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Metal nanostructures for non-enzymatic glucose sensing

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ABSTRACT

This review covers the recent development of metal nanostructures in electrochemical non-enzymatic glucose sensing. It highlights a variety of nanostructured materials including noble metals, other transition metals, bimetallic systems, and their hybrid with carbon-based nanomaterials. Particularly, attention is devoted to numerous approaches that have been implemented for improving the sensors performance by tailoring size, shape, composition, effective surface area, adsorption capability and electron-transfer properties. The correlation of the metal nanostructures to the glucose sensing performance is addressed with respect to the linear concentration range, sensitivity and detection limit. In overall, this review provides important clues from the recent scientific achievements of glucose sensor nanomaterials which will be essentially useful in designing better and more effective electrocatalysts for future electrochemical sensing industry.

1. Introduction

Diabetes mellitus is a group of metabolic diseases caused by high level of blood glucose in the body over a prolonged period. It is one of the primary causes of disability and mortality, as well as highly responsible for complications such as heart disease, amputation, renal failure and blindness. Globally, there are more than 220 million people affected by diabetes and the number of diabetic patients is projected to double within the next 20 years [1]. Its growing prevalence is certainly to be one of the most challenging health problems in the 21st century. So far, glucose control in diabetic patient is managed by regular monitoring of blood glucose to reveal individual patterns of glucose metabolism in the body, so that their treatment can be adjusted in order to achieve optimal glucose control. Therefore, it is of significant importance to develop a rapid, sensitive and reliable glucose sensor to monitor the blood glucose level with the aim of reducing the risk of disease complications.

The fifty years of glucose sensor progress can be summarised into three generations (Fig. 1) The first enzymatic glucose sensor was demonstrated by Clark and Lyons in the 1960s using glucose oxidase (GOx) enzyme [2]. GOx was immobilized over an oxygen electrode and the oxygen consumption by the enzyme-catalyzed reaction was monitored. This was further followed up by Updike and Hicks [3], and subsequently, Guilbault and Lubrano developed another glucose sensor for measuring blood glucose based on the hydrogen peroxide detection [4]. The first generation glucose sensors were then based on the oxidation of glucose by oxygen, catalyzed by the active component of GOx (i.e. flavin adenine dinucleotide) to yield the redox product of glucolactone and hydrogen peroxide. However, the major limitations of the first generation enzymatic glucose sensors are the strong dependence on oxygen and the co-existence of redox-active interference species in the blood. The second generation glucose sensor was introduced in the 1980s [5,6], making use of mediators to facilitate electron transfer. However, owning to the potential biotoxicity of mediators, the second generation glucose sensor is limited for in-vivo operation. Moreover, the presence of other redox-active species potentially competes with the mediators and thus affects the accuracy of the glucose sensor. The third generation of glucose sensor was introduced to remove the use of the mediator and its function was based on the direct transfer between the enzyme and the electrode. The significant lower operating potential minimises the electroactive species interferences. However, due to its relatively smaller linear range of the third generation in comparison to the first and second generation glucose sensors, further development of glucose sensor is highly desirable.

1.1. Non-enzymatic glucose sensing

Over the last five decades, enzymatic glucose sensors have prevalently dominated the glucose sensing research and development as well as the glucose sensing industry. However, there are a number of shortcomings associated with enzymatic glucose sensors that hinder their further development. Examples include complicated enzyme immobilization procedures, critical operating conditions such as optimum temperature, humidity and pH, and chemical instability [7]. Furthermore, enzymatic glucose sensors have short shelf life owning to the intrinsic nature of the enzymes and generally they are only allowed for single use. These limitations result in high fabrication cost and become

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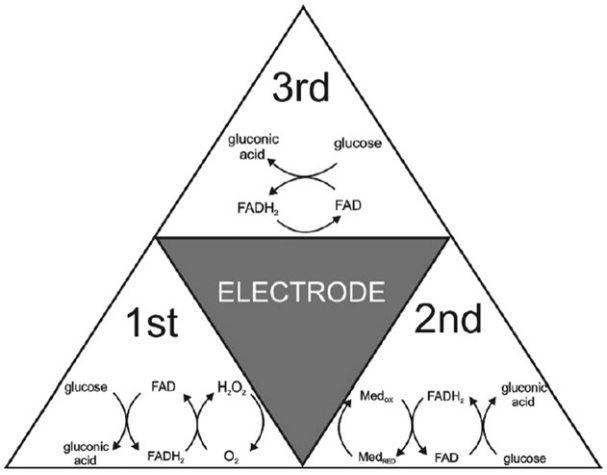

Fig. 1. Schematic illustration of enzymatic glucose oxidation mechanism for first, second and third generation biosensors.
Reproduced with permission from [102].

challenging for the accelerating number of diabetic patients, particularly in the developing countries. In recent years, much research has centered on the non-enzymatic glucose sensors to alleviate the limitation of enzymatic glucose sensors. The rapid advancement in nanoscience and nanotechnology has introduced new innovative approaches for the development of non-enzymatic glucose sensors. A number of nanostructured electrocatalysts such as metals, bimetallic systems and their hybrid with carbon-based nanomaterials were chosen to study and develop as non-enzymatic glucose sensors. These nanostructured materials in glucose oxidation has established themselves as an important tool in non-enzymatic glucose sensing due to their unique capabilities to enhance mass transport and sensing performance with high effective surface area [8–11]. Herein, this review attempts to highlight the important advancement in the development of various metal nanostructures in glucose sensing including noble metals (Au, Pd, Pt), other transition metals (Ni, Cu), bimetallic systems, and their hybrid with carbon-based nanomaterials. In this aspect, more attention is devoted to the tailoring of the particle size, shape, surface morphology of nanostructured materials and their glucose oxidation activity. These studies provide important clues on the recent progress of glucose sensor nanomaterials and also can be very useful in the process of designing better electrocatalysts in the future.

