

Hybrid nanoparticles based on gold and bimetallic cyanide complexes for magnetism, catalysis, and biomedicine



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Memoria presentada por Shoaib Azeem para aspirar al grado de

Doctor en Nanociencia y Nanotecnología

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Que la memoria presentada por D. Shoaib Azeem con el título “Hybrid nanoparticles based on gold and bimetallic cyanide complexes for magnetism, catalysis, and biomedicine” corresponde a su Tesis Doctoral y ha sido realizada bajo su dirección y tutorización en el Instituto de Ciencia Molecular, autorizando mediante este escrito la presentación de la misma para optar al grado de Doctor.

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"It is not the strongest of the species that survive, nor the most intelligent,
but the one most responsive to change."

Charles Darwin

“To my beloved parents, whose unwavering support and guidance have shaped my journey, and to my late grandparents, whose wisdom and love continue to inspire me.”

Acknowledgments

As I reach the culmination of this journey, I find myself reflecting on the people who have made this endeavor possible. Completing a PhD is far from a solitary pursuit, rather it is a shared experience, built on the encouragement, wisdom, and support of many.

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challenges far more bearable. To those who have been a part of this experience, whether through insightful feedback, helping hands in the lab, or much-needed coffee breaks, I truly appreciate you.

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Finally, to those who may not be named here but have played a role, however small, in this journey, thank you. Every kind word, every bit of advice, every shared struggle has contributed to this achievement.

This thesis stands as a testament not only to years of research but also to the strength of the community that has supported me. I am deeply grateful to each and every one of you.

Abbreviations

CP	Coordination polymer
PB	Prussian Blue
PBA	Prussian Blue Analogues
NPs	Nanoparticles
Au	Gold
NSp	Nanosphere
NRd	Nanorod
NSt	Nanostar
fcc	face-centered cubic
ORR	Oxygen reduction reaction
OER	Oxygen evolution reaction
FDA	Food and Drug Administration
MRI	Magnetic Resonance Imaging
PD	Photodynamic
PDT	Photodynamic therapy
PTT	Photothermal therapies
ROS	Reactive Oxygen Species
TMB	3,3',5,5'-tetramethylbenzidine
POMs	Polyoxometalates

TEOS	Tetraethyl orthosilicate
APTMS	3-aminopropyltrimethoxysilane
TMDs	Transition metal dichalcogenides
LSPR	Localized surface plasmon resonance
SERS	Surface-Enhanced Raman Spectroscopy
HAuCl ₄	Chloroauric acid
NIR	Near-infrared
4-MPy	4-Mercapto pyridine
DOX	Doxorubicin
PEG	Polyethylene Glycol
XPS	X-ray photoelectron spectroscopy
DLS	Dynamic light scattering
ATR-FTIR	Attenuated Total Reflectance Fourier transform infrared spectroscopy
TEM	Transmission electron microscopy
HR-TEM	High-resolution transmission electron microscopy
EDX	Energy-dispersive X-ray spectroscopy
PXRD	Powder X-ray diffraction
ED	Electron diffraction
SQUID	Super Conducting Quantum Interference Device

M/H	Magnetization curves
χ	Magnetic susceptibility
T _c	Curie temperatures
FC	DC field-cooled
FCM	Field cooled mode
CV	Cyclic voltammetry
LSV	The linear sweep voltammetry
η	Overpotential
log j	Logarithm of the current density
CTAB	Hexadecyltrimethylammonium bromide
RDE	Rotating disk electrode
NHE	Normal hydrogen electrode
h ν	Light irradiation

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Motivation, Objectives and Structure of the Thesis

In the last decade, nanotechnology has boosted the interest in hybrid nanomaterials. These materials two (or more) nanoparticles (NPs) in a complementary manner, giving rise to enhanced performance characteristics. In this context, Prussian Blue Analogues (PBAs) have attracted great interest due to their structural versatility, tunable properties, and ease of integration with other materials at the nanoscale. Their open lattice structure allows for chemical composition modifications, enabling the adjustment of their magnetic, catalytic, and electrochemical properties. Additionally, their ability to host ions and molecules makes them attractive for biomedical applications.

To enhance the efficiency of PBAs in specific applications, it is often necessary to improve their intrinsic properties or incorporate new functionalities. In this regard, the combination of PBAs with Au NPs has proven to be a highly effective strategy. Au NPs exhibit exceptional chemical stability, unique optical properties, precise control over size and shape, and a wide range of applications. Their integration with PBAs not only enhances thermal and electrical conductivity but also introduces additional optical effects through localized surface plasmon resonance (LSPR), expanding their potential applications.

Among the possible heterostructures that can be formed by combining these materials at the nanoscale, core@shell structures stand out due to the strong interaction between the two materials, which can generate new properties or enhance existing ones beyond the simple sum of the individual properties of each material.

However, the preparation of Au@PBA structures presents significant synthetic challenges because the cyanide used in PBA synthesis can attack gold (oxidizing and dissolving it), which limits the stability of colloidal gold NPs and complicates the formation of a uniform PBA shell. Therefore, more synthetic methods need to be developed to overcome these limitations and enable the efficient integration of gold and PBAs.

Thus, the main objective of this thesis is to develop and explore Au@PBA NPs with a focus on their synthesis, characterization, and potential applications in catalysis, magnetism, and biomedicine. By leveraging the synergistic properties of Au and PBAs, we aim to enhance catalytic efficiency, explore photomagnetic behavior, and assess biomedical functionalities such as drug delivery and photothermal therapy (PTT).

This thesis is organized into four chapters:

- **Chapter 1** provides an overview of the fundamentals of PBAs and Au NPs. It also discusses the most relevant heterostructures and the Au@PBA syntheses developed to date.
- **Chapter 2** describes the synthetic route developed for obtaining core@shell Au@PBA NPs (with CsNiFe as the PBA). This chapter details the experimental conditions and key parameters used in the synthesis, ensuring reproducibility and stability. A thorough characterization of the structural, optical, magnetic, and catalytic properties of the hybrid nanoparticles is presented. Additionally, the catalytic efficiency of different Au@PBA NPs in the oxygen evolution reaction is analyzed.

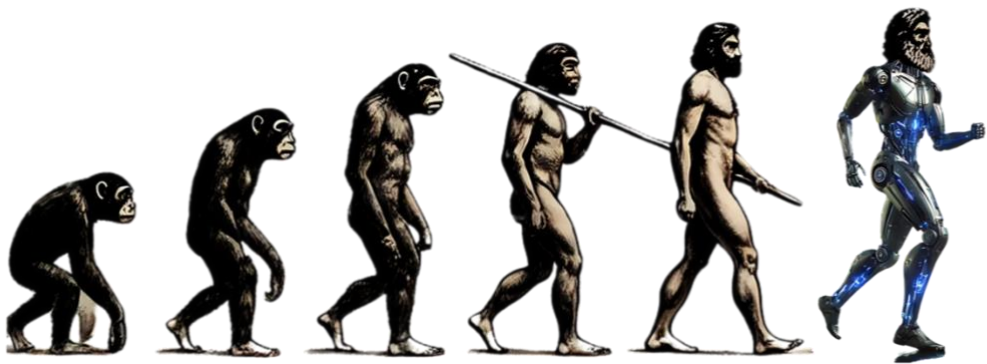
- **Chapter 3** investigates the photomagnetic properties of Au@PBA hybrid nanoparticles. It explores structural and magnetic changes induced by overgrowing a CsCoFe PBA compound around Au NPs. The chapter focuses on analyzing the photomagnetic response as a function of PBA coating thickness and the effect of dissolving the central gold core.
- **Chapter 4** examines the biomedical applicability of Au@CsMnFe NPs. It evaluates their stability in physiological media and their ability to release drugs in a controlled manner. Specifically, the potential for controlled drug release and their application in PTT through near-infrared (NIR) light irradiation are investigated.

Finally, the thesis concludes by summarizing the key findings. By establishing new synthesis protocols, this work represents a significant advancement in the development of novel heterostructures based on Au and PBAs.

Chapter

1

Introduction



1.1 Prussian Blue Analogues

1.1.1 Prussian Blue, the first coordination polymer

Even if the term “coordination polymer” (CP) started to appear at the end of the 20th century, the current extensive interest in CPs started after the reports of Robson, Hoskins, and coworkers in the early 1990s.^{1–3} A CP is a material that has a polymeric structure built from the association of metal ions and bridging organic linkers (ligands) forming coordination bonds that extend in one, two or three directions of space leading to networks with different dimensionalities as shown in Figure 1.1. The wide variety of metal cations and ligands affords a vast number of possible combinations and, therefore, structures and topologies. The judicious choice of metals and ligands is crucial for obtaining a targeted structure.⁴

The metal ions are usually d-transition metals and/or f-transition metals. Generally, d-transition metals have been more popular due in part to the relatively predictable nature of their coordination geometries. For d-transition metals, the field is dominated by the first-row elements (plus Zn, Cd, Hg, Ag and, to a less extent, Au, Pd, Pt). Their low cost, earth abundance, kinetic lability and stability explain why the research on these d-transition metal-containing CPs is predominant compared to the rest.⁵ Additionally, the use of first row transition metal ions can result in magnetic, optic and catalytic properties, leading to a wide range of applications (Figure 1.1).

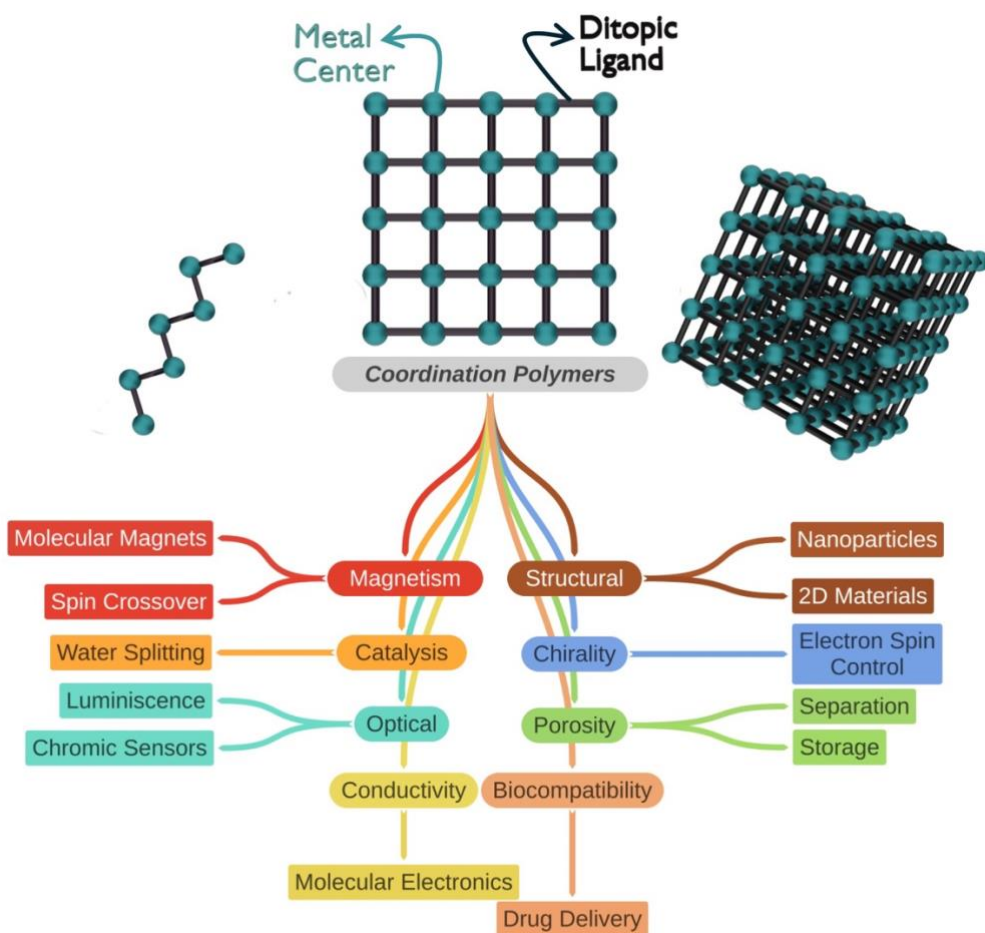
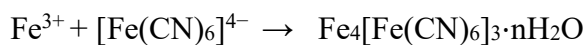


Figure 1.1: Schematic representation and the diverse functionalities of coordination polymers.

Ferric hexacyanoferrate (II), the first CP ever reported, is widely recognized as Prussian Blue (PB), a compound discovered in the early 18th century. In Figure 1.2, the historical timeline of PB can be seen. According to a book published by Georg Ernst Stahl (1660 – 1734), this discovery was made by an accidental contamination of potash and hexacyanoferrate by a color maker named Diesbach.⁶ Due to a shortage of potash, he borrowed some contaminated iron cyanide potash, which led to an unexpected chemical

reaction forming a vivid blue precipitate. This residue was called PB and used as a pigment in many paintings.⁶ The reaction that took place was:



By the 19th century, chemists started to explore modifications of the original PB compound. By using other metal ions along with iron, they created a range of compounds with varying colors. These compounds are nowadays known as Prussian Blue Analogues (PBAs).^{5,7} Indeed, when analyzing their crystallographic structure, these compounds were found to exhibit structural similarities to PB, therefore, they began to be described collectively as its analogues. These structural insights not only deepened the understanding of PB and PBAs but also paved the way for the design of new materials with specific properties. Nowadays, PB and its analogues are exploited in various applications.⁸ For example, PB is used as a remedy for heavy metal poisoning, while PBAs are being explored in energy storage. Moreover, their tunable magnetic and optical properties make them interesting candidates for use in technologies such as electrocatalysts, molecular electronics, and magneto-optical devices.⁹⁻¹⁵

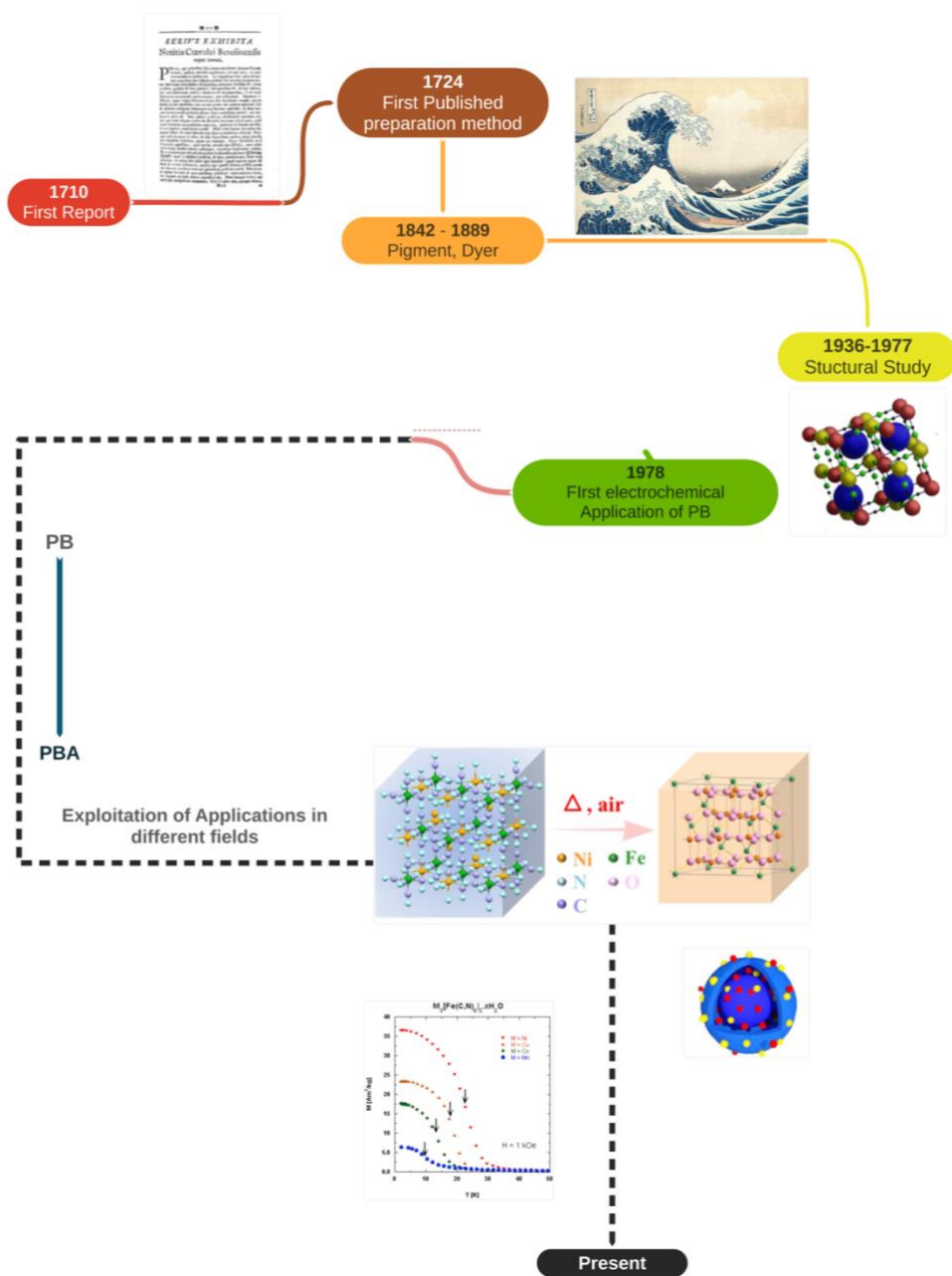


Figure 1.2: Historical timeline of PB and PBAs, from first report to modern research.

1.1.2 Structure of Prussian Blue Analogue

The first reported PB presented a face-centered cubic (fcc) structure, with alternating Fe^{II} and Fe^{III} metallic ions that are connected by cyanide ligands, representing the formula $\text{Fe}^{\text{III}}_4[\text{Fe}^{\text{II}}(\text{CN})_6]_3 \cdot n\text{H}_2\text{O}$. It exhibits an intense blue color due to an intervalence charge transfer band associated with the $\text{Fe}^{\text{II}}\text{-CN-Fe}^{\text{III}}$ mixed-valence unit.^{16,17}

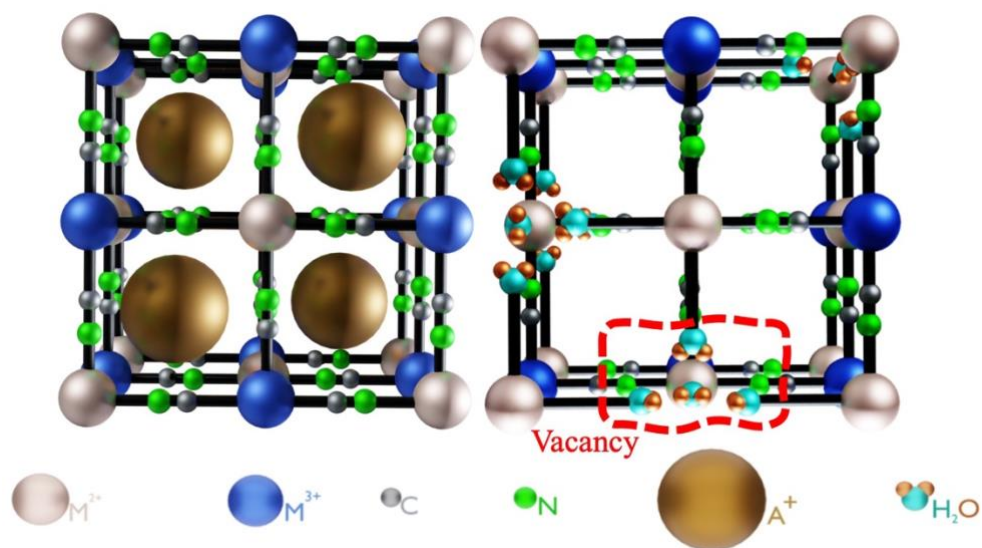


Figure 1.3: Crystal structure of PBAs with and without vacancies.

