0.99d+0
              go to 77777
            end if
          else
            FLAGY=1
            goto 88888
          end if
        else
          FLAGX=1
          goto 99999
        end if
        if(((TMP1.LE.MAX1(1)).and.(TMP1.GE.MIN1(1)))
     $  .and.((TMP2.LE.MAX1(2)).and.(TMP2.GE.MIN1(2)))
```

```
     $  .and.((TMP3.LE.MAX2(3)).and.(TMP3.GE.MIN1(3)))) then
           IX=IX+1
           goto 9999
         else
           RW(N,1,1)=TMP1
           RW(N,2,1)=TMP2
           RW(N,3,1)=TMP3
           RW(N,1,2)=RW(N,1,1)-DXHY
           RW(N,2,2)=RW(N,2,1)+DYHY
           RW(N,3,2)=RW(N,3,1)
           RW(N,1,3)=RW(N,1,1)+DXHY
           RW(N,2,3)=RW(N,2,1)+DYHY
           RW(N,3,3)=RW(N,3,1)
           IX=IX+1
         end if
88888 if(FLAGY.EQ.1) then
       IX=1
       IY=1
       IZ=IZ+1
       goto 9999
      end if
99999 if(FLAGX.EQ.1) then
       IX=1
       IY=IY+1
       goto 9999
      end if
1000  continue
      return
      end
*************************************************************************
```

** RANDOM.....This function generates random numbers in the range 0.0 TO 1.0. It is a modification of the RANDOM subroutine in V.A. Dyck, J.D. Lawson and J.A. Smith, "FORTRAN 77: an introduction to structured problem solving", Prentice-Hall, New Jersey (1984).Modifications include the use of a 97-element array to shuffle the generated random deviates. This is the technique used with the RAN0, RAN1, and RAN2 functions in W.H. Press, B.P. Flannery, S.A. Teukolsky and W.T. Vetterling, "Numerical Recipes: The Art of Scientific Computing (FORTRAN Vers.)",Cambridge University Press,Cambridge (1989). This modified generator is used since it is easy to keep track of the current value of the seed (iseed). This is necessary in Monte Carlo simulations so that a simulation may be continued using the same series of random numbers if desired. Note : The constants used in this generator are for use on a 32 bit machine only (e.g. VAX, DecStation). It is not suitable for use on machines with other than 32 bit word sizes. Version 1.0 February,1992. Trevor Creamer. The code was obtained from the following web site:http://euripides.gws.uky.edu/~trevor/Public/random_f.html

```
*************************************************************************
```

```
      double precision function RANDOM(ISEED)
      implicit               NONE
*****************************************************************************
      integer        I,ISEED,MBIG1,MBIG2,MBIG3
      double precision N1,N2,RSMALL,RAN(97)
      logical        LFIRST
      data           MBIG1,MBIG2  /843314861,453816693/
      data           MBIG3,RSMALL /2147483647,0.4656612d-9/
      data           LFIRST,RAN   /.true.,97*0.0d+0/
C *****************************************************
C ** initialization of shuffling arry (1st call)   **
C *****************************************************
      if(LFIRST)then
        write(9,*)
        write(9,*) 'PARAMETERS FOR THE RANDOM # GENERATOR'
        write(9,*) MBIG1,MBIG2
        write(9,*) MBIG3,RSMALL
        do 1000 I=1,97
          ISEED=ISEED*MBIG1+MBIG2
          if(ISEED.lt.0)then
            ISEED=ISEED+MBIG3+1
          endif
          RAN(I)=dble(ISEED)*RSMALL
1000     continue
        LFIRST=.false.
      endif
C *****************************************************
C ** generation of a new random deviate using a linear congruential generator **
C *****************************************************
      ISEED=ISEED*MBIG1+MBIG2
      if(ISEED.lt.0)then
        ISEED=ISEED+MBIG3+1
      endif
      N1=dble(ISEED)*RSMALL
C *****************************************************
C ** use the new deviate to select one from the shuffling array and then replace the selected one in the array with the
newly generated deviate*
C *****************************************************
      I=idint(N1*97.0d+0)+1
      N2=RAN(I)
      RAN(I)=N1
      RANDOM=N2
```

```
      return
      end
*************************************************************************
** DISTWMSURF.....subroutine which calculates the squared distance between the atoms of the chosen molecules and the sites of the surfaces. **
*************************************************************************
      subroutine DISTWMSURF(D2SURF1,D2SURF2,RSURF,RM,NSURF,LX,LY)
      implicit NONE
      integer N,I,NSURF
      double precision LX,LY,DELX,DELY,DELZ1,DELZ2,CORX,CORY
      double precision D2SURF1(3,600),D2SURF2(3,600)
      double precision RM(3,3),RSURF(600,3)
      do 2000 N=1,NSURF
        DELX=RSURF(N,1)-RM(1,1)
        CORX=LX*dnint(DELX/LX)
        DELY=RSURF(N,2)-RM(2,1)
        CORY=LY*dnint(DELY/LY)
        do 2100 I=1,3
          DELX=RSURF(N,1)-RM(1,I)-CORX
          DELY=RSURF(N,2)-RM(2,I)-CORY
          DELZ1=RSURF(N,3)-RM(3,I)
          DELZ2=-RSURF(N,3)-RM(3,I)
          D2SURF1(I,N)=DELX*DELX+DELY*DELY+DELZ1*DELZ1
          D2SURF2(I,N)=DELX*DELX+DELY*DELY+DELZ2*DELZ2
2100     continue
2000  continue
      return
      end
*****************************************************
* PDBOUT: this subroutine generates a PDB output file. You can view it through RASMOL.          **
*****************************************************
      subroutine PDBOUT(RSURF,RW,PEPCORD1,PEPCORD2,FILENAME,NATOM,
     1                  NMOLW,NSURF,AA,ATOM,GROUP)
      implicit none
      character FILENAME*15
      integer NATOM,NMOLW,NSURF
      integer M,K,ALA,LYS
      integer N,H,CA,CB1,CB2,C,O,CG,CD,CE,NZ,HZ1,HZ2,HZ3
      integer AA(200),ATOM(200),GROUP(200)
      double precision RSURF(600,3),RW(2000,3,3),PEPCORD1(200,3)
      double precision PEPCORD2(200,3)
      ALA=1
```

```
 LYS=2
 C  =1
 CA =2
 CB1=3
 CB2=4
 CG =5
 H  =6
 N  =7
 O  =8
 CD =9
 CE =10
 NZ =11
 HZ1=12
 HZ2=13
 HZ3=14
 open(unit=8,file=FILENAME,status='unknown',form='formatted')
 write(8,*)'HEADER'
 do 223 M=1,NATOM
  if(ATOM(M).EQ.C) then
    if(AA(M).EQ.ALA) then
    write(8,950) M,GROUP(M),PEPCORD1(M,1),
1             PEPCORD1(M,2),PEPCORD1(M,3)
    else if(AA(M).EQ.LYS) then
    write(8,937) M,GROUP(M),PEPCORD1(M,1),
1             PEPCORD1(M,2),PEPCORD1(M,3)
    end if
  else if(ATOM(M).EQ.CA) then
    if(AA(M).EQ.ALA) then
    write(8,951) M,GROUP(M),PEPCORD1(M,1),
1             PEPCORD1(M,2),PEPCORD1(M,3)
    else if(AA(M).EQ.LYS) then
    write(8,938) M,GROUP(M),PEPCORD1(M,1),
1             PEPCORD1(M,2),PEPCORD1(M,3)
    end if
  else if(ATOM(M).EQ.CB1) then
    if(AA(M).EQ.ALA) then
    write(8,952) M,GROUP(M),PEPCORD1(M,1),
1             PEPCORD1(M,2),PEPCORD1(M,3)
    else if(AA(M).EQ.LYS) then
    write(8,939) M,GROUP(M),PEPCORD1(M,1),
1             PEPCORD1(M,2),PEPCORD1(M,3)
    end if
```

```
      else if(ATOM(M).EQ.CB2) then
       if(AA(M).EQ.ALA) then
       write(8,953) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       else if(AA(M).EQ.LYS) then
       write(8,940) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       end if
      else if(ATOM(M).EQ.CG) then
       if(AA(M).EQ.ALA) then
       write(8,954) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       else if(AA(M).EQ.LYS) then
       write(8,941) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       end if
      else if(ATOM(M).EQ.CD) then
       if(AA(M).EQ.ALA) then
       write(8,955) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       else if(AA(M).EQ.LYS) then
       write(8,942) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       end if
      else if(ATOM(M).EQ.CE) then
       if(AA(M).EQ.ALA) then
       write(8,956) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       else if(AA(M).EQ.LYS) then
       write(8,943) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       end if
      else if(ATOM(M).EQ.H) then
       if(AA(M).EQ.ALA) then
       write(8,957) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       else if(AA(M).EQ.LYS) then
       write(8,944) M,GROUP(M),PEPCORD1(M,1),
     1            PEPCORD1(M,2),PEPCORD1(M,3)
       end if
      else if(ATOM(M).EQ.N) then
       if(AA(M).EQ.ALA) then
```

```
      write(8,958) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      else if(AA(M).EQ.LYS) then
      write(8,945) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      end if
    else if(ATOM(M).EQ.NZ) then
      if(AA(M).EQ.ALA) then
      write(8,959) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      else if(AA(M).EQ.LYS) then
      write(8,946) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      end if
    else if(ATOM(M).EQ.O) then
      if(AA(M).EQ.ALA) then
      write(8,960) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      else if(AA(M).EQ.LYS) then
      write(8,947) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      end if
    else if(ATOM(M).EQ.HZ1) then
      if(AA(M).EQ.ALA) then
      write(8,961) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      else if(AA(M).EQ.LYS) then
      write(8,948) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      end if
    else if(ATOM(M).EQ.HZ2) then
      if(AA(M).EQ.ALA) then
      write(8,962) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      else if(AA(M).EQ.LYS) then
      write(8,949) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
      end if
    else if(ATOM(M).EQ.HZ3) then
      if(AA(M).EQ.ALA) then
      write(8,963) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
```

```
        else if(AA(M).EQ.LYS) then
        write(8,850) M,GROUP(M),PEPCORD1(M,1),
     1             PEPCORD1(M,2),PEPCORD1(M,3)
        end if
      end if
  223 continue
      do 230 M=1,NATOM
      if(ATOM(M).EQ.C) then
        if(AA(M).EQ.ALA) then
        write(8,950) M,GROUP(M),PEPCORD2(M,1),
     1             PEPCORD2(M,2),PEPCORD2(M,3)
        else if(AA(M).EQ.LYS) then
        write(8,937) M,GROUP(M),PEPCORD2(M,1),
     1             PEPCORD2(M,2),PEPCORD2(M,3)
        end if
       else if(ATOM(M).EQ.CA) then
        if(AA(M).EQ.ALA) then
        write(8,951) M,GROUP(M),PEPCORD2(M,1),
     1             PEPCORD2(M,2),PEPCORD2(M,3)
        else if(AA(M).EQ.LYS) then
        write(8,938) M,GROUP(M),PEPCORD2(M,1),
     1             PEPCORD2(M,2),PEPCORD2(M,3)
        end if
      else if(ATOM(M).EQ.CB1) then
        if(AA(M).EQ.ALA) then
        write(8,952) M,GROUP(M),PEPCORD2(M,1),
     1             PEPCORD2(M,2),PEPCORD2(M,3)
        else if(AA(M).EQ.LYS) then
        write(8,939) M,GROUP(M),PEPCORD2(M,1),
     1             PEPCORD2(M,2),PEPCORD2(M,3)
        end if
      else if(ATOM(M).EQ.CB2) then
        if(AA(M).EQ.ALA) then
        write(8,953) M,GROUP(M),PEPCORD2(M,1),
     1             PEPCORD2(M,2),PEPCORD2(M,3)
        else if(AA(M).EQ.LYS) then
        write(8,940) M,GROUP(M),PEPCORD2(M,1),
     1             PEPCORD2(M,2),PEPCORD2(M,3)
        end if
      else if(ATOM(M).EQ.CG) then
        if(AA(M).EQ.ALA) then
        write(8,954) M,GROUP(M),PEPCORD2(M,1),
```

```
1               PEPCORD2(M,2),PEPCORD2(M,3)
     else if(AA(M).EQ.LYS) then
     write(8,941) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     end if
   else if(ATOM(M).EQ.CD) then
     if(AA(M).EQ.ALA) then
     write(8,955) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     else if(AA(M).EQ.LYS) then
     write(8,942) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     end if
   else if(ATOM(M).EQ.CE) then
     if(AA(M).EQ.ALA) then
     write(8,956) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     else if(AA(M).EQ.LYS) then
     write(8,943) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     end if
   else if(ATOM(M).EQ.H) then
     if(AA(M).EQ.ALA) then
     write(8,957) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     else if(AA(M).EQ.LYS) then
     write(8,944) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     end if
   else if(ATOM(M).EQ.N) then
     if(AA(M).EQ.ALA) then
     write(8,958) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     else if(AA(M).EQ.LYS) then
     write(8,945) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     end if
   else if(ATOM(M).EQ.NZ) then
     if(AA(M).EQ.ALA) then
     write(8,959) M,GROUP(M),PEPCORD2(M,1),
1               PEPCORD2(M,2),PEPCORD2(M,3)
     else if(AA(M).EQ.LYS) then
```

```
        write(8,946) M,GROUP(M),PEPCORD2(M,1),
     1              PEPCORD2(M,2),PEPCORD2(M,3)
        end if
       else if(ATOM(M).EQ.O) then
        if(AA(M).EQ.ALA) then
        write(8,960) M,GROUP(M),PEPCORD2(M,1),
     1              PEPCORD2(M,2),PEPCORD2(M,3)
        else if(AA(M).EQ.LYS) then
        write(8,947) M,GROUP(M),PEPCORD2(M,1),
     1              PEPCORD2(M,2),PEPCORD2(M,3)
        end if
       else if(ATOM(M).EQ.HZ1) then
        if(AA(M).EQ.ALA) then
        write(8,961) M,GROUP(M),PEPCORD2(M,1),
     1              PEPCORD2(M,2),PEPCORD2(M,3)
        else if(AA(M).EQ.LYS) then
        write(8,948) M,GROUP(M),PEPCORD2(M,1),
     1              PEPCORD2(M,2),PEPCORD2(M,3)
        end if
       else if(ATOM(M).EQ.HZ2) then
        if(AA(M).EQ.ALA) then
        write(8,962) M,GROUP(M),PEPCORD2(M,1),
     1              PEPCORD2(M,2),PEPCORD2(M,3)
        else if(AA(M).EQ.LYS) then
        write(8,949) M,GROUP(M),PEPCORD2(M,1),
     1              PEPCORD2(M,2),PEPCORD2(M,3)
        end if
       else if(ATOM(M).EQ.HZ3) then
        if(AA(M).EQ.ALA) then
        write(8,963) M,GROUP(M),PEPCORD2(M,1),
     1              PEPCORD2(M,2),PEPCORD2(M,3)
        else if(AA(M).EQ.LYS) then
        write(8,850) M,GROUP(M),PEPCORD2(M,1),
     1              PEPCORD2(M,2),PEPCORD2(M,3)
        end if
       end if
230    continue
       K=NATOM
       do 224 M=1,NMOLW
        K=K+1
        write(8,964) K,9,RW(M,1,1),RW(M,2,1),RW(M,3,1)
        K=K+1
```

```
      write(8,965) K,10,RW(M,1,2),RW(M,2,2),RW(M,3,2)
      K=K+1
      write(8,965) K,10,RW(M,1,3),RW(M,2,3),RW(M,3,3)
224   continue
    do 226 M=1,NSURF
      K=K+1
      write(8,966) K,11,RSURF(M,1),RSURF(M,2),RSURF(M,3)
      K=K+1
      write(8,966) K,12,RSURF(M,1),RSURF(M,2),-RSURF(M,3)
226   continue
937   format('ATOM  ',I5,1x,' C  ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
938   format('ATOM  ',I5,1x,' CA ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
939   format('ATOM  ',I5,1x,' CB1',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
940   format('ATOM  ',I5,1x,' CB2',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
941   format('ATOM  ',I5,1x,' CG ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
942   format('ATOM  ',I5,1x,' CD ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
943   format('ATOM  ',I5,1x,' CE ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
944   format('ATOM  ',I5,1x,' H  ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
945   format('ATOM  ',I5,1x,' N  ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
946   format('ATOM  ',I5,1x,' NZ ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
947   format('ATOM  ',I5,1x,' O  ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
948   format('ATOM  ',I5,1x,' HZ1',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
949   format('ATOM  ',I5,1x,' HZ2',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
850   format('ATOM  ',I5,1x,' HZ3',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
950   format('ATOM  ',I5,1x,' C  ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
951   format('ATOM  ',I5,1x,' CA ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
952   format('ATOM  ',I5,1x,' CB1',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
953   format('ATOM  ',I5,1x,' CB2',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
954   format('ATOM  ',I5,1x,' CG ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
955   format('ATOM  ',I5,1x,' CD ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
956   format('ATOM  ',I5,1x,' CE ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
957   format('ATOM  ',I5,1x,' H  ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
958   format('ATOM  ',I5,1x,' N  ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
959   format('ATOM  ',I5,1x,' NZ ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
960   format('ATOM  ',I5,1x,' O  ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
961   format('ATOM  ',I5,1x,' HZ1',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
962   format('ATOM  ',I5,1x,' HZ2',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
963   format('ATOM  ',I5,1x,' HZ3',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
964   format('ATOM  ',I5,1x,' OW ',1x,'H2O',2x,I4,4x,f8.3,f8.3,f8.3)
965   format('ATOM  ',I5,1x,' HW ',1x,'H2O',2x,I4,4x,f8.3,f8.3,f8.3)
966   format('ATOM  ',I5,1x,' CH2',1x,'SUF',2x,I4,4x,f8.3,f8.3,f8.3)
    close(8)
```

```
      return
      end
*************************************************************************
** DISTWMPEP.....subroutine which calculates the squared distances between the atoms of the chosen molecule and the atoms of the closest images of the remaining molecules in the system.          **
*************************************************************************
      subroutine DISTWMPEP(D2MPEP,PEPCORD,NATOM,RM,LX,LY,COM)
      implicit   NONE
      integer    N,I,NATOM
      double precision DELX,DELY,DELZ,LX,LY,CORX,CORY
      double precision D2MPEP(200,3),RM(3,3),COM(3)
      double precision PEPCORD(200,3)
C ************************************************
C ** SQUARED DISTANCES.                    **
C ** note that the minimum image convention is applied only to oxygen pairs.              **
C ************************************************
      DELX=RM(1,1)-COM(1)
      CORX=LX*dnint(DELX/LX)
      DELY=RM(2,1)-COM(2)
      CORY=LY*dnint(DELY/LY)
      do 1010 I=1,3
        do 1020 N=1,NATOM
          DELX=RM(1,I)-PEPCORD(N,1)-CORX
          DELY=RM(2,I)-PEPCORD(N,2)-CORY
          DELZ=RM(3,I)-PEPCORD(N,3)
          D2MPEP(N,I)=DELX*DELX+DELY*DELY+DELZ*DELZ
1020  continue
1010  continue
      return
      end
*************************************************************************
** DISTPP.....subroutine which calculates the squared distances between the atoms of the chosen peptide molecule and the atoms of the closest images of the remaining peptide molecules in the system.**
*************************************************************************
      subroutine DISTPP(D2PP,PEPCORD1,PEPCORD2,NATOM,LX,LY,COM1,COM2)
      implicit   NONE
      integer    N,I,NATOM
      double precision DELX,DELY,DELZ,LX,LY,CORX,CORY
      double precision D2PP(200,200),COM1(3),COM2(3)
      double precision PEPCORD1(200,3),PEPCORD2(200,3)
C ************************************************
C ** SQUARED DISTANCES.                    **
```

```
C ** note that the minimum image convention is applied only to COM                **
C ***************************************************
      DELX=COM1(1)-COM2(1)
      CORX=LX*dnint(DELX/LX)
      DELY=COM1(2)-COM2(2)
      CORY=LY*dnint(DELY/LY)
      do 1011 I=1,NATOM
        do 1021 N=1,NATOM
          DELX=PEPCORD1(I,1)-PEPCORD2(N,1)-CORX
          DELY=PEPCORD1(I,2)-PEPCORD2(N,2)-CORY
          DELZ=PEPCORD1(I,3)-PEPCORD2(N,3)
          D2PP(N,I)=DELX*DELX+DELY*DELY+DELZ*DELZ
1021  continue
1011  continue
      return
      end
*************************************************************************
** DISTPEPSF.....subroutine which calculates the squared distance between the atoms of the chosen molecules and the sites of the surfaces. **
*************************************************************************
      subroutine DISTPEPSF(D2PEPSF1,D2PEPSF2,RSURF,NSURF,PEPCORD1,NATOM,
     1          LX,LY,COM)
      implicit NONE
      integer N,M,NSURF,NATOM
      double precision LX,LY,DELX,DELY,DELZ1,DELZ2,CORX,CORY
      double precision D2PEPSF1(200,600),D2PEPSF2(200,600)
      double precision PEPCORD1(200,3)
      double precision RSURF(600,3),COM(3)
      do 2000 N=1,NSURF
        DELX=RSURF(N,1)-COM(1)
        CORX=LX*dnint(DELX/LX)
        DELY=RSURF(N,2)-COM(2)
        CORY=LY*dnint(DELY/LY)
        do 2100 M=1,NATOM
          DELX=RSURF(N,1)-PEPCORD1(M,1)-CORX
          DELY=RSURF(N,2)-PEPCORD1(M,2)-CORY
          DELZ1=RSURF(N,3)-PEPCORD1(M,3)
          DELZ2=-RSURF(N,3)-PEPCORD1(M,3)
          D2PEPSF1(M,N)=DELX*DELX+DELY*DELY+DELZ1*DELZ1
          D2PEPSF2(M,N)=DELX*DELX+DELY*DELY+DELZ2*DELZ2
2100    continue
2000  continue
```

```
      return
      end

*************************************************************************
** NRGPEPSF: subroutine which calculates the potential energy "felt"by a chosen molecule.  **
*************************************************************************
      subroutine NRGPEPSF(A12PX,C6PX,QCONPX,VPEPSF,D2PEPSF1,D2PEPSF2,
     1              NSURF,NATOM)
      implicit   NONE
*************************************************************************
      integer         M,N,NSURF,NATOM
      double precision D6,D12,VPEPSF,DSURF
      double precision D2PEPSF1(200,600),D2PEPSF2(200,600)
      double precision A12PX(200,2),C6PX(200,2),QCONPX(200,2)
      VPEPSF=0.d+0
      do 2000 M=1,NATOM
        do 2100 N=1,NSURF
        DSURF=dsqrt(D2PEPSF1(M,N))
        D6=D2PEPSF1(M,N)**3
        D12=D6*D6
        VPEPSF=VPEPSF+A12PX(M,1)/D12-C6PX(M,1)/D6
     1       +QCONPX(M,1)/DSURF
        DSURF=dsqrt(D2PEPSF2(M,N))
        D6=D2PEPSF2(M,N)**3
        D12=D6*D6
        VPEPSF=VPEPSF+A12PX(M,2)/D12-C6PX(M,2)/D6
     1       +QCONPX(M,2)/DSURF
2100    continue
2000  continue
      return
      end
*************************************************************************
** NRGWMPEP: subroutine which calculates the potential energy "felt" by a chosen molecule.
*************************************************************************
      subroutine NRGWMPEP(D2MPEP,A12PX,C6PX,QCONPX,VMPEP,NATOM)
      implicit   NONE
*************************************************************************
      integer         M,I,NATOM
      double precision VMPEP,D,D6,D12
      double precision A12PX(200,3),C6PX(200,3),QCONPX(200,3)
      double precision D2MPEP(200,3)
C *************************************************
```

```
C ** ENERGY CALCULATION.
C ** the calculation includes all pairs of atoms in the chosen molecule and the closest images of the remaining molecules.          **
C ***************************************************
      VMPEP=0.d+0
      do 1000 I=1,3
        do 1010 M=1,NATOM
        D=dsqrt(D2MPEP(M,I))
        D6=D2MPEP(M,I)**3
        D12=D6*D6
        VMPEP=VMPEP+A12PX(M,I)/D12-C6PX(M,I)/D6+QCONPX(M,I)/D
1010    continue
1000  continue
      return
      end
*************************************************************************
** NRGPP: subroutine which calculates the potential energy "felt" by a chosen peptide molecule from the atoms of the remaining peptides.**
*************************************************************************
      subroutine NRGPP(D2PP,A12PP,C6PP,QCONPP,VPP,NATOM)
      implicit   NONE
*************************************************************************
      integer         M,I,NATOM
      double precision VPP,D,D6,D12
      double precision A12PP(200,200),C6PP(200,200),QCONPP(200,200)
      double precision D2PP(200,200)
C ***************************************************
C ** ENERGY CALCULATION.                    **
C ** the calculation includes all pairs of atoms in the chosen molecule and the closest images of the remaining molecules. **
C ***************************************************
      VPP=0.d+0
      do 1001 I=1,NATOM
        do 1011 M=1,NATOM
        D=dsqrt(D2PP(M,I))
        D6=D2PP(M,I)**3
        D12=D6*D6
        VPP=VPP+A12PP(M,I)/D12-C6PP(M,I)/D6+QCONPP(M,I)/D
1011    continue
1001  continue
      return
      end
```

