A typical drug design approach for AIDS in HIV genomics using various MD methods

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ABSTRACT

In our work we are working with HIV genomes and AIDS proteins. In our method we are performing sequence alignment using Needleman Wunch algorithm of development and application the approach to calculate free energy and entropy by using non-physical, alchemical path through a thermodynamic series while the drug will interact with the protein. Here we are working in the principle based on protein-protein, protein-peptide, protein-ligand, virtual screening and compulsory free energy estimation for HIV genomics and AIDS proteins. For sequence comparison we are using Needleman Wunch algorithm.

INTRODUCTION

Bioinformatics is an arena that improves technique and software outfits to realize biological information. It pools mathematics, computer science and statistics. Aim of bioinformatics is to Advance and appliance computer programs that allow effective access to, use and controlling of, various types of biological information.

The use of computer and information technologies with numerous types of problems in Chemistry is seminophobic. Chemophthalmics is a scientific field of chemistry, computer science, and information sciences. Cheminformatics uses several parameters to describe pharmaceutical designs that combine with the use of Cheminformatics as the primary application for storage and indexing.

Molecular Dynamics (MD) is a computer model that studies both physical and molecular motions. Annals and molecules allow interacting with the dynamic of the system by providing a fixed time. Using MD, we calculate entropy and free energy.

LITERATURE SURVEY

Bin Zou et al describes The advancement of lead particles will help us to pick just powerful wires to treat particular maladies. Subsequently, the PC technique in the objective acknowledgment and forecast of new medications has been vital. (Maithri et al., 2016) describes Proteomics Group, John Curtin School of Medical Research, The Australian National University, Canberra ACT 0200, Australia 2ANU Supercomputer Facility, The Australian National University: The application of molecular dynamics simulation in lead screening virtual screening is both effective and practical. However, screening for various target proteins requires further optimization of computational scheme. (Duan et al., 2015) Lead revelation through looking of ligand databases with atomic docking procedures speaks to an alluring contrasting option to high-throughput irregular screening. (Ma et al., 2013) In this perspective article, we propose that the true limiting fac-
tor for molecular dynamics is rather the high hardware and electrical power costs "which "constrain not only the length of runs but also the number that can be performed concurrently. (Harvey and Fabritiis, 2012) Drug repositioning by structure-based virtual screening: This audit condenses the essential standards and most recent advancements of structure-based virtual screening and features the solid cooperative energies of PC innovation in medicate repositioning (Okimoto et al., 2009) A Review: The advancement of lead particles will help us to pick just powerful wires to treat particular maladies. Subsequently, the PC technique in the objective acknowledgment and forecast of new medicaments has been vital (Alonso et al., 2006) The application of molecular dynamics simulation in lead screening virtual screening is both effective and practical. However, screening for various target proteins requires further optimization of the computational scheme (Gschwend et al., 1996). Bipin Nair B. J et-al work provided lot of findings in regards with the discovery of drugs for the cancer treatment. The notable point is that, the computational methods which are all they specified can able to compare the performance and effect of drugs (B.J et al., 2018a) had taken the advantage of machine learning algorithms for the prediction and representation of drug interaction in hematic disease affected individuals on the basis of blood coagulation (B.J et al., 2018b). Through venn diagram visualization (J et al., 2018) identified the evolutionary relationships of various species. They had applied various clustering algorithms on different species data set and noted the efficient one and created phylogenetic tree and finally identified the evolutionary relationship (J et al., 2018)"

**Proposed Work**

A typical drug design approach for AIDS in HIV GENOMICS using various MD simulation method::Sequence Alignment in bioinformatics is a way of arranging of RNA,DNA or Protein to identify areas of functional, structural, or dependence between the sequences. Aligned sequences of amino acid and nucleotide residues are represented by rack inside a matrix. Between the residues gaps are inserted, so that identical characters are allied in consecutive columns. Tertiary structure prediction-The function of a protein is deeply linked to its structure in Figure 7 ,so solving protein 3D is the key to understand the biological purposes of a proteins. Resolving protein three-dimensional structure is a complex process, Hence, each protein family has a number of recent efforts to determine the representation of the representative system, but the number of known protein structures is reduced by the number of known protein ranges. The third structure of proteins which is shown in Fig.5 it will be called as tertiary structure of protein it predicts the amino acid has been developed directly from the ranges to fill this gap. These structural predictions show the limited number of protein element in the algorithm which will be shown in Figure 1 as the the flow of the work .

