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Molecular Docking Simplified: Literature Review

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Abstract

Molecular docking is the prominent method for structural analysis and designing of drugs which is assisted by computer programs. The aim of docking is to predict the binding between two molecule ligand and receptor when they bind to form stable complex. The ligand could be any macromolecule but mainly this method is performed with protein of known 3-D structure. Fruitful docking method utilizes a scoring function which appropriately ranks the docking candidates. It could be utilized for performing hypothetical screening of huge collection of diverse compounds which rank the results and proposes the hypothesis of process leading to ligand blockage to intended target which is not found appropriate for the process of lead optimization which aims to increase the promising compound for enhancing its effectiveness, decreased toxicity or enhanced absorption. Beside all this, the setup of input structure for docking is as critical as the docking itself. The evaluation of the result of algorithms which could perform a broad search of design space and ignores local optima named stochastic search could also few times found to be unclear. As molecular docking had become important for drug designing so the reliable theories for this includes sampling algorithms scoring function. The distinction among the docking software and approaches of molecular docking had been mention. Also recently developed docking software Local Move Monte Carlo (LMMC) is mentioned which provides potent solution towards flexible receptor docking programs. Beside all these things, applications of molecular docking have also been described.

Docking is basically a process which identifies appropriate positions of molecule with other when bound together for forming stable orientation of complex. The understanding of suitable conformation may be utilized for predicting the power of involvement in affinity of binding among two molecules with the utilization of scoring which helps in predicting the binding capability between two molecules after they have been docked. The involvement of macromolecules biologically admissible like lipids, carbohydrates, protein performs significant function in cell signaling. Moreover, the comparable orientation among 2 binding molecules could also affect the kind of signal produced. Though docking is helpful for both providing strength and type of signal produced. This technique basically works both structural and computer assisted drug designing and to identify the binding in between ligand and protein in which three dimension structure of protein is already known. Successful method of docking identifies high dimensional spaces prominently and scoring function utilization results in appropriate ranking of candidate docking. Docking can also be involve in performing screening virtually on huge libraries of molecules and give the structural hypothesis of the process ligand inhibits the target which critically leads to optimization.

Key words: Docking, Ligand, Receptor, Docking tools, Drug Designing, Scoring Function, Docking Program.

Prospective of molecular docking

Molecular docking is performed mainly by two types of approaches -

Stimulation approach

This approach works through separation of ligand and target by the physical distance and afterwards ligand is permitted to associate into the groove of indented target following multiple number of moves in their conformational

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space. The movement involves structural variation of ligand which could be either internally or externally and between ligand and receptor ligand in entire move limits the release of energy. The approach is found to be more appropriate for accepting flexibility of ligand. Further, it leads greater access towards molecular identification between ligand and target. Though longer extent of time is required for estimating excellent docked conformer because of huge amount of removal of energy from particular conformational change. Currently, quick optimization technique and grid based methods had been dominantly transforming this disadvantage to make stimulation method more user friendly.[1-3]

Shape complementarity

This approach involves ligand and target as structural surface characteristic which gives molecular interaction. The surface of target had been associated from solvent attainable surface area and ligand molecular surface should show matching illustration with target surface area. This complementation between two surfaces, shape matching helps in identifying the ligand indentation for ligand on its desired surface. As for example, protein as a target molecule hydrophobicity found to be analyzed through turns present in main chain atoms. This method is preferred as more fast and involves various ligands scanning in very less time for searching the expected binding properties of ligand on their intended target of molecular surface.[4,5]

Types of docking

Molecular docking utilizes the search algorithms like genetic algorithm, fragment based algorithm, fragment based algorithms and molecular dynamics. Beside all these, there are some tools such as DOCK, GOLD, Flex and ICM which are mainly utilized for high throughput docking simulations. There are also multiple types of molecular docking procedure associated with either ligand/target which could be flexible or rigid based on docking stimulations objectives.[6,7] Molecular flexibility of protein –ligand and mutual adaptation of ligand with its receptor is important for knowing the ligand binding and protein function. One of the challenges in molecular docking is to account the adaptation in docking calculations.

