Applications of Molecular Docking in Biological Sciences

Erman Salih Istifli
Department of Biology, Faculty of Science and Literature, Cukurova University, Adana, Türkiye
esistifli@cu.edu.tr; ermansalih@gmail.com

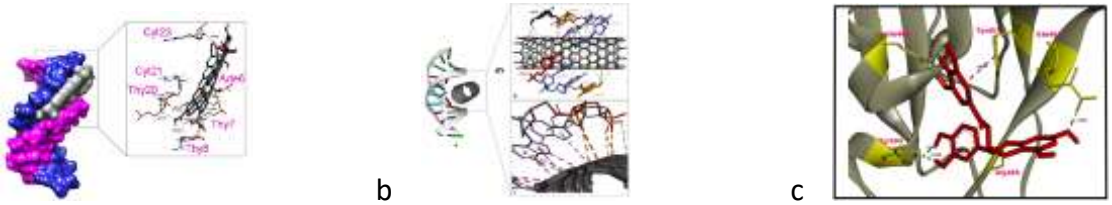
The submicroscopic details of interactions between small molecules and macromolecules, or between macromolecules themselves (i.e., DNA-ligand, protein-ligand, DNA-protein, protein-protein), are of critical importance for elucidation of the biochemical reactions occurring at the cellular level and the molecular-level understanding of the specific responses that emerge as a result of these reactions. In this context, molecular docking is one of the most significant computational techniques of the past 20 years, and perhaps one of the most frequently used techniques in deciphering biological molecular phenomena. Molecular docking has the ability to reveal the conformational orientation, binding affinities, and intermolecular interactions formed between numerous molecules, making it a powerful and indispensable tool in understanding cellular phenomena [1].

In the field of biological sciences, the molecular docking technique is widely applicable and provides valuable mechanistic and molecular-level insights into experimental results. This technique is extensively utilized in disciplines such as genetics, biochemistry, pharmaceutical chemistry, pharmacy, microbiology, molecular biology, and toxicology [2]. Furthermore, molecular docking plays a crucial role in studying the molecular-level interactions between synthetic chemicals (e.g., carbon nanotubes, pillararenes, nanoparticles, nanocomposites, etc.) used alone or as drug carriers against their respective receptors, particularly in targeting cancer cells. Additionally, molecular docking is frequently employed in the 3D orientation prediction of DNA-protein and protein-protein complexes whose crystallographic structures remain unelucidated. Strikingly, the inherent nature of molecular docking, which is based on biochemistry and biophysics, has allowed it to take place even in the COVID-19 pandemic, which has severely affected the world agenda, societies, and the global economy for about 2 years. This method has ultimately become a principle component in bioinformatics-based drug-discovery campaigns against the SARS-CoV-2 virus [3].

Through our experimental and computational molecular docking studies conducted with several research groups, the molecular complexes formed between synthetic or organic small molecules and macromolecular targets such as DNA/proteins (i.e. AChE, BChE, alpha-glucosidase, alpha-amylase, tyrosinase, spike, TMPRSS2, cathepsins) have been characterized in 3D, and the resulting non-bonded interactions have also been successfully demonstrated. The data obtained from molecular docking simulations serve as a starting point to define the biochemical events occurring between ligands and their specific receptors more clearly and contribute to a better understanding of the underlying biological phenomena.

References

[1] X.Y. Meng, H.X. Zhang, M. Mezei, M. Cui, Molecular docking: a powerful approach for structure-based drug discovery, Curr Comput Aided Drug Des, 7 (2011) 146-157.
[2] L. Pinzi, G. Rastelli, Molecular Docking: Shifting Paradigms in Drug Discovery, Int J Mol Sci, 20 (2019).
[3] E.S. Istifli, P.A. Netz, A. Sihoglu Tepe, M.T. Husunet, C. Sarikurkcu, B. Tepe, In silico analysis of the interactions of certain flavonoids with the receptor-binding domain of 2019 novel coronavirus and cellular proteases and their pharmacokinetic properties, J Biomol Struct Dyn, (2020) 1-15.



a b c

Figure 1: Molecular complexes of a. DNA-graphene, b. DNA-nanotube, and c. Spike-epicatechin gallate