POLITECNICO DI TORINO

Master's Degree in Nanotechonolgy for ICT



Nickel and Zinc Ferrite Nanoparticles Tailored Screen Printed Electrode for Non-Enzymatic Electrochemical Sensing

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Abstract

This work aims to develop a fast, cheap, and easy-to-use non-enzymatic sensor for paracetamol detection. Non-enzymatic electrochemical sensing was selected because of the electrochemical activity of paracetamol and the easy and cheap way of sensing it using the commercially available Screen-printed carbon electrodes (SPCEs). In order to improve the sensing, five concentrations of zinc ferrite ($Zn_xFe_{1-x}O_4$, x from 0.2 to 1 with step of 0.2) nanoparticles, five concentrations of nickel ferrite ($Ni_xFe_{1-x}O_4$, x from 0.2 to 1) nanoparticles, and magnetite nanoparticles were synthesized using an auto-precipitation method followed by a hydrothermal synthesis. Nanoparticles act as catalytic agents, improving the electron transfer rate and, therefore, the sensitivity and the limit of detection (LOD). These new materials' quality has been tested by means of SEM imaging, XRD, and Raman spectroscopy. The SEM imaging highlight that the synthesized nanoparticle formed agglomerates of micrometric size while the XRD and Raman were used to check the composition.

Four 3:1 Weigth/Volume (w/V) dispersions of each ferrite were done using deionized (DI) water, ethanol, methanol, and a 10% V/V solution of isopropanol in DI water. C11L Screen Printed Carbon Electrodes (SPCEs) with $0.12cm^2$ carbon working electrode, carbon counter electrode, and Ag/AgCl reference electrode were bought from Dropsens. The synthesized nanoparticles were deposited on top of several SPCEs using drop-casting, a simple technique based on putting a drop of the dispersed ferrite on top of the electrode and leaving it dry. Cyclic voltammetry (CV) was used to test bare and coated electrodes in 1 mM paracetamol solution in 0.1M PBS. The volume of the drop and the solvent of the dispersion were the first two variables optimized. After various optimizations step, ethanol resulted as the best solvent and $2.5\mu L$ as the best drop volume. An increase of around 35% of the oxidation's peak current with respect to the bare electrode was observed. Using the optimized conditions, a kinetic characterization was performed; in particular, electron transfer coefficient (α) and kinetic rate constant (k) were calculated using Laviron equations.

Calibration curves were obtained for the bare and the best materials, using seven known concentrations from 0 mM to 3 mM paracetamol in 0.1 M PBS

solution, plotting the oxidation's peak currents with respect to the concentration. Three electrodes for each used material were measured for the calibration curve to have an inter-sensor error. Higher sensitivity was observed for all modified electrodes compared to the bare electrode. Quantitatively, the bare electrode has a sensitivity of $26.8 \pm 1.3 \mu A/mM$ with a limit of detection (LOD) of $6.9 \pm 0.3 \mu M$. The performances of the coated electrodes are similar; the best material seems to be the zinc ferrite, with a sensitivity of $34.9 \pm 0.7 \mu A/mM$ and a LOD of $15.5 \pm 0.3 \mu M$. So a final increase of around 29% in the sensitivity was achieved. Finally, chronoamperometry measurements were done to calculate the active area of the electrodes resulting in $0.67 \pm 0.18 \text{ cm}^2$ for the zinc ferrite electrode. This work can be further developed: by trying in-flow measurements, checking the selectivity using other analytes, and developing a custom portable potentiostat to make possible in-situ measurements.

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Acronyms

 ${\bf CPEs}$ Carbon Paste Electrodes.

 ${\bf CQDs}$ Carbon Quantum Dots.

 ${\bf CV}$ Cyclic Voltammetry.

DI deionized.

DPV Differential pulse voltammetry.

FCC Face Cube Centered.

FE-SEM Field Emission Scanning Electron Microscopy.

FIA Flow Injection Analysis.

GCEs Glassy Carbon Electrodes.

 ${\bf LoD}$ Limit of Detection.

MWCNTs Multi-Walled Carbon Nanotubes.

NMR Nuclear Magnetic Resonance.

PBS Phospate-Buffered Saline.

PCM Paracetamol.

PEG Polyethylene Glycol.

POC Point-of-Care.

SERS Surface-Enhanced Raman Scattering.

SPCEs Screen Printed Carbon Electrodes.

- **SPEs** Screen Printed Electrodes.
- ${\bf SWV}$ Square wave Voltammetry.
- $\mathbf{w/V}$ Weigth/Volume.
- ${\bf XRD}$ X-Ray Diffraction.

Chapter 1 Introduction

Nowadays, nanomaterials and nanoparticles are widely used due to their improved performance compared to the respective bulk materials. Nanoparticles can be classified according to size, shape, and surface properties. Usually, a particle can be defined as a nanoparticle if it has at least one dimension less than 100 nm. They can show different shapes: flakes, rods, flowers, and spheres. Nanoparticles are used in the drug delivery system for cancer therapy [1], in different imaging techniques such as Nuclear Magnetic Resonance (NMR) spectroscopy [2], Surface-Enhanced Raman Scattering (SERS) [3], microwave imaging [4], and in biosensing applications [5]. Electrochemical sensors represent an important class of biosensors widely used in our everyday life. Environmental monitoring, health and instrumentation sensors, and machine sensors are examples of electrochemical sensors' applications. In recent decades, the incorporation of nanotechnology and, in particular, nanoparticles has significantly impacted the development of nanosensors mainly because of the surface-to-volume ratio, one of the most important characteristics of nanometric size [6]. Nanoparticles also act as catalytic agents and, if their size is comparable with the electron De Broglie wavelength, can enhance the electron transfer rate due to quantum effects. The use of nanoparticles in the electrochemical sensors can improve the sensitivity and the Limit of Detection (LoD), taking advantage not only of the excellent electron transfer rate and catalytic proprieties but also of the more extensive active surface area. Biosensors based on electrochemical sensing typically have a bio-recognition layer that affects selectivity. Depending on this layer is possible to divide electrochemical biosensors into DNA-based, enzyme-based, and electro-catalytic-based sensors [7]... It is also possible to classify electrochemical sensors based on the technique used to transduce the signal. Amperometric detection catches the electric current produced by redox reactions. Potentiometric detection measures the change in potential at electrodes due to ions or chemical reactions at an electrode. Conductometric detection measures the changes in resistance associated with the changes in the overall ionic medium between the electrodes.



(a) Screen Printed Electrodes (SPEs) with carbon working and counter electrode, Ag reference electrode.

(b) SPEs with gold working and counter electrode, silver reference electrode.

Figure 1.1: Example of SPEs. Reprinted from [8]

SPEs are electrochemical sensors built by printing different kinds of ink on plastic or ceramic substrates; allowing quick, low-budget, in-situ measurements with high reproducibility, sensitivity, and accuracy [9]. The composition of the electrodes determines their selectivity and sensitivity. As shown in Figure 1.1, SPEs comprises working, reference, and counter electrodes, permitting them to be used in several set-ups for different measurements. Carbon is often used for its excellent properties: low background currents, chemically inert, and larger potential windows [10, 11]. Another great feature of SPEs is that the surface can be easily modified with nanoparticles that enhance the electron transfer and help reach higher sensitivities.

1.1 Project aim

This work's aim was to synthesize different zinc and nickel ferrite materials and use them to improve the performance of non-enzymatic electrochemical sensors. I used a carbon SPEs as the base sensor, which I coated with my synthesized materials. After the materials' characterization and the coating process's optimization, these new sensors were thoroughly characterized: electron transfer coefficient, kinetic rate constant, sensitivity, and LoD were analyzed. All these parameters were compared to find the best sensor that can be used for different applications.

1.2 Electrochemical sensing of paracetamol

Paracetamol (PCM), also known as Acetaminophen (Figure 1.2), is a widely used medication employed in the treatment of fever and mild to moderate pain.



Figure 1.2: Skeletal formula of paracetamol (N-(4-Hydroxyphenyl)acetamide).

