Applications of Gold Nanomaterials in Biomedicine

Jiangxu Wu[1,*,†], Zikai Wang[2,†]

[1] School of Biology & Basic Medical Sciences, Suzhou Medical College of Soochow University, Suzhou, Jiangsu province, 215000, China

[2] The Second Middle School, Qingdao, Shandong province, 266000, China

* Corresponding Author Email: 1930401069@stu.suda.edu.cn

† These authors contributed equally.

Abstract. With more deeply recent researches and studies about nanomaterials, such as nanoparticles, nanospheres and nanoshells, scientists found that nanomaterials have some specific advantages in terms of physical and chemical, optical, nuclear characteristics due to quantum size effect, which are ideally satisfied strict demand of high sensitivity and accuracy of biosensors. Nowadays, nanomaterials are widely used in the detection and treatment in medical domain. Among many categories of nanoparticles, gold nanomaterials are the most attractive one. As a result, this research mainly introduces a number of applications based on gold nanomaterials in different fields, such as DNA detection, cell imaging, protein detection and disease treatment. It will hope this research would expand the knowledge sight of advanced nanotechnology of readers. However, there also have many aspects of applications of gold nanomaterials waited to be found in future.

Keywords: Gold nanomaterials, Biological medicine, Detection, Disease treatment.

1. Introduction

Biomedicine is a crossing subject including the medicine, biology and bioscience, and its basic task is using biotechnology and bioengineering technique to solve medical questions. It is also the base of academic research and innovation of biomedical information, medical imaging technology, gene chips, proteomics, material science and chemistry and modern systems. There are many diseases which are hard to cure, so what it needs to do is to detect it as early as possible. In this regard, one presentative molecular, such as a special protein or a small piece of RNA or some signal molecular, can be followed and used for monitoring disease.

Medical physics direction which including biological signalling and medicine image two aspect. The field of biological signalling is concentrated in some processing, and identification of human physiological signals. It needs to measure blood pressure and many other different signals in your body. For biomechanical direction, this direction is based on utilizing three-dimensional modelling software builds models and using finite analysis software to analyze various types of situations. The three-dimension image can be used to describe the unfamiliar protein. For biomaterial direction, biological materials are the material basis to produce various artificial organs, or the materials which is used for biological molecular detection, like the nanopore used for detection. Its main research is biocompatibility and biological activity issues, which can largely increase the success rate of organ transplantation. In addition, the more sensitive and collective biosensor is potential. Meanwhile, the nanomaterials are the most potential and hot one [1].

But now, biomedicine has hit several major bottlenecks. Many incurable diseases emerge and make the difficult situation, like some typical diseases, including cancer, neurodegenerative disease, Parkinson and Alzheimer. More and more researchers are focusing their research direction on these current difficulties to overcome the disease. This is also the future trend of biomedicine development. It is well known that Tau protein is one of biomarkers of Alzheimer, there are many difficulties of its detection, low concentration in blood, difficulty of getting cerebral fluid, which has low accuracy [2]. With the society advancing incessantly, medical workers constantly raise their expected standards and requirements to medical equipment. Nowadays, to have a better curative effect of treatment, practitioners no longer focus on qualitative analysis of biomedical samples, but quantitative analysis.

They want to see how many target substrates are in sample and how they react with other molecules. However, previous sensor merely has few contributions to solve such difficulties due to their poor accuracy and resolution. In fact, the target biomolecule are usually 100 times smaller than the diameter of a human hair. It's hard to detect them by behind hind equipment. To have a clearer perspective of tiny molecules, it needs to enter the new frontier to detect it by the nanomaterial to increase the accuracy.

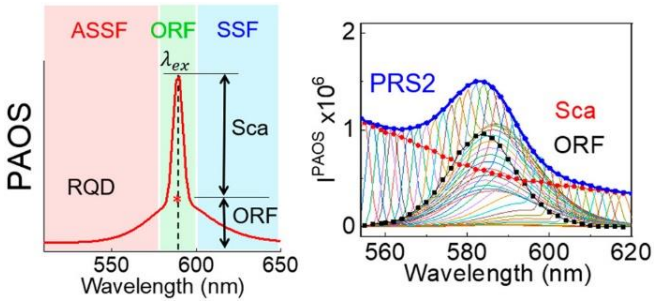


Figure 1. The optical properties of the used nanomaterials in solutions [7].

