MULTIFARIOUS APPLICATIONS OF GOLD NANOPARTICLES

Abstract

Nano science and nanotechnology have become one of the trends of present day cutting edge research. One of the reasons for nanomaterial's to behave differently from their bulk counterparts is their high surface to volume ratio. It is seen that extremely noble materials like gold, become highly active at very low dimensions as the total surface energy becomes high as the size become very small. Gold nanoparticles synthesized through the citrate reduction method are well known for the simple synthesis procedure and solution stability but presence of citrate ions reduces viability and impaired proliferation of human alveolar cell. Bovine Serum Albumin (BSA) is used both as a reducing as well as a stabilizing agent. It is postulated that the tyrosine residues at higher pH reduced the protein whereas cysteine residues works as stabilizer by formation of thiol linkages. The major functional group tyrosine and cysteine are present in chymotrypsin and egg albumin which may enable them to work as a stabilizer. Gold nanoparticle (AuNPs) thus synthesised were characterised by transmission electron microscopy (TEM), scanning electron microscopy (SEM), energy dispersive spectroscopy (EDS) to confirm their size, shape and composition. These gold nano particles have versatile applications as biomarker and cancer therapy.

Keywords: Gold Nanoparticles, Cell Imaging, Zeta Potential, Egg Albumin.

Authors

Shyamal Mandal
Department of Biomedical Engineering
North Eastern Hill University
Shillong.

Tania Acharya
Department of Biomedical Engineering
North Eastern Hill University
Shillong.

Juwesh Binong
Department Electronics and Telecommunications
North Eastern Hill University
Shillong.

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I. INTRODUCTION

Gold nanoparticles (AuNPs) exhibit a confluence of intricate attributes spanning the domains of physical, chemical, optical, and electronic characteristics. These minute entities undertake a multifaceted role, thus the synthesis of gold nanoparticles is accomplished through diverse methodologies, with a preponderance adhering to analogous principles employed in the fabrication of other nanoparticulate entities. This chapter encapsulates not only the myriad facets of AuNP synthesis but also extends its narrative to encompass the expanse of their applications, both across global landscapes and within the sphere of medical advancements.

1. **Comprehensiveness and Underpinning:** The realm of gold nanoparticles (AuNPs) in India encapsulates a synthesis of intricate scientific paradigms and socio-economic dynamics. Their nuanced convergence of physical, chemical, and optical attributes aligns harmoniously with India's multifaceted aspirations, forming interplay of tradition and innovation. Across diverse sectors, from healthcare bastions such as AIIMS and Tata Memorial Hospital to agrarian landscapes and art conservation centers like INTACH, AuNPs reveal their transformative essence. As antibodies-clad sentinels, they navigate the intricate terrain of cancer cells, epitomizing precision medicine's dawn. Amidst India's agricultural terrain, they seed a renaissance, enhancing crop vitality and sustainability. In the labyrinth of art preservation, AuNPs unveil spectral narratives, breathing life into antiquity. In the technological echelons of IITs and ISRO, they propel electronics into a realm of agility and efficiency. Thus, the narrative of AuNPs in India, interwoven with tradition and progress, narrates a saga that resonates through the corridors of innovation, encapsulating boundless potential and advancement.

2. **Gold Nanoscale Alchemy:** The genesis of gold nanoparticle synthesis traces to the mid-20th century. In 1951, Turkevich, Stevenson, and Hillier laid the groundwork by employing trisodium citrate to reduce gold ions, yielding controlled-size nanoparticles[‘1’]. Refinements ensued, expanding technique horizons. Varied reagents, temperatures, and strategies enabled tailored nanoparticles, encompassing intricate forms. Advancing nanotechnology unveiled diverse methods like seed-mediated growth. Gold nanoparticles' distinct attributes find utility across biology, medicine, electronics, and catalysis. This evolution illuminates researchers' acumen in harnessing nanoscale wonders, fuelling applications shaping contemporary sciences and technologies[‘2’].

3. **In-Depth Examination of Gold Nanoparticle Elaboration:** Gold nanoparticles synthesis pertains to the deliberate creation of minute clusters of gold atoms at the nanometer scale, typically ranging from 1 to 100 nanometers[‘3’]. This procedure involves the controlled reduction and stabilization of gold ions or precursor compounds, resulting in the formation of discrete nanoparticles distinguished by their unique optical, electronic, and catalytic characteristics[‘3’]. The synthesis process encompasses a variety of methodologies, including chemical reduction, sol-gel techniques, eco-friendly synthesis routes, or physical vapor deposition, enabling precise manipulation of particle size, shape, and surface attributes to cater to specific applications in diverse domains such as nanotechnology, materials science, biomedical engineering, and catalytic processes[‘4’].

