Chapter 1

Introduction

Poly-elemental nanoparticles (PENPs)[1], consisting of four or more elements integrated within a single nanoparticle, are garnering significant attention in recent years due to their exceptional properties and versatility across various applications. These nanoparticles combine the unique attributes of multiple elements, leading to enhanced material properties compared to single-element nanoparticles. Their advantages include superior mechanical strength, improved thermal stability, greater resistance to fatigue, fracture, or corrosion, and enhanced functional performance in demanding environments.

Poly-elemental nanoparticles have found applications in the field of catalysis[2–4] majorly. However, it can have potential applications in optics[5, 6], electronics[7], chemical sensors[8, 9], drug delivery[10, 11], etc. In general, poly-elemental nanoparticles are broadly categorised as (Figure 1.1):

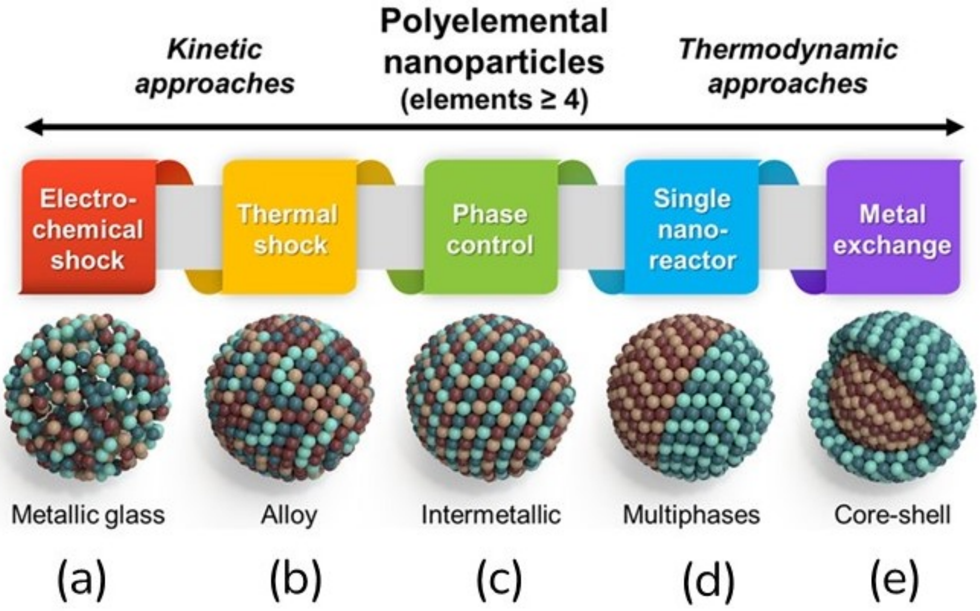

Figure 1.1: Schematic illustration of the structure of Poly-elemental nanoparticles (a) Metallic glasses, (b) High-Entropy alloys, (c) Intermetallic Compounds, (d) Multiphase Poly Elemental Nanoparticles, (e) Core-Shell. (Image is taken from ref[1])

1. **Metallic glasses:** These amorphous nanoparticles are synthesized using methods like electrochemical shock[12], where rapid deposition and mixing prevent crystallisation, resulting in a disordered atomic structure shown in Figure 1.1(a). This approach relies heavily on kinetic control to bypass thermodynamic constraints.
2. **High-Entropy alloys:** These possess a uniform mixture of different elements (Figure 1.1 (b))and are made by using thermal shock methods,[13] where rapid heating and cooling at high temperatures promote the homogeneous mixing of multiple elements. This technique combines both thermodynamic and kinetic aspects to achieve uniform alloys.
3. **Intermetallic Compounds:** Intermetallic compound PENPs are structured with precise atomic arrangements resulting from specific combinations of metallic or non-metallic elements (Figure 1.1(c)). These crystalline materials are synthesized through phase control techniques[14, 15], which ensure precise atomic arrangements by manipulating the growth conditions to favour specific stoichiometries. This method often involves a balance of thermodynamic stability and controlled nucleation. These ordered crystalline materials excel in hardness and thermal conductivity, making them invaluable for advanced technological applications.
4. **Multiphase Poly Elemental Nanoparticles:** It consists of distinct compositional phases (Figure 1.1 (d)), these nanoparticles are often synthesized in single nanoreactors, such as those formed by scanning probe block copolymer lithography (SPBCL).[16, 17] This method uses spatial confinement to control the nucleation and growth of different phases within a single particle.
5. **Core-Shell:** Core-Shell PENPs feature a stratified architecture with an elemental core encased by one or more outer shells (Figure 1.1 (e)). These layered nanoparticles are typically produced using metal exchange techniques[18], where sequential addition or replacement of elements forms distinct core-shell architectures. This thermodynamically driven approach enables precise control over the elemental layering, enabling highly specialized functionalities such as targeted drug delivery or

environmental remediation.

Many methods are used to fabricate poly elemental nanoparticles involve complex synthetic approaches. It is challenging to control all crystal structures, compositions, and heterostructures of phases and interfaces with Poly-elemental nanoparticles.

Many conventional methods[19], such as impregnation[20], chemical reductions[21], etc., are for the synthesis of Poly-elemental nanoparticles, but there are several challenges. In the impregnation method [20, 22], metal salts are deposited onto a porous support material, such as silica or carbon, by soaking the support in a solution of the metal precursors. After drying, thermal treatment or reduction is applied to convert the precursors into metallic nanoparticles. While this method is simple and scalable, it typically results in non-uniform particle size and composition, making it less effective for complex PENPs.

Similarly, the chemical reduction method[21] involves reducing metal ions from their precursors using agents like sodium borohydride or hydrazine in a solution-phase reaction. Stabilizers or surfactants are often used to control particle size and prevent aggregation, but achieving homogeneous mixing of multiple elements can be challenging due to differences in the reduction potentials of the metals.

Additional approaches, such as co-precipitation[23], sol-gel synthesis[24], and thermal decomposition[25], have also been employed. Co-precipitation[23] involves the simultaneous precipitation of multiple metal ions by adding a precipitating agent, followed by calcination or reduction, but precise stoichiometric control remains difficult.

The sol-gel method[26] uses hydrolysis and condensation of metal precursors to create gels that can be calcined or reduced into nanoparticles, offering high-purity materials but requiring careful control of reaction conditions.