Nanotechnology developed quickly in the last 40 years [3]. It makes a huge effect on how the way medical worker do the quantitative analysis to the target biomedical samples. The nanomaterials are the base of the nanotechnology. According to its special chemical and physical properties compared with traditional previous technique, like thermal conductivity, magnetism, electrical properties, optical properties, and catalytic performance, the nanotechnology has its unparalleled advantages in biomedical detection [4].

Nanomaterials have extraordinary specific heat coefficient and thermal expansion coefficient. Usually, their numerical values are greater than homogeneous coarse-grained material's and non-crystalline material's, what is affected by atomic coupling weaken and low atomic density [5]. The resistance of nanomaterials is also greater than congeneric coarse-grained materials. And in some special case, it could even cause the insulator translation. As a result, nanoelectronic device made of nanomaterials has the characteristic of ultra-high-speed, ultra-high-capacity, and ultra-low power consumption. The reflectivity of nanomaterial is super low, so it would result nanomaterial absorb most of the light and energy and makes the particles dark. In addition, the absorption band of the nanomaterials usually moves in the direction of short wave.

Thanks to such incomparable advantages, nanomaterials can perfectly match the standards of biosensors, like multifunction and fast response. Besides, as the component of biosensors, nanomaterials also have benefit in widely use, high sensitivity, good selectivity, and wide detection range. After the application of nanomaterials in biosensors, the detection performance has been significantly enhanced, and lots of new types of biosensors has been inviting. The amazing physical and chemical characteristics of nanomaterials make it easy to analysis cells or biomolecules and reduce the time interval of analysis them. Some of techniques could show how much degree that the test taker is ill. And some of nanotechnology could extinguish different types of protein in unprocessed bio samples, even the sequence of DNA.

Based on a variety of unique characters of nanomaterials, scientists have invented plenty of meaningful nanomaterials-based analysis methods in biomedicine. Herein, the research will describe the applications of gold nanomaterials in biomedicine for different needs

2. Applications of different gold nanomaterials in biomedicine

2.1. Disease detection

Gold nanoclusters (AuNCs), which is less than 2 nm, and it is consisted of many gold atoms, showing excellent optical properties [7], as shown in Figure 1. AuNCs can be produced with different

templates or ligand, including DNA template, protein template and thiolate ligands [8]. Protein is the most important part in human body, and also many early detection tags of disease. Using AuNCs as the sensing probes, AuNCs-based analysis method has been developed and be used to detect protein [6] [10], as shown in Figure 2. In addition to detecting one protein at a time, new sensing strategy is proposed that many proteins can be detected at the same time [11] [12].

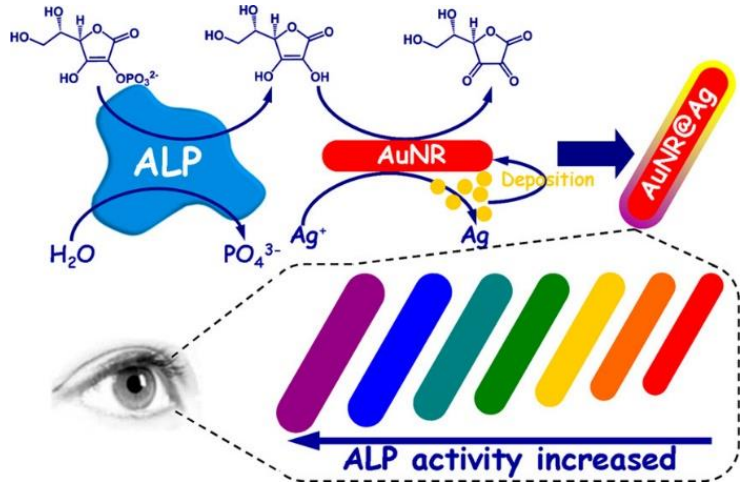


Figure 2. Scheme of the developed method for detection of phosphatase activity [10].

Many diseases are due to the quality and quantity change of enzyme [13-18]. When the biological molecular, like proteins and peptides meet the nanoparticle, a corona will be generated quickly on the surface of nanoparticle. At first, this corona just includes the richest protein with low affinity. This stage is called soft corona. Gradually, it is replaced by high affinity protein which have lower abundance. According to this, a change in the affinity and abundance of peptide in bigger protein can be used to control the composition of protein corona [19].