```
**************************************************************************
** MOVEPEP.....subroutine which randomly displaces a molecule. the displacement is performed as a translational displacement of the molecule coupled with a rotational displacement about the position of the oxygen atom. **
**************************************************************************
      subroutine MOVEPEP(NATOM,PEPCORD1,COM,MXTPEP,MXRPEP,
     1                   LX,LY,LZ,ISEED)
      implicit   NONE
      external   MULTMAT,RANDOM
**************************************************************************
      integer         I,M,ISEED,NATOM
      double precision LX,LY,LZ,DELC,MXTPEP,MXRPEP,THX,THY,THZ
      double precision COSX,SINX,COSY,SINY,COSZ,SINZ
      double precision ROTX(3,3),ROTY(3,3),ROTZ(3,3),TMP1(3,3)
      double precision TMP2(3,3),COM(3)
      double precision PEPCORD1(200,3),RHYOLD(3,200),RHYNEW(3,200)
      double precision RANDOM,L(3)
      L(1)=LX
      L(2)=LY
      L(3)=LZ
C *****************************************************
C ** HYDROGEN COORDINATE MATRIX.                  **
C ** the positions of the hydrogen atoms are defined relative to the oxygen atom.       **
C *****************************************************
      do 1000 M=1,NATOM
        do 1010 I=1,3
          RHYOLD(I,M)=PEPCORD1(M,I)-COM(I)
1010  continue
1000  continue
c *****************************************************
C ** RANDOM ROTATION.                          **
C *****************************************************
      THX=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MXRPEP
      THY=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MXRPEP
      THZ=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MXRPEP
      COSX=dcos(THX)
      SINX=dsin(THX)
      COSY=dcos(THY)
      SINY=dsin(THY)
      COSZ=dcos(THZ)
      SINZ=dsin(THZ)
      ROTX(1,1)=1.0d+0
      ROTX(1,2)=0.0d+0
```

```
      ROTX(1,3)=0.0d+0
      ROTX(2,1)=0.0d+0
      ROTX(2,2)=COSX
      ROTX(2,3)=-SINX
      ROTX(3,1)=0.0d+0
      ROTX(3,2)=SINX
      ROTX(3,3)=COSX
      ROTY(1,1)=COSY
      ROTY(1,2)=0.0d+0
      ROTY(1,3)=-SINY
      ROTY(2,1)=0.0d+0
      ROTY(2,2)=1.0d+0
      ROTY(2,3)=0.0d+0
      ROTY(3,1)=SINY
      ROTY(3,2)=0.0d+0
      ROTY(3,3)=COSY
      ROTZ(1,1)=COSZ
      ROTZ(1,2)=-SINZ
      ROTZ(1,3)=0.0d+0
      ROTZ(2,1)=SINZ
      ROTZ(2,2)=COSZ
      ROTZ(2,3)=0.0d+0
      ROTZ(3,1)=0.0d+0
      ROTZ(3,2)=0.0d+0
      ROTZ(3,3)=1.0d+0
      call MULTMAT(ROTX,ROTY,3,3,3,TMP1)
      call MULTMAT(TMP1,ROTZ,3,3,3,TMP2)
      call MULTMAT(TMP2,RHYOLD,3,3,NATOM,RHYNEW)
C *************************************************
C ** RANDOM TRANSLATION.                  **
C *************************************************
      do 100 I=1,3
        DELC=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MXTPEP*L(I)/LX
        COM(I)=COM(I)+DELC
        if(I.NE.3) then
          COM(I)=COM(I)-L(I)*dnint(COM(I)/L(I))
        end if
        do 110 M=1,NATOM
          PEPCORD1(M,I)=COM(I)+RHYNEW(I,M)
110     continue
100   continue
      return
```

```
      end
*************************************************************************
** SUBROUTINE WHICH CALCULATES THE ENERGY OF THE PEPTIDE MOLECULE ******
*************************************************************************
      SUBROUTINE pepenrg(confgE,APEP,CPEP,QPEP,PEPCORD1,NATOM,
     1   phi,psi,v1,v2,v3,v4,v5,v6,RESNUM)
      integer NATOM,M
      integer I,RESNUM
      double precision PEPCORD1(200,3),APEP(200),CPEP(200),QPEP(200)
      double precision QFACTP,TEMP,A12P(200,200),C6P(200,200)
      double precision QCONP(200,200)
      double precision AP(200,200),CP(200,200)
      double precision D2PEP(200,200),DELX,DELY,DELZ
      double precision PVPEP,DSURF,D6,D12,VTOR
      double precision phi(20),psi(20),confgE
      double precision v1,v2,v3,v4,v5,v6
c *************************************************************************
c ** The non-bonded interaction energy calculations **
c *************************************************************************
c *************     LJ Potential Calculations   *****************
      TEMP=298.0
      QFACTP=1.671d+5/TEMP
      do 200 M=1,NATOM-1
      do 201 I=M+1,NATOM
        AP(M,I)=dsqrt( APEP(M)*APEP(I) )
        CP(M,I)=dsqrt( CPEP(M)*CPEP(I) )
 201    continue
 200    continue
      do 202 M=1,NATOM-1
         do 203 I=M+1,NATOM
          A12P(M,I)=(AP(M,I)**12)/TEMP
          C6P(M,I)=(CP(M,I)**6)/TEMP
          QCONP(M,I)=QFACTP*QPEP(M)*QPEP(I)
 203       continue
 202    continue
      A12P(1,2)=0.0d+0
      A12P(1,3)=0.0d+0
      A12P(1,4)=0.0d+0
      A12P(1,5)=0.0d+0
      A12P(2,1)=0.0d+0
      A12P(2,3)=0.0d+0
      A12P(3,1)=0.0d+0
```

```
A12P(3,2)=0.0d+0
A12P(3,4)=0.0d+0
A12P(3,5)=0.0d+0
A12P(3,6)=0.0d+0
A12P(3,7)=0.0d+0
A12P(4,1)=0.0d+0
A12P(4,3)=0.0d+0
A12P(4,5)=0.0d+0
A12P(5,1)=0.0d+0
A12P(5,3)=0.0d+0
A12P(5,4)=0.0d+0
A12P(5,6)=0.0d+0
A12P(5,7)=0.0d+0
A12P(5,8)=0.0d+0
A12P(5,9)=0.0d+0
A12P(6,3)=0.0d+0
A12P(6,5)=0.0d+0
A12P(6,7)=0.0d+0
A12P(7,3)=0.0d+0
A12P(7,5)=0.0d+0
A12P(7,6)=0.0d+0
A12P(7,8)=0.0d+0
A12P(7,9)=0.0d+0
A12P(7,10)=0.0d+0
A12P(7,11)=0.0d+0
A12P(8,5)=0.0d+0
A12P(8,7)=0.0d+0
A12P(8,9)=0.0d+0
A12P(9,5)=0.0d+0
A12P(9,7)=0.0d+0
A12P(9,8)=0.0d+0
A12P(9,10)=0.0d+0
A12P(9,11)=0.0d+0
A12P(9,12)=0.0d+0
A12P(9,13)=0.0d+0
A12P(10,9)=0.0d+0
A12P(10,7)=0.0d+0
A12P(10,11)=0.0d+0
A12P(11,7)=0.0d+0
A12P(11,9)=0.0d+0
A12P(11,10)=0.0d+0
A12P(11,12)=0.0d+0
```

```
A12P(11,13)=0.0d+0
A12P(11,14)=0.0d+0
A12P(11,15)=0.0d+0
A12P(12,11)=0.0d+0
A12P(12,9)=0.0d+0
A12P(12,13)=0.0d+0
A12P(13,9)=0.0d+0
A12P(13,12)=0.0d+0
A12P(13,11)=0.0d+0
A12P(13,14)=0.0d+0
A12P(13,15)=0.0d+0
A12P(13,16)=0.0d+0
A12P(13,17)=0.0d+0
A12P(14,11)=0.0d+0
A12P(14,13)=0.0d+0
A12P(14,15)=0.0d+0
A12P(15,11)=0.0d+0
A12P(15,13)=0.0d+0
A12P(15,14)=0.0d+0
A12P(15,16)=0.0d+0
A12P(15,17)=0.0d+0
A12P(15,18)=0.0d+0
A12P(15,19)=0.0d+0
A12P(16,13)=0.0d+0
A12P(16,15)=0.0d+0
A12P(16,17)=0.0d+0
A12P(17,13)=0.0d+0
A12P(17,15)=0.0d+0
A12P(17,16)=0.0d+0
A12P(17,18)=0.0d+0
A12P(17,19)=0.0d+0
A12P(17,20)=0.0d+0
A12P(17,21)=0.0d+0
A12P(18,15)=0.0d+0
A12P(18,17)=0.0d+0
A12P(18,19)=0.0d+0
A12P(19,15)=0.0d+0
A12P(19,17)=0.0d+0
A12P(19,18)=0.0d+0
A12P(19,20)=0.0d+0
A12P(19,21)=0.0d+0
A12P(19,22)=0.0d+0
```

A12P(19,23)=0.0d+0
A12P(20,17)=0.0d+0
A12P(20,19)=0.0d+0
A12P(20,21)=0.0d+0
A12P(21,17)=0.0d+0
A12P(21,19)=0.0d+0
A12P(21,20)=0.0d+0
A12P(21,22)=0.0d+0
A12P(21,23)=0.0d+0
A12P(21,24)=0.0d+0
A12P(21,25)=0.0d+0
A12P(22,19)=0.0d+0
A12P(22,21)=0.0d+0
A12P(22,23)=0.0d+0
A12P(23,19)=0.0d+0
A12P(23,22)=0.0d+0
A12P(23,21)=0.0d+0
A12P(23,24)=0.0d+0
A12P(23,25)=0.0d+0
A12P(23,26)=0.0d+0
A12P(23,27)=0.0d+0
A12P(24,21)=0.0d+0
A12P(24,23)=0.0d+0
A12P(24,25)=0.0d+0
A12P(25,21)=0.0d+0
A12P(25,23)=0.0d+0
A12P(25,24)=0.0d+0
A12P(25,26)=0.0d+0
A12P(25,27)=0.0d+0
A12P(25,28)=0.0d+0
A12P(25,29)=0.0d+0
A12P(26,23)=0.0d+0
A12P(26,25)=0.0d+0
A12P(26,27)=0.0d+0
A12P(27,23)=0.0d+0
A12P(27,25)=0.0d+0
A12P(27,26)=0.0d+0
A12P(27,28)=0.0d+0
A12P(27,29)=0.0d+0
A12P(27,30)=0.0d+0
A12P(27,31)=0.0d+0
A12P(28,25)=0.0d+0

```
A12P(28,27)=0.0d+0
A12P(28,29)=0.0d+0
A12P(29,25)=0.0d+0
A12P(29,27)=0.0d+0
A12P(29,28)=0.0d+0
A12P(29,30)=0.0d+0
A12P(29,31)=0.0d+0
A12P(29,32)=0.0d+0
A12P(29,33)=0.0d+0
A12P(30,27)=0.0d+0
A12P(30,29)=0.0d+0
A12P(30,31)=0.0d+0
A12P(31,27)=0.0d+0
A12P(31,29)=0.0d+0
A12P(31,30)=0.0d+0
A12P(31,32)=0.0d+0
A12P(31,33)=0.0d+0
A12P(31,34)=0.0d+0
A12P(31,42)=0.0d+0
A12P(32,29)=0.0d+0
A12P(32,31)=0.0d+0
A12P(32,33)=0.0d+0
A12P(33,29)=0.0d+0
A12P(33,31)=0.0d+0
A12P(33,32)=0.0d+0
A12P(33,34)=0.0d+0
A12P(33,35)=0.0d+0
A12P(33,42)=0.0d+0
A12P(33,43)=0.0d+0
A12P(33,44)=0.0d+0
A12P(34,33)=0.0d+0
A12P(34,31)=0.0d+0
A12P(34,42)=0.0d+0
A12P(34,35)=0.0d+0
A12P(34,36)=0.0d+0
A12P(35,33)=0.0d+0
A12P(35,34)=0.0d+0
A12P(35,36)=0.0d+0
A12P(35,37)=0.0d+0
A12P(36,34)=0.0d+0
A12P(36,35)=0.0d+0
A12P(36,37)=0.0d+0
```

```
A12P(36,38)=0.0d+0
A12P(37,35)=0.0d+0
A12P(37,36)=0.0d+0
A12P(37,38)=0.0d+0
A12P(37,39)=0.0d+0
A12P(37,40)=0.0d+0
A12P(38,36)=0.0d+0
A12P(38,37)=0.0d+0
A12P(38,39)=0.0d+0
A12P(38,40)=0.0d+0
A12P(38,41)=0.0d+0
A12P(39,37)=0.0d+0
A12P(39,38)=0.0d+0
A12P(39,40)=0.0d+0
A12P(39,41)=0.0d+0
A12P(40,37)=0.0d+0
A12P(40,38)=0.0d+0
A12P(40,39)=0.0d+0
A12P(40,41)=0.0d+0
A12P(41,37)=0.0d+0
A12P(41,38)=0.0d+0
A12P(41,39)=0.0d+0
A12P(41,40)=0.0d+0
A12P(42,31)=0.0d+0
A12P(42,33)=0.0d+0
A12P(42,34)=0.0d+0
A12P(42,43)=0.0d+0
A12P(42,44)=0.0d+0
A12P(42,45)=0.0d+0
A12P(42,46)=0.0d+0
A12P(43,33)=0.0d+0
A12P(43,42)=0.0d+0
A12P(43,44)=0.0d+0
A12P(44,33)=0.0d+0
A12P(44,42)=0.0d+0
A12P(44,43)=0.0d+0
A12P(44,45)=0.0d+0
A12P(44,46)=0.0d+0
A12P(44,47)=0.0d+0
A12P(44,55)=0.0d+0
A12P(45,42)=0.0d+0
A12P(45,44)=0.0d+0
```

```
A12P(45,46)=0.0d+0
A12P(46,42)=0.0d+0
A12P(46,44)=0.0d+0
A12P(46,45)=0.0d+0
A12P(46,47)=0.0d+0
A12P(46,48)=0.0d+0
A12P(46,55)=0.0d+0
A12P(46,56)=0.0d+0
A12P(46,57)=0.0d+0
A12P(47,44)=0.0d+0
A12P(47,46)=0.0d+0
A12P(47,48)=0.0d+0
A12P(47,49)=0.0d+0
A12P(47,55)=0.0d+0
A12P(48,46)=0.0d+0
A12P(48,47)=0.0d+0
A12P(48,49)=0.0d+0
A12P(48,50)=0.0d+0
A12P(49,47)=0.0d+0
A12P(49,48)=0.0d+0
A12P(49,50)=0.0d+0
A12P(49,51)=0.0d+0
A12P(50,49)=0.0d+0
A12P(50,48)=0.0d+0
A12P(50,51)=0.0d+0
A12P(50,52)=0.0d+0
A12P(50,53)=0.0d+0
A12P(51,49)=0.0d+0
A12P(51,50)=0.0d+0
A12P(51,52)=0.0d+0
A12P(51,53)=0.0d+0
A12P(51,54)=0.0d+0
A12P(52,50)=0.0d+0
A12P(52,51)=0.0d+0
A12P(52,53)=0.0d+0
A12P(52,54)=0.0d+0
A12P(53,50)=0.0d+0
A12P(53,51)=0.0d+0
A12P(53,52)=0.0d+0
A12P(53,54)=0.0d+0
A12P(54,50)=0.0d+0
A12P(54,51)=0.0d+0
```

A12P(54,52)=0.0d+0
A12P(54,53)=0.0d+0
A12P(55,44)=0.0d+0
A12P(55,46)=0.0d+0
A12P(55,47)=0.0d+0
A12P(55,56)=0.0d+0
A12P(55,57)=0.0d+0
A12P(55,58)=0.0d+0
A12P(56,46)=0.0d+0
A12P(56,55)=0.0d+0
A12P(56,57)=0.0d+0
A12P(57,46)=0.0d+0
A12P(57,55)=0.0d+0
A12P(57,56)=0.0d+0
A12P(57,58)=0.0d+0
A12P(57,59)=0.0d+0
A12P(57,60)=0.0d+0
A12P(57,68)=0.0d+0
A12P(58,55)=0.0d+0
A12P(58,57)=0.0d+0
A12P(58,59)=0.0d+0
A12P(59,55)=0.0d+0
A12P(59,57)=0.0d+0
A12P(59,58)=0.0d+0
A12P(59,60)=0.0d+0
A12P(59,61)=0.0d+0
A12P(59,68)=0.0d+0
A12P(59,69)=0.0d+0
A12P(59,70)=0.0d+0
A12P(60,57)=0.0d+0
A12P(60,59)=0.0d+0
A12P(60,68)=0.0d+0
A12P(60,61)=0.0d+0
A12P(60,62)=0.0d+0
A12P(61,59)=0.0d+0
A12P(61,60)=0.0d+0
A12P(61,62)=0.0d+0
A12P(61,63)=0.0d+0
A12P(62,60)=0.0d+0
A12P(62,61)=0.0d+0
A12P(62,63)=0.0d+0
A12P(62,64)=0.0d+0

A12P(63,61)=0.0d+0
A12P(63,62)=0.0d+0
A12P(63,64)=0.0d+0
A12P(63,65)=0.0d+0
A12P(63,66)=0.0d+0
A12P(63,67)=0.0d+0
A12P(64,65)=0.0d+0
A12P(64,66)=0.0d+0
A12P(64,67)=0.0d+0
A12P(64,62)=0.0d+0
A12P(64,63)=0.0d+0
A12P(65,63)=0.0d+0
A12P(65,64)=0.0d+0
A12P(65,66)=0.0d+0
A12P(65,67)=0.0d+0
A12P(66,63)=0.0d+0
A12P(66,64)=0.0d+0
A12P(66,65)=0.0d+0
A12P(66,67)=0.0d+0
A12P(67,63)=0.0d+0
A12P(67,64)=0.0d+0
A12P(67,65)=0.0d+0
A12P(67,66)=0.0d+0
A12P(68,57)=0.0d+0
A12P(68,59)=0.0d+0
A12P(68,60)=0.0d+0
A12P(68,69)=0.0d+0
A12P(68,70)=0.0d+0
A12P(68,71)=0.0d+0
A12P(68,72)=0.0d+0
A12P(69,59)=0.0d+0
A12P(69,68)=0.0d+0
A12P(69,70)=0.0d+0
A12P(70,59)=0.0d+0
A12P(70,68)=0.0d+0
A12P(70,69)=0.0d+0
A12P(70,71)=0.0d+0
A12P(70,72)=0.0d+0
A12P(70,73)=0.0d+0
A12P(70,81)=0.0d+0
A12P(71,68)=0.0d+0
A12P(71,70)=0.0d+0

```
A12P(71,72)=0.0d+0
A12P(72,68)=0.0d+0
A12P(72,70)=0.0d+0
A12P(72,71)=0.0d+0
A12P(72,81)=0.0d+0
A12P(72,82)=0.0d+0
A12P(72,83)=0.0d+0
A12P(72,73)=0.0d+0
A12P(72,74)=0.0d+0
A12P(73,70)=0.0d+0
A12P(73,72)=0.0d+0
A12P(73,81)=0.0d+0
A12P(73,74)=0.0d+0
A12P(73,75)=0.0d+0
A12P(74,72)=0.0d+0
A12P(74,73)=0.0d+0
A12P(74,75)=0.0d+0
A12P(74,76)=0.0d+0
A12P(75,73)=0.0d+0
A12P(75,74)=0.0d+0
A12P(75,76)=0.0d+0
A12P(75,77)=0.0d+0
A12P(76,75)=0.0d+0
A12P(76,74)=0.0d+0
A12P(76,77)=0.0d+0
A12P(76,78)=0.0d+0
A12P(76,79)=0.0d+0
A12P(76,80)=0.0d+0
A12P(77,75)=0.0d+0
A12P(77,76)=0.0d+0
A12P(77,78)=0.0d+0
A12P(77,79)=0.0d+0
A12P(77,80)=0.0d+0
A12P(78,76)=0.0d+0
A12P(78,77)=0.0d+0
A12P(78,79)=0.0d+0
A12P(78,80)=0.0d+0
A12P(79,76)=0.0d+0
A12P(79,77)=0.0d+0
A12P(79,78)=0.0d+0
A12P(79,80)=0.0d+0
A12P(80,79)=0.0d+0
```

A12P(80,76)=0.0d+0
A12P(80,77)=0.0d+0
A12P(80,78)=0.0d+0
A12P(81,70)=0.0d+0
A12P(81,72)=0.0d+0
A12P(81,73)=0.0d+0
A12P(81,82)=0.0d+0
A12P(81,83)=0.0d+0
A12P(81,84)=0.0d+0
A12P(82,72)=0.0d+0
A12P(82,81)=0.0d+0
A12P(82,83)=0.0d+0
A12P(82,84)=0.0d+0
A12P(83,81)=0.0d+0
A12P(83,82)=0.0d+0
A12P(83,72)=0.0d+0
A12P(83,84)=0.0d+0
A12P(83,85)=0.0d+0
A12P(83,86)=0.0d+0
A12P(83,94)=0.0d+0
A12P(84,81)=0.0d+0
A12P(84,83)=0.0d+0
A12P(84,85)=0.0d+0
A12P(85,81)=0.0d+0
A12P(85,83)=0.0d+0
A12P(85,84)=0.0d+0
A12P(85,86)=0.0d+0
A12P(85,87)=0.0d+0
A12P(85,94)=0.0d+0
A12P(85,95)=0.0d+0
A12P(86,87)=0.0d+0
A12P(86,88)=0.0d+0
A12P(86,83)=0.0d+0
A12P(86,85)=0.0d+0
A12P(86,94)=0.0d+0
A12P(87,88)=0.0d+0
A12P(87,89)=0.0d+0
A12P(87,85)=0.0d+0
A12P(87,86)=0.0d+0
A12P(88,86)=0.0d+0
A12P(88,87)=0.0d+0
A12P(88,89)=0.0d+0

