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MOLECULAR DOCKING: A REVIEW

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ABSTRACT

It was the most popular and integrity part of computational data based screening method of compounds in Pharmaceutical Research for drug Discovery efforts. The molecular docking is an important part of virtual screening, means "Ligand-based Screening" to find out the active compound as a template and also focus on comparative molecular similarity analysis of compounds with known and unknown activity by algorithm method. Docking is one of the best data-based screening methodology of virtual screening for ligand which minimized the works cost by filtering and also helps to predicted the toxicity study for designing the formulation or synthesis of New Chemical Entity(NCE) in now a day of Pharmaceutical Research Developments.

Key Words: Molecular docking, Computational chemistry (Insilico Methods), Scoring, Docking soft wares.

INTRODUCTION

Molecular docking is an important tool of molecular modeling system which provides to teach us the ligand-protein interaction through four force fields by orientation and translation. It is also welly known as a "Ligand-based Screening Method" in which a small organic molecule having drug liking property or drug molecule is interacting with target protein or receptor through intra or inter molecular binding reasons like hydrogen bonds, vandar waal

bonds etc. This binding conformation will be confirmed by each translation and orientation of ligand-protein complexations and it was observed in visualizing docking windows like Hex-6.3, Argus Lab. 4.0.1 and MVD 5.0.5 by algorithm methods.

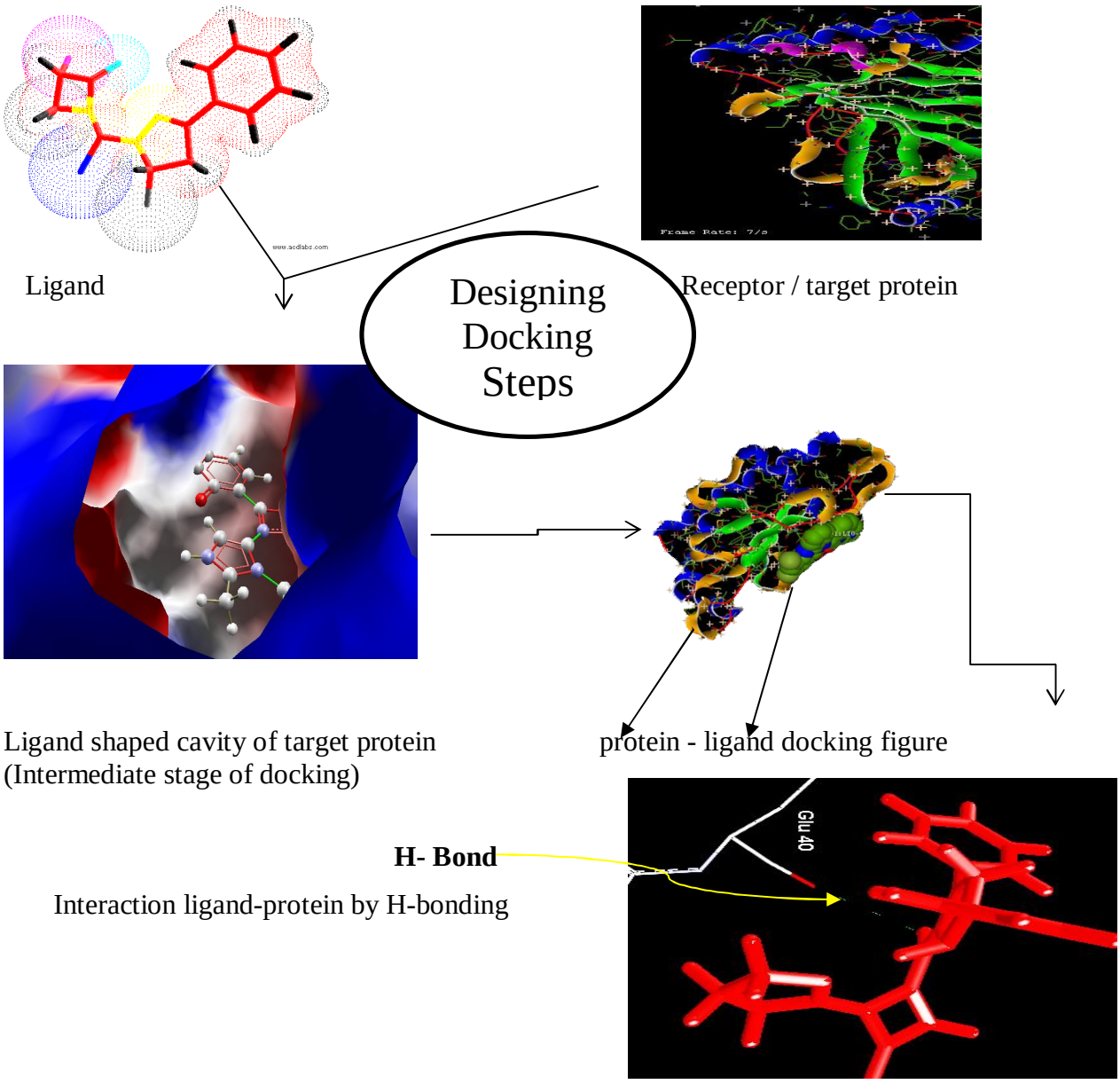


Fig-01

Each iteration of ligand-protein bond complexation will be predicted the binding free energy which is known as pose energy of that conformation. The binding free energy will be depended in the shape or searching space of cavity of protein or receptor and the negative geometry of complexed pair of ligand-protein will be reflected the minimum binding free energy. This minimum negative binding free energy is predicted the best pose of that stable conformation which may or may not be reflected towards the biological indices.

Various computational software methodologies were already used for explaining the ligand-protein or protein-protein or protein-DNA interaction for designing the geometrical conformations of those bond complexations. Among of them, few software like Hex 6.3, ArgusLab.4.0.1 and MVD 5.0.5 were reflected its knowledge to us for designing and described the developing methodologies of molecular docking systems. the developing methodologies of molecular docking systems.

COMPUTATIONAL CHEMISTRY

Basic concept of docking[1]

Docking" is defined as the identification of the low-energy binding modes of a small molecule, or ligand, within the active site of a macromolecule, or receptor, whose structure is known. A compound that interacts strongly with, or binds, a receptor associated with a disease may inhibit its function and thus act as a drug. Solving the docking problem computationally requires an accurate representation of the molecular energetic as well as an efficient algorithm to search the potential binding modes. Shortly it is known as the “Computational simulation of a candidate ligand binding to a receptor”.