It has antipyretic and analgesic effects and is commonly used for several symptoms: fever, headache, and other pain treatments. When taken as an overdose, paracetamol has a direct hepatoxic potential and can cause acute liver injury and death from acute liver failure [12]. Therefore, an accurate, fast, simple, low-cost, and easily applicable method is needed to measure its concentration in pharmaceutical applications and biological fluids. Several techniques can be used to detect paracetamol, such as chromatography-mass spectrometry, spectroscopic methods, capillary electrophoresis methods, water analysis, and electrochemical methods [13]. Most of these techniques are time-consuming, expensive, and not applicable at the Point-of-Care (POC). Since paracetamol is electrochemically active, electrochemical methods are the most suitable to determine paracetamol concentration. In Table 1.1 and Table 1.2 are reported examples of paracetamol sensors coated with non-carbon-based and carbon-based nanoparticles. As we can see, many different materials have been tested for improvement in paracetamol sensing. Also, different types of working electrodes are employed; the most common are Carbon Paste Electrodes (CPEs), Glassy Carbon Electrodes (GCEs) and Screen Printed Carbon Electrodes (SPCEs).

| WE | Modifier | methods | linearity | LOD (μM) | Refs. |
|------|---------------------------------|---------------|---------------|---------------|-------|
| CPE | $ZMS-5/TiO_2$ | DPV | 2.5-110 | 0.58 | [14] |
| CPE | Fe_2O_3 | DPV | 2 - 150 | 1.16 | [15] |
| CPE | $Au@Fe_3O_4$ | DPV | 0.1 - 70 | 0.045 | [16] |
| SPCE | $\mathrm{Bi}_{2}\mathrm{O}_{2}$ | DPV | 0.5 - 1250 | 0.03 | [17] |
| GCE | $\mathrm{Bi}_{2}\mathrm{O}_{3}$ | CV | 0.5 - 1500 | 0.2 | [18] |
| SPCE | CeO_2 | DPV | 0.09-100 | 0.051 | [19] |
| GCE | $Fe_2O_3@SnO_2$ | DPV | 4.5 - 876 | 0.2 | [20] |
| CPE | $ZnFe_2O_4$ | DPV | 6.5 - 135 | 0.4 | [21] |
| CPE | ZnS | DPV | 1-15 | 0.041 | [22] |
| GCE | NI-Al/HCF-LDH | Amperometry | 3-1500 | 0.8 | [23] |
| GCE | Au/SDS-LDH | DPV | 0.5 - 400 | 0.13 | [24] |
| CPE | PANI/TPA | DPV | 0.9-1900 | 0.2 | [25] |
| SPCE | PEDOT | FIA | 0.5-600 | 0.16 | [26] |
| | | DPV | 4-400 | 1.39 | |
| | | CV | 10-1000 | 3.71 | |
| GCE | PEDOT | DPV | 2.5 - 150 | 1.13 | [27] |
| GCE | Poly-AHMP | DPV | 2-20 | 0.15 | [28] |
| GCE | Poly-(L-cysteine) | Linear sweep | 0.2-100 | 0.05 | [29] |
| | | Voltammetry | | | |
| GCE | Poly-(L-histidine)/ | DPV | 0.8-100 | 0.077 | |
| | acetylene black | | | | |
| GCE | Poli-(diglycolic acid) | CV | 0.02 - 500 | 0.0076 | [30] |
| GCE | Poly (nile blue) | DPV | 0.2 - 16.2 | 0.08 | [31] |
| GCE | Poly(chromium Schiff | DPV | 0.008 - 0.125 | 0.0068 | [32] |
| | base complex) | | | | |

Introduction

Table 1.1: PCM sensors based on non-carbon nanostructure modified electrodes.Reprinted from [33].

1.3 Electrochemical theory

Electrochemistry is a branch of chemistry related to the combination of chemical and electrical effects. An oxidation-reduction reaction is a chemical reaction involving the transfer of electrons from a species A that oxidizes to a species B that reduces. The electron transfer happens between molecules or from the molecule-electrode interaction due to the difference in their energy level. The electrode-molecule transfer occurs when the energy level is changed with an external voltage, and the electron can tunnel through the barrier. The energy needed for the transfer is provided by the energy difference between the initial and final state. When the transfer is between molecules, we are talking about homogeneous transfer; when it is between electrode and molecule is a heterogeneous transfer [50]. An electrochemical setup is made of at least two electrodes, but three are used in most

| WE | Modifier | methods | linearity | LOD (μM) | Refs. |
|------|-----------------------|-------------|--------------|---------------|-------|
| CPE | MWCNTs | SWV | 2-200 | 0.8 | [34] |
| CPE | Gr | SWV | 2.5 - 143 | 0.6 | [35] |
| GCE | GO | Amperometry | 0.1 - 430 | 0.021 | [36] |
| GCE | Gr | SWV | 0.1-20 | 0.032 | [37] |
| GCE | Gr nanoflakes | Amperometry | 0.0001 - 300 | 0.00043 | [38] |
| GCE | ERGO | SWV | 0.05 - 0.1 | 0.25 | [39] |
| GCE | ERGO | Amperometry | 0.005-4 | 0.0021 | [40] |
| CPE | MWCNTs | DPV | 39.4 - 146.3 | 2.1 | [41] |
| CPE | MWCNTs | SWV | 0.0002 - 15 | 0.00009 | [42] |
| SPCE | MWCNTs | FIA | 0.25 - 10 | 0.1 | [43] |
| GCE | MWCNTs | DPV | 3-300 | 0.6 | [44] |
| GCE | C_{60} | DPV | 50-1500 | 50 | [45] |
| SPCE | C ₆₀ black | DPV | 1-300 | 0.01 | [46] |
| GCE | $C_{60}MWCNT$ | DPV | 0.5 - 2000 | 0.035 | [47] |
| GCE | N-CQDs | DPV | 0.5 - 600 | 0.157 | [48] |
| GCE | CQDs-Gr | DPV | 0.001-10 | 0.00038 | [49] |

Introduction

Table 1.2: PCT sensors based on carbon nanostructure modified electrodes.Reprinted from [33].

cases, as shown in figure 1.3. The working electrode is where the redox reaction occurs efficiently. The reference electrode provides the potential needed for the proper redox reaction. The counter electrode catches the redox's current. Usually, the working electrode is made of an inert conductive material such as carbon, gold, or platinum; the reference electrode can be made of Ag, Ag/Agcl, or SCE.

1.3.1 Mass transport

In an electrochemical reaction involving electrodes, the reaction takes place in the electrode-solution interface. It is crucial to analyze how the reactants come, and the product goes away from the interface. There are three possible kinds of motions in an electrolyte solution: diffusion, migration, and convection. With the experimental condition normally used, it is possible to neglect the convection. It is pretty challenging to describe the motion of a particle under the effect of two kinds of forces, so the experimental conditions are fixed to make one of the two negligible. In particular, for this work, only diffusion has to be present, so a highly concentrated salt solution is used to lower the potential gradient across the solution. In this way, the migration, proportional to the potential difference, becomes negligible.

Let us consider the case of a typical electrochemical cell (as the one shown in



Figure 1.3: Three electrodes electrochemical cell scheme: an adjustable voltage source apply a voltage between the working electrode and the reference electrode. At the same time, an amperemeter measures the current flowing in the counter electrode. Reprinted from [51]

figure 1.3), with the three electrodes immersed in an electrolyte solution in the presence of an electrochemically active analyte. When a positive potential is applied, an oxidation reaction can occur. Close to the interface where the reaction occurs (i.e. the working electrode), part of the analyte is oxidized, so its concentration is not uniform in all the solutions. This gradient of concentration determines a mass flow:

$$\vec{J_m} = -D\vec{\nabla}C(\vec{x},t). \tag{1.1}$$

Equation 1.1 is the first Fick's law. $\vec{J_m}$ is the diffusion flux, and C is the concentration in the function of space and time. The coefficient of proportionality D is called diffusion coefficient. Its value depends on the electrostatic interaction between diffusing and solvent molecules (usual water)[51].

From Equation 1.1, using the continuity equation of the flux, it is possible to obtain the variation of concentration, in a certain volume, over time in function of the variation over space:

$$\frac{\partial C(\vec{x},t)}{\partial t} = D\nabla^2 C(\vec{x},t).$$
(1.2)

Equation 1.2 is the second Fick's law. Usually, the interface where the reaction takes place is planar, so it's possible to rewrite this equation in only one dimension,

neglecting the y and z components of the diffusion:

$$\frac{\partial C(\vec{x},t)}{\partial t} = D \frac{\partial^2 C(\vec{x},t)}{\partial x^2}.$$
(1.3)

Equation 1.3 will be used in the next sections to explain other important equations of electrochemistry.