```
      A12P(88,90)=0.0d+0
      A12P(89,87)=0.0d+0
      A12P(89,88)=0.0d+0
      A12P(89,90)=0.0d+0
      A12P(89,91)=0.0d+0
      A12P(89,92)=0.0d+0
      A12P(89,93)=0.0d+0
      A12P(90,88)=0.0d+0
      A12P(90,89)=0.0d+0
      A12P(90,91)=0.0d+0
      A12P(90,92)=0.0d+0
      A12P(90,93)=0.0d+0
      A12P(91,89)=0.0d+0
      A12P(91,90)=0.0d+0
      A12P(91,92)=0.0d+0
      A12P(91,93)=0.0d+0
      A12P(92,90)=0.0d+0
      A12P(92,91)=0.0d+0
      A12P(92,93)=0.0d+0
      A12P(92,89)=0.0d+0
      A12P(93,89)=0.0d+0
      A12P(93,90)=0.0d+0
      A12P(93,91)=0.0d+0
      A12P(93,92)=0.0d+0
      A12P(94,95)=0.0d+0
      A12P(94,85)=0.0d+0
      A12P(94,86)=0.0d+0
      A12P(95,94)=0.0d+0
      A12P(95,85)=0.0d+0
*****************************************************************
      C6P(1,2)=0.0d+0
      C6P(1,3)=0.0d+0
      C6P(1,4)=0.0d+0
      C6P(1,5)=0.0d+0
      C6P(2,1)=0.0d+0
      C6P(2,3)=0.0d+0
      C6P(3,1)=0.0d+0
      C6P(3,2)=0.0d+0
      C6P(3,4)=0.0d+0
      C6P(3,5)=0.0d+0
      C6P(3,6)=0.0d+0
      C6P(3,7)=0.0d+0
```

C6P(4,1)=0.0d+0
C6P(4,3)=0.0d+0
C6P(4,5)=0.0d+0
C6P(5,1)=0.0d+0
C6P(5,3)=0.0d+0
C6P(5,4)=0.0d+0
C6P(5,6)=0.0d+0
C6P(5,7)=0.0d+0
C6P(5,8)=0.0d+0
C6P(5,9)=0.0d+0
C6P(6,3)=0.0d+0
C6P(6,5)=0.0d+0
C6P(6,7)=0.0d+0
C6P(7,3)=0.0d+0
C6P(7,5)=0.0d+0
C6P(7,6)=0.0d+0
C6P(7,8)=0.0d+0
C6P(7,9)=0.0d+0
C6P(7,10)=0.0d+0
C6P(7,11)=0.0d+0
C6P(8,5)=0.0d+0
C6P(8,7)=0.0d+0
C6P(8,9)=0.0d+0
C6P(9,5)=0.0d+0
C6P(9,7)=0.0d+0
C6P(9,8)=0.0d+0
C6P(9,10)=0.0d+0
C6P(9,11)=0.0d+0
C6P(9,12)=0.0d+0
C6P(9,13)=0.0d+0
C6P(10,9)=0.0d+0
C6P(10,7)=0.0d+0
C6P(10,11)=0.0d+0
C6P(11,7)=0.0d+0
C6P(11,9)=0.0d+0
C6P(11,10)=0.0d+0
C6P(11,12)=0.0d+0
C6P(11,13)=0.0d+0
C6P(11,14)=0.0d+0
C6P(11,15)=0.0d+0
C6P(12,11)=0.0d+0
C6P(12,9)=0.0d+0

C6P(12,13)=0.0d+0
C6P(13,9)=0.0d+0
C6P(13,12)=0.0d+0
C6P(13,11)=0.0d+0
C6P(13,14)=0.0d+0
C6P(13,15)=0.0d+0
C6P(13,16)=0.0d+0
C6P(13,17)=0.0d+0
C6P(14,11)=0.0d+0
C6P(14,13)=0.0d+0
C6P(14,15)=0.0d+0
C6P(15,11)=0.0d+0
C6P(15,13)=0.0d+0
C6P(15,14)=0.0d+0
C6P(15,16)=0.0d+0
C6P(15,17)=0.0d+0
C6P(15,18)=0.0d+0
C6P(15,19)=0.0d+0
C6P(16,13)=0.0d+0
C6P(16,15)=0.0d+0
C6P(16,17)=0.0d+0
C6P(17,13)=0.0d+0
C6P(17,15)=0.0d+0
C6P(17,16)=0.0d+0
C6P(17,18)=0.0d+0
C6P(17,19)=0.0d+0
C6P(17,20)=0.0d+0
C6P(17,21)=0.0d+0
C6P(18,15)=0.0d+0
C6P(18,17)=0.0d+0
C6P(18,19)=0.0d+0
C6P(19,15)=0.0d+0
C6P(19,17)=0.0d+0
C6P(19,18)=0.0d+0
C6P(19,20)=0.0d+0
C6P(19,21)=0.0d+0
C6P(19,22)=0.0d+0
C6P(19,23)=0.0d+0
C6P(20,17)=0.0d+0
C6P(20,19)=0.0d+0
C6P(20,21)=0.0d+0
C6P(21,17)=0.0d+0

C6P(21,19)=0.0d+0
C6P(21,20)=0.0d+0
C6P(21,22)=0.0d+0
C6P(21,23)=0.0d+0
C6P(21,24)=0.0d+0
C6P(21,25)=0.0d+0
C6P(22,19)=0.0d+0
C6P(22,21)=0.0d+0
C6P(22,23)=0.0d+0
C6P(23,19)=0.0d+0
C6P(23,22)=0.0d+0
C6P(23,21)=0.0d+0
C6P(23,24)=0.0d+0
C6P(23,25)=0.0d+0
C6P(23,26)=0.0d+0
C6P(23,27)=0.0d+0
C6P(24,21)=0.0d+0
C6P(24,23)=0.0d+0
C6P(24,25)=0.0d+0
C6P(25,21)=0.0d+0
C6P(25,23)=0.0d+0
C6P(25,24)=0.0d+0
C6P(25,26)=0.0d+0
C6P(25,27)=0.0d+0
C6P(25,28)=0.0d+0
C6P(25,29)=0.0d+0
C6P(26,23)=0.0d+0
C6P(26,25)=0.0d+0
C6P(26,27)=0.0d+0
C6P(27,23)=0.0d+0
C6P(27,25)=0.0d+0
C6P(27,26)=0.0d+0
C6P(27,28)=0.0d+0
C6P(27,29)=0.0d+0
C6P(27,30)=0.0d+0
C6P(27,31)=0.0d+0
C6P(28,25)=0.0d+0
C6P(28,27)=0.0d+0
C6P(28,29)=0.0d+0
C6P(29,25)=0.0d+0
C6P(29,27)=0.0d+0
C6P(29,28)=0.0d+0

C6P(29,30)=0.0d+0
C6P(29,31)=0.0d+0
C6P(29,32)=0.0d+0
C6P(29,33)=0.0d+0
C6P(30,27)=0.0d+0
C6P(30,29)=0.0d+0
C6P(30,31)=0.0d+0
C6P(31,27)=0.0d+0
C6P(31,29)=0.0d+0
C6P(31,30)=0.0d+0
C6P(31,32)=0.0d+0
C6P(31,33)=0.0d+0
C6P(31,34)=0.0d+0
C6P(31,42)=0.0d+0
C6P(32,29)=0.0d+0
C6P(32,31)=0.0d+0
C6P(32,33)=0.0d+0
C6P(33,29)=0.0d+0
C6P(33,31)=0.0d+0
C6P(33,32)=0.0d+0
C6P(33,34)=0.0d+0
C6P(33,35)=0.0d+0
C6P(33,42)=0.0d+0
C6P(33,43)=0.0d+0
C6P(33,44)=0.0d+0
C6P(34,33)=0.0d+0
C6P(34,31)=0.0d+0
C6P(34,42)=0.0d+0
C6P(34,35)=0.0d+0
C6P(34,36)=0.0d+0
C6P(35,33)=0.0d+0
C6P(35,34)=0.0d+0
C6P(35,36)=0.0d+0
C6P(35,37)=0.0d+0
C6P(36,34)=0.0d+0
C6P(36,35)=0.0d+0
C6P(36,37)=0.0d+0
C6P(36,38)=0.0d+0
C6P(37,35)=0.0d+0
C6P(37,36)=0.0d+0
C6P(37,38)=0.0d+0
C6P(37,39)=0.0d+0

C6P(37,40)=0.0d+0
C6P(38,36)=0.0d+0
C6P(38,37)=0.0d+0
C6P(38,39)=0.0d+0
C6P(38,40)=0.0d+0
C6P(38,41)=0.0d+0
C6P(39,37)=0.0d+0
C6P(39,38)=0.0d+0
C6P(39,40)=0.0d+0
C6P(39,41)=0.0d+0
C6P(40,37)=0.0d+0
C6P(40,38)=0.0d+0
C6P(40,39)=0.0d+0
C6P(40,41)=0.0d+0
C6P(41,37)=0.0d+0
C6P(41,38)=0.0d+0
C6P(41,39)=0.0d+0
C6P(41,40)=0.0d+0
C6P(42,31)=0.0d+0
C6P(42,33)=0.0d+0
C6P(42,34)=0.0d+0
C6P(42,43)=0.0d+0
C6P(42,44)=0.0d+0
C6P(42,45)=0.0d+0
C6P(42,46)=0.0d+0
C6P(43,33)=0.0d+0
C6P(43,42)=0.0d+0
C6P(43,44)=0.0d+0
C6P(44,33)=0.0d+0
C6P(44,42)=0.0d+0
C6P(44,43)=0.0d+0
C6P(44,45)=0.0d+0
C6P(44,46)=0.0d+0
C6P(44,47)=0.0d+0
C6P(44,55)=0.0d+0
C6P(45,42)=0.0d+0
C6P(45,44)=0.0d+0
C6P(45,46)=0.0d+0
C6P(46,42)=0.0d+0
C6P(46,44)=0.0d+0
C6P(46,45)=0.0d+0
C6P(46,47)=0.0d+0

C6P(46,48)=0.0d+0
C6P(46,55)=0.0d+0
C6P(46,56)=0.0d+0
C6P(46,57)=0.0d+0
C6P(47,44)=0.0d+0
C6P(47,46)=0.0d+0
C6P(47,48)=0.0d+0
C6P(47,49)=0.0d+0
C6P(47,55)=0.0d+0
C6P(48,46)=0.0d+0
C6P(48,47)=0.0d+0
C6P(48,49)=0.0d+0
C6P(48,50)=0.0d+0
C6P(49,47)=0.0d+0
C6P(49,48)=0.0d+0
C6P(49,50)=0.0d+0
C6P(49,51)=0.0d+0
C6P(50,49)=0.0d+0
C6P(50,48)=0.0d+0
C6P(50,51)=0.0d+0
C6P(50,52)=0.0d+0
C6P(50,53)=0.0d+0
C6P(51,49)=0.0d+0
C6P(51,50)=0.0d+0
C6P(51,52)=0.0d+0
C6P(51,53)=0.0d+0
C6P(51,54)=0.0d+0
C6P(52,50)=0.0d+0
C6P(52,51)=0.0d+0
C6P(52,53)=0.0d+0
C6P(52,54)=0.0d+0
C6P(53,50)=0.0d+0
C6P(53,51)=0.0d+0
C6P(53,52)=0.0d+0
C6P(53,54)=0.0d+0
C6P(54,50)=0.0d+0
C6P(54,51)=0.0d+0
C6P(54,52)=0.0d+0
C6P(54,53)=0.0d+0
C6P(55,44)=0.0d+0
C6P(55,46)=0.0d+0
C6P(55,47)=0.0d+0

C6P(55,56)=0.0d+0
C6P(55,57)=0.0d+0
C6P(55,58)=0.0d+0
C6P(56,46)=0.0d+0
C6P(56,55)=0.0d+0
C6P(56,57)=0.0d+0
C6P(57,46)=0.0d+0
C6P(57,55)=0.0d+0
C6P(57,56)=0.0d+0
C6P(57,58)=0.0d+0
C6P(57,59)=0.0d+0
C6P(57,60)=0.0d+0
C6P(57,68)=0.0d+0
C6P(58,55)=0.0d+0
C6P(58,57)=0.0d+0
C6P(58,59)=0.0d+0
C6P(59,55)=0.0d+0
C6P(59,57)=0.0d+0
C6P(59,58)=0.0d+0
C6P(59,60)=0.0d+0
C6P(59,61)=0.0d+0
C6P(59,68)=0.0d+0
C6P(59,69)=0.0d+0
C6P(59,70)=0.0d+0
C6P(60,57)=0.0d+0
C6P(60,59)=0.0d+0
C6P(60,68)=0.0d+0
C6P(60,61)=0.0d+0
C6P(60,62)=0.0d+0
C6P(61,59)=0.0d+0
C6P(61,60)=0.0d+0
C6P(61,62)=0.0d+0
C6P(61,63)=0.0d+0
C6P(62,60)=0.0d+0
C6P(62,61)=0.0d+0
C6P(62,63)=0.0d+0
C6P(62,64)=0.0d+0
C6P(63,61)=0.0d+0
C6P(63,62)=0.0d+0
C6P(63,64)=0.0d+0
C6P(63,65)=0.0d+0
C6P(63,66)=0.0d+0

C6P(63,67)=0.0d+0
C6P(64,65)=0.0d+0
C6P(64,66)=0.0d+0
C6P(64,67)=0.0d+0
C6P(64,62)=0.0d+0
C6P(64,63)=0.0d+0
C6P(65,63)=0.0d+0
C6P(65,64)=0.0d+0
C6P(65,66)=0.0d+0
C6P(65,67)=0.0d+0
C6P(66,63)=0.0d+0
C6P(66,64)=0.0d+0
C6P(66,65)=0.0d+0
C6P(66,67)=0.0d+0
C6P(67,63)=0.0d+0
C6P(67,64)=0.0d+0
C6P(67,65)=0.0d+0
C6P(67,66)=0.0d+0
C6P(68,57)=0.0d+0
C6P(68,59)=0.0d+0
C6P(68,60)=0.0d+0
C6P(68,69)=0.0d+0
C6P(68,70)=0.0d+0
C6P(68,71)=0.0d+0
C6P(68,72)=0.0d+0
C6P(69,59)=0.0d+0
C6P(69,68)=0.0d+0
C6P(69,70)=0.0d+0
C6P(70,59)=0.0d+0
C6P(70,68)=0.0d+0
C6P(70,69)=0.0d+0
C6P(70,71)=0.0d+0
C6P(70,72)=0.0d+0
C6P(70,73)=0.0d+0
C6P(70,81)=0.0d+0
C6P(71,68)=0.0d+0
C6P(71,70)=0.0d+0
C6P(71,72)=0.0d+0
C6P(72,68)=0.0d+0
C6P(72,70)=0.0d+0
C6P(72,71)=0.0d+0
C6P(72,81)=0.0d+0

C6P(72,82)=0.0d+0
C6P(72,83)=0.0d+0
C6P(72,73)=0.0d+0
C6P(72,74)=0.0d+0
C6P(73,70)=0.0d+0
C6P(73,72)=0.0d+0
C6P(73,81)=0.0d+0
C6P(73,74)=0.0d+0
C6P(73,75)=0.0d+0
C6P(74,72)=0.0d+0
C6P(74,73)=0.0d+0
C6P(74,75)=0.0d+0
C6P(74,76)=0.0d+0
C6P(75,73)=0.0d+0
C6P(75,74)=0.0d+0
C6P(75,76)=0.0d+0
C6P(75,77)=0.0d+0
C6P(76,75)=0.0d+0
C6P(76,74)=0.0d+0
C6P(76,77)=0.0d+0
C6P(76,78)=0.0d+0
C6P(76,79)=0.0d+0
C6P(76,80)=0.0d+0
C6P(77,75)=0.0d+0
C6P(77,76)=0.0d+0
C6P(77,78)=0.0d+0
C6P(77,79)=0.0d+0
C6P(77,80)=0.0d+0
C6P(78,76)=0.0d+0
C6P(78,77)=0.0d+0
C6P(78,79)=0.0d+0
C6P(78,80)=0.0d+0
C6P(79,76)=0.0d+0
C6P(79,77)=0.0d+0
C6P(79,78)=0.0d+0
C6P(79,80)=0.0d+0
C6P(80,79)=0.0d+0
C6P(80,76)=0.0d+0
C6P(80,77)=0.0d+0
C6P(80,78)=0.0d+0
C6P(81,70)=0.0d+0
C6P(81,72)=0.0d+0

C6P(81,73)=0.0d+0
C6P(81,82)=0.0d+0
C6P(81,83)=0.0d+0
C6P(81,84)=0.0d+0
C6P(82,72)=0.0d+0
C6P(82,81)=0.0d+0
C6P(82,83)=0.0d+0
C6P(82,84)=0.0d+0
C6P(83,81)=0.0d+0
C6P(83,82)=0.0d+0
C6P(83,72)=0.0d+0
C6P(83,84)=0.0d+0
C6P(83,85)=0.0d+0
C6P(83,86)=0.0d+0
C6P(83,94)=0.0d+0
C6P(84,81)=0.0d+0
C6P(84,83)=0.0d+0
C6P(84,85)=0.0d+0
C6P(85,81)=0.0d+0
C6P(85,83)=0.0d+0
C6P(85,84)=0.0d+0
C6P(85,86)=0.0d+0
C6P(85,87)=0.0d+0
C6P(85,94)=0.0d+0
C6P(85,95)=0.0d+0
C6P(86,87)=0.0d+0
C6P(86,88)=0.0d+0
C6P(86,83)=0.0d+0
C6P(86,85)=0.0d+0
C6P(86,94)=0.0d+0
C6P(87,88)=0.0d+0
C6P(87,89)=0.0d+0
C6P(87,85)=0.0d+0
C6P(87,86)=0.0d+0
C6P(88,86)=0.0d+0
C6P(88,87)=0.0d+0
C6P(88,89)=0.0d+0
C6P(88,90)=0.0d+0
C6P(89,87)=0.0d+0
C6P(89,88)=0.0d+0
C6P(89,90)=0.0d+0
C6P(89,91)=0.0d+0

```
      C6P(89,92)=0.0d+0
      C6P(89,93)=0.0d+0
      C6P(90,88)=0.0d+0
      C6P(90,89)=0.0d+0
      C6P(90,91)=0.0d+0
      C6P(90,92)=0.0d+0
      C6P(90,93)=0.0d+0
      C6P(91,89)=0.0d+0
      C6P(91,90)=0.0d+0
      C6P(91,92)=0.0d+0
      C6P(91,93)=0.0d+0
      C6P(92,90)=0.0d+0
      C6P(92,91)=0.0d+0
      C6P(92,93)=0.0d+0
      C6P(92,89)=0.0d+0
      C6P(93,89)=0.0d+0
      C6P(93,90)=0.0d+0
      C6P(93,91)=0.0d+0
      C6P(93,92)=0.0d+0
      C6P(94,95)=0.0d+0
      C6P(94,85)=0.0d+0
      C6P(94,86)=0.0d+0
      C6P(95,94)=0.0d+0
      C6P(95,85)=0.0d+0
     do 204 M=1,NATOM-1
       do 205 I=M+1,NATOM
         DELX=PEPCORD1(I,1)-PEPCORD1(M,1)
         DELY=PEPCORD1(I,2)-PEPCORD1(M,2)
         DELZ=PEPCORD1(I,3)-PEPCORD1(M,3)
         D2PEP(M,I)=DELX*DELX+DELY*DELY+DELZ*DELZ
205     continue
204   continue
      PVPEP=0.d+0
     do 206 M=1,NATOM-1
       do 207 I=M+1,NATOM
      DSURF=dsqrt(D2PEP(M,I))
      D6=(DSURF)**6
      D12=(DSURF)**12
      PVPEP=PVPEP + A12P(M,I)/D12 - C6P(M,I)/D6
     1       + QCONP(M,I)/DSURF
207     continue
206     continue
```

```
c            write(*,*)'Total Potential '
c            write(*,208) PVPEP
c 208        format(f15.3)
c ***********************************************
c ** Torsional Energy(VTOR) Calculations **
c ***********************************************
      VTOR=0.0d+0
      do i=1,RESNUM
       VTOR=VTOR + 0.5d+0*v1*(1.0d+0 - dcos(phi(i)))
     1    + 0.5d+0*v2*(1.0d+0 - dcos(2.0d+0*phi(i)))
     1    + 0.5d+0*v3*(1.0d+0 + dcos(3.0d+0*phi(i)))
      enddo
      do j=1,RESNUM
      VTOR=VTOR + 0.5d+0*v4*(1.0d+0 - dcos(psi(j)))
     1     + 0.5d+0*v5*(1.0d+0 - dcos(2.0d+0*psi(j)))
     1     + 0.5d+0*v6*(1.0d+0 + dcos(3.0d+0*psi(j)))
      enddo
C            write(*,*)'VTOR',VTOR
       CLOSE(10)
       confgE=VTOR+PVPEP
c            write(*,*)'Total Confirmational energy of peptide'
c            write(*,*)'ConfgE=',confgE
       RETURN
       END
*************************************************************************
** SUMBINPEP..subroutine which collects the data for the number of atoms in each bin. **
*************************************************************************
      subroutine SUMBINPEP(PEPCORD1,LZ,NMOLW,NATOM,RXMAX2,
     1 DELR,DELZ,D2WPEP,COSSUM,COSSQSUM,ZPEPSUM,NEND,CEND,GRPWSUM,
     1 NEIBOURWSUM,HB,NHB,COM)
      implicit   NONE
      integer J,N,M,BIN,NMOLW,NATOM,BINZ,NHB,NEND,CEND
      integer ZPEPSUM(2000,3)
      integer GRPWSUM(600,2,100),HB(100),NEIBOURWSUM(100)
      double precision D,DSQ,RXMAX2,DELR,DELZ,LZ,HALFLZ
      double precision DISTMINW
      double precision PEPCORD1(200,3),COM(3),COSSQ
      double precision D2WPEP(200,2000,3)
      double precision DELTX,DELTY,DELTZ,COSSUM,COSSQSUM,LNC
C ***************************************************
C ** COLLECTION OF DATA.                  **
C ***************************************************
```

```
      HALFLZ=LZ/2.d+0
      DISTMINW=3.3d+0
** Z profile of 1st, last, and COM positions
** 1st atom
       BINZ=idint((PEPCORD1(1,3)+HALFLZ)/DELZ)+1
       ZPEPSUM(BINZ,1)=ZPEPSUM(BINZ,1)+1
** COM
       BINZ=idint((COM(3)+HALFLZ)/DELZ)+1
       ZPEPSUM(BINZ,2)=ZPEPSUM(BINZ,2)+1
** last atom
       BINZ=idint((PEPCORD1(NATOM,3)+HALFLZ)/DELZ)+1
       ZPEPSUM(BINZ,3)=ZPEPSUM(BINZ,3)+1
**Order Parameter (from NEND to CEND)
      DELTX=PEPCORD1(NEND,1)-PEPCORD1(CEND,1)
      DELTY=PEPCORD1(NEND,2)-PEPCORD1(CEND,2)
      DELTZ=PEPCORD1(NEND,3)-PEPCORD1(CEND,3)
      LNC=dsqrt(DELTX*DELTX+DELTY*DELTY+DELTZ*DELTZ)
      COSSQ=DELTZ/LNC
      COSSUM=COSSUM+COSSQ
      COSSQ=COSSQ*COSSQ
      COSSQSUM=COSSQSUM+COSSQ
**PEPTIDE-WATER PCF and nearest neighbor
      do 1500 M=1,NMOLW
        do 1400 N=1,NHB
          DSQ=D2WPEP(HB(N),M,1)
          if(DSQ.LE.RXMAX2) then
            D=dsqrt(DSQ)
            if(D.LE.DISTMINW) then
              NEIBOURWSUM(N)=NEIBOURWSUM(N)+1
            end if
            BIN=idint(D/DELR-0.5d+0)+1
            GRPWSUM(BIN,1,N)=GRPWSUM(BIN,1,N)+1
          end if
          do 1410 J=2,3
            DSQ=D2WPEP(HB(N),M,J)
            if(DSQ.LE.RXMAX2) then
              D=dsqrt(DSQ)
              BIN=idint(D/DELR-0.5d+0)+1
              GRPWSUM(BIN,2,N)=GRPWSUM(BIN,2,N)+1
            end if
1410        continue
1400      continue
```

```
1500  continue
      return
      end
**************************************************************************
** TORSION ..... subroutine to give the torsional rotation by changing coordinates of the peptide atoms
**************************************************************************
      subroutine TORSION(NATOM,PEPCORD1,maxpsi,maxphi,phi,psi,
     &  COM,AW,RESNUM,ISEED)
      integer ISEED,NATOM,RESNUM
      integer k1,k2,k3,n3,n4,k4,N
      double precision PEPCORD1(200,3)
      double precision COM(3),CM(3),AWS,AW(200)
      double precision RANDOM
      double precision u(20,3),s(3),w(3),x(3),maxpsi,cpsi(20)
      double precision phi(20),psi(20),magu(20),magv(20)
      double precision v(20,3),t(3),y(3),z(3),maxphi,cphi(20)
c u vector is to be used as reference vector for psi angle (about Calpha - C) rotation
c there are 8 Calpha - C bonds, so 8 u vectors
      do I=1,3
      CM(I)=0.0D+0
      enddo
      AWS=0.0D+0
      do i=1,RESNUM
      cpsi(i)=(2.0d+0*RANDOM(ISEED)-1.0d+0)*maxpsi
      cphi(i)=(2.0d+0*RANDOM(ISEED)-1.0d+0)*maxphi
      enddo
      do i=1,RESNUM
      phi(i)=phi(i) + cphi(i)
      psi(i)=psi(i) + cpsi(i)
      enddo
      do 45 k1=1,RESNUM
      if (k1 .le. 5) then
      u(k1,1)=PEPCORD1(6*k1-1,1) - PEPCORD1(6*k1-3,1)
      u(k1,2)=PEPCORD1(6*k1-1,2) - PEPCORD1(6*k1-3,2)
      u(k1,3)=PEPCORD1(6*k1-1,3) - PEPCORD1(6*k1-3,3)
      else
      u(k1,1)=PEPCORD1((13*(k1-3))+3,1) - PEPCORD1((13*(k1-3))-6,1)
      u(k1,2)=PEPCORD1((13*(k1-3))+3,2) - PEPCORD1((13*(k1-3))-6,2)
      u(k1,3)=PEPCORD1((13*(k1-3))+3,3) - PEPCORD1((13*(k1-3))-6,3)
      endif
c magnitude of reference vector u
      magu(k1)=sqrt((u(k1,1))**2 + (u(k1,2))**2 + (u(k1,3))**2)
```

```
 45     continue
c v vector is to be used as reference vector for phi angle (about N - Calpha) rotation
c there are 8 N - Calpha bonds, so 8 v vectors
       do 47 k2=1,RESNUM
       if (k2 .le. 5) then
       v(k2,1)=PEPCORD1(6*k2-3,1) - PEPCORD1(6*k2-5,1)
       v(k2,2)=PEPCORD1(6*k2-3,2) - PEPCORD1(6*k2-5,2)
       v(k2,3)=PEPCORD1(6*k2-3,3) - PEPCORD1(6*k2-5,3)
       else
       v(k2,1)=PEPCORD1((13*(k2-3))-6,1) - PEPCORD1((13*(k2-3))-8,1)
       v(k2,2)=PEPCORD1((13*(k2-3))-6,2) - PEPCORD1((13*(k2-3))-8,2)
       v(k2,3)=PEPCORD1((13*(k2-3))-6,3) - PEPCORD1((13*(k2-3))-8,3)
       endif
c magnitude of reference vector v
       magv(k2)=sqrt((v(k2,1))**2 + (v(k2,2))**2 + (v(k2,3))**2)
 47    continue
c FOR PSI (Calpha-C) rotation calculations for atom coordinates when the right
c bond C - N is rotated, all the atoms on the right are mapped
       do 49 k3=1,RESNUM
       IF (K3 .LE. 5) THEN
       n3=6*k3-1
       else
       n3=13*(k3-3)+3
       endif
       do 50 N=n3+1,NATOM
       s(1)=PEPCORD1(N,1)-PEPCORD1(n3,1)
       s(2)=PEPCORD1(N,2)-PEPCORD1(n3,2)
       s(3)=PEPCORD1(N,3)-PEPCORD1(n3,3)
       w(1)=(1.0d+0/magu(k3))*(u(k3,2)*s(3) - u(k3,3)*s(2) )
       w(2)=(1.0d+0/magu(k3))*(u(k3,3)*s(1) - u(k3,1)*s(3) )
       w(3)=(1.0d+0/magu(k3))*(u(k3,1)*s(2) - u(k3,2)*s(1) )
       x(1)=(1.0d+0/magu(k3))*(u(k3,2)*w(3) - u(k3,3)*w(2) )
       x(2)=(1.0d+0/magu(k3))*(u(k3,3)*w(1) - u(k3,1)*w(3) )
       x(3)=(1.0d+0/magu(k3))*(u(k3,1)*w(2) - u(k3,2)*w(1) )
       PEPCORD1(N,1)=PEPCORD1(N,1) + w(1)*dsin(cpsi(k3))
     1   + x(1)*(1.0d+0-dcos(cpsi(k3)))
       PEPCORD1(N,2)=PEPCORD1(N,2) + w(2)*dsin(cpsi(k3))
     1   + x(2)*(1.0d+0-dcos(cpsi(k3)))
       PEPCORD1(N,3)=PEPCORD1(N,3) + w(3)*dsin(cpsi(k3))
     1   + x(3)*(1.0d+0-dcos(cpsi(k3)))
 50    continue
 49    continue
```

