Empirical Study of Noise Dependence in Electrochemical Sensors

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Abstract—**We report the experimental study of noise in electrochemical biosensors as related to voltage and concentration. A comparison with experiments is performed for H_2O_2 and Ferrocyanide with bare sensors, and with sensors functionalized with Multi-Walled Carbon Nanotubes (MWCNT) modified electrodes. Chronoamperometry measurements at different voltages were carried out, followed by fast Fourier transform analysis of noise at different concentration of analyte to understand the effect of concentration and voltage on the noise** *Power Spectral Density* **(PSD) and the** *Signal over Noise* **(SNR) ratio. Experimental results demonstrate the presence of 1/f noise and its dependence on the state variables. The parameters of 1/f noise i.e. the amplitude coefficient and frequency power coefficients are extracted by curve fitting, and are characterized by comparing the coefficient in different molecules, electrodes, voltages and concentration.**

Keywords— SNR; flicker noise; MWCNT; voltage and concentration effect; H_2O_2; Ferrocyanide; chronoamperometry.

I. INTRODUCTION

Understanding the noise mechanism would open up a possibility to attain an accurate electrical response for in-vivo detection of analytes. Several attempts have been made to integrate electrochemical sensors in order to determine the content of biological analyte [1-4]. The ability of an electrochemical system to perceive small changes in the signal brings uncertainty and limits the sensor to make precise measurements. A better understanding of noise sources in electrochemical sensing is necessary to design the next generation devices for high sensitivity bio-sensing applications. Such understanding is also very useful to develop new models for the electrochemical sensors that can improve chip design simulations.

Over the last decades, Nanomaterials have attracted a great attention in biosensor applications due to their unique physical and chemical properties, which led to biosensors with high sensitivity and stability [5, 6]. Their ability as an electrode modifier has been widely investigated to enhance the efficiency of biosensors [7]. An example is the use of *multi-walled carbon nanotubes* (MWCNT), which results in better decrease of charge transfer resistance and mass transfer impedance [7-9].

In general, the noise fluctuations found in nature falls into three classes according to their spectral densities: thermal noise; shot noise; and flicker noise [10].

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The Johnson-Nyquist thermal current noise of a resistor has a PSD is given by:

$$S_R = 4kT/R \qquad (1)$$

Shot noise is a type of electronic noise, which originates from the discrete nature of electric charge. Shot noise is temperature and frequency independent, in contrast to thermal noise, which is proportional to temperature, and flicker noise, which has a spectral density that decreases with the frequency. Since both thermal noise and shot noise are constant in frequency they are also called white noise.

Flicker noise, or 1/f noise, is a process with a frequency spectrum such that the power spectral density of the noise is proportional to the reciprocal of frequency. The 1/f noise is the dominant noise source in low frequencies for the devices that exhibits this kind of noise.

In this work, we study experimentally the noise of biosensors under different conditions in the domain of low frequencies. The effect of the applied voltage and the analyte concentration on the noise level is investigated. The effect of using sensing electrodes functionalized with MWCNT on the parameters of the flicker noise is also investigated. To study the effect of the molecule nature on the noise level, two different target molecules, i.e. H_2O_2 and Ferrocyanide are chosen because of their popularity in electrochemical detection of biocompounds. The measurement method is described in section II. Section III presents the measurement results and the related discussion.

II. MEASUREMENT METHOD

A. Chemicals

Graphite Screen- Printed Electrodes (SPE) (model DRP-C110 from DropSens, Spain), Multi-walled carbon nanotubes and Multi walled carbon nanotubes functionalized with COOH group were purchased from Dropsens (Spain). The electrodes were made of graphite working electrode of 2 mm^2, a graphite counter electrode, and a reference electrode made of Ag/AgCl. Multi walled carbon nanotubes of diameter 10 nm and length 1-2 μm were purchased in powder form (90% purity), and subsequently diluted in chloroform to the concentration of 1mg/ml [17] Potassium Ferrocyanide in the form of powder and hydrogen peroxide (30% vol) are purchased from Sigma. All solutions were prepared using 0.01 M Phosphate Buffer Saline (PBS,Sigma) at pH 7.4.
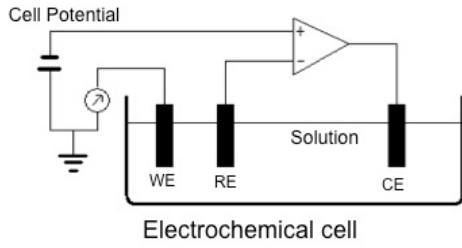
Fig. 1. Setup for Chronoamperometry measurement. A fixed voltage is applied between working electrode (WE) and the reference electrode (RE) and the current flowing between the WE and the counter electrode (CE) is measured.
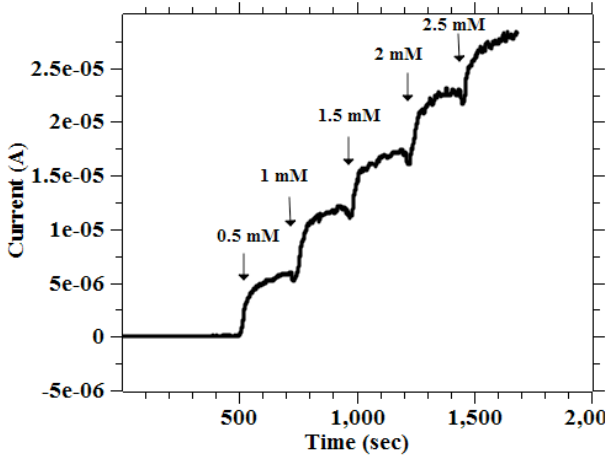

