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iBET: Immersive visualization of biological electron-transfer dynamics

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ABSTRACT

Recently, we presented a computational framework named VizBET to simulate and visualize biological electron-transfer (ET) dynamics. The visualization process was encapsulated as a plugin to the Visual Molecular Dynamics (VMD) software. However, the user's ability to understand complex, multidimensional ET pathways was severely limited when visualized in 2D on traditional computer monitors. To provide a more accurate representation with enhanced depth perception, we here present an extension of VizBET named iBET to render the VMD model of ET dynamics in a commodity virtual reality (VR) platform. The paper describes detailed procedures to export VMD models into the Unity game engine and render it in an Oculus Rift head mounted display. With the increasing availability of low-cost VR systems like the Rift and rich programmability of game engines, the iBET framework provides a powerful means to explore and understand not only biological ET processes but also a unique experiential tool for broad scientific communities.

1. Introduction

Reduction and oxidation (redox) reactions govern a variety of biological energy-conversion processes, including respiration. Electron transfer (ET) within and across biological molecules is the key process that essentially dictates these redox reactions [1]. Visualizing ET [2] could provide key insight into understanding these fundamental processes and possibly controlling them for a wide range of applications including renewable energy and wastewater treatment [3]. To provide better insight into the dynamics of biological ET processes, we have recently developed a computational framework named VizBET [4]. For simulating and visualizing ET dynamics in a multi-cytochrome complex, for instance, VizBET consists of an entire workflow of homology modeling, protein docking, molecular dynamics (MD) simulation, binding free energy computations, kinetic Monte Carlo (KMC) simulation of ET dynamics [5], and visualization of KMC simulation as a plugin to the widely used Visual Molecular Dynamics (VMD) software [6].

While VizBET was used successfully to reveal nonequilibrium phase transitions in biological ET [4], for more complex ET pathways, the user's ability to understand these processes was rather limited due to its 2-dimensional (2D) rendering on traditional computer monitors. Virtual reality (VR) technologies immerse the user within three-dimensional (3D) models and allow them to navigate through the environment [7]. This type of immersive experience provides the user with the necessary perceptive depth to enhance their understanding of the ET processes being rendered. The head mounted display (HMD) is one of the earliest VR technologies, starting with an early effort by Ivan Sutherland in 1960s [8]. Currently, there is a resurgence of interest in HMD technologies with the advent of low-cost commodity HMDs such as the Oculus Rift [9]. Thus far, however, applications for devices like the Rift have largely been limited to computer games. Reports on biomolecular visualization using the Rift are scarce [10], and we have not found any description of general procedures for scientists to export their

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visual models from standard biomolecular visualization software such as VMD to the Oculus platform.

In this paper, we present an extension of VizBET named iBET (immersion in Biological Electron Transfer) to render VMD models of ET dynamics for display on the Oculus Rift HMD. The paper describes detailed procedures to export the VMD model into the Unity game engine [11] and render it for the Rift. Unity is a cross-platform game engine used to develop video games for personal computers (PCs), consoles, mobile devices, and websites. With the increasing availability of low-cost VR platforms, including smartphone-based VR [12], iBET provides a powerful and uniquely accessible means for understanding, not only biological ET processes, but also a wide variety of complex dynamical systems. The main contribution of this paper is to introduce commodity VR devices and game engines as a common desktop tool for a broad community of scientists, by providing step-by-step explanations of the procedure and an archive of resources that can be easily extended to other applications.

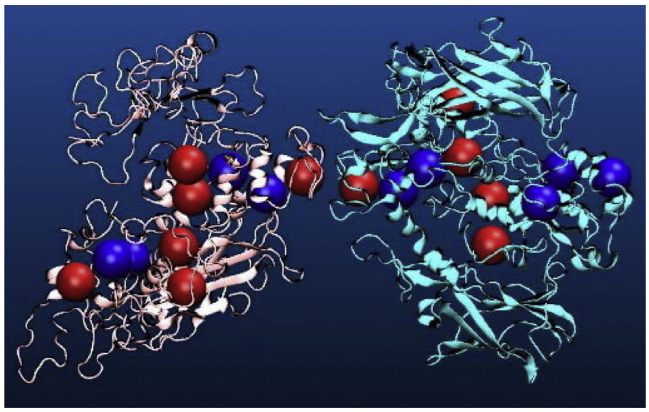

Fig. 2. A snapshot of VizBET visualization of ET dynamics in a cytochrome complex. Fe atoms are represented as spheres, and are overlaid with the NewCartoon representation of the entire protein complex, where two cytochromes named MtrF and OmcA are represented in magenta and cyan shades, respectively. Fe^{2+} and Fe^{3+} are represented by red and blue spheres, respectively. The figure shows a single snapshot from a KMC simulation.