The replacement of either Fe^{III} or Fe^{II} with other transition metal ions leads to the formation of PBAs with formula $\text{A}_x\text{M}^{\text{II}}_x[\text{M}'^{\text{III}}(\text{CN})_6]_y \cdot n\text{H}_2\text{O}$, (where A is an alkali cation (e.g. Na^+ , K^+ , Rb^+ , and Cs^+)) where M and M' are transition metal ions such as Fe, Co, Ni, and Mn (Figure 1.3). Note that the cubic structure is maintained, however, in this case, the oxidation states of the metallic species are reversed compared to PB: M^{II} is linked to the cyanide through the nitrogen atom, while M'^{III} is connected to the cyanide through the carbon atom. In this context, the framework is still formed by cyanide linkers,

and the tetrahedral sites of the fcc structure can be occupied by alkali ions that compensate for the negative charge of the network. If these alkali ions are removed, vacancies in hexacyanometalate species are generated and the vacant sites are filled with residual water molecules occupying the coordination sphere of M^{III} metal ions. These vacancies give rise to an open pathway within the 3D network, which is usually occupied by a network of H-bonded water molecules.^{5,18,19}

This ability to incorporate alkali ions, vacancies and variable oxidation states among the transition metals contributes to their structural complexity and versatility. The capability of hosting various guest species and the presence of vacancies makes them to exhibit various electronic, magnetic, and catalytic properties. In fact, the properties of PBAs are intrinsically linked to their structural features, making them highly adaptable materials with a range of potential functionalities. Hence, PBAs offer several advantages in comparison to other conventional inorganic materials because of their different tunable properties, processability, and chemical versatility.^{5,18,20}

1.1.3 Properties and Application of PBAs

PBAs' applications are extensive and diverse, extending far beyond a single area of study. In this regard, these materials are utilized in various scientific fields, including energy storage, catalysis, environmental remediation, magnetism, and medicine, highlighting their versatile nature and significant potential for innovation across multiple disciplines.²¹

1.1.3.1 Electrochemistry

Due to their specific open framework structure with CN^- bridges between metal centers, PBAs are promising cathode materials for sodium and potassium ion batteries. Moreover, PBAs have demonstrated high specific capacity, excellent cycling stability, and compatibility with aqueous electrolytes. These characteristics make PBAs highly suitable for energy storage applications where long life cycle and cost efficiency are critical. In addition to their role in energy storage, PBAs have shown potential in various applications as electrocatalysts, including in fuel cells and metal-air batteries. Electrocatalysis involves the acceleration of electrochemical reactions, where PBAs are particularly effective due to the redox active metal centres, their ability to tailor electronic properties through compositional modifications, and the inherent porosity, which leads to high surface areas. For example, key reactions in which PBAs have demonstrated effectiveness are the oxygen reduction reaction (ORR) and oxygen evolution reaction (OER). Typically, these reactions are slow, and they require efficient catalyst to improve the reaction rate and reduced energy losses. PBAs incorporating first-row transition metals, including cobalt, nickel, chromium, and iron, have emerged as highly effective catalysts for the OER. These materials display high

electrochemical activity comparable to those of conventional metal oxides at alkaline conditions.^{22,23} On the other hand, the reduction of hydrogen peroxide is another well-known reaction that PBAs of FeFe and CoFe can successfully catalyse. Thus, by introduction of specific metal ions or creation of structural defects within the PBA lattice, researchers have been able to optimise the catalytic properties of PBAs, making them highly effective for electrochemically detecting this molecule.^{24,25}

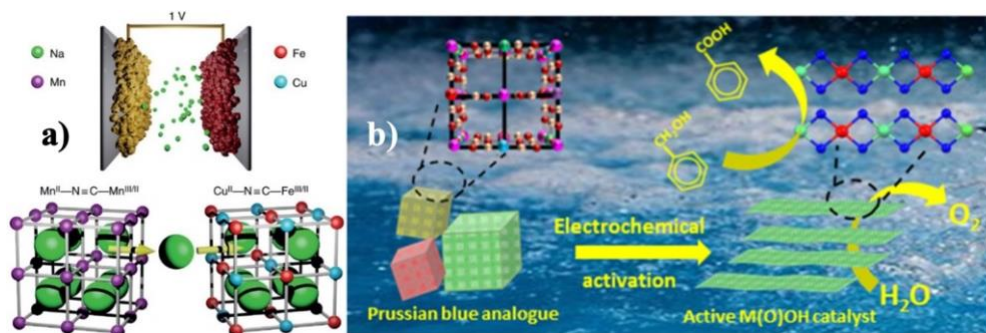


Figure 1.4: (a) Structural representation of PBAs in electrochemical cells, reproduced with permission from Nature Springer 26, (b) Schematic illustration of the electrochemical activation of PBAs into active metal hydroxide ($M(OH)_2$) catalysts for OER adapted with permission from 27.

1.1.3.2 Magnetism

Materials with the PB structure are exciting molecule-based magnets for several reasons. The metal centres are covalently linked into a three-dimensional network, and a wide range of metals with varying spin states and oxidation states can be incorporated into the structure. Additionally, the bridging cyanide ligands facilitate strong magnetic exchange couplings between paramagnetic centres, providing significant control over the nature and strength of the local magnetic interactions.^{17,28,29}

Considerable improvements in magnetic ordering temperatures have been made possible thanks to the PBAs' chemical flexibility (Figure 1.5). For instance, in vanadium-chromium (VCr) PBAs,^{17,28} the magnetic ordering temperature has been raised from a low of 5 K in conventional PB to ambient temperature. Besides these characteristics, some PBAs also show photomagnetic characteristics, a phenomenon attributed to a metal-to-metal charge transfer under the influence of external light. The first characteristic of photo magnetism was observed in CoFe PBA films.¹³ The combination of these magnetic properties with their easy processability underscores the potential of PBAs for advanced applications in nanotechnology.

In this sense, the significant advantage of PBAs is the tuning of their magnetic properties, which can be adjusted by altering their composition and structure during their preparation. Depending on the specific metal ions involved and their arrangement within the crystal lattice, they can exhibit behaviour such as ferromagnetism, antiferromagnetism, or ferrimagnetism. This tunability is crucial for applications that require precise control over magnetic properties such as data storage or spintronic devices. For example, in cobalt-iron PBAs magnetic interactions can be manipulated by the change of oxidation states of metal ions or by the introduction of vacancies or different alkali cations.¹⁷ In this way, it is possible to influence the magnetic ordering temperature, the strength of magnetic interactions, and the overall magnetic moment of the material. Such control is essential for developing materials that can function effectively in advanced magnetic applications.

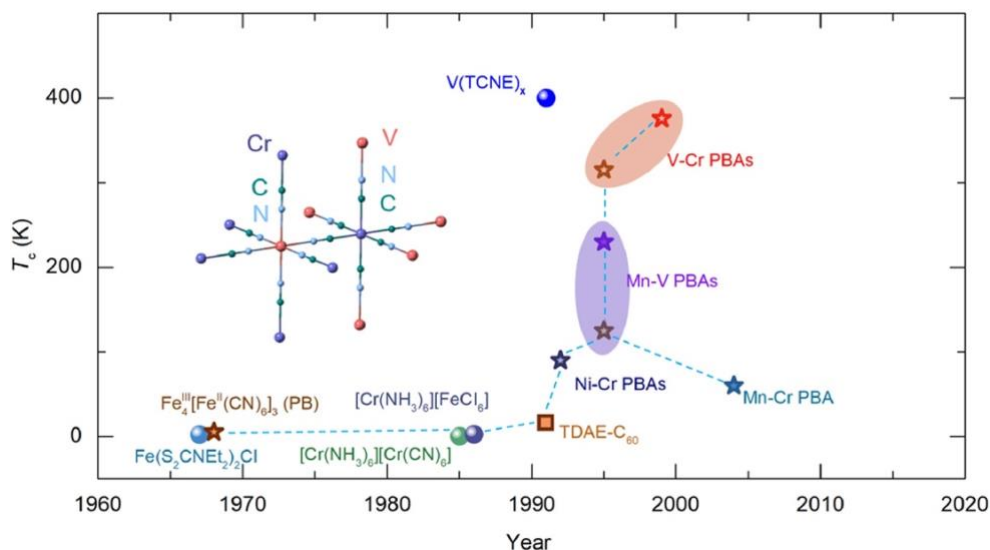


Figure 1.5: Temperature evolution of various PBAs over the years, reprinted from 30.

1.1.3.3 Biomedicine

PB is known for its biocompatibility, making it suitable for various biomedical applications. In fact, it was approved by the Food and Drug Administration (FDA) for its use in treating certain types of heavy metal poisoning. In the case of PBAs, they also inherit many of the desirable properties of PB, such as biocompatibility and stability. Moreover, the optical and magnetic characteristics of PBAs make them valuable in a variety of biomedical applications such as diagnostic imaging, therapeutic interventions, drug delivery and biosensing.^{31–33}

- i) PBAs have been extensively studied as contrast agents in diagnostic imaging techniques such as magnetic resonance imaging (MRI) and photo acoustic imaging. The use of iron-based PBAs enhances the contrast in MRI which provide clear and more detailed images of biological tissues. Full acoustic imaging which combines optical, and ultrasound imaging also benefits from the use of PBAs as contrast

agents because the strong absorption of near-infrared light generates ultrasonic waves upon light absorption, which enables the construction of high-resolution images of deep tissue structures.^{34,35}

- ii) In therapeutic applications, particularly in photodynamic (PD) and photothermal therapies (PTT), PBAs have shown significant potential. In PTT, PBA nanoparticles (NPs) are used to convert light into heat, which has been investigated to selectively destroy cancer cells. Compared to traditional cancer treatments, this approach offers a less invasive alternative as PBA NPs can be targeted to specific tumour sites. Photodynamic therapy (PDT) is another area where PBAs are showing promise. When these materials are exposed to light, they can generate reactive oxygen species (ROS) which damage cellular components and can lead to the targeted destruction of cancer cells. This precise targeting of cancerous tissues by the generation of ROS with light reduces the risk of side effects associated with conventional therapies.^{36–38}
- iii) PBAs have also found applications in biosensing, where their catalytic properties are leveraged in detecting various biomolecules. For example, in electrochemical biosensors, they catalyse the reduction of hydrogen peroxide, a reaction commonly used for the detection of glucose and other important biomolecules. The high sensitivity of these materials makes them ideal for using medical diagnostics, such as glucose monitoring in diabetes management.^{39,40}
- iv) PBAs have been extensively researched as drug delivery systems because of their porous structures. They have the capability to encapsulate therapeutic agents within their pores and can then be released in a controlled manner at the desired site of action. PBAs are

also being explored for their potential in delivering genetic material such as DNA or RNA for gene therapy applications. The ability of PBAs to protect these fragile molecules during the drug delivery and release in response to specific stimuli makes them promising vectors for gene therapy.^{41–44}

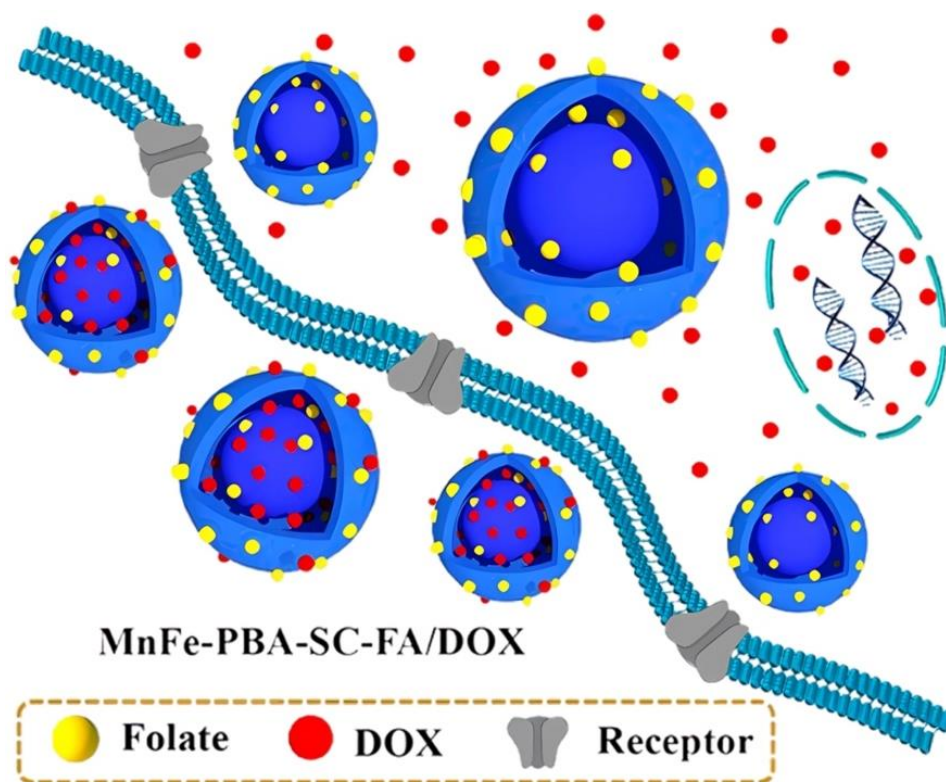


Figure 1.6: Illustration of MnFe-PBA-SC-FA/DOX nanostructures designed for targeted drug delivery, reprinted with permission from 12.

1.1.4 Synthesis of Prussian Blue Analogues

Since the accidental discovery of PB, the synthesis has evolved significantly, and various methods have been developed to control the structural and functional properties of these versatile materials. PB and PBA materials possess unique physical and chemical properties that can be finely tuned, in particular at the nanoscale. For instance, they can be synthesized as stable colloidal solutions in water, remaining stable for several years, and their size can be precisely adjusted from 2 to 200 nm depending on the synthetic conditions employed. In this way, this tunability has enabled the design of PBAs in various morphologies, including discrete NPs, hollow nanostructures,²² thin films,⁴⁵ nanowires,¹⁶ and sophisticated core@shell architectures formed by integrating different PBAs or combining a PBA with other materials. Such structural and compositional versatility allows for the tailored development of PBAs for specific applications, ranging from biomedicine to catalysis and energy storage.⁶ Over the years the following methods have been the most commonly used for synthesizing PBA materials:

- Co-precipitation method
- Hydrothermal synthesis
- Electrochemical synthesis
- Template-assisted

Each of these synthetic methods is chosen based on the specific needed requirements, as offers benefits for synthesizing PBAs with unique morphologies or tuning properties suitable for specialized applications

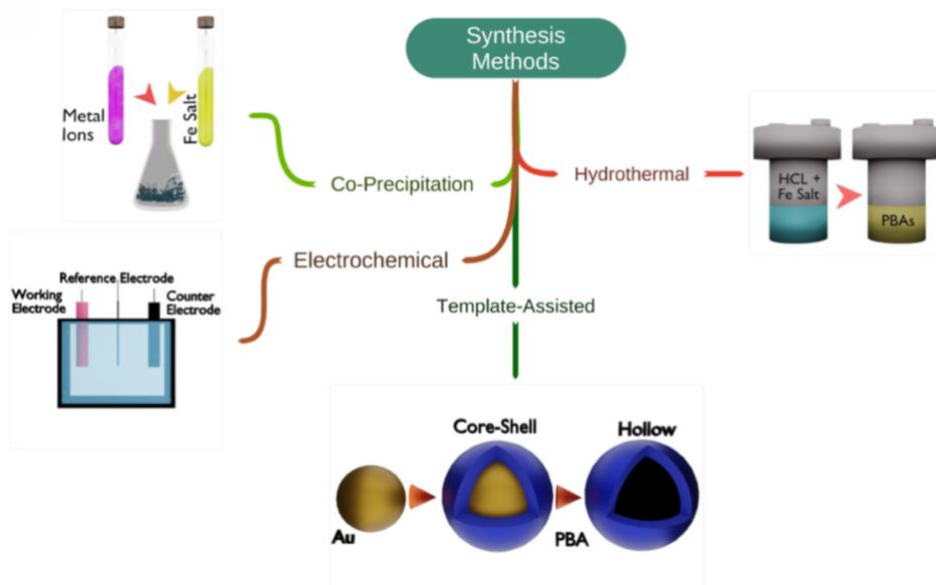


Figure 1.7: Overview of various synthesis methods of PBAs.

1.1.4.1 Co-precipitation Method

Co-precipitation methods have become one of the most widely used procedures for the synthesis of PBAs owing to their simplicity and scalability. Typically, this method involves mixing metal ions with (e.g. Fe^{2+} , Ni^{2+} , Co^{2+}) with hexacyanometallate ions (e.g. $\text{Fe}(\text{CN})_6^{3-}$, $\text{Cr}(\text{CN})_6^{3-}$) in aqueous solution that results in the formation of PBAs through a precipitation reaction. By controlling key factors such as pH, temperature, and concentration during the synthesis, researchers can optimize crystallinity and particle size.^{46–51}

1.1.4.2 Hydrothermal Synthesis

Another method, known as hydrothermal synthesis, involves reacting hexacyanometallate compounds with metal ions in a sealed autoclave under high temperature and pressure. This procedure produces highly crystalline PBAs with well-defined particle sizes and shapes. Researchers have been able to manipulate structural features like vacancies and phases by adjusting parameters such as temperature, pressure, and time for the reaction to take place. This approach gives rise to the formation of PBAs which are desirable for applications requiring a well-defined structure, like magnetism and batteries.^{52–54}

1.1.4.3 Electrochemical Synthesis

PBAs can be formed on an electrode surface by electrochemical reduction or oxidation of metal ions in the presence of hexacyanometallate ions. This technique is useful for the precise deposition of PBAs on conductive substrates, making it suitable for applications in electrochemical and magneto-optical devices. The thickness and composition of the PBA films can be controlled by modifying parameters such as applied voltage, time, pH and reactant concentration, leading to highly pure and crystalline film materials.^{55,56}

1.1.4.4 Template-Assisted Method

Template-assisted synthesis of PBAs is a versatile and widely used method for engineering complex nanostructures, particularly core@shell structures. In this approach, a template (e.g., gold, silica or carbon matrices),

is used to guide the formation of a shell. The easy processability of PBAs allows them to grow uniformly as a shell around many template cores under controlled conditions, resulting in well-defined core@shell nanostructures (see description in section 1.2.1.1) with different possible morphologies. Interestingly, once the PBA shell is formed, the template can be removed by techniques like chemical etching or thermal treatment, giving rise to a highly ordered, porous hollow nanostructure. The preparation of core@shell nanostructures is especially valuable for combining the unique properties of PBAs with those of the core material. This approach offers a powerful platform for designing PBAs with enhanced functionalities, making them ideal for a wide range of applications such as catalysis, energy storage, and sensing.^{57–60}

1.2 Hybridization of Prussian Blue Analogues

Hybrid materials are materials that combine two or more distinct components to create a new material with properties that are not present in the individual components. These materials often exhibit synergistic effects, where the combination of different materials results in enhanced or tailored characteristics, such as improved mechanical strength, electrical conductivity, or catalytic activity. In this context, the use of coordination compounds, particularly PBAs, in hybrid nanostructures as functional materials is a rapidly growing area of research in materials science. PBAs are especially attractive for hybridization due to their unique structural versatility, tunable properties, and ability to integrate easily with other materials at the nanoscale.^{61–63}

1.2.1 PBA-based heterostructures

PB and PBAs can be easily combined with other nanomaterials at the nanoscale, forming different heterostructures, each offering unique interactions. The most popular heterostructures are:

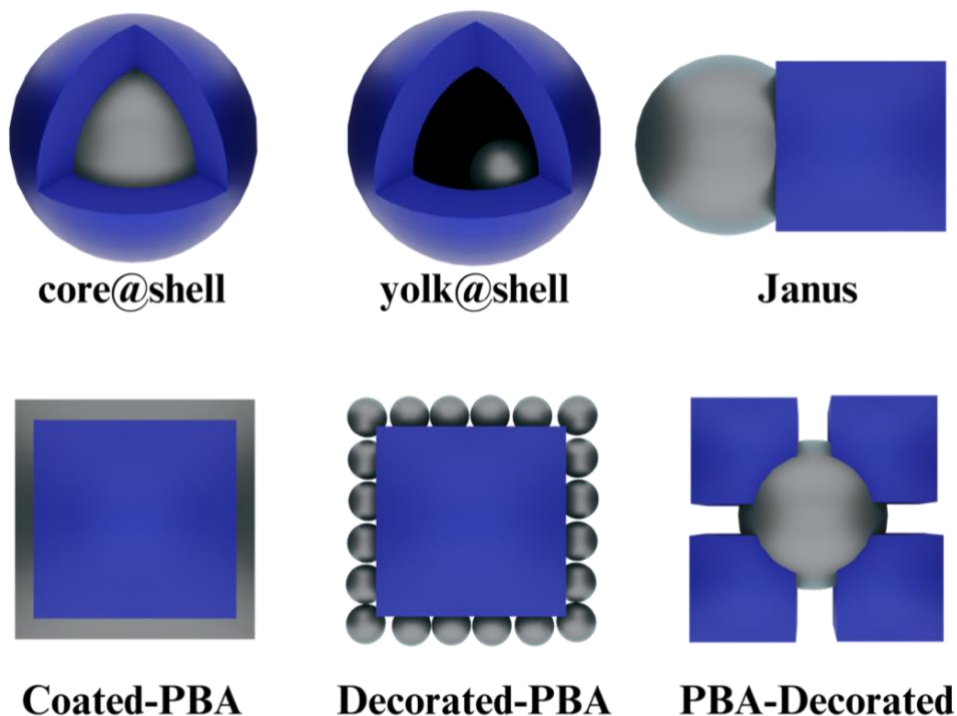


Figure 1.8: Representation of various hybrids of PBAs.

