Mesoporous silica-based materials for use in electrochemical enzyme nanobiosensors

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Biology and medicine have seen great advancements in the development of enzyme nanobiosensors capable of characterizing and quantifying biomolecules.

   We provide an overview of mesoporous silica (MPS)-based enzyme nanobiosensors developed for biological and medical applications, and we describe significant advances in these technologies.

   We review progress in constructing high-performance electrochemical enzyme biosensors. We also discuss:
- **WMCM-41 and SBA-15-modified and MPS composite electrodes for enzyme biosensing;**
- **incorporation of biorecognition elements into MPS material electrodes for enzyme biosensing; and,**
- **MCM-41 and SBA-15-supported electrocatalytic MPS-based electrochemical enzyme biosensors.**
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1. Introduction

1.1. Porous materials, concept, and classifications

Porous materials have attracted considerable attention since the 1960s because of their wide variety of scientific and technological applications. In its most generalized definition, the term ''pore'' means a limited space or cavity in a continuous material. Porous materials comprise from inorganic compounds (e.g., aluminosilicates) to biological membranes and tissues. According to the International Union of Pure and Applied Chemistry, pores are classified into three categories: micropores (<2 nm), mesopores (2–50 nm), and macropores (>50 nm).

Fundamental and applied research dealing with novel silica-based mesoporous materials aims to improve template-synthesis strategies, chemical modification of porous materials via molecular chemistry, construction of nanostructures of metals and metal oxides with controlled interior nanospace, reticular design of metal-organic frameworks (MOFs) with pore sizes ranging from the micropore to the mesopore scales, among others. Porous materials are useful (e.g., sensing, catalysis, shape-selective and size-selective absorption and adsorption of reagents, gas storage, and electrode materials) [1].

Because of the considerable variety of materials that can be classified as porous, several classifications can be proposed. Thus, according to the distribution of pores within the material, we can distinguish between regular and irregular porous materials, whereas, according to the size distribution of pores, we can distinguish between uniformly-sized and non-uniformly-sized porous materials.

From a structural point of view, porous materials can be viewed as the result of building blocks following an order of construction that can extend from cm to nm levels. Porous materials can range from highly-ordered crystalline materials (e.g., aluminosilicates or MOFs) to amorphous sol-gel compounds, polymers and fibers. This review focuses on materials that have porous structures.

Although it does not exhaust the entire range of porous materials, the list attempts

to cover those that can be described in terms of extended porous structures and whose electrochemistry has been extensively studied. In addition, since 1990, there has been growing interest in the preparation of nanostructures of metal and metal oxides with controlled interior nanospace, whereas a variety of nanoscopic porogens (e.g., dendrimers, cross-linked and core-corona nanoparticles (NPs), hybrid copolymers, and cage supramolecules) are currently subject to intensive research [2].

The most relevant characteristic of porous materials is the highly effective surface/volume relationship, usually expressed in terms of specific surface area (area per mass unit), which can be determined from nitrogen adsorption/desorption data. Different methods are available for determining the specific surface area (Brunauer-Emmett-Teller, Langmuir, and Kaganer), micropore volume (t-plot, as, and Dubinin-Astakhov), and mesopore diameter [3]. Table 1 summarizes the values of specific surface area for selected porous materials.

In recent years, more attractive possibilities have arisen by the development of various new silica materials with ordered structures. Compared to polymers, inorganic mesoporous material is an excellent support for molecular catalysts due to its excellent thermal and chemical stability. But highly hydrothermally stable mesoporous material has not only all the virtues of inorganic material but also a large specific surface area, well-defined tunable pore sizes and an adjustable hydrophobic or hydrophilic character, which provides great opportunities for immobilization of large catalytic species and catalytic conversion of bulky organic substrates [4]. One of the best-known newly discovered mesoporous silicas (MPSs) is the Santa Barbara Amorphous material, SBA-15, which is a structurally well-ordered mesoporous material with a narrow pore-size distribution of 1.5–300 Å. It has regular, cylindrical, ordered hexagonal pores, with a narrow pore-size distribution and large surface area [5].

There are a few papers about the modification and the application of SBA-15 with heteropolyacid [6,7]. SBA-15 was characterized by scanning electron microscopy (SEM), X-ray diffraction (XRD), and transmission electron microscopy (TEM). The X-ray pattern of SBA-15 prepared with poly (ethylene oxide)-block-poly (propylene oxide)-block-poly (ethylene oxide) ($EO_{20}PO_{70}EO_{20}$) (Pluronic P123) in Fig. 1 shows four well-resolved peaks that could be indexed as the (100), (110), (200), and (210) diffraction peaks associated with space group (p6mm) hexagonal symmetry. Three additional peaks appeared in the 2θ range 2.5–3.5° that could be indexed as the (300), (220), and (310) scattering reflections, respectively. The intense (100) peak reflected a d-spacing of 87 Å, which corresponded to a large unit cell parameter ($a = 90$ Å) [8,9]. As shown in Fig. 2, the TEM image of the Soxhleted SBA-15 confirmed that SBA-15 had a two-dimensional p6mm hexagonal structure with a well-ordered hexagonal array and a one-dimensional channel structure. The average distance between mesopores was estimated to be about 100 Å, which was consistent with that determined from XRD data [8].

SEM could be used to determination the size and the morphology of SBA-15, as shown in Fig. 3. SBA-15 images revealed that it comprised many rope-like domains with relatively uniform sizes.

1.2. Principles of biosensor function and electrochemical enzyme sensors

Since the first biosensors were reported in the early 1960s [10], there has been an explosive growth of research activities in this area [11–13]. Biosensors have seen a wide variety of applications primarily in two major areas, biological monitoring and environmental sensing. This review covers the recent, significant advances in biosensor technologies for the analysis of samples of biological and biomedical interest. It is not meant to be a comprehensive review, but rather a critical review, presenting a selection of the significant advances in the field of biosensors.

All molecule-based biosensors rely on highly-specific recognition events to detect their target analytes. The essential role of the sensor is to provide a suitable platform that facilitates formation of the probe-target complex in such a way that the binding event triggers a usable signal for electronic read-out. The minimal elements of any biosensor include a molecular recognition layer and a signal transducer that can be coupled to an appropriate read-out device. Enzymes are especially suitable for biosensing applications, because the base-pairing interactions between complementary sequences are both specific and robust.

Biosensors can be classified either by bioreceptor or transducer type. A bioreceptor is a biological molecular species (e.g., an antibody, an enzyme, a protein, or a nucleic acid) or a living biological system (e.g., cells, tissue, or whole organisms) that utilizes a biochemical mechanism for recognition. The sampling component of a biosensor contains a bio-sensitive layer. The layer can contain bioreceptors or be made of bioreceptors covalently attached to the transducer. The most common forms of bioreceptors used in biosensing are based on

(1) antibody/antigen interactions;
(2) nucleic-acid interactions;
(3) enzymatic interactions;
(4) cellular interactions (i.e. microorganisms, or proteins); and,
(5) interactions using biomimetic materials (i.e. synthetic bioreceptors).

For transducer classification, conventional techniques include: