Bioelectrochemistry and Biosensors
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Editorial

Bioelectrochemistry & *Biosensors*-Inaugural Issue: In Memory of Leland Charles Clark—"Father" of Biosensors

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Bioelectrochemistry is the study of the effect of applied electrical potential on biochemical changes in the solution-transducer interface and vice versa. In other words, it is the combination of physical chemistry and biochemistry concerned with the interconversion of biochemical, chemical, and electrical energy.

Biosensorics is an applied direction combining biochemistry, chemistry, material science, and engineering focused on the development of advanced systems and devices measuring biochemical or chemical reactions by generating signals proportional to the concentration of a target analyte in the tested sample.

Here we are pleased to introduce a new international, peer-reviewed, open-access, multidisciplinary journal *Bioelectrochemistry & Biosensors* (*BEBS*) which is focused on novel approaches in Bioelectrochemistry, Biosensors, Bioactuators, and Bioelectronic systems and devices. The journal is a forum for the entire bioelectrochemistry and biosensors interested community and is intended as a journal of choice for researchers coming from varied scientific branches. The journal covers the wide breadth of bioelectrochemical and biosensors sciences, including bioelectrochemistry, bioanalytical science, bioelectrochemical energy conversion and storage, biomaterials science and biomembranes, bioengineering, and all the related areas in between.

The editor team is committed to a fair and efficient evaluation process while the prominent experts in the fields provide a highly qualified review of the submitted papers. We thank them for all their efforts in starting this new journal, and we look forward to your next submission to *BEBS*.

The 1st *BEBS* issue honors Prof. Leland Charles Clark who is the "Father" of bioelectrochemical sensors and it is dedicated to the 20th anniversary of his passing (4 December 1918–25 September 2005). We look forward to your contribution to the Issue in his memory taking into account his essential impact on the fields of Bioelectrochemistry & Biosensors.

Leland Charles Clark (Figure 1) [1,2] was an American biochemist famous mostly for inventing an electrochemical device (Clark electrode) for measuring O_2 concentration in liquids, later converted him into the very first electrochemical biosensor upon placing glucose oxidase (GO_x) enzyme on a membrane coating the electrode compartment. Therefore, Clark is recognized as a "father of biosensors". The modern-day glucose biosensors used daily by millions of diabetics are conceptually based on his research (still technically being very different).

The Clark electrode is an electrode that measures oxygen concentration in a liquid using a platinum (Pt) working electrode according to the net reaction:

$$O_2 + 4\,e^- + 4\,H^+ \rightarrow 2\,H_2O$$

The Pt electrode is negatively polarized vs. Ag/AgCl reference electrode to allow the concentration-limited cathodic (reductive) current. Both electrodes (Pt and Ag/AgCl) are placed into a sensor compartment filled with an electrolyte solution (usually saturated aqueous KCl solution). The compartment is closed with an O_2-permeable membrane (using a Teflon membrane), which allows only O_2 penetration into the measuring compartment and restricts other redox species from getting inside the O_2 sensor. This membrane provides the current-response only dependent on the O_2 concentration in the analyzed liquid.

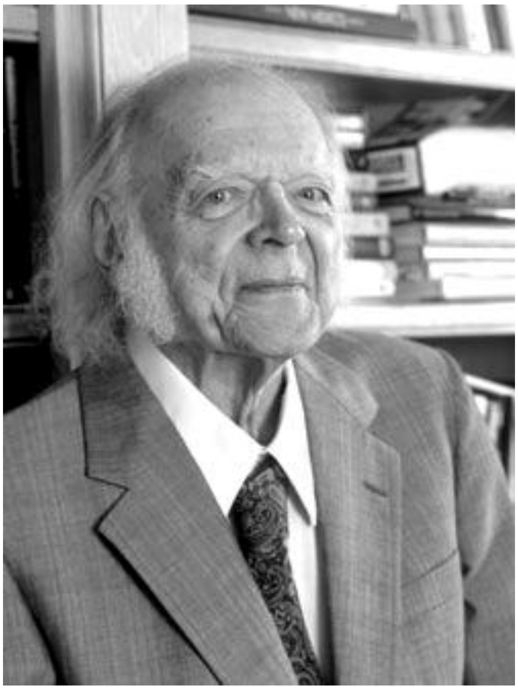

Figure 1. Portrait of Dr. Leland C. Clark, Jr. on or about the date of being awarded the 2005 Fritz J. and Dolores H. Russ Prize, "*for bioengineering membrane-based sensors in medical, food, and environmental applications*". Reproduced from [2].