1.2. Electrochemical glucose sensing

There are several detection methods that have been developed for glucose sensing including electrochemistry, colorimetry, conductometry, optical rotation, and fluorescent spectroscopy [7]. Of these, majority of the electrochemical glucose sensors are based on the electrochemical techniques because of their simplicity, selectivity, and portability. Moreover, electrochemical techniques show low detection limit, rapid response time, excellent stability and low cost [7,12]. Today, electrochemical sensing for the monitoring of glucose concentration is mostly operated in amperometric mode. During glucose measurement, a small drop of blood to be tested is placed on a disposable electrochemical test strip that contains electrodes (i.e. reference, working and auxiliary counter electrodes) while a fixed potential is applied at the working electrode. Glucose in the blood subsequently undergoes a chemical reaction with the enzymes immobilized on the electrode and current flows as electrons are produced while glucose is oxidized at the working electrode. In principle, these electrons generated are measured in the form of electric current (i.e. the charge passing through the electrode) and this is proportional to the glucose concentration.

2. Metal nanostructures for glucose sensing

Nanostructured metals have received tremendous interests because of their extremely small feature size, exhibiting superior properties compared to their bulk counterparts, thus making them suitable for a wide range of applications. The distinct superiority of the nanometer dimensions is the increase in surface area to volume ratio and the key benefit is that the percentage of surface atoms becomes significant. This is particularly advantageous in catalysis reactions because the increase in surface atoms can lead to an increase in reactivity of the material [13–15]. For this reason, nanostructured metals have thus received significant attention in multiple areas of research [16–19]. Likewise, application of nanostructured metals in electrochemical sensing has gained increasing popularity for the development of next generation non-enzymatic glucose sensors [20]. Metal nanostructures with controlled size, shape, architecture, and composition are very appealing considering that their physicochemical properties vary accordingly and thus their electrocatalytic glucose sensing performance [20]. Considerable attentions have been paid to the study of the correlation of metal nanostructures to their electrocatalytic properties to investigate mass transport and electron transfer kinetics for enhancing their performance [8–11,21]. According to the literature, most metallic nanomaterials for non-enzymatic glucose sensing are mostly focussed on the transition metals including the noble metals. Particularly, the use of the noble metal nanostructures (i.e. Au, Pd and Pt) and their bimetallic nanostructures for glucose sensing was widely studied due to their high catalytic activity (Table 1).

2.1. Noble metal nanomaterials

2.1.1. Gold

Nanostructured Au has attracted an enormous amount of interest for biological application and biosensing owning to their unique optical, physical and catalytic properties [22–26]. Particularly, nanostructured Au has demonstrated excellent performance for the electrochemical glucose oxidation. Kurniawan et al. studied the electrochemical sensing of glucose using Au nanoparticles (Nps) prepared by layer-by-layer deposition on thin Au electrodes [27]. The Au Nps sensor showed superior

Table 1
List of noble metal non-enzymatic glucose sensors. The table is presented with respect to electrode materials, sensitivity, linear range, limit of detection and publication year.

Electrode composition	Sensitivity ($mA\ mM^{-1}\ cm^{-2}$)	Linear range (mM)	LOD (μM)	Year	Ref.
Gold					
Au Nps	1.79×10^{-4}	0–8	0.05	2006	[28]
Au Nps	0.16	0–8	0.5	2006	[27]
Macroporous Au	0.0466	0.005–10	3.2	2008	[32]
Au nanowire array	0.309	1–10	50	2009	[30]
Au nanotube array	1.13×10^{-4}	1–42.5	10	2009	[29]
Au Nps	–	0.4–10.7	370	2009	[103]
Au particles/MWCNTs[a]	–	0.2–40	50	2014	[104]
Au Nps/graphene	4.56×10^{-3}	0.1–16	–	2015	[34]
Palladium					
Pd Nps/SWNTs[b]	1.6×10^{-4}	0.5–17	0.2	2009	[38]
Pd Nps/CNTs	0.0114	0–46	–	2010	[36]
Pd Nps/graphene	0.0312	0.001–1	0.2	2011	[105]
Pd Nps/graphene	–	0.01–5	1	2011	[35]
Pd Nps/graphene oxide	–	0.2–10	–	2012	[39]
Platinum					
Pt nanotube arrays	1×10^{-4}	2–14	1	2005	[43]
Pt Nps	0.1377	0.2–3.2	5	2007	[106]
Nanoporous Pt	0.642	0.1–1.5	–	2008	[107]
Pt 3D dendritic structure	0.0121	1–20	1.2	2013	[44]
Pt nanoflower	0.011	1–7	–	2014	[47]
Pt Nps/graphene	6.36×10^{-3}	0.01–12.55	1	2015	[46]

List of abbreviations: a — multi-walled carbon nanotubes, b — single-walled carbon nanotubes.