1.2.1.1 Core@shell PBA NPs

These nanostructures consist of a core material, such as metals or metal oxides, encapsulated within a PB or PBA shell, enabling the properties of both the core and the shell to be precisely tailored by adjusting the core-to-shell size ratio. Thanks to the strong interaction between the core and shell materials, synergistic effects can emerge, leading to enhanced properties (e.g.,

the stability, catalytic activity, and distinct optical and electrochemical properties). For instance, $\text{Fe}_3\text{O}_4@\text{PB}$ nanostructures have shown promise in MRI-guided PTT, thanks to their tunable optical and magnetic properties. Regarding their preparation, methods are often based on template-assisted approaches. However, their synthesis can be challenging, requiring meticulous control over conditions to avoid undesirable problems such as aggregation, incomplete coverage, or cyanide-etching of the core.^{64–67}

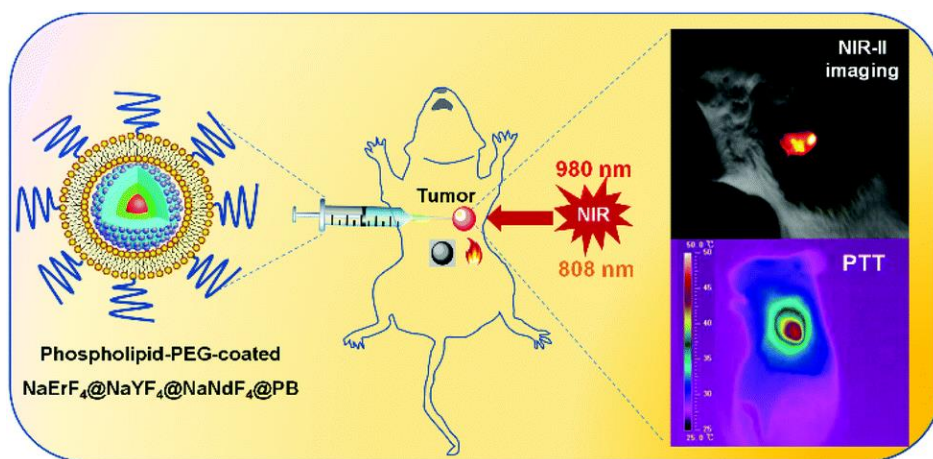


Figure 1.9: Illustration of a phospholipid-PEG-coated $\text{NaErF}_4@\text{NaYF}_4@\text{NaNbF}_4@\text{PB}$ NP system for targeted tumor therapy reproduced from 68 with permission from Royal Society of Chemistry.

1.2.1.2 Yolk@shell PBA NPs

Yolk@shell nanostructures have emerged as a versatile class of materials that combine the advantages of both hollow and core@shell architectures. These structures typically feature a core particle enclosed within a hollow shell, creating a distinctive core-void-shell configuration that offers high surface area, low density, and the ability to independently modify both core and shell. The distinctive design of yolk@shell structures involving PB and PBAs creates a cavity that can potentially interact with the

environment, thanks to the inherent porosity of the PBA shell. This feature enables enhanced reactivity and adsorption capabilities, making these structures especially useful in biomedicine or environmental remediation.^{69–}

71

The development of *yolk@shell* nanostructures leverages multiple synthetic techniques to achieve precise control over particle morphology and composition (Figure 10a). However, preparing these structures can be challenging due to difficulties in achieving uniform shell thickness and maintaining shell integrity. Careful optimization of reaction conditions is crucial to overcome these obstacles and ensure the desired structure and functionality.

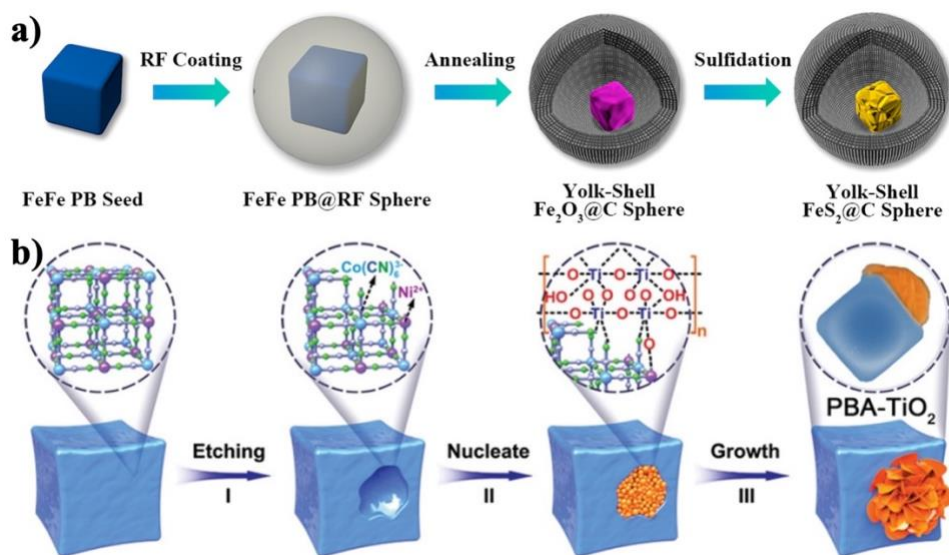


Figure 1.10: (a) Synthesis process for *yolk@shell* FeS_2 @C spheres starting from a PB seed reprinted with permission from 69, (b) Growth stages of PBA- TiO_2 Janus NPs reprinted with permission from 72.

1.2.1.3 Janus PBA

Dumbbell or Janus nanostructures exhibit an asymmetric design in which two distinct regions of a single particle are composed of different materials, such as a PBA on one side and another material on the opposite side. This anisotropy provides dual functionalities within a single particle, making them ideal candidates for applications that require bifunctional properties. These materials are typically connected through direct chemical bonding, electrostatic interactions, or epitaxial growth at the interface, ensuring strong adhesion between the two domains.

The synthesis of Janus structures presents several challenges, as it requires precise control over nucleation and growth. Various synthetic approaches have been developed, including heterogeneous nucleation, selective surface modification, and controlled assembly techniques. One of the key difficulties lies in preventing uncontrolled deposition of nanoparticles onto the other, which could lead to undesired aggregation or loss of anisotropy. Additionally, ensuring a stable interface between the two materials is crucial for maintaining their distinct functionalities.⁷²

An example of this design is the PBA-TiO₂ Janus heterostructure, which integrates PBA single particles with TiO₂ 2D nanocrystals (Figure 1.10b). The strong interface between the two components facilitates efficient charge separation and transfer, which is particularly advantageous for photocatalytic applications.⁷²

1.2.1.4 Coated-PBA

Coated-PBA nanostructures consist of PBAs as cores, encapsulated within an inorganic shell such as metal oxides (e.g., SiO₂ or TiO₂). This coating strategy enhances the stability of PBAs while introducing additional functionalities, such as optical properties, or controlled surface reactivity. Unlike other structures, these coated systems are designed to limit the direct interaction of PBAs with the environment, making them more suitable for applications where high stability is required. For example, SiO₂ coatings provide a protective layer that prevents PBA degradation in some aqueous or oxidative environments while enabling surface functionalization (Figure 1.11a). Similarly, TiO₂ coatings can introduce photocatalytic properties, expanding the potential applications of these nanostructures. However, a key limitation of coated-PBA nanostructures is the reduced accessibility of their inner framework, as the dense inorganic shell can hinder ion exchange and limit electrochemical activity, which are typically advantageous features of PBAs. The synthesis of these nanostructures generally involves methods such as sol-gel processing, co-precipitation, and surface-controlled deposition techniques.^{73–75}

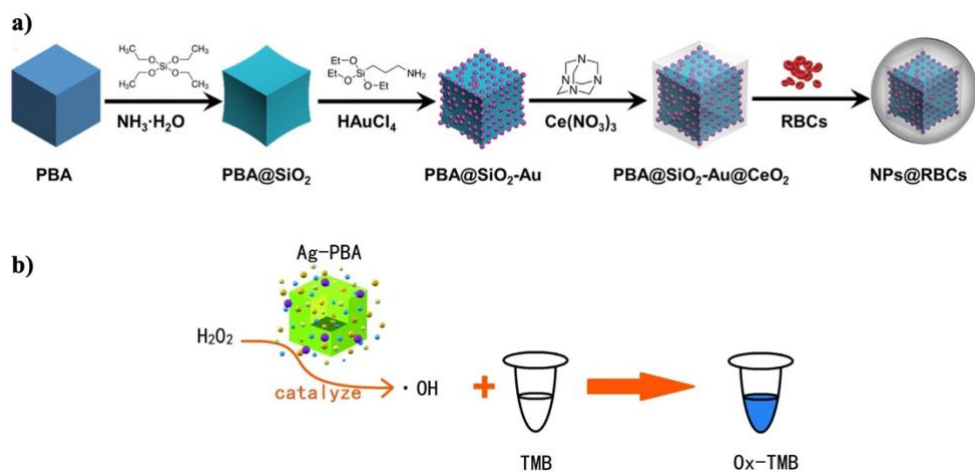


Figure 1.11: (a) Synthesis and application of $\text{PBA@SiO}_2\text{-Au@CeO}_2$ NPs functionalized with red blood cells adapted with permission from 75, (b) The catalytic activity of Ag coated PBA used with permission from 76, permission conveyed through Copyright Clearance Center, Inc.

1.2.1.5 Decorated PBA

Decorated PBA NPs are obtained by attaching smaller NPs onto larger PBA particles. This strategy adds to the PBAs while additional functionalities to the PBAs, such as improved electrochemical or catalytic activity. For instance, silver ions were anchored to PBAs forming Ag-PBA nanozymes (Figure 1.11b), which exhibit high catalytic efficiency in oxidation reactions, such as the oxidation of 3,3',5,5'-tetramethylbenzidine (TMB) in the presence of hydrogen peroxide (H_2O_2). Notably, the interaction between the environment and both NP surfaces can allow for cascade reactions, where multiple catalytic steps can occur sequentially within a single nanostructure. This is particularly beneficial in complex catalytic processes, as the different sites within the decorated particles can facilitate the conversion of substrates in a stepwise manner, enhancing reaction efficiency and selectivity. The

preparation of these heterostructures is relatively straightforward. Common synthesis methods include seed-mediated assembly, electrostatic adsorption, and bridging ligand strategies, which allow for controlled deposition of smaller NPs onto the PBA surfaces. However, there are challenges in achieving a uniform distribution of NPs, ensuring strong interfacial adhesion, and preventing unwanted aggregation during synthesis.^{76,77}

1.2.1.6 PBA Decorated

This heterostructure represents the complementary case of the previous one. Here, larger inorganic NPs are decorated with smaller PBA NPs. In this approach, the PBA NPs are typically anchored to the surface of the larger core through electrostatic interactions or other surface functionalization techniques. The synthesis of these heterostructures can follow similar procedures to those used in the preparation of decorated-PBA nanostructures.⁷⁷

1.2.2 Examples of hybrid PBA

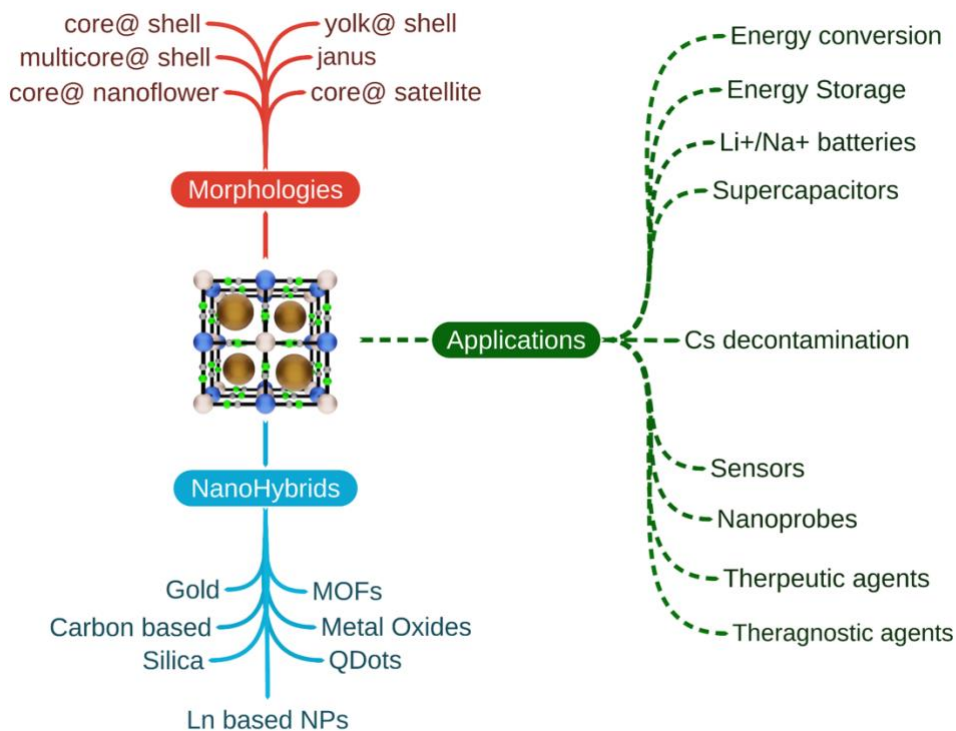


Figure 1.12: Schematic of PBA NPs, showing their hybrid structures, varied morphologies, and broad applications.

The versatility of PBAs is demonstrated not only by their easy preparation but also by their ability to be combined with a wide range of inorganic materials. These include metals, metal oxides, metal sulfides, carbon-based nanomaterials, and more recent additions like silica, metal oxides, and polyoxometalates (POMs). This simple integration with other inorganic components allows for the development of materials with tailored functionalities and improved performance. Some examples of such hybrid nanomaterials are:

1.2.2.1 PBA-SiO₂

A heterostructure made of PBA with silica (SiO₂) was developed by synthesizing Co₃[Co(CN)₆]₂ nanocubes coated with a silica layer functionalized with amino groups using organ silanes such as tetraethyl orthosilicate (TEOS) and 3-aminopropyltrimethoxysilane (APTMS). This hybrid material exhibits multi-redox behavior and fast electron transfer processes even with the dielectric coating of SiO₂. The incorporation of silica not only improves the stability and surface area of the PBA but also enables further functionalization, showing potential for use in electrochemical biosensors due to its robust and modifiable surface.⁷⁸

1.2.2.2 PBA-TMDs

PBAs and transition metal dichalcogenide (TMD) layers have been combined to enhance electrocatalytic OER under light irradiation. By incorporating the intrinsic electrocatalytic properties of TMDs with the light-responsive behavior of PBA, these materials display improved OER performance, including reduced overpotential and increased current density, attributed to the PBA porous structure, engineered surface defects, and abundant oxygen vacancies of TMDs.⁷⁹

1.2.2.3 PBA-POMs

Nanostructures of PBA and POMS have been synthesized by using the hydrothermal method where MnFe PBA cubes are etched with a strong acid that results in a hollow cube with enhanced electrocatalytic properties. This hollow structure not only increases the exposure of active sites but also

facilitated electron transport which improved the catalytic activity towards OER. The optimized PBA@POM exhibits low overpotentials and enhanced activity due to the structural evolution induced by POM, by providing more active sites, and better charge transfer. This study showed the potential and efficiency of PBA@POM hybrids in renewable energy technologies.⁸⁰

1.2.2.4 PBA-Fe₃O₄

Co₃[Co(CN)₆]₂/Fe₃O₄ has been prepared using a self-assembly process where the magnetic Fe₃O₄ NPs is adsorbed onto the nanocubes of cobalt PBA. Carvalho *et al.* concluded that the enhanced electrochemical performance of these material arises from the Co^{II}/Co^{III} redox process in the PBA, while the magnetite NPs retain their superparamagnetic properties. Through cyclic voltammetry, they observed an increase in Faradaic currents compared to the isolated PBA. They attributed this increase to the supramolecular charge transfer between the PBA and the magnetic NPs. This synergistic property is a combination of electrochemical activity with magnetic response.⁸¹

1.2.2.5 PBA-Metallic NPs

Pt/PB hybrid nanoparticles have been synthesized by reducing K₂PtCl₆ in a PB colloidal solution. In this heterostructure, Pt covers partly the surface of PB NPs. 1,3-Propanedithiol was used to anchor the Pt-modified PB NPs onto Au electrodes via strong metal–sulfur interactions. Electrochemical studies showed that these Pt/PB NPs maintain their PB redox activity and

thus, this heterostructure can serve to anchor PB on electrodes for electroanalytical applications.⁸²

1.3 Au-Prussian Blue Analogues heterostructures

Among the many possible inorganic materials to which PBA can be combined, Au NPs are particularly attractive due to the potential synergistic effects that can emerge. This is possible due to their exceptional chemical stability, their unique optical properties, their size and shape chemical control, and their variety of applications.

