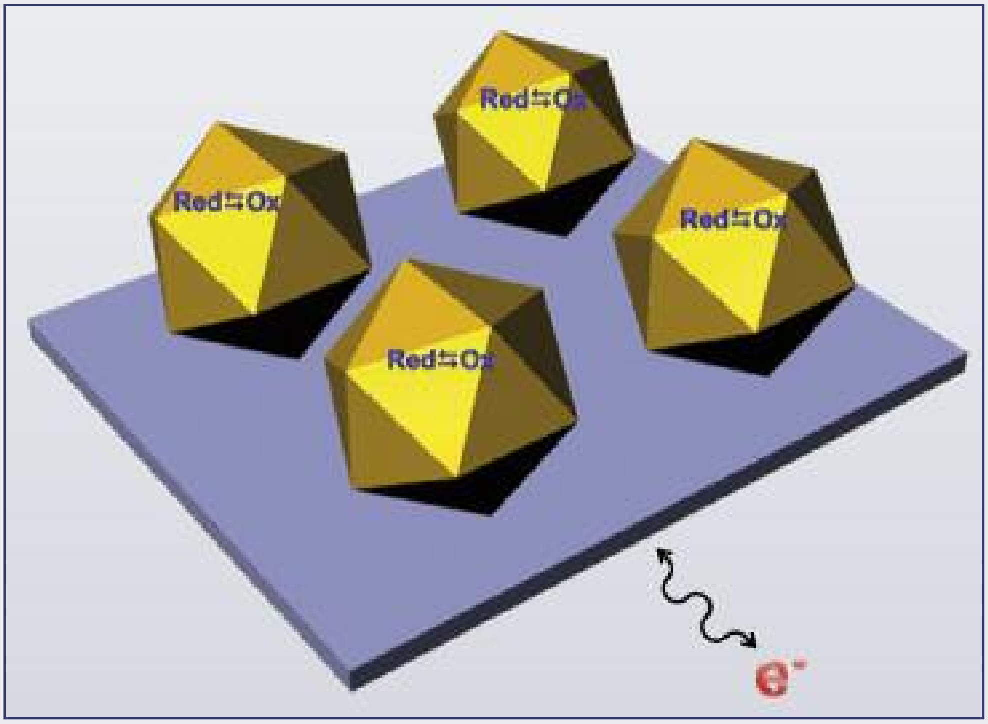

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Au NANOPARTICLES IN ELECTROANALYSIS

The review presents an overview on the use of electrode surfaces modified by Au nanoparticles in electroanalysis. These devices result very promising for the development of amperometric sensors and biosensors capable to quantify different inorganic, organic and biological analytes with extraordinary high sensitivity and low detection limit.

In the last two decades chemical sensing has attracted the attention of a growing number of scientists interested in developing new analytical devices useful for the rapid and specific chemical detection. The attention is motivated by the stringent demands for control systems, especially related to the industrial production processes, environmental monitoring, food safety, biomedical analyses and, not least of all, the security world, including the detection of drugs, explosives and chemical warfare agents. In all these fields, amperometric sensors have assumed great importance, since similar devices are very cheap, sensitive, rapid and easy to use. In addition, they allow on-line detection, especially important in the control of production processes and, whenever necessary, they can be easily miniaturised. Very widely diffused amperometric sensors consist of bare metal electrodes, typically Pt and Au, or carbon under different forms, such as graphite or glassy carbon. Although bare electrodes are still commonly used, they suffer from many drawbacks, such as the poor selectivity, the high limit of detection, the limited number of detectable chemical species and the dramatic fouling of the electrode surface, taking place due to adsorptions of species arising from the electrochemical processes. In order to solve these problems, and to significantly improve the performances of the amperometric sensors, most of the research efforts are today spent to suitably modify the electrode surfaces. The possibility to use different materials as electrode modifiers takes advantage of the huge progresses made in the development of very innovative materials useful for the electrochemical detection. In particular, great attention has been devoted to electrode coatings based on different conductive materials, which permit effective charge transfer from the underlying electrode substrate to the solution. With this respect, many different conductive organic polymers (polyaniline, polypyrrole and polythiophene derivatives), metal nanoparticles and carbon nanotubes have been deeply investigated. In this review, the attention is pointed to the use of Au nanoparticles (AuNPs) for electroanalytical applications, due to the polyvalent role of such a material, as described hereafter. Owing to the huge number of published papers concerning this particular application of AuNPs, it is important to underline that the reference list reported here concentrates only to some selected examples, chosen to give a general picture of the potentiality of such a nanomaterial in electroanalysis.

