

Politecnico di Torino

MASTER'S DEGREE IN NANOTECHNOLOGIES FOR ICTS

Master Thesis

Modelling the Bi-based clusters effect on the electron transfer to Paracetamol: from physics to computation

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Abstract

Theoretical model and computational analysis are exploited to estimate the electron transfer (ET) due to Paracetamol oxidation. Functionalized electrode surface through $HO-BiONO_3$ based nanocomposite have shown to improve the electrochemical sensor performance from previous experiments. The main aim is to build up an hypothetical transition state (HTS) model to look at the Bismuth cluster effects on electron transfer rate constant. First, the HTS model based on 2-Bi atoms cluster is studied as a minimum unit to have a two electron oxidation process as the Paracetamol one. Then, 3-Bi atoms cluser based model is drawn to examine a situation in which a free site is close to active sites. For both the two cases, simulations are performed on several clusters that differ in the functional groups bonded with Bi atoms. The presence of probable contaminants after a pretreatment in H_2SO_4 are studied in this way. Indeed, HTS molecular structure from simulations shows how orientation in space and relative position of Paracetamol and Bismuth functional groups lead to steric hindrance due to electron clouds repulsion. This together with the atoms electrostatic interactions define the HTS conformation and provide the interacting distance and the electronic properties affecting the ET rate constant. It is observed how some functional groups could be preferable resulting in less distorted structure: huge atoms hindrance can hardly influence length bonds and angles due to large functional groups approach. Molecular mechanics method based on MM+ forces field and quantum mechanics semiempirical method are used to perform the computational simulations. MM+ treats the system as made by springs and exploits Hook's law based equations. Indeed, it is useful to perform a first geometry optimization of the molecular structure but it is not suitable to provide electronic properties information. The many body system is further optimized with a quantum mechanics simulation. In that case, Schrödinger equation is solved according to the semiempirical method and the basis set choosen: PM3 in that case. The method is Hartree Fock (HF) based and the basis set parameters defining the electron wavefunctions: s and p orbitals formed this basis set. Moreover, PM3 also introduces some approximations to reduce the number of integral to be solved according to the neglect differential of diatomic overlap method: too iterations will results in a time consuming process not suitable for large system. Finally, the ET rate constant values is determined by using the computational data within a physical theoretical model. It comes from Marcus model and differ from it in some assumptions regarding the solvation effect of the electrolyte solution. To have a complete description of the ET between the electrode and the organic com-

To have a complete description of the ET between the electrode and the organic compound, differential equations (PDE) problem based on Fick's laws are used as well to analyse spontaneous diffusion and define the reacting specie concentrations at the surface.

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Chapter 1

Introduction

Electrochemical sensors have acquired a great interest during the last decades. They are large exploited in organic molecules detection for environmental protection, food safety and different medicine applications [1]. For instance, gas sensors are hugely exploited to control air pollution. There are also applications in agriculture to keep on a safe level the pesticide consume and other poisonous agents. Detection of toxins in food is developing too.

Regarding the medical applications, theranostic devices are developing basing on electrochemical sensor to improve the tumor cell detections and providing a better targeting drug release thanks to nanocarriers structures. Another example is related to point-of-care diagnostic: it is becoming one of the many research field to some disease like diabates. Investigations on glucose detection sensor have lead on many improvements in terms of portability and reduction of detection time. Moreover, some advantages come from the non-enzymatic nature of the reacting specie with the analyte [2]. Indeed, many issues associated to enzymatic sensor are due to huge depedence on biofluid features and surrounded ambient: temperature, humidity and pH have a negative effect on sensor reproducibility and stability. Metallic nanocomposite are used to overcome this problem. However, it is not the same if transition metals are used since they suffer in terms of reproducibility and also selectivity when interefering specie are there together with the analyte [3].

Bismuth based nanocompounds covering electrode surface seem to improve the electron transfer rate during detection analysis and give better electrochemical measurements [2]: high sensitivity and selectivity for analyte, low cost of fabrication, low limit of detection (LOD), good reproducibility and stability in time.

Cyclic voltagramm is the electrochemical tecnique for the evaluation of these properties. The current is measured as function of the applied voltage that changes according to a scan rate value; the CV curves look like the graph in figure 1.1: the two peaks are the anodic and cathodic peaks potentials from which the reduction potential can be derived [4]. Changing in analyte concentration or electrolyte pH give different current response to the same applied voltage [6]. Moreover, calibration plot from CV data allows to keep information on sensivity and LOD[7]. It is also possible to estimate the electron transfer rate knowing the redox potential by exploiting the Laviron equations [8].

Neverthless, these measurements and calculations do not provide any detailed information about what happens at the electrode/analyte interface that allows the electron



Figure 1.1: CV for Fe^{+2}/Fe^{+3} in acqueos solution [5].

transfer process. It strictly depends on analyte orientations with respect to the electrode surface or better the single active site on the total area. Looking for that means to determine the distance of closest approach at which the analyte adsorption on the electrode surface occurs. Besides that, it must be considered that the nanostructures active sites are not uniformily distributed on the electrode surface. Indeed, nanostructures can have some sides reacher in active sites than the other. Finally, the electrode surface can be thought as formed from many island with different electrochemistry activity.

Previous experiment [9] shows how several Bismuth nanostructures improve the electron transfer and the sensor quality in terms selectivity, LOD, sensitivity and so on. The aim of this thesis is to exploit computational method to analyse what can happens in proximity of a single active site when the electrode is functionalized with that nanostructure. Then, a comparison between this nanocomposite tailored with different functional groups are performed in order to further support or not the idea of a "fragment" electrode surface.

1.1 Electrochemical biosensor

Electrochemical sensor working method is based on the charge transfer process at the electrode surface due to oxyreductive (REDOX) reaction. This is traslated in a mesurable electric signal (current, potential or capacitance depending on the measuring way) that allows to qualitative describe the sensor properties. In details, a sensor is typically constituted from a three electrode system [10]:

- working electrode at which electron transfer occurs;
- reference electrode ensuring a known potential to keep a reference for the mea-

sured potential; the potential is applied between WE and RE;

• counter electrode to ensure that the current will be measured between WE and CE.

Nanostructures deposited on the WE surface are devoted to the analyte recogniton process by ensuring a rapid and in-situ detection. Chemical and physical features of nanocomposite are the main affecting parameters on sensor quality. Indeed, detection process must be accurate and precise and nanostructures must be choosen to ensure the best in terms of the main following properties:

- sensitivity that means how much the sensor response change as a function of analyte concentration;

- limit of detection (LOD) defining the minimum detectable concentration.

Strictly referring to biosensor, nanofunctionalization layer must be highly selective with respect the analyte by ensuring the same response if organic acid or other compounds are in solution. This becames the most important point if one think to immunosensors whose aim is to ensure the antibody-antigen recognition.

The electron transfer rate constant will also depence on the experimental measure conditions. Since the electrochemical system consists in an electrode surface, it is proved how the electron transfer rate changes depending on the applied voltage [11]. In particular by looking at the Tafel equation it can be observed an exponential behaviour of current vs overpotential η [12]:

$$\eta_{a,c} = \pm \frac{2.3RT}{nF} ln(\frac{i_{a,c}}{i_0})$$
(1.1)

where the sign depends on anodic a or cathodic c process, R is the gas constant, T the temperature, F the Faraday constant and n the electrons number involved in the redox reaction, $i_{a,c}$ are the current and i_0 is the exchange current density. By reversing the equation, the current exponentially depends on overpotential: it is the mass trasport to plays an important role by limiting the amount of reactants at the electrode surface and changing the observed behaviour of the current itself. Consequence, the current flowing will depende on itòò.

1.2 Theoretical study

Electrochemical sensor work well both in fluid and when the electrolyte solution is drop on modiefied electrode surface. This because there is no dependence on the "thickness" of the electrolyte but only on the analyte concentration going to react on the active area. Fick's laws model the analyte mass trasport up to the electrode surface while DLVO theory (from B.Derjaguin, L.Landau, E.Verwey and T.Overbeek) describes what happens at the interface electrode/analyte in terms of interactig force as a consequence of counter particles positions.

On the other hand, it could be interesting to go more on microscopic to understand how and why the electron transfer occurs. It will not only a matter of energy levels variantion of two reacting specie, but it will also depends on atoms analyte rearragement in proximity of the active sites. Marcus theory will be the starting point to build up a satisfying model for that.