1.3.1 Optical properties of Au NPs

Au NPs have a rich history that dates back to ancient times, with strong evidence of their use in stained glass windows and ceramics because of their optical properties. However, the history of Au NPs has evolved significantly since their initial exploration by Michael Faraday in 1857. Faraday demonstrated that when gold was reduced to nanometer dimensions, ended up exhibiting an intense red color, a phenomenon that now is called localized surface plasmon resonance (LSPR). In this phenomenon, when the electromagnetic radiation interacts with metallic NPs much smaller than its wavelength, electrons at the metal surface are excited and undergo collective oscillations in response to the incident light's frequency, relative to the stationary positive ions. These oscillations result in a localized electric field around the NP, extending into the surrounding dielectric medium over several nanometers, which enhances the local electromagnetic field intensity by several orders of magnitude. For noble metal NPs, such as those of gold or

silver, this resonant behavior typically occurs in the UV-visible spectrum, producing characteristic absorption peaks in this region. The resonance frequency is sensitive to factors such as the metal type, particle size, morphology, and the surrounding environment^{83–87} (Figure 1.13). For instance, spherical Au NPs generally show a plasmon resonance peak between 500 and 550 nm in the visible range, while anisotropic NPs can display different resonant frequency modes. In the case of nanorods (NRs), their spectra exhibit two plasmon bands associated with LSPRs along their length and across their diameter. These frequency resonances related to anisotropic NPs are much more sensitive than the LSPR from spherical NPs and have been extensively applied for sensing.^{88–92}

Plasmons offer a range of applications, such as enhancing local electric fields for Surface-Enhanced Raman Spectroscopy (SERS), generating localized heating through the photothermal effect, and enabling color detection thanks to the plasmon sensitivity. Moreover, Au NPs are particularly advantageous due to their unique properties, including easy surface functionalization, low toxicity, high stability, and excellent electrical and thermal conductivity. These features have allowed Au NPs to play a pivotal role in developing new applications across materials science, electrochemistry, and biomedicine.^{90,93}

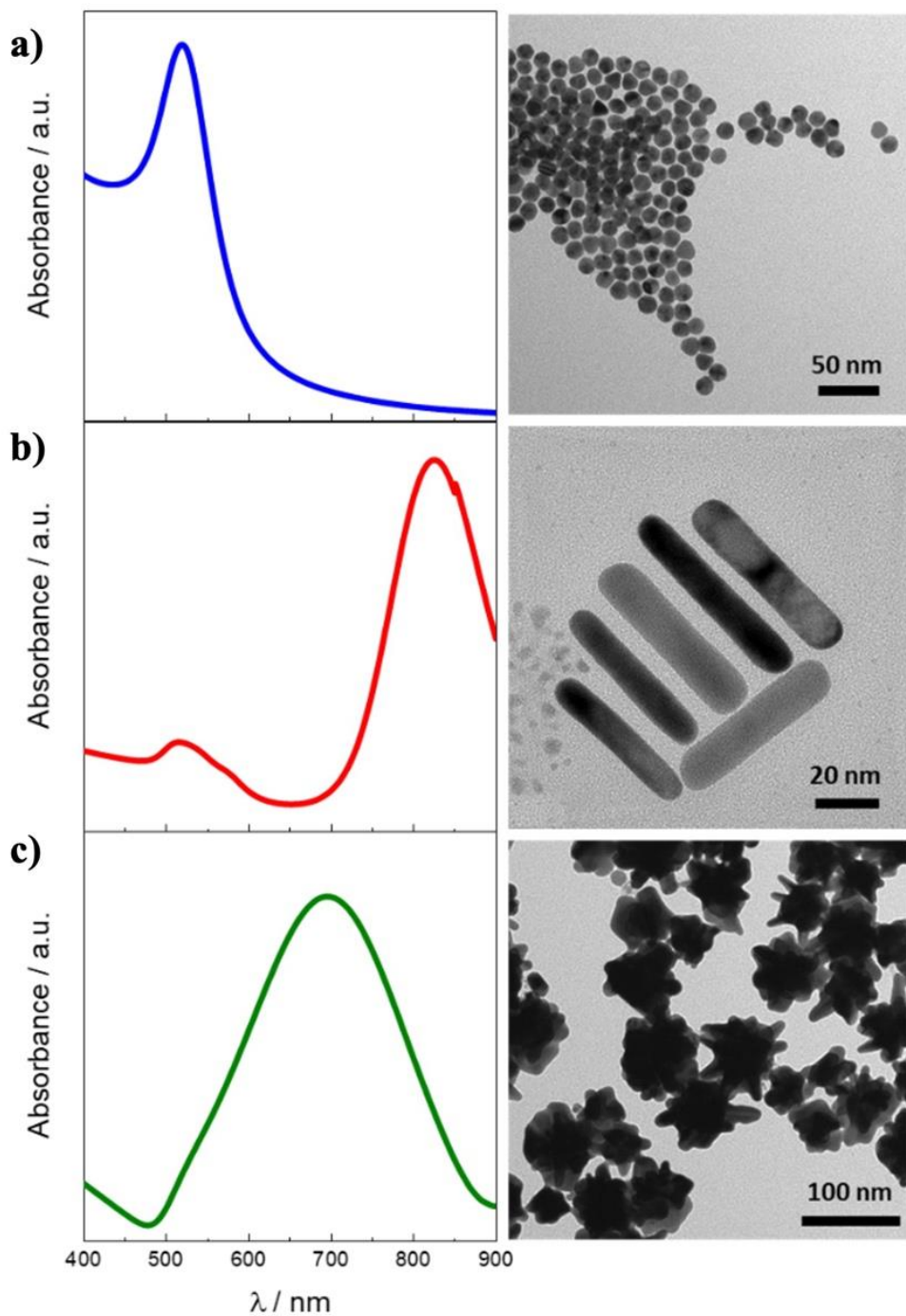


Figure 1.13: Spectral and morphological analysis of Au NPs: (a) spherical, (b) rod-shaped, and (c) star-shaped structures.

1.3.2 Synthesis of Au NPs

The distinctive optical properties of Au NPs are achieved by modifying the size and shape. Typically, this is achieved using colloidal approaches, where Au NPs are formed by the aggregation of gold atoms that are produced from the reduction of ions present in a solution.

Au NP obtained by colloidal synthesis comprises three parts: i) inner Au atoms (central atoms), ii) atoms exposed to the surface (surface atoms) and iii) surface-protecting organic ligands (capping agents) or surfactants. Central Au atoms determine the crystallinity of the nanostructure, whereas the structure of the surface atoms form surface facets and edges that will dictate their reactivity, including the catalytic activity. The surfactant is anchored on the surface atoms, stabilizing them and providing surface functionality.^{91,94}

In the early 20th century, significant advances in colloidal chemistry led to improved methods for synthesizing and stabilizing Au NPs. However, it was not until the latter half of the century that these particles became the focus of extensive research across various scientific disciplines. A pivotal development came in 1951 with the Turkevich method, which standardized the production of spherical Au NPs by reducing chloroauric acid (HAuCl_4) with citric acid in boiling water. In this process, citrate acts simultaneously as a reducing and stabilizing agent, which facilitated the reproducible synthesis of Au NPs and paved the way for broader applications and further exploration.^{95,96}

In 1973, Frens expanded on this approach by adjusting the ratio of gold to citrate, allowing precise control over particle size in the range of 10 to 100 nm. Moving into the early 1990s, interest grew in the shape-controlled

synthesis of gold nanostructures. Pioneering work by Masuda, Martin, and others utilized electrochemical reduction to produce AuNRd. While these methods generated relatively uniform structures, the large size (around 100 nm) and low yield presented challenges in achieving distinct optical properties.^{97,98}

A significant breakthrough occurred a decade later with the development of a seeded growth technique, which allowed for the high-yield production of monodisperse AuNRd. This two-step process first involved creating single-crystal seed particles, followed by their controlled growth into anisotropic shapes under carefully managed conditions in an aqueous surfactant medium. This method enabled the fine-tuning of the nanorod aspect ratio, allowing for the modulation of their longitudinal plasmon resonance from the visible to the near-infrared (NIR) spectrum, a feature highly beneficial for biomedical applications.^{99–101}

Due to its precise control over particle morphology and size, seed-mediated growth became the preferred method for synthesizing anisotropic NPs with diverse shapes. By 2008, Huang and colleagues had adapted this strategy to create gold nanostars (AuNSt), characterized by multiple sharp branches that serve as “hot spots” to significantly amplify local electromagnetic fields. These unique optical properties, particularly their tunable plasmon bands in the NIR region, have made AuNSt valuable in a variety of scientific and technological applications.^{102,103}

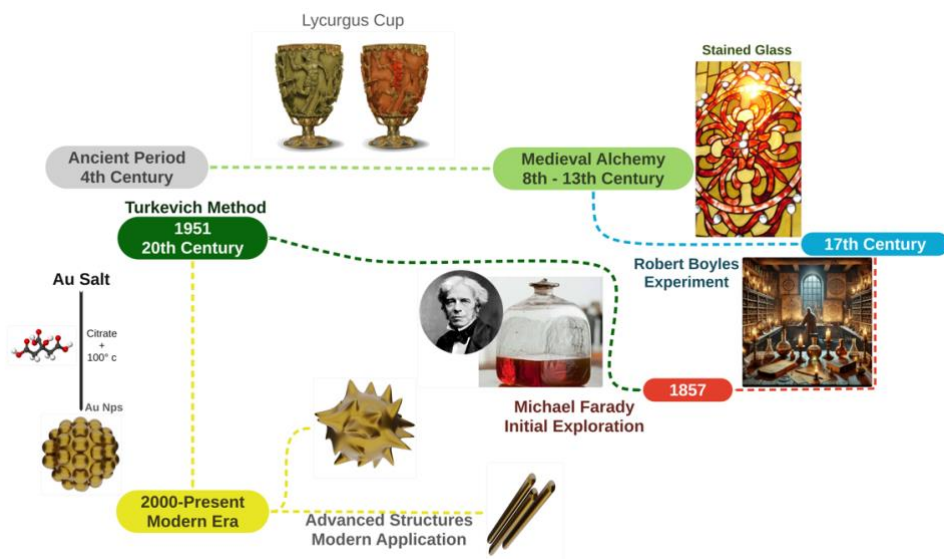


Figure 1.14: Historical timeline of Au NPs, from ancient applications to modern advancements.

1.3.3 Synthesis and properties of Au-PBA nanostructures

Early combinations of Au NPs and PBAs were realized via electrochemical deposition of PB onto gold surfaces, forming hybrid films on electrodes, which constrained their practical applications due to limited structural flexibility.^{104–107} The first example of PB coating directly on Au NPs was achieved by Xia through a colloidal approach where Au NPs catalyzed the reduction of ferric ions, precisely controlling the formation of PB. Subsequently, PB NPs decorated with Au NPs were synthesized using albumin as a linking agent, employing thiolate linkages and alkylamines to connect the two components; however, the protein layer hindered direct contact between the PB and Au systems. To address this limitation, PB@Au core-satellite NPs were developed, employing diverse organic polymers and surface modifications as linkers.^{107–110}

Further works led to the formation of core@shell nanostructures, where a PB shell was grown on citrate-stabilized Au cores, achieving well-defined structures. Another approach involved the initial etching of Au cores with cyanide ions (CN^-), anchoring these ligands around the Au surface before forming the PB shell. In these methods, Au NPs are initially stabilized with citrate, which is subsequently replaced by CN^- ligands, derived from ferricyanide precursors, to facilitate shell growth. Despite this, the reactive nature of cyanides complicates the use of anisotropic Au NPs, as they are highly susceptible to etching. Nevertheless, these methods have been optimized for biomedical applications, leveraging PB's suitability as a theragnostic nanomaterial. Au-PB hybrids have shown potential *in vivo* for computed tomography and PTT, demonstrating enhanced diagnostic precision, therapeutic efficacy, and biological stability (Figure 1.15).^{111–115}

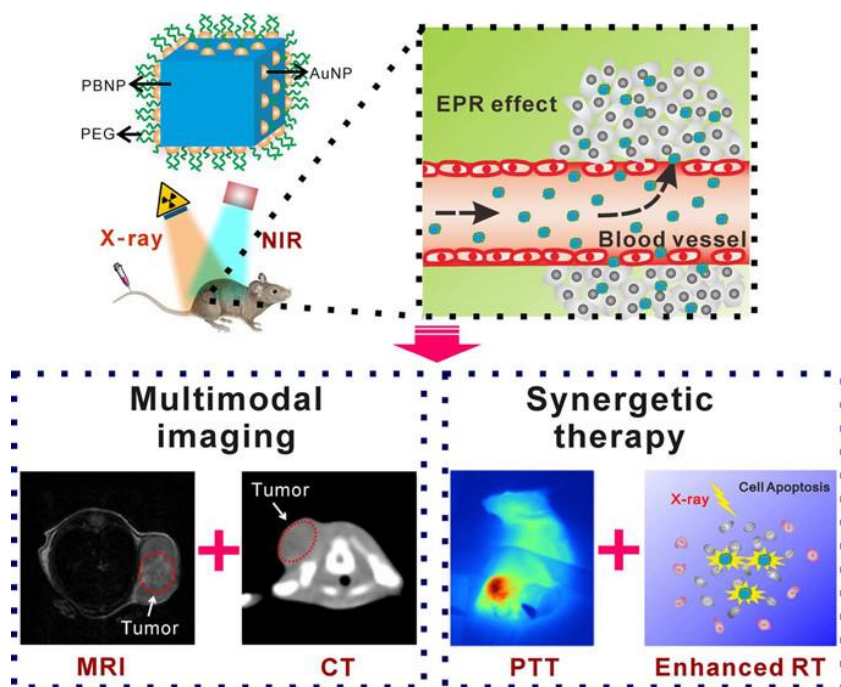


Figure 1.15: Multimodal imaging and synergistic therapy using PBA Au hybrid NPs.

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Recent studies include PB@polyacrylic acid/Au Janus NPs synthesized using polyacrylic acid domains as templates for selective Au NP growth. This design enhances NIR light absorption and offers optimal spacing for drug loading. In parallel, complex Au@PB yolk@shell nanocubes were created using Au@Ag nanocubes as sacrificial templates under mild conditions, where Ag shells guide the formation of PB shells via the reaction of $[\text{Fe}(\text{CN})_6]^{3-}$ with Fe(III).¹¹⁶ These yolk@shell nanostructures feature high surface areas, enabling effective drug encapsulation, such as doxorubicin, for chemo dynamic cancer therapy.

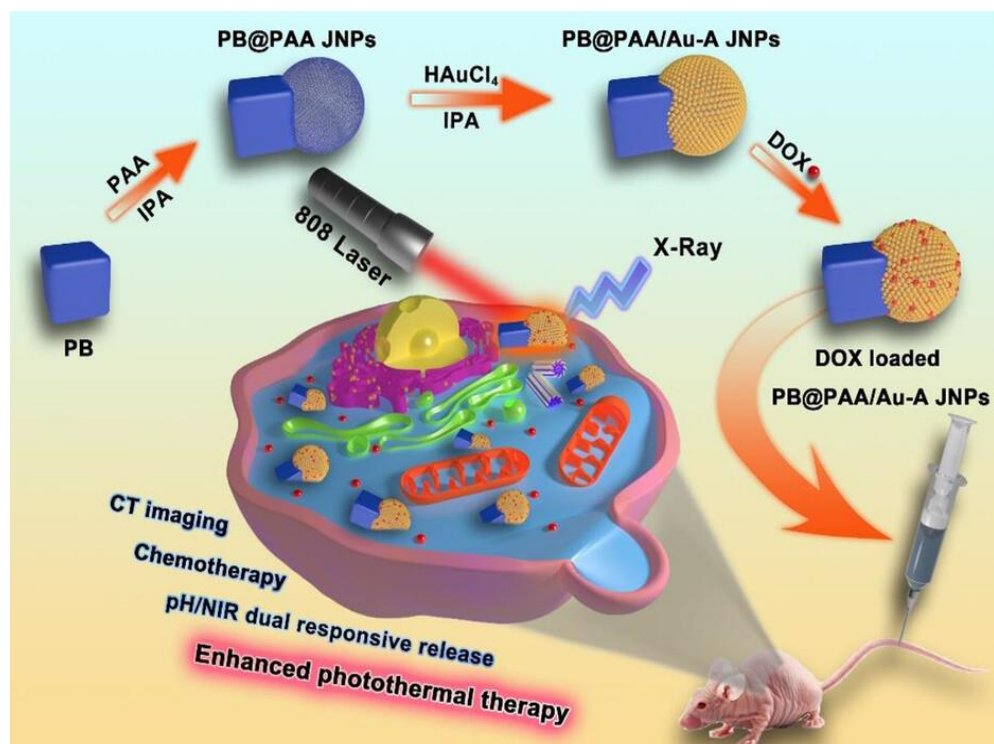
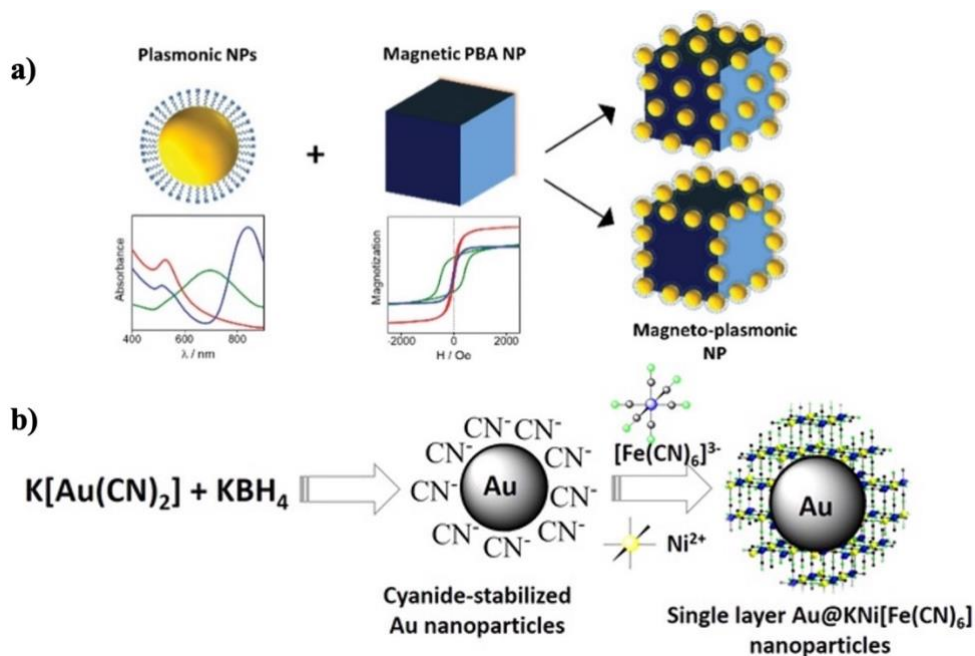


Figure 1.16: Illustration of the preparation and application of DOX-loaded PB@PAA/Au-A Janus NPs. Reprinted with permission from 116.

To expand beyond Au nanospheres and PB, a general synthetic route for obtaining hybrid Au-PBA magneto-plasmonic nanostructures was developed, employing various cubic PBAs decorated with Au NPs of different shapes linked via bridging molecules (Figure 1.17 (a)). This protocol allows tuning the plasmon band across the visible spectrum and permits the enhancement of the magneto-optical properties through plasmonic coupling. Complementarily, magneto-plasmonic core@satellite PBA@Au-Ag nano heterostructures were synthesized by Mamontova et al. using post-synthetic adsorption of a $[\text{AuI}_2\text{AgI}_2(\text{C}_6\text{F}_5)_4(\text{OEt}_2)_2]_n$ complex on ferromagnetic PBAs, altering magnetic properties and exhibiting spin-glass behavior due to ultra-small Au-Ag satellites, while also enhancing catalytic performance in the reduction of 4-nitrophenol. Furthermore, hybrid PB@AuNPs@MnO₂ structures have been created for magnetic resonance imaging and enhanced antitumor therapy, leveraging the catalytic properties of Au and PB for generating reactive oxygen species.^{117–119}

Despite these advancements, synthesizing Au@PBA heterostructures remains challenging due to the reactivity of cyanides, which can etch Au^{120–123} during PBA synthesis. To address this, Marin-Pasturel et al. introduced a method involving cyanide-stabilized Au NPs formed by reducing $[\text{Au}(\text{CN})_2]^-$ with sodium borohydride, followed by stepwise growth of multiple PBA shells. This strategy avoids Au dissolution but results in an intermediate reduced PBA layer, minimizing direct electronic interactions between the plasmonic Au core and the PBA shell. The introduction of Au NPs inside these core@shell structures resulted in the enhancement of the catalytic activity of the PBA shell. Specifically, the close contact between both materials gives rise to a synergistic effect where the Au core increases the

electrochemical activity and the electrochemical stability of the PBA, while the PBA shell protects Au from its electrochemical oxidation.



The association of Au NPs with PBAs in an appropriate heterostructure can result in enhanced properties due to the synergistic interaction between the two components. This interaction can involve electronic, structural, and magnetic coupling, leading to novel functions that go beyond the sum of their individual properties. In this way, the mutual influence between Au and PBA can enable the development of hybrid nanostructures with optimized functionalities of interest in catalysis, magnetism and biomedicine.

