Inverse design of biomimetic organic molecules with tailored spectroscopic properties

ABSTRACT: The project aims at the computational design of organic chromophores that are of great relevance from a biological and/or technological point of view as they feature peculiar steady-state and time-resolved optical spectroscopic properties. Starting from the simulations of absorption electronic (linear) spectra of well-known chromophores, target properties (such as energetic gaps, fundamental transition energies and transition dipole moments) will be used to define reward functions that can be employed in machine learning algorithm for the inverse design of new molecules, analogues to bio-organic chromophores. In fact, in order to investigate the behavior of standard biological dyes, such as DNA/RNA nucleobases and retinal chromophores, such molecular analogues can be considered to help in performing experimental studies. The results will be used to extend this design for molecules featuring specific properties in both pump-probe electronic and Raman types of nonlinear spectroscopies.

ABSTRACT: Il progetto mira alla progettazione computazionale di cromofori organici di grande rilevanza dal punto di vista biologico e tecnologico per le loro peculiari proprietà spettroscopiche. Partendo dalle simulazioni degli spettri elettronici di assorbimento di cromofori noti, le proprietà target (come gap energetici, energie di transizione fondamentali e momenti di dipolo di transizione) verranno utilizzate per definire funzioni ricompensa da impiegare in algoritmi 'machine learning' per la progettazione inversa di nuove molecole, analoghe ai cromofori bio-organici. Infatti, al fine di studiare il comportamento di cromofori biologici standard, come le basi azotate del DNA/RNA e i cromofori retinalici, tali analoghi molecolari possono risultare molto utili nell'esecuzione di studi sperimentali. I risultati verranno utilizzati per estendere questa progettazione molecolare a molecole dotate di proprietà specifiche nelle spettroscopie non lineari di tipo Pump-Probe e Raman.

Research Project: Understanding the photo-reaction mechanisms of biological systems is of fundamental importance for a variety of technological applications, such as the design of photochromic molecular switches and photosynthetic systems, as well as in biosensing or in the evaluation of health risks, for instance related to skin damage upon irradiation. Due to the complexity of photo-induced phenomena, giving a coherent picture of the photoreaction pathways is challenging and the aggregation phenomena often play a vital role. Sometimes even the interpretation of conventional UV-vis absorption spectra is not as straightforward as expected.

The project, thus, will first investigate absorption spectra of the target organic chromophores to provide reward functions that can be used in machine learning techniques for molecular design. For a good accuracy of the simulated absorption spectra the employment of various QM methodologies (such as TD-DFT and MC-SCF) and benchmark studies is quite important. Given the high computational cost of QM computations, the screening of many molecules is unfeasible. At the same time, choosing appropriate molecular analogues of DNA/RNA nucleobases and retinal chromophores is quite important to perform specific spectroscopic investigations such as pump-probe electronic and Raman nonlinear spectroscopies.

The theoretical study planned in this project will use reinforcement learning technique to rapidly design molecular analogues of bio-organic chromophores that will largely facilitate the experimental investigations, shedding light into the behavior of standard biological dyes, such as DNA/RNA nucleobases and retinal chromophores.

Activity Plan:

1. Simulations (TD-DFT and MC-SCF) of linear absorption spectra of target organic chromophores
   1.1 DNA/RNA nucleobases
   1.2 Retinal chromophores

2 Analysis of theoretical data and definition of reward functions
3 Reinforcement learning design of bio-chromophores' analogues
   3.1 Exploration of the chemical space and characterization of key features
   3.2 QM and QM/MM simulations of selected analouges

4 Extension to time-resolved spectroscopies
   4.1 Characterization of reward function for pump-probe electronic spectra
   4.2 Characterization of reward function for pump-probe Raman spectra
   4.3 Selection of bio-chromophores' analogues for pump-probe electronic spectroscopy
   4.4 Selection of bio-chromophores' analogues for pump-probe Raman spectroscopy