ELECTROANALYTICAL STRATEGIES AND METHODOLOGIES FOR THE DETECTION OF NITRIC OXIDE AND REDUCED OXYGEN-ASSOCIATED SPECIES IN BIOLOGICAL SYSTEMS

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Nitric oxide, NO, is one of the ten smallest molecules found in nature and interest in its direct and real-time measurement originated from studies of its role as physiological messenger and cytotoxic agent in several biological systems [1]. Indeed, biologically, NO was first characterized in 1987 as endothelia-derived relaxing factor and it was reported that it is produced by endothelial cells in blood vessels and diffuses to the adjacent smooth muscles to cause vasodilatation [2]. Since this initial report that resulted in R. E. Furchgott, L. J. Ignarro and F. Murad receiving the Nobel Prize in Physiology and Medicine in 1998, there has been an explosion of research activity showing that NO release occurs not only from endothelial cells but also from neuronal, tumoral and immune system cells etc. The huge and intense research activities in these fields have resulted in more than 204,000 papers being published in the literature during the last 15 years. Many of the numerous properties of NO – that enable it to carry out its diverse physiological functions - also present considerable problems when attempting its detection and quantification in biological systems. NO is a free radical – that reacts very fast with oxygen, peroxides, \( \text{O}_2^- \) (superoxide \( \text{O}_2^{-} \)) and metals (and metalloproteins). This explains its fleeting existence and extremely low concentrations in biological systems [3].

The only strategies that allow direct, real time, label free and \textit{in vivo} detection of NO, \( \text{O}_2^- \) and their associated product \( \text{ONOO}^- \) are those based on the use of ultramicroelectrodes [4]. Indeed, micro electrode design and fabrication are now reaching very high levels of sophistication, hence actively contribute to the promotion of the use of electrochemical techniques for \textit{in vivo} NO, \( \text{O}_2^- \) and \( \text{ONOO}^- \) determination by offering the following characteristics: (i) good selectivity and efficient discrimination against other species with selectivity factors \( > 100 \); (ii) good sensitivity towards the desired analyte down to the nanomolar range; (iii) fast response within the millisecond scale time; (iv) long-term stability over 1-2 hours; (v) small size of around 10-50 \( \mu \text{m} \) to offer non invasive and non destructive close proximity to the site of release (single cells, organelles) and (vi) ease of handling.

We present an overview of the successes and challenges still faced in the detection of NO, \( \text{O}_2^- \) and \( \text{ONOO}^- \) in biological media. We provide a full discussion on the electrochemical analyses of each of these species and we summarize the significant research contributions towards the development of sensors for individual and simultaneous detection of these species. We emphasize the importance of understanding the potential interferents in developing such sensors. We show that significant advances have been made with regards to detection of NO in biological media leading to the development of marketable NO sensors, though there is room for improvement in terms of interferences. A brief outlook into the future perspectives of the use of multi electrochemical array sensor for simultaneous detection of NO, \( \text{O}_2^- \) and \( \text{ONOO}^- \) is presented.

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References