From a general point of view, NPs can be defined as the constituents of extremely fine powder (1-100 nm size), being usually considered transitional between the clusters, i.e. aggregates of few atoms, and the bulk scale. NPs possess a particularly high surface/volume ratio: when NPs are fixed on an electrode surface, an increased electroactive area is obtained with respect to bulk materials, resulting in improved sensor sensitivity. NPs posses a polyhedric shape, which makes a large fraction of atoms to be located in the correspondence to defects such as vertexes and corners; this aspect is particularly important in the case of small NPs, i.e. under 20 nm size. For this reason, metals under the form of NPs possess (electro)catalytic properties by far superior to those of bulk systems. Among different metal NPs, the performances of AuNPs in many different catalytic processes are well known, as quite recently reported on this journal [1]. Finally, confinement of the electrons in regions of nanometric dimension leads to special optical properties; as an example, AuNPs possess a colour ranging from red to violet, depending on the size and distance between adjacent NPs. This peculiar property has been exploited for the development of optical sensors.

Applications in the field of sensors taking advantages of these properties are reported hereafter.

Selected examples of amperometric sensors based on AuNPs

Analysis of heavy metals

Anodic stripping voltammetry at mercury electrodes is considered an effective technique for metal trace analysis. Compared to atomic spectroscopies, it is cheaper and easier to use. Many efforts are spent developing new electrode materials able to replace Hg, due to the high toxicity of this metal. Although Au electrodes often lead to more sensitive responses than other metals, the very long cleaning procedures necessary to restore the electrode surface and the fairly high limit of detection toward different metals prevent the practical use of such an electrode material. In this case, the use of Au nanostructured surfaces allows for notable lowering of the detection limit, thanks to the large surface, and for easy renewal of the electrode surface. This methodology has been successfully employed to develop very promising amperometric sensors for heavy metal detection, such as Hg, Pb, Cu, Sb and As [2-4].

Analysis of organic species

The well known (electro)catalytic properties of AuNPs can be successfully exploited in the development of amperometric sensors suitable for detection of many organic species, which presents drawbacks when bare electrode surfaces are used. As an example, AuNP based amperometric sensors have been developed for detecting different neurotransmitters, such as dopamine [5-7] and epinephrine [8]. For both analytes the presence of AuNPs was found to induce electrocatalytic effects that significantly improve the sensitivity and the detection limit of the sensor. The advantages induced by the presence of AuNPs are particularly evident in the case of the determination of dopamine, which suffers from the interference of ascorbic acid, present in large concentration in biological fluids; these organic species are oxidised at very similar potentials on bare metal electrodes. Different AuNP modified electrodes [5-7] have been proposed in order to overcome this problem: the electrocatalytic properties of AuNPs allow the oxidation of ascorbic acid at less positive potentials, leading to good resolution of the responses due to the different species. Analogous electrode systems were also used to simply detect ascorbic acid in a different context [9], by considering uric acid as an interferent.

Nitrite determination also takes advantages of the peculiar properties of AuNPs [10, 11]. The relevant electrochemical devices are competitive with different analytical techniques, such as ionic chromatography and UV-Vis spectroscopy.

AuNP modified electrodes have been successfully employed to develop quite interesting non-enzymatic sensors for glucose and H_2O_2; the resulting devices can be used in several environments in which the enzyme is inactive. In the case of sensors for glucose [12, 13], the electrocatalytic properties of AuNPs allow oxidation without needing the enzymatic redox mediator; furthermore, the surface poisoning that affects bare Au surfaces is prevented. Non enzymatic electrodes were also developed for the detection of H_2O_2 [14, 15]; in this case, the use of AuNP based electrodes allows the registration of the electrochemical process at very low potentials, coupled to significant increment of the current, with respect to the bare Au electrodes.

By activating electrochemical processes similar to those of glucose oxidation, AuNP modified electrodes are also suitable to catalytically oxidise alcohols, such as methanol and ethanol [16, 17]. Although the catalytic mechanisms involved in the latter case have been studied in detail [17] and are at the basis of the development of direct methanol fuel cells [18], no attempt has been made so far to develop amperometric sensors for the quantification of methanol and different aliphatic alcohols.

