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5 **Preparation and Functionalization of Gold**
6 **Nanoparticles**
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11 **IGNÁC CAPEK**

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14 **Abstract** — The abilities to control the size of gold nanoparticles and to manipulate them on
15 a nanometer scale are priority subjects in the field of nanotechnology. To synthesize gold
16 nanomaterials in controlled sizes and dimensions, various approaches have been developed. These
17 systems can be made up of several different microenvironments: a continuous medium formed
18 by the alkane or water, a disperse phase formed by microdroplets, micelles or surface active
19 compounds and a tensioactive film, which separates the hydrophilic phase from the alkane and
20 allows the solubilization to occur. Micelle or microemulsion approach allows for a unique
21 encapsulated volume of controllable size through which reactions and subsequent development
22 of metal and metallic compounds can be produced. The precipitation of prime nanoparticles is
23 based on the supersaturation of solution by reactants and stabilization of formed nanoparticles
24 by surfactants. The existence of these microenvironments gives these systems a particular ability
25 to modulate the chemical reactivity due to the compartmentalization of the reactants in different
26 microenvironments. These nanoparticles have become the focus of intensive research due to their
27 unique applications in mesoscopic physics and in the fabrication of nanoscale devices.

28 **Keywords** : *Gold nanoparticles, preparation, passivation, functionalization and Ostwald ripening.*
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31 **INTRODUCTION**

32 While the most ancient use of colloidal gold is believed to have been in Egypt by
33 alchemists, the brilliant colors of nanosized colloidal particles of silver, gold and
34 copper were used in staining glasses as back as the 17th century. The use of gold
35 colloid in biological applications began in 1971, when the immunogold staining
36 procedure was invented.
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1 The preparation of noble metal nanoparticles has received considerable attention
2 in recent decades because nanoparticles possess unconventional physical and chemical
3 properties [1] Nanoparticles exhibit novel material properties which largely differ from
4 the bulk materials due to these small sizes, including quantum size effect on
5 photochemistry, nonlinear optical properties of semiconductor or the emergence of
6 metallic properties with the size of the particles [2]. As nanomaterials of noble metals,
7 gold nanoparticles have extensive applications, such as antibacterial materials [3],
8 antistatic materials, cryogenic superconducting materials [4], biosensor materials and
9 so on.

10 Many nanogold-based environmental technologies (e.g., sensors, sorbents,
11 reactants...) are under very active research and development, and are expected to
12 emerge as the next generation environmental technologies to improve or replace
13 various conventional environmental technologies in the near future [5]. Some of the
14 most promising near term realizations of nanotechnology are at the interface of
15 physical, chemical and biological systems. Because many biomolecules have specific
16 binding properties in self-assembly processes, they are attractive materials for
17 nanotechnology.
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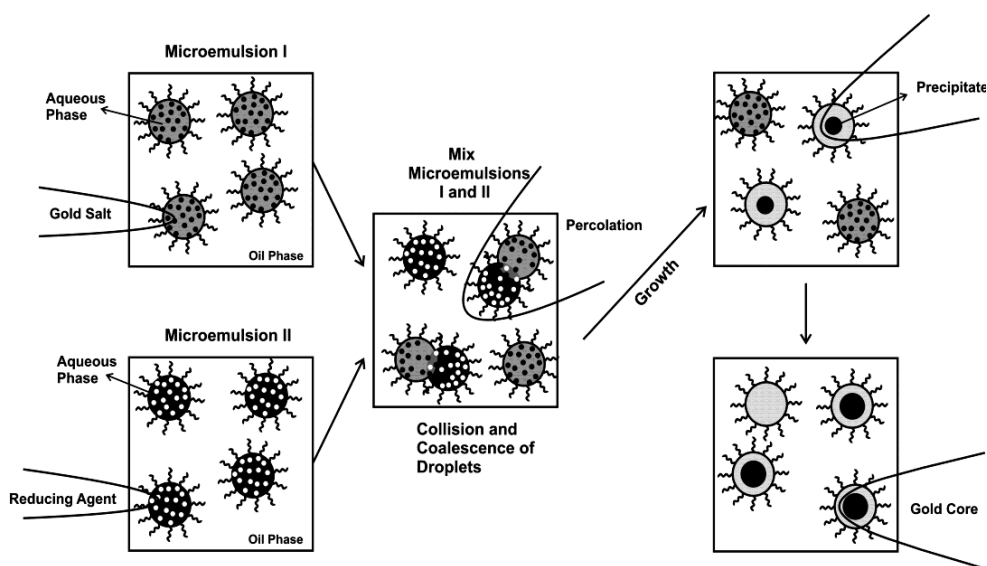
19 Most existing approaches explore the strong affinity of thiols to gold [6] and
20 the use of disulfides [7] and thioethers [8] as capping agents as well. Polymers
21 functionalized with molecular recognition groups [9], thioacetate groups [10] and
22 tetradentate thioether ligands [11] have recently been used to mediate the formation
23 of spherical or related assemblies of gold nanoparticles. These approaches have shown
24 remarkable capabilities in assembling nanoparticles into functional nanostructures, the
25 ability to control their size and shape.
26