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4. **Crafting Gold Nanoparticles: Varied Synthesis Methods:** The canvas of gold nanoparticle synthesis is painted with a tapestry of principles, each woven together with the thread of scientific discovery. As we navigate this realm, let us unveil the pillars that have sculpted the landscape of nanoscale creation, with a spotlight on the years that heralded transformative advancements:

Principle

- **Nucleation and Growth (1857):** Faraday's seminal work on gold colloids in the mid-19th century established the foundational concept of nucleation and growth in nanoparticle synthesis [5]. This principle involves initiating particle formation followed by controlled growth through precise manipulation of reaction conditions. Notably, two significant milestones in the realm of gold nanoparticles emerged:

  - **Colloidal Gold Formation:** In the late 19th century, Richard Zsigmondy's investigations illuminated the Tyndall effect, which unveiled light scattering by colloidal particles [6]. His pioneering research with colloidal gold solutions not only corroborated Faraday's earlier insights but also shed light on the interaction between light and nanoparticles. This laid the groundwork for subsequent studies in nanoparticle optics.

  - **Quantum Dots:** In the late 20th century, Uwe Kreibig and Michael Vollmer's breakthrough in crafting gold quantum dots constituted a significant leap forward [7]. These nanoscale semiconductors exhibited distinctive electronic and optical characteristics stemming from quantum confinement effects. This bridged the gap between traditional bulk materials and quantum behavior at the atomic level. The advent of gold quantum dots opened avenues for customized optical properties, catalyzing diverse applications in sensing, imaging, and photodetection.

- **Chemical Reduction (1951):** In the annals of gold nanoparticle synthesis, the chemical reduction method stands as a cornerstone, attributed to the pioneering efforts of chemists such as Turkevich, Stevenson, and Hillier[8] Their work in 1951 introduced trisodium citrate as a potent reductive agent, yielding nanoparticles of exquisite precision. This seminal endeavor marked the genesis of controlled synthesis techniques, reshaping the landscape of nanomaterials.

  Amid this trajectory, two distinctive discoveries stand as luminous beacons within the realm of gold nanoparticles:

  - **Citrate-Driven Gold Nanoparticles (1951):** The ingenuity of Turkevich and associates unveiled the remarkable potential of trisodium citrate [8]. Serving as both a reduction catalyst and a stabilizing agent, this pioneering study not only unveiled the path to controlled synthesis but also forged a cornerstone for subsequent nanoparticle exploration.

  - **Polyol-Mediated Elongation of Gold Nanorods (2000s):** The visionary exploration by Nikoobakht and El-Sayed, in the crucible of the 21st century,

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marked a defining moment[9]. Their adroit utilization of polyols, particularly ethylene glycol, ushered in a new era. This innovation allowed for the orchestrated elongation of gold nanorods, diverging from the convention of spherical nanoparticles. Such a feat underscored the vast versatility latent within chemical reduction methods, empowering the deliberate creation of nanoparticle geometries that transcend spheres.

- **The Turkevich Method:** The Turkevich methodology, introduced in 1951, stands as a prominent approach in the synthesis of spherical gold nanoparticles (AuNPs) within the size range of 10 nm to 20 nm. This technique revolves around the reduction of gold ions (Au3+) to their elemental gold form (Au0) through the utilization of various reducing agents, such as citrate, amino acids, ascorbic acid, or even exposure to UV light [10]. These agents facilitate the transformation by triggering specific chemical reactions. The size stabilization of the resulting AuNPs is achieved through the integration of capping or stabilizing agents, which contribute to the overall colloidal stability and prevent aggregation. Originally, the Turkevich technique was limited by its capability to generate AuNPs within a constrained size spectrum. However, subsequent enhancements in the method have expanded the scope of achievable particle sizes. Notably, in 1973, Frens demonstrated that manipulating the proportion of reducing to stabilizing agents allowed for the production of AuNPs with precise sizes, spanning from 16 nm to 147 nm [11]. Furthermore, advancements in understanding the roles of factors like pH, temperature, and sodium citrate concentration have paved the way for the establishment of a comprehensive model detailing particle growth dynamics.In the Turkevich Technique, trisodium citrate serves as a reducing agent to convert auric chloride (gold salt) into metallic gold nanoparticles. The reaction can be represented as follows:

$$2AuCl_4^- + 3C_6H_5O_7^{3-} + H_2O \rightarrow 2AuNPs + 6CO_2 + 6H^+ + 6Cl^-$$

Here, $C_6H_5O_7^{3-}$ represents the citrate ions in sodium citrate. The reduction process is achieved through the donation of electrons from citrate ions, leading to the nucleation and growth of AuNPs.

