

Short Note

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Short Note

Virtual Reality in Protein Visualization

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Abstract

Proteins are the building blocks of all living beings. They are composed of amino acid sequences which are folded into sheets, helices and loops which ultimately gives them complex tertiary structure with domains and scaffolds. The quaternary structure is gained by combination of two or more subunits. The structural organization of these protein gives them spatial arrangement that allows for specific interactions with other molecules. These interaction sites are of utmost interest to biologists for their use as drug targets. The visualization of these sites has been traditionally done by pictorial representation which may or may not have some 3D detailing. Software platforms help in visualization of these interactive site. However, such images are mere projections of the actual structure where users can shuffle through various angles of protein view. The virtual reality platform allows the user to visualize actual 3D structure of protein models in an immersive environment that gives better details of the interaction sites. This in turn helps in selecting binding sites for docking ligands and designing molecules of interest. The present study summarizes the advances in protein structure visualization as well the advantages of VR platforms in this aspect.

Keywords: 3D view; protein structure; binding sites; docking; ligand

Introduction

Proteins are the building blocks of nature. They are composed of amino acid chains connected by peptide bonds and called polypeptides. These sequences are highly specific and dictated by the nucleotide sequences of the nucleic acid. The amino acid sequence results in protein folding into Alpha helices or pleated sheets -the secondary structure. These are again folded into tertiary structures. The tertiary structures or units which may be similar or different are then combined into quaternary structures forming homogenous or heterogenous subunits of the protein respectively. They may or may not have non peptide motifs attached (Figure 1).

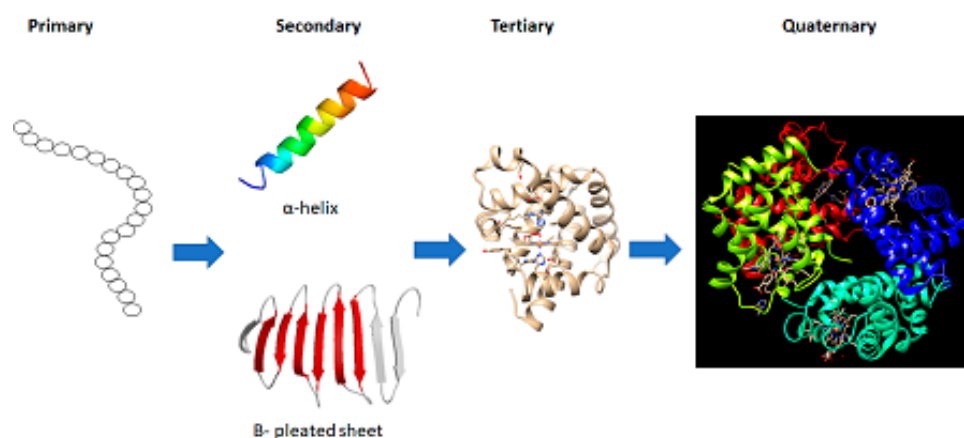


Figure 1. shows levels of protein structural organization.

The function of protein varies from providing the structure to cells to enzyme catalysis, mechanical functions, cell cycle, immune response etc [1–4]. The study of proteins and their function can be done in vitro (for cellular), in vivo (for cellular, tissue or whole organism), and in silico

(computation-based approach). The protein molecule can be obtained in a crystal form. This crystal is then placed on a goniometer which exposes it to x-rays at various angles. The diffracted monochromatic beam of x rays generates patterns which are reflections and vary according to the electron density at the position where it hits the crystal. This data is then converted using Fourier transformation into electron density maps. This combined with the chemical information about the crystal are then used to generate 3d structure of the molecule. The interpretation of the electron density map is vital to the generation of 3-D structure of the protein molecule. The representation of protein structure and interaction has been based on pictorial images. Such images may contain details of the structural organization with some 2D detailing like binding pockets and grooves. However, a deeper view and topology of such binding sites on protein is lacking. To overcome this computational approach is required. This allows for 2D view of the protein molecule and to certain extent the 3D structure can be projected on the screen where a person can rotate the molecule to visualize its structure and binding sites. A comprehensive detail of the binding site which is given by such 3D projections on 2D screen lack the details of binding which can be overcome with a complete view of the molecule in true 3D view. The functional and structural characterization of proteins demands the use of state-of-the-art 3D visualization. This necessitates the for use of VR. The use of VR in electron density map analysis allows for protein structure determination in an interactive environment. It also allows for the determination of protein -protein, and protein-ligand interaction which is an ardent requirement for developing targeted drugs [5–8]. The development of new advanced computation facility has helped in the generation and implementation of new algorithms for generating precise structures of the proteins. Softwares that made the protein structure visualization possible include Protein VR which is a web based application are listed in Table 1. FunFOLD2 is another webserver that allows 3D viewing of proteins and has the special ability to predict protein function [12]. FORECAST allows protein alignment quality assessment . This is a crucial step in template based protein structure prediction [13]. CAPSID is a program for protein-protein and protein RNA interaction display. RaptorX increases alignment accuracy for protein structure prediction [14].