1.2.1 Fick's laws of diffusion

According to what it is said about the sensor properties, electron transfer process can be improved by increasing the amount of analyte particles at the interface. This can be easy handle by dropping a specific molar concentrated solution of the detectable compound [9]. However, if the sensor is immersed in solution with a certain concentration, it is quite impossibile to keep the same solute amount at the electrode surface: mass trasport phenomena are involved. This mainly occurs due to a concentration gradient within the solution that spontaneously leads a diffusion movement [10]. Fick's laws are equations describing spontaneous diffusion phenomena [13]. The first one defines the directional mass flow \vec{J} as a function of the concentration c variation in space as follows:

$$\vec{J} = -D\nabla c(\vec{x}, t) \tag{1.2}$$

that can be rewritten as unidimensional equation only by supposing the diffusion process mainly occuring in the direction perpendicularly to the electrode surface.

$$j = -D\frac{\partial c}{\partial x} \tag{1.3}$$

The first Fick's law defines the proportionality constant between the mass flow and the concentration variation: D is the diffusion coefficient of the analyte and it depends on the specific electrolyte solution in which it is immersed. Its value depends on the solute/solvent interaction and it is measured as $[m^2s^{-1}]$. The minus sign means that the molar flux moves from high solute concentration to low solute concentration. The second Fick's law defines how the concentration changes as a function of time:

$$\frac{\partial c}{\partial t} = -D \frac{\partial^2 c}{\partial x^2} \tag{1.4}$$

The last equation must be solved to obtain the profile concentration of the analyte in order to know its amount reaching the electrode surface. Since second Fick's law is a partial derivative equation, some boundaries conditions (BC) must be applied. To do that, it must be defined a reference system by supposing to have the electrode at the right hand side (x=0) and the solute is added from the left hand side (x = x_{end}) with a concentration c_i . It must be introduce a subscript *i* since two different partial differential equations (PDE) problems must be solved for both oxidizing c_O concentration and reducing c_R one with relative BC. In details:

-at initial time (t=0) it is defined a concentration c_i constant at each distance from the electrode surface;

-at x_{end} the concentration is assumed to remain fixed at the initial one;

-to define the BC at the electrode side two further assumptions must be considered as follows

$$\frac{c_O}{c_R} = const \tag{1.5}$$

$$D_O \frac{\partial c_O}{\partial x} = -D_R \frac{\partial c_R}{\partial x} \tag{1.6}$$

where the equation 1.5 comes from the assumption that the potential at the electrode surface is mantained fixed such that the potential difference between the electrode potential and reference one gives a constant concentrations specie ratio from Nernst equation

$$E = E^0 + \frac{RT}{nF} ln \frac{a_O}{a_R} \tag{1.7}$$

Here, the ratio $\frac{a_0}{a_R}$ is the activity specie concentration and it can be taken equal to the concentration ratio when the solution is very dilute (concentration less than $10^{-3}M$) [14]; *E* is the reduction potential and E_0 is the Standard reduction potential associated to the reference electrode.

The equation 1.6 supposes that the flux of oxidazing specie is equal to that of reducing one $j_O = -j_R$ that means when an oxidizing molecule reach the electrode surface an oxidazed one is releases from that in the opposite side: in that case the system is in stationary condition.

All these assumption leads to the following PDE formulation:

$$\begin{cases} \frac{\partial c_i}{\partial t} = -D_i \frac{\partial^2 c_i}{\partial x^2} \\ c_i(x, t=0) = \\ c_i(x=0, t) = const_i \\ c_i(x=x_{end}, t) = c_i \\ (\frac{\partial c_i}{\partial x})_{x=0} = \frac{c_i(x_{end}) - c_i(0)}{\delta_i} \end{cases}$$

Finally, the profile concentration as function of time is obtain by solving the PDE problem and its behaviour looks like figure 1.2 [15].



Distance from electrode surface

Figure 1.2: Oxidizing specie diffusion profile concentration as function of time. Figures adapted from [15].

The last equation is obtained through PDE Laplace transformation. The term δ_i is called diffusion layer length and it defines as the maximum distance from the electrode surface within that the analyte concentration changes with respect the bulk electrolyte solution figure 1.3. It is given as follows:

$$\delta_i = \sqrt{\pi D_i t} \tag{1.8}$$

where t is the diffusion time.



Figure 1.3: Diffusion profile concentration of redox specie at a certain time. Figures adapted from [15]

1.2.2 DLVO theory describes EDL electrostratic interactions

Mass trasport at the electrode surface is not the only phenomena affecting the reacting specie concentration. Indeed, a solide surface immersed in an electrolyte solution will be charged due to dissociation of surface groups or adsorption of some solution ions. This leads to electrostatic interactions at the interface among surface and charged particles. This further holds if one think to the effect on ions of an applied voltage at the electrode surface. This is described through the electrical double layer structure (EDL).

An electrochemical system can be divided in three parts: the Stern layer plus the diffusion layer and the bulk electrolyte solution already analysed in the previous section. The diffusion layer is just a region close to the electrode in which ions are free to move. On the contrary, it is in the Stern layer that surface charge induces the interaction between electrode and ions of opposite sign by forming the so called EDL. This induces an accumulation of opposite charge out of the EDL that leads to an electrostatic potential decreasing by moving far from the surface along x as follows:

$$\Psi = \Psi(x=0)e^{-\overline{\lambda_D}} \tag{1.9}$$

In details, the drop of the electrostatic potential occurs at the Debye length λ_D that ideally identifies the separation between EDL and diffusion layer. At this shear plane the potential is called zeta-potential and it is defined as follows:

$$\zeta = \frac{\sigma_e D}{\sigma \lambda_D} \tag{1.10}$$

where D is again the diffusion coefficient, σ_e is the surface charge, σ is the conductivity. The λ_D can be written as follows:

$$\lambda_D = \sqrt{\frac{\varepsilon D}{\sigma}} \tag{1.11}$$

where ε is the dieletric constant.

Acting on these two parameters through the applied voltage or by changing the medium conductivity allows to modify the energy barrier that reacting specie must be overcome in order to have a stable interaction at the electrode surface. DLVO theory describe the potential at the surface and the forces involved. According to that, the total interaction energy depends on repulsive electrostatic forces and the attractive Van der Waals one. The electrostatic forces are referred to interaction between charges and polar medium, thus they define a Coloumb potential. Van der Waals interaction is due to attractive interactions between fluctuating dipoles particles. Indeed, also a neutral particles can interact if its electron distribution is such that a dipole arises. The two contributions are summed one of each other at any distance from the electrode by giving the total interaction energy in figure 1.4.



Figure 1.4: Interaction energy vs separation distance according to DLVO theory [16].

Finally, it can be conclude that the electron transfer will depend on the reacting specie concentration reaching the electrode at a favourable distance to interact with the nanoparticles surface. Electrokinetics evaluation suggests that this distance must be of the particle size order. However, this will be explained better in the following.

1.2.3 Electron transfer rate model

Electron trasfer process during a redox reaction consists on an electron moving from a donor specie to an acceptor one without involving a bond formation or break between the two reactants. This passage is due to the difference in energy state level of the reacting specie. In particular, electron typically moves from the highest occupied molecular orbital (HOMO) of the donor specie to the lowest unoccupied molecular orbital (LUMO) of the acceptor one. Electron transfer theory develops a mathematical and physical formulation to describes the parameters affecting the rate at which the process occurs. In 1956, R.A.Marcus provides a first theory by explaining many factors to determine the electron transfer rate constant as follows:

$$k = A e^{-\frac{E^*}{k_B T}} \tag{1.12}$$

where A is a preexponential constant, k_B is the Boltzmann constan, T is the temperature and E^* is the activation energy.

To understand this simple formula, the potential energy surface (PES) must be introduced with the Transition state theory [17]. Figure 1.5 shows how the ET from a specie M_1 to a specie M_2 according to the following reaction: $M_1^- + M_2 \rightarrow M_1 + M_2^-$



Figure 1.5: Electron transfer in step: initial coordinate Q_i , transition state Q_t and final coordinate Q_f . Figure adapted from [17].

At the beginning the electron is localized on M_1^- having longer bond length than M_2 at the initial coordinates Q_i . In order to go from initial to final state Q_f , the molecules must arrenged in the transition state in order to satisfy the energy conservation and the Franck-Condon principle (fixed nuclear coordinates) during the ET. PES associated to that reaction in figure 1.6 shows two parabolic energy profiles for both the reactants and the products. The minimum of the curves identifies the initial Q_i and final nuclear coordinate Q_f . The transition state at the intersection point Q_t of the two curves identifies the point at which electron transfer occurs. As it can be seen from the graph, a certain amount of energy is required to bring the specie from the initial coordinates to the TS ones. This barrier energy is called activation energy and it is the E^* appearing in equation 1.12 and defining by Marcus as follows:

$$E^* = \frac{(\Delta E + \lambda)^2}{4\lambda} \tag{1.13}$$

where λ is called reorganization energy and describes the required energy to have the vertical electron excitation from the reactants curve to the product one; $\Delta E = \varepsilon_i^0 - \varepsilon_f^0$ is just an offset term between the two energy values of the curves at the stable configuration.

The huge approximation of the model is in the reorganization energy term [18]. Reactants reorganization in products is not only a matter of the reacting specie, but it also involves the interaction with the surrounding medium. Marcus theory treats this interaction according to the dieletric continuum theory [19]. Briefly, solvent medium is assumed as a single sphere interacting with the redox specie and λ is defined as follows:

$$\lambda = \frac{\Delta e^2}{2} \left(\frac{1}{\epsilon_{op}} - \frac{1}{\epsilon_s}\right) \left(\frac{1}{a} + \frac{1}{b} - \frac{2}{R}\right) \tag{1.14}$$

where Δe is the number of electron transfer during the reaction, ϵ_{op} and ϵ_s are the optical and static dieletric *a* and *b* are the radius of the reacting specie and *R* is their separation distance. Neverthless, from one side this allows to reduce the number of interactions that must be considered, from the other side the solvation effect to the reacting molecules is completely loose.



Figure 1.6: Potential energy surface explains the transition state [17].

In 1993, Tachiya [20] defined a generalization of Marcus equation to overcome this limitation. His approach consists on a redox reactions between two neutral specie A and B in solution. Considering a polar solvent, an electrostatic potential difference $e\Delta V = eV_A - eV_B$ between the two reactants exists and fluctuates according to the solvent motion. This means that the potential difference is not constant. By reminding to the transition state, the electron transfer occurs at specific nuclear coordinates at which the PES of the reactants and products match. Accordingly, Tachiya describes the initial state energy and the final state one: the potential satisfying the transition state theory is found when the two states have the same energy.