Lastly, thermal decomposition[25] decomposes organometallic precursors at high temperatures to produce nanoparticles, providing good control over size and shape but often being costly and less scalable. While these methods are foundational in nanoparticle synthesis, their inherent limitations drive the need for more advanced techniques to produce PENPs with precise structural and compositional control.

1.1 Self Assembly

Self-assembly is a process in which molecules or particles spontaneously organized into structured aggregates. This phenomenon relies on non-covalent interactions, such as van der Waals, electrostatic, hydrogen bonding, hydrophobic interactions, and capillary forces, which guide the molecules to adopt an ordered arrangement that minimizes the overall free energy of the system. Surfactants are a great example of amphiphilic molecules with hydrophilic heads and hydrophobic tails that reduce surface tension. Above a critical concentration, these molecules form micelles.

Self-assembly is essential in both natural systems, for example, the formation of cell membranes, protein folding, DNA double helix formation and engineered materials, where it is exploited to create nanostructures and advanced materials.

The lipid bilayers, where the constitutive material is lipid molecules having a hydrophilic head and hydrophobic tail groups, are broadly classified as amphiphiles.[27] Due to different molecular structures, they can form assemblies of different geometries, like cylinders, spheres, etc. Similarly, molecules with more complexity, such as proteins, are assembled to form these structures.[28] Conjugate complexes of molecules can lead to the formation of different assemblies, such as Sodium dodecyl sulfate (SDS) and Cyclodextrin.[29]

1.2 Surfactants

Surfactants, or surface-active agents, are amphiphilic molecules consisting of a polar, hydrophilic headgroup and a nonpolar, hydrophobic tail as shown in Figure 1.2(a). Despite their contrasting characteristics, these two regions remain inseparably bound by strong covalent bonds. This inherent paradox is elegantly resolved in nature through molecular self-assembly, an intriguing phenomenon where amphiphiles spontaneously organize into three-dimensional structures. These structures minimise contact between the polar and non-polar regions, creating distinct and separate domains. Surfactants exhibit remarkable structural diversity, with numerous variations in both their head and tail groups.

Surfactants are classified according to the polarity of the headgroup, which is either ionic or non-ionic. Further, ionic surfactants can be classified into three categories: anionic contains a negative functional group at their headgroup, e.g., alkyl sulfates, alkyl benzene sulphonates; cationic contain a positive functional group at their head, e.g. Cetyltrimethylammonium bromide (CTAB); zwitterionic carry both positive and negative charged sites in the headgroups e.g. amino acids. In the case of nonionic, there is no formally charged group on its head, but strong hydrophilic groups (-COOR, -OH, -C_2H_4O, etc.) are present, e.g. Tween20, TX100, etc.

Special surfactants, such as bolaamphiphiles with two head groups or Gemini surfactants with two head groups and two tails connected by a covalent linkage, further expand the structural repertoire. Moreover, surfactants with polymeric head and tail groups, like block copolymers, add another layer of complexity. This vast structural variability allows for extensive modulation of surfactants' solution behavior, interfacial properties, and practical applications, underscoring the long-standing interest in understanding the relationship between their molecular structure and physicochemical behavior.[30]

The type of structure formed depends on thermodynamic conditions and the presence of additional components, such as salts or other amphiphilic molecules. This self-assembly capability makes surfactants highly versatile, with applications ranging from traditional uses as detergents to advanced roles in nanotechnology. Despite extensive experimental and theoretical research, a complete molecular-level understanding of surfactant self-assembly remains elusive. Fundamental questions, such as whether micelles are spherical or elongated, are still in discussion. From a practical perspective, predicting key micelle characteristics based solely on the chemical structure of the surfactant molecule would be immensely valuable. Such predictive capability would enable the rational design of novel surfactant molecules tailored for specific applications.

1.3 Micellization

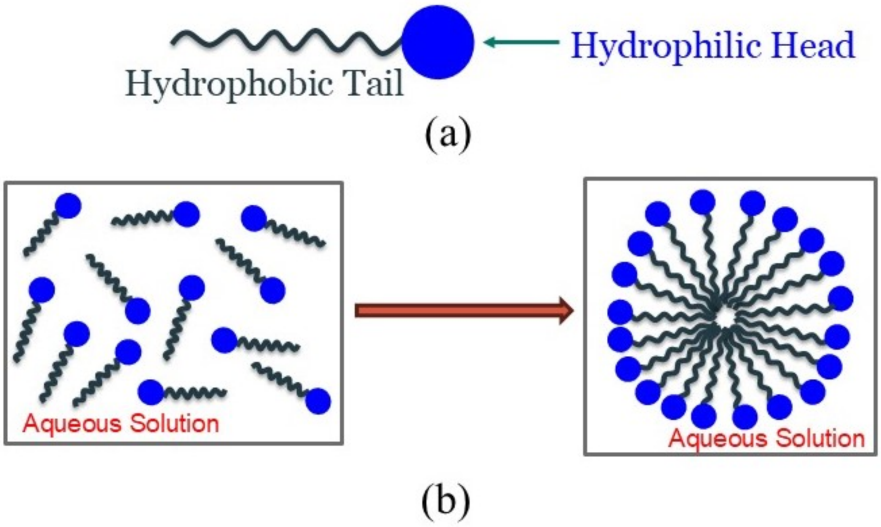

Figure 1.2: (a) Schematic representation of Surfactant Molecule (b) Micellization Process. Colour code: blue circles- hydrophilic heads, black curved lines- hydrophobic tails.

Micellization is a process in which an assembly of surfactant molecules in an aqueous solution forms micelles as shown in Figure 1.2(b) beyond a certain critical surfactant concentration, which is called critical micelle concentration (CMC). These micelles can adopt a variety of sizes and shapes: spherical, cylindrical, worm-like, globular, and lamellar structures. The specific size and shape of micelles are influenced by several factors, such as the surfactant concentration, temperature, ionic strength of the medium, and the molecular structure of the surfactant. This adaptability makes surfactants versatile tools across diverse scientific and industrial applications.