**Chou-Fasman Algorithm**

Step 1: Design the structure of ten drugs and protein
Step 2: Save drug and protein
Step 3: docking
Step 4: Drug-protein interaction
Step 5: Regain protein structure

**Chou–Fasman algorithm**

Step 1: probing linearly over and done with the sequence for a "nucleation" area of great helix or strand chance
Step 2: spreading the area until a succeeding four-residue window carries a chance of less than 1
Step 3: thresholds for helix and strand nucleations are continuous but not necessarily identical; initially 1.03 was fixed as helix limit and 1.00 for the strand limit.
Step 4: turn chance p(t) is determined as:
\[ p(t)=pt(j)+pt(j+1)*pt(j+2)+pt(j+3) \]

**Needleman-wunsch algorithm**

Step 1: take a sample of protein sequences
Step 2: compare the sequences
Step 3: find the similarity by
\[ \text{Similarity}=1(#\text{match})-1(#\text{mismatch})-2(#\text{gap}) \]

**Data Set**

- ITIADLMWCMICAIWVHKAWVMQQHV KMQWLDHDNLVCLQPWAGMWEM
- TFRGWCINLQVAMMFFCAIAMPIV QACTTPFDKRGGPRAHKQVDCQ
- QSYWVHFHKDTRPLSFSQDKDDGGL GLSREE-QQMANILCERNFAPAEPQVG
- TSEKTFGEIKVPTYCTGVHTISPTDA

**RESULTS AND DISCUSSION**

In our project we are collecting the AIDS HIV affected protein from protein data bank which is shown inFigure 2 as protein list from the protein
database and we are using Needleman wunch algorithm for the alignment of the selected proteins, then calculate similarity measure with normal sequence and affected sequence further applying redundancy which is described in Figure 3 as the proteins after redundancy test it will remove the duplicated proteins. Then we are going for the protein’s secondary structure prediction which will interpreted in Figure 4. Then we are making the drug existing for the HIV AIDS to interact with the af-
Figure 7: 3D-Structure of 1bd1

Figure 8: 3D- Structure of 1bdq

Figure 9: 3D- Structure of 1bdr

Figure 10: 3D- Structure of 1bh1

Figure 11: 3D-Structure of 1bl3

Figure 12: Graph showing efficiency
fected protein. Finally, we will summarize the result by plotting in a graph which is interpreted in Figure 12. Here 10 different drugs and protein results are interpreted in the following figures like Figures 6, 8, 9, 10, 11 and 12 shows the different protein list it will have been selected which are used for AID’s disease from Drug Bank. Comparing those drugs with their bond angle and free energy then finding the efficient drug. Changing the molecular structure of efficient drug by using a computational framework. Then collect the AIDS causing protein that will be represented in Figure 13 i.e. Amyloid beta from Protein Data Bank by using a docking tool checking the interaction between donepezil which will be described in Figure 14 and amyloid beta protein, checking whether the redesigned drug is efficient or not, visualizing the changes in our proposed work we are predicting suitable drug like Tenofovir disoproxil represented in Figure 15, which will also interact with AIDS causing proteins.

CONCLUSIONS

Since there are only a few drugs that help as a partial cure for AIDS disease, an effort has been put up to increase the efficiency of the drug by changing its molecular design. If 0.1% is increased, it will be an advantage to the medical field. Designing of the molecular structure of the available drugs by
the use of computational framework has been developed by us, after which all the molecular structures of the drug in .sdf format will be saved and proceed for interaction. Amyloid beta-protein sequence that has been collected from Protein Data Bank. Using docking which is interpreted in Figure 16 shows the structure after docking software, i.e. Pyrex, checking how the drug interacts with the protein and find which drug is the most efficient way which describes in Figure 17 as the physical property of a drug.

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