Surface active maghemite nanoparticles (SAMNs) is one technique of hard protein corona composition detection. A most important part is used to recognize properties. And after the complex generate, the MALDI-TOF mass spectrometry is applied to verify it. Meanwhile, it was already known that the surface has high selectivity for proteins [20].

Mastitis is a very severe bovine disease [21]. Advanced technology is lack of early diagnosis, and it just depends on some obvious change such as color of red, degree of swelling or changed consistency of milk, increased somatic cell count (SCC) [22]. Nowadays, it is found that SAMNs have ability to select caseins fragments specifically in milk from mastitis-affected cows [23]. Scientists have done an experiment that comparing healthy cows (high SCC) with unhealthy cows (low SCC) about protein consistency and abundance by SAMNs and then MALDI-TOF. The result shows the concentration of αs1-casein fragment is increased.

2.2. Imaging

Gold nanoparticles could be considered as a steady material in bio environment as a result of its specific stable chemical and physical structure and properties. It hardly reacts with other substance or element to form new compound. Gold atom has no radiation and toxicity. Therefore, it could be degraded in biological cell tissues without innocuously, which leads to be dissolved in injection solutions. Meanwhile, gold nanoparticles have unique optical characteristics, like high molar absorption coefficient and high fluorescence absorptivity and emissivity, which result the huge contribution in imaging.

Positron emission tomography (PET) is a kind of imaging technique based on nuclear technology. It's a non-invasive technology to provide information of 3-d whole body and ability to functions. The PET is not only used for medicine but also for basic research. It has widely applications for the study of metastasis of cancer and the imaging of oncology clinical medicine.

Gold nanoparticles are regularly used as contrast agent in PET. As the recent update in highly sensitive, stable, and biocompatible imaging agents [24]. Gold nanoparticles could be labelled in batches to save time and has extremely stable physical and chemical properties. Besides, it was harmless to patient's scanned organs. In other words, gold nanoparticles would not react with or destroy any biomaterials. The biological functions of cell tissue would not be changed, including the synthesis of proteins and enzymes. Gold nanoparticles in body would be expelled from kidney. A study concerned about the PEGylated crushed gold shell-radioactive 124 1-labelled gold core nanoballs to see whether gold nanoparticles are archive in imaging application with PET. The results showed that it had high sensitivity and hardly changed its structure [25]. Compared with the usual contrast agent made by Gadolinium and iodine, which are poisonous to body organs, gold nanoparticles are much safer and easier to use.

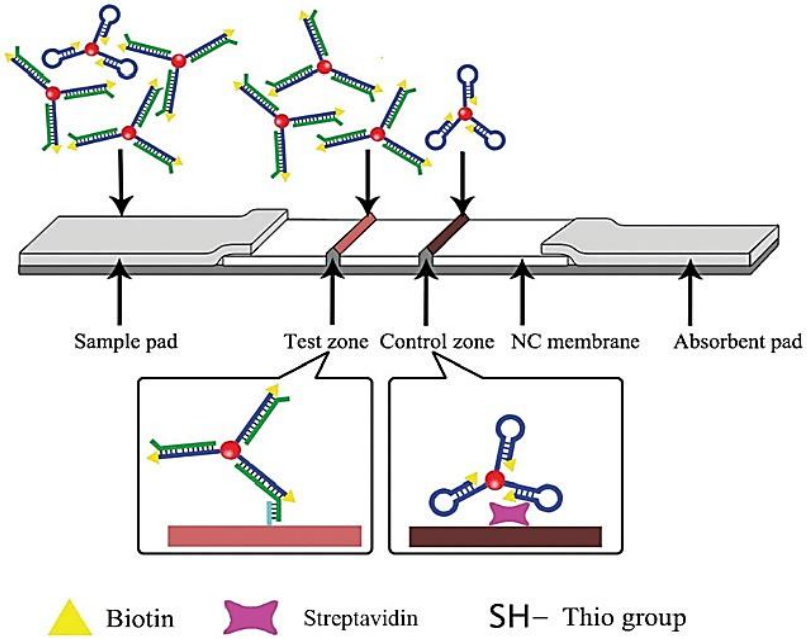


Figure 3. Scheme of the gold nanoparticles-based biosensor [27].