Fig. 2. Chronoamperometry measurement using MWCNT- SPE at 300 mV with 5 subsequent additions of 0.5 mM Ferrocyanide in PBS

B. Preparation of electrodes

Nano-structured SPEs were prepared by using MWCNT. To prepare the MWCNT modified SPEs, 30 μL of MWCNT-Chloroform solution was deposited by drop-casting in the steps of 6μL onto the working electrode and dried [9]. All the samples were freshly prepared and used the same day. When not is use, electrodes were stored at +4°C.

C. Apparatus

Chronoamperometry investigated the electrochemical response under aerobic conditions (Fig. 1). Electrochemical measurements were acquired by Versastat 3 potentiostat (Princeton Applied Technologies. The electrode was dipped into the PBS solution with a volume of 25 ml under stirring conditions. A volume of 25 μL per step of the analyte (solution of H_2O_2 or Ferrocyanide) was successively added into the solution with a time-step of 4 minutes. Each injection increases the concentration by 1mM.

I.   RESULTS AND DISCUSSION

Chronoamperometry measurements of H_2O_2 and Ferrocyanide were carried out on bare graphite SPE. Measurements are repeated using SPE with drop-casted MWCNT. There are four variables to each measurement. The
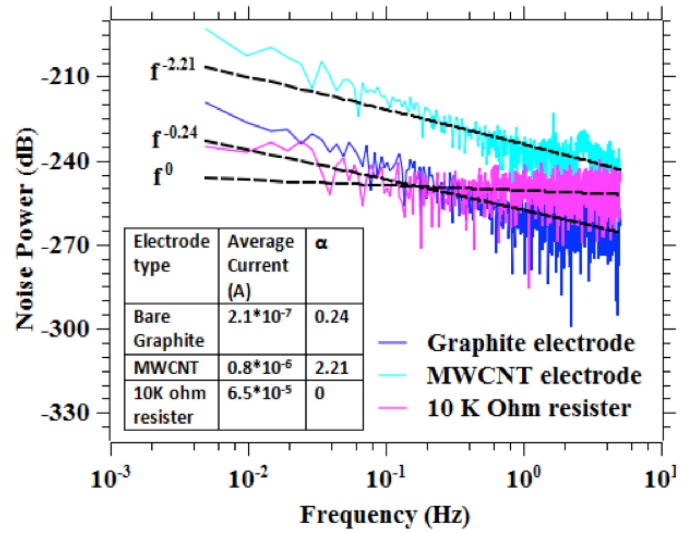

Fig. 3. Noise PSD in chronoamperometry measurement with bare and MWCNT electrodes and a 10 kOhm resistor. The H_2O_2 concentration is kept at 2mM and the applied voltage is 650 mV. The dashed lines represent the fits to $S(f) = A*I^2/f^\alpha$

applied voltage, analyte concentration, and the type of the analyte are three of them. The fourth variable is the presence of the MWCNT on the electrode. In the following subsections we discuss the effect of these four variables on the measured noise. To do this, we investigate the noise in frequency domain. The frequency spectrum of the noise is acquired by calculating the Fourier transform of the noise in time domain using the FFT algorithm. The time domain noise is extracted form the measurement data by subtracting the average sensor current form the measured current. The average current is considered the signal level of the biosensor. We assume that at frequencies lower than 10Hz the dominant noise source is the flicker noise. This is a reasonable assumption because the curve fitting with both flicker and white noise components gives negligible white noise compare to the flicker noise, and hardly changes the flicker noise parameters. Thus noise PSD is fitted to the flicker formula in order to extract the values of noise coefficients, A and α in