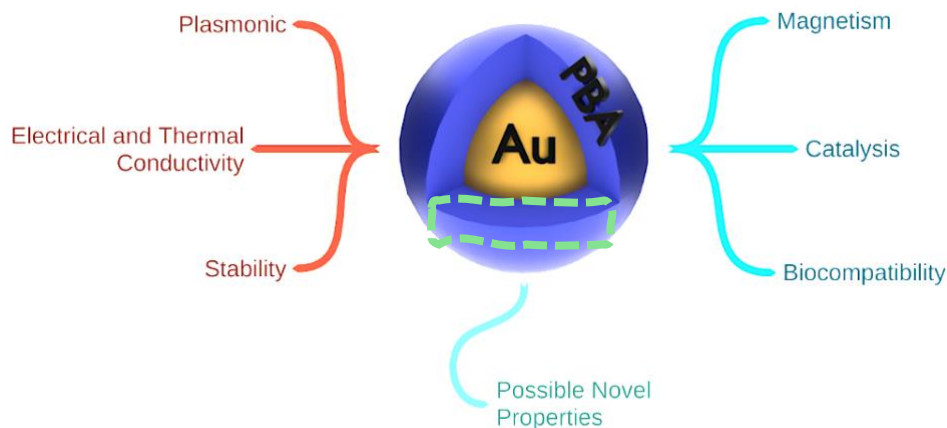


Figure 1.18: Illustration of Au@PBA core@shell NPs, leading to potential novel properties.

In catalysis, the elaboration of Au-PBA nanostructures can pave the way for catalyzing cascade processes and tandem reactions. Furthermore, Au can also enhance the catalytic performance of pristine PBA materials thanks to its high electrical conductivity (in electrocatalysis), or thanks to the plasmonic properties (in photocatalysis).^{110,124–126}

In molecular magnetism, Au plasmons have been proven to be highly effective for inducing the spin transition in spin crossover complexes through photo-thermal effects by light irradiation, and for electrically detecting and manipulating the spin state switching, which aids in their integration into molecular electronic and spintronic devices.¹²⁷ Another promising avenue is that of combining in a single structure Au NPs with optically active magnets based on PBA networks in order to get magneto-plasmonic effects, or even

more complex phenomena arising from the photo-magnetic properties exhibited by some of these magnets.¹¹⁹

In biomedical applications, the photo-thermal effect of Au NPs can facilitate the adsorption or desorption of molecules carried by these hybrid nanostructures. Thanks to that, their combination with the high surface area of PBAs can result in interesting usages for drug delivery.

It is important to remark that, among the different heterostructures, the core@shell nanostructure made of an Au core and a functional shell is the most popular because it maximizes the interaction between the two nano systems, thus favoring the appearance of synergistic effects. Therefore, developing new systematic protocols for easily covering Au NPs with different PBAs is essential because it will facilitate the study of potential novel functions and applications.

Chapter

2

Design of core@shell Nanoparticles Based on Gold and NiFe Prussian Blue Analogues Featuring Shape Dependent Electrochemical Activity

2.1 Introduction

The growing demand for sustainable energy has drawn attention to electrochemical water splitting as a cost-effective way to produce hydrogen. Nevertheless, its production generally also involves the oxygen evolution reaction (OER), an electrochemical process in which water is oxidized to release protons, electrons, and oxygen. This reaction requires high voltages mainly due to its slow kinetics (Figure 2.1), represents a significant efficiency loss in water-splitting systems and often requires an anode catalyst to reduce the energy barriers of the OER.¹²⁸

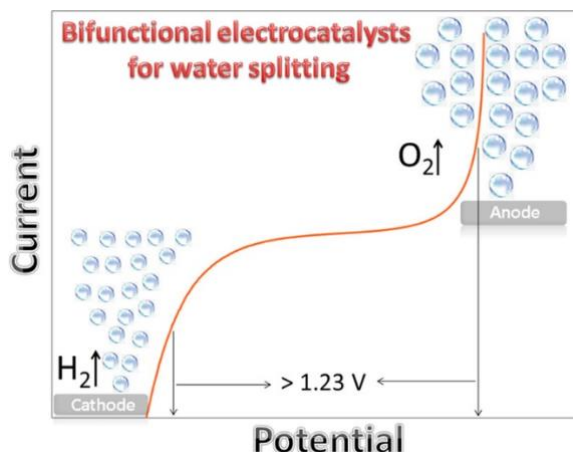


Figure 2.1: Schematic representation of bifunctional electrocatalysts for water splitting, showing the hydrogen evolution reaction (H₂ production) at the cathode and oxygen evolution reaction (O₂ production) at the anode Reprinted from 128.

In this context, many electrocatalysts based on earth-abundant electrocatalysts have been extensively studied.^{129–131} First-row transition metal oxides of Co, Fe, or Ni show extremely high activities but only at very high pH, where the corresponding half-cell reduction reaction (for example, the hydrogen production) is more problematic. Nonetheless, at low pH, most of the catalysts suffer corrosion. Thus, an efficient catalyst for OER at near-

neutral solution based on earth-abundant metals remains a significant challenge and highly desirable goal. In such conditions, benchmark materials are principally based on Ru or Ir oxides, affecting the cost of this technology considerably.^{132,133}

To this aim, Prussian Blue Analogues (PBAs) are interesting materials since they are robust in a wide range of pH, chemically tunable and based on earth-abundant metals. Importantly, they have shown promising performances comparable to those of many metal oxides and have become increasingly attractive as OER catalysts. Yet, at these conditions, their performance falls short of the current standard, iridium oxide.

Hence, to exploit their full electrocatalytic potential, the scientific community has pursued different approaches: such as expanding their catalytic surface area through the preparation of nanoobjects, synthesizing hybrid PBA heterostructures to produce synergistic effects^{134,135} and/or enhance the electrical conductivity of the insulating PBA,^{136–138} and increasing their intrinsic catalytic activity by incorporating defects/vacancies into the PBA structure.^{128–130} Nonetheless, a possibility that has been scarcely explored in PBAs for enhancing the catalytical activity of metallic centers is the formation of structural dislocations.¹³⁹ In this regard, recent reports indicate that preparing Pd@Pt core@shell nanoparticles (NPs) results in a strained Pt surface due to structural mismatch. Consequently, this configuration leads to a more efficient oxygen reduction reaction.^{140–143} Core@shell nanostructures, such as these, represent excellent examples of materials with structural dislocations due to the lattice mismatch between the core and shell materials, resulting in a distorted interface that affects the shell structure. Importantly, the level of dislocations in the shell is directly related

to factors such as shell thickness, core size, and shape, among others.¹⁴⁴ Taking this into account, we envisage the synthesis of core@shell nanostructures consisting of PBA overgrown around cores with tunable morphologies as an exciting pathway for significantly increasing PBA catalytic efficiencies.

Among the many inorganic materials with which PBA can be combined to form core@shell nanostructures, Au NPs are particularly appealing.¹⁴⁵ This combination results in NPs with a larger reactive surface area, a defective structure, and improved electrical conductivity.^{146,147} Furthermore, Au NPs can be synthesized in various sizes and shapes,¹⁴⁷ making them ideal templates for growing PBA shells. In this regard, the presence of a gold core can result in a notable enhancement of the PBA intrinsic properties and additional synergistic effects.^{144,146,148} Notably, Au@Fe^{III}Fe^{II} core@shell structures have attracted significant exposure for theranostic applications owing to the excellent photothermal conversion efficiency of Prussian Blue (PB) and the contrast-enhancing property of gold.^{147,149} The synthetic process of Au@Fe^{III}Fe^{II} is simple. It is based on the in situ reduction of [Fe^{III}(CN)₆]³⁻ on the Au surface accompanied by the presence of Fe^{III} ions. Nevertheless, the synthetic procedures to obtain other PBA shells in pure condition (M^{II}M^{III}), which are electrocatalytically more active, remain quite challenging because this usually involves the use of hexacyanometallate precursors in the +3 oxidation state. This constraint hampers the direct synthesis of PBAs with desired catalytic characteristics, including Ni^{II}Fe^{III}. To solve this problem, various routes for synthetic strategies that use cyanide functionalities as anchoring points for the polymerization of PBA have been investigated. However, these methods always undergo two major disadvantages: (i) etching of the Au core caused

by precursor cyanides, an effect particularly pronounced in anisotropic NPs,^{150,151} and (ii) the formation of a reduced PBA shell due to the use of reductants in order to prevent Au etching.^{136,152} The lower oxidation states reduce the OER performance of the material. Consequently, developing novel synthesis protocols that enable the direct formation of non-reduced PBAs on Au NPs is essential to fully harness their functional and synergistic properties.

To overcome these synthetic challenges, we introduce a novel strategy to synthesize a core@shell structure of Au and PBA while keeping their original states. In this research, we deliver a synthesis protocol where we have incorporated the concept of surface modification by using 4-Mercapto pyridine (4-MPy) as an anchoring molecule because of the strong thiol bonds,¹⁵² that function as a protection layer for the Au NPs from the cyanide ions of the hexacyanometallate while also acting as a bridge for the growth of PBAs on the surface of Au core. This method not only prevents the dissolution of the core but also retains the states of the PBAs. Moreover, this strategy gives us access to the successful synthesis of PBA shells on different Au anisotropic cores such as Au rods and Au stars, each causing a degree of structural distortions in the PBA shell resulting in the improvement of their electro catalytical properties.

2.2 Results and Discussion

We developed a two-step protocol to obtain the Au@PBA NPs with different core shapes (spheres, rods, and stars). Initially, the surface of the Au NPs is chemically modified using as anchoring molecule 4-MPy, which has a strong affinity towards the Au surface because of the thiols. This molecule facilitates the growth of the PBA shell while minimizing the Au etching by the cyanide species. The selection of 4-MPy was based on earlier research on the development of coordination polymers based on cyanides on 4-MPy self-assembled monolayers on gold. In this way, the presence of a N atom in the para-position with respect to the thiol group can facilitate the alignment between the core and the shell. High-resolution X-ray photoelectron spectroscopy (XPS) spectra demonstrate that the functionalization occurs through Au-S bonds, as can be seen in Figure 2.2 (a-b). The S2p spectra for different samples, Au surface where 4-MPy was drop-casted, Au@citrate and Au@CTAB as well with the functionalized 4-MPy can be seen which highlights the chemical states of sulfur in each case. The sulfur bands can be observed in the 4-MPy functionalized nanoforms. The main S2p_{3/2} peak at approximately 162.3 eV, is consistent with the expected signal that arises from the sulfur bound to Au, similar to that observed in self-assembled monolayers of 4-MPy on gold substrates. This suggests that the functionalization of the NPs mainly occurs by the formation of Au-S chemical bonds, thanks to the strong affinity of thiols towards metallic Au.¹⁵³

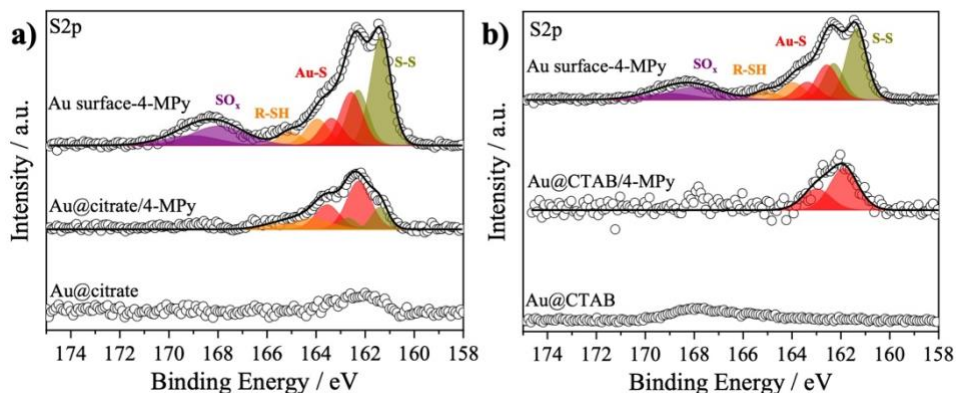


Figure 2.2: XPS spectra of the S2p region for Au@Citrate and Au@CTAB NPs functionalized with 4-MPy.

Since the 4-MPy is unable to adequately stabilize the different Au NPs in solution, a partial functionalization must take place to preserve the high colloidal stability of the NPs in solution. To achieve this, it is necessary to carefully regulate the 4-MPy concentration and ensure that there is not any additional absorption peak, as this would suggest aggregation as observed in Figure 2.3 (a).

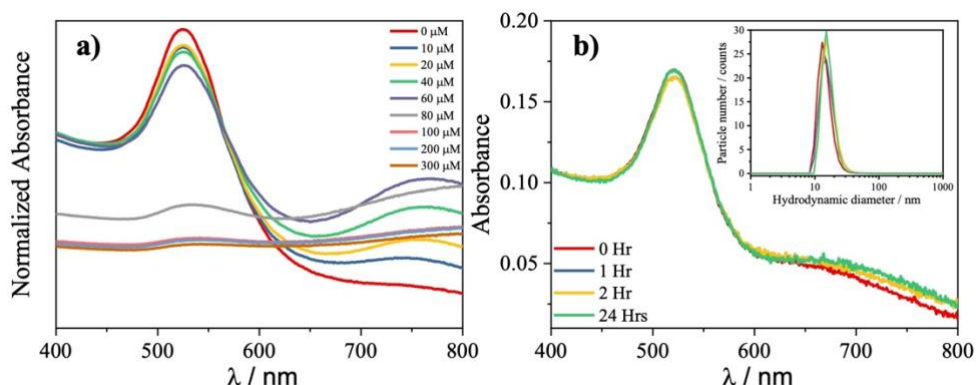


Figure 2.3: (a) UV-Vis absorbance spectra of Au@Citrate NPs at varying concentrations of 4-MPy (0-300 μM). (b) UV-Vis and DLS of Au NSp functionalized with 10 μM of 4-MPy over time of 24 hours.

For spherical Au NPs, we found that the maximum number of anchoring molecules on the Au surface while maintaining colloidal stability is achieved at an ideal 4-MPy: Au molar ratio of 0.002. The molar ratio must be increased by approximately 100 times to generate a uniform shell when using more stabilizing capping agents, such as CTAB for rods and stars. The aggregation can happen because of different factors, either charge imbalance or steric hindrance caused by the bonded 4-MPy molecules. To avoid this, we choose a concentration where the Au NPs are more colloiddally stable. Furthermore, we monitored this solution of Au@4MPy over a time period of 24 hours using UV-Vis and dynamic light scattering (DLS) as shown in Figure 2.3 (b). The characterization showed that there was no aggregation as well the system is colloiddally stable. The partial exchange of the ligand can also be observed by Attenuated Total Reflectance Fourier transform infrared spectroscopy (ATR-FTIR) spectra displayed in Fig 2.4 (a-b). The IR spectra provide a comparison of the surface chemistry changes in Au NPs surface before and after the addition of 4-MPy in the presence of citrate and CTAB. In both cases, the spectra of Au@Citrate and Au@CTAB exhibit minimal alterations following the addition of 4-MPy, and the distinctive peaks of 4-MPy are not discernible in the FTIR spectra. This indicates that although there may be some interaction between the NPs and 4-MPy, the functionalization is not fully evident in the FTIR results. However, XPS analysis as shown in Figure 2.1 (a-b) confirms the presence of thiol bonds, indicating that partial functionalization of the Au surface with 4-MPy that has occurred. This discrepancy suggests that the surface coverage of 4-MPy is likely low, making it difficult to detect in the FTIR spectra, despite the successful attachment of thiols as confirmed by XPS.

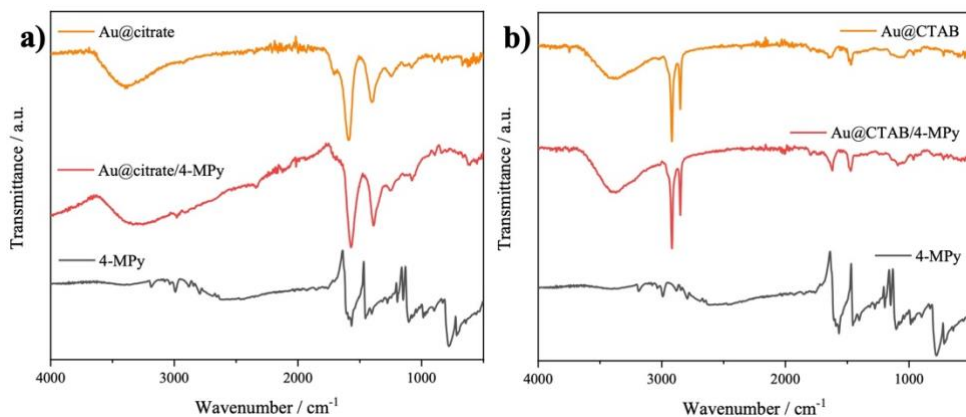


Figure 2.4: FTIR spectra of Au NPs before and after 4-MPy functionalization. (a) Au@citrate (b) Au@CTAB.

The second step involves the growth of PBA on the chemically modified surface of Au NPs (sphere, rods, and stars). It involves the simultaneous addition of the PBA precursors ($\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, CsCl , and $\text{K}_3\text{Fe}(\text{CN})_6$) to the colloidal solution. Here the choice of $\text{Ni}^{\text{II}}\text{Fe}^{\text{III}}$ -PBA is because of the pure ferromagnetic response and excellent OER catalytic properties exhibited by this PBA. Furthermore, Cs was selected as the counter-cation because of its size ($1.8 \text{ \AA}$), which closely matches the interstitial sites of the PBA. During the synthesis, a notable color change is observed confirming the formation of the shell, which is supported by the UV-Vis graphs displayed in Figure 2.5 (a-c). Normalized UV-Vis spectra show that plasmonic peaks red-shift to a few nm in all the cases (spheres, rods, and stars) indicating the alterations in the dielectric properties of the Au surface due to the interactions between the Au core and PBA shell. Notably, the plasmonic shifts for rods and stars are, as expected, more pronounced than for the spheres (Table 1), due to the higher optical sensibility of these anisotropic structures. Anisotropic structures have a more pronounced collective oscillation of the conduction band electrons compared to isotropic ones and thus, exhibit larger

shifts in their LSPR bands, as reflected by gold nanorods or nanostars compared to spherical NPs. Since the electric field is concentrated at points, tips or sharp edges, these modes are highly sensitive to small changes in their environment. These tip effects enhance the ability of the particle to sense changes in the local dielectric environment, that happens either because of a coating or change in the medium. As a result, even small changes in the outer surface geometry, such as shell formation or functionalization, alter the LSPR band position to a greater extent compared to spherical NPs.^{154–156}

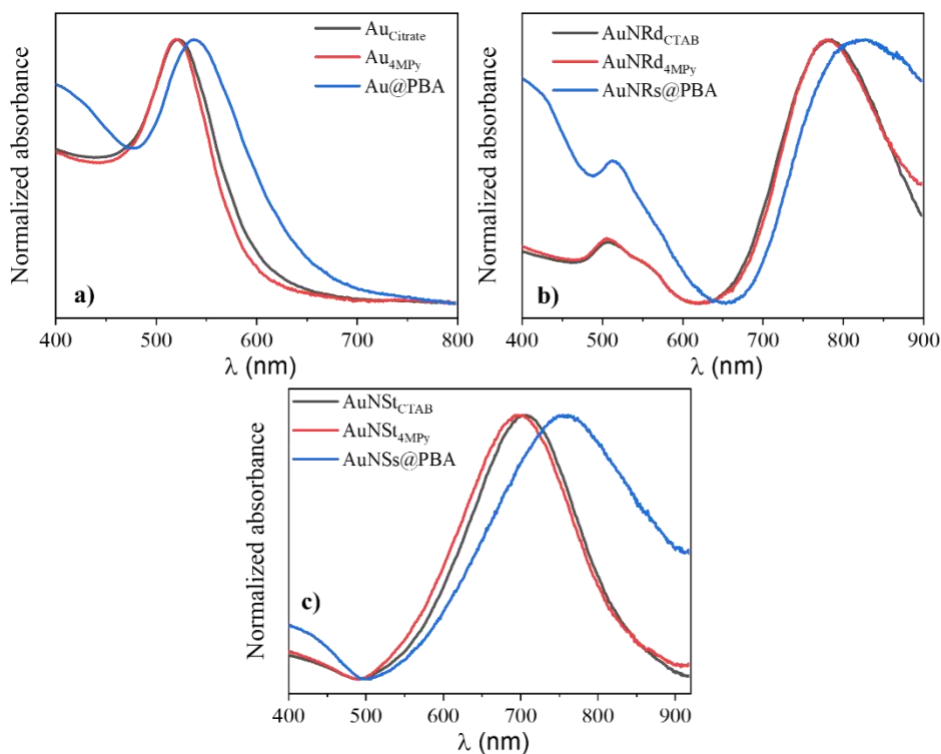


Figure 2.5: UV-Vis absorbance spectra comparing different gold NP morphologies with PBA shell. (a) Gold spheres (AuNSp) (b) Gold nanorods (AuNRd). (c) Gold nano stars (AuNSt).