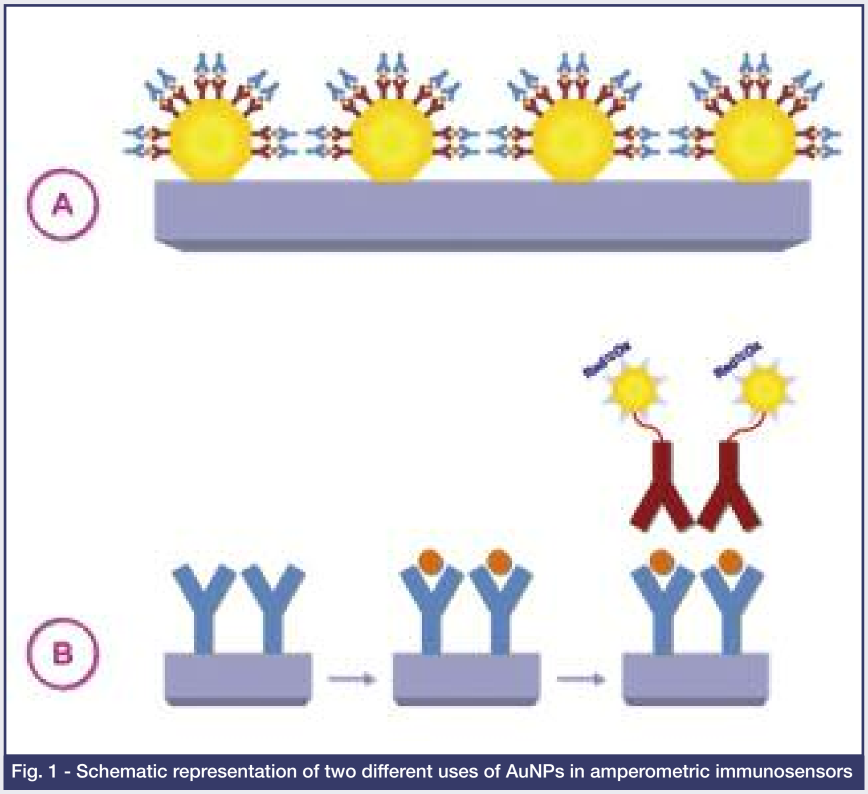

Fig. 1 - Schematic representation of two different uses of AuNPs in amperometric immunosensors

Biosensors

Nanomaterials strongly influence the development of new electrochemical biosensors. In particular, AuNPs constitute the substrate of choice for stable anchoring of biological elements, due to the peculiar affinity of Au toward different functional groups, such as thiols and amines, which are present in many biological species, such as enzymes, antibodies and DNA. Moreover, in similar systems the specificity of many biological species toward analytes of interest in medical diagnostics and in food safety results to be coupled to the extraordinary catalytic properties of the AuNPs. For all these reasons, the development of amperometric biosensors based on Au nanostructured surfaces constitutes nowadays the most important field of application of AuNPs in electroanalysis. The applications proposed range from redox protein based sensors, to genosensors and to immunosensors [19-21].

The enlarged surface area obtained through the formation of nanostructured surfaces allows the immobilisation of a higher number of recognition elements on the electrode surface, resulting in improved performances. In particular, many enzymatic electrodes, characterised by lower detection limits with respect to bare Au electrodes, have been developed. As an example of this class of sensors, the deposition of tyrosinase on Au nanostructured surfaces allows the development of biosensors for the detection of phenols and substituted phenols, achieving a limit of detection as low as 10^{-8} M [22, 23].

The possibility to detect extremely low concentrations of the target analyte is particularly important in the field of genosensors, where the early diagnosis of genetic DNA alteration requires the use of instrumental techniques capable to detect specific sequences of nucleobases at concentration levels down to 10^{-13} M [24].

By exploiting an analogous strategy, sensitivity and detection limits of several immunosensors have been significantly improved through immobilisation of antibodies on Au nanostructured electrodes [25, 26] (see Fig. 1A). Moreover, the sensitivity of immunoassays has been further improved by several orders of magnitude by selectively depositing AuNPs on antigen-antibody sandwich, which amplifies the electrochemical signal [25, 27, 28] (see Fig. 1B); the useful concentration range and the detection limit of the proposed sensors result comparable to those of classical ELISA tests.