```
c calculations for atom coordinates when the right bond C - N is rotated, all the atoms
c on the right are mapped
      do 51 k4=1,RESNUM
      IF (k4 .LE. 5) THEN
      n4=6*k4-3
      else
      n4=13*(k4-3)-6
      endif
      do 52 I=n4+1,NATOM
      t(1)=PEPCORD1(I,1)-PEPCORD1(n4,1)
      t(2)=PEPCORD1(I,2)-PEPCORD1(n4,2)
      t(3)=PEPCORD1(I,3)-PEPCORD1(n4,3)
      y(1)=(1.0d+0/magv(k4))*(v(k4,2)*t(3) - v(k4,3)*t(2) )
      y(2)=(1.0d+0/magv(k4))*(v(k4,3)*t(1) - v(k4,1)*t(3) )
      y(3)=(1.0d+0/magv(k4))*(v(k4,1)*t(2) - v(k4,2)*t(1) )
      z(1)=(1.0d+0/magv(k4))*(v(k4,2)*y(3) - v(k4,3)*y(2) )
      z(2)=(1.0d+0/magv(k4))*(v(k4,3)*y(1) - v(k4,1)*y(3) )
      z(3)=(1.0d+0/magv(k4))*(v(k4,1)*y(2) - v(k4,2)*y(1) )
      PEPCORD1(I,1)=PEPCORD1(I,1) + y(1)*dsin(cphi(k4))
     1    + z(1)*(1d+0-dcos(cphi(k4)))
      PEPCORD1(I,2)=PEPCORD1(I,2) + y(2)*dsin(cphi(k4))
     1    + z(2)*(1d+0-dcos(cphi(k4)))
      PEPCORD1(I,3)=PEPCORD1(I,3) + y(3)*dsin(cphi(k4))
     1    + z(3)*(1d+0-dcos(cphi(k4)))
   52   continue
   51   continue
      do I=1,3
      do M=1,NATOM
      CM(I)=CM(I)+PEPCORD1(M,I)*AW(M)
      enddo
      enddo
      do M=1,NATOM
      AWS=AWS+AW(M)
      enddo
      do I=1,3
      COM(I)=CM(I)/AWS
      enddo
      return
      end
```

APPENDIX B

INSTRUCTIONS TO RUN THE EXPLICIT MODEL CODE

The code 2pws.f simulates two identical peptides in bulk water (of explicit molecules) with two charged surfaces along the xy-plane on opposite sides of the box. The simulation is run by splitting the required total number of MC simulation steps in sets of no more than 40000 MC steps each. After completing a set, the input file required for the next set is generated and the simulation is continued. The simulation uses an input file for a run set, which is associated with system configuration files and output files.

Input data file (inputx.inp):

Each input data file describes the variables and file names for a simulation run set. They are named as 'inputx.inp', where 'x' denotes the serial number of the simulation run set, like 'input1.inp' for the first set of simulation run. The contents in an input data file (say inputx.inp) are described below,

0 or 1 or 2: Status of simulation set run (0-first run, 1-continuation, 2-Production).

'CFGx-1.out': Input configuration file from previous run set (x-1).

'CFGx.out': Output configuration file for next run set (x+1).

'outx.out': Output result file for the running simulation set (x).

'SYSTEM0.pdb': RasMol visualization file for the initial system configuration of the running simulation set (read only for first run, i.e. if x=1).

'SYSTEMx.pdb': RasMol visualization file for the final system configuration of the running simulation set (x).

NMOLW: Number of explicit water molecules in the simulation box, calculated to maintain 1 g/cm^3 of water density inside the simulation box.

NMCS: Number of Monte Carlo Steps in the simulation run set.

TEMP: Temperature of simulation run (selected 298K).

NSAVE: Simulation step interval between temporary variable storage (selected 500).

NADJUST: Simulation step interval between adjusting limits of molecular movement (selected 25).

'SURF.INP': Surface configuration file carrying data on the number of surface atoms, their coordinates and simulation box dimensions.

QSURF: Charge on the surface (selected 0.3 e)

'A5-I5.cod': Peptide configuration file generated by processing the data file obtained with ALCHEMY using GROMOS software, to put all the hydrogens in place which were not present in the original file. With all the hydrogens in place (H on N of –CONH and H of side chains of lysine) it is then processed again to get the center-of-mass at the origin to begin with. This final file is named as 'A5-L5.cod'. We have five ALA residues and five LYS residues in the peptide, with each LYS residue carrying a charge of '+1' while ALA is neutral.

VPEP: Peptide volume.

RESNUM: Number of peptide residues (10 for the selected peptide model).

For the first run set, the user needs to generate the input file (input1.inp) and the configuration files (A5-L5.cod and SURF.INP) for the selected simulation set-up, then for all other input files (for subsequent run sets) the user needs to only change names of the input configuration file, output configuration file, output file and RasMol file. Thus input data files for all simulation run sets required were created. Then before each

simulation run set (say set x), the only update needed in the FOTRAN code is to change the input file name (to inputx.inp); then compile the code and run.

APPENDIX C

IMPLICIT MODEL SIMULATION
PROGRAM CODE

```
c*Corrected Amol-Fuzz PEPTIDE_IMP-WATER_SURFACE code*******RUN:2.2(Correction for random intialization for peptide positions) MAX NMOLP = 50; MAX NATOM = 200; MAX NMCS = 50000;MAX RESNUM =20 MAX NSURF = 1000 Corrections to NCA and NCB variables**********************************
      program  main
      implicit NONE
      external INCONFIG,NRGTOT
      external RANDOM
      external PDBOUT
      external DISTPEPSF,NRGPEPSF
      external DISTPP,NRGPP
      external MOVEPEP,pepenrg,HPenrg
      external SUMBINPEP,TORSION,UHP_est,HBenrg_intra,HBenrg_inter
*************************************************************************
      integer I,ISEED,M,K,N,NMOLP,P,a,b
      integer NADJUST,NMCS,NMCSACC,NMCSOLD
      integer NMCSTMP,NPTS,NSAVE,RUNSTAT,STEP
      integer NSURF
      integer NBINZ,NCA(20),NCB(20)
      integer NATOM,NEND,CEND
      integer ATOM(200),AA(200),GROUP(200)
      integer ACCTOR,ACCPEP
      integer ZPEPSUM(50,2000,3)
      integer RESNUM
      double precision ACCPEPACC,ACCPEPTMP,AVGACCPEP
      double precision AVGACCTOR,ACCTORACC,ACCTORTMP
      double precision DELZ,CMM(3),r
      double precision AVGNRG
      double precision DELR,DELV,ESUM,ESUMACC,ESUMACCTMP
      double precision LMIN,PI,kB
      double precision LX,LY,LZ
      double precision QFACT,RANDOM,RXMAX,TEMP
      double precision V,VERR,VT,VTN
      double precision VERRSUM
      double precision QSURF,RSURF(1000,3)
      double precision AII(2),CII(2),Q(2)
      double precision VTOT(0:50001),VTOTPT(100)
      double precision PEPCORD(50,200,3),APEP(200),CPEP(200)
      double precision QPEP(200),AW(200)
      double precision phi(50,20),psi(50,20),COM(50,3)
      double precision v1,v2,v3,v4,v5,v6
```

```
      double precision A12PS(200,2),C6PS(200,2),QCONPS(200,2)
      double precision A12PP(200,200),C6PP(200,200),QCONPP(200,200)
      double precision UPEPMSFNEW,UPEPMSFOLD(50)
      double precision UPMPNEW,UPMPOLD(50)
      double precision PEPCORDOLD(200,3),COMOLD(3)
      double precision phiold(20),psiold(20)
      double precision PMCORD(200,3),COMM(3),phim(20),psim(20)
      double precision UHPO,UHBO,UHBIO,UHPN,UHBN,UHBIN,UHPM,UHBM,UHBIM
      double precision UHPA(50,20),UHPB(50,20),PUHPA(20),PUHPB(20)
      double precision MXTPEP,MXRPEP,maxpsi,maxphi
      double precision D2PEPSF1(200,1000),D2PEPSF2(200,1000)
      double precision D2PMPEP(200,50,200)
      double precision NEWPENRG,OLDPENRG(50)
      double precision VPEP,PE,PENTOT,AWS,UPSF,UP,UPMSF,UPMP
      double precision COSAVG(50),COSSQAVG(50),COSSQSUM(50),COSSUM(50)
      double precision ZPEP(50,2000,3)
      double precision ETED(50,50000),ETEDP(50,100)
      double precision CM(50,50000),CMP(50,100)
      double precision VPS(50,50000),VPEPT(50,50000)
      double precision VPSPT(50,100),VPEPTPT(50,100)
      double precision VPSS(50),VRESTI,VPEPTP(50),ETEDAVG(50),CMAVG(50)
      double precision VREST,UPEPSFI,UPEPPI,UPEPSF,UPEPP
      character CFGINP*15,CFGOUT*15,OUTPUT*15
      character TITLE*50,PDB*15,PDBI*15
      character SURFINP*15,SURFNAME*15
      character PEP*15
      parameter (PI=3.14159265d+0)
      parameter (kB=1.985878d-3)
C ***************************************************
C ** INPUT DATA.                                   **
C ***************************************************
      open(unit=5,file='input1.inp',status='unknown')
      read(5,*)
      read(5,*)
      read(5,*) TITLE
      read(5,100) RUNSTAT
      read(5,*) CFGINP
      read(5,*) CFGOUT
      read(5,*) OUTPUT
      read(5,*) PDB
      if (RUNSTAT.eq.0) then
        read(5,*) PDBI
```

```
      endif
      read(5,110) NMOLP
      if(NMOLP.gt.50) STOP 'Matrix size too small'
      read(5,120) NMCS
      if(NMCS.GT.50000) STOP 'Matrix size too small'
      read(5,140) TEMP
      read(5,*) NSAVE
      read(5,*) NADJUST
      read(5,*) SURFINP
      read(5,*) QSURF
      read(5,*) PEP
      read(5,*) VPEP
      read(5,*) RESNUM
100   format(i1)
110   format(i4)
120   format(i6)
140   format(f6.2)
      open(unit=88,file='phipsi',status='unknown')
      open(unit=7,file=SURFINP,status='unknown',form='formatted')
      read(7,*)
      read(7,*) NSURF
      if(NSURF.GT.1000) STOP 'Matrix size too small'
      do 105 N=1,NSURF
        read(7,222) (RSURF(N,I),I=1,3)
105   continue
222   format(f17.13,2x,f17.13,2x,f17.13)
      read(7,*) SURFNAME
      read(7,*) LX
      read(7,*) LY
      open(unit=9,file=OUTPUT,status='unknown',form='formatted')
C ****************************************************
C ** BOX DIMENSIONS & CONSTANTS FOR PCFs.        **
C ****************************************************
C**From the excel sheet calculations for NMOLP no of peptides***
      LZ=85.00D+0
C**a is rows along x-axis and b is rows along z-axis***********
      b=5
      r=dble(NMOLP)/dble(b)
      a=ceiling(r)
****************************************************
      NPTS=1
      if(NMCS.gt.100) then
```

```
        NPTS=NMCS/100
      end if
      MXTPEP=0.005
      MXRPEP=0.008
      maxpsi=0.005
      maxphi=0.005
      QFACT=1.671d+5/TEMP
      NMCSTMP=0
      ESUMACCTMP=0.d+0
      NMCSACC=0
      ESUMACC=0.d+0
      ESUM=0.d+0
      LMIN=LX
      if(LY.LT.LMIN) then
        LMIN=LY
      end if
      if(LZ.LT.LMIN) then
        LMIN=LZ
      end if
      RXMAX=LMIN/2.0d+0
      DELR=0.05d+0
      DELZ=DELR
      NBINZ=idint(LZ/DELZ)
      ACCPEP=0
      ACCTOR=0
      open(unit=2,file=CFGOUT,status='unknown',form='formatted')
*********************************************************************
***** Surface Parameters ***************************************
*********************************************************************
      AII(1)=6.344d+0
      CII(1)=10.152d+0
      AII(2)=AII(1)
      CII(2)=CII(1)
      Q(1)=QSURF
      Q(2)=-QSURF
C *****************************************************************
C ** INITIAL CONFIGURATION AND ENERGY.                        **
C ** RUNSTAT=0...cold start, call INCONFIG.                   **
C ** RUNSTAT=1...warm start, before equlibrium, read in coords.**
C ** RUNSTAT=2...1st data collecting run                      **
C ** RUNSTAT=3...collecting data (after 1st collecting run)    **
C *****************************************************************
```

```
      if(RUNSTAT.eq.0)then
        call INCONFIG(LX,LY,LZ,NMOLP,NATOM,PEPCORD,COM,APEP,
     &  CPEP,QPEP,AW,AA,ATOM,GROUP,NEND,CEND,phi,psi,
     &  v1,v2,v3,v4,v5,v6,RESNUM,NCA,NCB)
        do 1006 P=1,NMOLP
         COSSUM(P)=0.d+0
         COSSQSUM(P)=0.d+0
         do 8027 N=1,NBINZ
          do 3026 I=1,3
            ZPEPSUM(P,N,I)=0
3026       continue
8027      continue
1006     continue
      else
       open(unit=1,file=CFGINP,status='unknown',form='formatted')
        rewind(1)
        read(1,*)
        read(1,*) NATOM
        do 35500 M=1,NATOM
          read(1,889) AA(M),ATOM(M),GROUP(M),APEP(M),CPEP(M),QPEP(M),
     1      AW(M)
35500    continue
        do 35505 P=1,NMOLP
         do 35510 M=1,NATOM
          read(1,998) PEPCORD(P,M,1),PEPCORD(P,M,2),PEPCORD(P,M,3)
35510      continue
35505    continue
        do 35020 M=1,RESNUM
          read(1,23) NCA(M),NCB(M)
35020    continue
        do 35025 P=1,NMOLP
         read(1,777) (COM(P,I),I=1,3)
35025    continue
        read(1,*) NEND
        read(1,*) CEND
        do 35035 P=1,NMOLP
         do 35036 I=1,RESNUM
          read(1,1523)phi(P,I),psi(P,I)
35036     continue
35035    continue
        read(1,1524)v1,v2,v3,v4,v5,v6
889      format(5x,I3,1x,I3,1x,I4,1x,f8.3,f8.3,f8.3,f8.3)
```

```
998     format(3x,f8.3,f8.3,f8.3)
1523    format(5x,f8.3,5x,f8.3)
1524    format(f8.3,f8.3,f8.3,f8.3,f8.3,f8.3)
23      format(2x,i3,2x,i3)
777     format(f17.13,2x,f17.13,2x,f17.13)
      read(1,*) MXTPEP
      read(1,*) MXRPEP
      read(1,*) maxpsi
      read(1,*) maxphi
      if(RUNSTAT.ne.3)then
       do 1005 P=1,NMOLP
        COSSUM(P)=0.d+0
        COSSQSUM(P)=0.d+0
        do 1001 K=1,NBINZ
          do 1011 I=1,3
            ZPEPSUM(P,K,I)=0
1011        continue
1001      continue
1005    continue
      else
        read(1,*) NMCSACC
        read(1,*) ESUMACC
        read(1,*) ACCPEPACC
        read(1,*) ACCTORACC
        read(1,*)
        do 1003 P=1,NMOLP
         do 1004 K=1,NBINZ
          do 2478 I=1,3
            read(1,*) ZPEPSUM(P,K,I)
2478        continue
1004        continue
          read(1,*) COSSUM(P)
          read(1,*) COSSQSUM(P)
          read(1,*)
1003      continue
      end if
      close(1)
    endif
C *******************************************************
C ** PEPTIDE-SURFACE MODEL PARAMETERS.           **
C *******************************************************
    do 30172 M=1,NATOM
```

```
      do 30182 I=1,2
        A12PS(M,I)=(APEP(M)*AII(I))**6/TEMP
        C6PS(M,I)=(CPEP(M)*CII(I))**3/TEMP
        QCONPS(M,I)=QFACT*QPEP(M)*Q(I)
30182   continue
30172 continue
C ******************************************************
C ** PEPTIDE-PEPTIDE MODEL PARAMETERS.            **
C ******************************************************
    do 30173 M=1,NATOM
      do 30183 N=1,NATOM
        A12PP(M,N)=(APEP(M)*APEP(N))**6/TEMP
        C6PP(M,N)=(CPEP(M)*CPEP(N))**3/TEMP
        QCONPP(M,N)=QFACT*QPEP(M)*QPEP(N)
30183   continue
30173 continue

C****INITIAL PEPTIDE ENERGY CALCULATION**********
    call NRGTOT(V,LX,LY,LZ,NMOLP,A12PS,C6PS,QCONPS,A12PP,
   &    C6PP,QCONPP,NSURF,RSURF,NATOM,PEPCORD,COM,UPEPSFI,
   &    UPEPMSFOLD,UPEPPI,UPMPOLD,VRESTI)
    call UHP_est(UHPA,UHPB,NMOLP,NATOM,RESNUM,PEPCORD,NCA,NCB,
   &    COM,LX,LY,LZ)
    PENTOT = 0.0d+0
    UHBO = 0.0d+0
    UHBIO = 0.0d+0
    UHPO = 0.0d+0
    do 30174 P=1,NMOLP
     do 30176 M=1,NATOM
       do 30178 I=1,3
         PMCORD(M,I)=PEPCORD(P,M,I)
30178    continue
30176   continue
      do 30210 I=1,3
       COMM(I)=COM(P,I)
30210   continue
      do 30186 I=1,RESNUM
       phim(I)=phi(P,I)
       psim(I)=psi(P,I)
       PUHPA(I)=UHPA(P,I)
       PUHPB(I)=UHPB(P,I)
30186   continue
```

```
      call pepenrg(PE,APEP,CPEP,QPEP,PMCORD,NATOM,
     1   phim,psim,v1,v2,v3,v4,v5,v6,RESNUM)
      write(*,*)'PEPTIDE  ,  OLDPENRG'
      write(*,*)P,PE
      PENTOT=PENTOT+PE
      OLDPENRG(P)=PE
      call HPenrg(UHPM,RESNUM,TEMP,PUHPA,PUHPB,PI,kB)
      UHPO = UHPO + UHPM
      call HBenrg_intra(UHBM,PUHPA,RESNUM,NATOM,GROUP,ATOM,
     &       PMCORD,TEMP,COMM,LX,LY,LZ,PI,kB)
      UHBO = UHBO + UHBM
      call HBenrg_inter(UHBIM,PUHPA,UHPA,RESNUM,NMOLP,NATOM,
     &       GROUP,ATOM,PMCORD,PEPCORD,TEMP,P,COMM,COM,LX,LY,LZ,PI,kB)
      UHBIO = UHBIO + UHBIM
30174 continue
     UHBIO = 0.5d+0*UHBIO
     VT = V+PENTOT+UHPO+UHBO+UHBIO
     VTOT(0)=VT
     do P=1,NMOLP
      VPSS(P)=UPEPMSFOLD(P)
      VPEPTP(P)=UPMPOLD(P)
     end do
     write(*,*)'V-ENERGY  PENTOT    UHP      UHB      UHBI   '
     write(*,333)V,PENTOT,UHPO,UHBO,UHBIO
333   format(2x,f8.3,2x,f8.3,2x,f8.3,2x,f8.3,2x,f8.3)
     AVGACCPEP=0.5d+0
     AVGACCTOR=0.5d+0
     if (RUNSTAT.eq.0) then
      call PDBOUT(RSURF,PEPCORD,PDBI,NMOLP,NATOM,NSURF,AA,ATOM,GROUP)
     endif
C ***************************************************************
C ** MC STEPS. each MC step consists of an attempted move for each and every molecule in the system. Every NADJUST steps, maximum movements are adjusted for an acceptance rate of 0.50 Every NSAVE steps, configurations and results are saved for recovery in case the job is killed. *
C ***************************************************************
     do 10000 STEP=1,NMCS
       if(mod(STEP,NADJUST).eq.0) then
         AVGACCPEP=dble(ACCPEP)/(NMOLP*(STEP-1))
         AVGACCTOR=dble(ACCTOR)/(NMOLP*(STEP-1))
         if (AVGACCPEP.gt.0.50) then
           MXTPEP = MXTPEP * 1.1d+0
           MXRPEP = MXRPEP * 1.1d+0
```

```
      else
        MXTPEP = MXTPEP / 1.1d+0
        MXRPEP = MXRPEP / 1.1d+0
      end if
      if (AVGACCTOR.gt.0.50) then
        maxpsi = maxpsi * 1.1d+0
        maxphi = maxphi * 1.1d+0
      else
        maxpsi = maxpsi / 1.1d+0
        maxphi = maxphi / 1.1d+0
      end if
      if(mod(STEP,NSAVE).eq.0) then
        NMCSTMP=STEP-1
        ESUMACCTMP=ESUM
        ACCPEPTMP=ACCPEP
        ACCTORTMP=ACCTOR
        if(RUNSTAT.GE.2) then
         NMCSTMP=NMCSACC+STEP-1
         ESUMACCTMP=ESUMACC+ESUM
         ACCPEPTMP=ACCPEPACC+ACCPEP
         ACCTORTMP=ACCTORACC+ACCTOR
        end if
        open(unit=3,file='CFG.TMP',status='unknown',form=
     &          'formatted')
        rewind(3)
        do 34000 M=1,NATOM
          write(3,889) AA(M),ATOM(M),GROUP(M),APEP(M),CPEP(M),
     1                 QPEP(M), AW(M)
34000       continue
        do 34005 P=1,NMOLP
         do 34010 M=1,NATOM
         write(3,998) PEPCORD(P,M,1),PEPCORD(P,M,2),PEPCORD(P,M,3)
34010        continue
34005       continue
        do 35030 M=1,RESNUM
          write(3,23) NCA(M),NCB(M)
35030       continue
        do 35039 P=1,NMOLP
         write(3,777) (COM(P,I),I=1,3)
35039       continue
        write(3,*) NEND
        write(3,*) CEND
```

```
          do 35038 P=1,NMOLP
           do I=1,RESNUM
            write(3,1523)phi(P,I),psi(P,I)
           enddo
35038        continue
          write(3,1525)v1,v2,v3,v4,v5,v6
1525         format(f8.3,f8.3,f8.3,f8.3,f8.3,f8.3)
          write(3,*) MXTPEP
          write(3,*) MXRPEP
          write(3,*) maxpsi
          write(3,*) maxphi
          write(3,*) NMCSTMP
          write(3,*) ESUMACCTMP
          write(3,*) ACCPEPTMP
          write(3,*) ACCTORTMP
          write(3,*) 'STEP= ',STEP
          close(3)
        end if
      end if
********************** peptide movement ***************************
**TRANSLATIONAL(x,y and z direction) AND ROTATIONAL MOVEMEMNT

**PEPTIDE MOVEMENT**
      do 50050 P=1,NMOLP
        do 50052 M=1,NATOM
          do 50054 I=1,3
            PEPCORDOLD(M,I)=PEPCORD(P,M,I)
            PMCORD(M,I) = PEPCORD(P,M,I)
50054       continue
50052     continue
        do 50056 I=1,3
          COMOLD(I)=COM(P,I)
          COMM(I) = COM(P,I)
50056     continue
        call MOVEPEP(NATOM,PMCORD,COMM,MXTPEP,MXRPEP,
   &              LX,LY,LZ,ISEED)
        do 50062 M=1,NATOM
          do 50064 I=1,3
            PEPCORD(P,M,I) = PMCORD(M,I)
50064       continue
50062     continue
        do 50066 I=1,3
```

```
          COM(P,I)=COMM(I)
50066     continue
**TOTAL ENERGY CALCULATION**
          call UHP_est(UHPA,UHPB,NMOLP,NATOM,RESNUM,PEPCORD,NCA,NCB,
     &         COM,LX,LY,LZ)
          UPSF = 0.0d+0
          UP = 0.0d+0
          PENTOT = 0.0d+0
          UHPN = 0.0d+0
          UHBN = 0.0d+0
          UHBIN = 0.0d+0
          do 50113 K=1,NMOLP
           do 50115 M=1,NATOM
            do 50117 I=1,3
             PMCORD(M,I) = PEPCORD(K,M,I)
50117        continue
50115       continue
          do 50121 I=1,3
           COMM(I) = COM(K,I)
50121       continue
          do 50123 N=1,RESNUM
           phim(N)=phi(K,N)
           psim(N)=psi(K,N)
           PUHPA(N)=UHPA(K,N)
           PUHPB(N)=UHPB(K,N)
50123       continue
          call DISTPEPSF(D2PEPSF1,D2PEPSF2,RSURF,NSURF,
     &          PMCORD,NATOM,LX,LY,COMM)
          call NRGPEPSF(A12PS,C6PS,QCONPS,UPMSF,D2PEPSF1,
     &          D2PEPSF2,NSURF,NATOM)
          UPSF = UPSF+UPMSF
          if (K.eq.P) then
           UPEPMSFNEW=UPMSF
          end if
          call DISTPP(D2PMPEP,PMCORD,PEPCORD,K,NMOLP,NATOM,LX,LY,
     &          COM,COMM)
          call NRGPP(D2PMPEP,A12PP,C6PP,QCONPP,UPMP,K,NMOLP,NATOM)
          UP = UP+UPMP
          if (K.eq.P) then
           UPMPNEW=UPMP
          end if
          call pepenrg(PE,APEP,CPEP,QPEP,PMCORD,NATOM,
```

```
     &          phim,psim,v1,v2,v3,v4,v5,v6,RESNUM)
           PENTOT = PENTOT+PE
           if (K.eq.P) then
             NEWPENRG=PE
           end if
           call HPenrg(UHPM,RESNUM,TEMP,PUHPA,PUHPB,PI,kB)
           UHPN = UHPN+UHPM
           call HBenrg_intra(UHBM,PUHPA,RESNUM,NATOM,GROUP,ATOM,
     &          PMCORD,TEMP,COMM,LX,LY,LZ,PI,kB)
           UHBN = UHBN + UHBM
           call HBenrg_inter(UHBIM,PUHPA,UHPA,RESNUM,NMOLP,NATOM,GROUP
     &          ,ATOM,PMCORD,PEPCORD,TEMP,K,COMM,COM,LX,LY,LZ,PI,kB)
           UHBIN = UHBIN + UHBIM
50113      continue
          UP = 0.5d+0*UP
          UHBIN = 0.5d+0*UHBIN
          VTN = UPSF+UP+PENTOT+ UHPN + UHBN + UHBIN
          DELV = VTN - VT
         if((DELV.ge.0.0d+0).and.(dexp(-DELV).lt.RANDOM(ISEED)))then
           do 52000 N=1,NATOM
            do 53000 I=1,3
             PEPCORD(P,N,I)=PEPCORDOLD(N,I)
53000        continue
52000       continue
           do 54100 I=1,3
            COM(P,I)=COMOLD(I)
54100       continue
           call SUMBINPEP(PEPCORD,P,LZ,NATOM,DELZ,COSSUM,COSSQSUM,
     1          ZPEPSUM,NEND,CEND,COM)
          else
           VT=VTN
           VPSS(P)=VPSS(P)+UPEPMSFNEW-UPEPMSFOLD(P)
           VPEPTP(P)=VPEPTP(P)+UPMPNEW-UPMPOLD(P)
           ACCPEP=ACCPEP+1
           call SUMBINPEP(PEPCORD,P,LZ,NATOM,DELZ,COSSUM,
     1          COSSQSUM,ZPEPSUM,NEND,CEND,COM)
           OLDPENRG(P)=NEWPENRG
           UPEPMSFOLD(P)=UPEPMSFNEW
           UPMPOLD(P)=UPMPNEW
           UHPO=UHPN
           UHBO=UHBN
           UHBIO=UHBIN
```