Applications:

- predict binding modes of small molecule-protein complexes
- search databases of ligands for compounds that inhibit enzyme activity
- search databases of ligands for compounds that bind a particular protein
- search databases of ligands for compounds that bind nucleic acid targets
- examine possible binding orientations of protein-protein and protein-DNA complexes.
- help guide synthetic efforts by examining small molecules that are computationally derivatized
- many more …..

Ligand or **guest** or **key**[1]

It is the complementary partner molecule which binds to the receptor. Ligands are most often small molecules but could also be another biopolymer.

Character

- It should be chemically active and having drug like property.
- It has definite geometrical shape, size and surface area.
- It has must contained flexible bonds (soft and rigid bonds).
- It has a capacity to accept and donate the electrons.

Receptor (host or lock or Macromolecule or target protein)[1]

The "receiving" molecule, most commonly a protein or other biopolymer is known as receptor.

Binding mode[1]

The orientation of the ligand relative to the receptor as well as the conformation of the ligand and receptor when bound to each other is known as binding mode.

Pose - It is a candidature of ligand binding mode.

Scoring – The process of evaluating a particular pose by counting the number of favorable intermolecular interactions such as hydrogen bonds and hydrophobic contacts of ligand is known as scoring.

Ranking – The process of classifying which ligands are most likely to interact favorably to a particular receptor based on the predicted free-energy of binding.

Molecular Docking [(2, 3)]

Docking is an important part of drug designing field of molecular modeling system in which the orientation by means of interaction through H-bond or Vander Waal force of one molecule (ligand) to a second molecule(macro molecule or target protein) were bound with each other to form a stable complex. The orientation is directly referred to the strength of bond association or bond affinity between these two molecules and also predicted the scoring functions. The scoring function is directly influence the biological activity of that relevant molecule Docked.

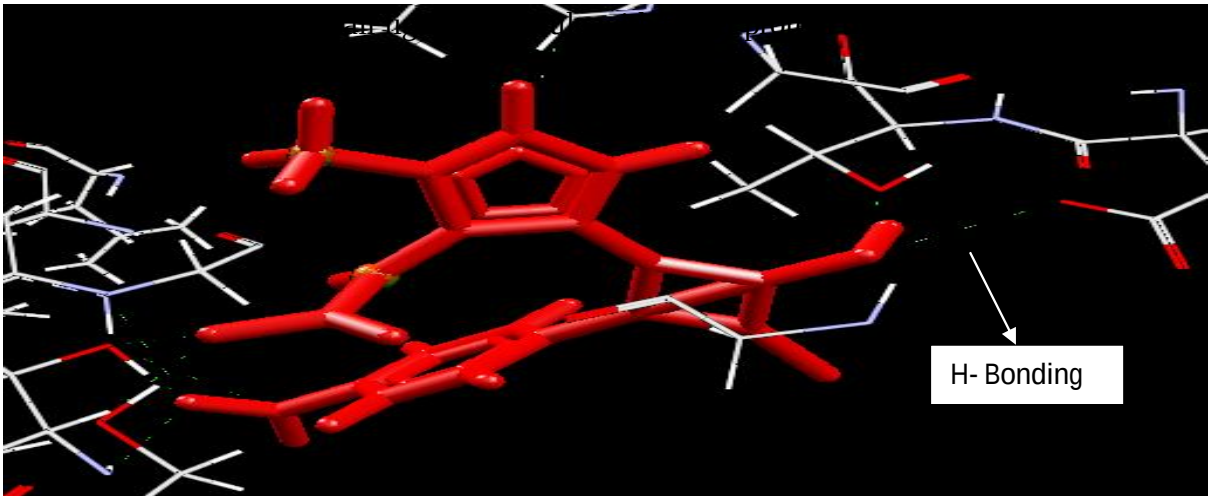


Figure-02: small ligand molecule with target protein through H-bonding

Molecular docking can be thought as a "Lock and Key theory" in which the number of different volume of cavities are present inside the target protein and are acted as Lock . While the small molecular volume of ligand or drug is acting as a key which is fitted in that cavity by orientation. The main focus the molecular docking is to be recognized the optimizing conformation and relative orientation of protein and ligand which minimized the free energy of the all system and will be predicted the best fitting area to define the best pose of ligand. The best pose of the ligand reveals the better biological activity of that compound.

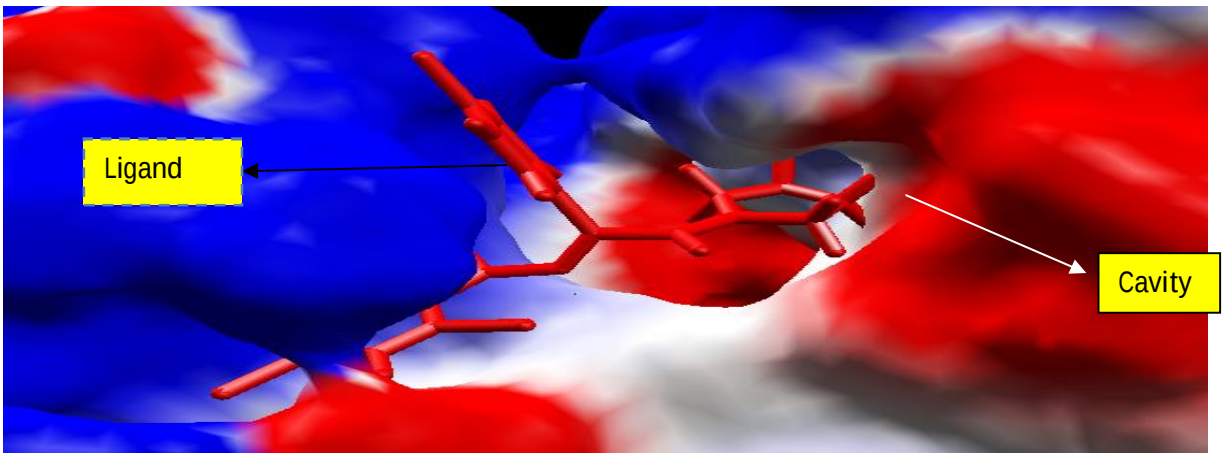


Fig.03: "Lock and Key Theory" (Ligand fixed in a cavity of target Protein)

Docking Approaches [4,5,6]

Particularly more than two popular docking approaches are utilized for dock preparation of ligand and protein molecules. Such are

- Matching of surface technique in both ligand and protein.
- Stimulation of docking process by pairing of ligand – protein interaction energy is calculated.
- The hydrophobic feature of protein in the main-chain atoms.
- Fourier shape descriptors technique.