2. Methods

2.1. System overview

To simulate ET dynamics in an assembly of proteins, the workflow of the VizBET framework [4] starts with the structures of individual protein molecules that are downloaded from the protein data bank (PDB) [13]. VizBET first pre-processes the PDB files to account for residues that were not resolved in the crystal structure with the aid of the homology-modeling web server, I-TASSER [14]. The structural outputs from this pre-processing step are then used as inputs to MD simulations that calculate the trajectories of all atoms by numerically integrating Newton's equations of motion. Individual protein configurations taken from the MD simulations are used as inputs to a protein-docking program, ZDOCK [15], to predict the structure of the protein complex. ZDOCK typically returns 2000 top configurations according to simple electrostatic and shape criteria. Our C-RANK program [4] screens these configurations into a small subset of biologically plausible configurations, according to structural and ET criteria. Subsequently, MD simulations are performed to re-solvate and relax the rigidly docked complex structure, while estimating the binding free energy with the MM/PBSA method [16]. Next, VizBET performs KMC simulations of ET dynamics [5] in the selected complex configurations. Finally, the visualization module named ETViz animates the ET dynamics in the KMC simulations [4].

At the final stage of the VizBET workflow lies the ETViz plugin [4] to the VMD software [6], which animates ET dynamics in KMC simulations using the Tcl scripting language [17] (Fig. 1). VMD is a molecular visualization program for large biomolecular systems using 3D graphics and built-in scripting. For this work, we have used VMD version 1.9.1. In the original VizBET, outputs from VMD were only rendered on a traditional computer monitor. Fig. 2 illustrates a visual output of VizBET, using ET in a complex of two cytochromes, MtrF and OmcA, as an example [4]. Such a cytochrome complex potentially plays an essential role for long-distance ET in bacterial nanowires produced by *Shewanella oneidensis* MR-1 [18,19]. Here, each decaheme cytochrome contains 10 heme groups. The iron (Fe) atom in each heme can exist in either of the two valence states, Fe^{2+} or Fe^{3+}. Conversion of the irons between Fe^{2+} and Fe^{3+} allows for the hopping of electrons between the hemes. KMC simulation simulates the hopping of electrons between Fe atoms, as well as the injection (*i.e.*, reduction) and ejection (*i.e.*, oxidation) of electrons.

The iBET framework enhances the perceptual depth over that of VizBET by exporting the visual output into VR instead of a 2D computer monitor (Fig. 1). We selected the Oculus Rift as our commodity device [9]. The system consists of a HMD and a head-movement sensor (Fig. 3). The HMD provides a stereoscopic 3D perspective to the user by showing images from different viewpoints to the left and right eyes. The sensor tracks the movement of the user's head to recalculate the images accordingly. In addition, the user navigates in the 3D model using a mouse and a keyboard. Optionally, a gamepad can be used as an input device for navigation. Porting the molecular model to VR is enabled by the Unity game engine [11]. In Unity, objects in the 3D model are manipulated and animated using the C# programming language [20] and can subsequently be rendered in VR (Alternatively, the JavaScript language [21] can be used for scripting.).

While there are many proprietary physics engines for game development, including CryEngine and Unreal Engine, Unity is one of the most widely used development platforms and one of the first (and only) to provide native support for the Oculus interface. Unity's personal license is free, widely available, and designed for easily accessible game development, making it an attractive option

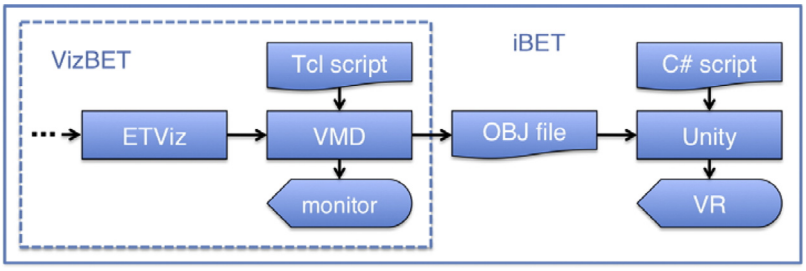

Fig. 1. Workflow of the iBET framework for immersive visualization of biological ET. The original VizBET framework is enclosed by the dashed lines, in which only the final stage (*i.e.*, the ETViz visualization module) is shown.