```
        end if
50050   continue
**********TORSION MOVEMENT**********
      do 54010 P=1,NMOLP
       do 54020 M=1,NATOM
        do 54030 I=1,3
         PEPCORDOLD(M,I)=PEPCORD(P,M,I)
         PMCORD(M,I)=PEPCORD(P,M,I)
54030     continue
54020     continue
       do 54050 I=1,3
        COMM(I)=COM(P,I)
        COMOLD(I)=COM(P,I)
54050     continue
       do 54040 I=1,RESNUM
        phiold(I)=phi(P,I)
        psiold(I)=psi(P,I)
        phim(I)=phi(P,I)
        psim(I)=psi(P,I)
54040     continue
**PEPTIDE MOVEMENT**
       call TORSION(NATOM,PMCORD,maxpsi,maxphi,phim,psim,
   &     COMM,AW,RESNUM,ISEED)
       do 51120 M=1,NATOM
        do 51130 I=1,3
         PEPCORD(P,M,I) = PMCORD(M,I)
51130     continue
51120     continue
       do 51140 I=1,3
        COM(P,I)=COMM(I)
51140     continue
       do 51150 I=1,RESNUM
        phi(P,I)=phim(I)
        psi(P,I)=psim(I)
51150     continue
**TOTAL ENERGY CALCULATION**
       call UHP_est(UHPA,UHPB,NMOLP,NATOM,RESNUM,PEPCORD,NCA,NCB,
   &       COM,LX,LY,LZ)
       UPSF = 0.0d+0
       UP = 0.0d+0
       PENTOT = 0.0d+0
       UHPN = 0.0d+0
```

```
      UHBN = 0.0d+0
      UHBIN = 0.0d+0
      do 51151 K=1,NMOLP
       do 51153 M=1,NATOM
        do 51155 I=1,3
         PMCORD(M,I) = PEPCORD(K,M,I)
51155     continue
51153     continue
      do 51157 I=1,3
       COMM(I) = COM(K,I)
51157     continue
      do 51159 N=1,RESNUM
       phim(N)=phi(K,N)
       psim(N)=psi(K,N)
       PUHPA(N)=UHPA(K,N)
       PUHPB(N)=UHPB(K,N)
51159     continue
      call DISTPEPSF(D2PEPSF1,D2PEPSF2,RSURF,NSURF,
     &          PMCORD,NATOM,LX,LY,COMM)
      call NRGPEPSF(A12PS,C6PS,QCONPS,UPMSF,D2PEPSF1,
     &          D2PEPSF2,NSURF,NATOM)
      UPSF = UPSF+UPMSF
      if (K.eq.P) then
       UPEPMSFNEW=UPMSF
      end if
      call DISTPP(D2PMPEP,PMCORD,PEPCORD,K,NMOLP,NATOM,LX,LY,
     &          COM,COMM)
      call NRGPP(D2PMPEP,A12PP,C6PP,QCONPP,UPMP,K,NMOLP,NATOM)
      UP = UP+UPMP
      if (K.eq.P) then
       UPMPNEW=UPMP
      end if
      call pepenrg(PE,APEP,CPEP,QPEP,PMCORD,NATOM,
     &       phim,psim,v1,v2,v3,v4,v5,v6,RESNUM)
      PENTOT = PENTOT+PE
      if (K.eq.P) then
       NEWPENRG=PE
      end if
      call HPenrg(UHPM,RESNUM,TEMP,PUHPA,PUHPB,PI,kB)
      UHPN = UHPN+UHPM
      call HBenrg_intra(UHBM,PUHPA,RESNUM,NATOM,GROUP,ATOM,
     &       PMCORD,TEMP,COMM,LX,LY,LZ,PI,kB)
```

```
        UHBN = UHBN + UHBM
        call HBenrg_inter(UHBIM,PUHPA,UHPA,RESNUM,NMOLP,NATOM,GROUP
     &         ,ATOM,PMCORD,PEPCORD,TEMP,K,COMM,COM,LX,LY,LZ,PI,kB)
        UHBIN = UHBIN + UHBIM
51151     continue
       UP = 0.5d+0*UP
       UHBIN = 0.5d+0*UHBIN
       VTN = UPSF+UP+PENTOT+ UHPN + UHBN + UHBIN
       DELV = VTN - VT
      if((DELV.ge.0.0d+0).and.(dexp(-DELV).lt.RANDOM(ISEED)))then
        do 52111 N=1,NATOM
         do 53111 I=1,3
          PEPCORD(P,N,I)=PEPCORDOLD(N,I)
53111       continue
52111      continue
        do I=1,3
         COM(P,I)=COMOLD(I)
        enddo
        do i=1,RESNUM
         phi(P,i)=phiold(i)
         psi(P,i)=psiold(i)
        enddo
        call SUMBINPEP(PEPCORD,P,LZ,NATOM,DELZ,COSSUM,COSSQSUM,
     1       ZPEPSUM,NEND,CEND,COM)
       else
        do i=1,RESNUM
         write(88,*)phi(P,i),psi(P,i)
        enddo
        VT=VTN
        VPSS(P)=VPSS(P)+UPEPMSFNEW-UPEPMSFOLD(P)
        VPEPTP(P)=VPEPTP(P)+UPMPNEW-UPMPOLD(P)
        ACCTOR=ACCTOR+1
        call SUMBINPEP(PEPCORD,P,LZ,NATOM,DELZ,COSSUM,COSSQSUM,
     1       ZPEPSUM,NEND,CEND,COM)
        UPEPMSFOLD(P)=UPEPMSFNEW
        OLDPENRG(P)=NEWPENRG
        UPMPOLD(P)=UPMPNEW
        UHPO=UHPN
        UHBO=UHBN
        UHBIO=UHBIN
       end if
4010   continue
```

```
**********************************************************************
      VTOT(STEP)=VT
      ESUM=ESUM+VTOT(STEP)
      do 10005 P=1,NMOLP
       VPS(P,STEP)=VPSS(P)
       VPEPT(P,STEP)=VPEPTP(P)
       ETED(P,STEP)=
     &   ( (PEPCORD(P,94,1)-PEPCORD(P,1,1))**2 +
     &   (PEPCORD(P,94,2)-PEPCORD(P,1,2))**2 +
     &   (PEPCORD(P,94,3)-PEPCORD(P,1,3))**2 )**0.5
       CM(P,STEP)=COM(P,3)
10005  continue
10000 continue
C****FINAL PEPTIDE ENERGY CALCULATION**********
     call NRGTOT(V,LX,LY,LZ,NMOLP,
    & A12PS,C6PS,QCONPS,A12PP,C6PP,QCONPP,NSURF,RSURF,NATOM,PEPCORD,
    & COM,UPEPSF,UPEPMSFOLD,UPEPP,UPMPOLD,VREST)
      call UHP_est(UHPA,UHPB,NMOLP,NATOM,RESNUM,PEPCORD,NCA,NCB,
    &    COM,LX,LY,LZ)
     PENTOT = 0.0d+0
     UHBN = 0.0d+0
     UHBIN = 0.0d+0
     UHPN = 0.0d+0
     do 10007 P=1,NMOLP
      do 10008 M=1,NATOM
       do 10012 I=1,3
         PMCORD(M,I)=PEPCORD(P,M,I)
10012    continue
10008  continue
      do 10030 I=1,3
       COMM(I)=COM(P,I)
10030  continue
      do 10022 I=1,RESNUM
       phim(I)=phi(P,I)
       psim(I)=psi(P,I)
       PUHPA(I)=UHPA(P,I)
       PUHPB(I)=UHPB(P,I)
10022  continue
      call pepenrg(PE,APEP,CPEP,QPEP,PMCORD,NATOM
    1      ,phim,psim,v1,v2,v3,v4,v5,v6,RESNUM)
      PENTOT = PENTOT + PE
      OLDPENRG(P)=PE
```

```
      call HPenrg(UHPM,RESNUM,TEMP,PUHPA,PUHPB,PI,kB)
      UHPN = UHPN + UHPM
      call HBenrg_intra(UHBM,PUHPA,RESNUM,NATOM,GROUP,ATOM,
     &      PMCORD,TEMP,COMM,LX,LY,LZ,PI,kB)
      UHBN = UHBN + UHBM
      call HBenrg_inter(UHBIM,PUHPA,UHPA,RESNUM,NMOLP,NATOM,
     &      GROUP,ATOM,PMCORD,PEPCORD,TEMP,P,COMM,COM,LX,LY,LZ,PI,kB)
      UHBIN = UHBIN + UHBIM
10007 continue
     UHBIN = 0.5d+0*UHBIN
     VT = V+PENTOT+UHPN+UHBN+UHBIN
     VTOT(NMCS+1)=VT
     NMCSOLD=NMCS
     if(RUNSTAT.GE.2) then
       NMCSACC=NMCSACC+NMCS
       ACCPEPACC=ACCPEPACC+ACCPEP
       ACCTORACC=ACCTORACC+ACCTOR
       NMCS=NMCSACC
     end if
C ***************************************************
C ** AVERAGES.                          **
C ** acceptance ratio. energy.  pair correlation functions.
C ***************************************************
     AVGACCPEP=dble(ACCPEP)/dble(NMOLP*NMCS)
     AVGACCTOR=dble(ACCTOR)/dble(NMOLP*NMCS)
     if(RUNSTAT.ge.2)then
       ESUMACC=ESUMACC+ESUM
       ESUM=ESUMACC
     end if
     AVGNRG=ESUM/dble(NMCS)
     do 13303 P=1,NMOLP
      do 13101 K=1,NBINZ
       do 13102 I=1,3
         ZPEP(P,K,I)=dble(ZPEPSUM(P,K,I))/dble(NMCS)
13102    continue
13101   continue
      COSAVG(P)=COSSUM(P)/NMCS
      COSSQAVG(P)=(COSSQSUM(P)*3.d+0-dble(NMCS))/(2.d+0*NMCS)
13303   continue
C ***************************************************
C ** OUTPUT DATA.                       **
C ** final configuration. acceptance ratios. energies. pair correlation functions.          **
```

```
C ************************************************
      write(9,*)
      write(9,*) '***********************************'
      write(9,*)
      write(9,*) 'GENERAL OUTPUT DATA'
      write(9,*)
      write(9,*) TITLE
      write(9,100) RUNSTAT
      write(9,*) CFGINP
      write(9,*) CFGOUT
      write(9,*) OUTPUT
      write(9,*) PDB
      write(9,*)'No of molecules of peptide'
      write(9,*) NMOLP
      write(9,*)'Total no of MC steps'
      write(9,120) NMCS
      write(9,140) TEMP
      write(9,*) NSAVE
      write(9,*) NADJUST
      write(9,*) SURFINP
      write(9,*) QSURF
      write(9,*) PEP
      write(9,*) VPEP
      write(9,*) NSURF
      write(9,*) SURFNAME
      write(9,*) LX,LY,LZ
      write(9,*)
      write(9,*) 'AVERAGE PEPTIDE MOVEMENT ACCEPTANCE RATIO'
      write(9,*) AVGACCPEP
      write(9,*) 'AVERAGE PEPTIDE TORSIONAL ACCEPTANCE RATIO'
      write(9,*) AVGACCTOR
      write(9,*) 'Maximum psi Movement of Peptide'
      write(9,*) maxpsi
      write(9,*) 'Maximum phi Movement of Peptide'
      write(9,*) maxphi
      write(9,*)
      write(9,*) 'INITIAL ENERGY'
      write(9,*) VTOT(0)
      write(9,*)
      write(9,*) 'ENERGIES (system and water)'
       do P=1,NMOLP
         ETEDAVG(P)=0.0d+0
```

```
        CMAVG(P)=0.0d+0
       end do
      do 3111 STEP=1,NMCSOLD
       if(mod(STEP,NPTS).eq.0)then
         N=STEP/NPTS
         VTOTPT(N)=VTOT(STEP)
         do P=1,NMOLP
          ETEDP(P,N)=ETED(P,STEP)
          CMP(P,N)=CM(P,STEP)
          VPSPT(P,N)=VPS(P,STEP)
          VPEPTPT(P,N)=VPEPT(P,STEP)
          ETEDAVG(P)=ETEDAVG(P)+ETED(P,STEP)
          CMAVG(P)=CMAVG(P)+CM(P,STEP)
         end do
       end if
3111  continue
      if (NMCSOLD.ge.100) then
       do P=1,NMOLP
        ETEDAVG(P)=ETEDAVG(P)/100
        CMAVG(P)=CMAVG(P)/100
       end do
      end if
      VERRSUM=0.d+0
      do 3000 N=1,100
        write(9,888) N*NPTS,VTOTPT(N)
        VERRSUM=VERRSUM+dabs(VTOTPT(N)-AVGNRG)
3000  continue
888   format('step=',I6,'<E>=',D18.10)
C     do 30005 N=1,100
C       write(9,8885) N*NPTS,VPSPT(N)
C30005 continue
C8885  format('step=',I6,'<VPS>=',D18.10)
      VERR=VERRSUM/100.0d+0
      write(9,*)
      write(9,*) 'FINAL ENERGY'
      write(9,*) VTOT(NMCSOLD+1)
      write(9,*) 'AVERAGE ENERGY & UNCERTAINTY'
      write(9,*) AVGNRG,VERR
      write(9,*)
      write(9,*)'Peptide ETED and CM'
C     do 8889 P=1,(NMOLP-1),2
C       do 8887 N=1,100
```

```
C         write(9,890) N*NPTS,P,ETEDP(P,N),P,CMP(P,N),(P+1),
C     &               ETEDP((P+1),N),(P+1),CMP((P+1),N)
C8887    continue
C8889  continue
C      if (mod(NMOLP,2).ne.0)then
C        do 8892 N=1,100
C         write(9,891) N*NPTS,NMOLP,ETEDP(NMOLP,N),NMOLP,CMP(NMOLP,N)
C8892    continue
C      end if
      do 10889 P=1,(NMOLP-1),2
        write(9,1090) P,ETEDAVG(P),P,CMAVG(P),(P+1),ETEDAVG(P+1),(P+1),
     &               CMAVG(P+1)
10889 continue
      if (mod(NMOLP,2).ne.0)then
        write(9,1091) NMOLP,ETEDAVG(NMOLP),NMOLP,CMAVG(NMOLP)
      end if
C890   format('STEP=',I6,'<ETEDP',I6,'>=',D18.10,'<CMP',I6,'>=',D18.10,
C     &      '<ETEDP',I6,'>=',D18.10,'<CMP',I6,'>=',D18.10)
C891   format('STEP=',I6,'<ETEDP',I6,'>=',D18.10,'<CMP',I6,'>=',D18.10)
1090  format('<ETEDAVG_PEP',I6,'>=',D18.10,'<CMAVG_PEP',I6,'>=',
     &      D18.10,'<ETEDAVG_PEP',I6,'>=',D18.10,'<CMAVG_PEP',I6,
     &      '>=',D18.10)
1091  format('<ETEDAVG_PEP',I6,'>=',D18.10,'<CMAVG_PEP',I6,'>='
     &      ,D18.10)
      write(9,*)
      write(9,*)'Peptide order parameter'
      do P=1,NMOLP-1,2
        write(9,895) P,COSAVG(P),COSSQAVG(P),(P+1),COSAVG(P+1),
     &       COSSQAVG(P+1)
      end do
      if (mod(NMOLP,2).ne.0)then
        write(9,896) NMOLP,COSAVG(NMOLP),COSSQAVG(NMOLP)
      end if
895   format('<PEPTIDE:',I6,'><COSAVG>=',D18.10,'<COSSQAVG>=',D18.10,3x,
     &      '<PEPTIDE:',I6,'><COSAVG>=',D18.10,'<COSSQAVG>=',D18.10,3x)
896   format('<PEPTIDE:',I6,'><COSAVG>=',D18.10,'<COSSQAVG>=',D18.10,3x)
      if (RUNSTAT.gt.1) then
        write(9,*)
        write(9,*) 'PEPTIDE Z position'
        do 4999 P=1,NMOLP-1,2
          do 5001 I=1,3
            write(9,977) P,I,(P+1),I
```

```
          do 5011 K=1,NBINZ
            write(9,996) ZPEP(P,K,I),ZPEP((P+1),K,I)
5011        continue
5001      continue
4999    continue
       if (mod(NMOLP,2).ne.0)then
         do 5002 I=1,3
          write(9,997) NMOLP,I
          do 5012 K=1,NBINZ
            write(9,1099) ZPEP(NMOLP,K,I)
5012        continue
5002      continue
       end if
977     format('PEPTIDE:',I6,'ZPEP',I6,6x,'PEPTIDE:',I6,'ZPEP',I6)
996     format(6x,f8.4,6x,f8.4)
997     format('PEPTIDE:',I6,'ZPEP',I6)
1099    format(6x,f8.4)
     endif
     close(9)
*************************************************************************
     write(2,*)NMOLP
     write(2,*) NATOM
     do 33000 M=1,NATOM
       write(2,889) AA(M),ATOM(M),GROUP(M),APEP(M),CPEP(M),QPEP(M)
    1   ,AW(M)
33000 continue
     do 33005 P=1,NMOLP
        do 33010 M=1,NATOM
          write(2,998) PEPCORD(P,M,1),PEPCORD(P,M,2),PEPCORD(P,M,3)
33010      continue
33005 continue
     do 35040 M=1,RESNUM
       write(2,23)NCA(M),NCB(M)
35040 continue
     do 35045 P=1,NMOLP
        write(2,777) (COM(P,I),I=1,3)
35045    continue
     write(2,*) NEND
     write(2,*) CEND
     do 35055 P=1,NMOLP
       do 35056 I=1,RESNUM
         write(2,1523)phi(P,I),psi(P,I)
```

```
35056    continue
35055 continue
      write(2,1524)v1,v2,v3,v4,v5,v6
      write(2,*) MXTPEP
      write(2,*) MXRPEP
      write(2,*) maxpsi
      write(2,*) maxphi
      if (RUNSTAT.gt.1) then
      write(2,*) NMCSACC
      write(2,*) ESUMACC
      write(2,*) ACCPEPACC
      write(2,*) ACCTORACC
      write(2,*) 'ZPEPSUM'
      do 1008 P=1,NMOLP
       do 1007 K=1,NBINZ
        do 41710 I=1,3
          write(2,*) ZPEPSUM(P,K,I)
41710    continue
1007    continue
        write(2,*) COSSUM(P)
        write(2,*) COSSQSUM(P)
        write(2,*) '**********************'
1008  continue
      write(2,*) 'STEP= ',NMCSOLD
      end if
      close(2)
      close(7)
      close(88)
      call PDBOUT(RSURF,PEPCORD,PDB,NMOLP,NATOM,NSURF,AA,ATOM,GROUP)

      stop
      end
```

****

** NRGTOT.....subroutine which calculates the total potential energy for any given configuration. for programming simplicity, the code is written to sum up the potential energies felt by each molecule and then divide this sum by a factor of 2 since each pair interaction is counted twice. **

****

```
      subroutine NRGTOT(V,LX,LY,LZ,NMOLP,
     & A12PS,C6PS,QCONPS,A12PP,C6PP,QCONPP,NSURF,RSURF,NATOM,PEPCORD,
     & COM,VPEPSF,VPMSF,VPEPP,VPMP,VREST)
      implicit   NONE
      external   DISTPEPSF
```

```
      external   NRGPEPSF
      external   DISTPP,NRGPP
*************************************************************************
      integer NSURF,NATOM,NMOLP
      integer P,M,I
      double precision V,VREST,LX,LY,LZ
      double precision RSURF(1000,3)
      double precision A12PS(200,2),C6PS(200,2),QCONPS(200,2)
      double precision A12PP(200,200),C6PP(200,200),QCONPP(200,200)
      double precision PEPCORD(50,200,3),COM(50,3)
      double precision VPEPSF,VPMSF(50),VPEPP,VPMP(50),VPSF,VP
      double precision D2PEPSF1(200,1000),D2PEPSF2(200,1000)
      double precision D2PEPP(200,50,200),PMCORD(200,3),COMM(3)
C ***************************************************
C ** TOTAL ENERGY.                        **
the calculation includes all pair interactions between a given molecule and the closest images of the remaining
molecules. **
C ***************************************************
      V=0.0d+0
      VREST=0.0d+0
      VPEPSF=0.0d+0
      VPEPP=0.0d+0
      do 1004 P=1,NMOLP
        do 61060 M=1,NATOM
         do 61070 I=1,3
           PMCORD(M,I)=PEPCORD(P,M,I)
61070     continue
61060   continue
       do 61090 I=1,3
          COMM(I)=COM(P,I)
61090   continue
** PEPTIDE-PEPTIDE **
       call DISTPP(D2PEPP,PMCORD,PEPCORD,P,NMOLP,NATOM,LX,LY,COM,COMM)
       call NRGPP(D2PEPP,A12PP,C6PP,QCONPP,VP,P,NMOLP,NATOM)
       VPMP(P)=VP
       VPEPP=VPEPP+VP
** PEPTIDE-SURFACE **
       call DISTPEPSF(D2PEPSF1,D2PEPSF2,RSURF,NSURF,PMCORD,
     1              NATOM,LX,LY,COMM)
       call NRGPEPSF(A12PS,C6PS,QCONPS,VPSF,D2PEPSF1,
     1              D2PEPSF2,NSURF,NATOM)
       VPEPSF = VPEPSF+VPSF
```

```
      VPMSF(P) = VPSF
1004  continue
      VPEPP=0.5*VPEPP
      V=VPEPSF+VPEPP
      VREST=VPEPSF
      return
      end
*************************************************************************
** DISTPEPSF.....subroutine which calculates the squared distance between the atoms of the chosen molecules and the sites of the surfaces. **
*************************************************************************
      subroutine DISTPEPSF(D2PEPSF1,D2PEPSF2,RSURF,NSURF,PMCORD,NATOM,
     1          LX,LY,COMM)
      implicit NONE
      integer N,M,NSURF,NATOM
      double precision LX,LY,DELX,DELY,DELZ1,DELZ2,CORX,CORY
      double precision D2PEPSF1(200,1000),D2PEPSF2(200,1000)
      double precision PMCORD(200,3)
      double precision RSURF(1000,3),COMM(3)
      do 2000 N=1,NSURF
        DELX=RSURF(N,1)-COMM(1)
        CORX=LX*dnint(DELX/LX)
        DELY=RSURF(N,2)-COMM(2)
        CORY=LY*dnint(DELY/LY)
        do 2100 M=1,NATOM
          DELX=RSURF(N,1)-PMCORD(M,1)-CORX
          DELY=RSURF(N,2)-PMCORD(M,2)-CORY
          DELZ1=RSURF(N,3)-PMCORD(M,3)
          DELZ2=-RSURF(N,3)-PMCORD(M,3)
          D2PEPSF1(M,N)=DELX*DELX+DELY*DELY+DELZ1*DELZ1
          D2PEPSF2(M,N)=DELX*DELX+DELY*DELY+DELZ2*DELZ2
2100     continue
2000  continue
      return
      end
*************************************************************************
** NRGPEPSF: subroutine which calculates the potential energy "felt" by a chosen molecule. **
*************************************************************************
      subroutine NRGPEPSF(A12PX,C6PX,QCONPX,VPEPSF,D2PEPSF1,D2PEPSF2,
     1              NSURF,NATOM)
      implicit   NONE
*************************************************************************
```

```
      integer         M,N,NSURF,NATOM
      double precision D6,D12,VPEPSF,DSURF
      double precision D2PEPSF1(200,1000),D2PEPSF2(200,1000)
      double precision A12PX(200,2),C6PX(200,2),QCONPX(200,2)
      VPEPSF=0.d+0
      do 2000 M=1,NATOM
        do 2100 N=1,NSURF
        DSURF=dsqrt(D2PEPSF1(M,N))
        D6=D2PEPSF1(M,N)**3
        D12=D2PEPSF1(M,N)**6
        VPEPSF=VPEPSF+A12PX(M,1)/D12-C6PX(M,1)/D6
     1       +QCONPX(M,1)/DSURF
        DSURF=dsqrt(D2PEPSF2(M,N))
        D6=D2PEPSF2(M,N)**3
        D12=D2PEPSF2(M,N)**6
        VPEPSF=VPEPSF+A12PX(M,2)/D12-C6PX(M,2)/D6
     1       +QCONPX(M,2)/DSURF
2100    continue
2000  continue
      return
      end
*************************************************************************
** DISTPP.....subroutine which calculates the squared distances between the atoms of the chosen peptide molecule and the atoms of the closest images of the remaining peptide molecules in the system.      **
*************************************************************************
      subroutine DISTPP(D2PP,PMCORD,PEPCORD,P,NMOLP,NATOM,LX,LY,
     &           COM,COMM)
      implicit   NONE
      integer    N,I,NATOM,P,Q,NMOLP
      double precision DELX,DELY,DELZ,LX,LY,CORX,CORY
      double precision D2PP(200,50,200),COM(50,3),COMM(3)
      double precision PEPCORD(50,200,3),PMCORD(200,3)
C ****************************************************
C ** SQUARED DISTANCES.                      **
C ** note that the minimum image convention is applied only to COM                      **
C ****************************************************
      do 1004 Q=1,NMOLP
        if(Q.ne.P)then
          DELX=COM(Q,1)-COMM(1)
          CORX=LX*dnint(DELX/LX)
          DELY=COM(Q,2)-COMM(2)
          CORY=LY*dnint(DELY/LY)
```

```
          do 1011 I=1,NATOM
            do 1021 N=1,NATOM
              DELX=PEPCORD(Q,N,1)-PMCORD(I,1)-CORX
              DELY=PEPCORD(Q,N,2)-PMCORD(I,2)-CORY
              DELZ=PEPCORD(Q,N,3)-PMCORD(I,3)
              D2PP(I,Q,N)=DELX*DELX+DELY*DELY+DELZ*DELZ
1021          continue
1011        continue
          end if
1004  continue
      return
      end
*************************************************************************
** NRGPP: subroutine which calculates the potential energy "felt" by a chosen peptide molecule from the atoms of the remaining peptides.**
*************************************************************************
      subroutine NRGPP(D2PP,A12PP,C6PP,QCONPP,VPP,P,NMOLP,NATOM)
      implicit   NONE
*************************************************************************
      integer         M,I,NATOM,P,Q,NMOLP
      double precision VPP,D,D6,D12
      double precision A12PP(200,200),C6PP(200,200),QCONPP(200,200)
      double precision D2PP(200,50,200)
C *****************************************************
C ** ENERGY CALCULATION.                    **
C ** the calculation includes all pairs of atoms in the chosen molecule and the closest images of the remaining molecules. **
C *****************************************************
      VPP=0.0d+0
      do 1001 I=1,NATOM
        do 1025 Q=1,NMOLP
          if (Q.ne.P)then
            do 1011 M=1,NATOM
              D=dsqrt(D2PP(I,Q,M))
              D6=(D2PP(I,Q,M))**3
              D12=(D2PP(I,Q,M))**6
              VPP=VPP+A12PP(I,M)/D12-C6PP(I,M)/D6+QCONPP(I,M)/D
1011          continue
          end if
1025    continue
1001  continue
      return
```

