Chapter 6

Gold-Polymer Nanocomposites for Bioimaging and Biosensing
6.1. Introduction

- Gold-polymer nanocomposites: a gold core coated with a polymer shell
- The first colloidal gold solution produced by Faraday in 1857
- Faraday’s gold

- Michael Faraday
- Gold colloids prepared by Faraday (ambient light) (1857)
- Electromagnetic rotation experiment of Faraday, ca. 1821
6.1. Introduction

- This solution, which is stored at the Royal Institute of Great Britain, has kept its red color until the present day.

- Faraday recognized that gold existed as very small discrete particles in the solution, and investigated the relationship between the solution’s color and the particle size of the gold.

- The origin of the relationship between gold compounds and the life sciences began during the era of the European alchemists.

- Although metallic gold and gold compounds had been believed to possess medical benefits until the early nineteenth century, today only one gold salt is unused medically, to treat rheumatism.

- During the early twentieth century, Lange conducted the first verifiable investigations into gold sols in the life sciences, in which a variation of the Zsigmondy flocculation test (면상반응) was used to identify degenerated proteins.
Gold salts describe ionic chemical compounds of gold. The term, which is a misnomer, has evolved into a synonym for the gold compounds used in medicine. The application of gold compounds to medicine is called “chrysotherapy” “aurotherapy.” The first reports of research in this area appeared in 1935, primarily to reduce inflammation and to slow disease progression in patients with rheumatoid arthritis.

Auranofin, in capsule form for oral administration, is marketed under the brand name Ridaura. Sodium aurothiomalate (Gold sodium thiomalate as brands Myocrisin UK, Aurolateor or Myochrysine U.S.) and aurothioglucose (Solganal in U.S.) are administered by injection.
6.1. Introduction

- Significant progress in the use of metal nanoparticles in the life sciences has been inspired by recent developments in nanotechnology, that have revealed the importance of metal nanoparticles for **nanodevices** and as **building blocks** in the creation of nanostructures.

- The rapid development of nanotechnologies such as **lithography**, which has been further accelerated in the semiconductor industries, has allowed research groups to manipulate **top-down patterning** at nanoscale levels.

- Meanwhile, supermolecular chemistry has enabled the fabrication of biomimetic architectures in the mesoscopic region.

- As with metal nanoparticles, gold nanoparticles and nanocomposites have been used primarily as building blocks, not only in **nanoengineering** but also in **the life sciences**, due to their versatile properties such as chemical stability (i.e., low toxicity), stable development of color, and ease of preparation and modification.
6.1. Introduction

- The properties of nanosized gold cores (such as the absorption of visible light, fluorescence quenching, electrochemical activity, mass enhancement, and light-heat conversion) are desirable features for applications in the life sciences.

- As conjugated polymers serve not only to stabilize gold nanocomposites in solution, but also offer several other attractive functions such as phase transition and recognition, the sophisticated combination of gold nanoparticles with functional polymers to form gold nanocomposites has allowed the development of a variety of versatile platforms.

- Gold nanocomposites have been studied intensively as diagnostic tools because gold cores develop a stable red color due to their surface plasmon resonance (SPR).
  - (ex) colorimetric assay using gold nanocomposites: the target DNA could be assayed with the naked eye.

- In this chapter, following a discussion of the preparation of gold nanocomposites, details are provided of the recent developments in imaging and assay systems, where gold nanocomposites function as the key materials.
6.2. Fabrication of Gold Nanocomposites

- 6.2 Fabrication of gold nanocomposites
  - 6.2.1 General aspects
  - 6.2.2 “Grafting-from” modifications
  - 6.2.3 “Grafting-to” modifications
  - 6.2.4 Post-modification
6.2. Fabrication of Gold Nanocomposites

- The conjugation of a polymer shell with the surface of a gold core is a crucial step in preparing gold nanocomposites.

- The different methods used to prepare gold nanocomposites are shown in Figure.
  - **Grafting-from**: a polymer chain is extended from the surface of the gold core
  - **Grafting-to**: a gold core is generated in polymer aggregates
  - **Post-modification**: the conjugation of as-prepared gold nanoparticles (AuNPs) with the polymer

- As-prepared AuNPs are required for the “grafting-from” and “post-modification” methods.