27 **SYNTHETIC APPROACHES**

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29 A number of techniques have been used for producing metal nanoparticles, including
30 vapor phase techniques [12], sol-gel methods [13], sputtering [14], precipitation [15],
31 soft- and hard-templates, chemical and bioreduction, synthesis in micellar solutions [16,
32 17], etc. Two main methods can be employed for the preparation of gold
33 nanoparticles: coprecipitation and chemical reduction. In both cases, the presence of
34 surfactant is required to govern the growth process. Typically, the coprecipitation
35 reactions involve the thermal decomposition of organometallic precursors [18]. The
36 chemical reduction occurring in colloidal assemblies is another approach for the
37 formation of size- and shape-controlled nanoparticles [19]. A major benefit of chemical
38 methods is their relatively inexpensive investment of capital equipment.
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1 The successful utilization of gold nanoparticles (AuNPs) in biological assays
 2 relies on the availability of synthetic methods generating nanoparticles with the desired
 3 characteristics, namely high solubility in water, and adequate morphology, size
 4 dispersion, and surface functionalities. Of the chemical processes, reverse micelle
 5 (microemulsion) synthesis has been recently demonstrated to be a viable method for
 6 producing a wide array of noble metal nanoparticles over a relatively narrow particle
 7 size distribution [20]. Reverse micelle synthesis utilizes the natural phenomenon
 8 involving the formation of spheroidal aggregates in a solution when a surfactant is
 9 introduced to an organic solvent, formed either in the presence or in the absence of
 10 water [21]. Micelle formation allows for a unique encapsulated volume of controllable
 11 size through which reactions and subsequent development of metal and metallic
 12 compounds can be produced. Aggregates containing ω ($=$ [water]/[surfactant], see
 13 above) of less than 15 can be called as reverse micelles and have hydrodynamic
 14 diameters in the range of 4-10 nm [22], whereas ω greater than 15 constitute
 15 microemulsions, which have a hydrodynamic diameter range between 5 and 50 nm.
 16 Once the right microemulsions are obtained, the method of particle preparation consists
 17 in mixing of two microemulsions carrying the appropriate reactants in order to obtain
 18 the nanoparticles [23,24] (Fig. 1).



38 Fig. 1. Proposed mechanism for the formation of gold nanoparticles by the microemulsion ap-
 39 proach.

1 Through controlling the amount of surfactant, water, reducing agent, gold salt,
2 the rate of reaction and the reaction temperature, inverse micelle synthesis usually
3 produces nanoparticles with the average particle size depending somewhat on the size
4 of the micelles. The gold colloid was prepared at room temperature using a
5 didodecyldimethylammonium bromide (DDAB)/water/toluene inverse micelle system
6 [25]. The gold particles have a wide size distribution, from tiny particles as small
7 as 1 nm to very large particles with the size of 80 nm. The large size distribution
8 was apparently caused by the inhomogeneous growth of the nanoparticles due to the
9 low DDAB concentration. The simplest approaches for isotropic and anisotropic
10 nanoparticle synthesis are various surfactant- or micelle-based methods [26].
11 Surfactant-based anisotropic micelle templates can be easily prepared [27]. For
12 example, the ~ 6 nm spherical micelles formed by a dilute (>1 mM) solution of
13 cetyltrimethyl ammonium bromide surfactant converts to cylindrical micelles at higher
14 concentrations (>20 mM), more elongated rodlike micelles in the presence of organic
15 solubilizes (Fig. 2, homogeneous and heterogeneous (seeded) nucleation) [28], and
16 wormlike micelle structures in the presence of salicylate [29]. Surfactant molecules
17 can be used as “simple” capping and stabilizing agents as in the organometallic
18 precursor decomposition reactions.