In the initial state, the energy contribution is due to only the interaction between permanent dipole moment of polar solvent as a function of their position r_i and orientation ρ_i :

$$E_i = \Pi(r_1, \rho_1, r_2, \rho_2, ..., r_N, \rho_N)$$
(1.15)

In the final state some other terms must be considered due to the interaction between the two solute and the solvent as follows:

$$E_f = \Pi(r_i, \rho_i) + IP - EA + e\Delta V - \Delta G_s^e - e^2/R$$
(1.16)

where IP and EA are the ionization potential and the electron affinity of donor and acceptor specie respectively, ΔG_s^e is the solvation energy due to electronic polarization, e^2/R is the Coloumb attractive energy. By imposing the energy conservation at the transition state, one obtains:

$$e\Delta V^* = -IP + EA + \Delta G_s^e + e^2/R \tag{1.17}$$

This allows to rewrite the Marcus ET rate as follows:

$$k = \frac{2\pi}{\hbar} J^2 \Phi(e\Delta V^*) \tag{1.18}$$

where $\Phi(e\Delta V^*)$ is the probability to have the ET at the TS; it is evaluated by studing the distribution of the electrostatic potential within the dieletric continuum model [20]. At the end, the electron transfer rate is calculated as follows:

$$k = \frac{2\pi}{\hbar} J^2 \frac{1}{\sqrt{4\pi k_B T \lambda}} e^{\frac{-(IP - EA - \Delta G_s^e - e^2/R)^2}{4k_B T \lambda}}$$
(1.19)

where λ is defined in equation 1.14 and the solvatation energy ΔG_s^e is given as follows [21]:

$$\Delta G_s^e = \frac{\Delta e^2}{2} (1 - \frac{1}{\epsilon_s}) (\frac{1}{a} + \frac{1}{b})$$
(1.20)

The term J is the transfer integral defining the orbital coupling between the interacting specie and it is given by Generalized Mulliken-Hush theory [22] as follows:

$$J = \frac{\mu_{12}\Delta E_{12}}{\sqrt{(\Delta\mu_{12})^2 + 4(\mu_{12})^2}}$$
(1.21)

where $\Delta \mu_{12}$ is the difference between the dipole moment of the two interacting specie, ΔE_{12} is the difference between their eigenstate involved in the reaction and μ_{12} is the transition dipole moment.

1.3 Computational methods

The theoretical study on the electron transfer implicitly needs to solve the many body system for the specie involved in the reaction. This system is typically described as made by electrons outer shell part plus nuclei (inner electrons shell+atom) and the associated Hamiltonian consists on five terms: two kinetic energy terms referred to both electrons and ions and three coulombic terms due to interactions between electrons, nuclei and electrons-nuclei. The wavefunctions, solutions of the associated Hamiltonian of the Schrödinger equation, will provide all the information required to estimate the electron transfer rate constant according to the Tachiya formula. Moreover, they should depend on both the electrons \bar{r}_i and ions coordinates \bar{R}_j :

$$\hat{H}\Psi(\bar{r_i},\bar{R_j}) = E_{tot}\Psi(\bar{r_i},\bar{R_j}) \tag{1.22}$$

where \hat{H} is the Hamiltonian operator describing the total energy of the system whose associated eigenvalue is the energy labelled with $E_t ot$ and $\Psi(\bar{r_i}, \bar{R_j})$ is the electron wavefunction depending on both electrons and ions coordinates. However, it is not so trivial to analytically solve it for a system of many atoms even if it can be solved for a small system like the Hydrogen atom

A first possible simplification comes from Hartree approach by introducing the following approximations:

- Born-Oppheneimer approximation allows to solve for fixed nuclear coordinates due to the difference in mass between electrons and ions $(m_{ions} \gg m_{e^-})$; the nuclei kinetic energy term is null and the electron-nuclei interaction V_{ext} is taken into account for fixed \bar{R}_j positions;

- Mean field approximation treats the $e^- \cdot e^-$ Coulomb repulsion in an effective way V_{int} that means each electrons undergoes a potential due to the presence of other electrons, but all of them are considered indipendent one of each other;

$$\left(-\frac{1}{2}\nabla_i^2 + V(\bar{x}_i)\right)\Psi_i(\bar{x}_i) = \varepsilon_i\Psi_i(\bar{x}_i) \tag{1.23}$$

where $V = V_{ext} + V_{int}$ and the wavefunction $\Psi_i(\bar{x}_i)$ is an indipendent electron wavefunction in which (\bar{x}_i) contains both spatial and spin coordinates.

Despite it is acceptable to consider the BO approximations by experimental proof, it is not the same about the wavefunction. Indeed, electrons correlation and its fermion nature is not taken into account since the wavefunction is not symmetric and does not satisfy the Pauli Principle.

Quantum-mechanical computational methods provide a mathematical formulation to overcome these issues. Their propose a still approximated but physically correct formulation of the Schrödinger problem on a specific formalism depending on the method choosen.

1.3.1 Ab-initio method

Ab-initio term refers to all these methods proposing a problem solution by only exploiting some physical constant as parameters (such as the electron mass or lattice parameters) [23, 24]. No experimental results are used, but the method is just developed according to quantum-physics principle.

There exist different Ab-initio method. Here, it can be introduced the simplest one, the Hartree Fock, that allows to obtain the following Hamiltonian for a system of n-electrons and m-atoms (express in atomic units):

$$\hat{H} = -\frac{1}{2} \nabla_i^2 \chi_i(\bar{x}_i) - \sum_{A=1}^m \frac{Z_A}{|\bar{r}_i - \bar{R}_A|} \chi_i(\bar{x}_i) + \sum_{j=1}^n \int (d\bar{x}_j) \frac{\chi_j(\bar{x}_j)^2}{|\bar{r}_i - \bar{r}_j|} - \sum_{j=1}^n \int (d\bar{x}_j) \chi_j^*(\bar{x}_j) \frac{1}{|\bar{r}_i - \bar{r}_j|} \chi_i^*(\bar{x}_j) \chi_j^*(\bar{x}_i)$$

$$(1.24)$$

where the terms are the electron e^- kinetic energy term, the e^- -core interaction, the $e^- - e^-$ Coulomb repulsion and the exchange term.

In addition to the Hartree approach, HF rewrites the wavefunction as a single Slater determinant: the wavefunctions are derived as a linear combination of Hartree product wavefunction in order to be antisymmetric (exchange effect) and form the basis set of the HF method.

The HF Hamiltonian is then solved self-consistently starting from an initial wavefunction guess belonging to the basis set. However, some advanced formulations such as post-HF method must be used in order to improve the accurancy and to introduce the so-called exchange correlation: the probability to find an electron i in a position r_i must depends on the probability to find another electron *j*. HF just introduces an exchange term to take into account of the correlation between two electrons having the same spin, but no correlation among all the electrons is considered. Moving to more detailed formalism can improve the wavefunctions accurancy, but this also becomes too time consuming.

1.3.2 Density functional theory

Density functional theory (DFT) is based on the assumption that all the system properties can be rewritten as functional of the electron density: it is given by the probability to have an electron i in a certain position r_i integrating over all the electron wavefunctions as follows [15]:

$$n(\bar{r}) = \sum_{i=1}^{n} \Psi_{i}^{*}(\bar{r}) \Psi_{i}(\bar{r})$$
(1.25)

The theory is based on the following Hohember-Khon theorems [25]:

- 1st theorem \rightarrow the external potential $V_{ext}(\bar{r})$ of a system of interacting particles is uniquely determined by the ground state $n_0(\bar{r})$ of this system except for a constant; - 2st theorem \rightarrow A universal functional for the energy $E[n(\bar{r})]$ of the density $n(\bar{r})$ can be defined, valid for any $V_{ext}(\bar{r})$. For any $V_{ext}(\bar{r})$, the exact ground state is the global minimum value of this functional $E[n(\bar{r})]$ and the the density that minimizes the functional is the exact ground state density $n_0(\bar{r})$.

Both the theorems are proved [26].

What these theorems say is that the many electron system can be solved by knowing the electron density at the ground state system $n_0(\bar{r})$ that only depends on three spatial variables. This is the first advantage if one thinks to the wavefunction whose depends on the spatial variables for each electron of the system (three times N-electrons). Additionally, this ground state density $n_0(\bar{r})$ determined the Hamiltonian of the system (from the 1st theorem) whose terms will be defined as functional of $n_0(\bar{r})$ itself as follows:

$$E[n(\bar{r})] = T[n(\bar{r})] + V_{e-e}[n(\bar{r})] + V_{ext}[n(\bar{r})]$$
(1.26)

where in order there are the electron kinetic term, the Coulomb $e^- \cdot e^-$ repulsion and the external potential due to nuclei and any other external field. The missing information is still the exchange correlation to consider all the electrons interactions. The solution comes from Kohn-Sham approach (1965) [27]. Their idea is to think on an auxiliary system of non-interacting particle whose $n_0(\bar{r})$ is the same of the original many interacting particle system. Starting from the ground state density, the functional $E_2[n(\bar{r})]$ for the auxiliary system that allows to correctly mimic that one of the interacting particle system must contains its own kinetic energy term, the Hartree term describing the electrons repulsion in a non interacting way, the external potential again and an additional term contained all the unknown information related to the correlation particles:

$$E_2[n(\bar{r})] = T_2[n(\bar{r})] + E_{Ha}[n(\bar{r})] + V_{ext2}[n(\bar{r})] + E_{xc}[n(\bar{r})]$$
(1.27)

Comparing the energy functional of the two system, an approximated form for $E_{xc}[n(\bar{r})]$ is obtained as difference between functional of the electron density: this means that also this term is a functional of the electron density and can be derived from that. Since all the other terms of the last equation are automatically defined if the ground

state density is known, the KS approach provides this final equation that can be solved in a self-consistent way:

$$\left[-\frac{1}{2}\nabla_{i}^{2} + V_{ext(\bar{r})} + V_{Ha}(\bar{r}) + V_{xc}(r)\right]\Psi_{i}(\bar{r}) = \varepsilon_{i}\Psi_{i}(\bar{r})$$
(1.28)

indeed, an initial guess electron density $[n(\bar{r})]$ is used to solve the KS equation since all the terms are functionals of the $[n(\bar{r})]$ and the wavefunction $\Psi_i(\bar{r})$ can be find. From that, it can be better estimated the $[n(\bar{r})]$ according to equation 1.25.