These approaches have significant advantages as well as some limitation. These are

Shape[7,8,9,10]

The shape or surface descriptors are the complementary features of geometrical matching for ligand and protein to make them dock able. In case of receptor, the molecular surface is described in terms of its solvent accessible surface area while the molecular surface of ligand is described in terms of its matching surface descriptions. The two surfaces amount are

needed for shape matching descriptions that may be helped to find out the pose of docking of target and ligand molecules. The shape complementarily methods can be quickly scanned through the several thousand ligands in a matter of seconds and figure out the actual active site of protein for binding.

Stimulation [(11)]

The stimulation is an important main part of docking process in which the ligand and protein are separated by certain physical distances. So that the ligand find its active site inside a target molecule (protein) after moving around the certain changing pose of conformational position in 3D space. The changes of conformation of ligand may be occurred due to flexibility and torsion of bond by moving in the mean of translations and rotations. Thus each conformational move in 3D space of ligand induces the total energy cost of the system. This is known as optimal energy of the system. Now a day the latest technique is used for the detection of optimal energy pose by grid-base which is also based on translation and rotation. The docking can be stimulated or gridded between

- Target protein (receptor) / small ligand.
- Protein / peptide.
- Protein / protein.
- Protein / nucleotide.

Mechanics Of Docking[11]

It was the structure based process of interaction between x-ray crystallographic structure of protein (derived from bioinformatics' centre) and potential uploaded ligand through H-bonding , vandal Waal and steric factors. These are successively organized by algorithm method which is finalized the scoring function of docking. Otherwise the docking program is depending upon the algorithm and scoring functions of ligand.

Search Algorithm[12]

It is the current computational based theory of all possible orientations and conformations of target protein paired up with ligand. It is impossible to exhaustively explore the searching space for all possible distortion of each molecular conformation by rotational and translational orientation of ligand to the relative protein. In the docking program, most of the ligand was set as flexible. While several approaches of protein were considered as flexible. Each snapshot pair of protein- ligand is referred as a pose.

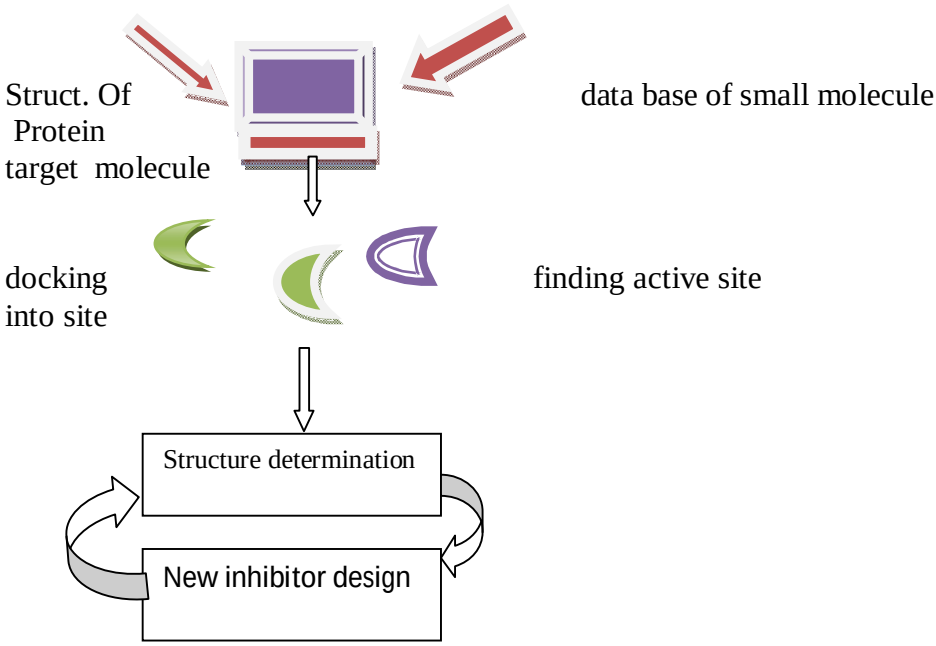


Fig.04:design and experimental testing of algorithms

A rigorous search algorithm will be exhaustively elucidating the all possible binds mode of ligand-target protein. All six degree of translational and rotational freedom of the ligand would be explored along with internal conformational degrees of freedom of ligand-protein. However, this is impractical due to the size of the search space. A simple system comprising a ligand with four rotatable bonds and six rigid body alignment parameters will be estimated in the searching work space. The alignment parameters are used to position the ligand relative to the protein in a cubic active site measuring $103^{o}A^{3}$. If the angles are considered in 10^{0} increments and translational parameters on a 0.5^{0}A grid, their approximately $4x10^{8}$rigid body degree of freedom to a sample which is corresponding to $4x10^{16}$configurations of the four rotatable torsions to be recognized in the searching space and the 10 configurations of the ligand-protein grid will be estimated within a second. Thus variety of conformational strategies of ligands were applied to the proteins, are

- Systematic or stochastic torsional searches about the rotatable bonds.
- Molecular dynamics stimulation.
- Genetic algorithm to evolve new low energy conformations.

Ligand Flexibility[13]

This is one of the main part of docking system in which ligand gives it conformations during the bind formation with the cavity of protein and also point out the force field energy of that reasonable conformation is known as pose energy.

Ligand RMSD[14,15]

The root mean square distance (RMSD) values were reported by three main approaches when "calculate_rmsd = yes". These values can be found in the header of the output MOL2 file or docking out file.

(1) Standard heavy-atom RMSD (HA_RMSDs): In this case the standard pair-wise RMSD can be calculated between the non-hydrogen atoms of a reference conformation *a* and a pose conformation *b* for a ligand with *N* total heavy atoms of index *i*.

$$HA\_RMSDs = \sqrt{\frac{1}{N}\sum_{i=1}^{N}\|a_i - b_i\|^2}$$

If the HA_RMSDs is "-1000.0", then there is an inconsistency in the number of heavy atoms between the reference and the docked conformer.