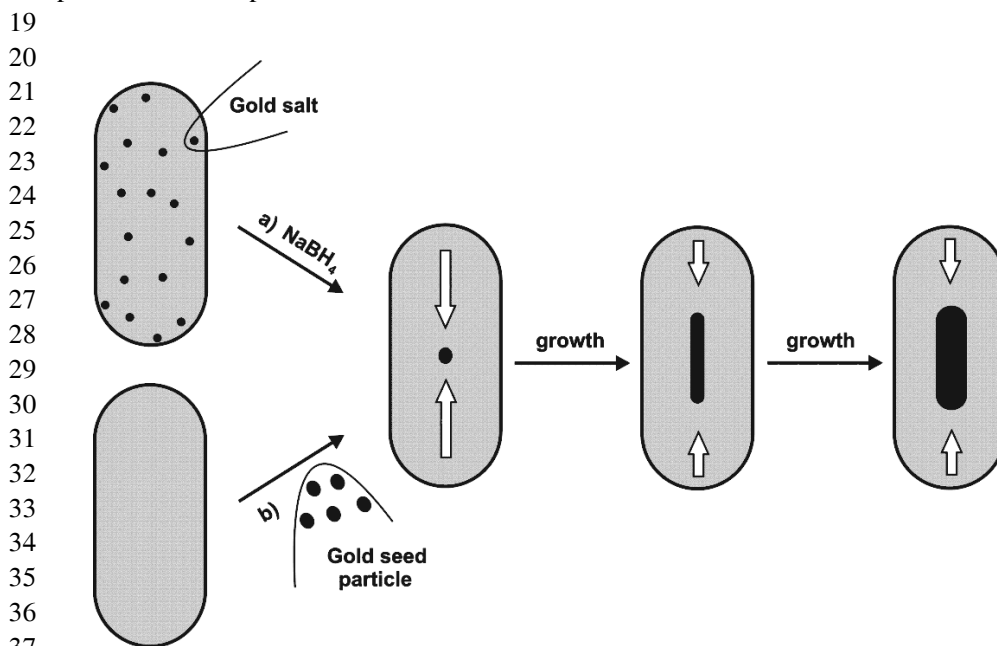
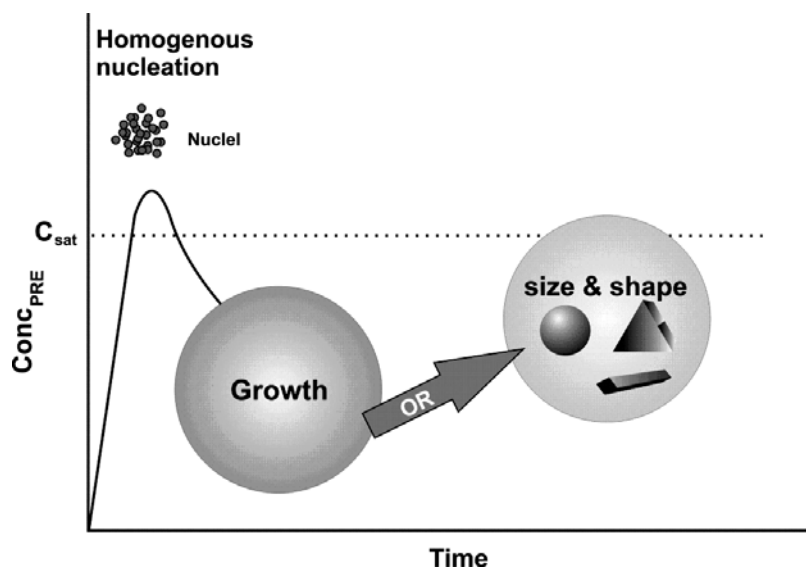


Fig. 2. Proposed rodlike particle nucleation for (a) borohydrate or Au seeded one.

1 The co-precipitation (homogeneous and heterogeneous nucleation) of prime
 2 nanoparticles is based on the supersaturation of solution by reactants such as
 3 precursors (metal salts), reducing agent, stabilizers, co-stabilizers, solvents (passivation)
 4 and additives (Fig. 3). The increased solubility of component in the continuous phase
 5 can be reached by the rising in temperature. The supersaturation state can be then
 6 reached by the reduction in temperature. Generation of supersaturation through in situ
 7 chemical reactions by converting highly soluble chemicals into less soluble chemicals
 8 is a good example of this approach. In a typical homogeneous nucleation synthesis
 9 consisting of one step process in which precursor (s), stabilizer(s) and other additives
 10 are stirred in the oil- or water-continuous phase and then treated by the heat [30].
 11 The heterogeneous nucleation of metal particles consists of several-steps process [31].
 12 In a typical heterogeneous nucleation the first step is the formation of the primary
 13 (seed) metal particles and then the growth of particles is achieved by the addition
 14 of precursor(s), stabilizer(s) and additives [32,33].

15 H. Hiramatsu and F. E. Osterloh have used a high-temperature solution-phase
 16 synthesis as an inexpensive, versatile, and very reproducible supersaturation method
 17 for the large-scale synthesis of organoamine-protected gold nanoparticles in the 6-21
 18 nm (Au) size ranges and with polydispersities as low as 7% [34]. In terms of
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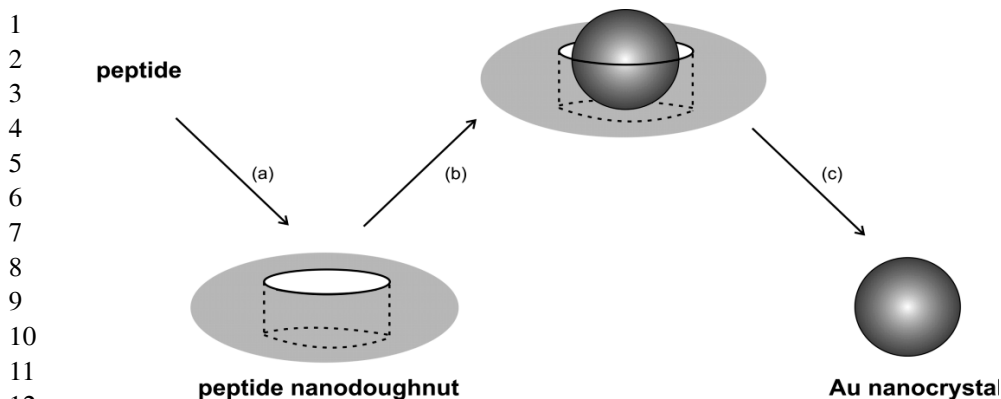


