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T01

Modeling Charge Transfer States in Phycobilisomes

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Abstract

Phycobilisomes are giant (~6 MDa) light-harvesting pigment-protein complexes of cyanobacteria and certain algae, responsible for harvesting sunlight and regulating the flow of absorbed energy to provide the photochemical reaction centres with a constant energy throughput. Single-molecule spectroscopy studies have identified the presence of strongly red-shifted and quenched emission states and they were hypothesised to originate from charge-transfer states residing on phycocyanobilin pigments in the core of phycobilisomes. The quenched states were suggested to be an important, rapidly activated photoprotective mechanism to protect the organism against high solar illumination. An investigation into the molecular origin of these states, the role of the background charge, amino-acid residues around the pigments, and the geometrical configuration of the pigments requires the use of atomistic simulations involving a state-of-the-art QM/MM computational microscope. In this work, the ground-state geometries of the trimeric core units of phycobilisomes retrieved from *Synechocystis* PCC 6803 and *Synechococcus* PCC 7002 were optimized using Density Functional Theory (DFT) employing the CAM-B3LYP exchange-correlation functional together with the 6-31+G* basis set. Linear-response time-dependent DFT (TD-DFT) was used to calculate the excited-state geometries. The results demonstrated that the coupling between the energy states in TD-DFT spectra would serve as a screening tool as a charge transfer states in light-harvesting pigments. Accordingly, care should be taken in considering the natural transition orbitals (NTOs) for CTS analysis. Therefore, a complete analysis of charge transfers energies, hole-electron distance, NTOs, and optimized charge transfer states are needed to confirm the presence of charge transfer states. Amino acids around the D-ring of the bilin have a strong potential to serve as electron acceptor.

T02

Computational investigations for the design of a Multimodal Innovative Theranostic Nanosystem (MITHOS)

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Drug delivery systems based on stimuli-responsive metal oxide nanoparticles (MeOx NPs) for cancer treatment gained interest in the past few years. Due to their enhanced targeting ability, they can limit the drugs toxic effects and allow for better tuning of the dose/response behavior [1, 2]. Biomedical MeOx NPs rely on NP surface functionalization with different agents, which allows their solubility, drug loading and specific targeting. Within the PRIN project MITHoS, functionalized NP are covered by a lipid membrane and used as an ultrasound-responsive carrier of the anti-cancer drug carfilzomib (CFZ) against multiple myeloma. Here, we used Molecular Dynamics (MD) simulations to investigate the structure and dynamics of these functionalized MeOx NPs and guide the design of better-performing theranostic agents. Our target NP is a ZnO NP functionalized with oleic acid (OLA) and 3-(aminopropyl)trimethoxysilane (APTMES) or N-(2-Aminoethyl)-3-aminopropyltrimethoxysilane (L-APTMES). We designed molecular models with a coarse-grained (CG) resolution of ZnO NPs, ligands, and CFZ drug. We performed metadynamics simulations to characterize CFZ adsorption on a ZnO surface functionalized with APTMES and L-APTMES with or without OLA in water and in ethanol. The free energies of adsorption profiles showed that using L-APTMES instead of APTMES can lead to a more efficient CFZ adsorption. The addition of OLA as a NP stabilizing agent in ethanol enlarged the range of attractive interaction between CFZ and the functionalized surface. When a lipid bilayer is added on top of the functionalized (OLA+L-APTMES) surface, we observe that its leaflets exhibit an asymmetric lipid distribution, due to their interactions with the ligand layer. Regarding CFZ, most of the molecules are most favorably adsorbed in the region delimited by the ligand layer and the lower lipid bilayer leaflet. In the next steps, we aim to investigate the possible mechanisms and the energetics of drug release.

[1] Dhas Namdev, et al., J Control Rel 333, 188 (2021).
[2] Anjum Sumaira, et al., Cancers 13.18, 4570 (2021).

