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Review

# Enzymatic fuel cells: Recent progress

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ABSTRACT

There is an increasing interest in replacing non-selective metal catalysts, currently used in low temperature fuel cells, with enzymes as catalysts. Specific oxidation of fuel and oxidant by enzymes as catalysts yields enzymatic fuel cells. If the catalysts can be immobilised at otherwise inert anode and cathode materials, this specificity of catalysis obviates the requirement for fuel cell casings and membranes permitting fuel cell configurations amenable to miniaturisation to be adopted. Such configurations have been proposed for application to niche areas of power generation: powering remotely located portable electronic devices, or implanted biomedical devices, for example. We focus in this review on recent efforts to improve electron transfer between the enzymes and electrodes, in the presence or absence of mediators, with most attention on research aimed at implantable or semi-implantable enzymatic fuel cells that harvest the body's own fuel, glucose, coupled to oxygen reduction, to provide power to biomedical devices. This ambitious goal is still at an early stage, with device power output and stability representing major challenges. A comparison of performance of enzymatic fuel cell electrodes and assembled fuel cells is attempted in this review, but is hampered in general by lack of availability of, and conformity to, standardised testing and reporting protocols for electrodes and cells. We therefore highlight reports that focus on this requirement. Ultimately, insight gained from enzymatic fuel cell research will lead to improved biomimetics of enzyme catalysts for fuel cell electrodes. These biomimetics will mimic enzyme catalytic sites and the structural flexibility of the protein assembly surrounding the catalytic site.


**Contents**



## 1. Introduction

Fuel cells transform chemical reactivity into electricity by oxidising fuel at the anode and reducing oxidant at the cathode using noble metal catalysts, providing electrical power output for as long as sufficient fuel and oxidant are available. Biofuel cells (BFCs) are low-temperature fuel cells that harness biological catalytic reactions, in place of metal catalysts in traditional low-temperature fuel cells, to generate electricity from electrolysis of fuel and oxidant. Due to nature's versatility, BFCs are not limited to use of hydrogen or methanol as a fuel, and can derive electrical power from a wide range of organic substrates. BFCs can be classified into those which utilise living cells (bacteria, algae) and those which utilise catalysts extracted from cells (enzymes, enzyme cascades and, more recently, mitochondria) as biological catalysts.

The use of living cells as catalysts in microbial fuel cells (MFCs) is an area that has received increased attention over the past decade, because of applications related to conversion of biomass into electricity [1–13]. Although MFC technology is unlikely to rival the more cost-effective biogas production technology via

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anaerobic digestion for large scale systems, niche applications for MFCs are emerging. For example, these microbial fuel cells have been proposed for application to providing power to devices deployed in remote regions or environments, such as marine deployed sensors [5]; to combine waste treatment or polishing by microbial anaerobic digestion with extraction of electrical power [1,3]; to act as self-powered bio-indicating sensors, for example for application to real-time monitoring of $BOD_5$ levels in wastewater treatment plants [9]. Furthermore microbial electrochemical systems that use the voltage of a waste (fuel)-oxidising microbial anode to offset electric power required for electrolytic production of value-added chemicals such as hydrogen, show potential [7].

Enzymatic fuel cells (EFCs) have been proposed that can catalyse oxidation of fuels at anodes and/or reduction of oxidants at cathodes to provide electrical power. Full EFCs have enzyme catalysts at both anode and cathode, whereas hybrid EFCs, where only one of the two electrodes are based on enzyme catalysis, whilst the other is based on traditional fuel cell or battery catalytic processes, have also been proposed.

Much attention has focused on proof of this concept and production of some prototype EFCs, because of advantages that the use of biologically derived catalysts can offer. These advantages range from the capacity to produce a wide range of catalysts based on sustainable (biological) processes, the versatility of the catalysts produced to oxidise/reduce a wide range of substrates under moderate conditions of pH and temperature, and the specificity of the catalytic reactions, permitting removal of separating membrane in some cases. Early EFCs sought to harness oxidation of in vivo glucose fuel, coupled to reduction of oxygen as oxidant, to power an artificial heart or to provide power to cardiac pacemakers [14]. It was soon realised, however, that power, and the stability of power output of the prototype devices could not match the battery technology that emerged during the 1970s for such applications. The recent resurgence in research activity in the area of EFCs is partly driven by progress in enzyme electrochemistry, particularly in terms of achieving higher, and increasingly stable, current densities at modified electrodes, and, in microelectronics, where ever smaller and lower-energy consuming devices are being manufactured. A potential application that has received much attention over the past decade is the development of miniature, membrane-less, semi-implantable EFCs to provide intermittent power to subcutaneously inserted glucose monitors that detect glucose levels in interstitial fluid over a period of several days [15–17]. Others have focused on the potential for EFCs to provide power to portable electronic devices [18,19].