The characteristics of the AuNPs also allow intimate contact between the reaction sites of the biological unit and the NP metal core. In particular, it was observed that redox active proteins can suitably rearrange on the AuNP surface, reducing the insulating effect of the polypeptide shell surrounding the redox centre. As a consequence, a direct electron transfer between the electrode and the redox centre becomes operative [29-31]. This aspect is of basic importance for the development of a new generation of amperometric biosensors, characterised by improved performances with respect to biosensors of first and second generation, which require the presence of a redox mediator. As an example, third generation of sensors for O_2 [29] and for H_2O_2 [30] were developed by directly depositing cytochrome C on AuNPs. Direct charge transfer is not possible when bare Au electrodes are used, since the redox centre of most oxidoreductases is electrically insulated by a protein shell [30]. An analogous approach has been followed for the development of enzymatic biosensors, based on a direct charge transfer between AuNP and horseradish peroxidase [32] or glucose oxidase [31, 33].

Deposition of AuNPs onto electrode surfaces

Electrochemical synthesis

The most spontaneous way to deposit AuNPs on a conductive surface is to perform an electrochemical reduction of a Au(III) salt, generally of $AuCl_4^-$. This process produces a layer of Au nanocrystals, homogenously distributed on the electrode surface. The conditions for the electrochemical deposition can be varied very easily, allowing the formation of a number of electrodes with NPs of different size, shape and spatial distribution [34].

The electrochemical deposition also allows the formation of three-dimensional Au nanostructures whose properties are, to a certain extent, very similar to those above described for AuNP modified electrodes. In particular, the deposition onto the electrode surface of a coating possessing open porosity leads to an efficient increase of the surface area and ensures accessibility of electroactive species to a wide number of electroactive sites. Hence, the sensitivity of the amperometric sensor is increased. As an example, Au sponges can be obtained by simply electrochemically dealloying Ag from Au/Ag alloy [35]. Alternatively, Au nanostructures were obtained by electroreduction of Au(III) salts on alumina [36] or on polycarbonate membranes [37], used as templates (see Fig. 2). Electrochemical measurements indicate that they can constitute very promising devices for electroanalytical tests, since these Au nanostructured surfaces possess high electrocatalytic activity toward different organic species.

Chemical synthesis

AuNPs can be synthesised in advance to the deposition onto the substrate surface. In this case, the organization of the nanoobjects on the electrode surface results in more controlled surface architectures, which are reported to be essential for the successful realization of a sensor. Only a very brief overview of the possible synthetic approaches is reported hereafter.

The different methods for the synthesis of AuNPs are based on two main strategies, i.e. the top-down and the bottom-up approaches. The top-down strategy is based on the subdivision of bulk metal into finely divided particles that can be collected under the form of solid powder, suspended inside a liquid or directly deposited onto the conductive support. The minute particles are usually obtained by physical methods, such as thermal evaporation, sputtering, or laser ablation. In most cases, these methods require the use of expensive and complex experimental apparatuses, thus preventing their wide use in the field of amperometric sensors. On the other hand, the bottom-up approach represents the most diffused strategy to obtain AuNPs with well controlled size, suitable for electroanalytical applications. In this case, AuNPs are generally obtained by chemical reduction of Au(III) salts by reducing agents, such as $NaBH_4$ or citric acid. When chemical synthetic methods are followed, an encapsulating agent has to be added to the reaction solution; the presence of this species, surrounding the metal cores, introduces repulsive steric or electrostatic interactions between the nanoobjects in solution, capable to prevent from NP aggregation. The choice of the proper encapsulating agent strongly conditions the properties of the resulting NP system, particularly with respect to the size, reactivity and accessibility to the metal core by the species in solution. This last aspect results particularly important in electroanalysis, in order to exploit the electrocatalytic properties of AuNPs at best. The lability of the organic shell also allows the AuNPs to be subsequently functionalised, e.g. by specific recognition elements, though a simple 'place exchange' reaction:

$$xR' + R_m\text{-NP} \rightarrow xR + R'_xR_{m-x}\text{-NP}$$

For this reason, AuNPs surrounded by very labile encapsulating agents, such as citrate, are generally more suitable for the development of amperometric sensors.