Despite the simplicity of the invented Clark electrode, the importance of this invention was immediately recognized, and when the paper was published (in 1953), it became one of the most cited papers in the life sciences [3]. The electrode, in its original form, has been in use in a broad range of applications requiring precision O_2 measurements for water quality, many medical and pharmacological situations, and food production. Clark's electrode allowed oxygen to be monitored actually during surgery, an invention that has saved millions of lives over the past half-century.

It is interesting to note that exactly the same device can be used for measuring H_2 concentration instead of O_2 when the Pt electrode is positively polarized (opposite to the case when O_2 is measured), then resulting in the H_2 electrochemical oxidation [4,5].

The first glucose biosensor (Figure 2) invented by Clark [6] was a simple device where the O_2-permeable membrane was functionalized with glucose oxidase (GO_x) enzyme consuming O_2 in the presence of glucose.

$$\text{glucose} + O_2 \xrightarrow[\text{GOx}]{} \text{gluconic acid} + H_2O_2$$

The O_2 concentration was inversely dependent on the glucose concentration, thus, the current response was decreased proportionally to the glucose concentration. The membrane performed two functions: (i) it provided support for the immobilized enzyme, and (ii) it restricted other redox species to penetrate inside the biosensor's compartment where both electrodes (Pt and Ag/AgCl) are located. The biosensor device provided a specific response to glucose concentration regardless of the complex biochemical composition of the analyzed biological liquid (e.g., blood).

Clark performed pioneering research on artificial heart-lung machines in the 1940s/50s (Figure 3A) and obtained over 25 patents. Particularly, he developed a fluorocarbon-based liquid that could be breathed successfully by mice in place of air [7], his lifelong goal of developing artificial blood remained unfulfilled at the time of his death, and is still not fully achieved now. He is the inventor of Oxycyte (based on perfluoro *tert*-butylcyclohexane) (Figure 3B), a third-generation perfluorocarbon (PFC) therapeutic oxygen carrier designed to enhance oxygen delivery to damaged tissues.

