Nanoparticles as biosensors components - a brief review

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Keywords: nanoparticles, biosensors.

Abstract

Biosensors are chemical sensors, in which recognition processes rely on biochemical mechanisms utilization. There are several kinds of nanoparticles that can be used as biosensors components. Most of them work as probes recognizing and differentiating an analyte of interest for diagnostic and screening purposes.

The probes are used to bind and signal the presence of a target in a sample by their color, mass, or other physical properties. This paper provides a brief description of the following nanoprobes: quantum dots, nanobarcodes, metallic nanobeads, silica nanoparticles, magnetic beads, carbon nanotubes, and nanopores.

1 Introduction

The most common definition of nanotechnology is that of manipulation, observation and measurement at a scale of less than 100 nanometers (one nanometer is one millionth of a millimetre). In biology and chemistry nanoscale operations are involved in the synthesis of inorganic, organic and hybrid nanomaterials for use in nanodevices, the development of novel nanoanalytical techniques, and the manipulation of biological molecules such as DNA and the evolution of molecular machines. This review is focused on the potential of nanotechnology in the developing and constructing artificial nanodevices, such as biosensors.

Biosensors consist of a biological element (responsible for sampling), and a physical element (transmitting sampling results for further processing) [1, 2]. The biological element of a biosensor contains a biosensitive layer, which can either contain bioreceptors or be made of bioreceptors covalently attached to the physical element. The type of biological element defines biological specificity conferring mechanism used. The physical element translate information from the biological element into a chemical or physical output signal with a defined sensitivity.

There are several kinds of nanoparticles that can be used as biosensors components. Most of them work as probes recognizing and differentiating an analyte of interest for diagnostic and screening purposes. In such applications biological molecular species are attached to the nanoparticles through a proprietary modification procedure. The probes are used then to bind and signal the presence of a target in a sample by their color, mass, or other physical properties. The other biosensors employ nanoparticles in a different way. They work as sieves through which charged molecules are transported in an electrical field.

In the next section a short description of nanoparticles used in biosensors as nanoprobes and nanosieves is provided.

2 Nanoparticles as parts of biosensors

Most of nanoparticles used in biosensors work as probes translating information from the biological element into measurable signal. Nanoparticles made of solid-state materials currently available (see Figure 1) are presented in the foregoing paragraphs.

Nanocrystals, quantum dots – these particles are inorganic crystals of cadmium selenide, 200–10000 atoms wide, coated with zinc sulphide. They emit fluorescent light when irradiated with low-energy light. The size of the dots (< 10 nm) determines the frequency of light emitted. The dots usually have a polymer coating with multivalent bio-conjugate attached, or are embedded into microbeads. Collection of dots of different size embedded to a given microbead emits distinct spectrum of colors - spectral bar code specific for this bead. Detection technique with the use of 10

intensity levels and 6 colors could theoretically provide 106 distinct codes. Quantum dots, for example CdSe-ZnS nanocrystals, do no emit in the near infrared, so they cannot be used for analysis in blood [3].
Area of use: multicolor optical coding for biological assays [4]; labelling of the breast cancer marker HeR2 on the surface of fixed and live cancer cells; stain actin and microtubule fibbers in the cytoplasm; detection of nuclear antigens in side nucleus [5]; immunohistochemical analysis of paraffin-embedded tissue sections [6]; *in vivo targeting* [7].

Nanobarcodes are cylindrical nanoparticles with specific patterns of submicron stripes of noble metal ions, produced by alternating electrochemical reduction of the appropriate metals. They are between 12 nm and 15 μm in width and 1-50 μm in length. The striping patterns make them distinctive under light, or fluorescent microscopy, or mass spectrometry. Nanobarcodes are easy to make in a nearly unlimited number of uniquely identified flavors [8, 9].
Area of use: coding in multiplexed assays for proteomics, population diagnostics and in point-of-care hand-held devices; proteins detection by either mass spectrometry or fluorescence measure.

Metallic nanobeads are made of noble metals with diameters between 15 to 60 nm [10, 11]. They can be detected by the transmissive and reflective light measure, plasmon resonance, quartz crystal microbalance, and differential pulse voltametry.
Area of use: cancer diagnosis [11]; DNA detection assay [10]; DNA diagnostics [12].

Silica nanoparticles are synthesized using standard water-in-oil microemulsion method (60nm in diameter.) They are silanised, and coated by oligonucleotide before use (DNA immobilization.) They are observable by fluorescence measurements methods [13].
Area of use: efficient nucleic acid hybridisation; detection of nanomolar range target DNA probes; ultrasmall nano-biosensors for trace analysis [13].

Ferrofluid magnetic nanoparticles are particles (25–100 nm in radius) consisting of a magnetic core surrounded by a polymeric layer (biological substrate) coated with affinity molecules, such as antibodies. Macro magnetic beads are bigger in size. They might be coated with streptavidin to bind to biotin with a single-stranded DNA probes specific for a bioagent or sample DNA attached. They are detectable trough amperometry or resistance measure. They can be also manipulated in a magnetic field [14].