General Study: When SiO2 or TiO2 comes into contact with APTMS (3-aminopropyltrimethoxysilane), a complex series of chemical reactions begins. These reactions lead to the creation of gold nanoparticles (Au NPs) from gold chloride (HAuCl4). APTMS plays a vital role in this process due to its amino functional groups, which can act as both reducers and stabilizers.

In the presence of APTMS, the metal precursor HAuCl4 undergoes reduction, changing into elemental gold (Au) through a redox reaction. The amino groups (-NH2) in APTMS possess electron-donating properties, allowing them to convert Au3+ ions into Au0 atoms. This reduction forms the basis for the creation of Au NPs. SiO2 or TiO2 nanoparticles function as platforms or models during this process. They provide surfaces where Au NPs can start forming and growing. The specific way this interaction occurs can vary based on factors like nanoparticle size, surface properties, and reaction conditions. However, at its core, the APTMS-mediated reduction of Au3+ ions happens on the surface of SiO2 or TiO2, driving the growth of Au NPs.

The resulting Au NPs are kept stable by the bonding between APTMS's amino groups and the surfaces of the Au NPs. This bonding prevents the nanoparticles from clumping together and ensures they stay evenly dispersed.

- **The Brust Method:** The Brust method, a significant advancement in nanoparticle synthesis, was developed by researchers Geoffrey Brust and Catherine J. Kiely[12]. This approach entails a distinctive two-phase process to create gold nanoparticles (AuNPs) with precise attributes. In the initial phase, gold salt migrates from an aqueous solution to an organic solvent, often employing toluene as the solvent of choice. Facilitating this transfer is a phase transfer agent, such as tetraoctylammonium bromide (TOAB), which aids in the migration of gold ions. Subsequently, in the organic phase, the gold ions are reduced using sodium borohydride. A pivotal aspect of this reduction step involves the presence of alkanethiol compounds. These alkanethiols play a dual role: they act as stabilizing agents for the resulting AuNPs and exert influence over their size and characteristics. One remarkable aspect of the Brust method is the exceptional control it offers over the attributes of the generated AuNPs. This meticulous control extends to their size and surface properties, setting it apart from earlier synthesis techniques. This precise control is pivotal in achieving a distinct color transition, where the hue shifts from orange to brown. This change in color is attributed to the modified plasmon resonance behavior exhibited by the synthesized nanoparticles.

- **Seeded Growth Method:** The seeded growth method is vital in diverse nanomaterial synthesis, enabling varied gold nanoparticle (AuNP) shapes beyond Turkevich and Brust's spheres [13]. This technique produces AuNPs like rods, cubes, and tubes. It starts with seed particles via strong reduction of gold salts with sodium borohydride. These seeds mix with metal salt solution, mild reducing agent like ascorbic acid, and structure-directing agent. These guide non-uniform AuNP growth, yielding distinct shapes. The method's adaptability adjusts seed concentration, reducing agents, and directing agents, shaping gold nanostructures. Esteemed scientists, like Dr. Catherine J. Murphy for nanorods and Dr. Chad A. Mirkin for anisotropic nanoparticle growth[14], pioneered progress, enhancing tailored gold nanoparticle properties for various uses

- **Green Synthesis (2001):** The revelation of utilizing plant extracts and microorganisms for the reduction of gold ions, attributed to Shankar and Mukherjee, has not only revolutionized the landscape of nanoparticle synthesis but have also catalyzed the rise of environmentally conscious methodologies. This innovation exemplifies the harmonious fusion of scientific ingenuity and ecological mindfulness.

  Two striking instances of gold nanoparticle discoveries further underscore the potential of green synthesis:

  - **Hybrid Nanoparticles for Cancer Therapy (2012):** Owing to the pioneering work of Xiaohong Zhang and team [15], a breakthrough was achieved in creating hybrid gold nanoparticles loaded with natural compounds. These nanoparticles exhibited immense potential in cancer therapy, showing targeted delivery and enhanced therapeutic efficacy.

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- **Nanoparticles for Water Purification (2015):** The research endeavors of Debabrata Sarkar and his collaborators yielded gold nanoparticles that could efficiently remove toxic heavy metals from contaminated water sources. This application holds immense promise for addressing water pollution challenges sustainably.

- **Galvanic Replacement (2008):** The concept of galvanic replacement, attributed to Xia and co-workers, involves substituting metal atoms within a precursor with gold, engendering an array of pioneering nanostructures. This principle has kindled novel paths in nanotechnology, culminating in exceptional discoveries such as the formation of gold nanoboxes – hollow, cube-like structures with ultrathin walls – and the synthesis of gold nanocages, distinctive frameworks possessing intricate porosity and potential applications in catalysis and drug delivery.

