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Electrode Technology relies upon a low Contact Impedance to the Body

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Description

In 2002, QUASAR developed a new class of bioelectric sensors that coupled to the body capacitively. These devices differ from previous capacitive electrodes in that they can tolerate very small capacitances to the source. Thus, the sensors can be operated at a standoff from the skin (up to several millimeters in practice), which makes it possible to measure the ECG through clothing.

Conventional wet electrode technology relies upon a low contact impedance to the body (typically <5 k Ω in clinical settings) to limit common-mode voltages appearing on the body and to reduce interference caused by picking up external signals. The high coupling impedance of the CCNE has necessitated the development of specialized capacitive sensing techniques. In the CCNE sensor, the amplifier electronics are shielded and placed as close as possible to the electrode to limit pickup of external signals.

Immunity to Common-Mode (CM) Signals

To provide immunity to common-mode (CM) signals appearing on the body, we operate the sensor in conjunction with the company's proprietary common-mode follower (CMF) technology. Due to its ultra-high input impedance (~1012 Ω), the CMF tracks the body-ground potential with a high degree of accuracy. This can then be used to dynamically reduce any CM signals by more than three orders of magnitude.

We are interested in enhancing storage, shelf-life and thermal stabilities of enzymes and proteins by covalent conjugation with water soluble, flexible polymers, such as poly (acrylic acid) (PAA). The synthesis and characterization of Hb-PAA nanoparticles using low molecular weight PAA (MW 8k) was reported earlier and these withstood steam sterilized conditions without significant loss of structure or biological activities. However, the particle nature of Hb-PAA-8k nanoparticle platform is not favorable for electrochemical application because Hb is encapsulated in the polymer nanoparticles, potentially hindering the accessibility of Hb active center to the electrode surface. Additionally, the nanoparticles limit the number of Hb molecules that could be brought close to the electrode surface and some Hb molecules may be far from the electrode surface. Conversely, protein-polymer nanogels could be more amenable to an enhance electrical contact between the redox active sites and the electrode surfaces.

Since the publication of the previous article, we have made considerable technical improvements to the CCNE technology. A new circuit design has improved sensor performance and also reduced sensor power consumption by the sensors to less than 400 µW. Further improvements include a reduction in the size of the sensor, improved robustness and reliability of the dielectric coating on the electrode, and a simplified manufacturing process to reduce the cost per sensor.

Capacitive Biosensors

To amend the above-mentioned issues, we currently report the use of high molecular weight PAA (MW 450k) to cross-link Hb molecules and form unique Hb-nanogels such that their thermal stability as well electroactivity at the electrode surface may be improved. This can be due to increased rigidity to the local environment surrounding Hb by the higher molecular weight polymer. The mole ratio of Hb:PAA was optimized and its molecular weight increased such that low overlap concentrations of the high molecular weight PAA would favor nanogel formation instead of nanoparticles. In addition, the mole ratio of the crosslinking reagent (carbodiimide) to the number of COOH groups of PAA that are available for linking to the protein has been optimized systematically to produce water-soluble, highly active and thermally stable nanogels. Furthermore, PAA matrix around Hb was further strengthened by cross-linking carboxylic acid groups of PAA with Tetraethylenepentamine (TEPA) or Polyenthyleneimine (PEI) using the carbodiimide chemistry.

The hybrid electrodes were referenced to a CMF placed upon the subject's right earlobe. The ground reference for the wet EEG electrodes was a standard pre-gelled disposable Ag/AgCl electrode placed upon a prepared site on the right ear. Improved thermal stabilities of enzyme electrodes will directly enhance the shelf life for storage at ambient temperatures and facilitate biocatalysis and electrocatalysis at higher temperatures. Particularly, steam-sterilizable bioelectrodes will be useful for biomedical applications. Therefore, there is an urgent need to develop methods to stabilize Hb, as an example, and characterize these new materials for use as bioelectrodes.

Among many redox proteins, met-hemoglobin (Hb) is considered as a model to study direct electrochemistry-based biosensors, because of its catalytic activity and commercial availability. Although hemoglobin comprises of four iron containing heme groups, its electron transfer activity is hindered due to the extended three dimensional protein envelope around the heme, which buries the electroactive centers away from the electrode surfaces. As a result, only a weak redox current appears with Hb-based electrodes on application of large over voltages. The electron transfer rate may be enhanced by the addition of promoters and mediators such as surfactants, polymers and specific nanomaterials. Using different techniques, Hb has been embedded in these films, which led to enhanced electron transfer rates, as well as better adhesion to the electrode surface. This facilitated the use of Hb-based electrodes for biosensing in food, pharmaceutical, clinical and environmental issues. Despite all this progress, a major concern and unmet challenge is the poor stability of Hb and Hb encapsulated derivatives under non-physiological environments, such as high temperatures, extreme pHs, and electrode surface.

It compares EEG signal fidelity between hybrid sensors and Ag/AgCl electrodes positioned at the exact center top of the head (Cz). The 4 second segment in the figure shows alpha activity measured by both electrodes. The plot also includes the Pearson correlation over 0.25 seconds. Very significant correlations, in excess of 90%, are evident throughout the record. One of the principal benefits of QUASAR's biosensor technology is the ease with which the sensors may be applied. For example, the CCNE sensors can be incorporated into a chair or bed for completely unobtrusive monitoring of ECGs. For EEG, a harness can be used to position the hybrid sensors and hold them comfortably against the scalp. The prototype harness can be attached by a novice without the aid of an EEG technician by using a simple combing motion to work the sensors through the hair. Ultimately, the sensors in the harness can be embedded in helmets for soldiers and athletes and inserted in a set of headphones or glasses.