1.3.2 Cottrell Equation and chronoamperometry

We want to calculate the current flowing at the interface. Solving Equation 1.3 is possible to know the exact number of electrons collected by the interface. Laplace transformations help us to simplify it:

$$s\hat{C}(x,s) - C(x,0^+) = D\frac{\partial^2 \hat{C}(x,s)}{\partial x^2},$$
(1.4)

where s is the Laplace Transform's independent variable. $\hat{C}(x,0)$ is related to the system's initial conditions. The initial conditions commonly used in electrochemistry are:

$$\begin{cases} C(x,0) = C_0\\ \lim_{x \to \infty} C(x,t) = C_0\\ \lim_{x \to \infty} C(0,t) = 0 \end{cases}$$
(1.5)

These initial conditions mean that our electrochemical system has the following features (i) at any point of the solution, the concentration of the metabolites is equal to C_0 ; (ii) Away from the interface, this concentration remains unchanged at any time; (iii) after a long time it becomes null at the interface (x=0). Using this condition to write

$$C(x,0^{+}) = C(x,0) = C(x \to \infty, t) = C_0$$
(1.6)

is possible to rewrite Equation 1.5 as

$$\frac{\partial^2 C(\hat{x}, s)}{\partial x^2} = -\frac{s}{D} C(\hat{x}, s) = -\frac{C_0}{D}$$
(1.7)

that is a second-order differential equation. Solving it and antitransforming to recover the time dependency we obtain

$$i(0,t) = \frac{nFA\sqrt{D}C(0,t)}{\sqrt{\pi t}}.$$
(1.8)

Equation 1.8 is Cottrell's equation; n is the number of electrons taking part in each redox reaction, A is the area of the electrode, and F is the Faraday constant. It is possible to obtain the relationship between the current increase and the analyte concentration:

$$\Delta i = \frac{nFA\sqrt{D}}{\sqrt{\pi\Delta t_0}}\Delta C \tag{1.9}$$

where Δt_0 is the time interval between analyte injection and the increment of the current [51].



Figure 1.4: Chronoamperometry technique. Reprinted from [51]

Chronoamperometry is an electrochemical technique obtained by applying a fixed potential across the interface and acquiring the current flowing as a function of time. It is described by Cottrell's equation (1.8), and the typical trend is the one shown in ref. Adding more analyte, we can see the step on the current followed by a decrease due to the root square dependence of current on time. The current step should have a linear dependence on concentration variation as described by Figure 1.4 left. The right part of Figure 1.4 shows the typical calibration curve for chronoamperometric measurements.

1.3.3 Nernst Equation

Let us consider a general redox reaction taking place at the working electrode surface in the form

$$O + e \underset{k_a}{\overset{k_c}{\longleftrightarrow}} R \tag{1.10}$$

where K_c and k_a are the cathodic and anodic kinetic rate constant:

$$\begin{cases} k_c = k_c^0 e^{-\frac{\Delta G_c}{RT}} \\ k_a = k_a^0 e^{-\frac{\Delta G_a}{RT}} \end{cases}$$
(1.11)

Substituting the Gibbs free energies:

$$\begin{cases} k_c = k_c^0 e^{-\frac{\Delta G_c^0 + \alpha n F(E - E^0)}{RT}} \\ k_a = k_a^0 e^{-\frac{\Delta G_a^0 - (1 - \alpha) n F(E - E^0)}{RT}} \end{cases}$$
(1.12)

As reported by Equation 1.12 the Gibbs energies depend on furnished external energy (E) with respect to the standard potential (E^0) as well on the free energies of reduction (ΔG_c^0) and oxidation (ΔG_a^0) . F is the Faraday constant, and α is the electron transfer coefficient, a parameter going from 0 (reduction) to 1 (oxidation). The perfect equilibrium between oxidation and a reduction process is obtained by imposing:

$$E = E_0; \quad \alpha = 0.5; \quad k_c = k_a \Rightarrow k_c^0 e^{-\frac{\Delta G_c^0}{RT}} = k_a^0 e^{-\frac{\Delta G_a^0}{RT}} \equiv k^0.$$
 (1.13)

Now it is possible to rewrite Equation 1.12 taking into account Equation 1.13:

$$\begin{cases} k_c = k^0 e^{-\frac{\alpha n F(E-E^0)}{RT}} \\ k_a = k^0 e^{\frac{(1-\alpha)n F(E-E^0)}{RT}} \end{cases}$$
(1.14)

The concentration of oxidized and reduced molecules determine the measured current at the working electrode's surface:

$$i = i_c - i_a = nFA[k_cC_O(0, t) - k_aC_R(0, t)].$$
(1.15)

So,

$$i = nFAk^{0} \left[C_{O}(0,t)e^{-\frac{\alpha nF(E-E^{0})}{RT}} - C_{R}(0,t)e^{\frac{(1-\alpha)nF(E-E^{0})}{RT}} \right].$$
 (1.16)

Equation 1.16 is a well-known electrochemistry equation widely used in problems requiring heterogeneous kinetics. The results obtained from this equation are known as the Butler-Volmer formulation of electrode kinetics[52] At the equilibrium, we have again

$$i = 0 \Rightarrow C_O(0, t) e^{-\frac{\alpha n F(E-E^0)}{RT}} = C_R(0, t) e^{\frac{(1-\alpha)n F(E-E^0)}{RT}}.$$
 (1.17)

Equation 1.17 can be rewritten in the form

$$\frac{C_O(0,t)}{C_R(0,t)} = e^{\frac{nF(E-E^0)}{RT}}$$
(1.18)

It means

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$$\frac{nF(E-E^0)}{RT} = ln \left[\frac{C_O(0,t)}{C_R(0,t)} \right]$$
(1.19)

and finally, we get the Nernst equation:

$$E = E^{0} + \frac{RT}{nF} ln \left[\frac{C_{O}(0,t)}{C_{R}(0,t)} \right].$$
 (1.20)

The Nernst equation (1.20) put in relations the oxidation/reduction peaks by analyte concentration [51].

1.3.4 Cyclic voltammetry

Cyclic Voltammetry (CV) is a widely used electrochemical technique employed to analyze redox reactions and electron transfer-initiated reactions as catalysis. As we can see from Figure 1.5a, every analyte has a different voltammogram form. If the analyte is not electrochemically active, it has a shape like the blue one with no peaks. An active electrochemical analyte can show multiple reduction/oxidation peaks. In Figure 1.5b are reported the two possible conventions used for CV [50]. In this work, I'll use the IUPAC convention.



Figure 1.5: On the left (1.5a) is reported an example of different voltammograms. On the x-axis is reported the potential imposed between the reference electrode and the working electrode of a 3-electrode electrochemical cell. On the y-axis, we have the measured current on the counter electrode. On the right (1.5b) are reported the US and IUPAC convention for CV measurements. Reprinted from [50]

In CV, we scan the voltage starting from a potential where the analyte is not electrochemically active, moving toward a positive potential, then a negative



Figure 1.6: On the left (1.6a) is reported a detailed voltammogram; on the right (1.6b) is reported the typical applied potential.Reprinted from [50].

potential, and finally coming back, completing the cycle. Meanwhile, the current between working and counter electrodes is measured and plotted as a function of the applied voltage. Typically a duck-shaped plot is obtained from which it is possible to extract the redox current peaks and the corresponding voltages. In Figure 1.6a, we can see a detailed voltammogram. The potential was scanned from -0.3V (point A) to 0.3V (point D) and back to -0.3V (point G), as shown in Figure 1.6b. Changing the potential, we are changing the potential barrier of the electrodes. Increasing the potential, the oxidation reactions become more probable, so we observe a higher current. Decreasing the potential, reducing reactions become more probable, so we measure a higher negative current. The peaks are present due to two phenomena: (i) the oxidation/reduction regulated by the Nernst equation (1.20); (ii) the analyte depletion by diffusion. Rewriting Nernst Equation:

$$ln\left[\frac{C_O(0,t)}{C_R(0,t)}\right] = \frac{nF}{RT}(E - E^0)$$
(1.21)

where E is the applied potential, and $E^0 = E^{\frac{1}{2}}$ is the standard potential of this redox couple, we explain why oxidation occurs only when $E > E^0$. Unfortunately, the Nernst equation works only for a limited amount of space (some nm) near the interface. The total current that we see depends on the mass transport phenomena in the solution. The non-zero current, even when no reactions occur, is the background current, also called non-Faradaic current, and it is usually subtracted. The procedure of subtracting the background current is called Baseline correction. As shown in Figure 1.6a, two straight lines have been drawn starting from the Introduction

oxidation/reduction bases. The oxidation peak (i_p, a) and reduction (i_p, c) peak are measured from these lines. After the Baseline correction, if the ratio of the peaks is equal to 1, the system is ideally reversible.

Randles-Sevčik Equation

The applied potential is not fixed, but, as already said, it changes in time:

$$E(t) = E_{initial} + \nu t. \tag{1.22}$$

Substituting it in Equation 1.18, we get

$$\frac{C_O(0,t)}{C_R(0,t)} = e^{\frac{nF(E_{initial} + \nu t - E^0)}{RT}}.$$
(1.23)

The time dependence of Equation 1.23 due to the voltage scan enters now in the general solution of Equation 1.7. After several calculations, and under the assumption of an electrochemically reversible electron transfer process involving freely diffusing redox species, it is possible to write the so-called *Randles-Sevčic* equation:

$$i_{peak}(t) \propto nFA \sqrt{\frac{nFD\nu}{RT}}C(0,t)$$
 (1.24)

Where n is the number of electrons involved in the redox reaction, F is the Faraday constant, A is the Area of the working electrode, D is the diffusion coefficient, and C is the concentration of the analyte. Equation 1.24 show that the maximum current peak is proportional to the analyte concentration at the interface. The coefficient of proportionality is determined numerically, equal to 0.446. The final version of the *Randles-Sevčic equation* is the following:

$$i_{peak}(t) = 0.446nFA\sqrt{\frac{nFD\nu}{RT}}C.$$
(1.25)

Equation 1.25 can be used to build a calibration curve for our system [51].