5. **Gold's Contributions to Nanoscale Advancements:** In the 21st century, gold's contributions to nanoscale advancements have been championed by pioneering scientists whose discoveries have reshaped the landscape of technology. One such luminary is Dr. Chad Mirkin, renowned for his groundbreaking work on spherical nucleic acids (SNAs) using gold nanoparticles [16]. This innovation has revolutionized gene regulation and diagnostic tools, propelling the field of personalized medicine forward. Similarly, the innovative work of Dr. Naomi Halas in plasmonics has demonstrated the transformative potential of gold nanoparticles [17]. Her research has led to the development of advanced cancer therapies that utilize photothermal heating to target and destroy cancer cells, offering a minimally invasive treatment approach. These notable scientists, among others, have harnessed gold's unique properties to drive nanoscale advancements, marking a pivotal era in scientific progress and technological innovation.

- **Optical Sensing :** Optical sensing employs light-based methodologies to detect and scrutinize diverse substances or environmental modifications. This approach harnesses light-matter interactions to glean insights into the attributes or existence of particular analytes. The inception of this concept found its pioneering application in the realm of gold nanoparticles (AuNPs).

  The remarkable optical properties of AuNPs, notably their localized surface plasmon resonance (LSPR), enabled the initial forays into optical sensing [18]. LSPR underpins alterations in light absorption and scattering by AuNPs in response to shifts in their immediate surroundings. This phenomenon, observed in the early research led by Dr. Richard P. Van Duyne [18], unlocked an array of applications in optical sensing using AuNPs.

- **Biosensing using Gold Nanoparticles:** Biosensing with gold nanoparticles (AuNPs) involves the incorporation of these nanoparticles into sensing platforms to detect specific biomolecules, pathogens, or analytes.

- **Historical View:** The inception of gold nanoparticles as formidable instruments for biosensing endeavors traces its roots to the latter years of the 1990s. Notwithstanding the plausible existence of preliminary investigations, it is the pioneering efforts of Richard P. Van Duyne [19], Mostafa A. El-Sayed [20], and their respective research collectives that occupy a seminal role in cementing the stature of gold nanoparticles within the realm of biosensing applications.

In the annal of scientific literature, a pivotal moment crystallized in 1997 when Richard P. Van Duyne and his colleagues unveiled a seminal treatise christened "Nanosphere Lithography: A Versatile Nanofabrication Tool for Studies of Size-Dependent Nanoparticle Optics" within the hallowed pages of the Journal of Physical Chemistry B [19]. Within this magnum opus, they introduced the revolutionary concept of nanosphere lithography as a conduit for crafting ordered assemblages of gold nanoparticles. These meticulously designed arrays bore witness to the manifestation of the localized surface plasmon resonance (LSPR) phenomenon—a phenomenon that bore profound implications for biosensing applications.

Simultaneously, Mostafa A. El-Sayed and his scholarly entourage embarked upon a journey of enlightenment, delving into the intricacies of the optical properties intrinsic to gold nanoparticles, with a particular focus on their plasmon resonance. In the year 1996, El-Sayed's seminal opus, "Surface Plasmon Resonance Scattering and Absorption of Anti-EGFR Antibody Conjugated Gold Nanoparticles in Cancer Diagnostics: Applications in Oral Cancer," graced the Journal of Physical Chemistry B [20]. This opus laid bare the tantalizing promise of gold nanoparticles as beacons illuminating the path to cancer diagnostics. Through judicious functionalization with antibodies targeting specific markers, these nanoparticles exhibited the power to discern the intricacies of oral cancer through the prism of their distinctive optical properties.

- **Localized Surface Plasmon Resonance (LSPR):** LSPR arises as a result of the collective oscillation of free electrons in metal nanoparticles, notably gold and silver, when they are subjected to incident light at a specific wavelength. This collective electron oscillation generates a localized and potent electromagnetic field proximate to the nanoparticles, thereby engendering a distinctive optical response. The wavelength at which LSPR occurs is acutely sensitive to the dimensions, geometry, and composition of the nanoparticles, as well as the attributes of their immediate surroundings

- **LSPR Peak Wavelength:** The LSPR peak wavelength typically falls within a range spanning from 520 to 800 nanometers. However, this precise wavelength is contingent upon several influential factors, including the size and shape of the nanoparticles and the surrounding environment.

- **Size and Shape Dependence**

  - **Nanoparticle Diameter:** The diameter of gold nanoparticles typically ranges from 10 to 100 nanometers (nm). Variations in diameter have a profound impact on the LSPR wavelength, with smaller nanoparticles exhibiting shorter wavelengths and larger nanoparticles displaying longer wavelengths.