Understanding the molecular driving forces behind micelle formation is a fascinating area of study. The forces at play include short-range van der Waals interactions, which bring the uncharged regions of surfactant molecules together, and long-range electrostatic interactions, which facilitate the aggregation of charged regions. The interplay between these opposing forces determines the formation and stability of the aggregated structures.[31]

To delve deeper into this phenomenon, one can start with the mass-action principle, describing the equilibrium between individual surfactant monomers (A) and micelles (A_n), where n represents the number of surfactant molecules in the micelle, and K_n is the equilibrium constant for this association:

$$nA \Longleftrightarrow A_n$$

Let C_n denote the concentration of micelles, C_1 the concentration of unassociated surfactant molecules, and C_T the total concentration of surfactant molecules in the system, all expressed in mole fractions. Then:

$$C_T = C_1 + nC_n$$

Assuming K_n can be expressed relative to an arbitrary concentration C_0 as $K_n = C_0^{(1-n)}$, the application of the mass-action principle, assuming ideal behavior, gives:

$$C_n = K_n(C_1)^n = C_0 \left(\frac{C_1}{C_0}\right)^n$$

$$C_T = C_1 + nC_0 \left(\frac{C_1}{C_0}\right)^n$$

For sufficiently large n, when $C_1 < C_0$, the micelle concentration C_n remains negligible, and the total concentration C_T is approximately equal to C_1.

This implies that C_1 cannot exceed C_0. When n is large enough, surfactants remain primarily as monomers below the concentration C_0, and above this threshold, all additional surfactant molecules form micelles. Thus, C_0 corresponds to the *critical micelle concentration (CMC)*.

1.3.1 Energetic Contributions to Micelle Formation

To estimate the energetic changes during micelle formation, the work involved in forming an aggregate from individual molecules is analyzed. One component of this work is the electrical energy, which arises due to the charged micelle surface. For a micelle with radius R and surface charge density σ_e, the work required to expand the micelle radius by a differential amount dR against Coulombic forces is proportional to $R^2 dR \sigma_e^2$. Integrating this, the total electrical work scales with R^3. Since the micelle surface area (R^2) is proportional to n, the number of surfactant molecules in the micelle, the electrical energy (W_e) required to create a micelle can be expressed as:

$$W_e = n^{3/2} w_e;$$

where, w_e is a fundamental energy constant reflecting the electrical energy contribution, independent of n.

The second contribution to the energy is from the favorable interactions among hydrocarbon tails, which involve short-range forces. This energy (W_m) is given by:

$$W_m = -n w_m$$

Here, w_m is another energy constant, with the negative sign indicating that these interactions are energetically favorable. The total energy of micelle formation is then:

$$W = W_e + W_m$$

The equilibrium micelle size n_0 is found by minimizing W, resulting in:

$$n_0 = \left[\frac{2}{3} \left(\frac{w_m}{w_e} \right) \right]^2$$

The corresponding energy of a stable micelle (W_0) is:

$$W_0 = -\frac{1}{3} n_0 w_m$$

From these equations, one can determine the critical micelle concentration (C_0) as:

$$W_0 = -k_B T \ln K_n = (n_0 - 1) k_B T \ln C_0$$

Alternatively, experimental values of n_0 and C_0 can be used to estimate the energy constants w_m and w_e.

Regarding micelle morphology, smaller aggregates typically adopt spherical shapes. However, when aggregation numbers increase, making the radius of a spherical micelle exceed the length of its surfactant tails, transitions to other shapes, such as rod-like, globular, or cylindrical forms, occur.

1.3.2 Generalized Free Energy Approach

A more generalized treatment of micellization involves considering the free energy of a system comprising monomers, aggregates of various sizes and shapes, and solvent molecules. The equilibrium condition corresponds to the free energy minimum, described by:

$$\mu_n = n\mu_1$$

$$\mu_n = \mu_n^0 + RT \ln C_n$$

$$\mu_1 = \mu_1^0 + RT \ln C_1$$

Here, μ_n^0 and μ_1^0 are the standard-state chemical potentials of aggregates of size n and monomers, respectively. Combining these equations gives the aggregate size distribution:

$$C_n = C_1^n \exp\left[-\frac{\Delta\mu_n^0}{k_B T}\right]$$

where $\Delta\mu_n^0$ is the standard free energy difference between a surfactant molecule in an aggregate of size n and a free monomer. This energy difference directly relates to the equilibrium constant K_n, allowing predictions of aggregation behaviour for systems of varying size and shape.

1.4 Self-Assembled Monolayer

When considering the self-assembly of amphiphilic molecules on a solid surface, as shown in Figure 1.3, similar theoretical principles apply as in bulk solution. However, additional factors specific to the solid substrate come into play. These include the crystallographic plane[33] of the surface, which influences the arrangement of the assembling molecules, and the surface's intrinsic properties, such as its hydrophilicity or hydrophobicity.[34–36] The assembly process is driven by short-range van der Waals forces and long-range electrostatic interactions, which may be enhanced by strong interactions such as hydrogen bonding [36] between the molecules and the surface. These forces collectively enable the formation of self-assembled monolayers (SAMs)[37, 38] and create structures as shown in Figures 1.3 and 1.4.[39] The resulting monolayer structures are determined by the interplay of molecular and surface interactions.

So, self-assembled monolayers are single-molecule-thick layers that form spontaneously when molecules adsorb onto a substrate as in Figure 1.4. For instance, alkanethiols can adhere to noble metals like gold, silver, and platinum, creating tightly packed and easily functionalised layers. SAM functionalisation enables applications in bioimaging, molecular detection, drug delivery, and catalysis, shown in Figure(1.5).[32]

1.5 Nucleation

Nucleation is the process in which nuclei act as templates for crystal growth. It can change the morphology and size of metal nanoclusters, affecting their electrical, optical, structural, and magnetic properties.[40–43] Different kinds of nucleation mechanisms are as follows:

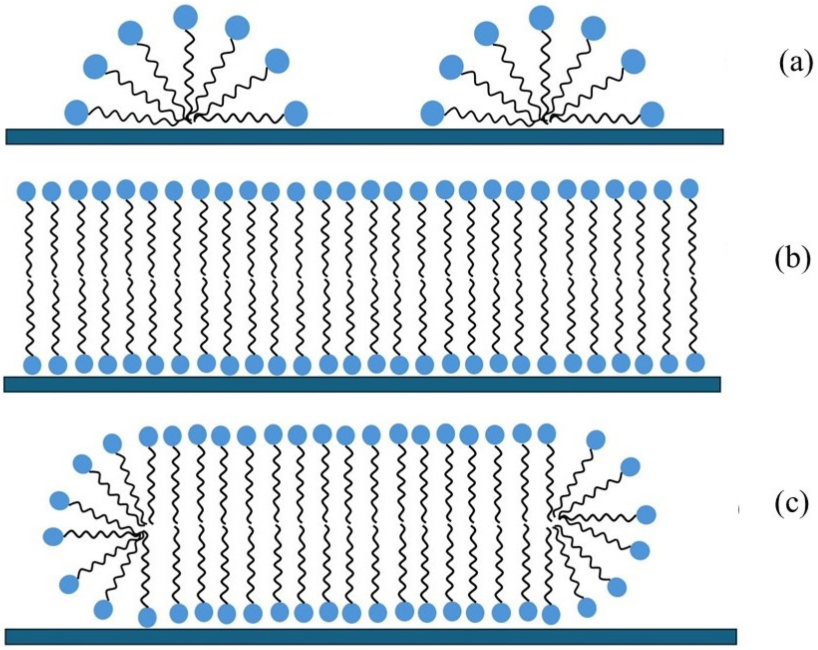

Figure 1.3: Self-assembly of surfactants/amphiphiles on (a) hydrophobic surface forming hemimicelles. (b) and (c) a hydrophilic surface forming lamellar and cylindrical bilayers. Colour code: blue circles-hydrophilic heads, black curved lines-hydrophobic tails.