1.3.5 Laviron Equations

We are interested in determining the kinetic rate constant (k) and the electron transfer coefficient (α) . Under the assumption of a diffusionless electrochemical system is possible to use two equations proposed by Laviron [53]. According to Laviron's theory, when it is possible to approximate the reaction as totally irreversible, the cathodic peak potential is

$$E_{p,c} = E^0 - \left(\frac{RT}{\alpha nF}\right) ln \left[\frac{\alpha}{|m|}\right], \qquad (1.26)$$

the anodic peak potential is

$$E_{p,ca} = E^0 + \left(\frac{RT}{(1-\alpha)nF}\right) ln \left[\frac{(1-\alpha)}{|m|}\right]$$
(1.27)

and m is:

$$m = \left(\frac{RT}{F}\right) \left(\frac{k}{n\nu}\right) \tag{1.28}$$

where $k = k_s$ as homogeneous rate constant or $k = Ak_{s,h}/V$ with $K_{s,h}$ as heterogeneous rate constant and V as volume. The totally irreversible approximation is considered by $m \to 0$ in particular when 1/|m| > 12 the approximation leads to an error smaller than 2%. The problem is that we don't know m a priori, so another condition has to be found. From a general equation proposed in [53] is possible to plot $n(E_{p,c} - E^0)$ and $n(E_{p,a} - E^0)$ as a function of $|m|^{-1}$. From the plot, we can clearly see that the condition $|m|^{-1} > 12$ can be replaced by $\Delta E_p > 200/n$ mV. Under this assumption we can determine α from equation 1.26 and 1.27. a plot of $E_p = f(\log \nu)$ yields to lines with a slope of

$$m_c = -2.3RT/\alpha nF \tag{1.29}$$

for the cathodic peak and

$$m_a = -2.3RT/(1-\alpha)nF$$
 (1.30)

for the anodic peak. Combining these two equations, α is determined:

$$\alpha = \frac{m_a}{m_a + m_c}.\tag{1.31}$$

The kinetic rate constant (k) can be calculated using this formula:

$$log(k) = \alpha log(1-\alpha) + (1-\alpha)log(\alpha) - log(\frac{RT}{nF\nu}) - \alpha(1-\alpha)\frac{nF\Delta E_p}{2.3RT}.$$
 (1.32)

If the condition of $\Delta E_p > 200/n$ mV is not satisfied, α can be approximately determined using different curves in [53].

1.4 Ferrite Materials

Inorganic Nanoparticles-based biosensors are gaining attention due to their low-cost production, physiochemical stability, biocompatibility, and eco-friendly characteristics [54]. A ferrite is a ceramic material derived from iron (III) oxides that shows ferrimagnetic properties [55]. Ferrites are classified into two categories: hard ferrites and soft ferrites. Hard ferrites have high coercitivity and are difficult to magnetize; therefore, they are used in making permanent magnets. On the other hand, soft ferrites have low coercitivity, meaning their magnetization can easily be altered. For that reason, they are a good conductor of magnetic field, and this property can be used in many electronics applications.



Figure 1.7: Spinel structure. Reprinted from [56]

Ferrites can have several structures: Spinel, reverse-spinel, hexagonal, garnets, and orthoferrite or perovskite structure, but the first two are the most common [57]. The materials chosen for this work, i.e., zinc and nickel ferrite, show spinel and reverse spinel structures. Spinel ferrites have the general molecular formula $A^{2+}B_2^{3+}O_4^{2-}$ where A^{2+} and B_2^{3+} are the divalent and trivalent cations occupying tetrahedral (A) and octahedral (B) interstitial positions of the Face Cube Centered (FCC) lattice formed by O^{2-} ions. An example of spinel structure is reported in Figure 1.7. Zinc ferrite $(ZnFe_2O_4)$ shows this structure: Zn^{2+} ions are in the A sites, Fe^{3+} in the B sites. Magnetite (Fe_3O_4) and nickel ferrite $(NiFe_2O_4)$ show a reverse-spinel structure where the Fe^{2+} or Ni^{2+} are in the B sites, and Fe^{3+} is equally distributed between A and B sites [58]. In Figure 1.8 is shown the magnetite's reverse-spinel structure. Depending on the preparation method, the final structure can also be a mix of the two.



Figure 1.8: Magnetite reverse-spinel structure. Reprinted from [59].

1.4.1 Ferrite nanoparticles synthesis

The synthesis of ferrites can be done using a top-down or bottom-up approach. In the top-down approach, the bulk material is ground into smaller parts to get nanometric size, while in the bottom-up there is a condensation of atoms or molecules in solution or in gas to form materials in nanometric size. There are several methods of synthesis of Ferrite nanoparticles such as sol-gel auto combustion [60, 61], co-precipitation [62], hydrothermal [63], ceramic processing, solid-state reaction, citrate precursor [64], sol-gel auto-ignition [65], oxidation process [66]... In the coprecipitation method, a stoichiometric ratio of divalent and trivalent transition metal salts is dissolved in an aqueous solution with continuous stirring. After reaching a suitable pH by adding an alkaline medium, the nanoparticles precipitate. A final dry and annealing step is required. The sol-gel method is a wet chemical method that involves multiple processes of hydrolysis, condensation, polymerization reaction of metal precursor, and finally, gel formation. If final annealing is required, we have the sol-gel auto-combustion method. The hydrothermal method involves mixing the precursors in stoichiometric ratios into a solvent, transferring the mixture into a sealed autoclave, and heating it in a furnace at a specific temperature and reaction time. In ceramic processing, also called solid-state reaction methods, a mixture of oxides, carbonates, oxalates, and other metal compounds are heated, pelletized, ground, and sintered until the desired phase of the materials is achieved. The citrate precursor method starts with mixing the appropriate stoichiometric amounts of metal salts. After a stirring process adding citric acid and heating at low temperature, a solid compound called precursor is formed. This precursor is calcinated and sintered, and finally, the nanoparticles are formed [66].

| Methods | Temperature (°C) | Advantages | Limitations |
|-------------------------------|------------------|---|---|
| Co-precipitation | 30-140 | Simple process | Poor crystallinity |
| | | Aqueous media | Very long reaction time required |
| | | Controlled size and morphology | Broad size distribution |
| | | Easily functionalized | |
| Hydrothermal | 100-200 | Scalable | Requirement of special reactor |
| | | Controlled size | High pressure required (> 2000PSI) |
| | | Aqueous media | High temperature |
| | | High yield | Long reaction time |
| Sol-gel method | 20-200 | Controlled size and shape | Takes longer time |
| | | Low cost | Yield is medium |
| Microwave hydrothermal method | 160 | Fast heating speed | - |
| | | Faster and economical | |
| | | Very fine nanoparticles produced | |
| | | Uniform morphology | |
| Combustion method | 480 | Less time and energy required | Very high temperature is required |
| | | Simple and effective method | |
| | | Versatile and fast | |
| | | Nanoparticles produced are pure and homogeneous | 5 |
| Solid state reaction method | 25 | No toxic and expensive solvent used | - |
| | | Facile and economic | |
| Oxidation process | 30 | Narrow size distribution | Irregular and elongated morphology of the product |
| - | | Uniform size | |

 Table 1.3: Comparison between ferrite synthesis methods. Reprinted from [55]

Introduction

Chapter 2

Materials and methods

2.1 Materials synthesis

Zinc ferrite and nickel ferrite materials were synthesized in Carbon group at Politecnico di Torino with the help of Mallikarjun Madagalam and Dr. Mattia Bartoli adapting the method suggested by MilošOgnjanović *et al* [67].

2.1.1 Chemicals

If not otherwise specified, all the following chemicals are from Sigma-Aldrich.