Table 1. Shows the list of some softwares for 3D and VR viewing of proteins.

Sl.No.	Software	Author	Link
1	Protein VR - Durrant lab (13)	Cassidy et al (2020)	http://durrantlab.com/protein-vr/
2	PEP Block builder VR (14)	Yallapragada 2021	https://github.com/TianshuXu/Pocket-Peptides-PC
3	Nanome (15)	Ramrez et al 2020	Learning organic chemistry with virtual reality IEEE Conference Publication IEEE Xplore
4	Raghav (16)	Raghav et al ()	APSSP2: Advanced Protein Secondary Structure Prediction Server (osdd.net)
5	PROtein VR (17)	Cassidy et al (2020)	ProteinVR – Durrant Lab (pitt.edu)
6	Peppy VR (18)		Peppy VR - Faculty of Science (sydney.edu.au)
7	ProMVR (19)		VR-тренажёры PROMVR – обучение безопасному поведению на производстве
8	CootVR (20)		cootVR (hamishtodd1.github.io)
9	Chimera X (21)	Peterson et al 2021	UCSF ChimeraX Home Page
10	IntFOLD (22)	Liam et al	https://www.reading.ac.uk/bioinf/IntFOLD/
11	RaptorX(23)	Peng et al	http://raptorx.uchicago.edu/
12	ESyPred3D (24)	Lambert et al 2002	ESyPred3D submitting form (unamur.be)
13	FunFOLD2 (25)	Roche et al 2013	http://www.reading.ac.uk/bioinf/FunFOLD/FunFOLD_form_2_0.html

14	FORECAST (26)		http://pbil.kaist.ac.kr/forecast
15	Capsid (27)	Peng et al 2011	Projects – CAPSID (loria.fr)
16	MODELLER (28)	Webb et al (2016)	

The ESyPred3D software is also used for alignment of protein for protein structure prediction. It uses neural network for this purpose. However the final 3D protein structure is built using MODELLER software [15]. IntFOLD can give tertiary structure and 3D model of protein, quality assessment, intrinsic order prediction, domain prediction and protein ligand prediction as well [16–18]. ProteinVR is a web based programme for viewing protein molecule in virtual reality. It can be used on any 3D viewing platform and VR head sets. It allows the user to schuffle through the molecule in an immersive environment unlike in 3 D where the user can see but not edit the molecule [19]. Nanome allows multiple users to interact in 3D scene and make changes to the molecular model. It allows live docking, molecular dynamics and property calculations [20]. Peppy VR allows for alteration of each amino acid in the predicted secondary structure. This feature allows for the evaluation of mutation on each amino acid on the protein structure [21]. ProMVR allows multiple users to come to gather in a virtual environment with the molecule. CootVR is used to develop 3D models based on Cryo EM and xRay crystallography data. This helps in reducing the time consumed in 3D model prediction [22]. ChimeraX has a virtual reality application which enables it to render 3D models for live interaction [23]. Confocal VR allows to view architecture in shared virtual space allow for virtual meeting . Molecular dynamics simulation live visualization can be done using VR.

Advantages and Future Perspectives

Molecular dynamics simulation has been used for studying the dynamics of molecular complexes. The ligand bound to a target is subjected to different conditions in-silico and the response of the system is analyzed. However, the size of such a system is restricted to several thousand atoms only. The use of VR approach has allowed the study of millions of molecules in a live interaction state [1]. Currently available VR software and gadgets are costly and require heavy computing facility. Immersive environment gives sickness to the user. This is the major disadvantage of VR. Automatization is also one feature which needs improvement. Controlling the sickness caused by VR is one of the major challenge apart from improvisation in the core area of visualization of protein molecule.

Conclusion

Virtual reality is a fine tool that has opened new horizon for drug discovery. It is expected that fresh techniques and apps will be available in short time that may make VR more easily applicable in drug designing. Overall success of this technique depends upon the outcome i.e. the drugs with precision. It will also help in discovering new protein molecules fro the whole genomics data.

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