METHODS OF DOCKING

Rigid ligand and rigid receptor

This method involves rigid objects of ligand and receptor with search space restricted with 3 translational and rotational degree of freedom. This docking method involves flexible ligand which is found to be named according to pre-computed series of ligand conformations and also could allow degree of overlapping among both ligand and protein. Initially known version of docking are DOCK and FLOG. Beside this, also few known program are FTDOK adopted the method through which ligand and receptor remains rigid at the time of docking process.[8-10] As DOCK is primarily known automated process of docking in which ligand docking into receptor site is found to be developing continually. This distinguishes the ligand and receptor as series of spheres which can overspread through clique process.[11,12] The ligand and receptor complex utilizes chemical and geometrical algorithms which could be scored through consideration of structural fit, pharmacophore similarity. The consideration of ligand flexibility involves increased construction process and comprehensive search are included in its improvised version. This comprehensive search arbitrary forms user-defined counts of conformers as numerous numbers of rotational bonds in ligand. The latest version of DOCK had included Assisted Model Building with Energy Refinement (AMBER) it is kind of software which helps in stimulating the forces score with implicit solvent.[13,14] Flexible Ligands Oriented on Grid (FLOG) is a search database which identifies the molecules complementary to large molecules receptor of know 3D structure. It forms ligand conformation on mathematical basis performed for molecular conformation called as distance geometry and utilizes a clique searching algorithm calculating the sets of distances. FLOG permits the users to elaborate the prominent points which could be involved in ligand and atom association. It could also be helpful if essential interaction have been known before the docking is to be performed.

FLEXIBLE LIGAND AND RIGID RECEPTOR

This system performed molecules with nature allowing induced fit parameter.[15,16] It is important to appraise the flexibilities of ligand-atom both as in cases both ligand and receptor modifies its conformation for forming a perfect fit complex with least energy but when receptor is flexible then cost become too high for it. Though, the perspective of this system is commonly been used as trade –off among reliability and computer assisted time used by ligand which is flexible and other side receptor being rigid at the time of docking. Nearly all the programs of docking had adopted this method like AutoDock, Flex.[17,18] AutoDock 3.0 inserts annealing, genetic algorithm process for making ligand flexible and receptor rigid. The scoring attribute is mainly based on AMBER which includes desolvation, interactions Vander waal, electrostatic, randomness or entropy conformational.

AutoDock 4.0 has the ability of modeling the flexibility of receptor by allowing side chains for mobility. Flexx utilizes an increased construction algorithm for sampling conformation of ligand. The fragment of base is firstly docked in active site through H-bond pairs complementing and aromatic interaction among ligand and protein. The remaining attributes are formed in sequence of rotational torsion angles which narrate for ligand flexibility.[19,20] The latest version consist electrostatic, lipophillic, aromatic interactions, H-bonds, rotational entropy. The interaction among functional groups has also been considered through allotment of geometry and type of groups.

Flexible ligand and flexible receptor

The internal movement of protein had been known to be nearly associated with ligand binding nature.[21,22] Insertion of flexibility to the receptor is a difficult task remarkably seen in docking area. The preferable utilization of molecular dynamics simulation can also represent entire degrees of freedom for the ligand and receptor complex, molecular dynamics had complication of inappropriate sampling. Also other hurdles are computational cost lead in prevention of this method to be utilized in huge analysis or screening of database. Additionally, multiple theories were presented for induced fit models, conformer induction selection is to be known for illustrating the ligand-protein association. Conformer selection means the method when a ligand discriminately binds to the appropriate conformation among number of protein conformations and induction associated with conformation shows a mechanism in which the ligand leads protein to the conformation which would not frequently unbound the state. Few of the incidence leads conformational transformation could be compared with partial refolding of protein. Multiple process are recently been formed for implementing the flexibility of receptor and easily available and known is soft docking which function by diminishing the vanderwall repulsive energy in scoring function and allows overlapping in between 2 atoms receptor and ligand.[23,24] This method not includes appropriate flexibility, though it had precedence of computational capability as coordinates of receptor are accurate through modification in van der wall variable. Another approach utilizes rotamer libraries for modeling receptor flexibility its significance includes relative