38 Fig. 3. Particle nucleation and growth processes (Conc_{PRE} denotes the precursor concentration
 39 [32]. Predzicit ciaru

1 achievable particles sizes, polydispersities, and simplicity (only three reagents,
2 tetrachloroauric acid, oleylamine, and a solvent are required) the method is superior
3 to that of Jana et al. [35]. The syntheses are fast, very reproducible, and simple.
4 The particles are stable in dried form and they can be easily modified with
5 hydrophobic and hydrophilic thiols to afford nanoparticles that are soluble in organic
6 solvents or in water.

7 Most commonly, gold nanoparticles are synthesized by chemical or
8 electrochemical reduction of a gold(III) precursor compound in the presence of a
9 capping agent, i.e. a compound able to bind to the nanoparticle surface blocking its
10 growth beyond the nanometer range and stabilizing the colloid in the particular solvent
11 used. Control over the shape and size of the AuNPs is usually achieved through the
12 careful selection of the experimental conditions, namely reducing agent, solvent,
13 reaction time, temperature, and capping agent. Controlled nucleation and separation
14 of nucleation from growth are the keys to synthesizing near-monodisperse gold
15 nanoparticles in the 1–15 nm size range [36]. This can be achieved either by providing
16 a controlled number of preformed gold nanoparticles as nucleation centers in a growth
17 medium where no secondary nucleation can occur—the seeding growth method [36]
18 - or by varying the ratio of strong and weak reducing agents [35]. Key goals in the
19 synthesis of nanoparticles are that the synthesis gives nanostructures of a specific size
20 and size distribution and that the synthesis is reproducible [37]. A common approach
21 is to use capping agents with strong affinity for gold, e.g. thiol capping agents. This
22 allows the synthesis of AuNPs but usually only soluble in organic solvents [6]. An
23 additional step is required for the extraction of the particles into water. Exchange
24 of strongly binding capping agents is, however, usually cumbersome, which makes
25 this type of AuNP less versatile for various modifications and biological applications.
26 The reverse is true for the capping agents with weak affinity for gold. The citrate
27 reduction method is the most commonly used method for preparation of spherical
28 AuNPs for biological assays due to its simplicity and high yield [38]. The use of
29 citrate as a capping agent is very convenient due to its easy post-synthesis treatment,
30 since it can be easily replaced by other capping agents, e.g. thiol capping agents,
31 bearing an appropriate functionality for binding of the biological analyte of interest.
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33 Djalali et al. have reported a novel method to produce gold nanoparticles in
34 soft templates (doughnut-shaped nanoreactors), peptide nanodoughnuts [39]. The nano-
35 doughnuts were self-assembled from peptides and organic gold salts. Various shapes
36 of peptide/protein assemblies have been produced in biomaterials [40]. Monodisperse
37 Au nanocrystals grew inside the cavities of peptide nanodoughnuts by the reduction
38 of Au ions trapped in the cavities and the resulting Au nanocrystals were extracted
39 by destroying the nano-doughnuts via long UV irradiation (Fig. 4. (a) peptide



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Fig. 4. Scheme for the peptide nanodoughnut formation.

16 monomers are self-assembled to the nanodoughnut in the presence of the organic gold
17 salts trimethylphosphine gold chloride (AuPMe_3Cl), (b) Au ions in the cavity are
18 reduced by short UV irradiation, and (c) longer UV irradiation (> 10 h) destroys
19 the nano-doughnut to release the Au nanocrystal) [41]. Because the peptide nano-
20 doughnuts already contained Au ions inside the cavities, Au nanocrystal synthesis was
21 completed in a simpler process as compared to that of micelle nanoreactors. Those
22 features may allow peptide nano-doughnuts to be applied in the fields of nanomaterial
23 syntheses, controlled release systems, and drug delivery.