In terms of shell formation, thanks to the presence of the N atom from the pyridine there are two possible anchoring points for the PBA, the pyridine for the Ni^{II} ions and the ferrocyanide that can interact with the gold through the CN^- . The interaction of both ions with the Au surface was explored independently by adding only one of the two ions on 4-MPy functionalized Au NSp (Figure 2.6). The presence of Ni^{II} (or $[\text{Fe}(\text{CN})_6]^{3-}$) ions were confirmed by XPS by looking at the Ni 2p (or Fe 2p) regions. However, it must be noted that adding only ferrocyanide causes the gold surface etching mediated by the CN groups. Therefore, 4-MPy is especially useful when forming PBA shells around gold cores, as it provides extra anchoring points for shell growth while reducing gold etching. In this way, the synthesis of anisotropic core shells is made possible.

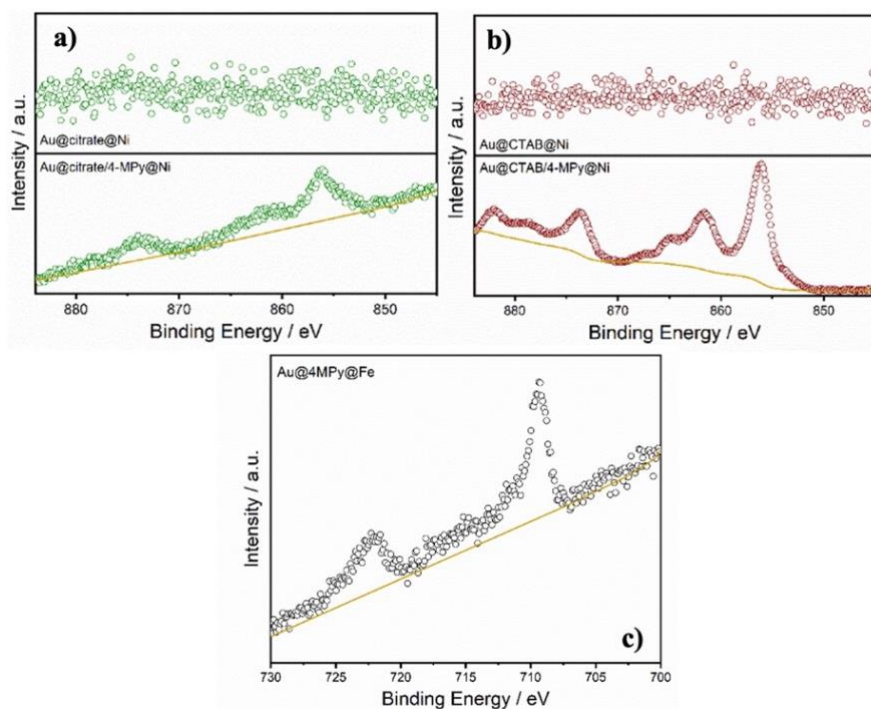


Figure 2.6: XPS spectra of Ni after functionalization of Au NPs with 4-MPy stabilized by (a) citrate. (b) CTAB. (c) XPS spectrum of Fe2p region after functionalization with 4MPy.

The size distribution and colloidal stability of the core@shell nanoparticles post synthesis were evaluated by DLS. The DLS analysis of the samples dispersed in water showed a narrow size distribution of the NPs as displayed in Figure 2.7 (a-c). Significantly, secondary peaks were not observed in DLS spectra, evidencing no aggregation in the solutions. Table 2.1 presents the summary of the hydrodynamic diameter and zeta potential characteristics for different morphologies through each step, AuNSp, AuNRd, and AuNSt functionalized with citrate, CTAB and thiol ligands of 4-MPy. The hydrodynamic diameter of spherical NPs remains approximately 13 nm for both AuNSp@citrate and AuNSp@citrate/4-MPy (no obvious change) but increases to ca. 47 nm in the case of AuNSp@NiFe, which provides evidence for shell growth. AuNRds demonstrates a consistent increase from 94 nm up to 147 nm while the the star-shaped NPs increased from 57 nm for AuNSt@CTAB to 130 nm for AuNSt@NiFe.

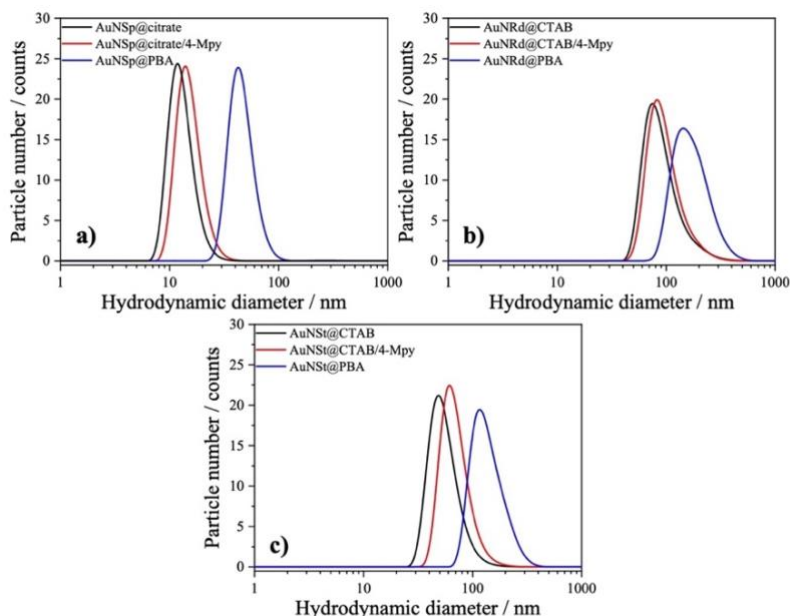


Figure 2.7: Dynamic Light Scattering plots for Au NPs, Au NPs with 4-MPy and Au NPs with a PBA shell.

On the other hand, Zeta potential indicates all types of spherical samples are negative with a small deviation, trending less negatively as being functionalized by 4-MPy and NiFe. The Z-potential measurements are shown in table 2.1, which were about -36 mV for spheres, -23 mV for rods and -20 mV for stars, demonstrating excellent colloidal stability of the nanoparticles. Strikingly, for anisotropic NPs, we also observed a prominent shift in the Z-potential from positive to negative upon the growth of the PBA shell. The positive surface charge was near 0 mV by functionalization with 4-MPy, thus charge reversal and aggregate formations are prevented in the shell formation process thanks to the use of 4-MPy.

Table 2.1: Hydrodynamic diameter and Zeta Potential values of the different colloidal suspensions.

Samples		Hydrodynamic diameter / nm	Zeta Potential / mV
Au Nanoparticles	AuNSp@citrate	13 ± 3	-41 ± 13
	AuNSp@citrate/4-MPy	13 ± 4	-39 ± 14
	AuNSp@NiFe	47 ± 20	-36 ± 14
	AuNRd@CTAB	94 ± 40	35 ± 43
	AuNRd@CTAB/4-MPy	100 ± 40	2 ± 15
	AuNRd@NiFe	147 ± 38	-24 ± 10
	AuNSt@CTAB	57 ± 19	35 ± 30
	AuNSt@CTAB/4-MPy	69 ± 20	-5 ± 13
	AuNSt@NiFe	130 ± 30	-20 ± 10

Next, we characterized the PBA shell by transmission electron microscopy (TEM), high-resolution transmission electron microscopy (HR-TEM) followed by energy-dispersive X-ray spectroscopy (EDX) mapping. As seen in Fig 2.8 (a-c) a clear core@shell structure with a narrow size distribution was distinguished in all cases proving the formation of a well-formed PBA shell with a size of ca. 15 nm as displayed in the histograms.

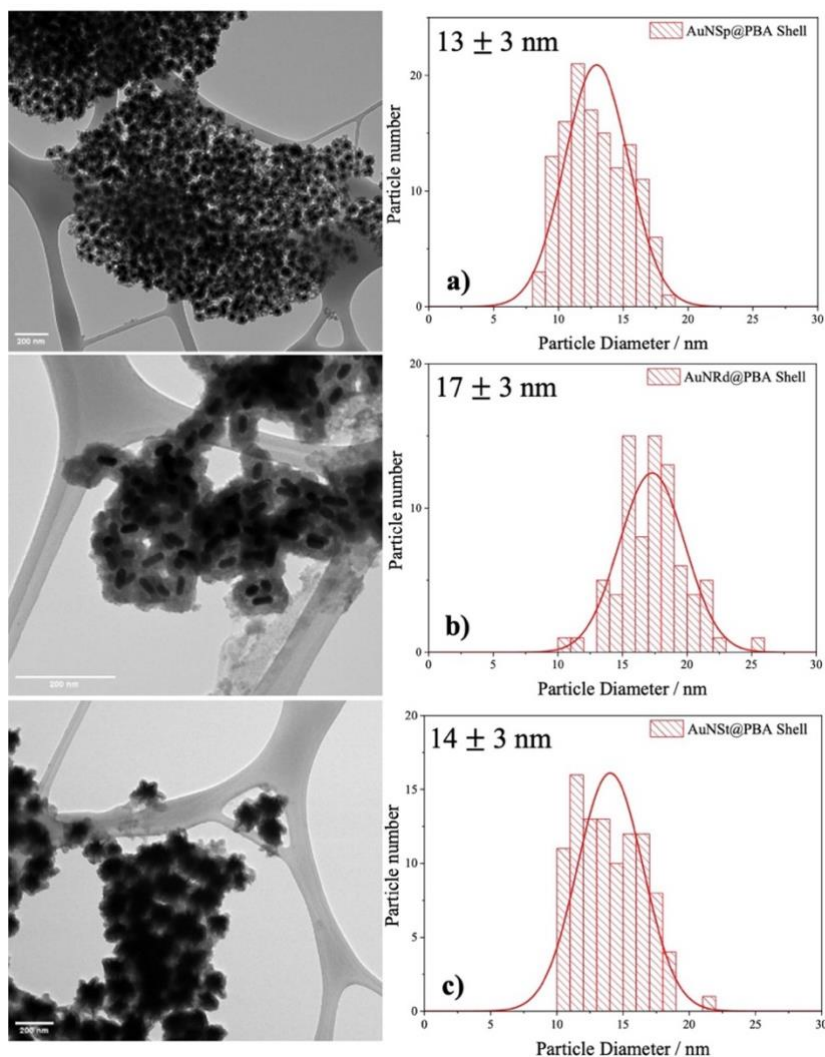


Figure 2.8: TEM images (left) and particle size distribution histograms (right) of different Au-based core@shell NPs. (a) AuNSp@PBA. (b) AuNRds@PBA. (c) AuNSt@PBA.

As illustrated in Figure 2.9 (a-c), EDX mapping was performed to investigate the physical indications of elements specifically Au as core, while Ni and Fe present separately within the grown shell. This established a reproducible synthesis of NiFe shell-coated core@shell NPs, showing consistent encapsulation by the NiFe shell around Au cores having spherical, rod-like and star-shaped particle geometries. In addition, the molecular formulas estimated by EDX show a comparable Cs:Ni:Fe ratio of approximately 0.6:1:0.86 as shown in table 2.2. This suggests the formation of the same PBA shell.

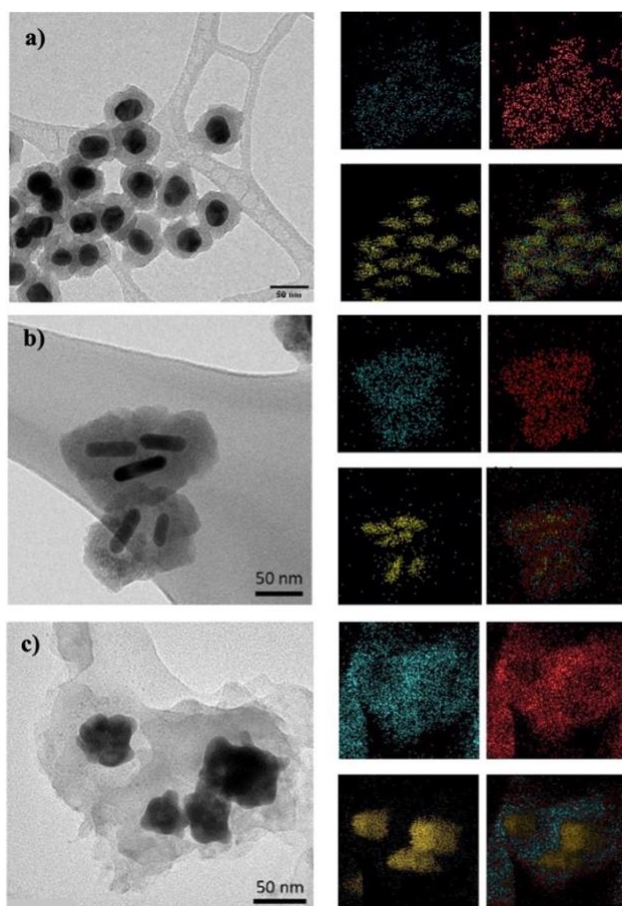


Figure 2.9: HR-TEM images Au@PBA core@shell NPs with corresponding Ni (cyan) and Fe (red) and Au (yellow) elemental maps (a) AuNSp (b) AuNRDs (c) AuNSt.

It is important to remark that, thanks to the use of 4-MPy, we obtained a well-defined core@shell structure in all cases (i.e. Au NSp, NRd and NSt). In contrast, in the absence of 4-MPy on the Au surface, dissolution of some edges of Au NPs occurs and aggregation is observed. In addition, the formation of the PBA shell remains incomplete, as observed in Figure 2.10 (a-c) the PBA tends to self-nucleate instead of forming a shell. Therefore, to grow a PBA shell, the surface of the colloidal Au NPs must be previously functionalized with 4-MPy.

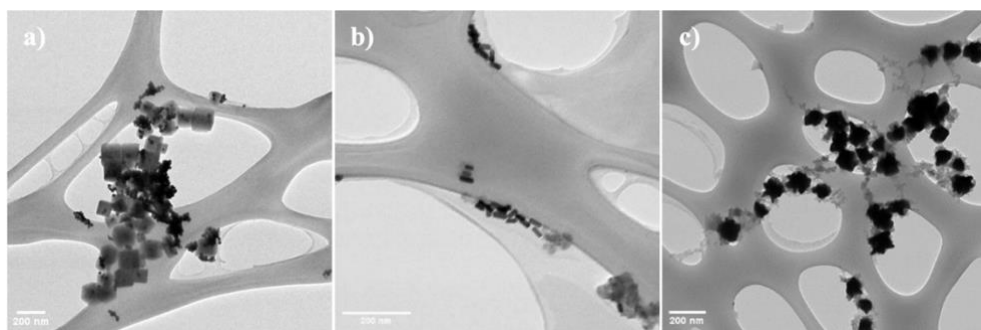


Figure 2.10: The TEM images demonstrate the impact of omitting 4-MPy on the formation of the PBA shell around Au NPs. (a) Au NSp, (b) Au NRd and (c) Au NSt.

After the visual identification of successful formation of core@shell NPs, the different nanoforms were characterized and compared to the pristine PBA by means of different techniques including XPS, powder X-ray diffraction (PXRD), and ATR-FTIR. Figure 2.11 (a) shows the XRD pattern collected for the different nanoforms. The same structure was observed in all the samples although a slight shift to higher angles was noticed for the PBA grown over gold cores. This shift could be attributed to some structural distortions causing a decrease in the Ni to Fe distance. By ATR-FTIR, the same vibrational modes were seen for the core@shells and the PBA as

observed in Figure 2.11 (b). This suggests that the synthesis process preserves the integrity of the PBA framework during the formation of the PBA shell.

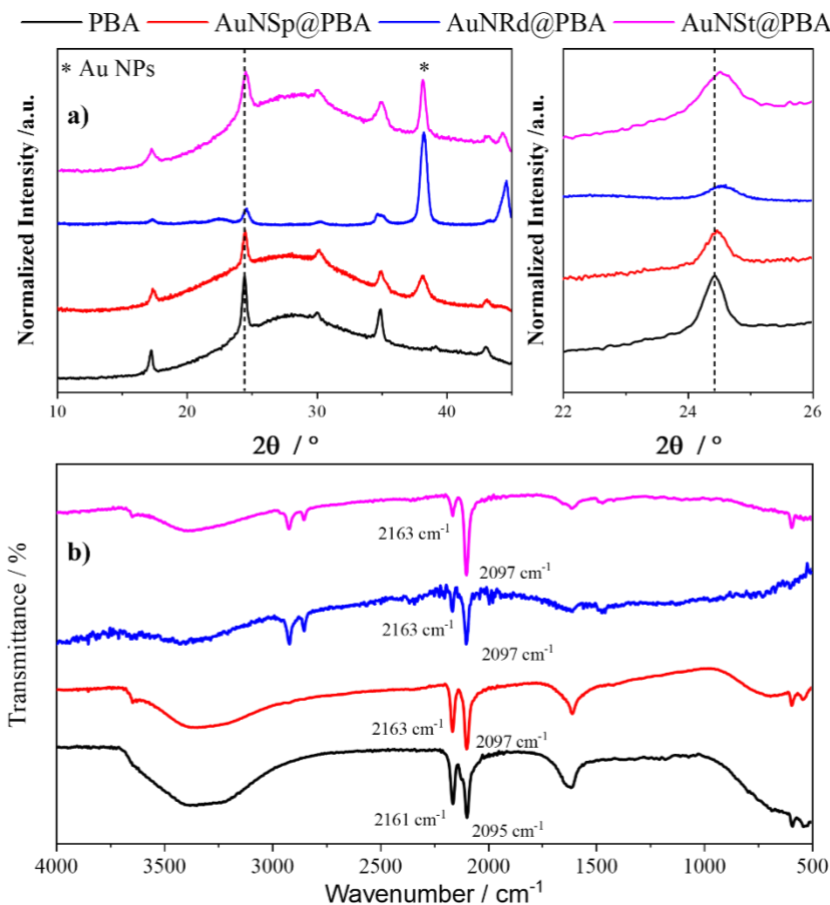


Figure 2.11: (a) XRD patterns of PBA, Au@PBA NPs showing characteristic peaks of PBA and Au NPs. (b) FTIR spectra of PBA and Au@PBA NPs, with prominent cyanide stretching vibrations.

The XPS spectra displayed in Figure 2.12 (a-b) illustrate the binding energy regions of Ni (2p) and Fe (2p) for a range of Au@PBA morphologies compared to pristine PBA. The Ni 2p spectra of the Au@PBA samples display a peak at approximately 855 eV, which provides further evidence that

Ni exists in the PBA shell as Ni^{II} . In the Fe 2p spectra, it indicates that on the surface, iron is present in the oxidation states of Fe^{II} and Fe^{III} .

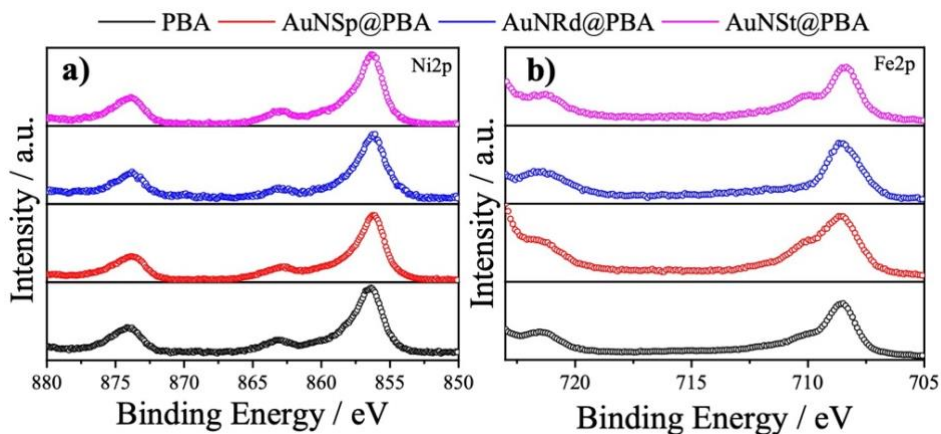


Figure 2.12: XPS spectra of Au@PBA NPs with different morphologies (spheres, rods, stars) compared with the pristine PBA. (a) Ni 2p region. (b) Fe 2p region.