(2) Minimum-distance heavy-atom RMSD (HA_RMSDm): The measurement of this case is based on the RMSD implementation used in Autodock Vina, or MVD 5.o.5 software, which does not explicitly enforce one-to-one mapping. Rather, atom pairings between reference conformation *a* and pose conformation *b* are determined by the minimum distance to any atom of the same element type, and it may be an under-prediction of the true RMSD.

$$RMSD_{\min}(A,B) = \sqrt{\frac{1}{N}\sum_{i=1}^{N}\left(\min_j \|a_i - b_j\|\right)^2}$$

$$HA\_RMSDm = \max\left(RMSD_{\min}(A,B), RMSD_{\min}(B,A)\right)$$

(3) Hungarian (symmetry-corrected) heavy-atom RMSD (HA_RMSDh): The final RMSD implementation is based on an *O (N^4)* implementation of the *Hungarian algorithm.*The algorithm solves the optimal assignment between a set of reference ligand atoms *a* and a set of pose ligand atoms *b* of the same size. For all groups of atoms of the same Sybyl atom type, a cost matrix *M* is populated where each matrix element *mij* is equal to the distance-squared between reference atom *ai* and pose atom *bj*. The Hungarian algorithm is used to determine one-to-one assignments between reference and pose ligand atoms such that the total distance between atoms is minimized. The new assignments *c(i)* are fed into the standard RMSD function in order to compute a symmetry-corrected RMSD. If the HA_RMSDh is "-1000.0", then there is an inconsistency in the number of atoms of at least one atom type between the reference and the docked conformer.

$$HA\_RMSDh = \sqrt{\frac{1}{N}\sum_{i=1}^{N}\|a_i - b_{c(i)}\|^2}$$

Receptor Flexibility[16]

It was the most sophisticated computational work of computer-assist drug designing during the docking period in which receptor was considered as flexible. A single fixed conformation will be obtained if the structure of protein was x-ray crystallographic in nature. The negative folded (posed energy) state of protein is characterized by collection of energetically equivalent conformations. If the condition of conformation structure of protein would be changed, as a result the folded energy will be shifted to another environment and introduction of ligand also changed with respective conformation. According to the binding conformation of the receptor may already be present in the ensemble of the protein conformations and ligand does not actively deform a fixed state of the protein, as generally inferred from 'induced fit' model.

Scoring Function [17, 18]

Scoring function is a mathematical method of virtual screening which predicted the non-covalent interaction between two molecules after docking of them. Normally a small organic molecule having drug liking property or drug molecule (ligand) and second one is biologically active target molecule of drug such target protein or receptor (which is derived from Protein Data Bank.). These scoring functions have also been obtained between the interactions of protein-protein or protein- DNA molecules.

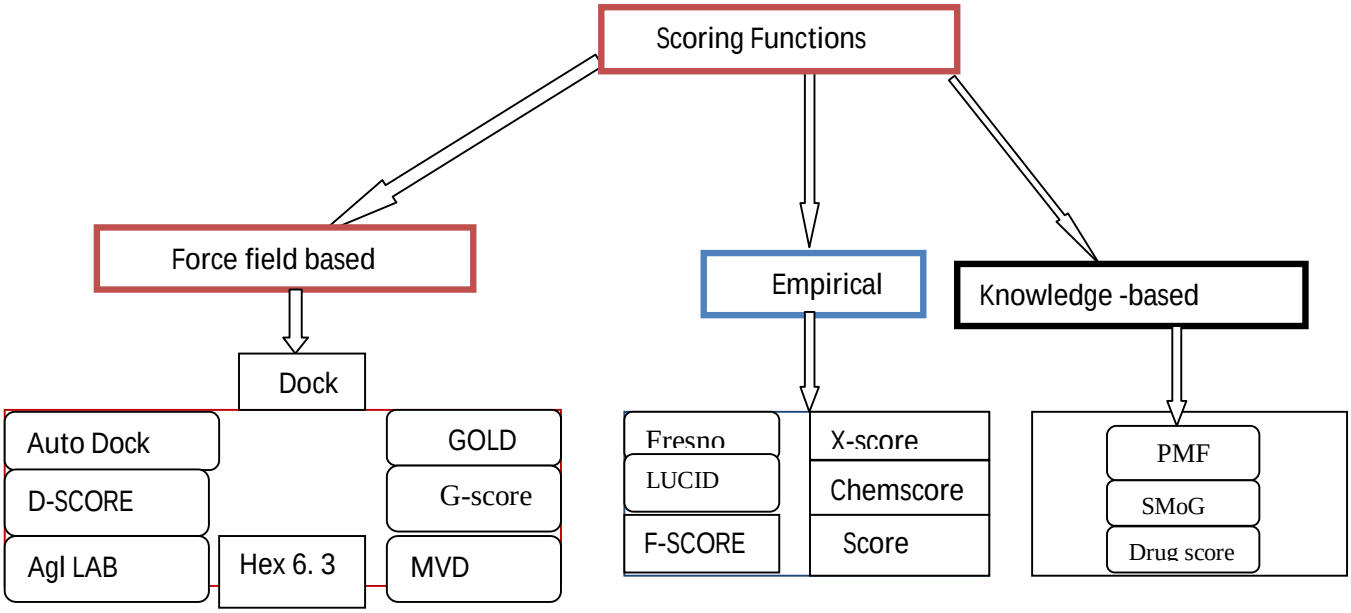
Always scoring function has been giving the pose input of favorable binding interaction ligand-protein. Most scoring functions are physical-based mechanics force fields that estimate the energy of poses and a low (negative) energy indicates the stable system which is a liking ligand- protein bond complexation. Actually the scoring function is composed of three different aspects that relevant to docking and design:

- Ranking of the configurations generated by docking search for one ligand interacting with given target protein. i. e. detected the best pose energy or best free energy.
- Ranking of different lignads with respect to the binding to one protein. i.e. prioritizing the binding affinity of ligand towards the protein.
- Ranking of one or different lignads with respect to their binding affinity to different proteins. This aspect is an essential and specific as consider.

Scoring methods can range from molecular mechanics force fields such as HEX: 6.3, Argus Lab: 4.0.1, MVD: 5.0.5, AMBER and OPLS OR CHARMM through the empirical free energy scoring function or knowledge based function. The currently available docking method utilizes the scoring function in one of two ways. The first approach uses the full

scoring function to rank a ligand protein conformation. The system is then modified by search algorithm and same function is applied to rank the new structure.

Docking method is a popular technique of molecular modeling to study the drugs excipient interaction which helps to visualize the types and sites of interactions in computer monitor. It also be reported study of various amino acids unit combine to get the cavity which has stable conformation with minimum energy. The cavity depth, diameter of a wider and narrower rim were calculated and compared with the literature values using DTMM package.



