Application of core-shell materials in glucose detection

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Abstract. The development of materials science can make people control material composition morphology through various means. The Core-shell nanoparticles is one of them. According to the adjustment of the shell and the core in a reasonable manner, we were able to prepare different kinds of personalized function materials. Therefore, it has a wide range of application in various fields. This paper focuses on the subdivision of glucose detection, and discusses the successful application of composite core-shell nanoparticles of metal materials and non-metal materials in glucose detection, as well as some existing problems that still need to be solved.

1. Introduction

As an essential energy substance for human survival, glucose has been widely used in food industry, biotechnology and other fields. Meanwhile, as one of the most important physiological indexes in human body, the research on glucose detection has been a hot spot in the sensor field[1]. With the continuous development of intelligent devices, people hope to detect glucose anytime and anywhere through a series of sensing devices, which puts forward higher requirements on the performance of sensors. The Common glucose sensors include electrochemical type, fuel cell type, optical type and so on. This paper mainly discusses the glucose sensor prepared by electrochemical method.

Glucose sensors based on electrochemical technology can be divided into enzymatic and non-enzymatic, the enzymatic has experienced three generations so far. The general principle of the three generation of enzymatic sensors is shown in Figure 1. The first generation of enzymatic sensor, invented by Clark et al., measured the amount of oxygen consumed by glucose oxidation or the

![Diagram of three generation enzymatic sensors](image)
amount of hydrogen peroxide generated. They were able to measure glucose in the blood by attaching glucose oxidase (GOx) to a platinum electrode[2], and the susceptibility of oxygen content to interference and the instability of hydrogen peroxide led to the advent of a second generation of enzymatic sensors. The second generation of sensors, using small molecules as electronic media, converts the change of substance content into the change of induced current on the electrode surface, and overcomes the interference caused by unstable dissolved oxygen and excessively high potential of hydrogen peroxide[3]. In order to further accelerate the reaction rate, the third generation of enzymatic sensor tries to make the active center of the enzyme directly contact with the electrode, so as to directly transfer electrons between GOx and the electrode surface. However, in either case, the issue of biocompatibility between electrodes and enzymes remains a challenge, as inactivation of the enzyme can lead to the failure of the sensor.

In the past half century, nanomaterials have developed rapidly, and their surface effects at the nanoscale have provided many interesting properties, including high specific surface area, etc. It brings great research potential for non-enzymatic electrochemical glucose detection[4]. The non-enzymatic electrochemical detection method can directly oxidize glucose on the electrode surface and generate a response current, which overcomes the high cost of maintaining enzyme activity. At the same time, with the continuous improvement of the synthesis process, some nanomaterials have realized controllable synthesis of size, shape and other properties, which has significant advantages in performance, sensitivity and selectivity. As one of the typical structures, core-shell materials have been widely used in sensing field, especially nano core-shell materials. According to the different composition of the core-shell material, it can be divided into inorganic and organic compounds, and there are four combinations. As more welcome is paid to functional nanomaterials with better properties, core-shell materials have gained more attention due to their diverse composition and synergistic effect. Moreover, core-shell material is also a kind of high-function material that can be flexibly controlled. Different composition and even different shape can produce very different characteristics. The synthesis and application of core-shell materials have been discussed in many literatures, but the application of glucose detection is rarely mentioned. Based on the research on the application of core-shell materials in glucose detection, this paper expounds the application progress and existing problems of core-shell materials in glucose detection, and looks forward to the future development direction.

2. Research on glucose sensor based on core-shell structure

At present, the electrode materials based on core-shell structure and used for glucose detection are mainly inorganic materials, and the inorganic materials are mainly metal materials. Meanwhile, a series of core-shell materials based on metal derivatives also have good performance. The results of these studies are described below. Among them, precious metals, such as platinum, were first used in the study of glucose sensor by Clerk et al., while precious metals also accounted for a certain proportion in the study of non-enzymatic glucose sensor. Kang et al. constructed a trimetal Au@PdPt core-shell structure with octahedral shape, in which not only a clear octahedral core was formed, but also a highly crystallized dendritic Pd-Pt shell, which had a good catalytic effect on the oxidation of organic matter[5]. And Wang et al. synthesized three Pd@Pt core-shell materials (octahedron, dodecahedron and cube) with different morphology to explore the influence of morphology on the catalytic oxidation of glucose in...
core-shell materials, and found that the Pd@Pt core-shell structure with octahedron morphology had relatively better catalytic performance[6].