speed of sampling and reducing hurdles. Internal Coordinates Mechanics (ICM) basically is a method of programming utilized for rotamer libraries with influential possibility which is combined with Monte Carlo search ligand conformation.[25,26] AutoDock 4 adapts a frequent process for dealing the flexibility of side chain flexibility.[27,28] Various receptors present in side chains could be opted from the users and sampled spontaneously from a ligand utilizing sample methods. Beside it other receptor part are handled rigidly from grid energy map at the time of sampling. It was established by Good ford and utilized for storing instructions, energy for receptor and simplifying binding energy computation among receptor- ligand. Even there is other option for dealing with flexibility of protein from using ensembles which are model of conformation which altogether work to elaborate the structure and flexibility of protein it corresponds with conformer selection theory.[29,30] In this approach ligand is independently docked in a sequence of rigid protein conformations instead of individual one and the obtained results are combined with appropriate method of option.[31,32] This method was mainly executed in DOCK, it forms an average potential energy grid of ensemble and stretched in various program in distinct method like FlexE.[33,34] It assembles various crystal structures particular proteins combining the identical parts while constructing the non-identical area as distinct approach. At the time of increased formation of ligand distinct conformation of proteins are sampled in combinational pattern. The increased scoring protein structure is opted on the basis of ligand and each substitute comparison. Hybrid method is also a plan to model the flexibility of receptor like glide a popularly known docking program.[35,36] Glides constructs a sequence of ranking filters for identifying the position and orientations of ligand inside the binding sites of receptor. Flexibility of ligand is tackled by the comprehensive identification of ligand torsion angle space. Primarily conformation of ligand are opted on the basis of torsion energies and docked to the binding site of receptor with soft potentials. Afterwards, rotamer investigations are utilized for receptor flexibility models, Fast Rigid Exhaustive Docking (FREDA) use a hybrid process which collaborate soft potential and multiple receptor conformations considering receptor flexibility. The maximizing approach based on mean-filed theory had been implemented for induced fit model between ligand-proteins. The process described here includes side chain flexibility or entire flexibility of receptor. This had been seen that loop formation in active site plays crucial function in ligand binding. Beside it few incidences had revealed that loop could undergo drastic conformational modifications where as in other parts of receptor there is bit of modifications on association between ligand and receptor. The entire scenario leads to process of flexibility in side chain which fails to illustrate the exact conformation of protein and full flexibility which seems to be computationally not useful.

Local Move Monte Carlo (LMMC)

It is basically a new method which aims towards sampling of ligand conformation inside the loop consisting active site. This sample for flexible receptor docking local movement initiated from the modification of one torsion angle followed by 6 subsequent torsion which permits remaining chain to be in their original place although preserving entire bonds length and angles. The LMMC associated work was primarily performed by Go and Scheraga they develop solution for system of equations describing the values of six torsion angles which preserves the backbone and bond lengths.[37,38] The other investigator Hoffmann *et al.* firstly implemented this method in polyalanine folding which includes an appropriate Jacobian for stabilizing the balance. Also, they showed this method samples the conformational space highly efficacious than individual move.[39,40] This process had also been performed on amino acid proline consisting peptides, proteins and nucleic acids.[41,42] The development of LMMC loop sampling address to predict the loop it performs with changing the backbone torsion angle further through 6 subsequent torsions allowing the remaining loop to be in their original position and preserves all the bond length and angles. The process which forms loop conformation on the basis of simple movement of torsion angles of side chains and local moves of backbone loops. Predictions for reducing computational cost for evaluation of energy grid based force filed developed for representing protein atmosphere and salvation effect. Stimulated annealing has been utilized for enhancing the capability this loop sampling method and finding less energy loop conformation. The quality of prediction was analyzed on the sequence of protein loops with already known crystal structure which had been earlier utilized by other for testing distinct loop prediction process.[43,44] This method could be useful for flexible receptor docking method which samples not only side chains but also backbone loops in protein and flexible ligand binding sites.

Molecular docking tools

The docking is basically a method in which ligand is positioned at active site of protein in 3-D spaces. Molecular docking requires two important aspects which are binding affinity among ligand and protein and correct posture of ligand in active site of target protein. Prediction of binding affinity is associated with distinct ligands obtained through assembly. Few of the ligand fit better than the other one. Prediction of pose is linked with same ligand molecules but distinct accommodation. The consideration is to predict the applicable top-score ligand among the set and their exact conformation in appropriate time limit without any mistake. The association between ligand and receptor is being estimated by their adequate complementarily in context of shape and physiological chemistry association with target protein. Molecular docking contains works on two basic steps searching and scoring. Searching depends on specific algorithm of search and explores potent binding poses. The scoring function is found to be crucial for reducing algorithm which depends on these functions.[45-48] There are various docking methods formed during last two decades among which DOCK 1.0 was firstly known automated molecular docking software program designed by Irwin Kuntz in 1982 for receptor-ligand docking.[49,50] Currently there are various docking tools available commonly used are AutoDock, DOCk, FLexX, GOLD, Ligandfit and also newly formed one are Glide, FRED, Surflex.[51-56] As the repercussion of enhanced number of available 3-D protein structures, molecular docking had being found as advantageous method in field of medicinal chemistry.[57,58] The formation and designing of drugs are dependent on the 3-D structure of protein and could be utilized through deriving the new ligand-protein with upgraded properties of binding.[59,60] The formation of drugs associated novel technique is conventional *in vitro* high throughput screening which is dominantly seen but it is costly. Although when structure of target is already been then virtual screening from protein- ligand docking could be the effective alternative.[61,62] Hence this provides a way for huge amount of compounds to be analyzed in opposition of target in instant and automated manner. Frequently used docking programs reported in few years are DOCK, FlexX and Glide.[63,64] As various programs are there on market than what is the basis through which one should choose a program. The option of docking tool should be opted on the basis of aim and objective of the work you have to perform associated with the project.