```
      end
*************************************************************************
** MULTMAT.....subroutine which multiplies two matrices.            **
*************************************************************************
      subroutine MULTMAT(A,B,ROW,MID,COL,AB)
      implicit   NONE
*************************************************************************
      integer         I,J,K,ROW,MID,COL
      double precision A(ROW,MID),B(MID,COL),AB(ROW,COL)
C ***************************************************
      do 1000 I=1,ROW
      do 1010 J=1,COL
        AB(I,J)=0.0d+0
      do 1020 K=1,MID
        AB(I,J)=AB(I,J)+A(I,K)*B(K,J)
1020  continue
1010  continue
1000  continue
      return
      end
*************************************************************************
** INCONFIG.....subroutine which sets up the initial configuration of water molecules for a cold start  **
*************************************************************************
      subroutine INCONFIG(LX,LY,LZ,NMOLP,NATOM,PEPCORD,COM,APEP,
     &  CPEP,QPEP,AW,AA,ATOM,GROUP,NEND,CEND,phi,psi,
     &  v1,v2,v3,v4,v5,v6,RESNUM,NCA,NCB)
      implicit   NONE
*************************************************************************
      integer I,M,P
      integer RESNUM
      integer NCA(20),NCB(20)
      integer NATOM,NEND,CEND,NMOLP
      integer ATOM(200),AA(200),GROUP(200)
      double precision LX,LY,LZ
      double precision PEPCORD(50,200,3),APEP(200),CPEP(200),QPEP(200)
      double precision COM(50,3)
      double precision phi(50,20),psi(50,20),AW(200)
      double precision v1,v2,v3,v4,v5,v6
      open(unit=10,file='Shake.cod',status='unknown',form='formatted')
      rewind(10)
      read(10,*)
      read(10,*) NATOM
```

```
      if(NATOM.GT.200) STOP 'Matrix size too small'
      do 35000 M=1,NATOM
       read(10,889)AA(M),ATOM(M),GROUP(M),APEP(M),CPEP(M),QPEP(M),AW(M)
35000 continue
      do 35020 P=1,NMOLP
       do 35030 M=1,NATOM
        read(10,998) PEPCORD(P,M,1),PEPCORD(P,M,2),PEPCORD(P,M,3)
35030   continue
35020 continue
      do 35010 M=1,RESNUM
       read(10,23) NCA(M),NCB(M)
35010 continue
      do 35040 P=1,NMOLP
         read(10,777) (COM(P,I),I=1,3)
35040    continue
      read(10,*) NEND
      read(10,*) CEND
      do 35050 p=1,NMOLP
       do 35060 I=1,RESNUM
        read(10,21)phi(P,I),psi(P,I)
35060   continue
35050 continue
      read(10,22)v1,v2,v3,v4,v5,v6
889   format(5x,I3,1x,I3,1x,I4,1x,f8.3,f8.3,f8.3,f8.3)
998   format(3x,f8.3,f8.3,f8.3)
21    format(5x,f8.3,5x,f8.3)
22    format(f8.3,f8.3,f8.3,f8.3,f8.3,f8.3)
23    format(2x,i3,2x,i3)
777   format(f17.13,2x,f17.13,2x,f17.13)
      close(10)
      return
      end
```

****

** RANDOM.....This function generates random numbers in the range 0.0 ** TO 1.0. It is a modification of the RANDOM subroutine in V.A. Dyck, J.D. Lawson and J.A. Smith, "FORTRAN 77: an introduction to structured problem solving", Prentice-Hall, New Jersey (1984). Please cut and paste here the subroutine RANDOM(ISEED) that can be found in the explicit code (Appendix A of this thesis). **

****

****

* PDBOUT: this subroutine generates a PDB output file. You can view it through RASMOL. **

****

```
 subroutine PDBOUT(RSURF,PEPCORD,FILENAME,NMOLP,NATOM,NSURF,
&                 AA,ATOM,GROUP)
 implicit none
 character FILENAME*15
 integer NATOM,NMOLP,NSURF
 integer M,ALA,LYS,P,K
 integer N,H,CA,CB1,CB2,C,O,CG,CD,CE,NZ,HZ1,HZ2,HZ3
 integer AA(200),ATOM(200),GROUP(200)
 double precision RSURF(1000,3),PEPCORD(50,200,3)
 ALA=1
 LYS=2
 C  =1
 CA =2
 CB1=3
 CB2=4
 CG =5
 H  =6
 N  =7
 O  =8
 CD =9
 CE =10
 NZ =11
 HZ1=12
 HZ2=13
 HZ3=14
 open(unit=8,file=FILENAME,status='unknown',form='formatted')
 write(8,*)'HEADER'
 do 190 P=1,NMOLP
  do 223 M=1,NATOM
    if(ATOM(M).EQ.C) then
      if(AA(M).EQ.ALA) then
        write(8,950) M,GROUP(M),PEPCORD(P,M,1),
1               PEPCORD(P,M,2),PEPCORD(P,M,3)
      else if(AA(M).EQ.LYS) then
        write(8,937) M,GROUP(M),PEPCORD(P,M,1),
1               PEPCORD(P,M,2),PEPCORD(P,M,3)
      end if
    else if(ATOM(M).EQ.CA) then
      if(AA(M).EQ.ALA) then
        write(8,951) M,GROUP(M),PEPCORD(P,M,1),
1               PEPCORD(P,M,2),PEPCORD(P,M,3)
      else if(AA(M).EQ.LYS) then
```

```
      write(8,938) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
     end if
    else if(ATOM(M).EQ.CB1) then
     if(AA(M).EQ.ALA) then
      write(8,952) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
    else if(AA(M).EQ.LYS) then
    write(8,939) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
    end if
    else if(ATOM(M).EQ.CB2) then
     if(AA(M).EQ.ALA) then
      write(8,953) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
    else if(AA(M).EQ.LYS) then
      write(8,940) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
    end if
    else if(ATOM(M).EQ.CG) then
     if(AA(M).EQ.ALA) then
      write(8,954) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
    else if(AA(M).EQ.LYS) then
     write(8,941) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
    end if
    else if(ATOM(M).EQ.CD) then
     if(AA(M).EQ.ALA) then
      write(8,955) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
    else if(AA(M).EQ.LYS) then
     write(8,942) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
    end if
    else if(ATOM(M).EQ.CE) then
     if(AA(M).EQ.ALA) then
      write(8,956) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
    else if(AA(M).EQ.LYS) then
     write(8,943) M,GROUP(M),PEPCORD(P,M,1),
1           PEPCORD(P,M,2),PEPCORD(P,M,3)
```

```
      end if
      else if(ATOM(M).EQ.H) then
       if(AA(M).EQ.ALA) then
        write(8,957) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      else if(AA(M).EQ.LYS) then
       write(8,944) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      end if
      else if(ATOM(M).EQ.N) then
       if(AA(M).EQ.ALA) then
        write(8,958) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      else if(AA(M).EQ.LYS) then
       write(8,945) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      end if
      else if(ATOM(M).EQ.NZ) then
       if(AA(M).EQ.ALA) then
        write(8,959) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      else if(AA(M).EQ.LYS) then
       write(8,946) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      end if
      else if(ATOM(M).EQ.O) then
       if(AA(M).EQ.ALA) then
        write(8,960) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      else if(AA(M).EQ.LYS) then
       write(8,947) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      end if
      else if(ATOM(M).EQ.HZ1) then
       if(AA(M).EQ.ALA) then
        write(8,961) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      else if(AA(M).EQ.LYS) then
       write(8,948) M,GROUP(M),PEPCORD(P,M,1),
     1          PEPCORD(P,M,2),PEPCORD(P,M,3)
      end if
      else if(ATOM(M).EQ.HZ2) then
```

```
          if(AA(M).EQ.ALA) then
            write(8,962) M,GROUP(M),PEPCORD(P,M,1),
     1             PEPCORD(P,M,2),PEPCORD(P,M,3)
          else if(AA(M).EQ.LYS) then
            write(8,949) M,GROUP(M),PEPCORD(P,M,1),
     1             PEPCORD(P,M,2),PEPCORD(P,M,3)
          end if
          else if(ATOM(M).EQ.HZ3) then
            if(AA(M).EQ.ALA) then
              write(8,963) M,GROUP(M),PEPCORD(P,M,1),
     1             PEPCORD(P,M,2),PEPCORD(P,M,3)
          else if(AA(M).EQ.LYS) then
            write(8,850) M,GROUP(M),PEPCORD(P,M,1),
     1             PEPCORD(P,M,2),PEPCORD(P,M,3)
          end if
        end if
  223   continue
  190   continue
        K=NATOM
        do 226 M=1,NSURF
          K=K+1
          write(8,966) K,11,RSURF(M,1),RSURF(M,2),RSURF(M,3)
          K=K+1
          write(8,966) K,12,RSURF(M,1),RSURF(M,2),-RSURF(M,3)
  226   continue
  937   format('ATOM  ',I5,1x,' C  ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  938   format('ATOM  ',I5,1x,' CA ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  939   format('ATOM  ',I5,1x,' CB1',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  940   format('ATOM  ',I5,1x,' CB2',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  941   format('ATOM  ',I5,1x,' CG ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  942   format('ATOM  ',I5,1x,' CD ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  943   format('ATOM  ',I5,1x,' CE ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  944   format('ATOM  ',I5,1x,' H  ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  945   format('ATOM  ',I5,1x,' N  ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  946   format('ATOM  ',I5,1x,' NZ ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  947   format('ATOM  ',I5,1x,' O  ',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  948   format('ATOM  ',I5,1x,' HZ1',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  949   format('ATOM  ',I5,1x,' HZ2',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  850   format('ATOM  ',I5,1x,' HZ3',1x,'LYS',2x,I4,4x,f8.3,f8.3,f8.3)
  950   format('ATOM  ',I5,1x,' C  ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
  951   format('ATOM  ',I5,1x,' CA ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
  952   format('ATOM  ',I5,1x,' CB1',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
```

```
953   format('ATOM  ',I5,1x,' CB2',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
954   format('ATOM  ',I5,1x,' CG ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
955   format('ATOM  ',I5,1x,' CD ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
956   format('ATOM  ',I5,1x,' CE ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
957   format('ATOM  ',I5,1x,' H  ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
958   format('ATOM  ',I5,1x,' N  ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
959   format('ATOM  ',I5,1x,' NZ ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
960   format('ATOM  ',I5,1x,' O  ',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
961   format('ATOM  ',I5,1x,' HZ1',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
962   format('ATOM  ',I5,1x,' HZ2',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
963   format('ATOM  ',I5,1x,' HZ3',1x,'ALA',2x,I4,4x,f8.3,f8.3,f8.3)
966   format('ATOM  ',I5,1x,' CH2',1x,'SUF',2x,I4,4x,f8.3,f8.3,f8.3)
      close(8)
      return
      end
*************************************************************************
** UHP_est... SUBROUTINE WHICH CALCULATES THE C_alf & C_beta DENSITY  **
** PARAMETER FOR EACH OF THE AMINO ACID FOR ALL THE PEPTIDE MOLECULES **
*************************************************************************
      subroutine UHP_est(UHPA,UHPB,NMOLP,NATOM,RESNUM,PEPCORD,NCA,NCB,
     &       COM,LX,LY,LZ)
      implicit none
      integer Q,C,K,i,r,NMOLP,NATOM,NCA(20),NCB(20)
      integer RESNUM
      double precision PEPCORD(50,200,3)
      double precision COM(50,3)
      double precision PPEPA_Ki(3),PPEPB_Ki(3),PPEPA_Qr(3),PPEPB_Qr(3)
      double precision LX,LY,LZ,PI
      double precision sigHP1,sigHP2,UHPATM,UHPBTM
      double precision CORX,CORY,DELX,DELY,DELZ,D
      double precision D2CAPCA(20,50,20),D2CBPCB(20,50,20)
      double precision UHPA(50,20),UHPB(50,20)
      parameter (PI=3.14159265d+0)
       sigHP1 = 3.5d+0
       sigHP2 = 9.5d+0
       do 515 K=1,NMOLP
        do 222 i=1,RESNUM
          do 224 C=1,3
            PPEPA_Ki(C)=PEPCORD(K,NCA(i),C)
            PPEPB_Ki(C)=PEPCORD(K,NCB(i),C)
224         continue
          do 226 Q=1,NMOLP
```

```
          DELX=COM(Q,1)-COM(K,1)
          CORX=LX*dnint(DELX/LX)
          DELY=COM(Q,2)-COM(K,2)
          CORY=LY*dnint(DELY/LY)
          do 228 r=1,RESNUM
           do 225 C=1,3
            PPEPA_Qr(C)=PEPCORD(Q,NCA(r),C)
            PPEPB_Qr(C)=PEPCORD(Q,NCB(r),C)
225         continue
           if ((Q.eq.K).and.(r.eq.i)) then
            D2CAPCA(i,Q,r)= 0.0d+0
            D2CBPCB(i,Q,r)= 0.0d+0
           else
            DELX=PPEPA_Qr(1)-PPEPA_Ki(1)-CORX
            DELY=PPEPA_Qr(2)-PPEPA_Ki(2)-CORY
            DELZ=PPEPA_Qr(3)-PPEPA_Ki(3)
            D2CAPCA(i,Q,r)=DELX*DELX+DELY*DELY+DELZ*DELZ
            DELX=PPEPB_Qr(1)-PPEPB_Ki(1)-CORX
            DELY=PPEPB_Qr(2)-PPEPB_Ki(2)-CORY
            DELZ=PPEPB_Qr(3)-PPEPB_Ki(3)
            D2CBPCB(i,Q,r)=DELX*DELX+DELY*DELY+DELZ*DELZ
           end if
228         continue
226        continue
222       continue
        do 232 i=1,RESNUM
         UHPATM=0.0d+0
         UHPBTM=0.0d+0
         do 234 Q=1,NMOLP
          do 236 r=1,RESNUM
           if ((Q.ne.K).or.((Q.eq.K).and.(r.ne.i))) then
            D=dsqrt(D2CAPCA(i,Q,r))
            if (D.lt.sigHP1) then
              UHPATM = UHPATM + 1d+0
            elseif (D.le.sigHP2) then
        UHPATM=UHPATM+(0.5*(1+ dcos(PI*(D-sigHP1)/(sigHP2-sigHP1))))
            end if
            D=dsqrt(D2CBPCB(i,Q,r))
            if (D.lt.sigHP1) then
              UHPBTM = UHPBTM + 1d+0
            elseif (D.le.sigHP2) then
        UHPBTM=UHPBTM+(0.5*(1+ dcos(PI*(D-sigHP1)/(sigHP2-sigHP1))))
```

```
              end if
             end if
236           continue
234         continue
           UHPA(K,i)=UHPATM
           UHPB(K,i)=UHPBTM
232       continue
515     continue
       return
       end
*************************************************************************
** HPenrg.....subroutine which calculates the Hydrophobic interactionenergy of the peptide molecule **
*************************************************************************
       subroutine HPenrg(VHPM,RESNUM,TEMP,UHPA,UHPB,PI,kB)
       implicit none
       integer M,i,mu
       integer RESNUM
       double precision TEMP,kB,PI
       double precision SHPA,SHPB,VHPA,VHPB,VHPM
       double precision etaHPA,etaHPB,epsHPA,epsHPB(20)
       double precision UHPA(20),UHPB(20)
        VHPM = 0d+0
        VHPA = 0d+0
        VHPB = 0d+0
c ** HP PARAMETERS FOR ALA-LYS BLOCK PEPTIDE ***
        etaHPA = 12d+0
        etaHPB = 12d+0
        epsHPA = 1.12d+0/(kB*TEMP)
        do 210 M=1,RESNUM
          if (M.le.5) then
            epsHPB(M)=0d+0
          else
            epsHPB(M)=2.8d+0/(kB*TEMP)
          end if
210       continue
c ********************************************************
c ** Hydrophobic Interaction (HP) Energy Calculations ***
c ********************************************************
       do 272 I=1,RESNUM
         if (UHPA(I).gt.etaHPA) then
           SHPA = 1d+0
         else
```

```
        SHPA = dcos(PI*(etaHPA-UHPA(I))/(2*etaHPA))
       end if
       VHPA = VHPA + SHPA
272    continue
      VHPA = epsHPA*VHPA
      do 274 mu=1,RESNUM
       if (UHPB(mu).gt.etaHPB) then
        SHPB = 1d+0
       else
        SHPB = dcos(PI*(etaHPB-UHPB(mu))/(2*etaHPB))
       end if
       VHPB = VHPB + (epsHPB(mu)*SHPB)
274    continue
      VHPM = -(VHPA + VHPB)
     return
      end
*************************************************************************
** HBenrg_intra.....subroutine which calculates the intra-molecular     **
** Hydrogen Bond interaction energy of the selected peptide molecule    **
*************************************************************************
      subroutine HBenrg_intra(VHB_intra,PUHPA,RESNUM,NATOM,GROUP,ATOM,
     1                PMCORD,TEMP,COMM,LX,LY,LZ,PI,kB)
      implicit none
      external SHB_est,VHB1_est,PPEPA_est
      integer I,II,JJ,RESNUM,NATOM,ATOM(200),GROUP(200)
      double precision PMCORD(200,3),PUHPA(20)
      double precision TEMP,kB,PI
      double precision SHB(20),SHBIJ,PMAMi(9,3),PMAMj(9,3)
      double precision VHB1SUM,VHB2SUM
      double precision sigHB,sigHB12,sigHB10,rHB0,epsHB
      double precision etaHBcMX,etaHBcMN,cHBc
      double precision LX,LY,LZ,COMM(3)
      double precision etaHBMX,etaHBMN,VHB_intra,VHB1
       VHB1SUM = 0d+0
       VHB2SUM = 0d+0
       VHB_intra= 0d+0
       sigHB = 2d+0
       rHB0 = 1.43d+0
       epsHB = 2.8d+0/(kB*TEMP)
       etaHBMX = 9d+0
       etaHBMN = 1d+0
       etaHBcMX = 12d+0
```

```
      etaHBcMN = 3d+0
      cHBc = 0.5d+0
C *********************************************
c ** Hydrogen Bond (HB) Energy Calculations ***
c *********************************************
      call SHB_est(SHB,PUHPA,RESNUM,etaHBMX,etaHBMN,PI)
      sigHB12=sigHB**12d+0
      sigHB10=sigHB**10d+0
**INTRA-MOLECULAR AMINO ACID INTERACTIONS
      do 320 JJ=1,RESNUM-3
       do 330 II=(JJ+3),RESNUM
        SHBIJ=(SHB(II)+SHB(JJ))/2d+0
        call PPEPA_est(PMAMi,NATOM,GROUP,ATOM,PMCORD,II)
        call PPEPA_est(PMAMj,NATOM,GROUP,ATOM,PMCORD,JJ)
** TO CALCULATE THE FIRST TERM OF HB INTERACTION FOR INTRA-MOLECULAR SCENARIO
        call VHB1_est(VHB1,PMAMi,PMAMj,LX,LY,LZ,sigHB12,sigHB10,
     &              COMM,COMM,SHBIJ,II,JJ)
        VHB1SUM= VHB1SUM + VHB1
330     continue
320     continue
** TO CALCULATE THE SECOND TERM OF HB INTERACTION FOR INTRA-MOLECULAR SCENARIO
      call SHB_est(SHB,PUHPA,RESNUM,etaHBcMX,etaHBcMN,PI)
      do 440 i=1,RESNUM
       VHB2SUM=VHB2SUM + SHB(i)
440     continue
      VHB_intra = epsHB*(VHB1SUM+(cHBc*VHB2SUM))
     return
     end
*************************************************************************
** SHB_est.....subroutine which calculates the switching function for AA local density in Hydrogen Bond interaction calculations **
*************************************************************************
     subroutine SHB_est(SHB,PUHPA,RESNUM,etaHBMX,etaHBMN,PI)
     implicit none
     integer i,RESNUM
     double precision SHB(20),PUHPA(20),etaHBMX,etaHBMN,PI
      do 310 i=1,RESNUM
       if (PUHPA(i).gt.etaHBMX) then
        SHB(i)=1d+0
       elseif (PUHPA(i).ge.etaHBMN) then
        SHB(i)=0.5d+0*(1d+0 + dcos(PI*(etaHBMX-PUHPA(i))/
     &          (etaHBMX-etaHBMN)))
```

```
        else
          SHB(i)=0d+0
        end if
310     continue
      return
      end
*************************************************************************
** HBenrg_inter.....subroutine which calculates the inter-molecular     **
** Hydrogen Bond interaction energy of the selected peptide molecule    **
*************************************************************************
      subroutine HBenrg_inter(VHB_inter,PUHPA,UHPA,RESNUM,NMOLP,NATOM,
     &           GROUP,ATOM,PMCORD_P,PEPCORD,TEMP,P,COM_P,COM,LX,LY,LZ,
     &           PI,kB)
      implicit none
      external SHB_est,VHB1_est,PPEPA_est
      integer i,k,l,P,NMOLP,Q
      integer II,JJ,RESNUM,NATOM,ATOM(200),GROUP(200)
      double precision PMCORD_P(200,3),PUHPA(20),PMCORD_Q(200,3)
      double precision TEMP,kB,PI,PEPCORD(50,200,3),QUHPA(20)
      double precision SHBP(20),SHBIJ,PMAMi(9,3),PMAMj(9,3),SHBQ(20)
      double precision VHB1SUM,UHPA(50,20)
      double precision sigHB,sigHB12,sigHB10,rHB0,epsHB
      double precision LX,LY,LZ,VHB_inter,VHB1
      double precision COM_P(3),COM(50,3),COM_Q(3)
      double precision etaHBMX,etaHBMN
       VHB1SUM = 0d+0
       VHB_inter= 0d+0
       sigHB = 2d+0
       rHB0 = 1.43d+0
       epsHB = 2.8d+0/(kB*TEMP)
       etaHBMX = 9d+0
       etaHBMN = 1d+0
c ***********************************************
c ** Hydrogen Bond (HB) Energy Calculations ***
c ***********************************************
       call SHB_est(SHBP,PUHPA,RESNUM,etaHBMX,etaHBMN,PI)
       sigHB12=sigHB**12d+0
       sigHB10=sigHB**10d+0
**INTER-MOLECULAR AMINO ACID INTERACTIONS
       do 510 JJ=1,RESNUM
         do 520 Q=1,NMOLP
           if (Q.ne.P) then
```

```
          do 522 k=1,NATOM
           do 524 l=1,3
            PMCORD_Q(k,l)=PEPCORD(Q,k,l)
524          continue
522         continue
          do 526 l=1,3
           COM_Q(l)=COM(Q,l)
526         continue
          do 530 i=1,RESNUM
           QUHPA(i)=UHPA(Q,i)
530         continue
          call SHB_est(SHBQ,QUHPA,RESNUM,etaHBMX,etaHBMN,PI)
          do 540 II=1,RESNUM
           SHBIJ=(SHBQ(II)+SHBP(JJ))/2
           call PPEPA_est(PMAMj,NATOM,GROUP,ATOM,PMCORD_P,JJ)
           call PPEPA_est(PMAMi,NATOM,GROUP,ATOM,PMCORD_Q,II)
** TO CALCULATE THE FIRST TERM OF HB INTERACTION FOR INTER-MOLECULE SCENARIO
           call VHB1_est(VHB1,PMAMi,PMAMj,LX,LY,LZ,sigHB12,
     &                sigHB10,COM_Q,COM_P,SHBIJ,II,JJ)
           VHB1SUM= VHB1SUM + VHB1
540         continue
         endif
520      continue
510     continue
       VHB_inter = epsHB*(VHB1SUM)
      return
      end
*************************************************************************
** PPEPA_est.....subroutine which returns the coordinates of atoms, interacting in HB model, for the selected amino acids (will be different for different amino acids)                **
*************************************************************************
     subroutine PPEPA_est(PEPAA,NATOM,GROUP,ATOM,PMCORD,AA)
     implicit none
     integer NATOM,GROUP(200),ATOM(200),AA,C,i,NATOM1,NATOM2
     double precision PEPAA(9,3),PMCORD(200,3)
      if (AA.le.5) then
       NATOM1 = 1
       NATOM2 = 30
      else
       NATOM1 = 31
       NATOM2 = NATOM
      endif
```

```
      do 340 i=NATOM1,NATOM2
        if (GROUP(i).eq.AA) then
         if (ATOM(i).eq.7) then
          do 350 C=1,3
           PEPAA(1,C)=PMCORD(i,C)
350        continue
         else if (ATOM(i).eq.6) then
          do 360 C=1,3
           PEPAA(2,C)=PMCORD(i,C)
360        continue
         else if (ATOM(i).eq.2) then
          do 370 C=1,3
           PEPAA(3,C)=PMCORD(i,C)
370        continue
         else if (ATOM(i).eq.1) then
          do 372 C=1,3
           PEPAA(4,C)=PMCORD(i,C)
372        continue
         else if (ATOM(i).eq.8) then
          do 374 C=1,3
           PEPAA(5,C)=PMCORD(i,C)
374        continue
         else if (ATOM(i).eq.11) then
          do 376 C=1,3
           PEPAA(6,C)=PMCORD(i,C)
376        continue
         else if (ATOM(i).eq.12) then
          do 378 C=1,3
           PEPAA(7,C)=PMCORD(i,C)
378        continue
         else if (ATOM(i).eq.13) then
          do 380 C=1,3
           PEPAA(8,C)=PMCORD(i,C)
380        continue
         else if (ATOM(i).eq.14) then
          do 382 C=1,3
           PEPAA(9,C)=PMCORD(i,C)
382        continue
         end if
        end if
340   continue
      return
```