Again, a failure comes from the exchange correlation since it is an estimation on an already trivial electron density! An accurate result is obtained in the local density approximation (LDA) of DFT in which the exchange term is evaluated as a function of the exchange correlation term of an homogeneous gas system [27]:

$$E_{xc}[n(\bar{r})] = \int d\bar{r}[n(\bar{r})]\epsilon_{xc}[n(\bar{r})]$$
(1.29)

The constant density of the last system leads to a good result for the exchange energy term $\epsilon_{xc}[n(\bar{r})]$ by exploiting Monte Carlo simulation [28].

1.3.3 Semi-empirical method

Semi-empirical methods are Hartre-Fock based as Ab-initio method. Ab-initio calculations consists on performing in a SCF way all the integrals concerning a certain own formalism to define the system properties. However, this method is not yet suitable by working with large system such as organic chemistry based [29]. The improvements in terms of computational cost comes from semi-empirical.

First of all, some system properties (such as heat of formation or geometry features) are known from experimental results and they can be used to easier determined the missing information. These data could be optimized according to the system under study and their validaty could be proved by performing DFT calculation on the same system [30]. In this way it is clear that the accurancy of semi-empirical method depends on the accurancy of the parameters exploited. At the best, if all the parameters are exactly known or perfectly determined from Ab-initio for instance, then semiempirical results surely reach high accurancy level [29]. However, the main point behind the semi-empirical idea is to use exact or theoretically justifiable parameters to obtain the better Hamiltonian solution; how much the method will be good depends on the error percentage between the obtained values and the experimental one.

The high computational cost of Ab-initio calculation is also reduced by appling some approximations on the calculated integrals of the choosen formalism (HF for instance). The basis set of all the semi-empirical methods is based on linear combination of molecular orbital involving just π -orbital (Hückel method) and also σ -orbitals (Extended Hückel method). Starting from that, methods differ in the added approximations to neglect some integrals, typically the two electrons repulsion [22]. These can be of two kinds:

- one-center if the repulsions is between two electrons whose wavefunctions are centered on the same atoms molecule;

- two-center if the repulsions is between two electrons whose wavefunction are centered on two different atoms (so two different orbitals) of a molecule.

The main methods can be then dived into three groups depending on the integrals

considered. Zero differential orbitals (ZDO) approximation holds for all of them according to all the two-electron integrals with different orbitals are neglected. Briefly, the others are describing in the following:

- Complete Neglect of Differential Overlap (CNDO) \rightarrow only outer valence electron interactions are considered;

- Intermediate Neglect of Differential Overlap (INDO) adds the one-center electron integral respulsion on the same atom (exchange integrals), but neglect all the two-center two electron integrals;

- Neglect of Diatomic Differential Overlap (NDDO) only neglects the two-center twoelectrons integrals belong to atomic orbitals of different atoms.

1.4 Paracetamol oxidation process

Paracetamol 1.7 (Acetaminophen or N-acetyl-p-aminophenol) is an analysic and antipyretic drug typically used to soothe pains of different nature: headache, toothache, backacke, cold and so on or to inhibit the rising of temperature in case of fever [31].



Figure 1.7: Paracetamol skeletal structure from [32].

If the recommended dose is overcame, it can damage liver or kidneys by causing hepatoxicity or nephrotoxicity [33]. Moreover, the merging of both Paracetamol and other compounds such as caffeine could also improves the impact of these side effects [34]. Finally, it is not irrelevant Paracetamol contribution as wastwater as other pharmaceutical compound [35]. In all these cases, the toxicity could be given more from Paracetamol metabolites due to its oxidation than the Paracetamol itself [36].

Biosensor research shows a great interest on Paracetamol sensing and also degredation of these metabolites through electrooxidation. In particular, a lot of experimental projects are oriented on the analysis of nanoparticles modified electrode as graphene modified glassy carbon electrode (GCE). Indeed, Paracetamol is an electroactive compound and that nanocomposite shows excellent electrocatalytic properties that favor the molecule detection with high sensitivity and selectivity, good stability and reducing detection time as it can be defined from CV results [32].

As regard the oxidation process, Paracetamol could not always undergone the same pathway. Possible pathway of Paracetamol oxidation to quinone (or 1,4 benzoquinone) is shown in figure 1.8 adapted from [37]. This process is based on generation of hydroxyl radical OH at the electrode surface (a graohite one in that case) thus water solution is needed. At the beginning, Paracetamol exchanges two electrons and two protons by giving as oxidation products the carboxylic acid CH₃COOH and the *p*aminophenol (C₆H₇NO). The last is one of the toxic metabolite. Thus, radicals favor intermediate products oxidation by leading to benzoquinone C₆H₄O₂ at the end.

It can be conclude that sensing issues to Paracetamol is not a metter of that molecule, but good detection (that means high sensitivity, low LOD value) must be also achieved to such metabolites. Again, electrochemical technique based on nanomaterial modified electrodes ensures fast and easy detection at low cost and can be exploited to simultaneously detect two different compounds [38].



Figure 1.8: Possible Paracetamol oxidation pathway through •OH generation adapted from [37].

1.5 Bismuth based electrode functionalization

Water pollutants have increased the interest in catalytic materials to favor the degration of such compounds. Micro and nano composites have an higher surface to volume ratio that improves the active area and can be easily dispersed in solution. However, immobilization on support should performed since it increases the catalytic effect by avoiding nanoparticles agglomeration [39]. In that sense, the research can be thought on two directions: looking for a best catalytist and for a support material satisfying certain physical and chemical requirements (inertness to the nanocomposite for instance). It is interesting that some catalytic properties are further improved if matching with a certain base support: graphene nanosheet bismuth oxide for instance [40]. Bi₂O₃ functionalized leads to a capacitive enhancement of graphene modified electrode ensuring a fast charge transport thanks to graphene electrical properties. It is also proved that bismuth modified nation electrode gives higher peaks current in CV analysis and lower LOD in simultaneously detection of Paracetamol and caffeine than the bare electrode [34]. Other improvements in Paracetamol detection are achieved through Bi oxide modifies GCE [6] while glucose detection is favoured from HO-BiONO₃ [2].

According to the experimental works above, Bismuth based compound seems to be really promising in electrochemical oxidation and photodegradation process acting as a catalyst. Indeed, it has good optical properties due to the low band gap that ensuring high absorption at visible light. Moreover, several synthesis or deposition tecnique of Bi oxynitrides such as HO-BiONO₃ allows to modified that band gap from 2.4 eV to 3.2 eV [41, 42].

1.6 Project aim

This graduation project is devoted to estimate the electron transfer rate constant due to Paracetamol oxidation by defining the parameters that influence the charge transfer at the interface oxide based electrode/organic compound. The oxidation process was studied by modelling the hypothetical transition state at which the two electrons transfer occurs according to the Paracetamol oxidation mechanism. In particular, it is assumed that the oxidation occurs as shown in figure 1.9: the intermediate state labelled with (b) has dashed lines to refer to those bonds that will change during the electron transfer process; it is supposed to move towards an advanced oxidation state labelled with (c): the Quinone. To accomplish, a physical model was defined and computational analysis were performed exploiting that intermediate state for Paracetamol.



Figure 1.9: Paracetamol oxidation mechanism: Paracetamol (a), Intermediate state (b), Quinone (c).

Chapter 2

Methods

The electrokinetics PDE problem is solved through the *pdepe* MATLAB function.Regarding the computational part, two chemistry software tools are exploited to build the molecule structure and obtain some parameters values:

- ChemDraw (CD) is a drawing tool used to design all the molecules involved in the system such Paracetamol and the Bismuth based groups;

- HyperChem (HC) is the simulation tool that allows to obtain all the need parameters by performing computational simulation.

2.1 Procedure and assumptions

Planar molecular structure are drawn in CD and imported on HC. A 3D structure is obtained in HC by the function *model build* for both Paracetamol and Bi clusters. Then, the simulations can start to evaluate the electronic properties and the geometry information required in the Generalized Marcus model. All these properties must be referred to the ground state energy of the molecule. Geometry optimization allows that by performing a potential energy V calculation as a function of molecule coordinates. This process is needed to look for the more stable configuration that means having a molecule in the minimum energy state (or at least in a local minimum). The potential energy must be minimized with respect to the system coordinates:

$$\frac{\partial V}{\partial r_i} = 0$$

The geometry optimization is first performed with MM+ and then with PM3. This is done for both Paracetamol and Bi-based structures. In particular, two different Bi clusters model the polymeric layer as shown in figure 2.1(a) and 2.1(b).



Figure 2.1: 2 Bi-atoms cluster (a), 3 Bi-atoms cluster(b).

The 2-Bi atoms cluster is assumed to be the minimum unit allowing the ET. Indeed, ET is depicted through two Bi-C "fake bonds" as shown in figure 2.2 by thinking that each couple exchanges just one electron and the two charged particles are simultaneosly acquired from Paracetamol (since the Paracetamol oxidation is a two electrons process [32]).



Figure 2.2: Transition state model.

The figure represents one of the HTS: indeed the TS is identified as a crossing point in the PES correspoding to a unique value of reaction coordinates defining the nuclear configurations of both reactants and products [19]. However, according to Tachiya [20] the ET can occurs depending on the probability to reach a certain $e\Delta V^*$ value of the electrostatic potential distribution. This condition could be verified at different rection coordinates that means the TS is not uniquely defined. For that reason, it is necessary to talk about "hypothetical" TS. Additionaly, transistion state must be analysed through in-situ spectrome

Moreover, it is observed after each simulation that the interaction distance between each Bi-C couple is not equal: the system is asymmetric, thus the average between them is kept within the model (the *R* parameter of reorganization energy in Tachiya [12]). It is accounted for that by considering the term $\Delta e = 2e$ on the reorganization energy term (eq.1.14).