In addition to precious metals, transition metals are more widely used in non-enzymatic glucose sensors. The transition metals are cheap, and the coupling reaction of transition metals represented by nickel and cobalt with glucose and the catalytic reaction of glucose are more sensitive than that of gold and platinum, so some researchers use transition metals or combine them with precious metals to form the core-shell electrode of composite materials. For example, Gao et al. prepared Au@Ni spherical gold nanoparticles with core-shell structure by reducing metal precursors with oleamide, which were resistant to interference of intermediates such as chloride ions, with a linear range width of up to 9.5 mM and a low detection limit of about 0.016 mM[7]. In another group of similar studies, Chen et al. used polyacrylamide as a reducing agent to deposit thin gold shells on the surface of copper with a three-dimensional structure with nanopores, which showed strong selectivity and stability[8]. Wang et al. prepared an Au@NiCo bell-shaped composite material, which is a hollow core-shell structure. The porous shell enables it to rapidly transfer reactants and products, which also enables its detection limit to reach an extremely low 0.028 uM, with a linear range width of about 12 mM, and a sensitivity of 864.7 μA mM⁻¹ cm⁻²[9]. Wu et al. constructed Cu@Ni core-shell nanostructures and introduced reduced graphene oxide (rGO) as a substrate, providing high electrical conductivity and a larger specific surface area[10]. Experiments have shown that this sensor has good sensing performance and glucose specific selectivity. The research on transition metals and composite materials with different core-shell morphology is still going on and there are still many problems to be solved. Performance data for all glucose sensors listed above are summarized in Table 1.

| Electrode Composition | Sensitivity (μA mM⁻¹ cm⁻²) | Linear range (mM) | LOD (μM) (S/N=3) | Response time (s) |
|-----------------------|-----------------------------|-------------------|------------------|------------------|
| Au@PdPt               | -                           | -                 | -                | -                |
| Pd@Pt                 | -                           | 0.25-6, 6-20       | 20.4             | -                |
| Au@Ni                 | 23.17                       | 0.5-10            | 0.0157           | 3                |
| Au@NiCo               | 864.7                       | 0.005-12          | 0.028            | -                |
| Au@3D porous Cu       | -                           | 1-24              | -                | -                |
| Cu@Ni/rGO             | 780                         | 0.001-4.1         | 0.5              | 3                |

2.2. Core-shell structure based on metal derivatives

Metal derivatives are also of great significance in the study of glucose sensing. Some researchers have found that the synergistic catalytic effect between metal oxides in composite binary nanocrystalline core-shell materials can significantly improve the electrocatalytic activity. In the study of Le et al., for example, they were prepared on stainless steel electrode with polyaniline as support material of Cu@CuO core-shell structure, with common distractors anti-interference (such as ascorbic acid maltose, etc.), and also has 25710 μA mM⁻¹ cm⁻² of high sensitivity, showing the metal and its oxide composite core-shell structure in the potential of the glucose sensing[11]. In Ding et al. ’s study, CuO@Co₃O₄ core-shell nanowires were constructed based on a stepwise synthesis method, in which the shell also has the characteristic of organic-metal frame (MOF)[12]. The glucose sensor prepared with this type of material has sensitivity up to 27778 μA mM⁻¹ cm⁻² and detection limit as low as 0.036 uM, and it has obvious advantages over the core-shell materials with only metal oxides. In addition to oxides, nitride has also been found to be useful in electrochemical applications, such as supercapacitors and lithium-ion batteries. The nitrides of some metals have potential for catalytic activity and are highly conductive, In the study by Deepalakshmi et al., they constructed a nitride nickel-cobalt core-shell nanostructure, modified with nitrogen-doped graphene, with a lower detection limit of 0.05uM, a wider linear range (2.008 μM-7.15 mM), and a sensitivity of 1803 μA mM⁻¹ cm⁻²[13]. Similarly, the role of metal sulfides in electrocatalysis has been gradually recognized by scholars. For example, copper sulfide, cobalt sulfide and other materials show excellent properties
similar to nitride in conductivity and stability, and have also been applied in the fields of supercapacitors. Yu et al., constructs the composite electrode include CuS nanoparticles with glassy carbon electrode (GCE), and glucose in surface oxidation mechanism was discussed[14]. Kannan and others to build the core-shell structure of Ni₃S₂/NiMoO₄ nano flake, among them, the presence of NiMoO₄ makes Ni₃S₂ has larger active surface area and more active site, the composite electrode showed strong selectivity, low detection limit and to 0.055 uM[15]. Some of the data referenced in this section is shown in Table 2.