- Iron(III) nitrate nonahydrate $Fe(NO_3)_3 \cdot 9H_2O$
- Iron(II) sulfate heptahydrate $FeSO_4 \cdot 7H_2O$
- Nickel(II) nitrate hexahydrate $Ni(NO_3)_2 \cdot 6H_2O$
- Zinc(II) nitrate hexahydrate $Zn(NO_3)_2 \cdot 6H_2O$
- Polyethylene Glycol (PEG) (MM=4000)
- Sodium hydroxide NaOH

2.1.2 Synthesis of $Zn_xFe_{1-x}O_4$ and $Ni_xFe_{1-x}O_4$

The synthesis was done using a co-precipitation method followed by a hydrothermal synthesis [67]. A stoichiometric amount of salts and 0.150 g of PEG were mixed in 15 ml of deionized (DI) water. The solution was put in stirring at 35°C for one hour. When the salts are completely dissolved, the right amount of 1M solution of NaOH was added to reach a pH equal to 10. When the hour passed, the solution was put inside a 25 ml Teflon container and placed inside an autoclave. The autoclave

was heated up in a furnace at 200°C for 1 hour. Finished the time the autoclave was cooled down and the nanoparticles had been synthesized. The solutions was decanted for 1 hour, the excess water was removed, and nanoparticles were dried in the oven for 24 hours. Finally, three washing steps were done to remove PEG and remaining reagents. Each washing step consists of adding 10 ml of DI water, sonication in an ultra-sound bath for 15 minutes, decantation, and removing the excess water. After 24 hours in the oven, the solid compound was smashed in a mortar to obtain the final nanoparticles' powder. The precise quantity for each ferrite is reported in table 2.1 and 2.2. The 1M solution of NaOH was prepared by adding DI water to 2.000 g of NaOH until a final volume of 50 ml is reached. The solution was put in stirring until NaOH is completely dissolved.

| х | $Fe(NO_3)_3$ (g) | $FeSO_4$ (g) | $Zn(NO_3)_2$ (g) | PEG(g) | 1M NaOH (mL) |
|-----|------------------|--------------|------------------|--------|--------------|
| 0 | 3.490 | 1.201 | 0 | 0.150 | 0.872 |
| 0.2 | 3.461 | 0.953 | 0.255 | 0.150 | 0.868 |
| 0.4 | 3.430 | 0.709 | 0.506 | 0.150 | 0.864 |
| 0.6 | 3.405 | 0.469 | 0.752 | 0.150 | 0.861 |
| 0.8 | 3.378 | 0.233 | 0.995 | 0.150 | 0.857 |
| 1 | 3.351 | 0 | 1.234 | 0.150 | 0.854 |

Table 2.1: $Zn_xFe_{1-x}O_4$ reagents.

| x | $Fe(NO_3)_3$ (g) | $FeSO_4$ (g) | $Ni(NO_3)_2$ (g) | PEG (g) | 1M NaOH (mL) |
|-----|------------------|--------------|------------------|---------|--------------|
| 0 | 3.490 | 1.201 | 0 | 0.150 | 0.872 |
| 0.2 | 3.481 | 0.958 | 0.251 | 0.150 | 0.871 |
| 0.4 | 3.472 | 0.717 | 0.500 | 0.150 | 0.870 |
| 0.6 | 3.464 | 0.477 | 0.748 | 0.150 | 0.868 |
| 0.8 | 3.455 | 0.238 | 0.995 | 0.150 | 0.867 |
| 1 | 3.447 | 0 | 1.241 | 0.150 | 0.866 |

Table 2.2: $Ni_x Fe_{1-x}O_4$ reagents.

2.2 Functionalization of the electrodes

2.2.1 Screen printed electrode functionalization

The used SPEs are the C11L by Dropsens, similar to the one reported in Figure 1.1a. C11L has the working and the counter electrode made of carbon, and the reference is made of Ag/agCl. The working electrode's area is 0.12 cm^2 . Four solvents

were used to disperse the synthesized ferrite materials: DI water, a 10% V/V DI solution of isopropanol in DI water, DI water, methanol, and ethanol. For each dispersion, 3mg of ferrite smashed in a mortar was added to 1 ml of solvent. After a sonification of 15 min in an ultrasound bath, the suspension was ready to use. Before the functionalization, the SPEs were washed with DI water, the excess water was removed with nitrogen flow, and the electrode was left drying for at least 3 hours. Inspired by the work of Mallikarjun *et al.* [68], the functionalization of the electrodes was done using the drop-casting technique. It consists of simply spreading a drop of selected volume on the surface of the working electrode and drying at room temperature for at least three hours[69]. Different Volume's drops were used: from $2.5\mu L$ to $12.5\mu L$.

2.3 Preparation of electrolytic solution

2.3.1 PBS preparation

Phospate-Buffered Saline (PBS) 0.2M solution was prepared by adding DI water to one tab of PBS by Sigma-Aldrich until reaching 10ml and sonicating in an ultrasound bath until wholly dissolved. PBS was conserved at 4°C.

2.3.2 Paracetamol solution preparation

Initially a 50mM paracetamol solution was prepared adding DI water to 0.189g of analytical grade paracetamol by Sigma-Aldrich until reaching 25ml in a flask. After that other concentration were prepared diluiting the concentrated solution as reported in Table 2.3. the paracetamol solution were conserved at 4°C.

| Final concentration (mM) | final volume (mL) | Volume of 50mM |
|--------------------------|-------------------|-----------------------|
| That concentration (mwr) | | initial solution (mL) |
| 0.2 | 25.0 | 0.050 |
| 1 | 25.0 | 0.50 |
| 2 | 25.0 | 1.00 |
| 3 | 25.0 | 1.50 |
| 4 | 25.0 | 2.00 |
| 5 | 25.0 | 2.50 |
| 6 | 25.0 | 3.00 |

| Table 2.3: Paracetamol | solution | preparation. |
|--------------------------------|----------|--------------|
|--------------------------------|----------|--------------|

2.3.3 Final electrolyte solutions preparation

At the use moment, the final solutions were prepared mixing in equal volume the PBS solution with one of the paracetamol solutions. the Final concentration is 0.1M PBS and half of the used paracetamol solution i.e. from 0.1mM to 3mM.

2.4 CV measurements

The CV measurements were performed using the potentiostat EA164 QuadStat by Edaq connected to the high resolution laboratory data recorder e-corder 821 by Edaq. Measured electrodes were connected to the potentiostat, and a drop of 100 μ L of the selected final electrolyte solution was put on top of the SPE, wholly covering the three electrodes. The applied potential ranged from -0.4 V to 0.8V between reference and working electrodes at a scan rate of 100 mV/s.

2.5 Chronoamperometric measurements

The Chronoamperometry measurements were performed using the potentiostat EA164 QuadStat by Edaq connected to the high-resolution laboratory data recorder e-corder 821 by Edaq. Measured electrodes were connected to the potentiostat, and a drop of 80 μ L of PBS was put on top of the SPE, covering the three electrodes. An external potential of 0.6 V is applied between the working and reference electrode, and the current between the working and the counter electrodes is measured as a function of time. A drop of 0.8 μ L of 50 mM paracetamol solution is added to reach a concentration of 0.495 mM. The effect of the addiction is measured.

Chapter 3 Results and Discussion

3.1 Characterization of materials

Raman spectroscopy, X-Ray Diffraction (XRD), and Field Emission Scanning Electron Microscopy (FE-SEM) have been used to characterize the materials: Raman spectroscopy is used to study the vibrational modes of the system, and XRD is helpful to understand the crystalline structure and to estimate the composition and finally with FE-SEM is possible to study the size, the shape and the distribution of synthesized materials.

3.1.1 X-ray diffraction

In Figure 3.1 and 3.2 are reported the X-ray diffraction spectra of some of my samples. Using QualX2 equipped by XRD databases, I analyzed the composition of my samples; the results are reported in Table 3.1.

| Sampla | theoretical composition | Estimated composition (Qualx2 databases) |
|----------------------------------|--|--|
| Sample | (% atomic) | (% weight) |
| Fe_3O_4 | $100\% \ \mathrm{Fe_3O_4}$ | $37\% \ \text{Fe}_2\text{O}_3, 36\% \ \text{FeO}, 27\% \ \text{Fe}_3\text{O}_4$ |
| Zna "Fos «Ou | 80% Eq. (), $20%$ $7n$ Eq. (), | 38% FeO, $22%$ Fe ₂ O ₃ , $19%$ ZnO, |
| 2110.21 62.804 | 0070 Fe304, 2070 Zhre204 | $15\% \text{ Fe}_3 \text{O}_4, 6\% \text{ ZnFe}_2 \text{O}_4$ |
| $Zn_{0.8}Fe_{2.2}O_4$ | $80\% \text{ ZnFe}_2O_4, 20\% \text{ Fe}_3O_4$ | $34\% \text{ Fe}_2\text{O}_3, 32\% \text{ ZnFe}_2\text{O}_4, 23\% \text{ Fe}_3\text{O}_4, 11\% \text{ ZnO}$ |
| NiFe ₂ O ₄ | $100\% NiFe_2O_4$ | $62\% \text{ Fe}_2\text{O}_3, 16\% \text{ Fe}_3\text{O}_4, 20\% \text{ Ni}_{1.47}\text{Fe}_{1.53}\text{O}_4$ |

 Table 3.1: Estimated materials' composition according to Qualx2 databases.