Then the simulations are repeted for the 3-Bi atoms cluster. The geometry optimization is performed two times in both the cases by cutting the fake bonds before to start the second simulation.

Finally, it must be considered solvation effect. Since the ET occurs on the "wetting" electrode side this could be modeled as acting on Paracetamol only: thus five water molecules surround the organic molecule to account for that: this number is the minimum amount of water molecules ensuring ET.

The last step is to repeat the procedure by supposing an electrode pretreatment in H_2SO_4 whose aim is to clean the surface by possible contaminants and to keep a more homogeneous deposition after the functionalization. However, it can be happen that the acid remove some NO_3 by replacing it with OH or SO_4 groups: this will hardly affect the final results.

2.1.1 Simulation methods

The simulations are performed firstly by optimizing the structure through molecular mechanics method, then through quantum mechanical method as it is said. This because no electric properties can be kept from the molecular mechanics simulation since it is a classical physics method in which the molecule is just treated as a mechanical spring system, thus $e^- \cdot e^-$ interactions are not taken into account.Bond interactions are modelled through elastic force: these are stretch and compress in order to reach the minimum energy state of the system (or at least a local minimum). In particular, forces field can be set to perform the simulation among several options that change one each other in the equations form. Since molecular mechanics exploits the classic mechanics equation, all forces field basis set reminds to Hooke's equation by changing in the form and the parameters exploited. In the simulations, the MM+ basis set is choosen since it is better that the other to treat organic molecules by considering both bonded and electrostatic interactions [43]. The main difference is a cubic term to model the stretch-bend motion in addition to the harmonic term as follows [44]:

$$E = const \times \Sigma_{\#bonds} \frac{1}{2} k (r - r_0)^2 [1 + switch(r - r_0, -\frac{1}{3}CS, -\frac{4}{3}CS)CS(r - r_0)]$$
(2.1)

where k is the force constant, r_0 is the equilibrium distance, CS is a cubic strech factor constant equals to -2.0 by default. The switch function allows to account for electrostatic interactions depending on the variation with respect equilibrium position $r - r_0$. In particular, it goes to 0 if the bond stretching from r_0 to r is larger than the threshold value $-\frac{4}{3}CS$ in order to go back to the harmonic equation. However, the method is not so reliable since the parameters are defined depending on the molecules type: atoms with same hybridation belong to the same type for instance.

This further leads to exploit quantum mechanical method since its philosophy is to only exploit physics constant as parameters. Semi-empirical is the method used in these simulations because DFT is as time consuming as Ab-initio method and both are not suitable for large system as the one under study to be performed on a common PC.

In details, PM3 (Parametrization method 3) basis set is choosen among the HC available method. It belongs to the NDDO, thus its basis set consists on s and p orbitals. PM3 differs from the other methods of the same group (MNDO or AM1) in the way to estimate the core-core repulsions between two atoms A and B [44]:

$$E_N(A,B) = Z_A Z_B \gamma_{AB} [1 + e^{-\alpha_A R_{AB}} + e^{-\alpha_B R_{AB}}] + \frac{Z_A Z_B}{R_{AB}} (\Sigma_k a_{kA} e^{[-b_{kA} (R_{AB} - c_{kA})^2]} + \Sigma_k a_{kB} e^{[-b_{kB} (R_{AB} - c_{kB})^2]})$$
(2.2)

where the first term just defines the core-core repulsion through the term γ_{AB} that takes into account the separation distance R_{AB} depedence (as it know, the repulsion does not immediately go as the inverse of R_{AB}) and the screening effect through the term in brackets; these two terms gives an overestimation of the repulsion term: PM3 adds the two parametrized Gaussian functions of the second term to reduce that. Additionally, the adjustable parameters are better optimized with respect to AM1 (in which the Gaussian functions are already exploited) since they are choosen by fitting on more experimental data. However, the best method is choosen depending on the system: for instance, PM3 is favourable to organic chemistry computations as Paracetamol.

2.1.2 Model validation

The electron transfer rate constant in a CdS-Phenol system is analysed before to start with the Paracetamol-Bismuth one [45]. This step is fundamental to be sure that the model holds. In details, it analyses the electrochemical redox process between a CdS powder and a Phenol molecule in solution simulated within a box contained water molecules. The box can not be used in the Paracetamol-Bi case because it implies to also have the electrode surface surrounded by water molecule. Indeed, image effect is automatically involved that means the system is replicated as mirrored outside the box. For the same reason, this simulation is in compliance with CdS-Phenol system. The box is shown in figure 2.3. The obtained ET rate constant is $k = 6.42 \times 10^{-5}$ s^{-1} comparable to the literature result equal to $k = 5.17 \times 10^{-5} s^{-1}$.



Figure 2.3: CdS-Phenol transition state model.

Chapter 3

Results

Two sections are devoted to the results. In the first the system electrokinetics is analysed by solving the PDE problem describing diffusion mass trasport.

In the second section, the HTS model are described in details for the several Bi based clusters. The ET rate are compared and also the activation energy is defined for all of them: here the activation energy is the energy required to reach a certain nuclear configuration such that the ET process could occurs.

3.1 Electrokinetics

The PDE problem is referred to a one dimensional system in which the maximum distance from the electrode surface is $0.2 \ mm$. The aim is to determine the profile concentration of oxidizing specie c_0 and reducing one c_R due to spontaneous diffusion after a certain time interval. The mass transport is supposed to occurs along the x-direction from the left side to the right one towards the electrode. The initial conditions and the BC are defined as follows according to what said in the introduction section:

 $\begin{aligned} - & \text{at } t = 0 \ \forall x \to c_O = 1mM, \ c_R = 0; \\ - & \text{at } x = x_{end} \ \forall t > 0 \to c_O = 1mM, \ c_R = 0; \\ - & \text{at } x = 0 \ \forall t > 0 \to c_O = c_R = 0.3 \ mM; \\ - & \text{at } x = 0 \ \forall t > 0 \to \frac{\partial c_O}{\partial t} = \frac{1 - c_O^0}{\delta}, \ \frac{\partial c_R}{\partial t} = \frac{-c_R^0}{\delta}. \end{aligned}$

It is choosen a time interval of diffusion equals to 1 s. The constant values of oxidizing specie concentration is choosen equals to 0.3 mM in order to have a smaller value than the initial one; the related reducing specie value is consequentely kept equal due to stationary condition. It is further assumed that the diffusion coefficients of oxidizing and reacting specie are equals and they are kept as the Paracetamol diffusion coefficient $D = 0.148 \cdot 10^{-9} m^2 s^{-1}$ that is experimentally obtain through CV measurements at scan rate 100 mV/s [9].

In figure 3.1(a) and 3.1(b) are respectively plotted the oxidizing and reducing specie concentrations as function of distance from electrod surface along the x-axis and as function of time along y-axis. A legend in the rhs of each map allows to understand the color and easily identified the initial and boundary conditions: indeed, a yellow

row marks out the homogeneous c_O at the initial time on the related plot while a blue line underlines the c_R absence on the other graph.



Figure 3.1: Oxidizing specie (a) and reducing specie (b) variation as function of time and distance.

The colours also underline the complementarity of the two figure due to stationary conditions: where the oxidizing concentration as its maximum value, the reducing one has the lowest. The concentration profile as function of distance at the end of diffusion time $t = 1 \ s$ is plotted in figure 3.2.



Figure 3.2: Profile concentration of oxidizing and reacting specie after $1 \ s$ of spontaneous diffusion: red line defines the diffusion layer length.

Both the two concentrations are costant and equals to the initial one at the farthest distance from the electrode and are constant at the closest one. Moreover, the minimum value of c_O coincides with the maximum one of c_R : this proves the stationary condition between the two fluxes. This means that neither accumulation of particles can occurs nor penetration within the electrode: the system is symmetric since each oxidizing molecules undergoes the reaction at the electrode surface and the oxidized one is immediately released (the same for reduction process). The red line determines the diffusion layer length according to what said in previous chapter and figure 1.3.



Figure 3.3: Profile concentration of oxidizing and reacting specie at ten time step.

The diffusion process smoothly reduces this influence on mass trasport by moving closer from that maximum length to electrode surface: the electrostatic electrode potential becomes more effective by leading the huge decreasing for oxidizing specie as shown in the figure (the opposite for reducing one since one must think that its initial concentration is zero).

Figure 3.3 shows the same profile concentration at ten different time step by proving again the expected change in slope: it is positive for the oxidizing specie and negative for the reducing one and decreases for both the cases along the time. This analysis is useful to prove some theoretical aspect of diffusion limited mass transport. However, it is an approximation since the redox site availability is not taken into account and the stationary condition on a symmetric system avoid particles accumulation: no EDL arises. If one consideres the formation of an EDL according to what said in previous section, the mass transport can not be diffusion limited yet since it will be also a charge trasport affected by electrostatic effect.

3.2 Computational results

Electron transfer rate constant values for each transition state model are shown together with the molecular structure model and the orbitals mapping. The last two are basically related to the affecting factors on molecular structure optimization: electron density distribution and steric hindrance. To have a reasonable comparison among all the models, they are presented into two separated groups: one is devoted to simulations involving the 2-Bi atoms cluster, the other one is dedicated to the case of 3-Bi atoms cluster. For both the case, it is described a general scheme as reference in order to understand the main variations and related effects on the results.



Figure 3.4: Paracetamol geometrical description.