24 When the peptide nanodoughnuts were reduced with a stronger reducing agent,
25 hydrazine hydrate, a striking difference was observed. Unlike the weak reduction with
26 the short UV irradiation, this stronger reduction produced gold nanocrystals after 20
27 min without forming the nanodoughnut-gold nanocrystal complexes. The diameter of
28 the Au nanocrystal produced with hydrazine hydrate is 23 nm in average, which is
29 larger and slightly more polydisperse as compared to the one produced by UV
30 irradiation. When the peptide monomers were self-assembled in the growth solution
31 without the organic gold salts, peptide nanotubes were formed instead of the peptide
32 nano-doughnuts [42]. Those nanotubes were assembled via intermolecular hydrogen
33 bonds between amide and carboxylic acid groups. Therefore, the addition of the
34 organic Au salts to the peptide monomer assembly likely has a significant influence
35 on those chemical interactions to alter the assembled structure. Because the
36 nanodoughnuts were not observed when an inorganic Au salt, HAuCl_4 , was incubated
37 in the peptide solution instead of AuPMe_3Cl , the ligand of this organic gold salt may
38 play an important role in the assembly of the nanodoughnuts. The IR investigation
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1 suggests that the organic Au salts are incorporated in the peptide self-assemblies and
2 contribute to the nanodoughnut formation. The amide peak shifts were observed in
3 amide-containing self-assembled monolayers, after gold salts were bound to their amide
4 groups [43]. When the peptide nano-doughnuts were weakly reduced by UV irradiation
5 in 20 min, gold nanocrystals were observed inside the doughnut cavities. The particles
6 in the center of the doughnut cavities are identified as gold nanocrystals from the
7 SFM phase images, the TEM images, and the electron diffractions. In fact, the
8 incorporation of the gold nanocrystal increases the mechanical strength of the peptide
9 nanodoughnut. After those samples were dried on mica surfaces, the peptide
10 nanodoughnuts without gold nanocrystals collapsed and displayed a deformed ring
11 shape, whereas the peptide nanodoughnuts with gold nanocrystals inside the cavities
12 showed a monodisperse and isotropic ring shape.

13 A solid-phase place exchange reaction can be also used to synthesize gold
14 nanoparticles with monofunctional group attached to the surface [44]. This approach
15 is based on a “catch and release” mechanism. Bifunctional thiol ligands with a
16 carboxylic end group were first immobilized on a solid support such as a polymer
17 resin with a controlled density. The density was low enough that neighboring thiol
18 ligands were far apart from each other. When the modified polymer support was
19 incubated in a butanethiol-protected gold nanoparticle solution, a one-to-one place
20 exchange reaction took place between the polymer-bound thiol ligands and the
21 nanoparticles. After cleaving off from the solid support, nanoparticles with a single
22 carboxylic group were obtained as the major product. Jacobson et al. published an
23 almost identical approach toward the synthesis of gold nanoparticles with a single
24 amino acid moiety [45]. These nanoparticles with a single functional group attached
25 can be treated as giant “molecules” and linked together into very sophisticated
26 structures through traditional chemical reactions, just like the total synthesis of
27 complicated natural product from small molecular units.

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29 **STABILIZATION**

31 Whether these gold colloids are stabilized or undergo aggregation depends on the net
32 potential of interparticle attraction and repulsion forces. The interparticle attraction
33 force is van der Waals force, which is responsible for the gold nanoparticle (AuNP)
34 aggregation. The two major repulsion forces that contribute to AuNP stabilization are
35 electrostatic and steric repulsion forces (Fig. 5) [46]. Electrostatic repulsion results
36 from the negatively or positively charged ionic groups at ionic stabilizers. The
37 charges, together with the counterions in the medium, form a repulsive electric double
38 layer that stabilizes colloids against van der Waals attraction [47]. The thickness of
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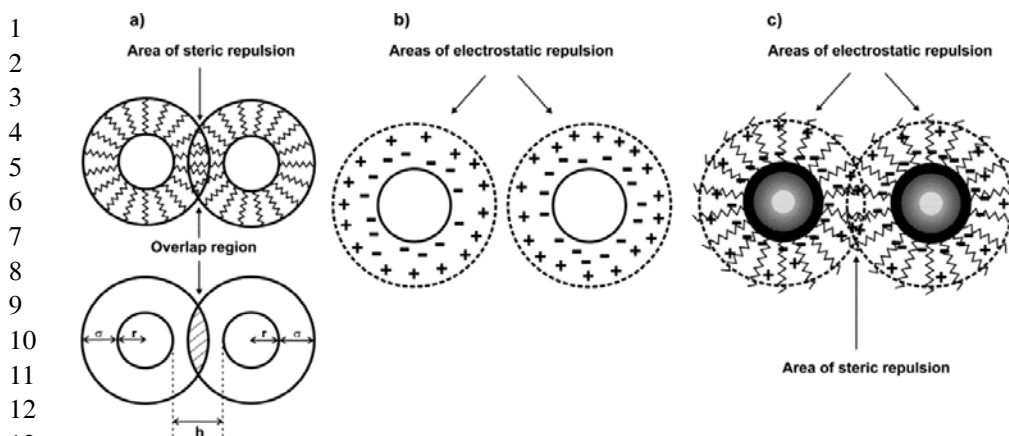


Fig. 5. Scheme of steric (a), electrostatic (b) and electrosteric (c) stabilization (where r is the radius of particle core and σ the thickness of particle shell).

the electric double layer is a measure of how far the repulsive potential extends from the colloid surface. A characteristic feature of the electrostatic repulsion force is that it is highly sensitive to the bulk ionic strength: the electrostatic repulsion force diminishes significantly at high salt concentration where electric double layer is highly suppressed.

