DockIt: Crowdsourcing Molecular Docking

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***Short Abstract* — Molecular binding is an important part of many biological mechanisms including immune system recognition and cell signaling. However, existing methods to predict bound states can be computationally expensive. We present DockIt, a computer game where players dock ligands to receptor proteins and find potentially bound states. Users are guided both visually and with haptic feedback. Ligand state transition roadmaps can be constructed incrementally using data crowdsourced from multiple players. The game also supports colored surface analysis displays. Our studies have shown users can find low potentially docked states and contribute toward refining motion planning queries.**

***Keywords* — Molecular docking, crowdsourcing**

I. Motivation

MOLECULAR BINDING has implications in the study of diseases, allergic responses, and many other biological processes. Molecular dynamics simulations can predict interactions between ligand and receptor proteins accurately at a high computational cost [1,2]. Probabilistic roadmaps built for protein binding can provide results at a reduced cost, but still require initial low potential energy states [3]. In this work, we aim to find potential ligand-receptor docked states by collecting data from *DockIt*, a crowdsourced interactive molecular docking puzzle game. The game allows users to fit ligands to receptors [4], where players are given both visual and haptic tactile feedback based on the potential energy between the molecules. The quality of the current fit is shown via a score based directly of the all-atom intermolecular energy. Surface analysis coloring, such as depicting surface electrostatics, can be implemented for use within the game.

II. DockIt

The molecular models used in *DockIt* were converted from RCSB data and assigned van der Waals and electrostatics parameters using the AMBER99 force field [2]. The all-atom model is used for potential energy calculation within the game but shown visually using an isosurface representation. Roadmaps are constructed from ligand states recorded as the user moves the ligand. Each ligand state is considered a roadmap node, and the edges represent transitions between two ligand states. Edge weights are given based on the difference in potential energy between two states. Shortest path queries are performed between two ligand states to predict ligand motion pathways.

A. User Study

A pilot study was performed with 24 participants assigned to one of four input devices. Users were aged from 18 to 66, with an average age of 30.2 years. The number of users with or without a technical background (biology or computation) was evenly split, 12 in each group.

B. Game Mechanics

Players can translate and rotate the ligand around the environment, move the camera for a better view, or let the game perform gradient descent toward the nearest minima. The user can see their current score and the best score for the current session. The best score encourages players to continue finding better potentially docked ligand states.

C. Input Devices

The four input devices used in the study vary by degrees of freedom for input and haptic feedback. First was the standard mouse and keyboard lacking any haptic feedback and only two degrees of manipulation at one time. The game controller had haptic vibration feedback and two degrees of manipulation. The Novint Falcon is a device that allows three degrees of haptic force feedback and manipulation, and the PHANToM input device allows six degrees of haptic force feedback and manipulation.

III. Results and Conclusions

DockIt users were able to find low energy potentially docked ligand states and ligand motion queries were refined as more user data was incorporated. Low energy states were found by users of all four devices, including the commodity game controller input device. *DockIt* can be adapted for use on mobile devices for future crowdsourcing scale studies.

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