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厦门大学

博 士 学 位 论 文

高性能电化学葡萄糖传感器的构建与研究

The study of electrochemical glucose sensor with high performance

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摘要

葡萄糖浓度的定量分析无论是对临床诊断，还是生态工程等众多领域均有至关重要的意义。尤其在临床方面，糖尿病已成为当今社会仅次于癌症和心脑血管疾病的第三大多发性疾病，特别的是由其可引出多种危害较大的并发症。每年糖尿病患者的数目都在不断增加，尤其是我国的糖尿病患者增速不可忽视。尽管没有完全治愈的方法，但是患者通过实时检测葡萄糖浓度可以有效避免并发症的发生。因此，开展快速精确实时地检测葡萄糖浓度的研究十分迫切。

电化学葡萄糖传感器凭借其特有的优势在众多检测技术中倍受青睐，但是无论是已商业化的酶传感器还是研究很热的无酶传感器，都有着各自的应用缺陷，综合性能都有不尽如人意的地方。对于经典酶传感器来说，易受氧浓度变化影响进而干扰检测结果准确性，并且无法实现稍高浓度葡萄糖的检测，受到酶的本身属性限制，传感器的重现性及稳定性差；对于无酶传感器来说，尽管可以避免酶电极的缺陷，研究越来越热，但也存在待改进的地方。其敏感材料主要的问题有：贵金属成本高并易于氯离子中毒失活，其他金属成本低但不稳定，金属氧化物稳定但灵敏度低，且无论是哪种敏感材料由于对于葡萄糖没有特异的专一性，无酶传感器的选择性较差，易受其他分析物质干扰。因此大部分的研究都是围绕如何改善传感器性能展开的。在本论文中我们主要是围绕敏感材料及材料与基体之间的固定方式这两方面展开探索研究，来改善电化学葡萄糖传感器的催化性能。

(1) 对于酶传感器来说，我们采用包埋法将葡萄糖氧化酶通过 PVP 包埋后固定于经拓扑绝缘体 Bi_2Te_3 改性过的玻碳电极上构建了酶电极。借助于拓扑绝缘体 Bi_2Te_3 特有的表面金属态，该特点有助于改善电子传输能力，该修饰电极在对葡萄糖进行检测时有效改善了酶电极易受氧浓度干扰这一问题，即使是在葡萄糖浓度高达 4 mM 时也呈现了 33.22 uA $mM^{-1}cm^{-2}$ 的灵敏度。而 PVP 包埋葡萄糖氧化酶后在增加酶与电极之间的作用的同时保持了酶的活性进而改善了酶电极的稳定性，该修饰电极即使是在经过近一个月的测试时，最终的电流信号也可保持在初始信号的 89%左右。

为了改善无酶传感器的综合性能，我们做了以下研究：

(2) 用简单的溶剂热法制备了形貌均匀的微球结构的多组分的 Ni-Mn 氧化物，并以其为敏感材料构建了无酶葡萄糖传感器。受益于镍系及锰系材料之间的协同作用，该传感器比很多已报道的单一的基于镍系或锰系材料的传感器来说催化效果更好，在+0.4V 的低电压下即可对葡萄糖实现高灵敏的检测，有效避免了其他分析物质的干扰，提高了传感器的选择性，特别是在人体血清样本分析中呈现了高的准确度。

(3) $NiMoO_4$ 具有钼酸盐的高的电导率同时具备 Ni 基高的催化活性，而且较贵金属经济，是无酶电化学葡萄糖传感器理想的敏感材料。将 $NiMoO_4$ 作为敏感材料构建了无酶电化学葡萄糖传感器，这也是 $NiMoO_4$ 在葡萄糖检测方面的首次探索。受益于 $NiMoO_4$ 各组分的协同作用，该传感器改善了无酶电化学传感器中贵金属所带来的高成本，金属氧化物所遇到的低灵敏度等问题，在葡萄糖浓度为 0.05 mM 到 14 mM 的如此宽的线性范围内呈现出了高达 389.9 uA mM^{-1} cm^{-2} 的灵敏度，低至 0.36 uM 的检测限，并且对葡萄糖的选择性极好，在实际血清样本分析中准确度较高。

(4) 我们从敏感材料及材料与基体之间的固定方式这两方面综合考虑探究改善无酶传感器的综合性能。传统的滴涂法虽说适用范围广，但是材料与电极之间的作用较弱，不利于传感器性能的提升。而基体生长法在增强两者之间的相互作用时，亦可减小接触电阻，进而有助于改善传感性能。考虑到碳纤维布的高电导率及良好的生物相容性，$NiCo_2O_4$ 高的电导率及葡萄糖催化活性等因素，我们以碳纤维布为基体生长 $NiCo_2O_4$ 纳米线阵列直接构建无酶电化学葡萄糖传感器。受益于 $NiCo_2O_4$ 纳米材料本身特点，基体生长优势及纳米线阵列特有的利于电子及质子传输的结构这几方面的综合作用，在进行葡萄糖检测时该传感器的灵敏度居然可以高达 6.027 mA mM^{-1}。

关键词：葡萄糖检测；电化学分析；酶电极；无酶传感器

Abstract

Quantificational glucose detection is very important not only to clinical diagnosis but also to other various ecological fields. Worldwide, diabetes has become the third multiple diseases behind cardiovascular diseases and cancer, which also leads to serious complications. The number of diabetes is growing from year to year, especially in our country, the growth rate has not been ignored. There is no cure for diabetes, but patients can reduce disease associated complications through the tight control of blood glucose level. Hence, how to reliably and fast detect glucose has always been an urgent task.