DOCKING SOFT WARES

Auto Dock[19]

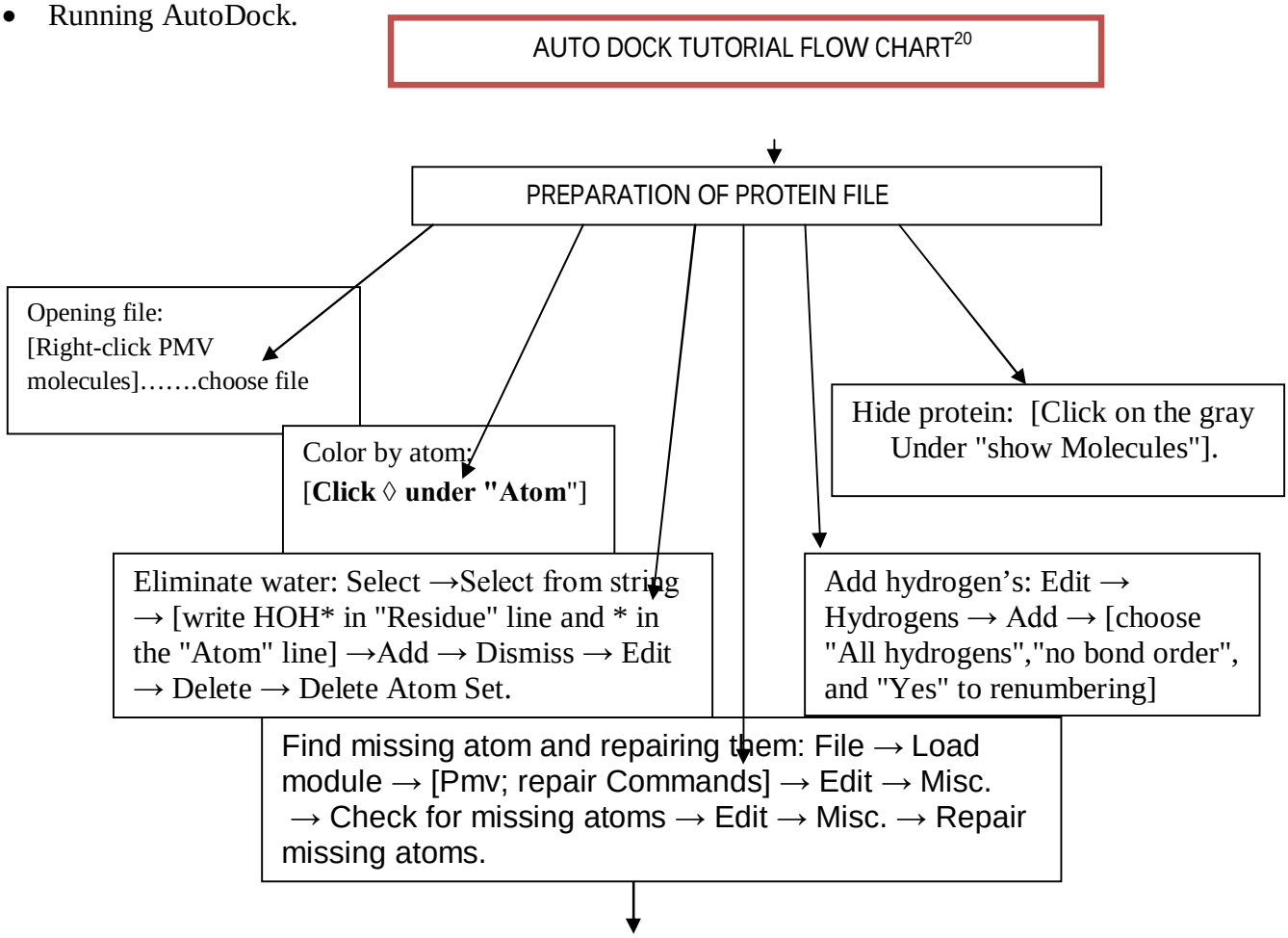
Auto dock is one of most cited molecular docking software in the earlier investigation of research fields for developing the ligand-protein interaction to finding the drug-likeness property of a molecule. Otherwise it also called as molecular activity developer software. The Auto dock consists two main soft ware programs such are

- For docking of the ligand to a set of grids describing the target protein.
- Auto Grid for pre-calculating these grids.

Auto dock Tools

- Preparing the Files
- .Editing the Protein PDB File with Auto Dock Tools (ADT)

- Preparing the Ligand File with ADT.
- Flexible Residues in the Protein
- Further Preparation of the Protein Files
- Open the Grid Options
- ready to run AutoGrid
- prepare the Docking Parameter file.
- Running AutoDock.



Preparing the Ligand

Make sure the ligand has all hydrogens added before working with ADT

↓

Toggle the "Auto Dock Tools" button

↓

Opening file: Ligand → Input → Open → All Files → [choose file] →Open

↓

Define torsions: * Ligand → Torsion Tree → Detect Root (this is the rigid part of the ligand) * Ligand → Torsion Tree → Choose Torsions → [either choose from the viewer

specific bonds, or use the widget to make certain bond types active (rotatable) or inactive (non-rota table). Amide bonds should NOT be active (colored pink)] → Done.

- Ligand → Torsion Tree → Set Number of Torsions → [choose the number of rotatable bonds that move the 'fewest' or 'most' atoms]

↓

Save ligand file: *** Ligand → Output → Save as PDBQT → [save with L. pdbqt].**

↓

Hide the ligand, as explained in (A5) for the protein

Preparing The Flexible Residue File

(Note: if you are planning rigid docking, ignore this section and do the following: **Grid** → Macromolecule → Open → [choose RH.pdb]. Auto Dock will automatically add charges and merge hydrogens. Save the object as RH. pdbqt and move to section D.)

↓

Flexible residues → Input → Choose molecule → [choose the original protein R.pdb] → Yes to merge non polar hydrogens (Auto Dock assigns charges + atom types to R.pdb, and merges nonpolar hydrogens).

↓

Select the residues to be flexible: Select → Select from string → ARG8 → Add → Dismiss**.**

↓

Define the rotatable bonds: Flexible residues → Choose torsions in currently Selected residues → [click on rotatable bonds to inactivate them or vice versa].

↓

Save the flexible residues: Flexible residues → Output → save flexible PDBQT → [save as R_flex. pdbqt].

↓

Save the rigid residues: Flexible residues → Output → save rigid PDBQT → [save as R_rigid.pdbqt.

↓

Delete this version of protein: Edit → Delete → Delete Molecule → [choose protein (R)] → Delete → Dismiss]

Running Auto Grid calculation

Open the rigid protein: Grid → Macromolecule → Open → [choose the rigid protein] → Yes to preserving the existing charges].

Prepare grid parameter file: Grid → Set Map Types → Choose Ligand →[choose the ligand already opened] → Accept

Set grid properties: Grid → Grid Box → [Set the grid dimensions, spacing, and center] → File → Close Saving Current.

Save the grid settings as GPf file: Grid → Output → Save GPF → [save as R.gpf].

[Make sure the AutoGrid executable is in the same directory as the input files].