Localized surface plasmon resonance (LSPR) is a physical phenomenon. When light is incident to the nanomaterials which consists of noble metal nanoparticles and the frequency of incident photon is similar to the vibration frequency of the nanometals conducting electrons, the resonance would happen. LSPR would cause three types of effects. First is leading to the surface enhanced spectroscopy, like surface enhanced fluorescent and surface enhanced infrared. Second result is wavelength selective absorption. Last one is resonance Rayleigh scattering. The scattering efficiencies are proportional to the dimensions of AuNPs. As a result, gold nanoparticles had wide applications in all kinds of fluorescent tests.

In this section, there are mainly 2 kinds of imaging methods [26]. One is dark field confocal imaging (DFCI) and the other one is optical coherence tomography (OCT).

2.3. Optical biosensors

Scientists now take advantages of a number of nanomaterials based on their optical characteristics, such as absorbance, reflectance, resonance, and luminescence to develop some optical DNA diagnostic systems [27], as shown in Figure 3.

Because of its advantages of high sensitivity, and simple operation, the fluorescence DNA biosensors has always been the focus of development in biomedicine. The alteration in fluorescence and luminescence of the transducer material upon analyte recognition will be recorded by the fluorescence-based optical biosensors. There are two components in such biosensors. One is probe

DNA molecule, working as recognition element. And the other one is transducer, a fluorescent nanomaterial. They are attached by each other. After the hybridization with the target DNA molecule and the semi conservative replication of them, the subsequent changes in density or position of the fluorescent nanomaterial would be recorded. A number of fluorescent DNA biosensors are invited on the foundation of a fluorescence resonance energy transfer (FRET) mechanism promotes and works as the basics of the invitation of a number of fluorescent DNA biosensors. The FRET represents the energy transfer between two adjacent molecules, fluorophore and quencher. When the distance between them is proper, fluorescent energy would be shifted from fluorophore to quencher. It's a non-radioactivity process. The FRET process would cause the change to the fluorescence intensity of the fluorophore (either an increase or decrease) [28].

Using the resonance properties of gold nanomaterials, surface enhanced Raman scattering (SERS)-based optical biosensors are widely developed in biomedicine [29] [30], as shown in Figure 4.

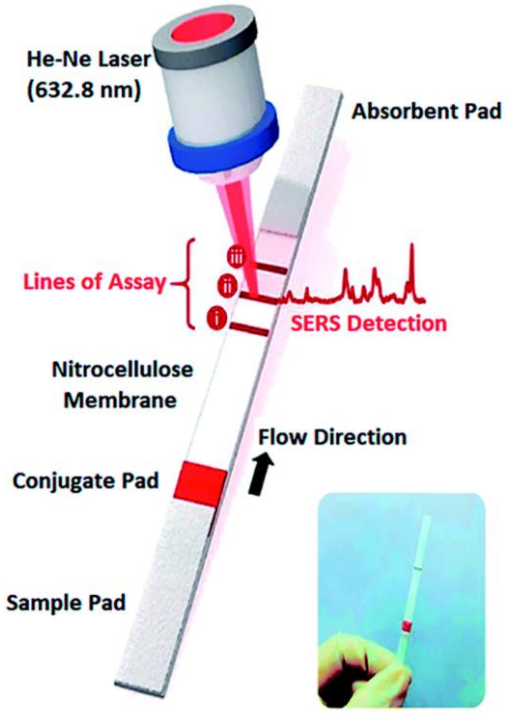


Figure 4. Scheme of the SERS-based biosensor [26].

3. Conclusions

In summary, the research clearly describes the applications of gold nanomaterials in biomedical field, which include detection of DNA and protein, as the photographic develop in visual technology, imaging and disease treatment because its special physical and chemical characteristics. This research mainly focuses on the gold nanomaterials which is very useful in positioning and detecting with its various advantages, like high chemical stability and catalytic activity. And this article is aimed to introduce the relationship between nanomaterial and biological medicine. Without doubt, nanotechnology plays an important role in pushing the development of biological medicine. But in my opinion, there are still some directions worth researching more, like using nanocluster to treat troublesome disease, such as neural disease, cancer cell expansion and autoimmunity disease. The applications of nanomaterials in biomedicine will achieve greater development in the future.

Authors' Contributions

Jiangxu Wu and Zikai Wang complete this work together.

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