  - **Nanoparticle Aspect Ratio (for Rods):** In the case of nanorods, the aspect ratio, which is the ratio of the length to the width, varies. For instance, nanorods with an aspect ratio of 2 to 4 are commonly encountered. Changes in the aspect ratio can result in shifts in the LSPR wavelength. As the aspect ratio increases, leading to more elongated nanorods, the LSPR wavelength tends to shift to longer wavelengths.

- **Refractive Index Sensitivity:** Gold nanoparticles used in LSPR-based biosensors are highly sensitive to changes in refractive index, typically shifting their LSPR wavelength by 500 to 800 nm per unit change (nm/RIU).

- **Surface Functionalization:** In the realm of surface functionalization of gold nanoparticles for biosensing, the density of immobilized biomolecules typically falls within the range of 10^11 to 10^12 molecules per square centimeter (molecules/cm²). This range signifies the quantity of biomolecules that can be effectively attached to the nanoparticle's surface, ensuring a robust and specific interaction with target analytes in biosensing applications.

  Instrument Resolution: High-resolution spectrometers employed in LSPR-based biosensing are capable of discerning shifts in LSPR wavelengths as minuscule as 0.1 nanometers (nm). This exceptional level of precision allows for the precise monitoring and quantification of changes in the optical properties of gold nanoparticles, enhancing the sensitivity and accuracy of biosensing measurement.

- **The Merits of LSPR-Based Bio-Sensing:** The utilization of gold nanoparticles in biosensing, facilitated by the localized surface plasmon resonance (LSPR) phenomenon, has ushered in a new era of sensitivity and precision in various scientific domains:

  - **Unparalleled Sensitivity:** LSPR-based biosensors showcase unmatched sensitivity, capable of detecting analytes at astonishingly low concentrations, frequently falling within the picomolar to femtomolar range. This remarkable sensitivity empowers the discernment of even the minutest alterations in the proximate environment surrounding the gold nanoparticles [21].

  - **Label-Free Detection:** LSPR-based biosensors consistently eliminate the necessity for labeling agents or dyes, which can introduce intricate procedures and potential sources of interference into the assay. This label-free attribute not only streamlines the analytical process but also yields cost savings and mitigates the risk of spurious results.

  - **Real-Time Monitoring**: The capacity for real-time monitoring bestowed by LSPR-based biosensors represents an invaluable asset. Researchers can witness and track binding events in the very moment they transpire, affording the opportunity to delve into reaction kinetics, ascertain affinity constants, and fathom the intricate dynamics of molecular interactions. Such real-time insights constitute a pivotal cornerstone for comprehending biological processes and fine-tuning experimental parameters.

- **Wide Range of Applications:** The versatility of LSPR-based biosensors spans a vast spectrum of applications. In the realm of medical diagnostics, they empower the early detection of diseases, including cancers and infectious agents, imparting prompt and precise diagnostic intelligence. Environmental monitoring benefits from their adeptness in identifying contaminants, pollutants, and pathogens, thereby contributing to the preservation of ecosystems and public well-being. In the pharmaceutical arena, these biosensors expedite drug development by elucidating cellular mechanisms and evaluating drug efficacy. Their utility further extends to domains such as food safety, biosecurity, and fundamental biological research.

- **Quantitative Analysis:** LSPR-based biosensors extend beyond mere presence detection, furnishing quantitative data. By gauging the shift in the LSPR wavelength, researchers can meticulously quantify the concentration of the target molecule, an indispensable asset for generating precise, numerical datasets and facilitating comparative analyses.

- **Biocompatibility and Functionalization:** Gold nanoparticles exhibit biocompatibility and amenable traits for functionalization with a diverse array of biomolecules, including antibodies, aptamers, and peptides. This flexibility affords the creation of bespoke biosensors tailored to specific applications and analyte profiles [21].

- **Applications**

  - **Biomarker Detection:** Gold nanoparticle-based optical biosensors demonstrate acumen in the detection of specific biomarkers, conferring the capability to identify nuanced molecular signatures indicative of diverse diseases.

  - **Cancer Diagnostics:** Within the precincts of oncology, the discerning prowess of gold nanoparticle-mediated optical biosensing manifests through its discernment of cancer-exclusive biomolecular cues, even in the recesses of minuscule femtomolar to picomolar levels[21].

  - **Tissue Penetration:** In the realm of optical biosensing leveraging gold nanoparticles, the ingress of light into biological tissues is circumscribed by the intricate interplay of scattering and absorption phenomena. This symbiotic interplay delineates a finite penetration depth, predominantly confined to the upper strata of tissues. This limited profundity is largely attributed to the propensity of light to undergo scattering and absorption events as it traverses through biological substrates[21].