$$N_{flicker} = S(f) = A \times I^2_{avg} / f^\alpha \qquad (2)$$

Where f is the frequency in Hz, I_{avg} is the average current of the biosensor. The noise coefficient A and the frequency power α are calculated from the PSD of the measured noise using the non-linear least-mean-square fitting method in matlab. The power of the average current is considered to be equal to two when *carbon nanotubes* (CNTs) are used [11-13] as well as when there are no MWCNTs on the electrodes. In this way A represents the inverse SNR of the measurement at 1Hz (Eq. 3). This curve fitting will make the comparisons among different measurements much easier since the SNR is more important in a measurement process than the noise itself.
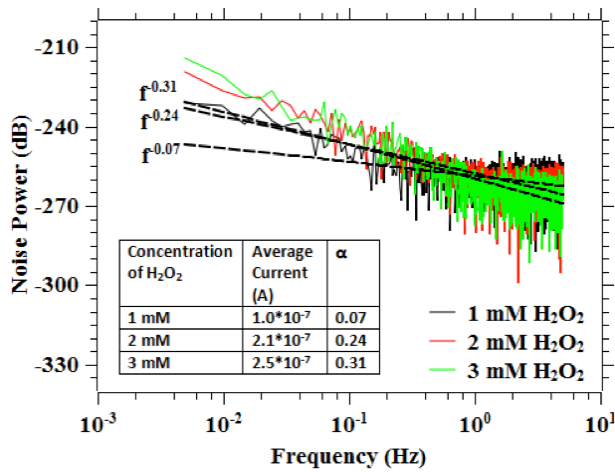
$$SNR = f^\alpha / A \qquad (3)$$

Fig. 4. *Noise PSD in chronoamperometry measurement of H_2O_2 in different concentrations. The applied voltage is 650 mV and bare graphite electrode is used.*
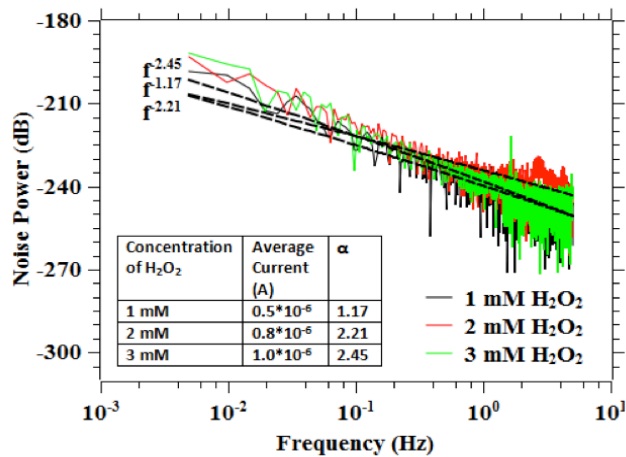

Fig. 5. *Noise PSD in chronoamperometry measurement of H_2O_2 in different concentrations. The applied voltage is 650 mV and MWCNT graphite electrode is used.*

Fig. 2 shows a sample chronoamperometry measurement of Ferrocyanide in PBS solution using bare graphite electrodes. Consequent increasing of the current is obtained by injecting the proper amount of the Ferrocyanide into the solution.

The applied voltage to the electrochemical cell, which is the voltage between the working electrode and the reference electrode, is kept at 300mV in this measurement.

Fig. 3 shows the noise PSD of three different measurements: chronoamperometry measurement on the detection of H_2O_2 is done using both bare graphite electrode and MWCNT-functionalized graphite electrode (at a fixed voltage of 650mV and a fixed concentration of 2mM). The same voltage is applied across a resistance and the resulted noise PSD is also shown in this figure for comparison. The primary result of this measurement is that the noise is much higher in electrodes with MWCNT than bare electrodes. The value of α is given for each PSD plot. It is zero for the measurement with the resistor, which means the instrument does not add any considerable flicker noise.
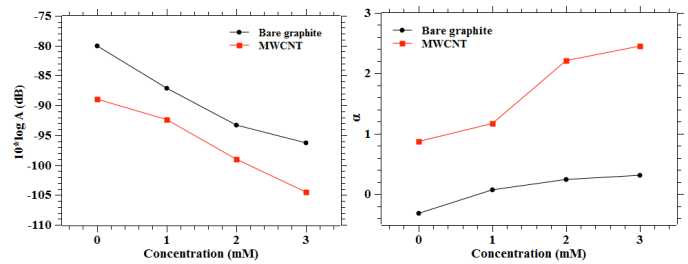

Fig. 6. *Estimated values of parameters A (left) and α (right) in $S(f) = A*F^2/f^\alpha$ versus concentration in H_2O_2 measurement with both bare electrodes and MWCNT electrodes. The applied voltage is 650mV in these measurements.*
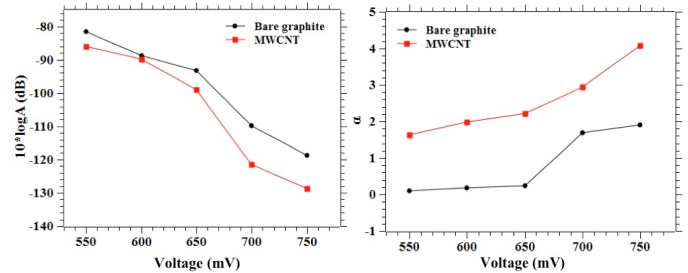