A first way to connect chemically synthesised AuNPs with the transducer lies in the construction of a carbon paste electrode, obtained by simply mixing AuNPs with graphite powder, using paraffin oil as a glue [22, 31]. However, when ordered nanostructures are sought, the anchoring of the pre-synthe-

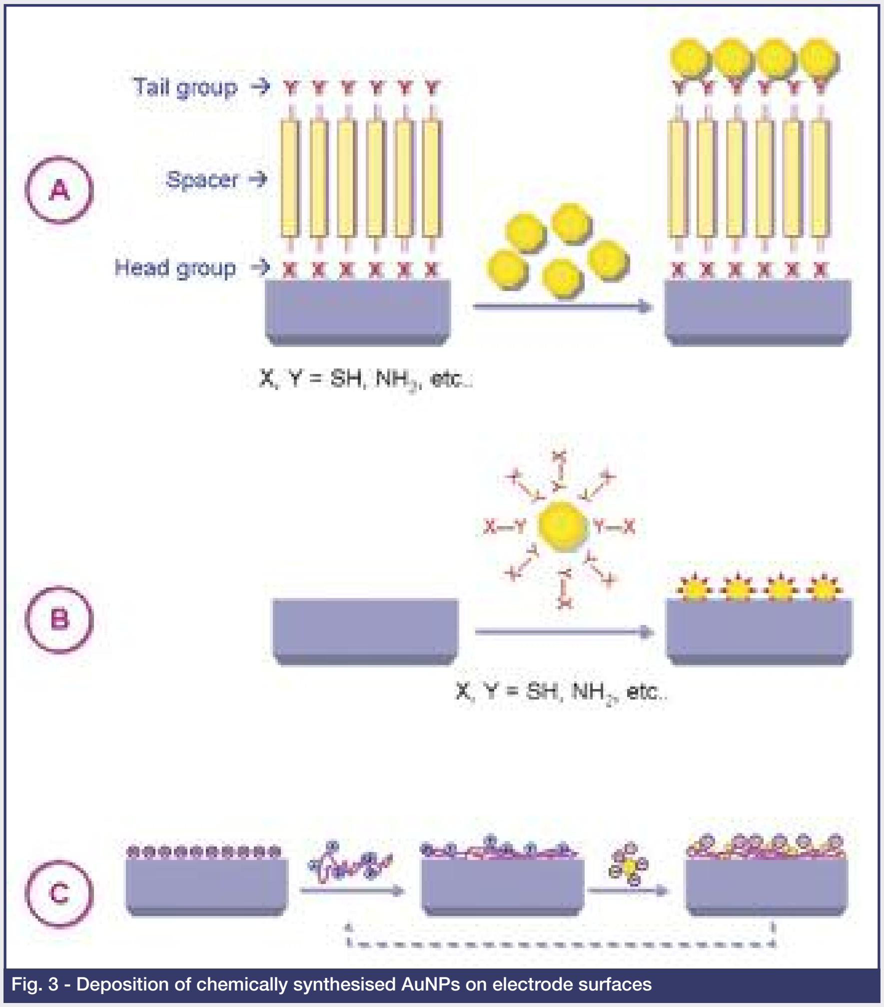

Fig. 3 - Deposition of chemically synthesised AuNPs on electrode surfaces

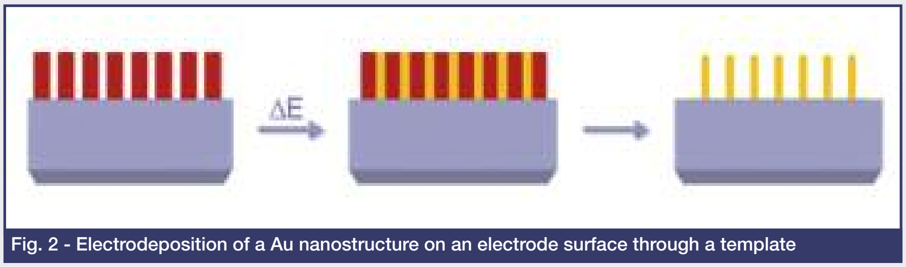

Fig. 2 - Electrodeposition of a Au nanostructure on an electrode surface through a template