Running: Run → Run AutoGrid → [make sure the program name has the right path, and that it is where the input files are] → Launch → [in the command prompt prompt, type "tail –f hsg1.glg" to follow the process] (Note: the AutoGrid calculation can be started directly from the command prompt by typing "autogrid4 –p hsg1.gpf –l hsg1.glg &")

Preparing The Docking Parameter File (.Dpf)

Specifying the rigid molecule: Docking → Macromolecule → Set Rigid Filename → [choose R_rigid.pdbqt]. (or RH. pdbqt for rigid docking)

Specifying the ligand: Docking → Ligand → Choose → [choose L.pdbqt] → [here you can set the initial location of the ligand] → Accept.

Specifying the flexible residues: Docking → Macromolecule → Set flexible Residues filename → [choose R_flex.pdbqt].

Setting the parameters for the chosen docking method: Docking → Search Parameters → Genetic Algorithm → [for 1st time, use the short number of evaluations (250,000), and for other runs choose the medium or long] → Accept.

Setting docking parameters: Docking → Docking Parameters → [choose the defaults].

Specifying the name of the ligand dpf file to be formed, containing the docking instructions: Docking → Output → Lamarckian GA → [type L.dpf].

Confirming the details of docking: Docking → Edit DPF → [make sure the right ligand pdbqt file name appears after the word "move", and that the right number of active torsions is specified].

Running Autodock 4

[Make sure the Auto Dock executable is in the same directory as the macromolecule, ligand, GPF, DPF and flex files (in case of flexible docking)].

Running: Run → Run Auto Dock... → Launch

WHEN RH AND LH ALREADY EXIST.

Protein

Grid → Macromolecule → choose RH.pdb → (charges & atom types assigned, nonpolar hydrogen merged) → File → save → write PDBQT → save as RH.pdbqt.

Ligand

Ligand → Input → Open → All Files → choose LH.pdb → (charges & atom types assigned, no polar hydrogen merged) → save as LH. Pdbqt.

Setting Docking parameters

Docking → Macromolecule → Set Rigid Filename → choose either RH.pdbqt or RH_rigid.pdbqt → Docking → Ligand → Choose → choose LH.pdbqt → set the rest of the docking parameters**.**

Running docking simulation.

Viewing Docking Results

Reading the docking log file (.dlg) **[**Toggle the "AutoDock Tools" button]. ____ Analyze → Dockings → Open → [choose L.dlg]. _____ Analyze → Conformations → Load → [double-click on each conformation to view it on screen].

Visualizing docked conformations

1. Analyze → Conformations → Play**...** (Note: & allows changing the ligand's color).

Hex 6.3[21]

Hex is an interactive superpostioning molecular graphics program for calculating docking modes of pairs of protein and DNA molecules. it can also be calculated protein – ligand docking, assuming that the ligand is rigid through *spherical polar Fourier* (SPF) correlations

to accelerate the calculations in their 3D shapes. In *Hex's* docking calculations, each molecule is modelled using 3D expansions of real orthogonal spherical polar basis functions to encode both surface shape and electrostatic charge and potential distributions. it represents the surface shapes of proteins using a two-term surface skin plus vander Waals steric density model, whereas the electrostatic model is derived from classical electrostatic theory. (Protein Docking Using Spherical Polar Fourier Correlations Copyright c 1996-2010 David W. Ritchie).

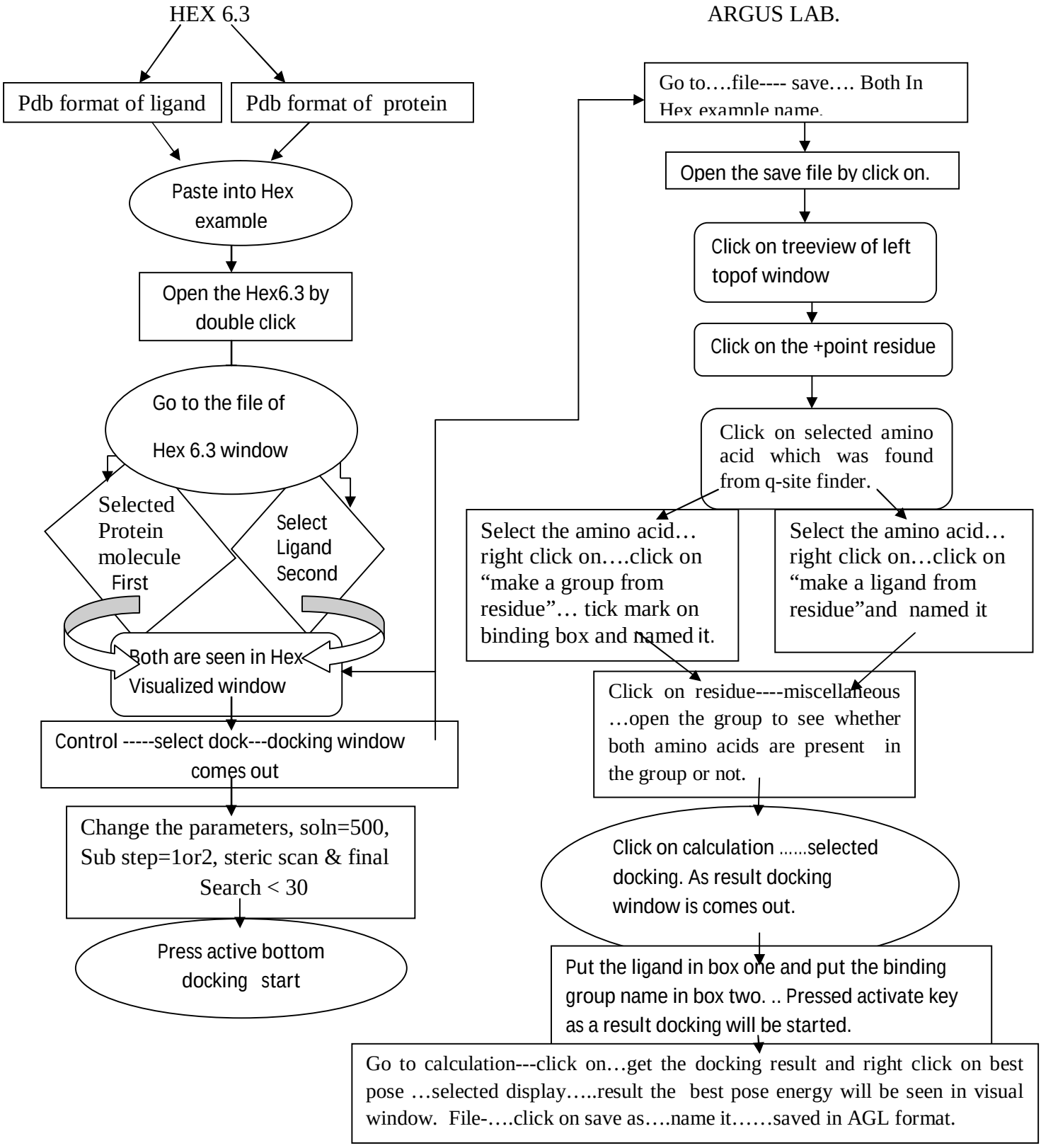
Argus Lab 4.O.1[22]