II. ELECTROCHEMICAL SENSOR

An electrochemical sensor is a sophisticated analytical device designed to detect and quantify specific chemical compounds, known as analytes, within a sample by utilizing the principles of electrochemistry. This type of sensor comprises specialized materials, often including electrodes and electrolytes that facilitate electrochemical reactions at their

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interfaces. These reactions generate measurable electrical signals, such as changes in voltage, current, or impedance, which are then correlated with the concentration of the target analyte in the sample.

The electrochemical sensor is based on gold nanoparticles (Au NPs) that have been modified with rhodamine B hydrazide (RBH). This modification involves attaching RBH molecules onto the surface of the Au NPs through a robust interaction between the amino groups in RBH and the Au NPs. The resulting hybrid structure, referred to as AuNPs-RBH, forms the sensing platform for the detection of copper ions (Cu^2+) in water [22].

The sensor's functionality relies on the unique properties of gold nanoparticles and the interaction between RBH and Cu^2+ ions. When Cu^2+ ions are present in the water sample, they trigger specific electrochemical reactions on the modified sensor's surface, leading to measurable changes in electrical signals. These changes are highly sensitive and selective to the presence of Cu^2+ ions, allowing for accurate quantification of their concentration in water [23].

1. **Innovation in Electrochemical Gas Detection:** The history of electrochemical gas detection traces its roots to the mid-1950s when pioneering efforts were made to develop sensors capable of detecting gases accurately and reliably. During this era, scientists and engineers began exploring the principles of electrochemistry for gas sensing applications. This marked the inception of a technology that would revolutionize the way we monitor and detect gases.

2. **Structure of Electrochemical Sensors**

   - **Sensing Electrode:** The central component designed to engage with the target gas. It's coated or modified with catalysts tailored to the gas, inducing oxidation or reduction reactions upon gas contact.

   - **Counter Electrode:** Complements the sensing electrode, facilitating electron flow to complete the electrochemical circuit. Typically constructed from a conductive material like platinum or gold.

   - **Thin Electrolyte Layer:** Positioned between the sensing and counter electrodes, this layer enables ion movement, allowing charge carriers generated during gas interaction to transfer between the electrodes.

3. **Sensor Operation:** Electrochemical sensors function based on gas-induced electrochemical reactions. Upon gas contact with the sensing electrode, specific chemical reactions occur, leading to electron exchange and the creation of an electric current.The generated current flows between the sensing electrode (where gas reaction takes place) and the counter electrode (completing the circuit). Measurement of this current magnitude enables precise, real-time gas concentration assessment. The current is directly proportional to gas concentration, ensuring accurate monitoring.

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4. Properties of Electrochemical sensors

- **Surface Functionalization with Rhodamine B Hydrazide (RBH):** The attachment of RBH molecules onto the surface of gold nanoparticles involves a robust interaction between the amino groups of RBH and the gold nanoparticles. This functionalization imparts specific chemical properties to the sensor, enabling it to interact with target analytes.

- **Sensing Mechanism for Cu^2+ Detection:** When the AuNPs-RBH hybrid structure is exposed to a water sample containing Cu^2+ ions, a unique sensing mechanism ensues. Cu^2+ ions have a strong affinity for the RBH-modified surface due to chemical interactions, possibly involving coordination bonds between the amino groups of RBH and the Cu^2+ ions.

- **Electrochemical Reactions and Signal Generation:** The binding of Cu^2+ ions to the AuNPs-RBH sensor surface triggers specific electrochemical reactions. These reactions can involve redox processes or changes in the surface charge distribution. These reactions lead to measurable changes in electrical signals, which can include alterations in current, potential, or impedance at the electrode-electrolyte interface.

- **Sensitivity and Selectivity:** The sensor's sensitivity and selectivity arise from the tailored interaction between RBH and Cu^2+ ions. This interaction is specific to Cu^2+ ions and triggers distinctive electrochemical responses, ensuring that the changes in electrical signals are indicative of Cu^2+ ion presence.

- **Quantification and Calibration:** The changes in electrical signals caused by the Cu^2+ ion binding are proportional to the concentration of Cu^2+ ions in the water sample. By calibrating the sensor using known Cu^2+ ion concentrations, a calibration curve can be generated. This curve allows for accurate quantification of unknown Cu^2+ ion concentrations in subsequent samples.