The computational method for screening of corporate libraries contains millions of compounds and the main criteria for it is reasonable time duration. The docking performing person should initiate from fast tools further by more accurate ones. Likewise leg and docking of simple type aims for designing drugs and its improvement needs utilization of suitable tool. In last

several decades various tools of protein ligand docking had been formed and results in multiple comparative program among them were made.[65,66] The comparative analysis of protein-ligand docking program is not that simple because each program had their own cost and benefits regarding to precision of docking, ranking and of time taken by the computational programs.[67,68] This is not found to be easy for establishing any form of conclusion as these programs are based on distinct docking approaches and utilization of different scoring function. As the users not have the control of access for entire docking codes and also it not all time utilizes test of adequate variation which ultimately results too few programs which will give the superior result than other one. Therefore, few advantages and disadvantages are revealed by current docking tools formed in last few years. Altogether, two approaches could be considered for comparative studied. The comparison could be performed in terms of accuracy, computation technique of screening for small molecules of libraries in oppose of target protein. Docking program could be selected for compounds which are active among the huge set of inactive compounds. Replicability and ranking precession are the secondary character among which could be compared, replicability means the number of times every program identifies the conformation of binding as its top-rank choice. Whereas docking precision is the point of concern, GOLD and Glide are mostly differentiated appropriately from other programs and also responsible for target protein type and properties of ligand.[69,70] The properties of ligand like molecular weight, rotatable bonds and polar atoms are studies frequently in the respect of docking performance. As commonly known fact is that accuracy of docking remarkably diminished for ligands with huge rotatable bonds number GOLD and CDOCKER are least liable in these aspects are the referred programs. The comparison associated with enrichment factor Glide and Surflex found to be more effective programs. Individual docking needs a time limit of few seconds to minute. In subject of docking performance user could opt a very instant tool in sequence to perform a virtual high or ultra-high throughput screening like Lig and Fit, FlexX are least considered for docking of huge assemble of ligand without any undesired huge matters from the air or water.

Applications of molecular docking

Though, this docking had been involved in exhibiting the viability through any biochemical process as executed before for any known experimental part of investigation. As there are few fields where molecular docking had been transformed to the findings. Mainly association between protein and micromolecules could predict the activation or drug binding properties of nucleic acid.[71] As this aspect forms the establishment between drug molecular structure and cytotoxicity. As this point consideration shows medicinal chemist are continually giving efforts for describing the process for drugs at molecular level in anticancer therapy through investigators the interaction mode among nucleic acid and drugs in the presence of copper.[72] Medicinal chemist performing *in silco* analyzed the main finding for predicting that the drug is interacting with DNA/ protein. Beside it, if docking program predicts the association between drug and macromolecules then it their experimental findings were available for finding out the method of complex. It will lead to formation of new anticancer drug. Therefore, this elucidation can be instrumental for finding the changes in drug which would lead to sequence or structural association with its target.[73]

Docking and G-protein-coupled receptors (GPCRs)

Docking of micro molecules to GPCR, the hurdle arise in the task depending upon the subfamily the target is associated with. The GPCRs play crucial role in various disease and shows major target class for drug discovery.[74,75] Structural analysis and determination for all the aminergic subfamilies have enabled the structure based ligand design for these receptors. The orthosteic binding site of receptor in these GPCR is associated through conserved sequence Aspragine 3.32 residue of third transmembrane helix inside bundle of transmembrane. This residue arbitrates a crucial salt bridge with the positively charged nitrogen atom of ligand. The hydrophobic fragment of ligand is located between transmembrane 3 and 6. In comparison of other class consisting receptor contains larger and more open or binding pockets which are lipophillic and could give more independence to ligand and form the appropriate prediction. As if there is not proper knowledge about binding sites so there should be comparison done in target protein with protein consisting identical function or with protein co-crystallized from other ligand. However, many of the cavity detection associated programs and online server are been shown by investigators, in inclusion of POCKET, SurNet, PASS, fpocket, eFindSite, and Cavitator.[76-79]