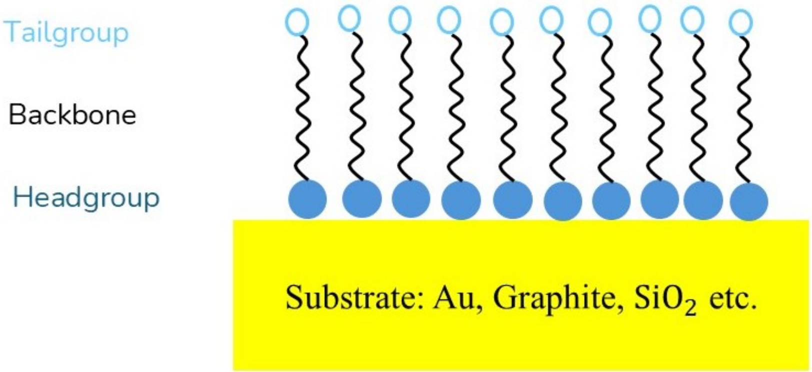

Figure 1.4: Typical diagram of self-assembled monolayer (SAM) formed by amphiphilic molecules on a substrate.

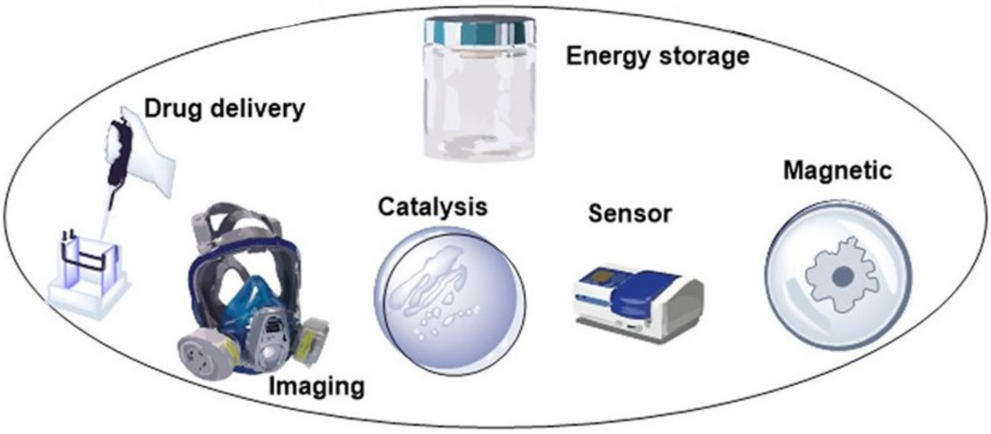

Figure 1.5: (a) Applications of SAMs.(Image is taken from ref[32])

1.5.1 Nucleation Mechanism

1. **Homogeneous Nucleation:** It occurs in a uniform medium without any pre-existing surface or foreign particles to assist the process. Atoms or ions spontaneously come together to form clusters, driven by supersaturation or high energy. However, such clusters must overcome a critical size to become stable; smaller clusters tend to dissolve due to their higher surface energy.

2. **Heterogeneous Nucleation:** It occurs on pre-existing surfaces, such as impurities, substrates, or interfaces, which lower the energy barrier for nucleation. This is the dominant mechanism in practical systems because it requires less energy compared to homogeneous nucleation.

3. **Seed Nucleation:** In this approach, pre-formed nuclei (or seeds) are intentionally introduced to guide the growth of nanoclusters. This method allows for better control over size, shape, and distribution.

1.6 Theories of Nucleation and Growth

Over the years, scientists have developed different mechanisms and theories to understand the nucleation and growth process of nanoparticles. These have been described by LaMer-Burst nucleation mechanisms[44], Oswald ripening[45], Finke-Watzky two-step

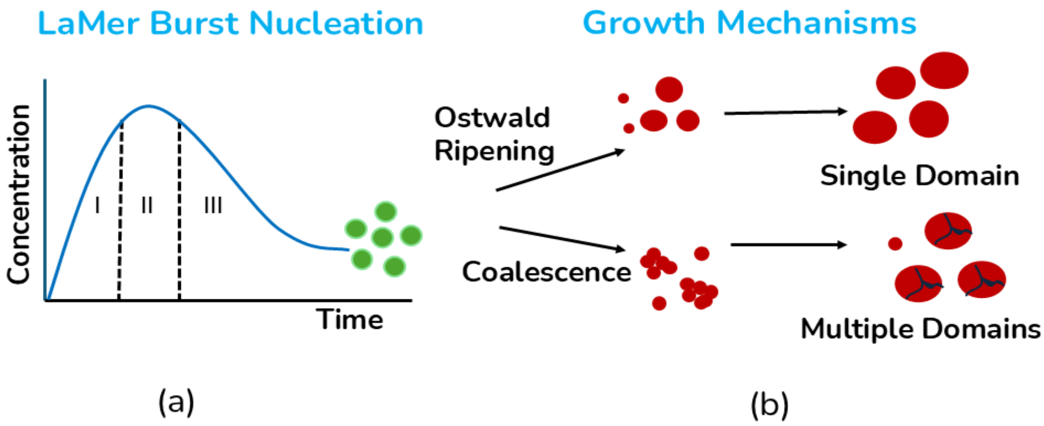

Figure 1.6: (a) LaMer- Burst Nucleation Mechanism, (b) Growth Mechanism (Image is taken from ref[48])

nucleation mechanism[46], coalescence and orientation attachment mechanism [47] and so forth.