Electrochemical glucose sensor with its unique advantages has been a focus among various detection mechanisms. But the overall performance of electrochemical glucose sensor can't meet the demands whether for enzymatic biosensors or for non-enzymatic biosensors. Enzymatic biosensors are vulnerable to oxygen concentration, which will interfere the accuracy of result and can't detect high glucose concentration. Enzymatic biosensors also have trouble with the stability and reproducibility, caused by inherent properties of enzyme. Though non-enzymatic biosensors can avoid the disadvantages of enzymatic biosensors and have been extensively researched in recent years, there is also a lot to be improved. The main questions of sensing materials for non-enzymatic glucose detection are: noble metals suffer from the high cost and poisoning caused by Cl^{-1}, transition metals with relatively low cost suffer from the instability, transition metal oxides with good stability suffer from low sensitivity. No matter which sensing material, the non-enzymatic biosensors suffer from bad selectivity and are vulnerable to interfere from other analyses. Hence all the research has aimed at improving sensing property of sensors. In this thesis, we mainly explore the methods to improve sensing property of electrochemical glucose sensor based on sensing materials and the modified technique between the materials and substrates.

(1) The enzymatic glucose sensor has been fabricated by modifying the GCE with the topological insulator Bi_2Te_3 and GOD which has already been immobilized by PVP.

Benefiting from the excellent surface conductivity of the topological insulator Bi_2Te_3, which contributes to the electron transfer, the Bi_2Te_3-PVP-GOD modified electrode has effectively improved the problem caused by the change of oxygen concentration and shown the high sensitivity of 33.22 uA $mM^{-1}cm^{-2}$ as the glucose concentration is up to 4.0 mM. More importantly, the Bi_2Te_3-PVP-GOD modified electrode has also displayed the good stability, which is ascribed to the immobilized GOD by PVP, which is benefit to enhancement function between GOD and substrate and remain GOD active at the same time. After nearly 30-day test, the final electrochemical signal accounts for about 89% of its original signal.

To improve sensing property of non-enzymatic glucose sensors, the research work has been done as follow:

(2) The muti-component nanocomposite of nickel and manganese oxides with a uniformly dispersed microspheric structure has been fabricated through a simple solvothermal method and employed as sensing materials for the non-enzymatic glucose detection. Benefiting from a synergistic effect in muti-component nanocomposite of nickel and manganese oxides, the Nafion/Mn-Ni-oxide/GCE has shown higher catalytic activity towards the oxidation of glucose in comparison with previously reported Mn-contained or Ni-contained sensors and presented the high sensitivity at a low applied potential of +0.40 V (vs. SCE), which can be beneficial to avoid interfering from other analyses and display a good selectivity. Moreover the high precision has been obtained as detecting glucose in human serum samples.

(3) $NiMoO_4$ has been considered as one of the most promising candidates for non-enzymatic glucose detection due to the high conductivity of metal molybdates and high catalytic activity of the Ni towards glucose oxidation. A non-enzymatic glucose sensor based on the $NiMoO_4$ nanorods has been fabricated for the first time. Benefiting from synergistic effects in $NiMoO_4$, the $NiMoO_4$ modified electrode has improved the issue of the high cost from the noble metal and the low sensitivity from metal oxides, which has shown the sensitivity as high as 389.9 uA mM^{-1} cm^{-2}, the detection limit as low as 0.36 uM in the wide liner range from 0.05 mM to14 mM. More importantly selectivity

and practicality of the modified electrode have been confirmed, too.

(4) We have took sensing materials and the modified technique between materials and substrates into consideration at the same time to improve the sensing performance. Though the drop-casting method can be used for various materials, function between materials and substrates is relatively weak, which is against the improvement of sensing property. Direct growth on the substrate can not only enhance the function between materials and substrates but also minimum resistivity simultaneously, which is benefit to the improvement of sensing property. Combining the high conductivity and good biological compatibility of the carbon fiber cloth with the high conductivity and high catalytic activity of the $NiCo_2O_4$, the $NiCo_2O_4$ nanowires arrays are deposited on carbon fiber cloth to be directly used as a non-enzymatic glucose sensor. Benefiting from combined effect of the own features of $NiCo_2O_4$, the advantage of direct growth on the substrates and the unique path of nanowires arrays which is benefit to transferring the proton or electron, the $NiCo_2O_4$/CFC has shown a sensitivity as high as 6.027 mA mM^{-1} when detecting glucose.

Key words: Glucose detection; Electrochemistry mechanisms; Enzymatic sensor; Non-enzymatic sensor

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