Our transition state consists on Paracetamol interacting with Bi cluster through its two carbon atoms and the interactions is modelled as a bond, at least in first approximation, as shown in figure 2.2. Looking at the "reacting" C atoms, one can think two geometrical reference as shown in figure 3.4:

- the symmetric axis passing through the C atoms that is a C_2 (by rotating of 180° the symmetry is mantained);

- the plane of symmetry on which the ring lies that is a reflection plane.

Similarly, a second plane is considered as that one in which the two Bi atoms lies.

By defining A the Paracetamol plane and B the Bismuth one, the orientation in space of the latter can be described as a function of two angles: - the dihedral angle α between the two plane as shown in figure 3.5(a);

- the angle β defining the rotation with respect the symmetric axis 3.5(b).



Figure 3.5: Dihedral angle α between the Paracetamol plane A and the Bismuth one B (a). Paracetamol rotation with respect symmetric axis (b).

3.2.1 2-Bismuth cluster

All the results are shown in table 3.1. The different cases are labelled with the functional groups connected to the two Bi atoms.

Bismuth case	ET rate constant $[s^{-1}]$	Activation energy $[eV]$
NO ₃ -NO ₃	$1.2 \cdot 10^{-3}$	9.3
OH-OH	$2.6 \cdot 10^{-3}$	10.89
NO ₃ -OH	$2.78 \cdot 10^{-2}$	7.46
OH-NO ₃	$6.9 \cdot 10^{-3}$	7.74
SO_4 - SO_4	$2.55 \cdot 10^{-4}$	6.75

Table 3.1: Electron transfer rate constant and activation energy for 2-Bi clusters

NO₃-NO₃ vs OH-OH

HTS model with a 2-Bi cluster are shown connecting with the same functional groups NO_3 in figure 3.6(a) and OH in figure 3.6(c). The two have the same order of magnitude of electron rate constant as it can be seen from the table 3.1 while the activation energy difference is almost 15%. The electron density distribution in shown in figure 3.6(b) and 3.6(d). By looking at the two structures, Paracetamol seems to have the same orientation with respect the plane of Bi clusters. Indeed, the angle α_1 associated to the NO₃-NO₃ case (blue planes) is just slightly greater than α_2 associated to the OH-OH one (yellowe planes) as shown in figure 3.7 by taking fixed the β angles (as it can be seen the C_2 Paracetamol axes are taken parallel for the two structures). However, the position of the functional groups with respect the Bi plane is really different. Indeed, the NO_3 group bonded with Bi (a) is above the Bi plane and moves closer to the Paracetamol nitro groups. This hugely affects the molecular conformation and it can be seen in the distorsion of the Bi-O bond on that side. The surroundend water molecules improve that distorsion and give a greater steric hindrace comparing with that in the right side in which there is just one water molecule. On the other hand, the OH-OH Bi-cluster have all the four identical functional groups below the Bi plane. This ensures a less steric effect since no strong repulsions between atoms electron clouds can arise in that case.



Figure 3.6: Molecular structure and electron density distribution of HTS with a 2-Bi clusters NO_3 - NO_3 (a),(b) and OH-OH (c),(d).



Figure 3.7: Overlapped molecular structure of HTS associated to the 2-Bi clusters NO₃-NO₃ (blue planes) and OH-OH (yellow planes): α angles comparison at fixed β .

NO₃-OH vs OH-NO₃

A comparison is made between the HTS based on 2-Bi cluster where the NO₃ group is bounded to Bi (a) and the hydroxyl group to Bi (b) 3.8(a) and viceversa 3.8(c).



Figure 3.8: Molecular structure and electron density distribution of HTS with a 2-Bi clusters NO₃-OH (a), (b) and OH-NO₃ (c), (d).

By looking at the two figures, it is more evident than the previous case the influence of the cluster NO₃ group. As it can be seen, the two clusters results quite specular in the conformation (despite the NO₃ position) but the steric effect is different since in the NO₃-OH the NO₃ group approaches the Paracetamol nitro group by leading to a more hindered side than the OH-NO₃. Indeed, in the second case the NO₃ is just close to the OH group of the organic compound. This affects the rotation of the Bi plane: the dihedral angle results larger in that case (α_2) as it is shown in 3.9 and this can be also depends on the NO₃ group position above the Bi plane. Also in that case the comparison assumes the same β angles. The activation energy changes by only 4% since the structures involved are the same in terms of atoms and it is less for NO₃-OH case. However, its different the effect on the ET rate constant since it is almost one order of magnitude greater than the OH-NO₃ despite the interaction distance is less for that case (according with the assumptions made in the previous section): $R_{OH-NO_3} = 3.5875 \ \dot{A} \ \text{and} \ R_{NO_3-OH} = 3.5506 \ \dot{A}.$

It can be supposed that some OH defects in the polymeric layer could favor the ET.



Figure 3.9: Overlapped molecular structure of HTS associated to the 2-Bi clusters NO₃-OH (blue planes) and OH-NO₃ (yellow planes): α angles comparison at fixed β .

SO_4 cases

The HTS associated to 2-Bi cluster in which both the Bi atoms are bonded to the SO_4 group is shown in figure 3.10(a).



Figure 3.10: Molecular structure (a) and electron density distribution (b) of HTS with a 2-Bi cluster SO_4 - SO_4 .

The molecular structure does not exhibit any distorsion in bonds or angles. However, the sulfur atoms are really massive. Indeed, an overlapping spheres molecular model better shows the steric hindrace due to the two S atoms as shown in figure 3.11: the yellow atoms are the S ones while the cyan atoms are the Bi ones. This results in a small ET rate constant if compared with the other values: it is the lowest among the 2-Bi cluster as shown in the table 3.1.

Some other cases are analysed to study the effect of SO_4 group in HTS.



Figure 3.11: Overlapping spheres molecular structure of HTS associated to the 2-Bi cluster SO_4 - SO_4 shows the steric hindrace due to S atoms.

Figure 3.12 shows the case in which the two NO₃ groups are replace by an SO₄ group bonded to Bi (a) and a OH group on the other side to Bi (b). It is clear how the SO₄ hugely affects the interaction distance R (in green) from the reacting Paracetamol C atom and the Bi (a): it is equal to 5.5385 \dot{A} much greater than the average R = 3.5368 \dot{A} .



Figure 3.12: Molecular structure of HTS associated to the 2-Bi cluster SO₄-OH.

The resulting ET rate constant of that HTS has an order of magnitude of $10^{+10} s^{-1}$. This can also depends on the position of sulfuric group with respect the Bi plane: figure 3.13(a) shows that the two sulfuric groups are on the same plane of Bi atoms in the case of SO₄- SO₄; on the other hand the sulfuric group is above that plane in the SO₄-OH case in figure 3.13(b) by more affecting the plane orietantion.

Another SO_4 based Bi cluster is simulated where only one NO_3 group is replaced as shown in 3.14(a). Also in that case the overlapping spheres molecular model in figure 3.14(b) underlines the hindrace due to SO_4 group close to the other two massive Bi atoms.



Figure 3.13: Comparison between the molecular structure HTS associated to 2-Bi clusters SO_4 - SO_4 (a) and SO_4 -OH (b).

Despite in the previous case the steric effets was mainly associated to the NO_3 , the figure explicitly shows the smaller region occupied by NO_3 if compared with that one of sulfur group. For that reason, the HTS associated to that cluster it is not shown since the structure can not be optimized.

It can be supposed that sulfuric group should not replace the NO₃ groups since there is not any improvements in terms of ET rate constant as consequence of the sulfur electronegativity (smaller than the nitrogen one). Additionally, the molecular structure can not be optimized due to the steric effect associated to SO₄ group.



Figure 3.14: Molecular structure (a) and overlapping sphere molecular model (b) of HTS with a 2-Bi cluster SO_4 -NO₃.

3.2.2 3-Bismuth cluster

All the results are shown in table 3.2. The different cases are labelled with the functional groups connected to the three Bi atoms of the chain.

Bismuth case	ET rate constant $[s^{-1}]$	Activation energy $[eV]$
NO ₃ -NO ₃ -NO ₃	$7.08 \cdot 10^{-5}$	7.34
NO ₃ -OH-NO ₃	$5.86 \cdot 10^{-2}$	5.75
NO ₃ -OH-OH	$8.46 \cdot 10^{-2}$	9.16
OH-OH-NO ₃	$8.30 \cdot 10^{-2}$	9.87

Table 3.2: Electron transfer rate constant and activation energy for 3-Bi clusters

NO₃-NO₃-NO₃ VS NO₃-OH-NO₃



Figure 3.15: Molecular structure and electron density distribution of HTS with a 3-Bi clusters NO₃-NO₃-NO₃ (a), (b) and NO₃-OH-NO₃ (c), (d).

The HTS regarding to NO_3 - NO_3 - NO_3 3-Bi cluster and NO_3 -OH- NO_3 one are respectively shown in figure 3.15(a) and figure 3.15(c). In that case it must be distinguished among the reacting Bi atoms and the non-reacting one. In the first case the two Bi atoms involved are the Bi labelled with (a) and the Bi (b); in the second case are the Bi (b) and the Bi (c). In both the case the Bi atoms must be adjacent one of each other.

By analising the HTS based on NO_3 - NO_3 - NO_3 cluster it can be seen that both the functional groups bonded with the reacting Bi atoms do not give any distorsion on

Bi bonds. They are quite close to the Bi plane; however the NO_3 bonded to the Bi (a) moves back with respect to the Paracetamol plane. This orientation reflects the rotation in front of the Paracetamol plane of the branch referred to non-reacting Bi (c) as it can be seen in figure 3.16(a).

The steric effect is more evident in the NO_3 -OH- NO_3 due to the orientation of the NO_3 group bonded with the non-reacting Bi atom. The reason is still the approach to the nitro group of the organic molecule. On the other side, the NO_3 group moves below the Bi plane while the OH group bonded to Bi (b) is almost on the same plane as it can be observed in figure 3.16(b).