1.6.1 LaMer- Brust nucleation

In LaMer- Brust nucleation,[44] as shown in Figure 1.6(a), it consists of three steps: (I) In the initial phase, the precursor concentration in the solution increases, leading to a supersaturated state. (II) Once the concentration reaches a critical supersaturation level, nucleation occurs suddenly, forming a large number of small nuclei in a short time. This rapid nucleation depletes the concentration of the precursors. (III) After the Brust nucleation, as the precursor concentration drops below the critical level, the growth phase begins. In this phase, existing nuclei grow by the addition of atoms from the surrounding solution. This growth phase continues until the precursor concentration becomes too low for further growth. The growth mechanisms consist of two steps:

1. **Oswald ripening:** The first mechanism is Oswald ripening[45], in Figure 1.6, in which smaller particles, which have higher surface energy, dissolve more easily into the surrounding solution. The dissolved particles then re-deposit onto larger particles, which have lower surface energy. This process continues, with larger particles growing and smaller ones shrinking until they dissolve completely. The result is an increase in the average particle size over time.

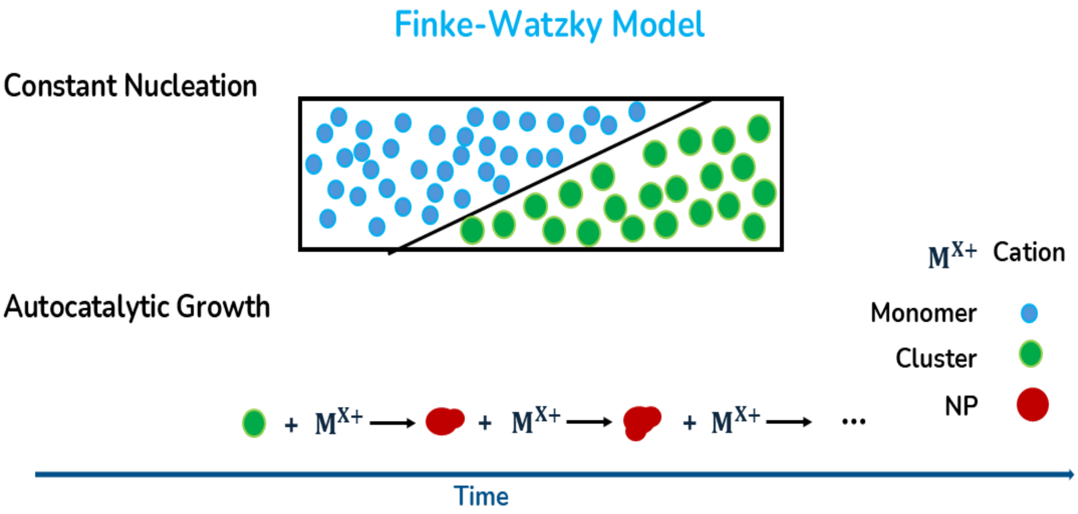

Figure 1.7: Finke-Watzky two-step nucleation Mechanism (Image is taken from ref[49])

2. **Coalescence:** Coalescence occurs when two or more nuclei come into close proximity, overcome their interfacial or repulsive energy barriers, and merge to form a single entity, as shown in Figure 1.6. The process is driven by the system's tendency to minimize its total free energy, often resulting in a reduction of the surface area-to-volume ratio and, consequently, the surface energy.

1.6.2 Finke-Watzky two-step nucleation mechanism

The third one is the Finke-Watzky two-step nucleation mechanism[46], in this mechanism, the first step involves a relatively slow, continuous nucleation process. This means nuclei form gradually rather than in a rapid burst, as seen in the LaMer-Brust mechanism. In the second step, the newly formed nuclei act as catalysts for further particle growth. This autocatalytic growth phase involves a continuous supply of precursors that allows for steady growth of the nuclei, as shown in Figure 1.7.

1.6.3 Coalescence and Orientation Attachment mechanism

The fourth one is the coalescence and orientation attachment mechanism[51]. In the coalescence mechanism, small particles collide due to Brownian motion or other forces, leading to the fusion of particles when they are close enough to overcome the repulsive

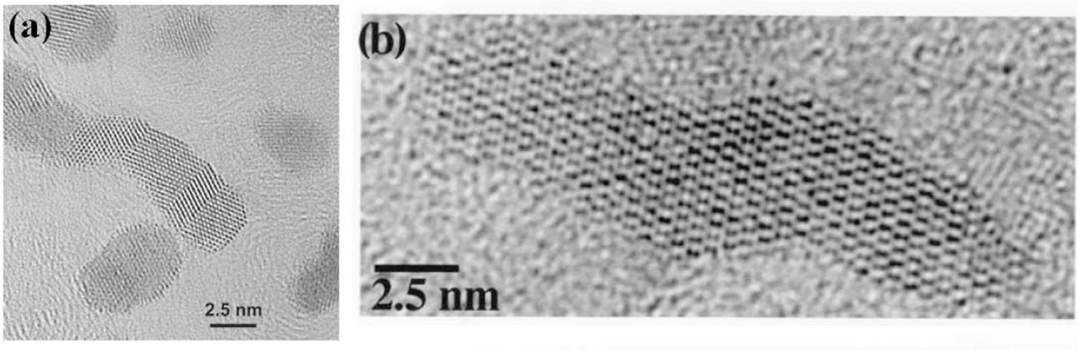

Figure 1.8: (a) Coalescence of platinum crystallites (b) Formation of titanium crystallites through orientated attachment (Image is taken from ref[50])

forces between them. After coalescence, larger particles are formed with a reduction in the overall surface area and surface energy. For the coalescence, there is no preference for attachment as shown in Figure 1.8(a). Whereas, in the orientation attachment mechanism, small particles or nanocrystals come into contact and align along particular crystal facets with matching lattice structures. Once aligned, the particles fuse along these planes, resulting in a single larger particle with a well-defined crystallographic orientation as shown in Figure 1.8(b). This process leads to elongated or anisotropic structures, such as nanorods, nanowires, or nanoplates.[47]

1.7 Literature Review

The self-assembly of nanoparticles has been a subject of significant interest in recent years, with various studies showcasing how nanoparticles can organize into ordered structures through interactions between their functionalised surfaces. For instance, Grest and colleagues investigated the self-assembly of alkyl thiol monolayers on gold nanoparticles at the water-vapor interface. Their research demonstrated that the assembly behavior is highly dependent on the chain length of the alkyl thiols and the specific functional groups present. These factors influenced the intermolecular interactions, leading to distinct patterns of assembly ranging from uniform monolayers to more complex hierarchical structures. This work underscores the role of molecular design in directing nanoparticle behavior and achieving desired assembly outcomes.[52]

