MGM's College of Engineering & Technology, Kamothe, Navi Mumbai

Department of Biotechnology

A.Y. 2018-19

Sem: VII **Class: BE**

Virtual Lab Experiments

Sub: Computer Aided Drug Design

Sr. No.	Name of the Experiment	Date of Perform	Time
1	Constructing computational model of a Molecule	05.10.18	02:00 pm – 04:00 pm
2	Introducing Hydrogen atoms to a Molecule	12.10.18	02:00 pm – 04:00 pm
3	Dihedral angle calculation of a molecule	12.10.18	04:00 pm – 06:00 pm

A molecule is a small chemical element that is made up of two or more atoms held together by chemical bonds. A molecule can be composed of either single kind of element (e.g. H2) or different kinds of elements (e.g. CO2). Molecules can be found in both living things and non living things. A drug is a small molecule that can interact, bind and finally control the function of biological receptors that helps to cure a disease. Receptors are proteins that interact with other biological molecules to maintain various cellular functions in body. Enzymes, hormone receptors, cell signaling receptors, neurotransmitter receptors etc. are some important receptors in our body. Drug design is a process of designing small drug molecules that can interact and bind to a target biomolecule. For example, Aspirin is a small pain killer drug molecule which contains nine carbon atoms, eight hydrogen atoms and four oxygen atoms. Design of the molecules should be complementary in shape and charge of the target. Molecular modeling includes computational techniques that are used to model a molecule. Drug designing by using these modeling techniques is referred to as computer-aided drug design. Computer based drug design is a fast, automatic, very low cost process. It

can be either target based or structure based design. Building a molecule using computer techniques is a very important step in drug deigning. There are so many computational tools available for building a molecule.

Hydrogen is the first element in periodic table with the symbol H. It is formed by a nucleus with one unit of positively charged proton and one unit of negatively charged electron. In normal conditions it is colorless, non-toxic, tasteless, odorless and highly explosive gas formed by diatomic molecules, H2. It is the most abundant chemical element and main compound of almost all organic matter. The atomic number of hydrogen is 1 and the atomic weight 1,00797 g/mol. Since hydrogen has the lowest atomic weight of any substance, it has very low density in its liquid and gaseous states.

There are three naturally occupying hydrogen isotopes are there. They are protium, deuterium and tritium. Protium contains a nucleus with a single proton and no neutron, Deuterium contains a single proton and single neutron. Tritium contains one proton and two neutrons. Proton has a positive electrical charge whereas an electron has a negative electrical charge. A neutron has no charge. The bonding between hydrogen atoms is strong. Since it is highly reactive, hydrogen can make bond with other elements also.

Most of the structure databases obtain the 3D structure of biological macromolecules from techniques like X-ray crystallography, NMR Spectroscopy, Small angle X-ray scattering, Electron microscopy etc. These files are saved in either pdb or mmCIF format and stored in the databases like PDB, Structure(NCBI) etc. In PDB, about 90% of the 3D structures are obtained through the method X-ray crystallography. In X-ray crystallography, the position of hydrogen atoms cannot be determined due to its small size, large thermal motion and lesser number of electrons. It has only 1 electron which does not get projected like the other atoms which has a bigger electronic cloud. So hydrogen is not included in the PDB files. Therefore only a part of the molecule may be included in almost all PBD entries. In the case of structure of symmetrical molecules in PDB entry, it includes only a single subunit of the complex. So the coordinates for quaternary structure of a protein should calculate from the coordinate of the subunit. Biologically, all the protein molecules have hydrogen atom and all the bonds are satisfied to obtain a stable conformation. When one does any analysis like docking with the protein molecule, the structures have to be added with hydrogen and satisfy the bonds. So this is an important step before any structure analysis.

A molecule is a small chemical element that is made up of two or more atoms held together by chemical bonds. A molecule can be composed of either single kind of element (e.g. H2) or different kinds of elements (e.g. CO2). These bonds are formed as a result of the sharing or

exchange of electrons among atoms of the molecule. Atoms have a tendency to attain more number of electrons towards itself thereby increasing stability. Bond length is the distance between the nuclei of two bonded atoms whereas bond angle is the angle formed betweeen two adjacent atoms in a molecule. They always range from 100- 180 degrees. Bond angle and bond length are the two important parameters which determine the shape and size of a molecule. The geometry of a molecule can be characterised by analysing the bond length and bond angle. These parameters can vary in their lentgth depending upon their bond multiplicity. They are shorter for a triple bond than for a single bond. Bond angles too vary in their angles from molecule to molecule depending upon on the electron structures of the molecule. Bond angles of molecules and ions are usually determined by VSEPR theory. Valence Shell Electron Pair Repulsion Theory or VSEPR theory are used to predict the shape of molecules based upon the extent of electron pair electrostatic repulsion.

A dihedral angle or torsion angle is the angle between two planes. It defines the conformations around rotatable bonds. The dihedral angle changes only with the distance between the first and fourth atoms; the other inter atomic distances are controlled by the chemical bond lengths and bond angles. Its value range from -180 to +180 degrees. The torsion angle is considered to be positive if a clockwise rotation is performed with the molecule and it will be negative when an anti clockwise rotation is performed with the molecule in its plane.