Molecular docking is instantly utilized for computer aided drug designing CADD which is basically a technique used for instant assessment of chemical libraries for guiding and enhancing the initial stage of development of new active compounds. This could be put in distinct stages of drug designing mechanism for predicting the binding of already known ligand and identifying the new and powerful ligand as a predictive tool. The molecular docking gives valuable data associated with site of binding pocket. Though, the success rate of docking could be enhanced through utilization of structural data obtained through technique Nuclear magnetic resonance (NMR) or X-ray crystallography providing the perception for favorable conformation of ligand.[80,81] Additionally distinct data like mutagenesis studies for providing the assumption of ligand-receptor complex. The increase count of X-ray structure associated with GPCR complex with distinct ligands like agonists fully, partially and this enhance the elucidation of intermolecular packing of these proteins. Though, distinct stimulatory condition of receptor induce different conformation for ligand binding site and contributes to complexity of exact prediction of probable ligand association with GPCRs. Evaluating the improvement of GPCR structure prediction and docking of ligand, large scale of GPCR modeling and docking analysis were organized.[82,83] As main aim of the analysis was ligand binding pose and their contacts with adjacent selected intended target. This analysis was performed firstly on adenosine receptor and ZM241385 ligand and various other model were also made in its competition which shows a large dispersal in prediction of exact ligand binding state for ligand and number of correct contacts. Therefore, least model was found to be appropriate for ligand and number of correct contacts. The more appropriate model was built by β2 adrenergic receptor structure which has sequence similar to A24 receptor of transmembrane domain. The most conquering prediction protocols were analyzed by utilization of micro molecule docking programs like GOLD, AutoDock, Glide and ICM.[84,85] The GPCR associated docking assessment consist 3 distinct classes of receptor which were analyzed mainly, dopamine D3 receptor in complex with eticlopride, chemokine receptor CXCR4 associate to isithiourea IT1t and CXCR4 bound with CVX15 peptide. The primary aim of these assessments of GPCR was to predict correct conformational position and atomic contacts among ligand and its binding pockets. The greater degree of accuracy was achieved in D3/ eticlopride it predicts the best conformational position of ligand and atomic contacts. GPCR docking also shown four targets in inclusion of two human receptor 5-hydroxy-tryptamine(5HT1B and 2B)against ergotamine and also smoothened homolog receptor in complex with LY_2940680 and SANT-1 were opted for evaluating the advancement in modeling and ligand docking in association of GPCR. There are various models submitted have predicted for

activation state of 5HT1B but could not reveal the 5HT2B influential state. Therefore, main aim of analysis for these receptor targets were prediction for binding position of ligand and its contact with nearby residues.

Drug designing

As for any enzymatic reaction, ligand binding is the main step and therefore, for their inhibition. Thus, an elaborated elucidation of interaction among micro molecules and proteins could vary from the essence of rational drug designing plan. This approach was considered on wider scale for designing molecules and addressing a larger range of major pathologies like cancer or cardiovascular disease. Another example in this context includes successfully utilization of docking for designing and leads to a new compounds a novel anti-infectious component against pathogen respectively and are the prominent cause of death in evolving countries. As these parasites which depend on the cascade for producing its isoprenoid compounds crucial for their survival. The next step of the pathway involves deduction of 1-deoxy-D-xylulose-5 phosphate catalyzed though 1-deoxy-d-xylulose-5 phosphate reductoisomerase. Additionally, mammals and animals does not depend on the methylerythritol 4-phosphate (MEP) pathway forming 1-deoxy-d-xylulose-5- phosphate reductoisomerase (DXR) an attractive component of target for searching the new family of drugs. As various inhibitors of DXR had been known and evaluated recently.[86,87] Therefore, motive of this subsection for presenting the utilization of structural data in sequence of improving the capability of new family of drugs. There was not any crystallographic structures data for DirectX Raytracing (DXR) of *Palsmodium falciparam* or Mycobacterium tuberculosis though molecular modeling based on structure of DXR. Though *E. coli* had provided helped various researchers for further describing the structure and function of enzyme and also gave the structure based design of inhibitor. Subsequently, DXR model of pathogen were formed and utilized for forming systematic screening process in sequence of recognizing the potent lead compound and afterwards these models were approved by X-ray crystallographic analysis.[88,89] Subsequently, on the account of quantitative structure activity relationship and crystallographic analysis of various new pyridine-consisting fosmidomycin derivatives were formed and synthesized and they emerged as a powerful inhibitor of DXR. Therefore, these molecules were found to be more active in comparison to fosmidomycin.[90] Currently, structure associated guide pattern and virtual screening were successfully implemented in sequence for identifying and evaluating new molecules with powerful inhibitor effect on Plasmodium falcipuram. These results summarized that significant exploration had been done in past and aim of achieving anti-malarial drugs which seems to be reachable.