```
      end
*************************************************************************
** VHB1_est.....subroutine which calculates the first term of the HB interaction energy estimation model **
*************************************************************************
      subroutine VHB1_est(VHB1,PPEPAi,PPEPAj,LX,LY,LZ,sigHB12,sigHB10,
     &           COMi,COMj,SHBIJ,II,JJ)
      implicit none
      integer j,i,flag,II,JJ,LIMi,LIMj
      double precision VHB1,PPEPAi(9,3),PPEPAj(9,3)
      double precision D2rij,rij,UHBij,sigHB12,sigHB10
      double precision DELX,DELY,DELZ,CORX,CORY
      double precision rij10,rij12,COMi(3),COMj(3)
      double precision LX,LY,LZ,SHBIJ
      VHB1 = 0.0d+0
      DELX=COMi(1)-COMj(1)
      CORX=LX*dnint(DELX/LX)
      DELY=COMi(2)-COMj(2)
      CORY=LY*dnint(DELY/LY)
      if ((II.le.5).and.(JJ.le.5)) then
**INTERACTION BETWEEN ATOMS OF ALA AMINO ACID UNITS**
        do 420 j=1,5
          do 430 i=1,5
            flag=0
            DELX=PPEPAi(i,1)-PPEPAj(j,1)-CORX
            DELY=PPEPAi(i,2)-PPEPAj(j,2)-CORY
            DELZ=PPEPAi(i,3)-PPEPAj(j,3)
            D2rij=DELX*DELX+DELY*DELY+DELZ*DELZ
            if (D2rij.gt.0.0d+0) then
             rij=dsqrt(D2rij)
             rij12 = D2rij**6d+0
             rij10 = D2rij**5d+0
             if(((j.eq.2).and.(i.eq.5)).or.((j.eq.5).and.(i.eq.2)))
     &          then
              flag=1
             else if ((j.eq.1).and.(i.eq.1)) then
              flag=2
             else if (((j.eq.3).and.(i.eq.1)).or.((j.eq.1).and.
     &                (i.eq.3))) then
              flag=2
             else if ((j.eq.4).and.(i.eq.4)) then
              flag=2
             else if (((j.eq.4).and.(i.eq.3)).or.((j.eq.3).and.
```

```
     &                (i.eq.4))) then
              flag=2
             end if
             if (flag.eq.1) then
               UHBij=(5d+0*(sigHB12/rij12))-(6d+0*(sigHB10/rij10))
             else if (flag.eq.2) then
               UHBij=(3d+0*(sigHB10/rij10))
             else
               UHBij=0
             end if
             VHB1 = VHB1 + (SHBIJ*UHBij)
            end if
430          continue
420        continue
       else if ((II.gt.5).and.(JJ.gt.5)) then
**INTERACTION BETWEEN ATOMS OF LYS AMINO ACID UNITS**
          do 425 j=1,9
            do 435 i=1,9
              flag=0
              DELX=PPEPAi(i,1)-PPEPAj(j,1)-CORX
              DELY=PPEPAi(i,2)-PPEPAj(j,2)-CORY
              DELZ=PPEPAi(i,3)-PPEPAj(j,3)
              D2rij=DELX*DELX+DELY*DELY+DELZ*DELZ
              if (D2rij.gt.0.0d+0) then
               rij=dsqrt(D2rij)
               rij12 = D2rij**6d+0
               rij10 = D2rij**5d+0
               if(((j.eq.2).and.(i.eq.5)).or.((j.eq.5).and.(i.eq.2)))
     &            then
                flag=1
               else if(((j.eq.7).and.(i.eq.5)).or.((j.eq.5).and.
     &                (i.eq.7))) then
                flag=1
               else if(((j.eq.8).and.(i.eq.5)).or.((j.eq.5).and.
     &                (i.eq.8))) then
                flag=1
              else if(((j.eq.9).and.(i.eq.5)).or.((j.eq.5).and.
     &                (i.eq.9))) then
                flag=1
               else if ((j.eq.1).and.(i.eq.1)) then
                flag=2
               else if (((j.eq.3).and.(i.eq.1)).or.((j.eq.1).and.
```

```
     &                (i.eq.3))) then
               flag=2
              else if (((j.eq.1).and.(i.eq.6)).or.((j.eq.6).and.
     &                (i.eq.1))) then
               flag=2
              else if ((j.eq.4).and.(i.eq.4)) then
               flag=2
              else if (((j.eq.4).and.(i.eq.3)).or.((j.eq.3).and.
     &                (i.eq.4))) then
               flag=2
              else if ((j.eq.6).and.(i.eq.6)) then
               flag=2
              else if (((j.eq.3).and.(i.eq.6)).or.((j.eq.6).and.
     &                (i.eq.3))) then
               flag=2
              end if
              if (flag.eq.1) then
                UHBij=(5d+0*(sigHB12/rij12))-(6d+0*(sigHB10/rij10))
              else if (flag.eq.2) then
                UHBij=(3d+0*(sigHB10/rij10))
              else
                UHBij=0
              end if
              VHB1 = VHB1 + (SHBIJ*UHBij)
             end if
435           continue
425         continue
        else
**INTERACTION BETWEEN ATOMS OF ALA -> LYS AMINO ACID UNITS**
          if((JJ.le.5).and.(II.gt.5)) then
            LIMj=5
            LIMi=9
          else
            LIMj=9
            LIMi=5
          endif
            do 445 j=1,LIMj
             do 455 i=1,LIMi
               flag=0
               DELX=PPEPAi(i,1)-PPEPAj(j,1)-CORX
               DELY=PPEPAi(i,2)-PPEPAj(j,2)-CORY
               DELZ=PPEPAi(i,3)-PPEPAj(j,3)
```

```
      D2rij=DELX*DELX+DELY*DELY+DELZ*DELZ
      if (D2rij.gt.0.0d+0) then
       rij=dsqrt(D2rij)
       rij12 = D2rij**6d+0
       rij10 = D2rij**5d+0
       if(((j.eq.2).and.(i.eq.5)).or.((j.eq.5).and.(i.eq.2)))
     &    then
        flag=1
       else if(((j.eq.7).and.(i.eq.5)).or.((j.eq.5).and.
     &          (i.eq.7))) then
        flag=1
       else if(((j.eq.8).and.(i.eq.5)).or.((j.eq.5).and.
     &          (i.eq.8))) then
        flag=1
       else if(((j.eq.9).and.(i.eq.5)).or.((j.eq.5).and.
     &          (i.eq.9))) then
        flag=1
       else if ((j.eq.1).and.(i.eq.1)) then
        flag=2
       else if (((j.eq.3).and.(i.eq.1)).or.((j.eq.1).and.
     &           (i.eq.3))) then
        flag=2
       else if (((j.eq.1).and.(i.eq.6)).or.((j.eq.6).and.
     &           (i.eq.1))) then
        flag=2
       else if ((j.eq.4).and.(i.eq.4)) then
        flag=2
       else if (((j.eq.4).and.(i.eq.3)).or.((j.eq.3).and.
     &           (i.eq.4))) then
        flag=2
       else if (((j.eq.3).and.(i.eq.6)).or.((j.eq.6).and.
     &           (i.eq.3))) then
        flag=2
       end if
       if (flag.eq.1) then
         UHBij=(5d+0*(sigHB12/rij12))-(6d+0*(sigHB10/rij10))
       else if (flag.eq.2) then
         UHBij=(3d+0*(sigHB10/rij10))
       else
         UHBij=0
       end if
       VHB1 = VHB1 + (SHBIJ*UHBij)
```

```
            end if
455          continue
445         continue
      endif

      return
      end
*************************************************************************
** MOVEPEP.....subroutine which randomly displaces a molecule. The displacement is performed as a translational displacement of the molecule coupled with a rotational displacement about the position of the oxygen atom. **
*************************************************************************
      subroutine MOVEPEP(NATOM,PMCORD,COMM,MXTPEP,MXRPEP,
     1                   LX,LY,LZ,ISEED)
      implicit   NONE
      external   MULTMAT,RANDOM
*************************************************************************
      integer         I,M,ISEED,NATOM
      double precision LX,LY,LZ,DELC,MXTPEP,MXRPEP,THX,THY,THZ
      double precision COSX,SINX,COSY,SINY,COSZ,SINZ
      double precision ROTX(3,3),ROTY(3,3),ROTZ(3,3),TMP1(3,3)
      double precision TMP2(3,3),COMM(3)
      double precision PMCORD(200,3),RHYOLD(3,200),RHYNEW(3,200)
      double precision RANDOM,L(3)
      L(1)=LX
      L(2)=LY
      L(3)=LZ
C ***************************************************
C ** PEPTIDE COORDINATE MATRIX.                  **
C ** the positions of the peptide atoms are defined relative to the COM point.          **
C ***************************************************
      do 1000 M=1,NATOM
        do 1010 I=1,3
          RHYOLD(I,M)=PMCORD(M,I)-COMM(I)
1010  continue
1000  continue
c ***************************************************
C ** RANDOM ROTATION.                          **
C ***************************************************
      THX=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MXRPEP
      THY=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MXRPEP
      THZ=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MXRPEP
     COSX=dcos(THX)
```

```
      SINX=dsin(THX)
      COSY=dcos(THY)
      SINY=dsin(THY)
      COSZ=dcos(THZ)
      SINZ=dsin(THZ)
      ROTX(1,1)=1.0d+0
      ROTX(1,2)=0.0d+0
      ROTX(1,3)=0.0d+0
      ROTX(2,1)=0.0d+0
      ROTX(2,2)=COSX
      ROTX(2,3)=-SINX
      ROTX(3,1)=0.0d+0
      ROTX(3,2)=SINX
      ROTX(3,3)=COSX
      ROTY(1,1)=COSY
      ROTY(1,2)=0.0d+0
      ROTY(1,3)=-SINY
      ROTY(2,1)=0.0d+0
      ROTY(2,2)=1.0d+0
      ROTY(2,3)=0.0d+0
      ROTY(3,1)=SINY
      ROTY(3,2)=0.0d+0
      ROTY(3,3)=COSY
      ROTZ(1,1)=COSZ
      ROTZ(1,2)=-SINZ
      ROTZ(1,3)=0.0d+0
      ROTZ(2,1)=SINZ
      ROTZ(2,2)=COSZ
      ROTZ(2,3)=0.0d+0
      ROTZ(3,1)=0.0d+0
      ROTZ(3,2)=0.0d+0
      ROTZ(3,3)=1.0d+0
      call MULTMAT(ROTX,ROTY,3,3,3,TMP1)
      call MULTMAT(TMP1,ROTZ,3,3,3,TMP2)
      call MULTMAT(TMP2,RHYOLD,3,3,NATOM,RHYNEW)
C ***************************************************
C ** RANDOM TRANSLATION.                    **
C ***************************************************
      do 100 I=1,3
        DELC=(2.0d+0*RANDOM(ISEED)-1.0d+0)*MXTPEP*L(I)/LX
        COMM(I)=COMM(I)+DELC
        if(I.ne.3) then
```

```
          COMM(I)=COMM(I)-L(I)*dnint(COMM(I)/L(I))
        end if
        do 110 M=1,NATOM
          PMCORD(M,I)=COMM(I)+RHYNEW(I,M)
110     continue
100   continue
      return
      end
*************************************************************************
** SUBROUTINE WHICH CALCULATES THE ENERGY OF THE PEPTIDE MOLECULE ******
*************************************************************************
      SUBROUTINE pepenrg(confgE,APEP,CPEP,QPEP,PEPCORD,NATOM,
     1   phi,psi,v1,v2,v3,v4,v5,v6,RESNUM)
      integer NATOM,M
      integer I,RESNUM
      double precision PEPCORD(200,3),APEP(200),CPEP(200),QPEP(200)
      double precision QFACTP,TEMP,A12P(200,200),C6P(200,200)
      double precision QCONP(200,200)
      double precision AP(200,200),CP(200,200)
      double precision D2PEP(200,200),DELX,DELY,DELZ
      double precision PVPEP,D,D6,D12,VTOR
      double precision phi(20),psi(20),confgE
      double precision v1,v2,v3,v4,v5,v6
c *********************************************************************
c ** The non-bonded interaction energy calculations **
c *********************************************************************
c ***************************************************************
c *************     LJ Potential Calculations   ****************
c ***************************************************************
      TEMP=298.0
      QFACTP=1.671d+5/TEMP
      do 200 M=1,NATOM-1
      do 201 I=M+1,NATOM
        AP(M,I)=dsqrt( APEP(M)*APEP(I) )
        CP(M,I)=dsqrt( CPEP(M)*CPEP(I) )
201     continue
200     continue
      do 202 M=1,NATOM-1
        do 203 I=M+1,NATOM
          A12P(M,I)=(AP(M,I)**12)/TEMP
          C6P(M,I)=(CP(M,I)**6)/TEMP
          QCONP(M,I)=QFACTP*QPEP(M)*QPEP(I)
```

```
 203       continue
 202    continue
C ** This section of this document is identical to the section of the explicit code starting on Page 98 of this thesis and therefore has been deleted.  Cut and paste here from Page 98 Line yy to Page 120 Line zz.  **
      do 204 M=1,NATOM-1
        do 205 I=M+1,NATOM
          DELX=PEPCORD(I,1)-PEPCORD(M,1)
          DELY=PEPCORD(I,2)-PEPCORD(M,2)
          DELZ=PEPCORD(I,3)-PEPCORD(M,3)
          D2PEP(M,I)=DELX*DELX+DELY*DELY+DELZ*DELZ
 205     continue
 204   continue
       PVPEP=0.d+0
      do 206 M=1,NATOM-1
        do 207 I=M+1,NATOM
       D=dsqrt(D2PEP(M,I))
       D6=(D2PEP(M,I))**3
       D12=(D2PEP(M,I))**6
       PVPEP=PVPEP + A12P(M,I)/D12 - C6P(M,I)/D6
     1       + QCONP(M,I)/D
 207     continue
 206     continue
c             write(*,*)'Total Potential '
c             write(*,208) PVPEP
c 208       format(f15.3)
c ***********************************************
c ** Torsional Energy(VTOR) Calculations **
c ***********************************************
      VTOR=0.0d+0
      do i=1,RESNUM
       VTOR=VTOR + 0.5d+0*v1*(1.0d+0 - dcos(phi(i)))
     1    + 0.5d+0*v2*(1.0d+0 - dcos(2.0d+0*phi(i)))
     1    + 0.5d+0*v3*(1.0d+0 + dcos(3.0d+0*phi(i)))
      enddo
      do j=1,RESNUM
      VTOR=VTOR + 0.5d+0*v4*(1.0d+0 - dcos(psi(j)))
     1     + 0.5d+0*v5*(1.0d+0 - dcos(2.0d+0*psi(j)))
     1     + 0.5d+0*v6*(1.0d+0 + dcos(3.0d+0*psi(j)))
      enddo
C             write(*,*)'VTOR',VTOR
       CLOSE(10)
       confgE=VTOR+PVPEP
```

```
c           write(*,*)'Total Confirmational energy of peptide'
c           write(*,*)'ConfgE=',confgE
      RETURN
      END
*************************************************************************
** SUMBINPEP..subroutine which collects the data for the number of atoms in each bin. **
*************************************************************************
      subroutine SUMBINPEP(PEPCORD,P,LZ,NATOM,
     1 DELZ,COSSUM,COSSQSUM,ZPEPSUM,NEND,CEND,COM)
      implicit   NONE
      integer NATOM,BINZ,NEND,CEND
      integer ZPEPSUM(50,2000,3),P
      double precision DELZ,LZ,HALFLZ
      double precision PEPCORD(50,200,3),COM(50,3),COSSQ
      double precision DELTX,DELTY,DELTZ,COSSUM(50),COSSQSUM(50),LNC
C ***************************************************
C ** COLLECTION OF DATA.                    **
C ***************************************************
      HALFLZ=LZ/2.d+0
** Z profile of 1st, last, and COM positions
** 1st atom
       BINZ=idint((PEPCORD(P,1,3)+HALFLZ)/DELZ)+1
       ZPEPSUM(P,BINZ,1)=ZPEPSUM(P,BINZ,1)+1
** COM
       BINZ=idint((COM(P,3)+HALFLZ)/DELZ)+1
       ZPEPSUM(P,BINZ,2)=ZPEPSUM(P,BINZ,2)+1
** last atom
       BINZ=idint((PEPCORD(P,NATOM,3)+HALFLZ)/DELZ)+1
       ZPEPSUM(P,BINZ,3)=ZPEPSUM(P,BINZ,3)+1
**Order Parameter (from NEND to CEND)
      DELTX=PEPCORD(P,NEND,1)-PEPCORD(P,CEND,1)
      DELTY=PEPCORD(P,NEND,2)-PEPCORD(P,CEND,2)
      DELTZ=PEPCORD(P,NEND,3)-PEPCORD(P,CEND,3)
      LNC=dsqrt(DELTX*DELTX+DELTY*DELTY+DELTZ*DELTZ)
      COSSQ=DELTZ/LNC
      COSSUM(P)=COSSUM(P)+COSSQ
      COSSQ=COSSQ*COSSQ
      COSSQSUM(P)=COSSQSUM(P)+COSSQ
      return
      end
*************************************************************************
** TORSION ..... subroutine to give the torsional rotation by changing coordinates of the peptide atoms
```

```
**************************************************************************
      subroutine TORSION(NATOM,PMCORD,maxpsi,maxphi,phim,psim,
     &  COMM,AW,RESNUM,ISEED)
      integer ISEED,NATOM,RESNUM
      integer k1,k2,k3,n3,n4,k4,N
      double precision PMCORD(200,3)
      double precision RANDOM
      double precision u(20,3),s(3),w(3),x(3),maxpsi,cpsi(20)
      double precision phim(20),psim(20),magu(20),magv(20)
      double precision v(20,3),t(3),y(3),z(3),maxphi,cphi(20)
      double precision CM(3),AWS,COMM(3),AW(200)
c u vector is to be used as reference vector for psi angle (about Calpha - C) rotation
c there are 8 Calpha - C bonds, so 8 u vectors
      do I=1,3
      CM(I)=0.0D+0
      enddo
      AWS=0.0D+0
      do i=1,RESNUM
      cpsi(i)=(2.0d+0*RANDOM(ISEED)-1.0d+0)*maxpsi
      cphi(i)=(2.0d+0*RANDOM(ISEED)-1.0d+0)*maxphi
      enddo
      do i=1,RESNUM
      phim(i)=phim(i) + cphi(i)
      psim(i)=psim(i) + cpsi(i)
      enddo
      do 45 k1=1,RESNUM
      if (k1 .le. 5) then
      u(k1,1)=PMCORD(6*k1-1,1) - PMCORD(6*k1-3,1)
      u(k1,2)=PMCORD(6*k1-1,2) - PMCORD(6*k1-3,2)
      u(k1,3)=PMCORD(6*k1-1,3) - PMCORD(6*k1-3,3)
      else
      u(k1,1)=PMCORD((13*(k1-3))+3,1) - PMCORD((13*(k1-3))-6,1)
      u(k1,2)=PMCORD((13*(k1-3))+3,2) - PMCORD((13*(k1-3))-6,2)
      u(k1,3)=PMCORD((13*(k1-3))+3,3) - PMCORD((13*(k1-3))-6,3)
      endif
c magnitude of reference vector u
      magu(k1)=sqrt((u(k1,1))**2 + (u(k1,2))**2 + (u(k1,3))**2)
 45   continue
c v vector is to be used as reference vector for phi angle (about N - Calpha) rotation
c there are 8 N - Calpha bonds, so 8 v vectors
      do 47 k2=1,RESNUM
      if (k2 .le. 5) then
```

```
      v(k2,1)=PMCORD(6*k2-3,1) - PMCORD(6*k2-5,1)
      v(k2,2)=PMCORD(6*k2-3,2) - PMCORD(6*k2-5,2)
      v(k2,3)=PMCORD(6*k2-3,3) - PMCORD(6*k2-5,3)
      else
      v(k2,1)=PMCORD((13*(k2-3))-6,1) - PMCORD((13*(k2-3))-8,1)
      v(k2,2)=PMCORD((13*(k2-3))-6,2) - PMCORD((13*(k2-3))-8,2)
      v(k2,3)=PMCORD((13*(k2-3))-6,3) - PMCORD((13*(k2-3))-8,3)
      endif
c magnitude of reference vector v
      magv(k2)=sqrt((v(k2,1))**2 + (v(k2,2))**2 + (v(k2,3))**2)
 47   continue
c FOR PSI (Calpha-C) rotation calculations for atom coordinates when the right
c bond C - N is rotated, all the atoms on the right are mapped
      do 49 k3=1,RESNUM
      IF (K3 .LE. 5) THEN
      n3=6*k3-1
      else
      n3=13*(k3-3)+3
      endif
      do 50 N=n3+1,NATOM
      s(1)=PMCORD(N,1)-PMCORD(n3,1)
      s(2)=PMCORD(N,2)-PMCORD(n3,2)
      s(3)=PMCORD(N,3)-PMCORD(n3,3)
      w(1)=(1.0d+0/magu(k3))*(u(k3,2)*s(3) - u(k3,3)*s(2) )
      w(2)=(1.0d+0/magu(k3))*(u(k3,3)*s(1) - u(k3,1)*s(3) )
      w(3)=(1.0d+0/magu(k3))*(u(k3,1)*s(2) - u(k3,2)*s(1) )
      x(1)=(1.0d+0/magu(k3))*(u(k3,2)*w(3) - u(k3,3)*w(2) )
      x(2)=(1.0d+0/magu(k3))*(u(k3,3)*w(1) - u(k3,1)*w(3) )
      x(3)=(1.0d+0/magu(k3))*(u(k3,1)*w(2) - u(k3,2)*w(1) )
      PMCORD(N,1)=PMCORD(N,1) + w(1)*dsin(cpsi(k3))
     1   + x(1)*(1.0d+0-dcos(cpsi(k3)))
      PMCORD(N,2)=PMCORD(N,2) + w(2)*dsin(cpsi(k3))
     1   + x(2)*(1.0d+0-dcos(cpsi(k3)))
      PMCORD(N,3)=PMCORD(N,3) + w(3)*dsin(cpsi(k3))
     1   + x(3)*(1.0d+0-dcos(cpsi(k3)))
 50   continue
 49   continue
c calculations for atom coordinates when the right bond C - N is rotated, all the atoms
c on the right are mapped
      do 51 k4=1,RESNUM
      IF (k4 .LE. 5) THEN
      n4=6*k4-3
```