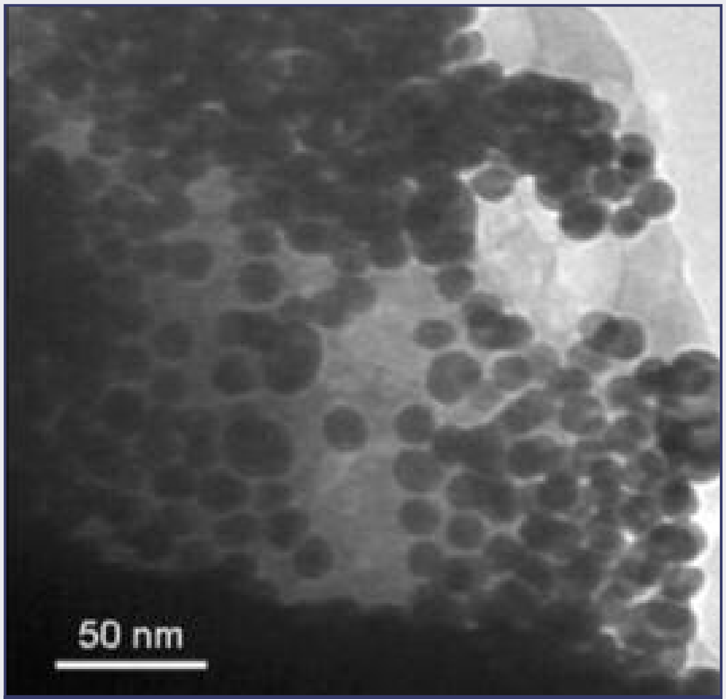

Fig. 4 - TEM image of an AuNP based electrode coating deposited through Layer-by-Layer technique

sised AuNPs on the support surface has been carried out by following a number of different methods; the most significant ones are schematically depicted in Fig. 3. In particular, it is possible to graft a monolayer of AuNPs on the outmost surface of a Self Assembled Monolayer (SAM) [5, 8, 9] (Fig. 3A). The chemical and physical properties of similar nanostructured coatings can be very easily tuned by changing the chemical composition of the head and tail groups, as well as of the spacer. In this case, -SH or -NH_2 tail groups are generally chosen, in order to take advantage of their chemical affinity to Au metal core. Alternatively, AuNPs dissolved in solution can be anchored directly on the substrate, taking advantage of the capability of the encapsulating layer to be grafted on the electrode surface [38] (Fig. 3B). Following whichever of these two strategies it is possible to repeat the deposition on the electrode substrate for a suitable number of times, in order to build up multilayers of NPs [38]. Finally, negatively or positively charged AuNPs can be made stably interact with electrode surfaces functionalised with chemical species containing groups bearing opposite charge (Fig. 3C). In this last case, the deposition of anionic and cationic layers can be repeated in order to obtain a film characterised by a well defined thickness and by a high metal loading [15, 26], as well evident from Fig. 4. Such a process is known as Layer-by-Layer deposition technique.

Other nanostructures, exhibiting properties similar to those reported for AuNPs, have been chemically synthesized in advance to their deposition onto the substrate surface [39]. Alternatively, nanostructures have been prepared directly on the electrode surface, through electroless deposition of Au inside nanoporous polycarbonate filters [40].

AuNP/conducting polymer composites

The performances of AuNPs in electroanalysis can be further improved after their dispersion in organic polymer matrices. The driving force to the development of these composite materials lies in the possibility to combine the properties of the matrix to those of the AuNPs described above, taking advantage of their synergic interaction. Although the use of many different organic polymer matrices has been reported in literature, we only discuss a few examples concerning the use of conducting polymers.

Conducting polymers (CP), which principally include polypyrrole, polyaniline and polythiophene derivatives, have attracted much interest in electroanalysis. Their success as electrode coatings is ascribed to the possibility to partially activate electrocatalytic processes, to increase the sensitivity of the sensor, which also results in low detection limits, and to reduce the fouling of the electrode surface [43].