- When considering the following modification steps, the most suitable methods of synthesizing AuNPs for life-science applications is in a homogeneous aqueous phase.
6.2 Fabrication of Gold Nanocomposites

- The generation of AuNPs in aqueous solution is easily achieved by using the correct reductant that will reduce gold salts to a zero-valent state.
  - In this respect, citrates have become one of the most commonly used reductants, as they serve not only as a reductant but also as a stabilizer for the generated AuNPs.
  - Both, the concentration and type of stabilizer will influence the particle size and the morphology of the AuNPs.
  - Moreover, stabilizers adsorbed onto AuNPs can serve as scaffolds at which the polymer chains are extended, via the “grafting-from” method, and play an important role in the “post-modification” method through replacement with polymer ligands.
6.2 Fabrication of gold nanocomposites

- A two-phase synthesis has also been recognized as an important method for preparing AuNPs, although this requires the use of water-immiscible organic solvents that will be unfavorable for bioassays.
  - In a two-phase synthesis, a water-immiscible organic phase containing an alkanethiol is contacted with an aqueous phase containing gold salts and reductants.
  - Then the AuNPs generated in the aqueous phase are extracted into the organic phase and stabilized by the alkanethiols.
  - Although, highly monodispersed AuNPs can be prepared using this technique, in order to be practically applicable the method requires a re-dispersion of the AuNPs into the aqueous phase in order to remove the organic solvent.

- Nonchemical methods have also been developed.
  - Laser irradiation, arc-discharge (아크방전), flame ionization
  - Biological syntheses using accumulated AuNPs in microorganisms
6.2 Fabrication of gold nanocomposites

- The shells of gold nanocomposite
  - Polymers (i.e., poly(N-isopropylacrylamide): recognition of analyte, formation of bridging structures, the catch-and-release of substances, stabilization of gold nanocomposites
  - Biopolymers: peptides and oligonucleotides

- The stability of gold nanocomposites
  - Polymers with functional groups containing sulfur atoms (e.g., a thiol group): chemical conjugation
  - Polymers without sulfur atoms: physical adsorbed

variously abbreviated PNIPA, PNIPAAm, PNIPAA or PNIPAm
6.2.2 “Grafting-from” modifications

- A modification technique that elongate polymer chains on the surface of planar gold substrates has been applied to the “grafting-from” modification of AuNP surface.

- Main advantages
  - The thickness of the polymer shell can be controlled easily with living polymerization
  - Various polymer architectures such as mesh, comb, and block can be designed
  - A high efficiency of polymer introduction can be achieved
6.2.2 “Grafting-from” modifications

- Initiators with sulfur atoms + surface of the gold cores via reversible addition-fragmentation chain-transfer (RAFT) reaction so as to provide gold nanocomposites of the core-shell type

6.2.2 “Grafting-from” modifications

- Biopolymers (oligonucleotides and peptides) can also be introduced with “grafting-from” methods.

Ref) Zhao W et al., Angew Chem Int Ed 2006;45:2409-2413
6.2.3 “Grafting-to” modifications

- The “grafting-to” modification, which refers to the evolution of gold cores in polymer aggregates, is another practical method for preparing gold nanocomposites.

- Advantages
  - The ease of synthesis
  - The extended availability of polymers
  - ‘single-pot’ reaction: laborious separation steps can be eliminated.

- The availability of various polymers allows the textural designs of gold nanocomposites to be expanded.
6.2.3 “Grafting-to” modifications

- Polymers terminated by a sulfur-containing groups: dithioester, trithioester, thiol, thioether, disulfide
6.2.3 “Grafting-to” modifications

- Polymers without sulfur atoms: the generated gold cores were conjugated with the polymers through multipoint physical adsorption

6.2.3 “Grafting-to” modifications

- The coated polymer layers in the composites are prone to detachment due to physical adsorption: crosslinking with polymer networks in preventing the detachment of physically adsorbed polymers.

- Another promising strategy to overcome detachment is to use either unimolecular micelles or stabilized micelles with crosslinking networks.

6.2.4 Post-Modification

- The conjugation of as-prepared AuNPs with as-prepared polymers is the most common and easiest way to prepare gold nanocomposites, mainly because the method is simple and effective at avoiding uncertain factors, such as the size and molecular weight distributions of AuNPs.

- Certain drawbacks
  - Low efficiency of polymer introduction due to steric hindrance
  - Unintended adsorption through polymer functional groups