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T03

Optimization of Post-Processing Tools for Collective Burst Mechanism of Angular Jumps in Water

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This study aimed to optimize the computational efficiency of an automated algorithm for detecting angular jumps in water molecules [1]. The protocol, which analyses dipole moment (DP), hydrogen-hydrogen (HH) vectors, and topological defects in hydrogen bonding across systems of varying sizes, faced performance bottlenecks as system size, trajectory length, and simulation time increased. These challenges led to frequent crashes and prolonged execution times. Initial tests of the DP and HH extraction tool revealed high memory consumption (**117 GB**) and long execution times (**4397 seconds**). To address these challenges, the MDAnalysis package was initially leveraged for input processing and benchmarked against the custom input processing approach. Results showed that converting XYZ trajectory files to binary reduces memory usage and processing time. Among various binary file reading techniques implemented, NumPy's frombuffer function performed best, reducing execution time and memory usage by up to **265-fold** compared to the original method, and **224-fold** relative to MDAnalysis. With optimized input handling, the serial version of the DP and HH extraction protocol ran approximately **3x** faster than the original. Implementing multiprocessing with up to 8 processes further improved performance, achieving a **14x** increase in speed while maintaining low memory usage **(~93 MB**) for all target analysis tasks. Quality checks on the molecular swing evaluation protocol was completed with updated jumps calculation protocol and plotting utilities. Additionally, the speed of the tool for calculating topological defects in hydrogen-bonded water molecules was enhanced using Numba's @njit decorator for functions. While the protocol undergoes further checks to produce a completely optimized automation, we tentatively conclude that binary formatting of custom trajectories coupled with the aforementioned Numpy routines enhanced computational efficiency of post-processing of large molecular dynamics simulations data.

[1] Offei-Danso et al. (2023). Nat. Commun., 14, 1345.

T04

Resveratrol interaction with model membrane system: an AFM Study

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Trans-resveratrol is a growing chemopreventative agent, due to its effect on cancer. Harnessing its chemotherapeutic potential is hampered by its poor pharmacokinetics. This study investigates the interaction of resveratrol with supported lipid bilayers using atomic force microscopy (AFM).

Resveratrol, a polyphenolic compound with known health benefits, was analyzed for its effects on lipid bilayer structure and stability. Supported lipid bilayers were prepared by DOPC, DSPC, and sphingomyelin with 7% and 33% cholesterol concentrations, on a mica substrate and exposed to 1µM, 5µM, and 10µM concentrations of resveratrol. AFM imaging revealed the deposition of resveratrol on the rafts, which caused an increase in the height of the rafts and alterations in surface roughness and raft thickness. These observations suggest that resveratrol interacts with lipid rafts in the 7% and 33% supported lipid bilayers, potentially influencing their fluidity. The study provides insights into the molecular interactions between resveratrol and lipid membranes, which may be relevant for understanding its bioactivity and therapeutic potential.

References

[1] Brittes, J., M. Lucio, C. Nunes, J. L. F. C. Lima, and Reis Y. "Effects of resveratrol on membrane biophysical properties: relevance for its pharmacological effects." Chemistry and physics of lipids 163, 747-754(2010).

[2] Longo, Elena, Federica Ciuchi, Rita Guzzi, Bruno Rizzuti, and Rosa Bartucci. "Resveratrol induces chain interdigitation in DPPC cell membrane model systems." Colloids and Surfaces B: Biointerfaces 148, 615-621(2016).

T05

Structural and biochemical characterization of iron-sulphur cluster containing helicases from pathogenic bacteria

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DNA helicases are essential enzymes for various cellular processes, including DNA replication, repair, and recombination. They are characterized by their DNA binding, ATP hydrolysis, strand separation, and translocation activities. Iron-sulphur helicases, such as DinG, play a crucial role in maintaining genomic integrity. *Mycobacterium tuberculosis*, responsible for tuberculosis (**TB**), and *Neisseria meningitidis*, causing meningococcal disease, are major health concerns in Sub-Saharan Africa. Given the prevalence of drug-resistant tuberculosis and meningococcal disease, targeting DinG from *Mycobacterium tuberculosis* (**MtDinG**) and *Neisseria meningitidis* **(NmDinG)** offers a promising strategy for developing novel antimicrobial agents. This presentation will discuss our ongoing efforts to characterize these helicases, including preliminary findings from protein production, purification, crystallization screening, as well as biochemical/biophysical studies. Our ultimate goal is to establish helicases as potential drug targets and develop novel inhibitors to combat these diseases.