Despite the NO₃-OH-NO₃ HTS could appeared more hindered, it has a lower activation energy of the transition state and an ET rate constant that is three order of magnitude greater than the NO₃-NO₃-NO₃ case. It can be thought again that the presence of some OH group should be improve the ET process. Moreover, replacing just one NO₃ group with a smaller functional group OH leads in a more energetically favorable molecular structure to ET process as it can be deduced from activation energy values in table 3.2.



Figure 3.16: Comparison between the nolecular structure HTS associated to the 3-Bi clusters NO_3-NO_3 (a) and $NO_3-OH-NO_3$ (b).

NO₃-OH-OH vs OH-OH-NO₃

Figures 3.17(a) and 3.17(c) show the molecular structures of two HTS based on 3-Bi clusters. In the NO₃-OH-OH case, the ET is supposed to invole the Bi (a) and Bi (b) one. The same for the OH-OH-NO₃ case that differ from the first in the position of the functional groups. Also that case compared two specular clusters with great differences in the conformations. Indeed, the steric effect is strongly visible in the NO₃-OH-OH based HTS due to the proximity between the cluster NO₃ group and the Paracetamol nitro group. In that case, the NO₃ is also above the Bi plane. On the contrary, it lies on that plane in the OH-OH-NO₃ case. Nevertless, no distorsion occurs and also the dihedral angles are similar as it can be seen in figure 3.18 where the blue planes and the α_1 angle are associated to the NO₃-OH-OH and the yellow planes and the α_2 angle are associated to the OH-OH-NO₃ one. Since no relevant differences occurs, the two HTS also have a variation between the two ET rate constant less than 2% as it can be seen in 3.2. The NO₃-OH-OH should promote a small activation energy (almost 10% less than the other case). However, the values are really similar one to each other for both the clusters. Thus, it could be say that the activation is strictly related to atoms forming the molecular structure as in the two specular case of NO_3 -OH and OH-NO₃ for the 2-Bi case. Despite that, the 3-Bi clusters also results in a similar ET rate constant while those associated to the 2-Bi clusters differ of one order of magnitude.



Figure 3.17: Molecular structure and electron density distribution of HTS with a 3-Bi clusters NO_3 -OH-OH (a), (b) and OH-OH-NO₃ (c), (d).



Figure 3.18: Overlapped molecular structure of HTS associated to the 3-Biclusters NO_3 -OH-OH (blue planes) and NO_3 -OH-OH (yellow planes).

Chapter 4

Conclusions

Electron transfer process at the interface Bi-oxide based surface electrode/Paracetamol is estimated through physical equations starting from computational results. This is done by building an hypotethical transition state to model the molecular structure when ET occurs at a single active site. Indeed, Bi cluster should not uniformily provide electroactive sites distribution that depends on nanostructures orientation. Additionally, adsorbed molecules on electrode surface can inhibit the availability of some sites. Simulations are also performed in order to keep information about not reactive sites influence on ET rate constant.

Solvation effect on Paracetamol is modeled through five water molecules whose distance from the organic compound is optmized through MM+ and semiempirical method. Further optimizations are performed on Paracetamol+Bi based structure to achieve the HTS conformation. Finally, the effects of an hypothetical H₂SO₄ pretreatment are analysed.

Results are summirezed in table 4.1 and show the effects of Bi cluster functional groups on final molecular structure. Bonds distorsion and rotation of Paracetamol molecule with respect Bi cluster through dihedral angles analysis are the main effects. For the 2-Bismuth clusters both symmetric and antisymmetric structures are simulated.

1. 1

	ET rate constant $[s^{-1}]$	Activation energy $[eV]$
2-Bi cluster		
NO ₃ -NO ₃	$1.2 \cdot 10^{-3}$	9.3
OH-OH	$2.6 \cdot 10^{-3}$	10.89
NO ₃ -OH	$2.78 \cdot 10^{-2}$	7.46
OH-NO ₃	$6.9 \cdot 10^{-3}$	7.74
SO ₄ -SO ₄	$2.55 \cdot 10^{-4}$	6.75
3-Bi cluster		
NO ₃ -NO ₃ -NO ₃	$7.08 \cdot 10^{-5}$	7.34
NO ₃ -OH-NO ₃	$5.86 \cdot 10^{-2}$	5.75
NO ₃ -OH-OH	$8.46 \cdot 10^{-2}$	9.16
OH-OH-NO ₃	$8.30 \cdot 10^{-2}$	9.87

Table 4.1: Results summary table for both 2-Bi clusters and 3-Bi ones.

The simplest case based on HO-BiONO₃ provides an ET rate constant equals to $1.2 \cdot 10^{-3} s^{-1}$ as it can be seen on the summary table 4.1. It is comparable with the experimental result equals to $(1.6 \pm 0.2) \cdot 10^{-3} s^{-1}$ obtained in [9] through CV data and exploiting Laviron equation. Neverthless, it has seen how the NO₃ group hugely affects the Bi-O bond due to steric effect. Keeping fixed β , better conformation is achieved with the symmetric OH-OH case where no steric effect arises. However, the ET rate constant is comparable with the previous case thus no enhancement could be given by an extended surface like that.

On the other hand, the rate constant is reduced by two order of magnitude if sulfuric groups are bonded on Bi atoms due to the huge hindrance of those. Additionally, it should be improbable that just one NO₃ group of the two bonded with reacting Bi atoms is replaced with SO₄ group since bond distorsions occur (probably associated to difference in electronegativity); similarly, a 2-Bi asymmetric cluster such as SO₄-OH results in an anacceptable ET rate constant of the order of $10^{+10} s^{-1}$ due to larger interaction distance *R* than the mean value one. Indeed, a distance of closest approach almost equals to 3.5368 \dot{A} can be estimated for the 2-Bi cluster.

Asymmetric structures should improve the charge transfer if OH group replaces one NO₃ as in the NO₃-OH and OH-NO₃ cases. This is also observed in the 3-Bi cluster cases where one or two OH groups are bonded with reacting or non-reacting Bi atoms: the ET rate constant is of the order $10^{-2} s^{-1}$ in all the cases simulated. Despite that, steric effects still hold in the 2-Bi asymmetric cluster if the NO₃ group is bonded with the Bi (a) or Bi (b) while neither distorsion nor relevant differences in dihedral angles are developed in the 3-Bi cases with two OH groups (NO₃-OH-OH vs OH-OH-NO₃). Finally, 3-Bi cluster NO₃-NO₃-NO₃ is compared with that one having a central OH group by giving an ET rate constant that is three order of magnitude less than the NO₃-OH-NO₃.

The table 4.1 also shown the activation energy meaning the energy required to achieve the system configuration such that the ET can occurs. Ideally, the higher is the activation energy the higher will be the energy needed to move on transition state coordinates, thus the lower will be the ET rate constant. However, this not exactly occurs: activation energy and ET rate constant are not linearly related and some other parameters such as geometrical ones affect the final results. Indeed, the NO₃-OH case and the NO₃-OH-OH have an ET of the same order of magnitude, but the first has an activation energy 20% less than the second case. This can be justified by considering that the reacting Bi atoms involved on the 3-Bi cluster are bonded with the same functional groups of the 2-Bi cluster by giving a comparable ET rate constant. Neverthless, having a third non-reacting Bi atom increases the system size: an higher activation energy could be reasonable.

On the contrary, it is evident that similar clusters such as the specular ones (NO₃-OH-OH and OH-OH-NO₃ or NO₃-OH and OH-NO₃) have almost the same activation energy since the same atoms undergo the geometry optimization. However, ET rate constant manteins the same order of magnitude just for the 3-Bi clusters and this could be explained by reffering to the different steric effect characterizing the two compared 2-Bi clusters.

In conclusion, it can be assume that the distribution of functional groups on Bi cluster is not uniform and will be depends on the nanocomposite functional groups. It can be also supposed that pretreatment becomes a fundamental steps to avoid further contaminants that can altered the performance if it can be performed by avoiding SO_4 attachments. On the contrary, having a more oxidezed electrode functionalizade layer should be improve the ET. Indeed, best results are obtained if at least one reacting Bi atom is bonded to an hydroxyl group. This could be related to the steric effect usually associated to NO_3 that can be counteracted from an OH group better than another NO_3 . Additionally, hindered groups generally move above the Bi planes by reducing the active sites exposure: this holds by looking at molecular structure such as 3.6(a) or 3.15(a) where no NO_3 is replaced.

Thus, the results suggest the positive effect of low oxigen reach surface. This could open the way to further synthetic adjustments for the improved surface tailoring of bismuth based nanocomposites.