Furthermore, as observed from the PXRD, the grown PBA shells on different nanoforms tend to show shifts that could be attributed to structural distortions. Therefore, we conducted a detailed analysis of the shell crystallographic structure at the interface of Au and PBA by HR-TEM. Firstly, a remarkable crystallinity was observed at 10 nm from the interface in all the heterostructures as seen in Figure 2.13. The Ni-Fe distances were calculated by filtering the most crystalline areas of different shells, which came out to be 5.1 Å in all cases, consistent with Ni-NC-Fe. The lattice discontinuity supports the presence of Fe-CN vacancies, which can be directly measured from the HR-TEM images, as observed in Figure 2.14 (a). Near the core, by the electron diffraction (ED) it is possible to observe the PBA pattern exhibiting two notable features: polycrystallinity, and distortion. These effects become more prominent as the core's anisotropy increases as shown in Figure 2.14 (b). AuNSp@PBA exhibits fewer crystalline domains

as compared to its rods and star analogues. The ED in Fig 2.14 (b) shows the change from cubic to more spherical pattern shifting in the case of anisotropic cores.

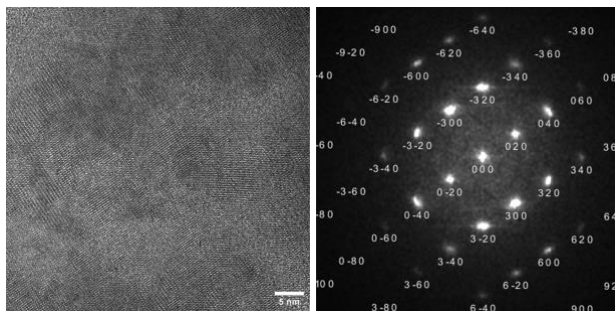


Figure 2.13: The crystallinity of the pristine PBA and corresponding electron diffraction (ED) pattern observed by HR-TEM.

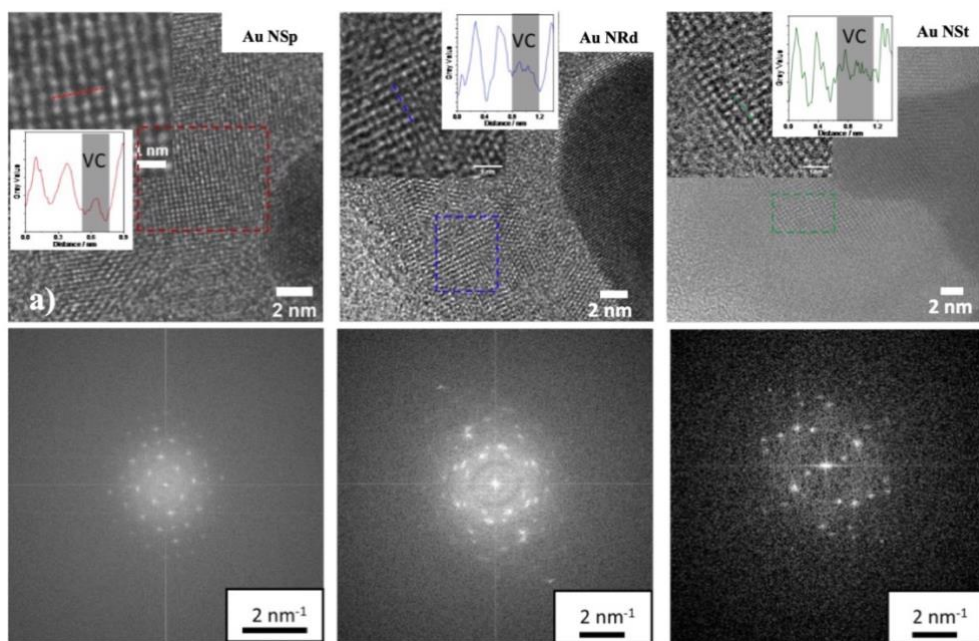


Figure 2.14: (a) HR-TEM and ED patterns of Au@PBA (NSp, NRds, and NSt) showing structural distortions near the Au-PBA interface, with insets displaying the reduction in diffraction planes (002 and 004).

These structural distortions are more evident from the reduction in the length of 002 and 004 diffraction planes, calculated from the ED images in Figure 2.14 (a) when compared to the crystallographic structure of pristine PBA shown in Figure 2.13. The Ni-Fe distance decreases by approximately 0.06 Å for spherical core, 0.08 Å for rods, and 0.1 Å for stars. Notably, as PBA grows further from the Au surface, this effect diminishes, and PBA regains its normal structure.

The structural distortions and the presence of polycrystallinity affect the magnetic response of the PBA. The magnetization curves observed by SQUID magnetometry in Figure 2.15 measured at 2K show a magnetic saturation near 3 μ_B at 7T for all the nanostructures including the pristine PBA and the core@shells confirming the main oxidation state of the PBA shell as Ni^{II} and Fe^{III}. Even though the value corresponds to the total spin $S=1.5$, a prominent decrease is observed in the coercive field of the core shells with an increase in core anisotropy (Table 2.2). From the temperature-dependent magnetic susceptibility, we can observe that all the NPs show a rise in magnetic response when decreasing the temperature. This response is attributable to the ferromagnetism of PBA. Even though the rapid magnetic response of all NPs, AuNSt@PBA exhibits a gradual increase in the magnetic response with a low T_c (Table 2.2). Such difference suggests that there are two types of magnetic responses in the case of AuNSt@PBA: a paramagnetic and a ferromagnetic response.

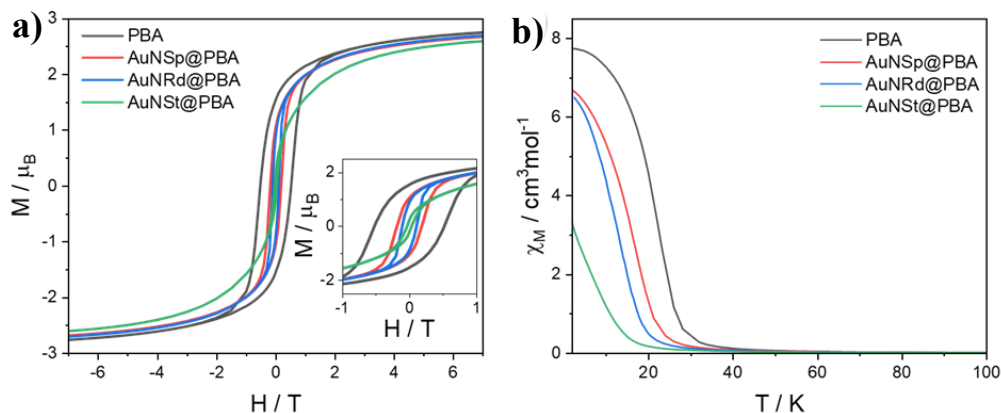


Figure 2.15: (a) Magnetization curves (M/H) (b) Temperature-dependent magnetic susceptibility (χ) of PBA and Au@PBA NPs.

Table 2.2: Molecular formulas, Curie temperatures (T_c), and coercive fields of pristine and core@shell nanostructures.

Samples	Molecular Formula	T_c / K	Coercive Field / T
PBA	$\text{Cs}_{0.61}\text{Ni}[\text{Fe}(\text{CN})_6]_{0.88}$	27.5	1.2
AuNSp@PBA	$\text{Au}_{1.12}\text{Cs}_{0.60}\text{Ni}[\text{Fe}(\text{CN})_6]_{0.86}$	22.9	0.4
AuNRd@PBA	$\text{Au}_{2.12}\text{Cs}_{0.69}\text{Ni}[\text{Fe}(\text{CN})_6]_{0.88}$	19.6	0.2
AuNSt@PBA	$\text{Au}_{1.31}\text{Cs}_{0.53}\text{Ni}[\text{Fe}(\text{CN})_6]_{0.84}$	13.3	0.07

To further validate this, AuNSt@PBA with shells thinner than 10 nm and thicker than 20 nm were prepared as shown in Figure 2.16 (c), and their magnetic properties were compared. As anticipated, the sample with the thinnest shell exhibited an almost entirely paramagnetic response, whereas the thickest shell displayed magnetic behavior nearly identical to that of bulk

PBA as can be seen in Figure 2.16 (a). These results align with previous ED experiments, which demonstrated that the influence of core anisotropy on the PBA crystalline structure diminishes beyond 10 nm from the Au surface. Consequently, for shells thinner than 10 nm, the Ni and Fe species are weakly coupled due to increased polycrystallinity and structural deformation, leading to a paramagnetic response. In contrast, regions farther from the Au surface exhibit the ferromagnetic behavior characteristic of strongly coupled Ni-NC-Fe species.

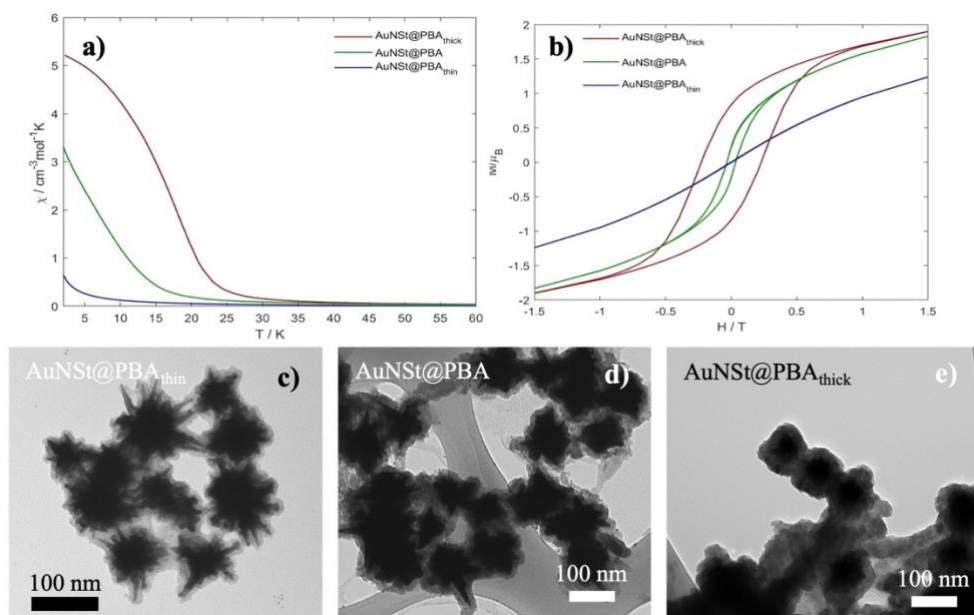


Figure 2.16: (a) Thermal magnetic susceptibility and (b) isothermal magnetization at 2K of AuNSt@PBA having a shell size below 10 nm (c), around 15 nm (d) and above 20 nm (e).

After characterizing the different PBA shells, we explored their performance as OER electrocatalysts, considering the potential positive effects of strain and smaller crystallite size on water-splitting electrocatalysis. Strain in the PBA structure can modify electronic properties by increasing the density of active sites, thereby enhancing the water-splitting reaction.^{157,158}

Additionally, smaller crystallite sizes expose more surface sites, particularly at edges where catalysis is most active, leading to a higher density of catalytic sites and improved charge transport, further boosting overall electrocatalytic performance.^{157,158}

To evaluate these effects, initially, the nanomaterials were activated by performing cyclic voltammetry (CV), as displayed in Figure 2.17 (a-d). From these CVs, electroactive species were estimated to facilitate the comparison of the catalytic activity.

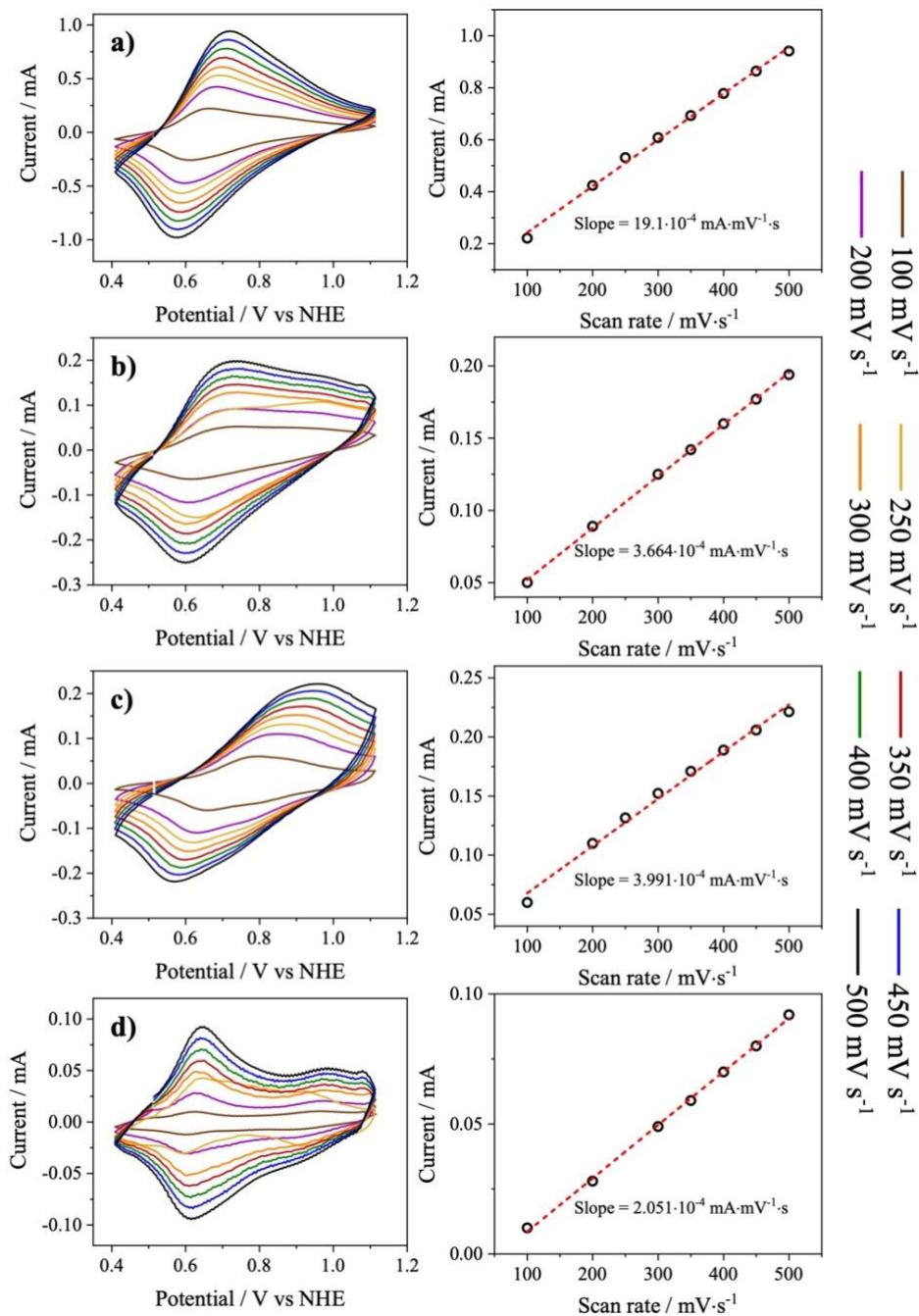


Figure 2.17: CV curves of the of (a) PBA (b) AuNSp@PBA (b) AuNRd@PBA and (d) AuNSt@PBA.

Next, the electrochemical performance was measured and compared by the linear sweep voltammetry (LSV) in Figure 2.18 (a). This experiment was conducted at a low scan rate of (5 mVs^{-1}) to minimize the capacitive current. To analyze the different electrochemical performances some key parameters were compared:

- (1) The current density recorded at an overpotential of 800 mV (Figure 2.18 (b)). A higher current density indicates more efficient charge transfer and a faster reaction rate. This parameter is crucial for evaluating the performance of electrocatalysts.
- (2) The Tafel slopes, calculated from the calculated by determining the slope of the linear region in a Tafel plot, where the overpotential (η) is plotted against the logarithm of the current density ($\log j$), typically using the equation $\eta = a + b \log(j)$, with b being the Tafel slope (Figure 2.18 (c)). This parameter indicates how much it is necessary to increase the overpotential to raise the reaction rate (thus, the current density) by an order of magnitude.

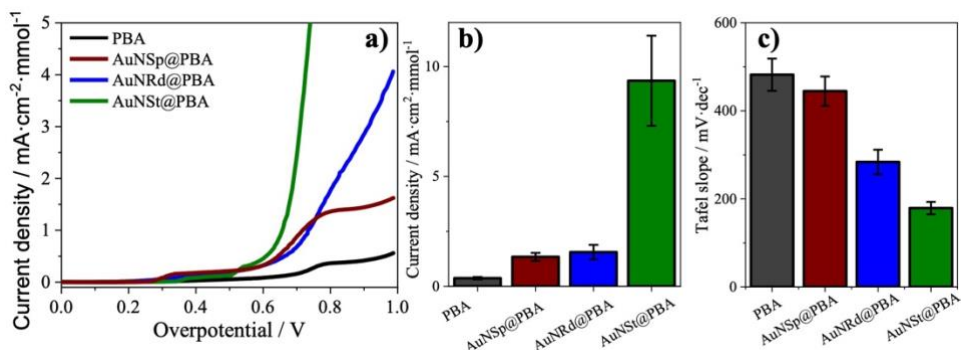


Figure 2.18: (a) LSV comparing the electrocatalytic activity, showing OER performance for different nanoforms. (b-c) Current density and Tafel slope comparison, highlighting improved performance for anisotropic core structures, especially NSt.

Since the samples may exhibit different electrochemical surface areas due to their different crystalline domain sizes, the electrochemical performance was normalized to the number of electroactive species with the aim of investigating the intrinsic catalytic activity of the PBA sites. The results demonstrate that the incorporation of an Au core into the PBA structure leads to an improvement in its performance. Notably, the current density is increased from 0.37 to 1.34 mA cm⁻² mmol⁻¹ (approximately 360% improvement), and the Tafel slope is slightly decreased by 38 mV dec⁻¹ when spherical Au cores are employed. It is noteworthy, that the displayed OER performance of the various Au@PBA NPs exhibits variation when the core shape is modified. Given that the PBA nanostructures in question exhibit a comparable composition and that their activity has been normalized in relation to their electroactive species, the observed discrepancy in OER performance can be attributed to the presence of structural distortions and multiple crystallographic domains. In this regard, it is evident that anisotropic NPs demonstrate superior performance compared to the spherical heterostructure, and their efficiency is enhanced with increasing structural distortions and polycrystallinity. In particular, the current density at 800 mV is increased by approximately 690 and 600 % for the star-shaped NPs, while the kinetic values are reduced by around 260 and 100 mV dec⁻¹ with respect to the spheres and rods, respectively.

The OER performance was evaluated by analyzing the current densities, which revealed that different anisotropic cores influence the activity differently, with improved performance compared to the spherical core. Among the tested nanoforms, the NSt demonstrated the highest enhancement, showing an approximately 600% increase in current density at 800 mV. Furthermore, the reaction kinetics were significantly improved, with a

reduction in Tafel slopes by approximately 260 mV dec^{-1} and 100 mV dec^{-1} compared to spheres and rods, respectively. These results highlight that selecting a core capable of inducing structural distortions and higher polycrystallinity in the PBA shell can substantially enhance the OER performance of the nanomaterial.

