PhD - Tangible molecular interface and augmented reality for molecular science and rational drug design (M/F)

keywords: Tangible Interface, Augmented Reality, Virtual Reality, Mixed Reality, Molecular Biology

Abstract: We propose to design, develop and evaluate a 3D interactive environment for molecular biology and rational drug design, combining tangible molecular interface and augmented reality. The aim is to augment a tangible molecular interface, with augmented reality features directly displayed on a modular, articulated, wireless and markerless physical molecular model. The main issue is to provide robust 6-degrees-of-freedom tracking of this tangible interface, to display in interactive time augmented reality features directly on the physical model during its construction and manipulation. The objective is to be able to benefit from the advantages of tangible interfaces in terms of direct interaction to build and manipulate molecules that intrinsically have many degrees of freedom, while offering at the same time the advantages of visualization, allowing dynamic management of the displays, adding new molecular components, changing its visual representation modes, and to provide innovative interactive and collaborative workspace dedicated to molecular biology and drug design.

From left to right, non-augmented tangible molecular interface prototype [5], a user manipulating a protein in augmented reality, an augmented reality artistic view of the Peppytide physical model [1]

Research issues: Manipulating biomolecules *in silico*, such as proteins and ligands, and study their molecular interactions remains a complex task, because classical 2D desktop interactive environments is still not suitable for numerical manipulations of inherently 3D, deformable and dynamic objects. It consequently slows down the efficiency and productivity of the experts in their drug design activity, especially because it requires to frequently change interaction context wasting a lot of time in data, between activities such as simulation, visualization, and data analysis. In the context of a user-centered methodology, complementary to high-throughput numerical or machine learning approaches, the aim of this work is to address this issue combining physical models [1], tangible interfaces [3] [4] [5] and augmented reality [2] to support the modular building of drug candidate and to facilitate the understanding of their biophysical interactions with their molecular environment.

More precisely, we target a scenario allowing to study the molecular interaction between a molecule as a drug candidate represented by a modular and deformable tangible interface and its target represented in augmented reality, such as large protein. Underlying this manipulation, a molecular simulation will be used to measure the geometric and biophysical affinities between the drug candidate and the active site of the virtual protein. Beyond the augmented representation of the target, it is planned to be able to augment this deformable tangible interface with augmented reality features, displayed directly on this tangible interface, as well as to change its visual representation modalities (color, type of molecular representation, feedback of biophysical interactions, etc.).

The implementation of this scenario requires to propose, design, implement and evaluate robust and efficient tracking approach, that is a challenge because of its deformable aspect of the tangible interface, overcoming the difficulty of fact that the interface is occluded by the user's hands during manipulation. This tracking is required to be able to display virtual elements directly on the interface during manipulation. It will be a question of combining optical tracking information classically used in virtual and augmented reality, with electronic embedded sensor-based tracking. The tangible interface is already available and provided by the project partners in the field of embedded electronics [5]. Once the scientific and technological issues have been overcome, especially about tracking, this platform dedicated to the rational design of medicines will be evaluated with experts of the molecular science field.

Application background: Most drugs are based on an active ingredient, which modulate molecular interactions involved in a disease according to a key-lock system. The key is the active principle, and the lock is often an active site on a protein. Proteins participate in cellular life, constituting the building blocks, the messengers, the transporters, the workers of the cellular machinery...

Two main principles make rational drug design difficult:
- This key-lock system does not only depend on geometric shape complementarities, but also on biophysical interactions (atomic, electrostatic, hydrophobic attractions and repulsions, etc.),
- The key, like the lock, i.e. the active ingredient molecule and its target, are often dynamic and deformable according to the degrees of freedom relative to the bonds between their atoms.

In order to design a drug, it is first necessary to identify the proteins and an active site on this protein, in order to correct a dysfunction related to an active site, using molecule as a drug candidate. Once a site has been identified, a commonly used methodology is based on the concept of a "pharmacophore", which consists of identifying patterns of biophysical properties and geometrical constraints (angles, distances...) which are designed to be complementary to the geometric and biophysical properties of the active site of the target. This pattern is used to carry out queries on banks of molecules, retaining as candidates only those that optimize these constraints. An important issue, "specificity", is to avoid that this drug also acts on other proteins and disrupts other molecular processes.

Context: The work will be carried out on the campus of the University of Paris Saclay in Orsay at the "Laboratoire Interdisciplinaire Pour les Sciences du Numérique" from 1 October 2022, in the "VENISE" Virtual and Augmented Reality research team. This work will be led in the context of molecular science and rational drug design. This project is funded by the French National Research Agency (ANR PIRATE 2021) led by Antoine Taly at Laboratoire de Biochimie Théorique. The partners of this project have multidisciplinary research background including computer science, electronics, molecular biology and pharmacy.

Salary : 2 135,00 € gross monthly. Additional remuneration is possible through teaching activities.

Requirements and skills: Applicants with a Master's degree or equivalent in Computer Science with excellent academic results. Practical experience and a good level in computer development (C++/C#) and 3D modelling and/or human computer interaction and/or XR is required. Basic knowledge in molecular biology would be appreciated. A strong level in english is required to be able to write scientific papers and talk at scientific conferences.

Available hardware and software environments: Augmented Reality headset (Hololens…) or/and Immersive Virtual Reality headset (Oculus, HTC Vive…). ART Tracking system. The developments will be done with the Unity 3D tool, in C#, using the available tracking libraries (ARToolkit, ARTTrack...). Molecular Visualisation and Interaction design will be done with Unity 3D.

Process: Interested candidates are required to send their applications on the dedicated CNRS website (https://emploi.cnrs.fr/Offres/Doctorant/UMR9015-NICFER-001/Default.aspx?lang=EN), and we advice moreover to send to supervisors a summary of their research interests, with names and contact information, at least two references, a list of publications and project by email with subject "PhD - Tangible molecular interface with augmented reality for molecular science and rational drug design"

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