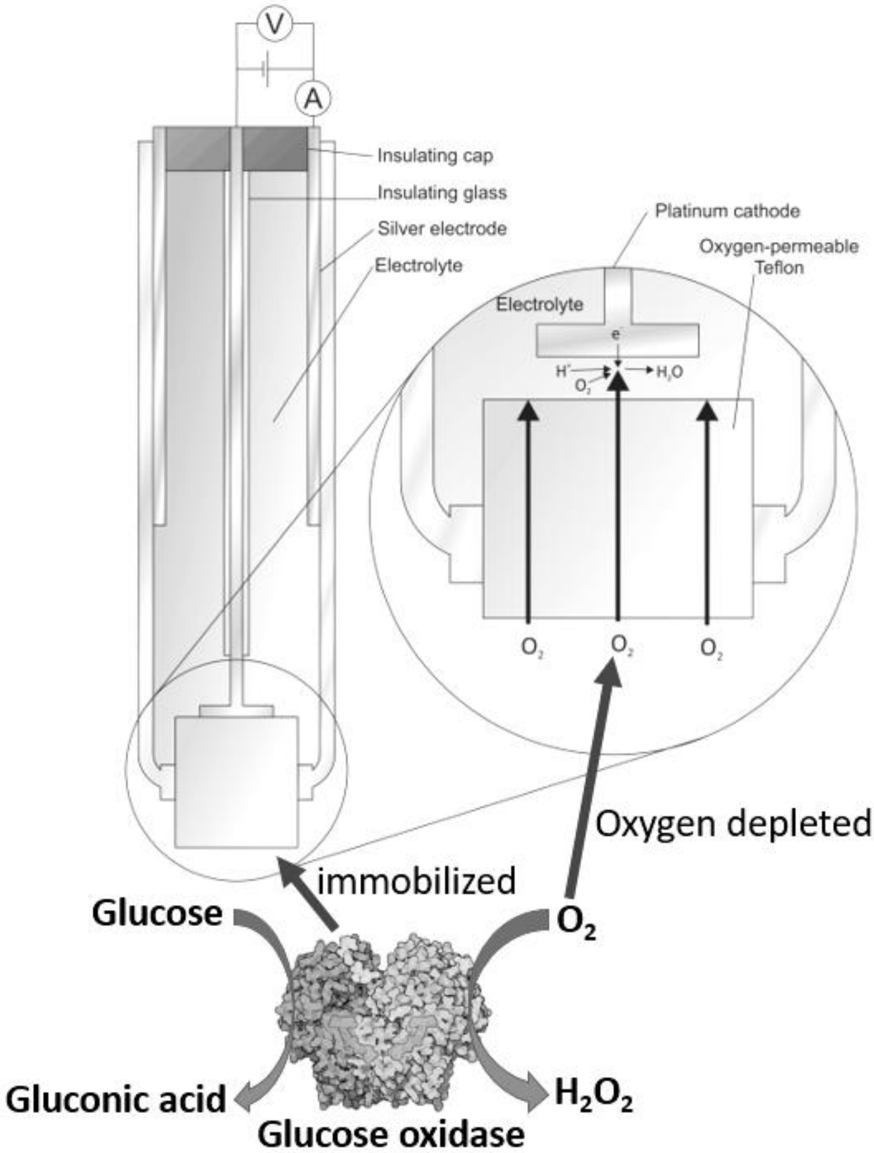

Figure 2. Schematic presentation of the first glucose biosensor based on the O_2 Clark electrode with the glucose oxidase enzyme immobilized at the O_2-permeable membrane. Notably, immobilization of other oxidase enzymes (e.g., lactate oxidase) consuming oxygen in the enzyme-catalyzed reaction can result in other biosensors operating according to the same concept. Reproduced from [2].

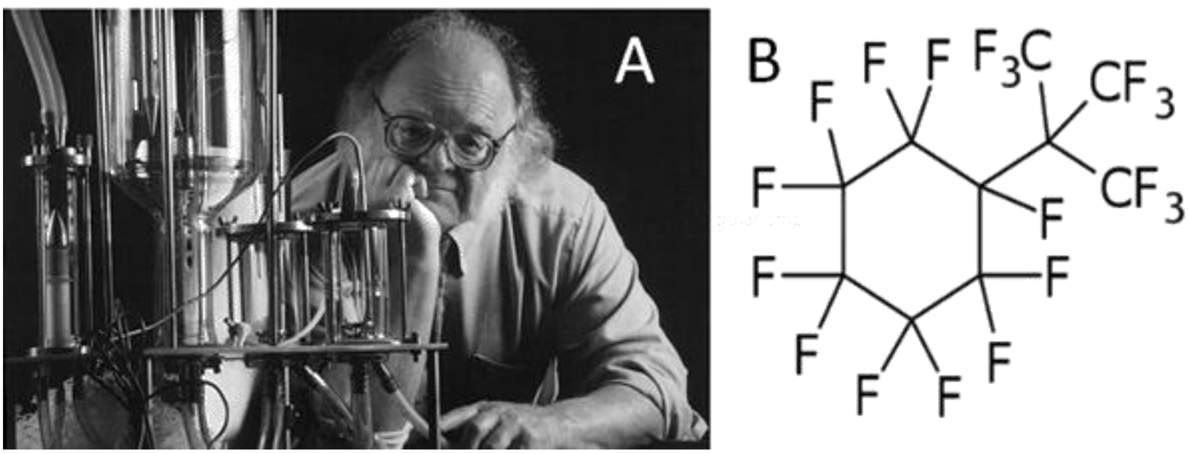

Figure 3. (**A**) Clark with a heart-lung machine. (**B**) Perfluoro *tert*-butylcyclohexane—artificial O_2 carrier claimed to carry oxygen with up to 5 times the efficiency of hemoglobin when used as an intravenous emulsion. Reproduced from [2].

Conflicts of Interest

The authors declare no conflict of interest.

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