A molecular modeling, graphics, and drug design program, contains Argus Dock which is the new drug docking code referred to both the GA Dock and Argus Dock docking engines, provides the Score scoring function with a preliminary set of parameters of following features:

- Ribbon rendering for proteins : with several coloring options.
- Solvent accessible surfaces.
- Display bumps and hydrogen bond monitors between ligands and protein targets Gaussian 98 & Gaussian 03 interfaces and are automatically added to the Calculation results in the Molecule Treeview.
- Molecule Treeview window: Molecule Treeview shows a treeview representation of the molecule and saves results of calculations that you have run. You can right-click on many calculated properties and select "render" or "animate" to see them on the screen.
- Builder Toolkit window: This window shows the palette of atoms, rings, and amino acids you can attach to the cursor and place in the molecule window.
- QuickPlot buttons for HOMO, LUMO, and ESP-mapped density surfaces. One click and all the essential calculations and surface preparation are done for you and the surface is rendered to the screen.
- Query the PDB database: download and display PDB files in one click**.**
- Calculation results and properties are saved to the Molecule Treeview.
- Docking results including poses that are renderable (right-click on a pose icon to see).
- UV/vis excited state results: by table and individually by excited state.
- Molecular orbital table
- Dipole moments (ground and excited state)
- Transition moments (length and velocity operator)

- Magnetic moments
- Mulliken, ZDO, Qeq charges
- Animate normal modes with a single click
- Thermochemical results from Gaussian calculations
- Copy/Paste Calculation results or properties to the Windows clipboard for easily adding to other Windows applications like Word or Excel. Right-click will also give you the option of saving to a formatted text file.
- Electric Field: SCF and CI, EHT, AM1, PM3, MNDO, ZINDO
- Display XYZ Cartesian axes.
- Orient the molecule in absolute coordinates and orientation.
- More extensive Atom Labeling including chiral centers.
- Invert chiral centers.
- Peptide builder : Easily build alpha helices, beta strands or specify the phi/psi angles yourself.
- Improved settings: Lighting, atom & background colors, electric field, display, and Quick Plot settings.
- Render peptide backbone as segments to simplify the display of large proteins.
- Set render mode and color for sets of atoms, residues, and user-defined groups.
- Color by molecule, by atomic number, by amino acid polarity, or user defined colors.
- Depth cueing.
- Turn on/off the use of fast-rendering during molecule moves.
- Make user-defined groups of atoms. Perform actions on these groups, such as selecting all neighbors' atoms or residues within a given distance.
- Improved support for hiding/showing complex sets of atoms, residues, and user-defined Groups.
- PDB files: improved support for atom and residue typing.
- Quick torsion and Quick bond length adjust (see Tips & Tricks).
- Performance enhancements and reduced memory footprint in handling systems with lots of rings.

Flow chart Representation of Hex [21] and ArgusLab[22] molecular docking



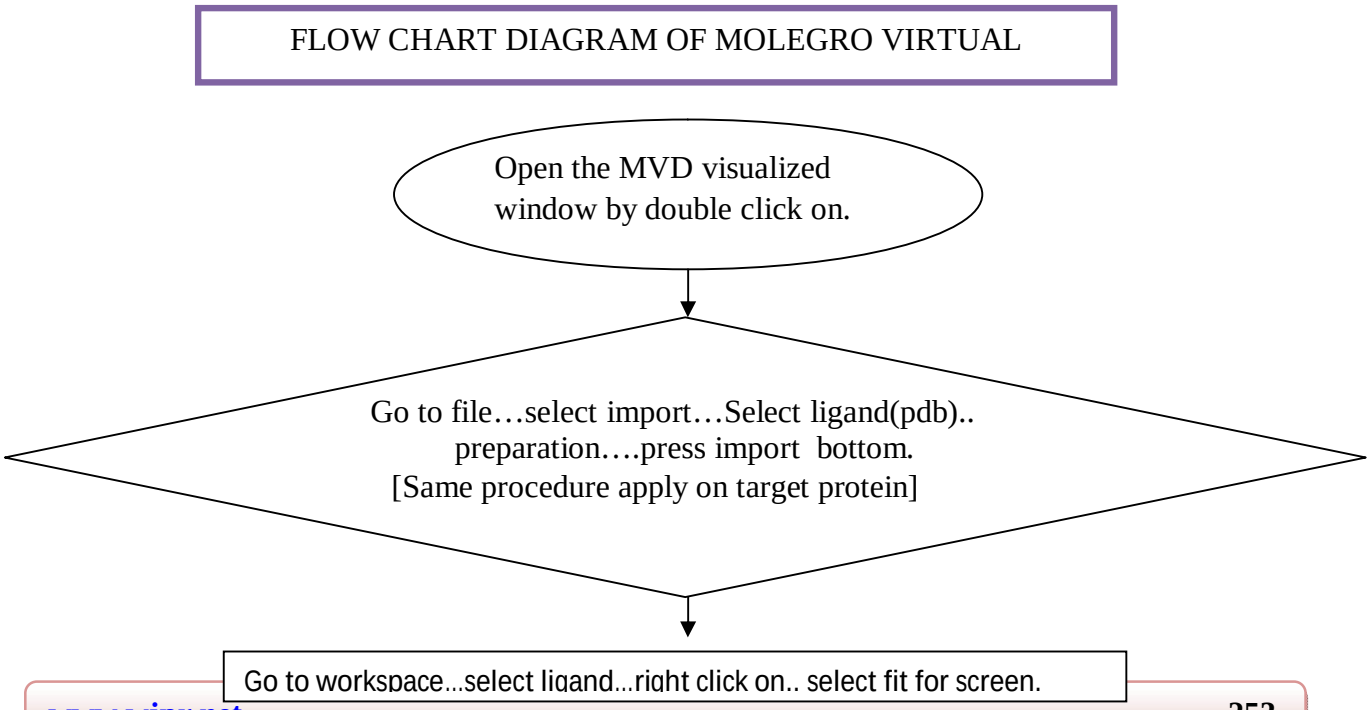
Molegro Virtual Docker[23]