Bibliography

- L. Rassaei, F. Marken, M. Sillanpää, M. Amiri, C. M. Cirtiu, and M. Sillanpää, "Nanoparticles in electrochemical sensors for environmental monitoring," *TrAC Trends in Analytical Chemistry*, vol. 30, no. 11, pp. 1704–1715, 2011.
- [2] G.-q. Liu, H. Zhong, X.-r. Li, K. Yang, F.-f. Jia, Z.-p. Cheng, L.-l. Zhang, J.z. Yin, L.-p. Guo, and H.-y. Qian, "Research on nonenzymatic electrochemical sensor using ho-biono3 nanocomposites for glucose detection," *Sensors and Actuators B: Chemical*, vol. 242, pp. 484–491, 2017.
- [3] W.-C. Lee, K.-B. Kim, N. Gurudatt, K. K. Hussain, C. S. Choi, D.-S. Park, and Y.-B. Shim, "Comparison of enzymatic and non-enzymatic glucose sensors based on hierarchical au-ni alloy with conductive polymer," *Biosensors and Bioelectronics*, vol. 130, pp. 48–54, 2019.
- [4] G. A. Mabbott, "An introduction to cyclic voltammetry," Journal of Chemical education, vol. 60, no. 9, p. 697, 1983.
- [5] S. Bilal, "Cyclic voltammetry," 2014.
- [6] M. Zidan, T. W. Tee, A. H. Abdullah, Z. Zainal, and G. J. Kheng, "Electrochemical oxidation of paracetamol mediated by nanoparticles bismuth oxide modified glassy carbon electrode," *Int. J. Electrochem. Sci*, vol. 6, pp. 279–288, 2011.
- [7] H. Bahramipur and F. Jalali, "Sensitive determination of paracetamol using a graphene-modified carbon-paste electrode," *African Journal of Pharmacy and Pharmacology*, vol. 6, no. 17, pp. 1298–1305, 2012.
- [8] E. Laviron, "General expression of the linear potential sweep voltammogram in the case of diffusionless electrochemical systems," *Journal of Electroanalytical Chemistry and Interfacial Electrochemistry*, vol. 101, no. 1, pp. 19–28, 1979.
- [9] M. Madagalam, C. Sandro, A. Tagliaferro, and M. Bartoli, Bismuthnanocomposites modified Screen Printed Carbon Electrodes for Non-Enzymatic Electrochemical Sensors. PhD thesis, Politecnico di Torino, 2020.
- [10] S. Carrara, "Nanotechnology to enhance electron transfer," in *Bio/CMOS Inter-faces and Co-Design*, pp. 157–183, Springer, 2013.
- [11] W. J. Albery, "Electrode kinetics," Philosophical Transactions of the Royal Society of London. Series A, Mathematical and Physical Sciences, vol. 302, no. 1468, pp. 221–235, 1981.

- [12] L. Gorker and V. Dimitrov, "Modified tafel equation for electroless metal deposition," Progress in Reaction Kinetics and Mechanism - PROG REACT KINET MECH, vol. 34, pp. 127–140, 06 2009.
- [13] A. Paul, T. Laurila, V. Vuorinen, and S. V. Divinski, *Fick's Laws of Diffusion*, pp. 115–139. Cham: Springer International Publishing, 2014.
- [14] M. Ciobanu, J. P. Wilburn, M. L. Krim, and D. E. Cliffel, "1 fundamentals," in *Handbook of Electrochemistry* (C. G. Zoski, ed.), pp. 3 – 29, Amsterdam: Elsevier, 2007.
- [15] F. Scholz, "Voltammetric techniques of analysis: the essentials," *ChemTexts*, vol. 1, no. 4, p. 17, 2015.
- [16] J. Adair, E. Suvaci, and J. Sindel, "Surface and colloid chemistry," 2001.
- [17] J. J. Kwiatkowski, "From molecules to mobilities: modelling charge transport in organic semiconductors," 2009.
- [18] K. A. Sharp, "Calculation of electron transfer reorganization energies using the finite difference poisson-boltzmann model," *Biophysical journal*, vol. 74, no. 3, pp. 1241–1250, 1998.
- [19] R. A. Marcus, "Chemical and electrochemical electron-transfer theory," Annual review of physical chemistry, vol. 15, no. 1, pp. 155–196, 1964.
- [20] M. Tachiya, "Generalization of the marcus equation for the electron-transfer rate," The Journal of Physical Chemistry, vol. 97, no. 22, pp. 5911–5916, 1993.
- [21] M. Tachiya and M. Hilczer, "Solvent effect on the electron transfer rate and the energy gap law," in AIP Conference Proceedings, vol. 298, pp. 447–459, American Institute of Physics, 1994.
- [22] R. J. Cave and M. D. Newton, "Generalization of the mulliken-hush treatment for the calculation of electron transfer matrix elements," *Chemical physics letters*, vol. 249, no. 1-2, pp. 15–19, 1996.
- [23] M. Towler, N. Allan, N. M. Harrison, V. Saunders, W. Mackrodt, and E. Apra, "Ab initio study of mno and nio," *Physical Review B*, vol. 50, no. 8, p. 5041, 1994.
- [24] M. Causa, R. Dovesi, C. Pisani, and C. Roetti, "Ab initio hartree-fock study of the mgo (001) surface," *Surface science*, vol. 175, no. 3, pp. 551–560, 1986.
- [25] D. Sholl and J. A. Steckel, Density functional theory: a practical introduction. John Wiley & Sons, 2011.
- [26] P. Hohenberg and W. Kohn, "Inhomogeneous electron gas," *Physical review*, vol. 136, no. 3B, p. B864, 1964.
- [27] N. Argaman and G. Makov, "Density functional theory: An introduction," American Journal of Physics, vol. 68, no. 1, pp. 69–79, 2000.
- [28] V. V. Karasiev, T. Sjostrom, J. Dufty, and S. Trickey, "Accurate homogeneous electron gas exchange-correlation free energy for local spin-density calculations," *Physical review letters*, vol. 112, no. 7, p. 076403, 2014.

- [29] K. F. Freed, "Theoretical foundations of purely semiempirical quantum chemistry," The Journal of Chemical Physics, vol. 60, no. 5, pp. 1765–1788, 1974.
- [30] J. J. Stewart, "Optimization of parameters for semiempirical methods iv: extension of mndo, am1, and pm3 to more main group elements," *Journal of Molecular Modeling*, vol. 10, no. 2, pp. 155–164, 2004.
- [31] X. ShangGuan, H. Zhang, and J. Zheng, "Electrochemical behavior and differential pulse voltammetric determination of paracetamol at a carbon ionic liquid electrode," *Analytical and bioanalytical chemistry*, vol. 391, no. 3, pp. 1049–1055, 2008.
- [32] X. Kang, J. Wang, H. Wu, J. Liu, I. A. Aksay, and Y. Lin, "A graphene-based electrochemical sensor for sensitive detection of paracetamol," *Talanta*, vol. 81, no. 3, pp. 754–759, 2010.
- [33] Y. Fan, J.-H. Liu, H.-T. Lu, and Q. Zhang, "Electrochemical behavior and voltammetric determination of paracetamol on nafion/tio2–graphene modified glassy carbon electrode," *Colloids and Surfaces B: Biointerfaces*, vol. 85, no. 2, pp. 289–292, 2011.
- [34] G. G. Graham, M. J. Davies, R. O. Day, A. Mohamudally, and K. F. Scott, "The modern pharmacology of paracetamol: therapeutic actions, mechanism of action, metabolism, toxicity and recent pharmacological findings," *Inflammopharmacol*ogy, vol. 21, no. 3, pp. 201–232, 2013.
- [35] G. Rebollar-Pérez, J. Campos-Terán, N. Ornelas-Soto, A. Méndez-Albores, and E. Torres, "Biosensors based on oxidative enzymes for detection of environmental pollutants," *Biocatalysis*, vol. 1, no. open-issue, pp. 118–129, 2016.
- [36] M. Á. López Zavala and C. R. Jaber Lara, "Degradation of paracetamol and its oxidation products in surface water by electrochemical oxidation," *Environmental* engineering science, vol. 35, no. 11, pp. 1248–1254, 2018.
- [37] S. Periyasamy and M. Muthuchamy, "Electrochemical oxidation of paracetamol in water by graphite anode: effect of ph, electrolyte concentration and current density," *Journal of environmental chemical engineering*, vol. 6, no. 6, pp. 7358– 7367, 2018.
- [38] J. Wang, H. Zhang, J. Zhao, R. Zhang, N. Zhao, H. Ren, and Y. Li, "Simultaneous determination of paracetamol and p-aminophenol using glassy carbon electrode modified with nitrogen-and sulfur-co-doped carbon dots," *Microchimica Acta*, vol. 186, no. 11, p. 733, 2019.
- [39] T. A. Gadhi, L. S. Gómez-Velázquez, M. Bizarro, A. Hernández-Gordillo, A. Tagliaferro, and S. E. Rodil, "Evaluation of the photodiscoloration efficiency of β-bi2o3 films deposited on different substrates by pneumatic spray pyrolysis," *Thin Solid Films*, vol. 638, pp. 119–126, 2017.
- [40] H.-W. Wang, Z.-A. Hu, Y.-Q. Chang, Y.-L. Chen, Z.-Q. Lei, Z.-Y. Zhang, and Y.-Y. Yang, "Facile solvothermal synthesis of a graphene nanosheet-bismuth oxide composite and its electrochemical characteristics," *Electrochimica Acta*, vol. 55, no. 28, pp. 8974–8980, 2010.

- [41] T. A. Gadhi, S. Hernández, M. Castellino, P. Jagdale, T. Husak, A. Hernández-Gordillo, A. Tagliaferro, and N. Russo, "Insights on the role of β -bi2o3/bi5o7no3 heterostructures synthesized by a scalable solid-state method for the sunlight-driven photocatalytic degradation of dyes," *Catalysis Today*, vol. 321, pp. 135–145, 2019.
- [42] J. Eberl and H. Kisch, "Visible light photo-oxidations in the presence of α-bi 2 o 3," *Photochemical & Photobiological Sciences*, vol. 7, no. 11, pp. 1400–1406, 2008.
- [43] A. Hocquet and M. Langgård, "An evaluation of the mm+ force field," Molecular modeling annual, vol. 4, no. 3, pp. 94–112, 1998.
- [44] R. HyperChem, "7.0 for windows, hypercube," 2002.
- [45] N. Serpone, P. Maruthamuthu, P. Pichat, E. Pelizzetti, and H. Hidaka, "Exploiting the interparticle electron transfer process in the photocatalysed oxidation of phenol, 2-chlorophenol and pentachlorophenol: chemical evidence for electron and hole transfer between coupled semiconductors," *Journal of Photochemistry* and Photobiology A: Chemistry, vol. 85, no. 3, pp. 247–255, 1995.

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