Fig. 7. *Estimated values of parameters A (left) and α (right) in $S(f) = A*F^2/f^\alpha$ versus the applied voltage. H_2O_2 concentration is 2mM and both bare and MWCNT graphite electrodes are used for comparison*

A. Effect of the analyte concentration and MWCNT

Fig. 4 and Fig. 5 show the noise PSD of different H_2O_2 concentrations measured with bare electrode and MWCNT-functionalized electrodes respectively. The estimated values of A and α from are plotted in Fig.6 versus the H_2O_2 concentration. The SNR of the measurement at 1Hz is about one order of magnitude higher when MWCNT are used. An increase in the SNR is achieved by increasing the concentration for both electrodes.

According to Fig. 6-right, the noise frequency power α increases with concentration for both target molecules. Higher α means that noise power decreases with a sharper slope when the frequency increases. From Eq. 3 and Fig. 6 we can conclude that SNR increases more rapidly by concentration in the case of MWCNT electrodes than in the case of bare electrode, at a given frequency of more than 1Hz.

On the other hand, assuming the measurements with both (MWCNTs and bare) electrodes have equal thermal noise, the increase of α and decrease of A with concentration implies that the noise corner frequency is lower in higher concentrations.

B. Effect of the aplied voltage

In order to investigate the dependence of A and frequency coefficient (α) on the applied voltage, a voltage between 550 mv to 750 mV is applied to the cell. The analyte concentration is set to 2mM and both bare graphite and MWCNT-graphite electrodes are investigated. The estimated values of A and α are presented in Fig. 7. The results show an increase in α by increasing the applied voltage for both kinds of electrodes. SNR at 1Hz also increases significantly with increasing the applied voltage.
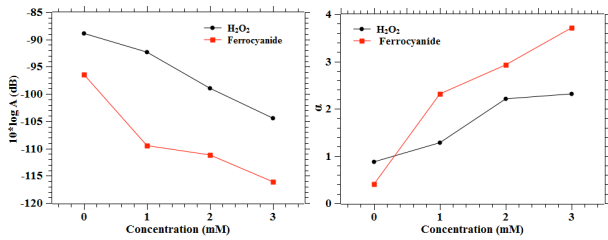
Fig. 8. *Estimated values of parameters A (left) and α (right) in S (f) = A*I²/fᵃ versus concentration in H_2O_2 and Ferrocyanide measurement. MWCNT electrode is used and the applied voltage is 650mV in these measurements.*

C. Effect of the target Molecule

Fig. 8 shows parameters A and α extracted from H_2O_2 and Ferrocyanide measurement by MWCNT electrodes at different concentrations. The SNR of the measurement at 1Hz is higher with Ferrocyanide than with H_2O_2 while for both molecules an increase in the SNR is achieved by increasing the concentration.

According to Fig. 8-right, the noise frequency power α increases with concentration for both target molecules. Both the average value of α and its increase rate with concentration is higher in the case of Ferrocyanide. In addition to having a higher SNR at 1Hz, noise with Ferrocyanide has also a higher corner frequency (assuming the same amount of thermal noise for both H_2O_2 and Ferrocyanide) and higher increase of SNR with frequency (according to Eq. 3).

II. CONCLUSIONS

In this paper, several experiments have been reported to understand the dependence of SNR on physical parameters, in order to properly design biochips with micro-nano-sensors with precise response.

Analyte type and concentration, as well as the measurement voltage dependants of 1/f noise are studied in MWCNT modified and bare graphite electrodes. The SNR of the measurement is investigated to compare the effect of each variable.

Measurements have shown that using MWCNTs increases the SNR of the measurement in all cases we studied. Moreover, the increase rate of SNR with frequency is higher for MWCNT electrode than for bare electrode.

We have demonstrated that the SNR of the measurement significantly increases for both kinds of electrodes with increasing analyte concentrations or applied voltage.

More interestingly, both parameters A and α in Eq. 1 depend on the applied voltage and analyte concentration. We are now developing a new model for the noise in electrochemical sensors that includes these dependencies.

Measurements show that SNR also depends on the type of analyte. For example Ferrocyanide measurements have higher SNR than H_2O_2 measurements under the same condition of concentration and applied voltage.

In summary we suggest the use of highest possible voltage, highest possible frequency, as well as the use of MWCNTs to achieve better SNR in chronoamperometry measurement of a fixed concentration of analyte.

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