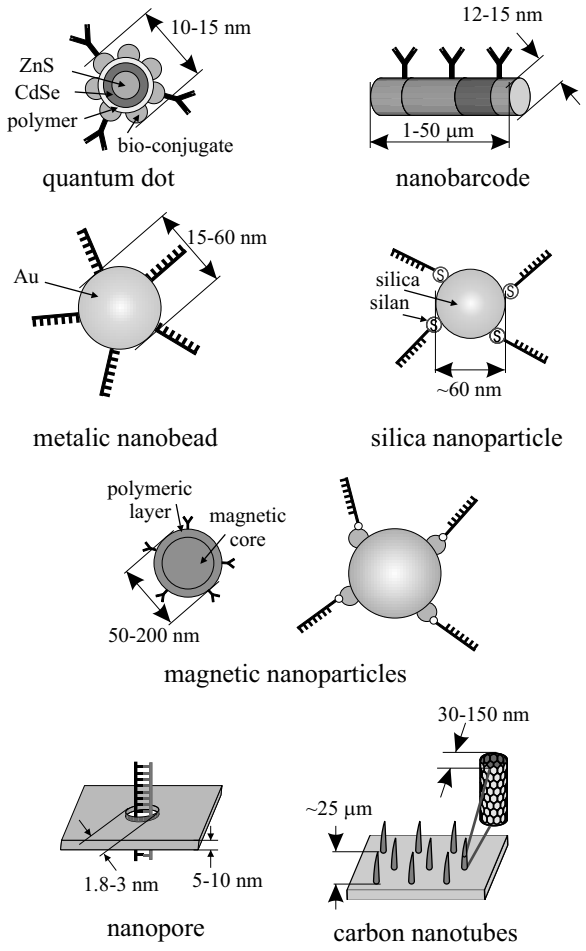

Figure 1: Schemes of different nanoparticles used for diagnostic and screening purposes.

Area of use: imaging specific molecular targets using nanoparticles as magnetic resonance contrast agents [15]; very sensitive cells or other tissue samples capture and/or separation.

Carbon nanotubes are carbon cylinders rising in the process of folding graphitic layers. The cylinders have remarkable strength and unique electrical properties making them insulting, semiconducting or conducting depending on their structure. They may be composed of a single shell single-walled nanotubes (SWNTs), or of several shells multi-walled nanotubes (MWNTs) [16, 17]. They are produced by microwave plasma enhanced chemical vapor deposition. Carbon nanotubes may be grown on a wide variety of substrates (including quartz and glass slides, platinum substrates) in the presence of catalyst (like nickel.)

Average length of these nanoparticles is of 25 mm order. Mean diameter may vary from 30 nm up to 150 nm. But with the use of super-lattice nanowire pattern transfer individual semiconductor nanowires can be created that are as little as 8 nm in diameter with the same distance between each wire [18]. In most cases electrical properties of carbon nanotubes are utilized for measurement purposes. When used in biosensing, carbon nanotubes have specific biomolecules attached. Area of use: promotion of electron transfer reactions when used to fabricate electrodes for the oxidation of biomolecules including dopamine, protein and b-nicotinamide adenine dinucleotide [19, 20]; extracellular analysis[21]; *in vivo* diagnostics.

Optical fibres are made from optical fibres pulled down to tips having distal end sizes of approximately 3060 nm. Fabrication procedure involves pulling from a larger silica optical fibre using a special fibre-pulling device what yields fibre with submicron diameters. One end of such fibre is polished from 600-mm silica/silica to a 0.3 mm finish. The other end is pulled then to a submicron length using a fibre puller. Thus the distal end of the fibre reaches 60 nm size. To prevent light leakage of the excitation light on the tapered side of the fibre, the side wall of the tapered end can be coated with a thin layer of silver, aluminium or gold (100-300 nm) leaving the distal end of the fibre free. These nanoparticles are not subject to electromagnetic interferences from static electricity, strong magnetic fields, or surface potentials. Fibreoptic nanoprobes can be covalently bound either with bioreceptors, such as antibodies, or with other, synthetic receptors, such as cyclodextrins [22, 23].
Area of use: in situ measurements of benzopyrene tetrol in single cells with the antibody-based nanoprobe [24, 1]; specific detection of target DNA at zeptomole levels, in the presence of non-cDNA [25]; analysis of mRNA isoforms in human cancer cell lines in conjunction with a new enzymatic detection method termed RNA-based annealing, selection and ligation (RASL) [26].

Nanopores are molecular-scale pores fabricated from variety solid-state materials (like silicon nitride) by ion-beam sculpting technique [27, 28]. The technique uses low-energy ion beams to slowly shape the surface of a material, while a feedback loop enables single-nanometre control over the pore dimension. Nanopores can be fabricated in two ways: they can be created from a cavity in the membrane under conditions where the sputtering erosion process dominates, or can be made by filling in larger pores under conditions where the lateral mass transport process dominates. The depth of nanopore fabricated in a membrane 510 nm thick is smaller than the molecule persistence length (50 nm for dsDNA), and a pore diameter 3-nm is slightly larger than the cross-sectional size of the molecule ($\sim$2 nm.) In another attempt nanopores are created as an array of cylindrical gold nanotubes with as small as 1.6 nm inner diameter [29]. Area of use: manipulation and electronically registering of single DNA molecules in aqueous solution [30]; discrimination and characteristic of unlabelled DNA molecules at low copy number [31].

3 Conclusion

This paper highlighted few examples of nanoparticles with their applications. Nowadays technology provides tools which allow researchers to produce several kinds of nanoparticles. Over the next couple of years it is widely anticipated that nanotechnology will continue to evolve and expand in many areas of life and science, and the achievements of nanotechnology will be applied in medical sciences, including diagnostics, drug delivery systems and patient treatment.

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