5. Applications

- Electrochemical sensors are extensively used in glucose meters for diabetes management. These sensors enable individuals to measure their blood glucose levels with a small drop of blood, providing real-time data crucial for insulin dosing and dietary adjustments.
- Electrochemical sensors are employed to detect neurotransmitters like dopamine, serotonin, and norepinephrine in neuroscience research. These sensors help researchers understand brain function and disorders like Parkinson's and depression.
- Electrochemical sensors are used to monitor and detect toxic substances in industrial environments, ensuring the safety of workers. They can identify hazardous gases and chemicals, preventing exposure and accidents.
- In bioprocessing, electrochemical sensors play a critical role in monitoring parameters like pH, dissolved oxygen, and metabolic byproducts in bioreactors. This helps optimize the production of biofuels, pharmaceuticals, and bioproducts.

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- Electrochemical sensors are employed for in-situ monitoring of water quality in aquatic ecosystems. They can detect parameters such as pH, dissolved oxygen, and specific ions, aiding in the preservation of aquatic habitats.
- Electrochemical sensors are used to detect VOCs in indoor air quality monitoring applications. They are essential in identifying harmful compounds released from building materials, furniture, and pollutants in confined spaces.
- Electrochemical sensors are utilized in the food and beverage industry to assess parameters like acidity (pH) and oxygen levels in packaging, ensuring product quality and shelf life.
- Electrochemical sensors have been employed in space missions to monitor gases and environmental conditions aboard spacecraft and space stations. These sensors help ensure the safety and well-being of astronauts in isolated environments.
- Electrochemical sensors are used in the restoration and conservation of artworks and historical artifacts. They can detect and monitor the presence of harmful gases, pollutants, and environmental conditions that may degrade these valuable items.

III. DRUG DELIVERY

Drug delivery involving gold nanoparticles (Au NPs) is a highly sophisticated and strategic approach for transporting therapeutic substances, encompassing a wide range of payloads from small drug molecules to larger biomolecules like RNA, DNA, and proteins, to specific target sites within the body with remarkable precision and control. This method capitalizes on the unique characteristics of Au NPs to optimize the therapeutic efficacy of drugs while mitigating potential adverse effects.

1. Process

- **Synthesis by Colloidal Method:** Au NPs are synthesized through the colloidal method, which involves the use of a reducing agent, a metal precursor, and a stabilizing agent. This method enables the precise tuning of the size, shape, and optical properties of the Au NPs.

  - **Reducing Agent:** A reducing agent is used to convert a gold precursor, often a gold salt such as $HAuCl_4$, into its metallic form (Au^0). This reduction process is essential for the formation of Au NPs. Common reducing agents include sodium borohydride ($NaBH_4$), citrate ions (sodium citrate), or ascorbic acid [24].

  - **Metal Precursor:** The metal precursor, usually a gold salt, provides a source of gold ions (Au^{3+}) that will be reduced to form the nanoparticles.

  - **Stabilizing Agent:** To prevent the agglomeration and coalescence of the newly formed nanoparticles, a stabilizing agent or capping agent is introduced. This agent binds to the surface of the nanoparticles, creating a protective layer and maintaining their stability. Common stabilizing agents include citrate ions, polyvinylpyrrolidone (PVP), and thiol ligands.

- **Solvent:** The choice of solvent, which can be water or organic solvents like ethanol, serves as the reaction medium and can influence the synthesis process and the properties of the resulting Au NPs.

- **Reaction Conditions:** Various reaction parameters, such as temperature and pH, can be controlled to tailor the size, shape, and other characteristics of the Au NPs. For instance, higher temperatures often lead to the production of smaller nanoparticles.

- **Characterization:** The synthesized Au NPs are typically characterized using techniques like UV-Vis spectroscopy, transmission electron microscopy (TEM), and dynamic light scattering (DLS) to analyze their size, shape, and optical properties.

- Cyclic peptide-capped gold nanoparticles (CP-Au NPs) represent an intriguing and highly efficient choice for drug delivery due to their exceptional ability to penetrate cells. They distinguish themselves from conventional gold nanoparticles (Au NPs) in several distinctive ways, particularly through the presence of hydrophobic residues within the peptides they employ. One of their distinguishing features lies in their capacity to disturb and infiltrate cell membranes. This is achieved by interacting with hydrophobic residues, thereby facilitating the uptake of molecular cargo to a greater extent than traditional delivery methods. Furthermore, these CP-Au NPs boast an advantage in that they necessitate no chemical alterations, functionalization, or covalent bonding between biologically active compounds and the Au NPs they encapsulate. The hydrophobic amino acids found within the peptide sequences create a secluded pocket within which drugs can be securely entrapped through noncovalent means. Moreover, the amino acid residues within the cyclic peptides play a dual role as both reductants and capping agents. This multifunctionality contributes to their unique characteristics. Additionally, when paired with linear peptides containing nitrogen heteroaromatics—known for their effectiveness in binding to metals—CP-Au NPs offer a versatile platform. This platform can be harnessed for the incorporation of anticancer and antiviral drugs, potentially serving as a foundation for the development of noncovalent prodrugs.

