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Biosensing of DNA damage in Alzheimer's disease by Computational and Experimental methods

DNA damage plays a pivotal role in the pathogenesis of Alzheimer's disease (AD) therefore, an innovative ss-DNA/dopamine/TiO2/FTO electrode strategy was developed to detect the genotoxicity upon photocatalytic reactions. This study involves a computational and electrochemical investigation towards the direct measurement of DNA damage. Computational chemistry was useful to resolve the intricate chemistry problems behind electrode constructions. The computational protocols were simultaneously carried out comprising of density functional theory (DFT) calculations, Metropolis Monte Carlo (MC) adsorption studies, and molecular dynamics (MD) simulations. The DFT calculations elucidated the structural, electronics, and optical properties of the electrode components resulting in a good agreement with the experimental parameters. The MC simulations carried out using simulated annealing predicted the adsorption process within layer-by-layer electrode as well generating reliable inputs prior to MD simulations. A 100 ns MD simulations were performed using a canonical ensemble provided information on the thermodynamics parameters such as total energy, temperature and potential energy profiles, including radius of gyrations and atomic density profiles. Binding energies calculated from the MD trajectories revealed increasing interaction energies for the layer-by-layer electrode, in agreement with the experimental characterization studies. Experimentally, the ss-DNA was electronically linked to TiO2/FTO surface through dopamine as a molecular anchor. Electrochemical measurements using cyclic voltammetry and electrochemical impedance spectroscopy were employed to characterize the electrode modifications. The square wave voltammetry was subsequently used to measure the DNA damage and the ability of antioxidant treatment using ascorbic acid (AA). The presence of AA significantly protected the DNA from the damage, and therefore used as a potential treatment in AD. The electrochemical characterizations were in a good agreement with the theoretical investigations (i.e. HOMO-LUMO DFT levels and binding energies). In addition, guanine residues predicted by DFT as the most reactive sites of the ss-DNA involved in the genotoxic reactions. Overall, the theoretical studies successfully validated the experimental study as well as providing the molecular basis of interaction phenomena towards electrode constructions. Our results highlight the potential application of this methodology to screen the genotoxicity in Alzheimer's, suggesting the important role of theoretical studies to predict the molecular interaction and validation of the DNA-based sensors and bioelectronics.

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