```
      else
      n4=13*(k4-3)-6
      endif
      do 52 I=n4+1,NATOM
      t(1)=PMCORD(I,1)-PMCORD(n4,1)
      t(2)=PMCORD(I,2)-PMCORD(n4,2)
      t(3)=PMCORD(I,3)-PMCORD(n4,3)
      y(1)=(1.0d+0/magv(k4))*(v(k4,2)*t(3) - v(k4,3)*t(2) )
      y(2)=(1.0d+0/magv(k4))*(v(k4,3)*t(1) - v(k4,1)*t(3) )
      y(3)=(1.0d+0/magv(k4))*(v(k4,1)*t(2) - v(k4,2)*t(1) )
      z(1)=(1.0d+0/magv(k4))*(v(k4,2)*y(3) - v(k4,3)*y(2) )
      z(2)=(1.0d+0/magv(k4))*(v(k4,3)*y(1) - v(k4,1)*y(3) )
      z(3)=(1.0d+0/magv(k4))*(v(k4,1)*y(2) - v(k4,2)*y(1) )
      PMCORD(I,1)=PMCORD(I,1) + y(1)*dsin(cphi(k4))
     1    + z(1)*(1d+0-dcos(cphi(k4)))
      PMCORD(I,2)=PMCORD(I,2) + y(2)*dsin(cphi(k4))
     1    + z(2)*(1d+0-dcos(cphi(k4)))
      PMCORD(I,3)=PMCORD(I,3) + y(3)*dsin(cphi(k4))
     1    + z(3)*(1d+0-dcos(cphi(k4)))
   52 continue
   51 continue
      do I=1,3
      do M=1,NATOM
      CM(I)=CM(I)+PMCORD(M,I)*AW(M)
      enddo
      enddo
      do M=1,NATOM
      AWS=AWS+AW(M)
      enddo
      do I=1,3
      COMM(I)=CM(I)/AWS
      enddo
      return
      end
```

APPENDIX D

INSTRUCTIONS TO RUN IMPLICIT MODEL CODE

The implicit model codes pw_imp.f (without surface) and pws_imp.f (with surface) can simulate up to 50 identical peptides (with a maximum of 20 residues each) in a pre-defined simulation box. Like the explicit model code, the simulation is run by splitting the required total number of MC simulation steps in sets of no more than 40,000 MC steps each. After completing a set, the input file required for the next set is generated and the simulation is continued. The simulation uses an input file for a run set, which is associated with system configuration files and output files.

For the implicit model codes, the input data file (inputx.inp) which describes the variables and file names for a simulation run set are written in similar fashion as that for the explicit model. The only difference is the absence of definitions for water molecules in the simulation box. All specific parameters for the HB/HP interaction model have to be set in their respective subroutines in the program code before the simulation run. Thus for running each set of MC simulations the only change to be made in the code is the input date file name for the next set of run. The code is then compiled and submitted for execution.

It should be noted that the attached implicit code to simulate multi-peptide-surface system takes the initial configuration from the output of the computational "shake" simulation. The configuration file (CFGxx.out) of the final set of computational "shake" simulations should be renamed as "shake.cod", which will be read in the INCONFIG( ) subroutine to assign initial configurations to the peptides. This subroutine should be modified if the peptides should be arranged in order inside the simulation box during initialization; where the peptide coordinates and parameters are read from the original peptide configuration file (for our model, the "A5-L5.cod" file).

APPENDIX E

EXPLICIT MODEL RESULTS

.1. Finite peptide concentrations

The diblock peptide used in this work consists of five alanine (ALA) residues followed by five lysine (LYS) residues. The residues were numbered as 1 to 5 for the first block of ALA and 6 to 10 for the LYS block for sake of identification. ALA is a nonpolar amino acid whereas LYS is a polar amino acid carrying a positive charge at pH 7. The selection of this peptide is based on the different hydrophobicities of the two amino acids. The peptide has an energy minimized α-helix conformation, for initial state, that was generated by using Alchemy software platform. All peptide atoms were treated explicitly except for the methyl groups, CH_x (x = 1-3), which were treated as united atoms. The peptide has a volume of 1200 $Å^3$ and an overall charge of +5e.

All water molecules were treated explicitly using the simple point charge (SPC) model. For the selected box size (27.748 Å X 24.030 Å X 38.00 Å), the number of water molecules was adjusted to maintain the desired solvent density to 1 g/cm^3 at a temperature of 298 K. The volume used in calculating solvent density was equal to the volume of the box minus the total volume occupied by the two peptides.

Two surfaces with opposing, but equal, charge density (0.10168 e/ $Å^2$) were placed at the two ends of the simulation box perpendicular to z-axis. Each surface is comprised of 226 united CH_2 atoms (with LJ parameters σ = 3.964 Å and ε = 70.49 K), arranged in face-centered cubic (fcc) 111 crystal lattice structure, with a lattice constant of 6.111 Å.

The interaction between any pair of sites, whether solute or solvent, is the spherically symmetric Lennard-Jones (LJ) plus a Coulomb term,

$$u_{\alpha\beta} = \left\{\frac{A_{\alpha\beta}}{r}\right\}^{12} - \left\{\frac{C_{\alpha\beta}}{r}\right\}^{6} + \frac{e^2 q_\alpha q_\beta}{4\pi\varepsilon_0}\left\{\frac{1}{r}\right\} \qquad \text{(E.1.1)}$$

Where, $A_{\alpha\beta}$ and $C_{\alpha\beta}$ are the repulsive and dispersive coefficients of the LJ potential, r is the distance between atoms α and β, q_α and q_β are the partial charges on atoms α and β respectively and ε_0 is the permittivity.

The contribution to the energy of the system by peptide conformation, consists of a nonbonded torsional energy along with the LJ and electrostatic interaction energies, as described above. The torsional energy is represented through a four term Fourier series,

$$E_{\text{torsion}} = \left(\frac{V_1}{2}\right)(1+\cos\theta) + \left(\frac{V_2}{2}\right)(1-\cos 2\theta) + \left(\frac{V_3}{2}\right)(1+\cos 3\theta) \qquad \text{(E.1.2)}$$

Where, θ is the torsion angle (either φ, rotation about N-C^α, or ψ, rotation about C-C^α). The coefficients, V_x (x=1-3), values are as per Table E.1.1.

Table E.1.1 Coefficients for torsional interactions

Coefficient	For ϕ (rotation about N-C^α)	For ψ (rotation about C^α-C)
V_1	0.000	1.849
V_2	0.000	0.950
V_3	1.498	0.840

The system's energy calculations include peptide-peptide, peptide-water, peptide-surface, water-water and water-surface interactions along with peptide intra-molecular interactions. All interactions were calculated using periodic boundary conditions using the minimum image convention and negating any edge effects.

Canonical ensemble MCMC simulations were carried out with the magnitudes of the maximum translational and rotational movements set separately for water and peptide molecules. They were adjusted every 25 steps throughout the simulation to maintain a 50% movement acceptance ratio. This was also applied to the torsional movements for the peptide molecules. Each simulation step consists of $N_{water} + N_{peptide}$ movements (N_{water} and $N_{peptide}$ are the number of water and peptide molecules respectively). In one step, a

molecule was subject to random translational, rotational or torsional (only for the peptide molecule) movement. Then the system's energy with the resulting conformation is estimated. The difference between the energy of the resulting conformation and the energy of the current conformation is subjected to the Metropolis criteria, to accept or reject the attempted move of the molecule. Movement for peptide-1 is followed by peptide-2 and then by each of the water molecules in a single simulation step. The simulation was run for 1.272 million steps to equilibration.

Figure E.1.1 shows the system's potential energy (PE) vs. the number of MC steps (NMCS). After 0.9 million MC steps the system energy approaches a minimum value and attains the equilibrium state.

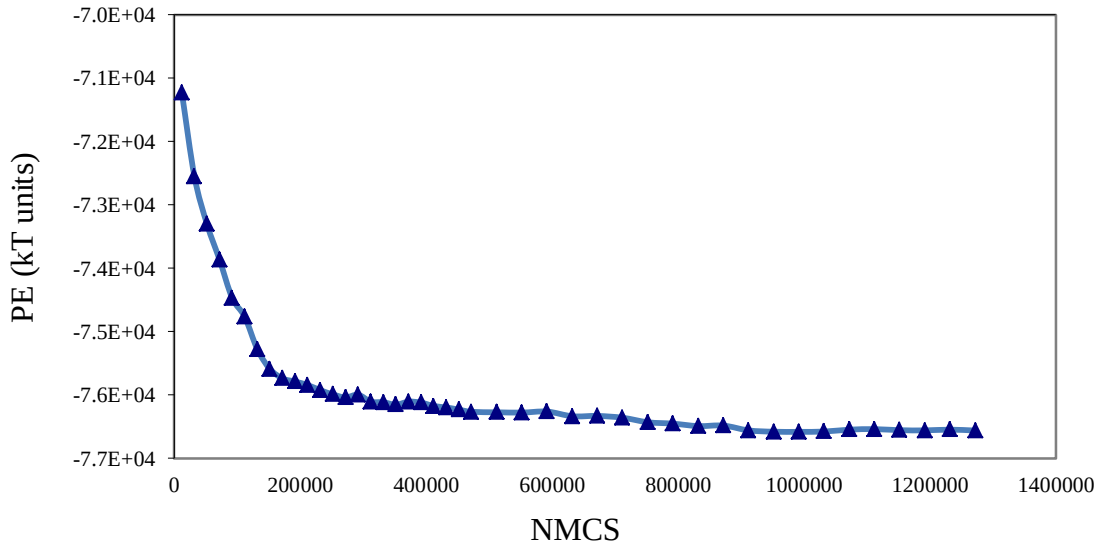


Figure E.1.1 Energy profile for 2-peptide(helix)-water-surface system.

Figures E.1.2 and E.1.3 show the z-location of the peptide's center of mass (COM) and peptide's end-to-end distance (dl), respectively, as functions of the NMCS. Here, the end-to-end distance is defined as the ensemble average of the distance separating the N-atom of the N-terminus ALA residue and the C^{α} atom of the C-terminus LYS residue.

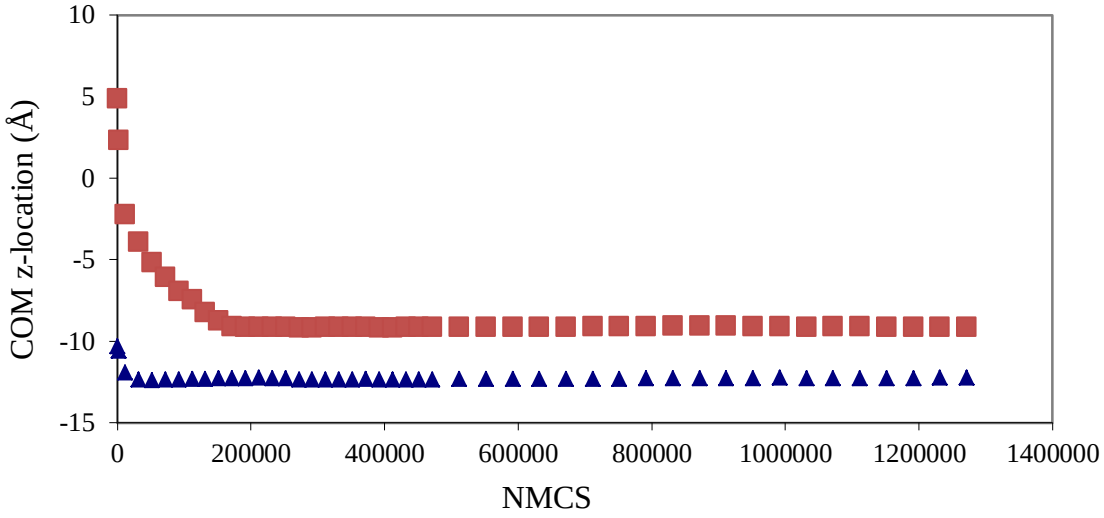


Figure E.1.2 COM z-location profile for 2-peptide(helix)-water-surface system

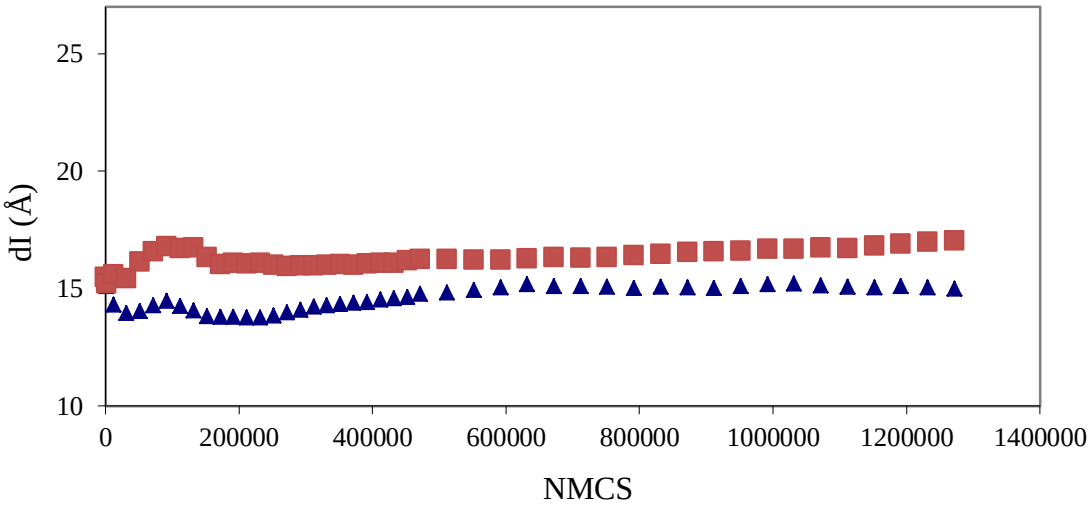
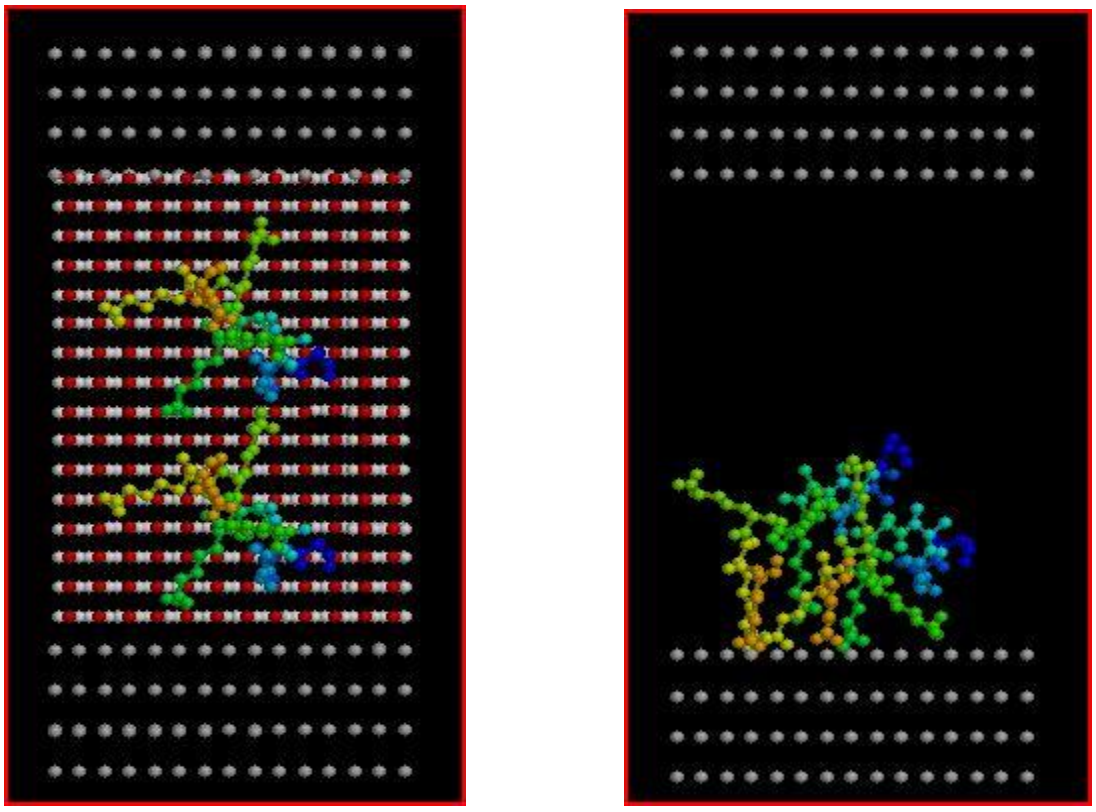


Figure E.1.3 Peptide end-to-end distance profile for 2-peptide(helix)-water-surface system.

Figure E.1.4 shows snapshots of the initial and final configuration states of the system. In Figure E1.4 (b) all water molecules were removed to ease the visualization of the peptides. As part of initialization, depicted in Figure E.1.4 (a), the water molecules were orderly arranged around the peptides, where for a molecule of water the oxygen atom is red and the hydrogen atoms are white. Different amino acids of the diblock

peptide model are displayed in different color shades: the ALA block end is dark blue, the LYS block end is orange, and the methyl groups of the surfaces grey. This color code is kept consistent for all our RasMol "Ball & Stick" graphic visualizations.



(a) (b)

Figure E.1.4 Snapshots of 2-peptide(helix)-water-surface system configuration using RasMol "Ball & Stick" graphics. (a) Initial state. (b) Final state.

The two peptides laid out along z-direction initially, with peptide-1 closer to the surface of complimentary electrostatic charge (negative charge) located at -19 Å on the z-axis, thus approaching the surface before peptide-2, which does so after 0.15 million MC steps. After reaching the surface, the peptide molecules lay flat on the surface to maximize the electrostatic interactions with the opposite charged surface. Both peptides changed their secondary structure upon adsorption (Figure E.1.3). The two peptides follow different paths in the end-to-end distance plot, although they were identical initially.

E.2 Mixing

Figures E.2.1 and E.2.2 show energy and end-to-end distance profiles, respectively, after 0.135 million MC steps. The initial and final system configuration snapshots are shown in Figures E.2.3 (a) and (b). For the sake of clarity the water molecules are not displayed in Figure E.2.3 (b).

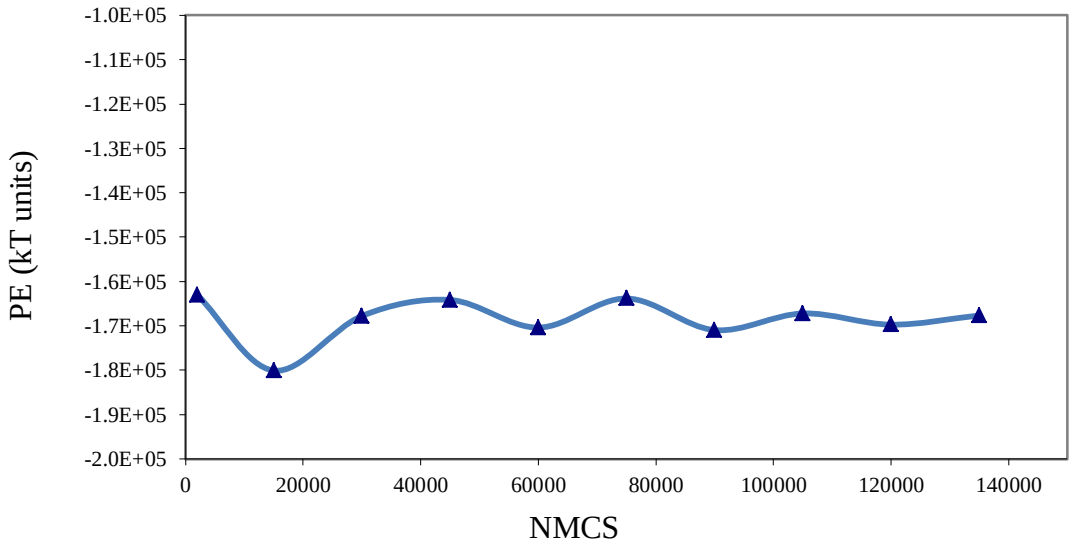


Figure E.2.1 Potential energy vs the number of Monte Carlo steps. Two peptides in explicit water in between surfaces of alternating polarity.

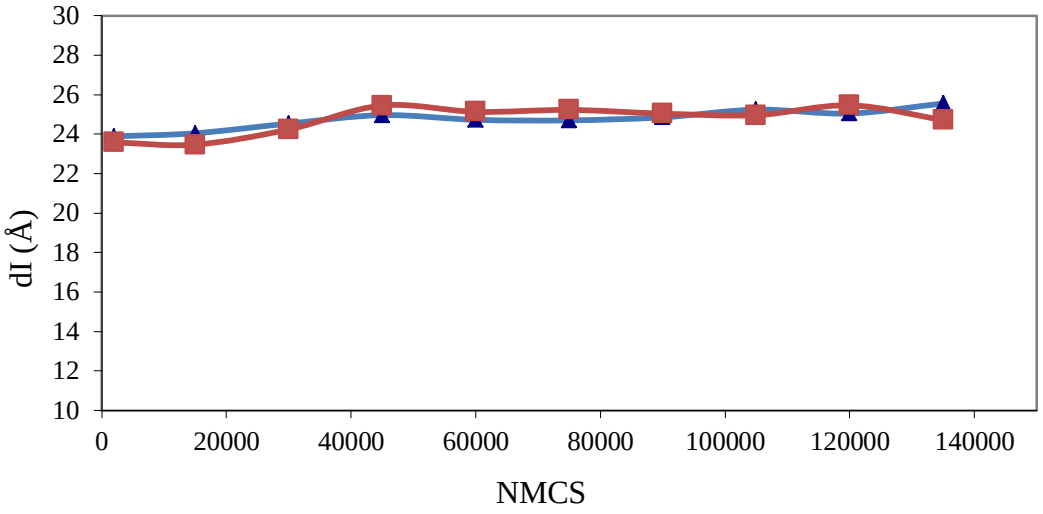
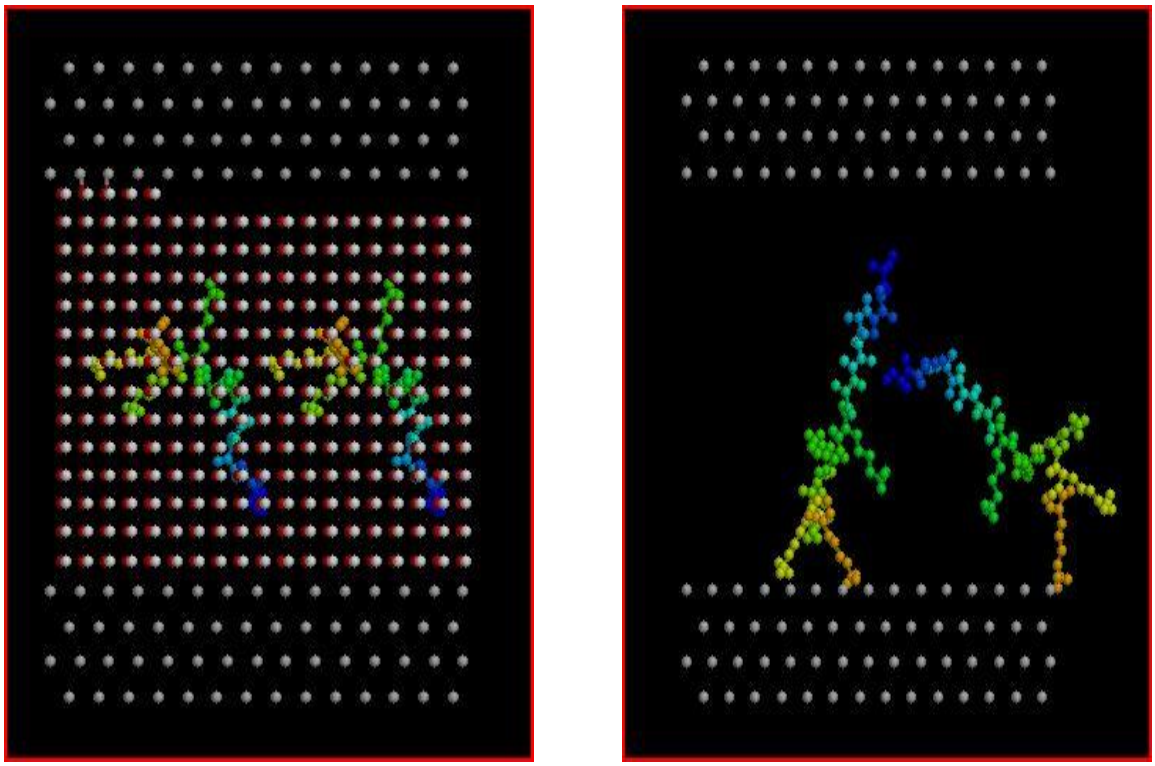


Figure E.2.2 Peptide end-to-end distance vs. the number of Monte Carlo steps. Two peptides in explicit water between two surfaces of alternating polarity.



(a) (b)

Figure E.2.3 RasMol "Ball & Stick" graphic view of initial and final system configuration. Two peptides in explicit water between two surfaces of alternating polarity.

BIBLIOGRAPHY

[1] Fink, A. L. Protein aggregation: folding aggregates, inclusion bodies and amyloid. Folding & Design 3:R9-R23; 1998.

[2] True, H. L., Lindquist, S. L. A yeast prion provides a mechanism for genetic variation and phenotypic diversity. Nature. 407:477-483; 2000.

[3] Dobson, C. M. Principles of protein folding, misfolding and aggregation. Seminars in Cell & Dev. Biol. 15:3-16; 2004.

[4] Feng, Y. W., Ooishi, A., Honda, S. Aggregation factor analysis for protein formulation by a systematic approach using FTIR, SEC and design of experiments techniques. J. of Pharm. and Biomed. Anal. 57:143–152; 2012.

[5]Cellar, T., Douma, R., Huebner, A., Prausnitz, J.; Blanch, H. Kinetic studies of protein L aggregation and disaggregation. Biophys. Chem. 125:350-359; 2007.

[6] Chi, E. Y., Krishnan, S.; Randolph, T. W., Carpenter, J. F. Physical Stability of Proteins in Aqueous Solution: Mechanism and Driving Forces in Nonnative Protein Aggregation. Pharmaceutical Res. 20:1325-1336; 2003.

[7] Taylor, D. R., Hooper, N. M. Role of lipid rafts in the processing of the pathogenic prion and Alzheimer's amyloid-β proteins. Seminars in Cell & Dev. Biol. 18:638-648; 2007.

[8] Giacomelli, C. E., Norde, W. Conformational Changes of the Amyloid β-Peptide (1–40) Adsorbed on Solid Surfaces. Macromol. Biosci. 5:401-407; 2005.

[9] Aisenbrey, C., Borowik, T., Bystrom, R., Bokvist, M., Lindstrom, F., Misiak, H., Sani, M.A., Grobner, G. How is protein aggregation in amyloidogenic diseases modulated by biological membranes? Eur. Biophys. J. 37:247-255; 2008.

[10] Wang, W., Nema, S., Teagarden, D. Protein aggregation - Pathways and influencing factors. Intern. J. Pharmaceutics 390:89-99; 2010.

[11] Sluzky, V., Tamada, J. A., Klibanov, A. M., Langer, R. Kinetics of insulin aggregation in aqueous solutions upon agitation in the presence of hydrophobic surfaces. Appl. Biol. Sci. 88:9377-9381; 1991.

[12] McMasters, M. J., Hammer, R. P., McCarley, R. L. Surface-Induced Aggregation of Beta Amyloid Peptide by ω-Substituted Alkanethiol Monolayers Supported on Gold. Langmuir 21:4464-4470; 2004.

[13] Radford, S. E. Protein folding: Progress made and promises ahead. TIBS 25:611-618; 2000.

[14] Karplus, M. The Levinthal paradox: yesterday and today. Folding and design 2:S69-S75; 1997.

[15] Roberts, C. J. Non-Native Protein Aggregation Kinetics. Biotechnology and bioengineering 98:927-938; 2007.

[16] Kunal, M.N. Formation of amyloid fibrils by diblock peptides. M.S. Thesis, Missouri S&T, 2012.

[17] Matysiak, S., Clementi, C. Optimal combination of theory and experiment for the characterization of the protein folding landscape of S6: How far can a minimalist model go? J. Mol. Biol. 343:235-248; 2004.

[18] Song, D., Forciniti, D. Monte Carlo simulations of peptide adsorption on solid surfaces. J. of Chem. Phys. 115:8089-8100; 2001.

[19] Mungikar, A., Forciniti, D. Molecular Simulations and Neutron Reflectivity studies of Peptides at Solid/liquid Interfaces. ChemPhysChem (Angewandte Chemie), 3: 993-999; 2002.

[20] Mungikar, A., Forciniti, D. Conformational Changes of Peptides at Solid/Liquid Interfaces: A Monte Carlo Study. Biomacromolecules, 5, 2147-2159; 2004.

[21] Mungikar, A., Forciniti, D. Effect of co-solvents on the adsorption of peptides at the solid-liquid interface. Biomacromolecules, 7: 239-251; 2006.

[22] Takada, S., Luthey-Schulten, Z., Wolynes, P. G. Folding dynamics with nonadditive forces: A simulation study of a designed helical protein and a random heteropolymer. J. of chem. Phys. 110:11616-11629; 1999.

VITA

Rehman Fazeem was born in Kannur, in the state of Kerala, India. He completed bachelors degree in Chemical Engineering from University of Kerala, Trivandrum, India, in May 2007. The same year in September he joined Engineers India Ltd. (EIL), New Delhi, as an Engineer in their Heat and Mass Transfer Division. In EIL, Rehman worked on designing and engineering processes and equipment for off-shore/on-shore gas processing facilities.

After resigning from EIL, Rehman joined Missouri S & T (MST), Rolla, MO, USA, in January 2011 to pursue M.S. degree in Chemical Engineering. He worked as a Graduate Assistant in MST, contributing in teaching and researching.

During M.S. degree, Rehman also worked as an intern in Mynah Technologies LLC, Chesterfield, MO, USA. For nine months in Mynah Technologies, starting August 2012, he worked on Control System Testing and Operator Training using real-time dynamic simulation platform of MiMiC software.