In a similar vein, Silva et al. employed molecular dynamics (MD) simulations to explore the self-assembly and structural evolution of nanoparticles. Their simulations provided a detailed picture of how nanoparticles transition from disordered states to highly ordered arrangements over time. The study vividly illustrated the dynamic nature of the assembly process. The progression observed in the simulations highlights key parameters, such as temperature, particle size, and interparticle forces, that drive the organization of nanoparticles into ordered structures.[53]

Self-assembled structures of amphiphiles are ubiquitous in nature.[54] Alkylthiol molecules form a monolayer on gold surfaces and provide easier functionalization of the gold surface. Ahn et al. demonstrated the evolution of self-assembled monolayer (SAM) of alkyl thiols on gold surfaces, detailing the progression from initial physisorption of individual molecules to the formation of densely packed, well-ordered layers. This transformation highlights the dynamic nature of SAM formation, where molecular interactions and surface characteristics guide the ultimate arrangement.[37]

A key feature of SAM is its tunability; by modifying the terminal functional groups of the alkyl chains, surface properties can be precisely controlled. For instance, Zheng et al. demonstrated how substituting a CH_3 terminal group with functional groups such as COOH, NH_2, or CN significantly alters the wettability of the surface.[55] This ability to engineer surface characteristics by molecular design underpins the versatility of SAM in various scientific and technological applications. The concept of functionalizing surfaces extends beyond planar substrates to include nanoparticles, where SAM play a transformative role. For example, SAM on nanoparticles can improve biocompatibility, target specificity, and dispersibility, enabling precise interactions in biological systems. Functional groups such as COOH or NH_2 can be used to conjugate biomolecules, facilitating applications in targeted drug delivery or biosensors. Similarly, thiol-functionalized nanoparticles have shown enhanced catalytic properties due to the controlled surface chemistry afforded by SAM.[56, 57] Moreover, the use of mixed thiol SAM introduces additional complexity and utility. By combining different thiol molecules within a single monolayer, researchers can create surfaces with tailored binding sites and selective interaction capabilities.[58] This approach has opened up opportunities for highly specific molecular recognition processes, such as selective capture of biomolecules, design of advanced sensors, and development of heterogeneous catalytic systems.[32] Mixed SAM also provide a platform for investigating cooperative or competitive molecular interactions on a nanoscale, which is essential for the design of multifunctional materials.

Ghorai and Glotzer have shown that alkyl thiol molecules form a highly packed, ordered monolayer on the gold nanoparticles; however, they are inclined at an angle. They have shown that long-range ordering of molecules at lower temperature, indicated by well-defined peaks in Radial Distribution Function (RDF) and with increasing temperature, the peak intensity decreases because the kinetic energy of molecules increases. This shows the absence of long-range ordering at an elevated temperature regime. Also, as carbon chain length increases, the molecular configuration changes from disordered to ordered and adopts an increasing tilt angle.[59]

The aggregation behavior of various surfactants in bulk solutions has been extensively investigated through both experimental and computational approaches. Key properties such as micelle sizes, shapes, shape transitions, critical micellar concentrations (CMC), and the effects of temperature on micelle sizes and shapes have been studied in detail. Theoretical studies have provided valuable insights into these phenomena.[60] Experimentally, techniques such as neutron scattering, light scattering, fluorescence probes, pressure perturbation calorimetry, differential scanning calorimetry, and isothermal titration calorimetry have been employed to explore these properties.[61–67]

Several methods have been described for the interactions between the aqueous solvent and micelles. Domínguez and Berkowitz performed molecular dynamics simulations of sodium dodecyl sulfate (SDS) monolayers at the water/carbon tetrachloride and water/vapour interfaces. They observed that SDS tails are more disordered and inclined at the water/vapour interface compared to the water/carbon tetrachloride interface.[68] Further, they investigated the surfactant mixtures of sodium dodecyl sulfate (SDS) and nonionic surfactants at the water/carbon tetrachloride interface and observed that SDS molecules were more disordered in mixtures compared to pure monolayers, while the nonionic surfactants exhibited straighter and longer hydrocarbon tails.[69]

Faramarzi et al. investigated the self-assembly of micelles starting from a random distribution of detergent molecules near the aggregation number (a_N) using molecular dynamics (MD) simulations and compared them with the simulations of preformed micelles to analyze their structural and dynamic properties.[70]

Chen and Panagiotopoulos proposed a new implicit solvent model to simulate surfactant micellization by leveraging solvent-accessible surface area (SASA) calculations to capture hydrophobic interactions. The model accurately predicted critical micelle concentration (cmc) and aggregation numbers, showing excellent transferability across different surfactants.[71]

In aqueous solution, the micelles can undergo sphere to cylinder transitions with an increase in the concentration of surfactants, as shown by Aswal et al., who investigated the transition for CTAB, cetyl trimethyl-ammonium chloride (CTAC) and Dodecyl trimethyl-ammonium bromide (DTAB). CTAC and DTAB remain spherical even at very high surfactant concentration, whereas CTAB micelles change their structure, confirmed by Small Angle Neutron Scattering (SANS) analysis. Cross-section area per unit volume increases, and peak position shifts to higher Q values (scattering factor) with the increase in hydrophobic tail length. The micelles of CTAB show a strong growth with the increase of concentration, and a sphere-to-cylinder transition of CTAB micelles occurs at 300 mM. Authors have also compared the structure of micelles of CTAB with CTAC and DTAB as a function of surfactant concentration. In CTAC, the hydrated size of the chloride ion is larger than that of the bromide ion in a CTAB molecule. This shows a slight increase in the size of micelles with an increase in surfactant concentrations. DTAB forms the smaller micelles in size because it has a shorter hydrophobic tail length as compared to that of CTAB.[72]

In the synthesis of metal nanoparticles, surfactants like CTAB can be used as a capping agent for the stability of the nanoparticles. Nikoobakht and El-Sayed have shown that

CTAB adsorbs in bilayers on gold nanorods, with the headgroup of one monolayer facing the gold surface and the other facing the solvent. They have used a mixture of CTAB as a cationic surfactant and TOAB (tetraoctylammonium bromide) as a co-surfactant. FTIR and TGA (Thermogravimetric Analysis) analysis indicated binding of surfactant headgroups to the surface of gold nanorods. At a temperature of 330 ^{o}C, desorption of the surfactants from the nanoparticle surfaces leaves the nanocrystals susceptible to transition from nanorods to nanospheres, as confirmed by the analysis of TEM images. [73]