Table 2. List of metals and their derivatives glucose sensors.

| Electrode Composition | Sensitivity (uA mM⁻¹ cm⁻²) | Linear range (mM) | LOD (uM) (S/N=3) | Response time (s) |
|-----------------------|---------------------------|-----------------|----------------|------------------|
| Cu@CuO                | 25710                     | 0.1-5           | 0.1             | -                |
| CuO@Co₃O₄             | 27778                     | 0.0001-1.3      | 0.036           | 1                |
| N-doped Ni/Co/N-doped graphene | 1803 | 0.002-7.15 | 0.05 | 3 |
| Ni₃S₂/NiMoO₄          | 10.49                     | -               | 0.055           | 1                |

2.3. Core-shell structure based on the mixture of non-metal and metal

In addition to the synergistic effect of multi-metals or multi-components to promote the electrocatalytic performance of the core shell materials, the shell protection of the metal core under relatively harsh external environment is also an important role. The test results in the references cited in this section are shown in Table 3.

Table 3. List of metallic and non-metallic glucose sensors.

| Electrode Composition | Sensitivity (uA mM⁻¹ cm⁻²) | Linear range (mM) | LOD (uM) (S/N=3) | Response time (s) |
|-----------------------|---------------------------|-----------------|----------------|------------------|
| Cu@C                  | 2565                      | 0.04-40         | 21.35           | -                |
| Ag@C                  | 24.65                     | 0.05-2.5        | 20              | -                |
| TiO₂/C                | 975.3                     | 0.001-7.658     | 0.6             | -                |
| NiO@C                 | 31370                     | 0.002-1.279     | 2               | -                |

Ye et al. constructed the Cu₂O@PVP precursor with the help of polyvinylpyrrolidone (PVP), and then obtained the Cu@C core-shell material after high temperature annealing, which has a wide linear range (0.04 mM-40 mM) and a high sensitivity (2565 uA mM⁻¹ cm⁻²). Meanwhile, it also has a good performance in the detection of human serum[16]. Zhou et al. prepared Ag@C core-shell nanostructures by wrapping silver particles in colloidal carbon. It is worth mentioning that this study focuses on the enzymatic glucose sensor. This design helps to fix the enzyme on the electrode and maintain its activity, which proves the good biocompatibility of nanocarbons[17]. Although non-enzymatic sensors are mainly discussed in this paper, enzymatic sensors are still the main commercially available products at the present stage. Therefore, the structure of this core-shell structure is also significant for the development of glucose sensors, and its detection limit is as low as 0.02mM, and it also has good long-term stability. Similarly, Wang et al. constructed TiO₂/C-based core-shell nanomaterials as the substrate and deposited Ni and Co nanoparticles in the form of alloy[18]. While taking full advantage of the strong conductivity of the substrate, they effectively avoided the aggregation of alloy particles on the surface and maintained the enzyme activity. The performance of non-enzymatic sensor in this field is also expected, Cui et al. prepared the precursor Ni(OH)₂/C by hydrothermal method, and obtained the NiO@C core-shell material by calcination. Its sensitivity for non-enzymatic glucose sensing is as high as 31370 uA mM⁻¹ cm⁻², and it also could resist common interferences such as sodium chloride, amino acids, ascorbic acid, and urea[19].
3. Conclusion
In recent years, there have been more and more studies on non-enzymatic glucose sensing, and researchers from all over the world are sparing no effort to use any possible material to improve glucose sensing performance, such as sensitivity, linear range, selectivity, detection limit, etc. In this paper, a series of applications of core-shell materials in the subfield of glucose sensing are reviewed, and the electrocatalysis of core-shell nanoparticles with different morphology prepared by intermetallic and intermetallic and non-metallic composites is discussed. Compared with the single electrocatalyst, core-shell material has become a promising nano-electrocatalytic material due to its advantages in plasticity and synergetic effect properties. Core-shell materials have strong catalytic ability to glucose, and some of them have high sensitivity. Core-shell materials have broad application prospects and development potential. In the future, they are likely to be more widely used in glucose sensing, until glucose sensors that can be used in real life scenarios can be developed. However, at present, not only the sensors prepared by core-shell materials, but also the non-enzymatic glucose sensors prepared by other methods or technologies have many problems in practical clinical application. Firstly, the technical parameters of the sensor tested using buffer or human serum in a laboratory environment cannot be directly transferred to actual use, from laboratory research and development to the realization of industrialization of this process, there are still many great uncertainty challenges. Secondly, as far as the properties of core-shell materials themselves are concerned, the interaction between core-shell and its specific influence on the electrocatalytic properties are still unclear. There is a ligand effect between core and shell, which will cause changes in the distribution of external charges of different metals, which may affect the electron layer structure of d-band, thus affecting the catalytic process. Nevertheless, researchers do not have a complete understanding of the behavior patterns of electrocatalysis affected by the changes in the core shell materials, and there are still some differences to be resolved. Core-shell materials provide a large imagination space for the future development of glucose sensing, and promote the industrialization of non-enzymatic glucose sensors prepared by core-shell materials and other means, which comes from the unremitting efforts of outstanding scholars all over the world who pay attention to this field.

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