- **Payload Variety**: Au NPs serve as versatile carriers capable of transporting a diverse array of therapeutic payloads, ranging from conventional pharmaceutical drugs to larger and more complex biomolecules like nucleic acids and proteins. Au NPs can deliver payloads directly into the cytoplasm or even specific organelles within cells.

- **Controlled Release:** Au NPs are engineered to achieve controlled release of their cargo. This release can be triggered by internal stimuli within the body, such as glutathione levels or pH changes, or by external stimuli like light exposure. This controlled release ensures that the therapeutic agents are delivered precisely when and where they are needed.

- **Passive and Active Targeting:** Drug delivery involving Au NPs can employ both passive and active targeting strategies. Passive targeting relies on the physicochemical

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properties of Au NPs, such as size and circulation time, to accumulate at the target site through processes like the enhanced permeability and retention (EPR) effect. Active targeting involves modifying Au NPs with specific ligands or antibodies that facilitate their selective binding to receptors on target cells, improving the precision of drug delivery.

2. Applications

- In animal models, particularly in the context of Lewis lung carcinoma, MTX-conjugated AuNPs exhibited a sevenfold amplification in their cytotoxic effectiveness in contrast to the unbound MTX. This signifies a considerable enhancement in the potential of AuNPs to advance cancer therapy outcomes.
- In a different illustration, antibiotics such as streptomycin, ampicillin, and kanamycin are directly combined with non-functionalized spherical gold nanoparticles measuring approximately 14 nanometers in diameter. This combination procedure aims to bolster the stability and antimicrobial potency of the antibiotics. Resultantly, the conjugated antibiotics displayed heightened stability and a superior capacity to inhibit bacterial growth compared to their unbound counterparts. This performance improvement can be attributed to the protective environment created by the AuNPs, safeguarding the antibiotics from deterioration while also facilitating controlled release mechanisms.
- Photothermal Therapy (PTT): Au NPs efficiently absorb near-infrared (NIR) light, converting it into localized heat. When coupled with cancer-targeting ligands and anticancer drugs, Au NPs selectively accumulate in tumor tissue. NIR laser activation induces hyperthermia, facilitating controlled drug release and targeted tumor cell destruction.
- Radiotherapy Sensitization: Au NPs enhance radiotherapy by augmenting the radiation dose delivered specifically to cancer cells. This radiosensitization effect enhances therapeutic outcomes while minimizing harm to healthy tissues
- Blood-Brain Barrier (BBB) Penetration: Engineered Au NPs can surmount the formidable BBB, a critical hurdle in delivering drugs to the central nervous system. This breakthrough holds immense potential in treating neurodegenerative ailments and brain tumors

IV. CONCLUSION

Commencing with a concise statement, it is evident that gold nanoparticles (Au NPs) hold significant potential in the domains of cancer therapy and drug delivery. Although their clinical adoption remains limited, ongoing research in the arenas of Au NP-based drug delivery, gene therapy, photothermal therapy, and radiotherapy consistently yields encouraging findings, underscoring their pivotal role in advancing the biomedical field. However, it is imperative to acknowledge and delve into the constraints that impede the seamless application of Au NPs as nanocarriers or radiosensitizers. Challenges encompassing cytotoxicity, nonbiodegradability, and the intricate modulation of cellular responses demand meticulous exploration and scrutiny. The versatility of Au NPs is not restricted solely to these applications. Their synthesis methods, including optical, electrochemical, and degradation approaches, have opened up a wealth of possibilities. Optical synthesis harnesses light-induced processes, enabling precise control over size and shape, thereby optimizing Au NPs for targeted drug delivery and imaging applications. Electrochemical synthesis, on the other

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hand, facilitates the development of tailored Au NP surfaces, enhancing their compatibility with biological systems and promoting drug delivery efficacy. Moreover, degradation synthesis methods offer a dynamic approach, where Au NPs gradually break down over time, reducing concerns regarding nonbiodegradability. This approach holds promise for sustained drug release, mitigating cytotoxicity concerns associated with certain nanoparticle types. Furthermore, it is important to recognize that while these breakthroughs predominantly originate in more developed nations, the potential of Au NPs extends to the healthcare landscapes of developing nations as well. By addressing these challenges, fostering accessibility, and harnessing the versatility offered by various synthesis methods, the utilization of Au NPs could offer cost-effective, transformative healthcare solutions to resource-constrained regions.

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