The effect of salt concentrations and compositions of different counter ions (NaCl and sodium salicylate) on sphere to cylinder transition in aqueous solution of CTAC surfactant using molecular dynamics simulation was reported by Wang and Larson. The chloride counterions associate weakly with the surface of CTAC micelles with increasing salt concentration. On the other hand, aromatic salicylate counter ions penetrate inside the micelle with their hydrophilic group staying in the surfactant headgroup region and hydrophobic group partially embedded into the hydrophobic core of the micelle. The strong association of salicylate counterions with surfactant headgroups leads to dense packing of surfactant molecules. Thus, reduces the surface area per surfactant molecules, and increases inter-micellar ordering of surfactant headgroups, favoring the formation of long threadlike micelles.[74]

In the case of computational studies, precisely molecular dynamics simulations, adequately accurate descriptions of force field parameters play a critical role in forming CTAB micelles in an aqueous solution along with counter ions. Silva et al. have shown the effect of force field parameters and different counterions on the formation of micelles. The authors used different parameters to model the interaction of bromide ions. They investigated that the CTAB micelle model does not form a perfectly spherical shape compared to CTAC. Also, chloride counter ions associate strongly on the surface of CTAC micelle, whereas bromide counter ions weakly associate on the surface of CTAB micelle. Therefore, the authors selected the CTAB model for the adsorption study on the gold surface. Adsorption of CTAB micelles on gold surface shows a pattern of cylindrical micelles occurs due to strong gold bromide interactions.[75]

Yuan et al. investigated the behavior of the CTAB monolayer at the air/water interface with time using molecular dynamics simulations. At the end of the simulation, they saw that changes in the electrostatic and hydrogen bonds between the headgroups and water molecules destroyed a slightly bent and ordered monolayer. [76]

Catá et al. also used MD to study CTAB micelles with increasing numbers of monomers at the interface between water and air. Authors have shown that the stability of spherical micelles increases with the number of molecules. For the characterization of micelles, authors have calculated radial number density for nitrogen, which gives an idea about inner and outer radii of layer of solvation, thus we can calculate thickness of the solvation layer.[77]

Fan et al. investigated the control of ice recrystallization using dilute surfactant solutions. They found that surfactants do not bind to ice but affect recrystallization by altering the distribution of counter ions and surfactants in the ice-water interface. Ionic surfactants such as SDS and DTAB initially increase ice grain size before reducing it at higher concentrations, while nonionic and zwitterionic surfactants cause a steady increase. [78]

Murphy and his group investigated the growth of gold and silver nanorods in the presence of aqueous CTAB and developed a seed-mediated growth mechanism. However, the aspect ratio of gold nanoparticles increases with the length chain of the surfactants. They proposed that the surfactants bind as a bilayer to the growing nanoparticle and assist in the nanoparticle elongation via a zipping mechanism. Inter-chain packing of the surfactants assists the formation of the nanorods.[79]

Perala et al. have used the two-phase Brust-Schiffrin method (BSM) for the synthesis of highly stable gold nanoparticles. In this two-phase synthesis, the metal precursor ($HAuCl_4$ for gold) is first transferred from an aqueous phase to an organic phase using tetraoctylammonium bromide (TOAB) as a phase transfer catalyst (PTC). When the organic phase comes into contact with an aqueous phase of sodium borohydride, a reducing agent, particles start to form. The nucleation of the reduced metal precursors, the growth of particles and their capping by alkanethiols lead to the synthesis of highly stable gold nanoparticles.

[80] Pérez-Juste et al. proposed electrochemical mechanism for gold nanorod formation. In this mechanism, $AuCl_4{}^-$ ions are bound to cationic micelles, displacing bromide ions. Then, reduction of $AuCl_4{}^-$ to $AuCl_2^-$ by ascorbate takes place on the micelle surface. $AuCl_2{}^-$ remains adsorbed to the micelle. The bound gold ions are transported to the growing seed particles. The interaction of the cationic micelles with the micelle-coated gold seed in a double layer controls this. Authors have also shown that using the different sized seed particles, size and aspect ratio of nanoparticles differ.[81]

Recently, Saurez-Lopez et al. have shown using Dissipative Particle Dynamics (DPD) simulations that surfactants are essential in regulating the nucleation and growth of gold nanoparticles. Similarly, Liu et al. have developed a coarse-grained model using a DPD approach to investigate the adsorption of CTAB molecules on the gold surfaces. The DPD model is unable to describe important properties related to CTAB ligands, including the deformation of the CTAB layer, the micellar/bilayer structure, and the ion distribution near the CTAB layer.

1.8 Research Gap

Based on the literature review, it is challenging to calculate properties accurately because the size of nanoparticles is below a few nanometres. Many methods used to fabricate PENP involve complex synthetic approaches. Controlling all crystal structures, compositions, and heterostructures of phases and interfaces with PENP is challenging. Many conventional methods, such as impregnation, chemical reductions, etc., are used for the synthesis of PENP, but there are several challenges. One significant challenge is controlling the size of PENP synthesized by conventional processes down to tens of nanometres with a narrow size distribution. Also, the conventional methods consist of several time-consuming steps. Moreover, the fabrication of PENP having more than four elements becomes incredibly challenging due to the immiscible nature of elements, leading to phase separation. This separation occurs due to differences in crystal structures, atomic sizes, mismatching valence electrons and their thermodynamic properties. Thus, it is essential to develop new methods for the more straightforward synthesis or fabrication of such an assembly. Apart from that, the characterization of poly-elemental nanoparticles is another challenge. The conventional methods used to prepare PENP are not scalable. A synthesis method that could be scalable is needed. Along with all these, optimization of the process with the properties of nanoparticles is also essential.

In this study, this problem can be addressed using molecular simulation tools. Using molecular simulations, we can suggest paths for the easier synthesis of the kinds of nanoparticles, considering a lower free energy barrier. It would also help us to understand the phenomenon by applying classical physics from the atomic scale. Furthermore, these experiments are hard, expensive, and difficult to carry out, so molecular simulation can be affordable to find the results of these experiments. Molecular simulations are one of the tools that can be used to calculate the properties and characterization of PENP. Each element has its own intrinsic properties that can thermodynamically induce phase transitions during the nucleation and growth of poly-elemental nanoparticles. Using molecular simulations, the measurement of those thermodynamic properties would be used to understand and predict the phase transition and phase equilibria. Estimation of free energies, radial distribution function, order parameter, excess entropy, etc. will be used for the characterization and feasibility of the processes. Further, the design of suitable surfactants will be carried out. The aim of the study is to develop a scalable path for easier preparation of PENP. This could be key to optimizing both nanomaterial synthesis and drug delivery systems.