As we can see, the exact molecular formula of my samples is only present for the magnetite. In the other case, we can see the presence of the zinc ferrite $(ZnFe_2O_4)$ or a particular nickel ferrite $(Ni_{1.47}Fe_{1.53}O_4)$ because the other ferrites, with different percentage of Zinc or Nickel, are not present in the databases. From this analysis,

I can conclude that my samples are what is expected for only around 30%; the other 70% is a mix of different iron oxides, zinc oxides, or Nickel oxides.



Figure 3.1: XRD of zinc Ferrites.



Figure 3.2: XRD of nickel ferrite.

3.1.2 Raman spectroscopy

In Figure 3.5 and 3.4 are reported the Raman spectra of the zinc and nickel ferrites samples. In Figure 3.3c is reported the Raman spectra of magnetite nanoparticles taken from [70]; the magnetite is evident from the 667 cm⁻¹ (A_{1g}) band present only in ferrite structures. The other peaks are also present in other iron oxides (hematite or maghemite) materials with a higher intensity with respect to magnetite. Hence, it is impossible to distinguish between them [70]. Also, for zinc and nickel ferrites, the important band to understand their presence is the A_{1g} placed around 680 cm⁻¹. The difference between them, and so between spinel and reverse-spinel structure, is the shoulder peak that moves from 656 cm⁻¹ for nickel ferrite to 621 cm⁻¹ for zinc ferrite, gradually increasing in intensity as shown in figure 3.3a and 3.3b [71]. As we said before, in my sample, there is a huge amount of iron oxides that have a Raman intensity much greater with respect to the magnetite and ferrites, so from Raman spectra, in my samples is not possible to say something about magnetite or ferrite presence. Still, I can conclude that other iron oxides are present.



Figure 3.3: Raman spectra of ferrite materials reprinted from [70, 71].



Figure 3.4: Raman spectra of zinc ferrites samples.



Figure 3.5: Raman spectra of Nickel ferrites samples.

3.1.3 SEM imaging

I performed FE-SEM characterization to identify the size, the shape and distribution of synthesized materials.



Figure 3.6: Sem images of (a and b) ZnFe_2O_4 coated electrodes with a magnification of 20k, (c) $\text{Zn}_{0.4}\text{Fe}_{2.6}\text{O}_4$ with a magnification of 20k.

In Figure 3.6 are reported the images of different zinc ferrites. In Figure 3.6a is shown a single zinc ferrite nanoparticles $(ZnFe_2O_4)$ with the typical form of a spinel structure crystal. Figure 3.6b shows a particle of zinc ferrite $(ZnFe_2O_4)$ of a dimension around $5\mu m$ that seems to be an aggregate of several sub-micrometric nanoparticles. In Figure 3.6c $(Zn_{0.4}Fe_{2.6}O_4)$, we can see the aggregation of several sphere nanoparticles, forming structures with different shapes of around $5\mu m$ dimension. In Figure 3.7a is reported the distribution of NiFe₂O₄ microparticles on top of carbon working electrodes; the distribution is quite regular. In Figure 3.7b, we can see that the shape and the dimension of NiFe₂O₄ are similar to the zinc ferrite ones. In Figure 3.7c and 3.7d, we can see that also, in this case, we have agglomerates but with a different structure.



Figure 3.7: SEM images of (a) distribution of NiFe₂O₄ microparticles on top of carbon working electrode with a surface distribution density of $0.0625mg/cm^2$, magnification of 2k; (b) NiFe₂O₄ sferical microparticles aglomerated, magnification of 20k; (c) (Ni_{0.6}Fe_{2.4}O₄) sintered nanoparticles of sub-micrometric size, magnification of 20k; (d) Ni_{0.6}Fe_{2.4}O₄) sintered nanoparticles with a magnification of 93.18k, in the lower right corner it is possible to recognize a typical spinel structure of a dimension around 400nm.

3.2 Electrochemical measurements

3.2.1 Measurement parameters optimization

Electrochemical measurements were done following the similar work done by Madagalam *et al.* [68]. The first step is optimizing the CV parameters.



Figure 3.8: CV of Bare Electrode in 0.1M PBS solution and 1 mM PCM in 0.1 M PBS solution at a scan rate of 100 mV/s.

In Figure 3.8 it is shown the cyclic voltammograms for PBS solution and PCM solution using the same parameters (PBS concentration, paracetamol concentration, potential starting point, minimum and maximum applied potentials, scan rate) used in [68] and reported in the Materials and methods section of this work. We can clearly see the oxidation and reduction peak only when paracetamol is present; the used parameters are also appropriate for this SPEs model. We are interested in the oxidation peak potential and current, so to have more precise data, I decided to repeat the measure (the CV) different times and compute the mean values of the oxidation peak potential and current with the associate standard errors. Repeating the CV various times, I noticed a strong diminishing trend of the oxidation peak current followed by a flat region as shown in Figure 3.9. Therefore, to have smaller error and comparable data, I decided, for each new electrode, to discard the first 15 CV cycles and consider the CV cycles from 16 to 20 as good data to compute the means values and associate standard errors. This protocol was used for all the work. The diminishing trend can be explained as a stabilization of the surface of the electrode. After the set-up of the potentiostat with the suitable measurement parameters and the optimization of the measuring process, the following step is the

optimization of the deposition process. The goals of this step are (i) to improve the oxidation peak current between the bare electrode and at least one of the modified electrodes (ii) to have a good reproducibility of the results.



Figure 3.9: Oxidation peak current as a function of the scan number for different materials: (a) bare electrode; (b) Fe_3O_4 ; (c) $NiFe_2O_4$; (d) $ZnFe_2O_4$. Testing solution: 0.1M PBS solution and 1 mM PCM in 0.1 M PBS solution at a scan rate of 100 mV/s. dispersion of materials in isopropil solution.

3.2.2 Deposition optimization

The first step is the optimization of the drop's volume. In Figure 3.10 are shown the cyclic voltammograms of different deposition quantities, and in Table 3.2 are reported the data regarding the oxidation peak with different depositions' volumes. The mean peak currents of the various electrodes are comparable, so it is impossible to use this parameter to select the best quantity to deposit. Instead, we can choose 2.5 μL as the best deposition quantity because of the smaller error associated. So from this point, I decided to perform all the coating using 2.5 μL material dispersion.



Figure 3.10: CV of Fe_3O_4 coated electrodes in 0.1M PBS solution and 1 mM PCM in 0.1 M PBS solution at a scan rate of 100 mV/s with different depositions volumes; Fe_3O_4 dispersed in DI water.

| Drop's Volume (μL) | Potential (mV) | Current (μA) |
|-------------------------|----------------|-------------------|
| Bare Electrode | 589 ± 2 | 29.5 ± 0.1 |
| 2.5 | 603 ± 3 | 31.4 ± 0.1 |
| 5 | 604 ± 2 | 31.9 ± 0.4 |
| 7.5 | 603 ± 1 | 32.2 ± 0.4 |
| 10 | 615 ± 3 | 30.6 ± 0.4 |
| 12.5 | 622 ± 3 | 31.1 ± 0.4 |

Table 3.2: Oxidation peak potential and corresponding peak current for Fe_3O_4 coated electrode with different deposition's volumes. Fe_3O_4 dispersed in DI water.

Cyclic voltammograms in Figure 3.10 show that, for the moment, there is no improvement with respect to the bare electrode because of the poor solubility of ferrites in water, so a 10% w/V solution of isopropanol in DI water was tried to improve the performance of the electrode. In Figure 3.11 and Table 3.3 are reported the cyclic voltammograms and the associated oxidation peak data of all the materials. We can see an improvement with respect to the bare electrode for some materials, but using only one electrode makes it impossible to say anything about the reproducibility of the result. Moreover, comparing the result of Fe₃O₄ dispersed in water with the same dispersed in isopropyl solution, we can see a