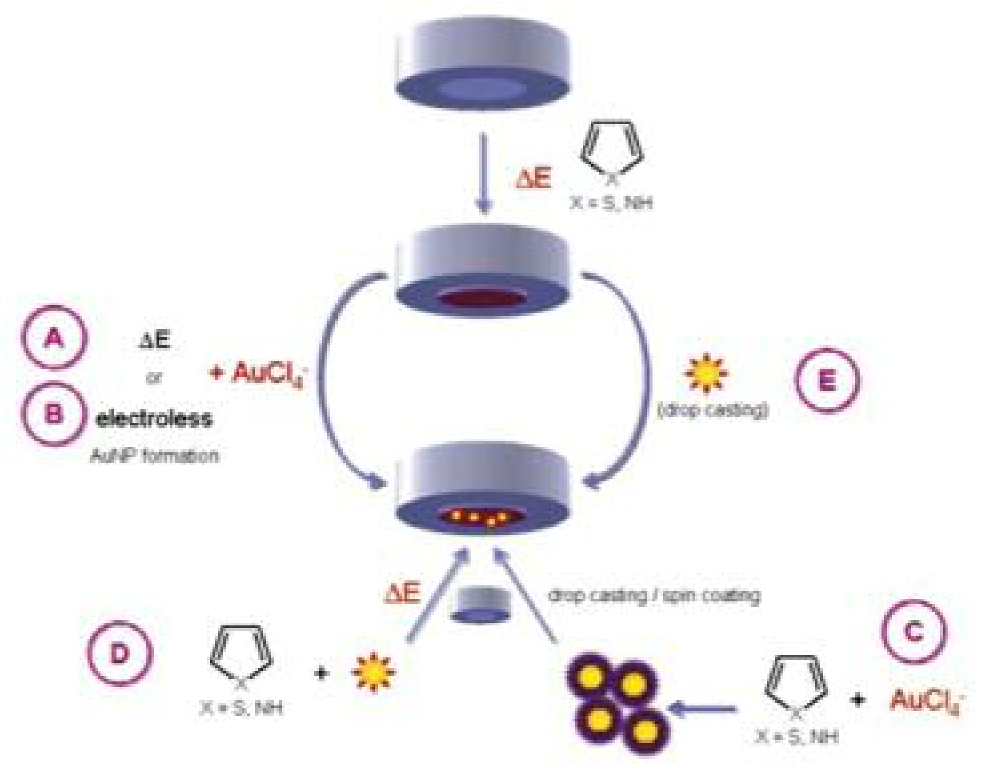

Fig. 5 - Different strategies to obtain AuNP/CP composites on electrode surfaces; the scheme reports the example of polypyrrole and polythiophene

Due to the porous nature, these materials allow a significant enlargement of the electrode active surface area leading to the deposition of a large number of AuNPs on pore surface. Moreover, the diffusion of the analytes to the NP surface is only partially hindered by the presence of such a microscopically porous support, and its conductive nature allows a profitable charge transfer throughout the film. Finally, the chemical affinity of the heteroatoms present in the polymeric backbone to the NP metal core allows stable interactions between the two components [41]; in this case, labile encapsulating agents are preferred, in order to favour this effect.

AuNP/CP composites can be prepared by following many different methods [42-44] as schematically outlined in Fig. 5. In particular, AuNPs can be generated before, concurrently or after the polymer formation. By considering the particular application of these composite materials, the most spontaneous and diffused synthetic method consists in a two-step electrochemical procedure: AuNPs are electrodeposited from Au(III) solution onto/into a pre-formed polymer electrode coating obtained through electrogeneration (Fig. 5A). Alternatively, metal ion reduction can be spontaneously induced on the CP-modified electrode surface, taking advantages of the capability of many CPs to be oxidised under very mild conditions, such as in the presence of Au(III) ions (Fig. 5B).

However, when a more strict control of the AuNP shape and dimension is sought, chemically synthesised AuNPs should be used. One of the most profitable approach consists in the use of the monomer, e.g. aniline, as the reductant for Au(III) ions: the reaction leads to the formation of AuNPs surrounded by the relevant conducting polymer; they are deposited onto the electrode surface in a following step, by simple drop casting or spin coating (Fig. 5C).

In addition, the formation of the conducting polymer can occur subsequently to AuNP chemical synthesis. As an example, the NPs can be dispersed in a solution containing the monomer and a supporting electrolyte; when the electrode is polarised at a potential suitable to induce polymerisation, the precipitation of polymer chains onto the electrode surface involves the inclusion of AuNPs inside the polymer coating [45] (Fig. 5D). Alternatively, chemically synthesised AuNPs can be deposited on the pre-synthesised polymer coating though drop casting (Fig. 5E).