The central hypothesis of this study is that surfactants and co-surfactants, such as CTAB, oleylamine (OLA), and hexadecanethiol (HDT), play a critical role in modulating the nucleation and growth of gold nanocrystals by altering micelle structure and reducing energy barriers associated with nucleate release and adsorption. By tailoring the micelle morphology and interaction with substrates, and by introducing functionalized molecules like thiols, it is possible to optimize the free energy landscape and achieve controlled nanocrystal synthesis. Additionally, this concept extends to the reverse process of controlled drug release, where molecular interactions and energy barriers within chitosan-based matrices can be engineered to enhance drug delivery efficiency.

1.9 Objectives

The aim is to develop a scalable path for easier preparation of poly-elemental nanoparticles via self-assembly of surfactant molecules. Here are the major objectives of this thesis: –

- Evaluated the micellar properties on the gold nanocrystals nucleation and growth.
- Calculated the free energy barriers for gold nucleates transitioning through the micelle core and adhering to the gold (111) surface using molecular dynamics (MD) simulations.
- Investigated influence of co-surfactants (e.g., oleylamine, thiols) on micelle stability, structural reorganization, and energy barrier reduction during nanocrystals formation.
- Investigated the role of thiolated layer on the gold surface in the reduction of energy barrier and spontaneity of the system in terms of change in free energy.
- Design a polymeric system for the encapsulation, stability, and controlled release of methotrexate for targeted drug delivery.

1.10 Nature and Scope of Present Work

The present thesis presents molecular dynamics (MD) simulation results on the structure and dynamics of micelle-mediated nucleation and growth of gold nanocrystals in aqueous solution at molecular and nanoscopic interfaces. The thesis consists of eight chapters, where the relevant introduction, conclusion and future prospects of related work are included in the respective chapters. As discussed in the Introduction section, due to the high energy demands associated with the high-temperature synthesis process of PENP, a solution-based process to synthesize it would be highly desired to reduce the energy demand. Understanding the nucleation of metals and their arrest in the solution phase is extremely important. We have used micelles to arrest the growth of the nano-clusters and investigated their subsequent voyage to a surface using computational techniques, which may contribute significantly to nanoparticle synthesis and pharmaceutical applications. In Chapter 1, the importance of studying the various nucleation and growth mechanisms, the self-assembly of surfactants, the role of surfactants and micelles in the nucleation and growth of gold nanocrystals, and the contribution of such studies in the understanding and engineering of self-assembled monolayers (SAMs) to synthesise poly-elemental nanoparticles through molecular simulations is highlighted. The significance of surfactants to the formation of micelles and the control of the size of gold nanoparticles is elaborated. The mention of the small amount of literature available on the behaviour of co-surfactants is worth noting. Finally, in the last part of Chapter 1, the nature and scope of the present thesis are discussed.

In Chapter 2, a general introduction to MD simulations is given, various mathematical equations involved are discussed, and methods adopted to solve these equations are presented. It also explains the motivation for the work carried out during the course of the thesis. Molecular dynamics simulations provide the time evolution of the phase-space in terms of trajectories, i.e. sets of positions and momenta of all the particles of the system. The various structural properties, such as Density profile, Radial Distribution Function, Radius of Gyration, thermodynamic and dynamic properties of the system, can be obtained from these microscopic variables by the application of classical statistical mechanics. Before proceeding with the simulations of the formation of spherical micelles in aqueous solutions, the bulk water system is simulated first to get acquainted with the tool of MD simulations. Various properties and results related to bulk water reported in the literature are reproduced as a learning exercise.

Moving further towards studying the behaviour of micelles in aqueous solutions, we carried out MD simulations for micellization of CTAB molecules in an aqueous solution to analyze the structural properties of various components of the surfactant in the aqueous solutions. The structural properties, such as density profile, radial distribution functions and radius of gyration of micelle formed by CTAB molecules are analyzed. Further, we studied how CTAB (cetyltrimethylammonium bromide) micelles act as templates to guide the formation of gold nanocrystals on a gold surface. We used molecular dynamics simulations to understand how CTAB stabilizes and controls the size and distribution of nanocrystals. To examine the release of gold nuclei from the micelle onto the substrate, we used an advanced simulation technique called umbrella sampling as discussed in Chapter 3 of the thesis.

Further, we have seen the effect of co-surfactant, oleylamine (OLA), with primary surfactant CTAB to modify micelle shape and lower the energy barrier, aiming to enhance the efficiency of nucleate release as discussed in Chapter 4. Notably, we have also seen that the OLA to CTAB molar ratio of 1:2 resulted in the formation of a well-structured and stable cylindrical micelle.

In a subsequent Chapter 5, we investigated the role of hexadecanethiol (HDT) as a co-surfactant in combination with oleylamine (OLA) and CTAB to enhance the micelle's ability to facilitate nanocrystal growth and nucleate release. The addition of HDT significantly altered the structure of the micelles, transforming them into cylindrical or rod-like shapes, similar to the effects observed with OLA.

In Chapter 6, we explored the use of thiol-functionalized surfaces to stabilize gold nucleates. We calculated the energy landscape using the potential of mean force (PMF) approach and found that thiol molecules significantly reduced the energy barrier for nucleate stabilization. Increasing the thiol density on the gold surface further enhanced hydrophobic interactions, leading to better stabilization and minimized energy requirements for nucleation.

Chapter 7 extended the study to drug delivery applications, focusing on the controlled release of methotrexate (MTX) using chitosan-based matrices. Chitosan (CS) chains were cross-linked with sodium tripolyphosphate (STPP) to create a stable carrier for MTX. We also examined how different concentrations of STPP affected drug release and found that optimizing STPP levels could fine-tune the release process. These findings suggest that chitosan nanoparticles are promising candidates for improving drug delivery efficiency and safety, particularly in cancer treatments like MTX therapy, as briefly discussed.

These chapters are followed by Chapter 8, which highlights the conclusions and important findings of the work. A brief summary of the work described so far has been presented in this chapter. This chapter also describes how the present work can be extended in the related field of research in the near future.