Figure 3.11: CV of (a) isopropil solution dispersion of $\text{Zn}_x\text{Fe}_{3-x}\text{O}_4$ coated electrodes in 1 mM PCM in 0.1 M PBS solution at a scan rate of 100 mV/s; (b) isopropil solution dispersion of $\text{Ni}_x\text{Fe}_{3-x}\text{O}_4$ coated electrodes in 1 mM PCM in 0.1 M PBS solution at a scan rate of 100 mV/s;

| Material | Potential (mV) | Current (μA) |
|----------------------------------|----------------|-------------------|
| Bare Electrode | 589 ± 2 | 30.8 ± 0.1 |
| Fe ₃ O ₄ | 534 ± 2 | 35.6 ± 0.1 |
| $Ni_{0.2}Fe_{2.8}O_4$ | 583 ± 2 | 31.1 ± 0.1 |
| $Ni_{0.4}Fe_{2.6}O_4$ | 614 ± 3 | 29.1 ± 0.1 |
| $Ni_{0.6}Fe_{2.4}O_4$ | 620 ± 4 | 28.7 ± 0.2 |
| $Ni_{0.8}Fe_{2.2}O_4$ | 580 ± 3 | 32.5 ± 0.1 |
| NiFe ₂ O ₄ | 575 ± 2 | 34.5 ± 0.1 |
| $Zn_{0.2}Fe_{2.8}O_4$ | 569 ± 2 | 33.7 ± 0.1 |
| $Zn_{0.4}Fe_{2.6}O_4$ | 601 ± 2 | 34.6 ± 0.1 |
| $Zn_{0.6}Fe_{2.4}O_4$ | 570 ± 2 | 31.2 ± 0.1 |
| $Zn_{0.8}Fe_{2.2}O_4$ | 551 ± 1 | 33.2 ± 0.1 |
| $ZnFe_2O_4$ | 546 ± 1 | 35.8 ± 0.1 |

Table 3.3: Mean oxidation peak potential and corresponding mean peak current for all the isopropranol solution dispersed samples coated electrodes in 1 mM PCM in 0.1 M PBS solution at a scan rate of 100 mV/s.

 Fe_3O_4 , $NiFe_2O_4$, and $ZnFe_2O_4$ were selected as the three best materials. Now

that the number of samples has been restricted, I did another optimization step by trying different solvents and using three electrodes for each material to test the reproducibility of the results.



Figure 3.12: (a) Bare and $ZnFe_2O_4$ coated electrodes mean oxidation peak current and relative inter-electrode standard error (n=3) for different volumes of depositions and different solvents; testing solution: 1 mM PCM in 0.1 M PBS solution at a scan rate of 100 mV/s. (b) CV of Fe₃O₄, NiFe₂O₄, ZnFe₂O₄ dispersed in ethanol coated electrodes in 1 mM PCM in 0.1 M PBS solution at a scan rate of 100 mV/s.

| Material | potential (mV) | current (μA) |
|----------------------------------|----------------|-------------------|
| Bare electrode | 629 ± 18 | 28.4 ± 0.5 |
| $ZnFe_2O_4$ | 516 ± 3 | 37.4 ± 0.7 |
| NiFe ₂ O ₄ | 513 ± 2 | 39.2 ± 0.2 |
| Fe ₃ O ₄ | 503 ± 7 | 39.7 ± 0.6 |

Table 3.4: Oxidation peak potential and corresponding peak current for the best material dispersed in ethanol; testing solution: 1 mM PCM in 0.1 M PBS solution at a scan rate of 100 mV/s.

In Figure 3.12a, we can see that the best compromise between a small error and a good improvement with respect to the bare electrode is to work with ethanol and a deposition volume of 2.5 μL . Also, the other two materials were tested with the selected conditions; the results are shown in Figure 3.12b and inTable 3.4.

Now, the improvement is around 37% with respect to the bare.

3.2.3 Kinetic analysis

Kinetic Analysis was performed by varying the scan rate from 15 to 250 mV/s in a testing solution of 1 mM PCM in 0.1 M PBS solution. The reduction peak at 15 mV/s is challenging to measure, so in further analysis, only the point from 50 to 250 mV/s in steps of 50 mV/s was considered. The results are shown in Figure 3.13. Based on this data, several analyses were performed: (i) the dependency of the oxidation peak current on the square root of the scan rate; (ii) the dependency of the peak potential and the peak-peak separation on the logarithm of the scan rate; (iii) the calculation of the electron transfer coefficient (α), the kinetic rate constant (k) and the diffusion coefficient.



Figure 3.13: CV with multiples scan rate of (a) bare electrode, (b) Fe_3O_4 coated electrode, (c) NiFe₂O₄ coated electrode, ZnFe₂O₄ coated electrode. All the dispersion were made in ethanol, testing solution: 1 mM PCM in 0.1 M PBS solution.



Figure 3.14: Linear regression of oxidation peak current with respect to $\sqrt{\nu}$ of (a) bare electrode, (b) Fe₃O₄ coated electrode, (c) NiFe₂O₄ coated electrode, ZnFe₂O₄ coated electrode.

| Material | I_{Pa} (μA) | \mathbb{R}^2 |
|----------------------------------|--------------------------|----------------|
| Bare | $3.87 \sqrt{\nu} + 6.00$ | 0.995 |
| Fe ₃ O ₄ | $4.00 \sqrt{\nu} + 3.96$ | 0.991 |
| NiFe ₂ O ₄ | $3.78 \sqrt{\nu} + 4.13$ | 0.999 |
| $ZnFe_2O_4$ | $3.65 \sqrt{\nu} + 1.96$ | 0.978 |

Table 3.5: Linear regression oxidation peak current equations with respect to $\sqrt{\nu}$ and determination coefficient R^2

Observing Figure 3.13 and 3.14 and the data reported in Table 3.5, we see the peak current increasing with the scan rate and, in particular, is clearly dependent on the square root of the scan rate as predicted from Randles-sevčik (1.25). According to this observation and what we already discussed in the introduction, the system involves freely diffusing redox species.



Figure 3.15: Linear regression of redox peaks potential with respect to $\ln(\nu)$ of (a) bare electrode, (b) Fe₃O₄ coated electrode, (c) NiFe₂O₄ coated electrode, ZnFe₂O₄ coated electrode.

In Figure 3.15 is reported, the redox peaks as a function of the logarithm of the scan rate of different materials. We can see that the peaks positions are shifting with the scan rate and vary linearly with respect to the logarithm of the scan rate. The linear regressions and the associated determination coefficients are reported in Table 3.6. Also, peak-peak separation is linear with respect to the logarithm of the scan rate; the graph is shown in Figure 3.16; the linear regressions with the

determination coefficient and the peak-peak separation at a scan rate of 100 mV/s are reported in Table 3.7.

| Material | E_{Pa} (mV) | \mathbb{R}^2 | E_{Pc} (mV) | \mathbf{R}^2 |
|-----------------|----------------------------|----------------|----------------------------|----------------|
| Bare electrode | $42.25 \ln(\nu) + 372.26$ | 0.984 | $-33.49 \ln(\nu) + 133.07$ | 0.979 |
| Fe_3O_4 | $28.94 \ln(\nu) + 360.06$ | 0.988 | $-35.25 \ln(\nu) + 204.66$ | 0.989 |
| $\rm NiFe_2O_4$ | $33.924 \ln(\nu) + 350.80$ | 0.994 | $-31.91 \ln(\nu) + 170.37$ | 0.997 |
| $ZnFe_2O_4$ | $18.98 \ln(\nu) + 441.19$ | 0.974 | $-16.33 \ln(\nu) + 54.32$ | 0.896 |

Table 3.6: Linear regression peaks potential equations with respect to $\ln(\nu)$ and determination coefficient \mathbb{R}^2



Figure 3.16: Linear regression of peak-peak separation with respect to $\ln(\nu)$ of (a) bare electrode, (b) Fe₃O₄ coated electrode, (c) NiFe₂O₄ coated electrode, ZnFe₂O₄ coated electrode.

| Material | $\Delta E_P (\mathrm{mV})$ | \mathbf{R}^2 | $\Delta E_P (\mathrm{mV})$ |
|-----------------------------|----------------------------|----------------|----------------------------|
| Bare electrode | $75.74 \ln(\nu) + 239.19$ | 0.983 | 585 ± 4 |
| $\mathrm{Fe}_3\mathrm{O}_4$ | $64.19 \ln(\nu) + 155.40$ | 0.989 | 445 ± 3 |
| $NiFe_2O_4$ | $65.83 \ln(\nu) + 180.43$ | 0.997 | 480 ± 5 |
| $ZnFe_2O_4$ | $35.31 \ln(\nu) + 386.87$ | 0.952 | 553 ± 4 |

Table 3.7: Linear regression of peak-peak separation (ΔE_P) with respect to $\ln(\nu)$, determination coefficient (\mathbb{R}^2), and peak-peak separation values at a scan rate of 100 mV/s with associate standard error.

| Material | α | n | k (ms ^{-1}) | $D (cm^2/s)$ |
|----------------------------------|-----------------|---|------------------------------------|----------------------|
| Bare electrode | 0.56 ± 0.08 | 2 | 0.22 ± 0.02 | $9.76 \cdot 10^{-7}$ |
| Fe_3O_4 | 0.45 ± 0.06 | 2 | 3.1 ± 0.1 | $1.91 \cdot 10^{-6}$ |
| NiFe ₂ O ₄ | 0.52 ± 0.04 | 2 | 1.49 ± 0.02 | $1.69 \cdot 10^{-6}$ |
| $ZnFe_2O_4$ | 0.54 ± 0.13 | 2 | 0.09 ± 0.03 | $1.86 \cdot 10^{-6}$ |

Table 3.8: Electron transfer coefficient (α), electron transfer number, kinetic rate constant (k) and diffusion coefficient (D) of paracetamol at a scan rate of 100 mV/s for bare and coated electrodes.