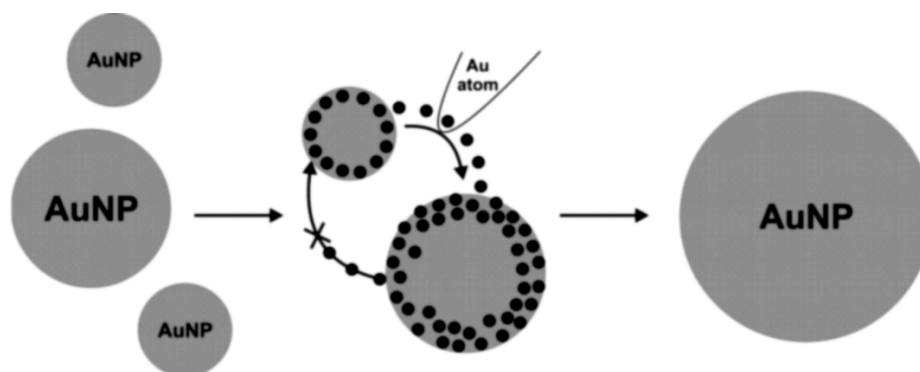
Steric stabilization (and/or polymeric stabilization) [46] is another key contribution to the repulsion forces in the current system. Amphiphilic block copolymers and/or macromolecules grafted on colloid surfaces impart a polymeric barrier that prevents colloids from coming close enough such that van der Waals attractive forces can dominate. Steric stabilization is highly dependent on the thickness of polymer layer and surface graft density. In general, thicker polymer layers and higher graft densities lead to more effective steric stabilization effect. A mixture of charged and uncharged stabilizers leads to the electrosteric stabilization.

RIPENING PROCESS

Under certain reaction conditions the large particles can grow on the expense of the small ones. This growth is called Ostwald ripening [48,49]. The decreased fraction of smaller particles can lead to the increase of particle uniformity. The "Ostwald ripening" (OR) process involves "the growth of larger particles (crystals) from those of smaller size which have a higher solubility than the larger ones" (Fig. 6) [50]. In their preparative solution, for example, a group of free standing crystallites with

1 unequal sizes in nonequilibrium form will further differentiate and redistribute
 2 themselves through the above solid–solution–solid process to achieve a more uniform
 3 size distribution (Fig. 6).

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19 Fig. 6. Ostwald ripening process.

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The passivation (wetting) of gold particle surface by solvents leads to the anchoring of particle surface atoms and their solution behaviour (they can be soluble in the solvent molecules). The penetration of solvent molecules into the particle surface volume is more pronounced for smaller nanoparticles. Thus, the partial release of these atoms from the particle surface is favoured by their interaction with the solvent molecules and their release is inversely proportional to the particle size. On the contrary the surface atoms of bigger nanoparticles are more incorporated into the particle core than the smaller ones. They are interacting with the larger number of core atoms than the surface atoms of smaller nanoparticle (Fig. 7).

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process results from the salvation of particle surface or the surface particle metal atoms.

The narrow size distribution of the particles is achieved by the remarkable procedure of “digestive ripening” [51]. This simple procedure is based on the reflux of a polydisperse nanoscale colloid for a certain amount of time, resulting in a dramatic improvement of the size distribution of the particles. The formation of gold monodisperse nanoparticles nanocrystals through a novel digestive ripening process and a temperature dependent size segregation process was reported by Lin et al. [25]. The authors [25] demonstrated a simple and straightforward approach to obtain narrow size distribution gold nanoparticles from a very polydisperse colloid by ligating the

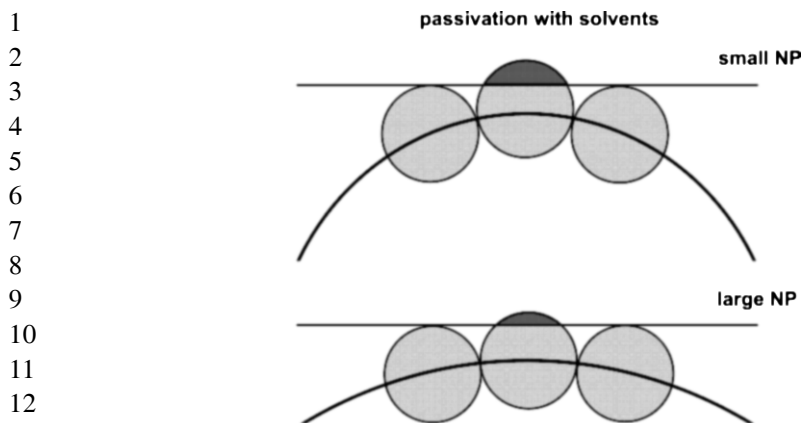


Fig. 7. Passivation of gold particle surface atoms by solvent.

nanoparticles with dodecanethiol followed by a digestive ripening process. Temperature induced size segregation can be used to further select the desired particle size.