Regardless of the intended application, the factors affecting cell voltage, current density, power density and operational stability of EFCs must be further investigated before commercial applications can be realised. Indeed, whether or not EFCs will ever meet the operational and cost requirements to compete in the marketplace remains open to debate. Nonetheless EFC research will aid in providing new insights into redox enzyme structure-activity and stability in solution and at surfaces, surface and immobilisation chemistry, and enzyme electrode electrochemistry and contribute to our fundamental understanding of catalysis, permitting future applications using biomimetics to be exploited.

This review is intended to provide a selective overview of challenges and recent developments in EFC research. Comprehensive reviews focused on EFCs, and aspects of EFC research, are available [15,20–31]. We focus here on research and challenges associated with development of miniaturised glucose oxidising, oxygen-reducing EFCs. Developments, focused on using other fuels, such as hydrogen, alcohols or other sugars, or oxidants will not be considered in detail.

## 2. Enzymatic fuel cells

A fuel cell in its most simple form consists of fuel and oxidant continuously passed over two electrodes: a fuel oxidising anode, and an oxidant reducing cathode connected to each other by an external load and separated by an electrolyte. Chemical fuel cells rely on non-selective metal catalysts, such as platinum and its alloys, to effect fuel oxidation and oxidant reduction. Recent fuel cell research focuses on the search for catalysts that are not as prone as platinum to de-activation through surface poisoning, on minimising catalyst loading to reduce costs, and on electrolyte properties to prevent fuel-oxidant crossover between half-cells [32,33]. In EFCs biological catalysts (enzymes) are used for fuel oxidation at the anode and oxidant reduction at the cathode. Appropriate choice of enzyme allows such reactions to occur under relatively mild conditions (neutral pH, ambient temperature) compared to conventional fuel cells. In addition, immobilisation of enzyme catalysts that are specific for a reaction (or class of substrate) on otherwise electrocatalytically inert electrodes such as carbon, can eliminate the need for separator and housing components required for conventional fuel cells [17]. Due to the exclusion of such components, enzymatic fuel cells have the capacity to be miniaturised, and consequently, micrometer dimension membrane-less EFCs have been developed [17,34–36].

The power output of an EFC is the product of the cell voltage and the current. Cell voltages depend on the fuel and oxidant selected, the rate of electron transfer, the current flowing, resistances within the cell (Ohmic losses) and mass transport processes. For example, the thermodynamic reversible cell voltage for the complete oxidation of glucose to carbon dioxide and water, Eq. (1), can be estimated as 1.24 V at 298 K, from standard Gibbs free energies of formation of all components in the reaction. This is the maximum cell voltage, under standard conditions, expected from an EFC displaying 100% coulombic efficiency with no overvoltages or ohmic losses. Whilst some effort has been focused on assembling multiple enzymes at the anode of an EFC to provide for extraction of up to 24 electrons from glucose [37–43], most EFC research has focused to date on use of a single enzyme at the anode to oxidise glucose to gluconolactone, Eq. (2), providing only 2 electrons per mole of glucose and a maximum reversible cell voltage of 1.18 V. The maximum cell voltages for EFCs are usually determined by the difference between the formal redox potentials ($E^{\circ\prime}$) of the redox enzyme cofactors, in the active site, utilised for the anode and cathode, depicted in the scheme in Fig. 1.

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O \quad (1)$$

$$C_6H_{12}O_6 + 1/2O_2 \rightarrow C_6H_{10}O_6 + H_2O \quad (2)$$

### 2.1. Enzyme electron transfer

Redox enzymes consist of an apoenzyme (the protein component of an enzyme) and cofactor(s): small nonproteinaceous electroactive species. The presence of the cofactor ensures electron transfer between enzyme and substrate/co-substrate. The cofactor can be tightly bound within the enzyme structure or released from the enzyme active site during the reaction. Common cofactors for glucose-oxidising enzymes include flavin adenine dinucleotide (FAD), nicotinamide adenine dinucleotide (NAD) and pyrroloquinoline quinone (PQQ) (Fig. 2).

For some redox enzymes that possess tightly bound cofactors in the active site electrons can be transferred directly from the enzyme to the electrode, as depicted in Fig. 3A, in a process referred to as direct electron transfer (DET). Although direct electron transfer has been reported on for a wide range of enzymes [21,28,44–46] several challenges need to be overcome to achieve significant rates of direct electron transfer, leading to appreciable current densities,