Patient comes with complications to clinician or physician. There can be a situation where Diagnosis can be made but conventional treatment method might not be available moreover, it may not be available in the near future too as drugs are discovered in years.

One of the benefits of Docking is that through this technique, we can find out a natural treatment which acts on the same pathway. Docking provides us the natural/dietary antagonist which is safer than the drugs available in market or can be used to treat such conditions where no drugs are available currently

Till the time the treatment arrives in its pure form or as an FDA approved drug, we can give these in natural forms as these are time tested.

Taking an example of IL-1 beta which is responsible for the many disease complications. The drugs available in market like Anakinra and Canakinumab have several adverse side effects on patients such as injection site reactions, headaches, increase in levels of cholesterol in their blood, and Macrophage Activation Syndrome (MAS).

Another benefit of Docking is that we can frame several unique and original research questions.

Objectives-
1. What is Molecular Docking?
2. WHY IS DOCKING IMPORTANT?
3. Benefits of Docking
4. Principle of docking
5. Work Flow

What is Molecular Docking

The experiment of how two or more molecular structures (for example, drugs, enzymes and proteins) are in contact with each other is called molecular docking.
In simple terms, docking is a mechanism for molecular modelling that predicts how a protein (enzyme) binds with small molecules (ligands). Ligands join a receptors or protein form a complex which is known as Protein Ligand complex.

WHY IS DOCKING IMPORTANT?

Signal Pathways:- In signal transduction, the interactions between biologically significant molecules, which including proteins, nucleic acids, carbohydrates and lipids play a major role. In addition, strongly connected partners' relative orientation might affect the type of signal generated (e.g., agonism vs antagonism). Docking is thus useful to predict the intensity and form of signal produced.

Drug-Designing:-

Molecular docking is one of the most used initial drug designing method especially when the 3D structure of the target protein is available. This technique can predict both the ligand-protein binding affinity and the protein–ligand complex structure that are useful for optimizing lead. These lead drug candidate can be use in drug development pipeline.

Benefits-
Drug discovery in wet laboratory research take year to find the lead drug molecules and it is very costly. Molecular docking cut down the time as well as cost of drug discovery.

Principle of docking
Molecular docking can be thought of as a 'lock and key' model, where you can find the right relative orientation of the 'key' that unlocks the 'lock' (where there is a keyhole on the surface of the lock, in which direction the key is to turn after inserting the lock etc.).

Work Flow-

The workflow divided in to following segments
1-Receptor Preparation, which has two different parts – Correcting Charges & Energy Minimization
2-Site Map
3-Ligand Preparation
4-Receptor Grid Generation
5-Docking

The Details of each segment is as follows

Binding site

a. **Receptor Preparation**
   Removing unwanted molecule and water, adding Hydrogen atom, correcting charges and performing energy minimization
   Correcting charges is needed to correct because different amino acid carry different charges at different pH and hence Glide is used to correct the charges at pH 7.2-7.4 (physiological pH).
   In energy minimization, a high energy system shows high reactivity and instability, so we have to make the receptor and ligand molecule into its minimum energy configuration for best docking result.

b. **Site Map**
   A crucial factor in drug design is the knowledge of the structure and function of protein active sites. SiteMap's validated binding site identification will enable scientists to classify binding sites with high confidence and to estimate the druggability of these sites.

c. **Ligand Preparation**

Add hydrogen atoms, neutralize charged groups, generate ionization states, generate tautomer, generate low-energy ring conformations, Optimize the geometries.
Tautomers are structural isomers of chemical compounds that readily interconvert between to form.

d. Receptor Grid Generation

Finding the active binding site on target and writing grid file for site specific docking
The **active site** consists of amino acid residues that form temporary bonds with the substrate (**binding site**) and residues that catalyse a reaction of that substrate (catalytic **site**).

Grid file- Coordinate of binding site on protein written in grid file, where the drug or ligand will be bind.

e. Docking

Output score and protein ligand complex

Output score= docking score, or emodel score
protein ligand complex= ligand join on receptor or protein form a complex which known as protein ligand complex (binding pose). (see figure in slide 2)

2. How do we come to a conclusion that the more negative is the value, the better it is?

Binding energy (docking score) is the result of molecular docking, which gives the idea about binding affinity or strength of interaction of the ligand with the receptors. Binding energy is always reported in negative values that means the greater the negative value of binding energy, the stronger the interaction is and vice versa.