The digestive ripening process is the key step for formation of a monodisperse colloid from the polydisperse Au-toluene-thiol colloid, e.g., [52]. The procedure involves heating under reflux of a certain amount of Au-toluene-thiol colloid. The heating temperature is the boiling point of the colloidal solution. A polydisperse colloid containing particles with sizes ranging from 1 to 40 nm is transformed into an almost monodisperse colloid with particle sizes of about 4–4.5 nm. The average size diameter is 4.5 nm and the size distribution is log normal, as typical for colloidal systems. The authors [25] demonstrated a simple and straightforward approach to obtain narrow size distribution gold nanoparticles from a very polydisperse colloid by ligating the nanoparticles with dodecanethiol followed by a digestive ripening process. Temperature induced size segregation can be used to further select the desired particle size. The UV/vis absorption spectrum of the colloid after cooling to room temperature shows an appearance of a definite plasmon absorption maximum at 513 nm, which is in agreement with the size and monodispersity of the obtained particles. The UV/vis absorption spectrum of colloid 2 is in agreement with the sizes of the particles observed in TEM. It is characterized by a broad plasmon absorption band with no definite maximum [53].

Heating of Au-toluene-thiol colloid under reflux results in a dramatic narrowing of the particle size distribution [54]. TEM studies of a hot colloidal solution show

1 formation of spherically shaped particles with sizes of about 4 nm. They have a
2 tendency to organize into 2D layers. Some of the particles from the hot colloid
3 organize in nice 3D structures. The remarkable effect of the digestive ripening
4 procedure is the great improvement of the size distribution. The amazing result is
5 that the particles predominantly organize on the TEM grid in large 3D structures in
6 only about 15 min after the digestive ripening process is finished. A small number
7 of areas of 2D arrangement are also observed. Even larger 3D structures ($>3\ \mu\text{m}$)
8 are observed. The results suggest that the activation energy for 2D organization is
9 lower compared to that of 3D organization. Of course, one of the most interesting
10 features of the synthetic sequence reported herein is the digestive ripening step, and
11 the mechanism for this remarkable process is not entirely clear. Only a few useful
12 facts are known. First of all, nanoparticles are the necessary starting material; that
13 is, normal gold powder is not susceptible to digestive ripening, showing again that
14 nanosized particles are intrinsically more chemically reactive than bulk samples [55].
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16 17 **FUNCTIONALIZATION**

18 The ligand exchange reaction is an extremely versatile tool for the preparation of
19 functionalized metal nanoparticles [56]. This method is fast and simple to use; it allows
20 one to introduce functional groups that are incompatible with other methods for
21 nanoparticle synthesis. A report by the R. W. Murray group suggests a new role of
22 reaction conditions in mediating the exchange reaction [57]. It was demonstrated that
23 triphenylphosphine (TPP)-stabilized gold nanoparticles [58] undergo ligand exchange
24 reactions with a few ω -functionalized thiols to produce *functionalized* nanoparticles
25 that preserve the core dimensions of the precursor particles but exhibit highly
26 increased stability against heat, aggregation, and decomposition [59]. The strong
27 interaction between n-alkylthiols and the gold surface provides the most popular
28 method for the attachment of molecular groups [60]. Such bonding is convenient to
29 engineer, but is reversible at moderate temperatures and kinetically unstable with
30 respect to movement of thiols on the surface [60]. Thus, groups that are deposited
31 onto a metallic surface cannot be precisely fixed with respect to one another, although
32 average spacing can be arranged by diluting the monolayer of functionalized alkylthiols
33 with analogues lacking the functional group [61]. Precise, angstrom-level control of
34 reactivity in nanotechnology requires nanoscale building blocks of known structure
35 at atomic resolution. 60 vynechana
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37 The passivation of gold particles with acetone leads to the gold-acetone colloid
38 (1) which has a brown color, particles well-dispersed in solvent and particles ranging
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1 from 10 to 50 nm in pure acetone solvent [54]. The addition of toluene changes the
2 color of the Au-acetone-toluene-thiol colloid to a dark brown color (colloid 2). TEM
3 studies of this colloid show particles ranging from 5 to 40 nm with no definite
4 geometrical shapes [52]. Both stabilization (steric and electrostatic) processes take place
5 during the warm up step, which has to be carried out slowly in order to ensure good
6 stabilization. Au-toluene-thiol colloid (colloid 2) was obtained by vacuum evaporation
7 of all the acetone from colloid 1. Drastic change of the size and shape of the particles
8 is characteristic at this stage. Nearly spherical particles with sizes in the range of
9 1-6 nm are dominant. There are also a small number of larger particles (10-40 nm)
10 like those in the initial acetone-containing colloid (colloid 1). One possible explanation
11 for the change of size and shape of the gold particles induced by the removal of
12 acetone is due to the change in interaction particle-solvent. In colloid 1 the amount
13 of acetone is in great excess. In great excess of acetone the gold particles are strongly
14 solvated by acetone and the attachment of dodecanethiol (RSH) molecules on the
15 particles' surface is suppressed. Acetone, with its nonbonding electron pairs, can serve
16 as a reasonably good ligand for gold but can only compete with RSH at high acetone
17 concentrations. Therefore, as acetone is removed, the thiol competes better and better.
18 This effect would be enhanced by the fact that the long-chained thiol is less soluble
19 in acetone than in toluene. Acetone acts as a preliminary stabilizing agent, which is
20 substituted by dodecanethiol molecules when acetone is evaporated. This ensures good
21 dispersity of the thiol-ligated gold particles in the toluene medium. In addition, toluene
22 is anticipated to achieve much better wetting of the thiol molecules on the gold
23 particles' surface compared to the more polar solvent acetone. In favor of this are
24 results obtained for the wetting of undecanethiol self-assembled monolayers on gold
25 surface by water and hexadecane [62]. It was found that hexadecane as a nonpolar
26 solvent wetted the thiol molecules on the gold surface much better compared to water
27 [62]. It is reasonable to expect a similar wetting trend for acetone, hexane, toluene,
28 etc. due to their different polarities.