In the last decade, a wide number of papers reported the synthesis and the chemical-physical characterisations of many different AuNP/CP composite materials. These studies are fundamental in order to clarify the interactions between the organic and the inorganic component and demonstrate the potentialities of these materials as electrode coatings. However, only few applications in the field of amperometric sensors are reported so far. Similar composite materials have proved to be very profitable, with respect to the two single components, in the selective detection of uric acid or dopamine in the presence of high concentrations of ascorbic acid [45, 46]. In many cases, the polymer matrix is recognized to be responsible for the increased resolution of the signals, which implies selectivity, while AuNPs improve the sensitivity and lower the detection limit to nanomolar level. As an example, Fig. 6 reports the comparison between dopamine determination with a AuNP/CP and with a pure CP modified electrodes; in this case, poly(3,4-ethylendioxithiophene) (PEDOT) was used as the conductive organic matrix and AuNPs were included inside the coating during the polymer electrogeneration.

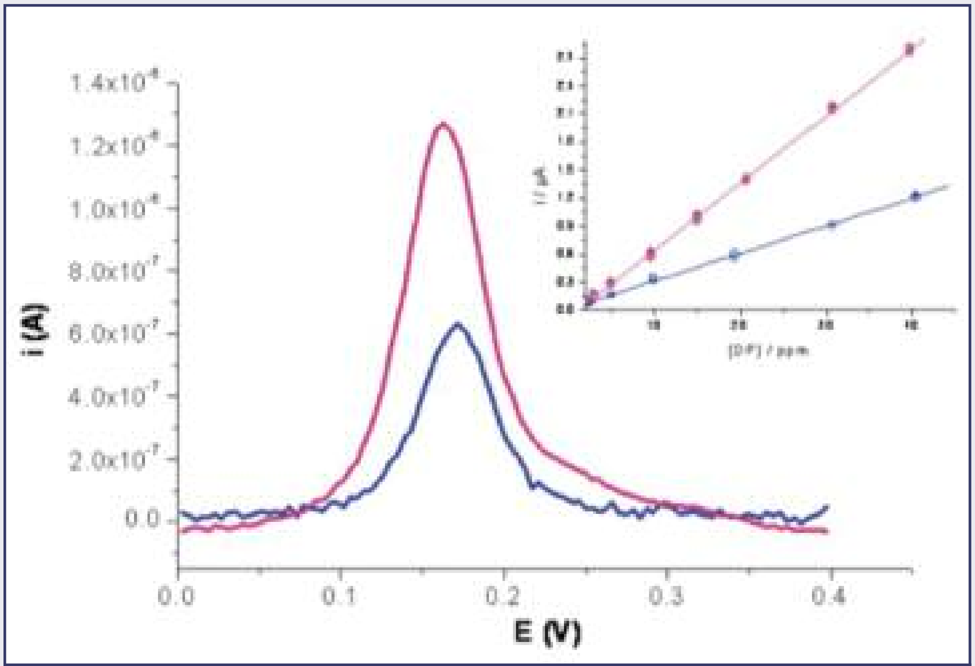

Fig. 6 - Dopamine determination at PEDOT (blue line) and AuNP/PEDOT composite (red line) modified electrodes. Differential pulse voltammetries recorded in phosphate buffer solution

The possibility to deposit a large number of AuNPs on an electrode surface also allows very low limit of detections for As [47] and Hg [48] to be reached; the performances of these amperometric sensors result competitive with inductively coupled plasma detections. Very recently, an innovative application of AuNP/CP modified electrodes in the field of sensing has been proposed; similar electrodes have been tested as elements of so-called electronic tongues. In this case, electrodes modified with a PEDOT coating containing AuNPs show good classification ability of different wines [49].

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RIASSUNTO

Nanoparticelle di oro in elettroanalisi

La review presenta una panoramica sull'uso di elettrodi modificati da nanoparticelle di oro in campo elettroanalitico. Questi dispositivi risultano particolarmente promettenti per lo sviluppo di sensori e biosensori amperometrici capaci di rilevare diversi analiti organici, inorganici e biologici con elevata sensibilità e bassi limiti di rilevabilità.