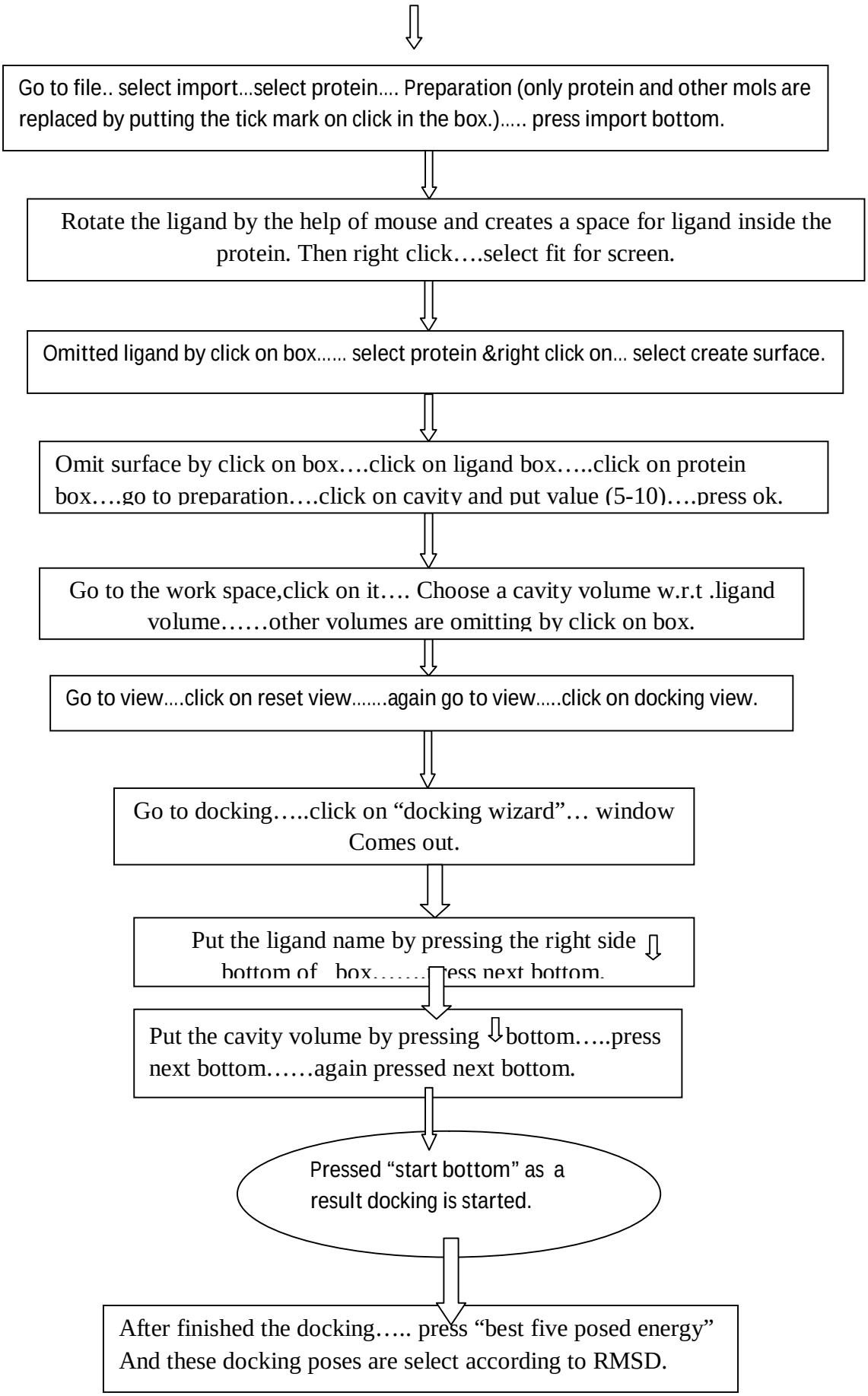
Molegro Virtual Docker (MVD) is an integrated Computational modeller of modern drug design environment for studying and predicting how ligands interact through hydrogen bond with macro molecules. The identification of ligand binding modes is done by iteratively evaluating a number of candidate solutions (ligand conformations) and estimating the energy of their interactions with the macromolecule. The highest scoring solutions are returned for further analysis. MVD requires a three-dimensional structure of both protein and ligand (usually derived from X-ray/NMR experiments or homology modeling). MVD performs flexible ligand docking, so the optimal geometry of the ligand will be determined during the docking.

Protein- Ligand Docking

Predict how small flexible molecules interact with a protein receptor and Screen databases for potential drug candidates or refine existing leads.

- Predict potential binding sites.
- Protein binding pocket flexibility.
- Visually inspect docking predictions with relevant interactions.
- Repair, mutate, or minimize side chains before docking.
- Displaceable water model.
- Import and export of industry standard file formats (PDB, Mol2, SDF).
- Automated preparation of input structures.




Go to file.. select import...select protein.... Preparation (only protein and other mols are replaced by putting the tick mark on click in the box.)..... press import bottom.
Rotate the ligand by the help of mouse and creates a space for ligand inside the protein. Then right click….select fit for screen.
Omitted ligand by click on box..... select protein &right click on... select create surface.
Omit surface by click on box….click on ligand box…..click on protein box….go to preparation….click on cavity and put value (5-10)….press ok.
Go to the work space,click on it…. Choose a cavity volume w.r.t .ligand volume……other volumes are omitting by click on box.
Go to view....click on reset view.....again go to view.....click on docking view.
Go to docking…..click on "docking wizard"… window Comes out.
Put the ligand name by pressing the right side
Put the cavity volume by pressing bottom…..press next bottom……again pressed next bottom.
Pressed "start bottom" as a result docking is started.
After finished the docking….. press "best five posed energy" And these docking poses are select according to RMSD.

SIGNIFICANCE

The binding interaction between of a small organic molecule (ligand) with enzymatic protein may result in activation or inhibition of the enzyme. If the protein is receptor, ligand binding may be resulted in agonist or antagonist. Docking may be applied to:

- The complexed ligand-protein orientation will be given the scoring function of ligand in Hit representation of insilico method.
- The docking can be optimized the ligand orientation conformation and formed the stable configuration which is referred to best pose of ligand and it will be predicted the certain biological activities.
- The docking method is helped to search the estimate of binding affinity of ligands toward the target protein.
- Understanding the binding mode principle for optimizing the standard leading molecule.

CONCLUSION

Molecular docking is one of the most popular and user friendly computational technology which helps in investigating, interpreting, explaining and identification of molecular properties by using of three –dimensional structure. Molecular docking also tries predict the structure of inter molecular interaction complexation formed between two or more constituent molecules. This techniques are applied in computational chemistry, computational biology and material science for studying the molecular system ranging from small organic molecule to macro (large) biological molecules and materials assemblies. Presently, most of the docking programs are used to stimulate the binding of a flexible ligand to a rigid biology receptor. This model does not reflect the actual physical process of bonding but eventually it prevents the correct identification of potential drug candidatures.

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