30 Although gold nanoparticles can be prepared from various materials by several
31 methods [63], the coupling and functionalization with biological components has only
32 been carried out with a limited number of chemical methods. To apply gold colloids
33 in newly developed biomodifying medical assay systems, a simple and facile means
34 of anchoring different ligand biomolecules onto particle surfaces are strongly required
35 as well as the stability in the physiological condition should be improved. Particularly,
36 color changes induced by the association of nanometer-sized gold particles provide
37 a basis of a simple yet highly selective method for detecting specific biological
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1 reactions between anchored ligand molecules and receptor molecules in the milieu.
2 Colloidal gold nanoparticles, in particular, have found application in a variety of assay
3 formats in which analyte binding is coupled to particle adsorption. With decreasing
4 gold colloidal particle size, however, colloidal stability decreases significantly due to
5 increased particle surface energy. Such gold nanoparticles aggregate in high ionic
6 strength milieu as well as adsorb biomolecules such as proteins and DNA
7 nonspecifically, resulting in reduced sensitivity and selectivity when used as colloidal
8 sensor systems in biological fluids.

9
10 Functionalization of gold nanoparticles involves the use of functional ligands
11 in which a moiety is used for anchorage to the particle while the other is directed
12 to the outer-surface for specific interaction with biomolecules. For example, thiol-
13 modified oligonucleotides have been used to functionalize AuNPs for specific detection
14 of nucleic acid sequences in biological samples. Functionalization of Au-NPs with
15 biomolecules other than nucleic acids has also been used in order to develop
16 methodologies suitable for clinical diagnostics. These include : 1) antibodies for signal
17 enhancement in immunoassays [64]; 2) carbohydrate functionalization to study specific
18 molecular interactions [65]; and 3) surface functionalization with ligands that can be
19 tailored for specific protein binding [66] or direct binding of peptides and proteins
20 to the Au-nanoparticle surface [67].

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22 CONCLUSION

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24 Gold nanomaterials have been synthesized using a variety of methods. Two main
25 approaches for the preparation of gold nanoparticles precipitation and chemical
26 reduction were discussed. In both cases, the presence of surfactant is required to
27 initiate the particle nucleation and govern the growth process. The precipitation of
28 prime nanoparticles is based on the supersaturation of solution by reactants and
29 additives. Generation of supersaturation through in situ chemical reactions by
30 converting highly soluble chemicals into less soluble chemicals is a good example
31 of this approach. The reverse microemulsion synthesis has been recently demonstrated
32 to be a viable method for producing a wide array of gold nanoparticles over a
33 relatively narrow particle size distribution. A major benefit of chemical methods is
34 their relatively inexpensive investment of capital equipment.

35
36 There are several reasons for the synthesis and use of AuNPs in nanotechnology
37 as well as in nanomedicine. (i) First of all, gold compounds have long been used in
38 medicine throughout the history of civilization. (ii) It is easy to synthesize AuNPs
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1 by several simple, economically cheap, safe and reliable (above mentioned) methods;
2 (iii) it can be synthesized from sizes of 2–500 nm by changing the reaction
3 parameters; (iv) it can be easily synthesized with different shapes (spheres, rods, tubes,
4 wires, ribbons, plate, cubic, hexagonal, triangular) using soft and hard templates and
5 changing reaction conditions; (v) due to the presence of a negative charge on the
6 surface of AuNPs, they are highly reactive, which helps to modify the surface of
7 AuNPs using several biomolecules. Due to the strong interaction between the gold
8 surface and thiol/amine containing molecules (organic molecules, DNA, protein,
9 enzyme etc.) the surface of AuNPs can be easily modified or functionalized and (vii)
10 finally, it is well established that AuNPs are biocompatible and non-toxic.
11

12 **ACKNOWLEDGEMENT**

14 This research was supported by the APVV-0125-11 project.
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16 **LITERATURE**

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