For paracetamol, the theoretical electron transfer number (n) is equal to 2, so the condition $n\Delta E_P > 200mV$ is satisfied. We can now apply the theory explained in Table 3.6. Electron transfer coefficient is calculated using Equation 1.31 and experimental electron transfer number can be found using Equation 1.30 or 1.29. The kinetic rate constant is calculated using Equation 1.32, and the associate error is calculated propagating the error on ΔE_P and α . The diffusion coefficient is calculated from the Randles-Sevcik equation (1.25) using the geometrical area of the electrode equal to 0.12 cm². Results are reported in Table 3.8. Fe₃O₄ electrode has the highest kinetic rate constant, meaning that it is involved in faster reaction transfer with respect to the other electrodes and also has the lowest over potential. The diffusion coefficient of the coated electrodes is quite similar and around the double one of the bare electrode.

3.2.4 Calibration curves

Calibration curves were performed to calculate the sensors' sensitivity and limit of detection. In Figure 3.17 are shown the calibration curves for the bare electrode and the three best materials.



Figure 3.17: Calibration curve for different electrodes.

Calibration curves were done using the usual measurement process described in subsection 3.2.1 for the first concentration and then performing six more CV cycles for each other concentration, and considering as good measurement the last five for each concentration. Three electrodes for each material were used to check reproducibility and to have inter-electrode errors that must be considered due to the use and trash nature of SPEs. The error reported in the Figure 3.17 is the inter-electrode error calculated as the standard error of each electrode's mean oxidation current peak. We have three measures for each concentration, so we obtain three calibration curves for each material by interpolating them with a linear model. The final calibration curve is calculated as a mean of the slopes of the three calibrations, which is the same as interpolating the mean values of the three measurements for each concentration directly. The associate error is calculated as the standard error of the three different slopes. In Table 3.9 are reported, the linear regression of the mean oxidation current peak as a function of the concentration and the relative determination coefficient. In Table 3.10 are reported the values of

| the | e sensitivity | (i.e. | the slope | of the | $\operatorname{calibration}$ | curve) | with | the | $\operatorname{associate}$ | error | and |
|-----|----------------|--------|-----------|--------|------------------------------|--------|------|-----|----------------------------|------------------------|-----|
| the | e limit of det | tectio | on. | | | | | | | | |

| Material | I_{Pa} (μA) | \mathbf{R}^2 |
|-------------|----------------------|----------------|
| Bare | 26.8 C | 0.921 |
| Fe_3O_4 | 32.8 C | 0.954 |
| $NiFe_2O_4$ | 34.0 C | 0.977 |
| $ZnFe_2O_4$ | 34.9 C | 0.989 |

Table 3.9: Linear regression of oxidation peak current with respect to the concentration (C) and relative determination coefficient

| Material | Sensitivity $(\mu A/mM)$ | LoD (μM) |
|----------------------------------|--------------------------|----------------|
| Bare | 26.8 ± 1.3 | 6.9 ± 0.3 |
| Fe ₃ O ₄ | 32.8 ± 1.2 | 15.4 ± 0.6 |
| NiFe ₂ O ₄ | 34.0 ± 0.9 | 31.1 ± 1.1 |
| $ZnFe_2O_4$ | 34.9 ± 0.7 | 15.5 ± 0.3 |

Table 3.10: Sensitivity and limit of detection with associate inter-electrode errors for different materials.

The limit of detection is calculated as

$$LOD = \frac{K * \delta I}{S} \tag{3.1}$$

where k is k is the parameter for the statistical level of confidence $(k = 1 \text{ for a } 66\% \text{ confidence level}, k = 2 \text{ for } 86\%, k = 3 \text{ for } 99.7\%), \delta I$ is the error of the blank measurement of the current and S is the sensitivity. The error of the limit of detection is calculated by propagating the error on the error of the blank current and the error on the sensitivity. Also, in this case, I decided to use inter-electrode error to calculate the detection limit. The error of blank measurement is calculated as a standard error, so the standard deviation on the error of the blank measurement becomes:

$$\sigma(\delta I) = \delta I \sqrt{1 - \frac{2}{n-1} \cdot \left(\frac{\Gamma(n/2)}{\Gamma(\frac{n-1}{2})}\right)^2}$$
(3.2)

where n is the number of measurements equal to three in my case.

Looking at the Calibration curve (Figure 3.17), we can see that all the materials, but mainly the bare electrodes, are not perfectly linear with the increasing of concentrations. We had always considered the scan from 16 to 20 of our electrodes; in this case, using the same electrodes for all the concentrations, we are changing the number of scansions considered, in particular, doing six CV cycles each for each concentration the higher concentrations are the most affected by this change. In Figure 3.18, I analyzed the behavior of a bare electrode and a zinc ferrite coated electrode for 120 cycles. We can see that changing the working region of the electrode can affect the performance; with higher concentration, this phenomenon is enhanced.



Figure 3.18: Bare and zinc ferrite electrodes oxidation current peaks as a function of the scan number for 120 scans at 100 mV/s. Testing solution: 1 mM PCM in 0.1 M PBS solution.

3.2.5 Chronoamperometry measurement

Chronoamperommetry was done for three $ZnFe_2O_4$ coated electrodes to estimate the active area of my electrodes. In Figure 3.19 is reported the chronoamperometry



Figure 3.19: Chronoamperometry measurement of $ZnFe_2O_4$ coated electrode.

graph for a zinc ferrite coated electrode; we can see a peak for each addiction of paracetamol in the testing solution. By means of the Cottrell law (Equation 1.9) using the height of the peak as Δi , the rising time as Δt_0 , the already calculated diffusion coefficient, and knowing ΔC , it is possible to compute the active area of the electrode. An average of over three electrodes have been done to have a more precise result. The active area of the zinc ferrite electrodes resulted being $0.67 \pm 0.18 cm^2$, around six times greater than the geometrical area.

Chapter 4 Conclusions

Eleven different zinc and nickel ferrites have been successfully synthesized using a co-precipitation method followed by hydrothermal synthesis. XRD showed a purity of around 30%.

New electrochemical sensors have been developed modifying the surface of SPCEs using the synthesized materials by means of the drop-casting technique. SEM images of the electrodes showed a uniform distribution of spherical micrometric size nanoparticles agglomeration. These sensor were tested by CV experiments to measure 1 mM paracetamol in 0.1M PBS solution at a scan rate of 100 mV/s. preliminary experiments showed that ethanol is the best solvent to disperse the ferrites materials, and $2.5\mu L$ resulted in the best drop volume. $ZnFe_2O_4$, $NiFe_2O_4$, Fe_3O_4 resulted as the three best materials with an enhancement with respect to the bare of around 37%. Kinetic analysis has been performed by varying the scan rate, showing that the electrochemical system is a freely diffusing quasi-reversible system. Redox peak currents were varying linearly with the square root of the scan rate, and redox peak positions and peak-peak separation were varying linearly with the logarithm of the scan rate. Kinetic constant rate (k), electron transfer coefficient (α) , and electron transfer number (n) were calculated using the Laviron model. The electron transfer number matches the expected one found in the literature. The diffusion coefficient (D) of paracetamol was computed using the Radles-Sevcik equation approximating the electroactive area with the geometrical area. From a kinetic point of view, magnetite is the best material having the greater kinetic constant rate (3.1 ms^{-1}) and less peak-peak separation (445 mV), meaning that it is involved in quicker reactions. Calibration curves were obtained performing CV for different analyte concentrations (0.5 mM to 3mM). Three electrodes for each material were used to allow inter-electrode error computation. The three kind of coated electrodes and Bare electrodes showed good linearity. Sensitivities were computed using the slope of the linear fitting. Both the sensitivities resulted better compared to the bare electrode. Reaching also the limit of detection, the

best material is the zinc ferrite, which has a sensitivity of $34.9 \pm 0.7 \ \mu A/mM$ and a LOD of $15.5 \pm 0.3 \ \mu M$. A repetitive scan of the electrodes, monitoring the oxidation peak current as a function of the scan number, showed that the electrode was unstable. Therefore selecting the better operation windows and changing electrodes for each concentration is possible to improve the sensitivity further. Chronoamperometry was done to estimate the active area of the electrodes. Zinc ferrite electrodes' mean electrochemical active area resulted in $0.67 \pm 0.18 cm^2$.

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