Molecular docking in COVID-19

As if now, not any exact cure of COVID-19 is found. The ongoing research had lead to development of molecules precursors which could act as potent antiviral drug as oppose to any disease. As various studies were performed for forming natural compounds which could act as powerful antiviral compound for inhibiting the virus SARS-CoV-2 Mpro doing so neutralizing the virulence. As more than 100 powerful antiviral natural compounds were found previously and were observed from the databases. The active site for the enzyme protease found through utilization of MetaPocket 2.0.[91] The docking was performed by AutoDock 4 accompanying supporting software which elucidates the interaction between ligand and Mpro. Among the various compound docked few were reported with high bonding energies.[92] The aflavin 3-30 digallate, rutin, hypericin, robustaflavone, solenoid had been shown as powerful inhibitor against protease. Also the drug atazanavir, saquinavir and darunavir were seen as potent inhibitor against protease and interact very efficiently than any other natural compounds. The investigations also revealed the pharmacokinetics, toxicity and productivity of drugs which are being utilized currently and reused against COVID-19 from utilization of docking. The approved drugs also contains high binding energies and the count of H-bonds established with Mpro were seen to be low in against H-bonds formed with natural compound utilized in study. Naturally found flavonoids, terpenoids, alkaloids, phenolics, tannins, and sapon in compounds are metabolites of plant and they do not have neither kind of property mutagen or carcinogen. As is not any side effects were caused due to natural compounds. Molecular dynamics was conducted 50 times for evaluating the stability and flexibility utilizing desmond package, Schrodinger and the result found that both protein and ligand were stable in entire stimulation. Entirely, phytocompunds are the major part of our diet and have emerged as a powerful antiviral compound in oppose of COVID-19 and anyone could prevent this infection by utilizing it.[93]

The research could conduct in a way for discovering the natural antiviral compounds. Therefore, various studies have given the instant and broad perception had result to visualizing the library of compounds. Though, these studies will aim toward the virulent protein of COIVD-19 from *in-silco* studies in future. Also *in-vitro* and *vivo* clinical trials with finest compound showed the capability of inhibition towards protease. The development in nanotechnology had provided the exploration in drug delivery system utilizing nano-syntheisized metal oxide and polymeric nano particle transporter. The nano materials had increased the various attributes, like electrical, optical, physical, and chemical properties, high surface area, and permeability. Also additionaly studies have aimed towards natural compounds as capping and deducting agents onto metals nanoparticles which will definitely give the fruitful aspect towards the treatment of COVID-19 infection.

CONCLUSION

As molecular docking had provided help in various fields there are also few hurdles which should be rectified mainly in methods of docking in which receptors are flexible backbone flexibility and mobility of various main receptor associated secondary elements involved with binding of ligand and catalyst are the main hurdles. Few methods were found which could deal with side chain flexibility and found to be efficacious and appropriate in many incidences. Regarding worldwide flexibility an ensemble is basically model which deals with describing the flexibility of proteins it had been known as a prominent solution works accordingly with the conformer selection. This provides an effective path to gain and choose relevant structure of protein utilized in docking which concludes that structure which is suitable fit in should be added in ensembles. Apart from this, computational cost is also the other problem in the molecular docking. Scoring function is also one of the components cost that has been enhanced in docking. The molecular docking shows that computational aspects have the capability of screening and strike from a vast database and forms new micro molecules. Though, interaction amongst micro-molecules and receptors are now also relevant on experimental technique. Exact and least computational cost of scoring function could also provide docking application at new stage.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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