Lastly, we evaluated the impact of the shell thickness on the catalytic activity by studying the performance of the most active heterostructure (AuNSt@PBA) exhibiting different shell thicknesses: below 10 nm, around 15 nm, and above 20 nm. As shown in Figure 2.19, NPs with less than 10 nm shell perform similarly to those with 15 nm. This could be attributed to the intrinsic porosity of PBAs, which facilitates ion diffusion, allowing catalytic activity to extend beyond the outer surface into the inner structure, accessing internal active sites. However, when the shell thickness exceeds 20 nm, the NPs exhibit a lower catalytic activity than those with thinner shells likely due to a reduced accessibility to strained active sites.

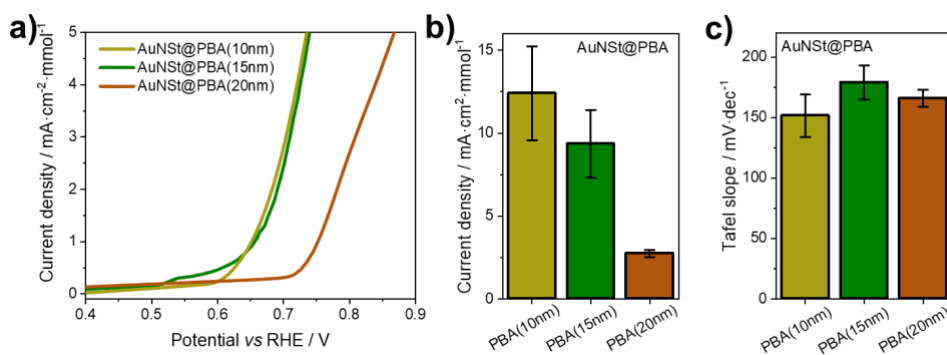


Figure 2.19: a) LSV of the AuNSt@PBA with different PBA shell thicknesses recorded at 5 mVs^{-1} in NaPi (0.1 M) buffer solution at pH 6.9 with NaNO_3 (1 M) as electrolyte. Current density values were normalized to the number of electroactive species. b) Current densities obtained at an overpotential of 800 mV vs OER. c) Tafel slopes calculated from LSV data.

2.3 Conclusions

In this work, we have employed 4-MPy to functionalize different Au NPs (spheres, rods, and stars) to grow magnetic PBA as shells. This approach provides different advantages. Firstly, it prevents Au etching caused by the cyanide ions present in the precursor solution permitting to use anisotropic Au cores. Secondly, it enables the growth of PBA in the absence of a reducing agent and thus, it allows for the synthesis of non-reduced PBA shells. Notably, depending on the core shape, the overgrown PBA shows different degrees of structural distortions and polycrystallinity. Both effects enhance the influence on magnetic exchange coupling, which is reduced from 2.3 cm^{-1} to 0.5 cm^{-1} when comparing bare $\text{CsNi}[\text{Fe}(\text{CN})_6]$ to a star-shaped PBA structure. Furthermore, structural distortions and polycrystallinity have an impact on the OER electrocatalytical performance. The heterostructures containing the star-shaped core (i.e. with higher structural distortions and polycrystallinity) improve the onset potential and the Tafel slope significantly as compared to the pristine PBA, resulting in a tenfold enhancement of the electrochemical activity. Therefore, this work demonstrates the use of 4-MPY for the growth of non-reduced PBA on different Au core morphologies and their advantage to tune the physical properties of the resulting shell.

2.4 Experimental Details

2.4.1 Materials

All chemical reagents were obtained from commercial suppliers and used as received without further purification. Silver nitrate was purchased from Alfa Aesar. Chloroauric acid (HAuCl_4), L-ascorbic acid, potassium iodide, sodium citrate tribasic dihydrate, hexadecyltrimethylammonium bromide (CTAB), sodium borohydride, 4-mercaptopyridine (95%), cesium chloride (CsCl), nickel (II) chloride ($\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$), and potassium hexacyanoferrate ($\text{K}_3[\text{Fe}(\text{CN})_6]$) were purchased from Sigma-Aldrich. Ultrapure water ($18.2 \text{ M}\Omega \text{ cm}$) was used for all syntheses.

2.4.2 Synthesis of Gold NPs

2.4.2.1 Gold Nanospheres

Au nanospheres were synthesized using the standard Turkevich method.¹⁵⁹ Briefly, 100 mL of a 0.5 mM HAuCl_4 solution was heated to boiling, and 31 mg of sodium citrate was added with constant stirring. The solution color changed from pale yellow to grey within one minute, indicating the formation of Au colloids, and subsequently darkened to deep wine over 2–3 minutes.

2.4.2.2 Gold Nanorods

AuNRd were prepared via a seed-mediated growth method. Initially, 25 μL of 50 mM HAuCl_4 was added to 4.7 mL of 0.1 M CTAB and stirred for 5 min. Then, 300 μL of freshly prepared 10 mM NaBH_4 was rapidly injected under vigorous stirring, followed by a 10s stirring period. The resulting seeds were left undisturbed for 1 h at 30°C . For the growth of

AuNRd, 190 μL of 1 M HCl and 100 μL of 50 mM HAuCl_4 were added to 10 mL of 0.1 M CTAB,

stirred for 5 min and mixed with 120 μL of 0.01 M AgNO_3 . Subsequently, 80 μL of 0.1 M ascorbic acid was added, and the solution was thoroughly shaken until colorless. Finally, 24 μL of the seed solution was added, shaken, and incubated at 30°C for 2 h. The resulting AuNRd were washed twice with water to remove excess surfactants.

2.4.2.3 Gold Nano stars

Au nano stars were synthesized via a seeded growth process using citrate-stabilized Au nanospheres as seeds. For the growth solution, 10 μL of 1 M HCl was added to 10 mL of 0.25 mM HAuCl_4 , followed by the addition of 100 μL of 0.5 mM seed solution. Aqueous solutions of 50 μL of 0.1 M ascorbic acid and 100 μL of 1 mM AgNO_3 were then added simultaneously. CTAB (0.2 mL, 0.1 M) was used as a capping agent. The solution was incubated for 30 min, after which the AuNSTs were collected and ready for further use.

2.4.2.4 Synthesis of Prussian Blue Analogues NPs

NiFe-PBA NPs were synthesized by simultaneously adding two aqueous solutions: (i) 40 mL of 10 mM $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ and (ii) 40 mL of 10 mM $\text{K}_3[\text{Fe}(\text{CN})_6]$ and 50 mM CsCl. The reaction mixture was stirred at room temperature for 30 min, followed by centrifugation at 11,000 rpm for 20 min. The final solution was washed with water and centrifuged at 13,000 rpm for 15 min, repeating this process three times to ensure purity.

2.4.3 Synthesis of Core@Shell NPs

2.4.3.1 AuNSp@PBA

In 10 ml of 0.5mM gold nanospheres, 10 μ L of 1 mM 4-mercaptopyridine (4-MPy) was added, and the mixture was stirred for 20 min to allow 4-MPy to bind to the Au surface. The solution was then washed with water (9,000 rpm, 20 min) to remove excess citrate and 4-MPy. For PBA shell growth, two precursor solutions were prepared: (i) 10 mM NiCl_2 and (ii) 10 mM $\text{K}_3[\text{Fe}(\text{CN})_6]$ and 50 mM CsCl. A total of 100 μ L of each precursor was simultaneously added to the colloidal Au@4-MPy NPs under vigorous stirring, with an addition rate of 10 μ L per 20 seconds. The final solution was stirred for 20 min and centrifuged at 13,000 rpm for 15 min, repeating the washing step three times.

2.4.3.2 AuNRd@PBA

A 1 mL aliquot of 1 mM 4-MPy was added to 4.5 mL of AuNRd(0.5 mM) under stirring at 1,100 rpm to functionalize the Au surface. After 20 min, the solution was centrifuged at 3,000 rpm for 30 min and redispersed in 10 mL of water. For PBA growth, two precursor solutions were prepared: (i) 5 mM NiCl_2 and (ii) 5 mM $\text{K}_3[\text{Fe}(\text{CN})_6]$ and 25 mM CsCl. The precursors (100 μ L each) were simultaneously added to the Au@4-MPy solution under vigorous stirring, with an addition rate of 10 μ L per 20 seconds. The final solution was stirred for 20 min and centrifuged at 3,000 rpm for 30 min, repeating the washing step three times.

2.4.3.3 AuNSt@PBA

A 1 mL aliquot of 1 mM 4-MPy was added to 4.5 mL of AuNSts (0.5 mM), mixed with 0.5 mL of water, and stirred at 1,100 rpm for 20 min. The mixture was then centrifuged at 3,000 rpm for 30 min to remove excess

CTAB and 4-MPy and redispersed in 10 mL of ultrapure water. For PBA shell growth, two precursor solutions were prepared: (i) 5 mM NiCl_2 and (ii) 5 mM $\text{K}_3[\text{Fe}(\text{CN})_6]$ and 25 mM CsCl. A total of 100 μL of each precursor was added under vigorous stirring, at a rate of 10 μL per 20 seconds. The final solution was stirred for 20 min, centrifuged at 3,000 rpm for 30 min, and washed three times with water.

2.5 Physical Characterizations

2.5.1 UV-Visible Spectroscopy

UV-Vis absorption spectra were recorded using a ThermoFisher Multiskan SkyHigh microplate spectrophotometer, covering a wavelength range of 300–900 nm. Measurements were conducted in Thermo Scientific clear flat-bottom, immune non-sterile 96-well plates, with 300 μ L of each sample added per well.

2.5.2 Dynamic Light Scattering

Dynamic Light Scattering (DLS) were performed with a Zetasizer Nano ZS instrument (Malvern Instruments Ltd.).

2.5.3 Transmission Electron Microscopy

TEM analysis was performed on a JEOL 300 ARM microscope operating at 80 kV and a Tecnai G2 F20 microscope at 200 kV. Samples were prepared by drop-casting suspensions onto lacey Formvar/carbon-coated copper grids (300 mesh). The electron microscopy experiments were as well performed on the ePSIC AT Diamond Synchrotron, United Kingdom (proposal number MG35687).

2.5.4 Attenuated Total Reflectance Fourier-Transform Infrared Spectroscopy

ATR-FTIR spectra were collected using an Agilent Cary 630 FTIR spectrometer in the range of 4000–500 cm^{-1} , without the use of KBr pellets.

2.5.5 X-Ray Photoelectron Spectroscopy

XPS analysis was conducted on a K-Alpha Thermo Scientific spectrometer using Al K α radiation (1486.6 eV) from a twin crystal monochromator. The focused X-ray spot (400 μ m major axis) was produced at 30 mA and 2 kV. The alpha hemispherical analyzer was operated in constant energy mode, with survey scan pass energies of 200 eV and 50 eV for narrow scans. Data analysis was performed using Avantage software, with a background function used for baseline correction. Charge compensation was provided by a dual system flood gun delivering low-energy electrons and argon ions.

2.5.6 Powder X-Ray Diffraction

PXRD patterns were recorded using a PANalytical Empyrean diffractometer with Cu K α radiation ($\lambda = 1.5418$ Å) and a PIXcel detector, operating at 40 mA and 45 kV, at room temperature.

2.5.7 Magnetic Measurements

Magnetic properties were measured using a Quantum Design MPMS XL-5 SQUID susceptometer. DC field-cooled (FC) magnetization measurements were conducted under an applied magnetic field of 100 Oe, while isothermal magnetization at 2 K was measured between -7 and +7 T. Diamagnetic corrections were applied using Pascal's constants, considering the molecular formulas determined from energy-dispersive X-ray spectroscopy (EDX). The masses used for PBA, AuNSp@PBA, AuNRd@PBA, and AuNSt@PBA samples were 2.15, 0.40, 0.05, and 0.15 mg, respectively.

2.5.8 Electrochemical Characterization

2.5.8.1 Electrode Preparation

Electrodes were prepared by dispersing 1 mg of powdered material with 0.5 mg of acetylene black in a mixture of 200 μL water and ethanol (1:1) and 8 μL of Nafion (10%). The mixture was sonicated to achieve a well-dispersed suspension. Then, 5 μL of this suspension was drop-cast onto a polished (0.05 μm alumina powder) 3 mm diameter glassy carbon electrode. The solvent was evaporated at room temperature, resulting in an electrode PBA mass loading of approximately $0.34 \text{ mg}\cdot\text{cm}^{-2}$.

2.5.8.2 Electrochemical Measurement

Electrochemical experiments were performed in a three-electrode cell using a glassy carbon rotating disk electrode (RDE) as the working electrode, a platinum foil as the counter electrode, and a silver/silver chloride (Ag/AgCl, 3 M KCl) reference electrode. Potentials were referenced to the oxygen evolution overpotential or the normal hydrogen electrode (NHE). Measurements were conducted using an Autolab PGSTAT 128N potentiostat/galvanostat, with at least two replicates per sample. LSV was performed at a scan rate of $5 \text{ mV}\cdot\text{s}^{-1}$ and 1600 rpm in an argon-purged 0.1 M sodium phosphate buffer solution (pH 6.9) containing 1 M NaNO_3 as the electrolyte. Cyclic voltammetry (CV) was performed at varying scan rates to activate the electrocatalysts. The concentration of redox-active Ni centers was determined from the slope of the peak current vs. scan rate relationship.

Chapter

3

Inducing Photomagnetic Properties in Au@CsCoFe core@shell Nanostructures

3.1 Introduction

In recent years, switchable materials have emerged as highly interesting candidates because of their ability to transition between two states in response to an external stimulus such as light or temperature.^{160–162} This exceptional property makes them promise for sensors, molecular switches, and memory storage.^{162–164} Among them, systems able to be controlled with light are particularly appealing due to the precision and controllable nature of light as an external stimulus. The use of molecular materials, particularly photo-switchable ones, represents a significant advantage because they allow for reversible and highly precise manipulation of magnetic properties, offering a level of control that is difficult to achieve with traditional inorganic materials. This molecular level tunability opens up new possibilities for developing magnetic storage devices.^{164–166}

In this context, Prussian Blue Analogues (PBAs) are one of the most interesting coordination compounds and molecular materials that can exhibit photo-induced magnetism. Especially, CoFe-PBAs, or $\text{Co}^{\text{III}}\text{Fe}^{\text{II}}$ PBA, with molecular formula $\text{A}_x\text{Co}[\text{Fe}(\text{CN})_6]_y \cdot z\text{H}_2\text{O}$ (A = alkali metal), are the most researched because of their response to light, adjustable chemical composition, and ease of processing. Under light irradiation at low temperatures (<20 K), these cyano-bridged coordination polymers show reversible photomagnetic activity, changing from a diamagnetic low-spin $\text{Co}^{\text{III}}\text{Fe}^{\text{II}}$ state ($S = 0$) to a ferrimagnetic high-spin $\text{Co}^{\text{II}}\text{Fe}^{\text{III}}$ state ($S = 3/2$) (Figure 3.1). Because of their tunable magnetic characteristics and versatile chemical composition, CoFe-PBAs have received increasing attention.^{164,167–}

To maximize their efficiency, however, precise synthesis control is essential because their photomagnetic response is affected by several variables, including the presence of alkali ions, structural vacancies, and metal ion oxidation states. The cyanide ligands act as a conduit for electron transfer, facilitating the transition between the two magnetic states.

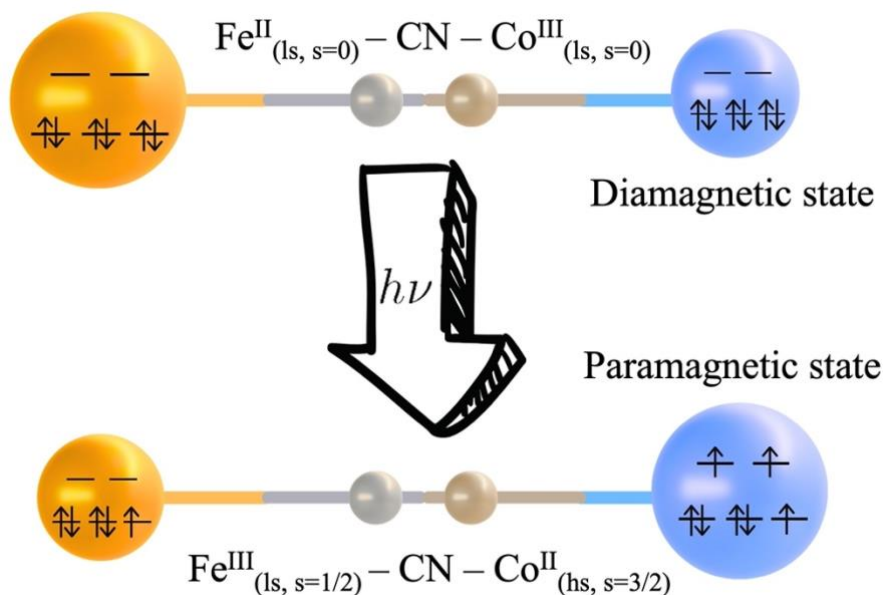


Figure 3.1: Schematic of the light-induced electron transfer process in CoFe PBAs showing the transition between $\text{Fe}^{\text{II}} \text{Co}^{\text{III}}$ and $\text{Fe}^{\text{III}} \text{Co}^{\text{II}}$ states under light irradiation ($h\nu$).

Even though these materials exhibit interesting properties, creating photoactive heterostructures that combine photo-switching with additional characteristics in a single entity is an interesting challenge. The formation of core@shell nanostructures offers a viable path to the appearance of new properties by combining the two components. For example, heterostructures of magnetic/photomagnetic PBA CsNiCr@CoFe NPs showed a homogeneous reversal of magnetization.¹⁷⁰ Also in another study, the capacity of RbCoFe@CrCr core@shell structures to optically switch

magnetization at temperatures higher than liquid nitrogen was studied.¹⁷¹ However, there have been no reports of hybrid core@shell nanostructures including other materials. Instead, photomagnetic core@shell systems have only been created by epitaxially growing PBAs around other PBA cores. Of especial interest is the combination of a metallic core with PBAs and other coordination polymers because it can result in enhanced properties and synergistic effects. For instance, the introduction of Au cores can improve the electrical readability of switching insulating systems.^{171–174}

In this work, we report the development of core@shell nanostructures consisting of Au NPs as cores and photomagnetic CsCoFe PBA shells with adjustable thicknesses by using the aforementioned synthesis protocol. We found that, when the shell becomes thicker, the PBA contains more diamagnetic $\text{Co}^{\text{III}}\text{Fe}^{\text{II}}$ species and its photomagnetic activity is higher. Interestingly, from these heterostructures, hollow CsCoFe NPs can be prepared by etching the gold cores, which significantly affects the photomagnetic properties. Still, for the bigger hollow NPs, photomagnetic properties can be observed. By studying these heterostructures, we aim to gain a deeper understanding of the impact of structural modifications on the photomagnetic response. This research opens up new possibilities for the design of multifunctional nanomaterials with combined photomagnetic and plasmonic properties, enabling efficient electrical reading of magnetic PBAs.

3.2 Results And Discussion

We utilized the synthetic approach reported in Chapter 2 to functionalize the surface of spherical Au NPs with 4-mercaptopyridine (4-MPy) to facilitate the formation of a photomagnetic CsCoFe PBA shell. As previously shown, the 4-MPy thiol groups bind onto the Au NP surface.^{175–178} CsCoFe PBA shell was formed by slowly and simultaneously adding precursors ($\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, CsCl and $\text{K}_3\text{Fe}(\text{CN})_6$) into a colloidal solution containing the 4-MPy-modified Au NPs. To manage the shell thickness, a third step was introduced where the precursor volumes were controlled.

During the synthesis, a change in color of the solution was observed suggesting the formation of the shell, although the complete color change was observed after 24 hours, suggesting the complete formation of the shell. This change in color can be attributed to the change in the refractive index of the Au surface to the surrounding resulting in the alteration of dielectric properties around the Au surface.^{179–181} This indicated the interaction between the Au NPs and the PBA shell. After each growth step, the solutions were subject to UV-Vis spectrometry and an indication of the growth was observed (Figure 3.2 (a)) by a shift of the plasmon band to higher wavelengths. Notably, in case of the thicker shell, a reduction in absorbance value and a wider plasmonic peak were observed that can be attributed to the presence of larger distance from Au surface to the shell as well to the formation of some aggregates.^{180,182,183}

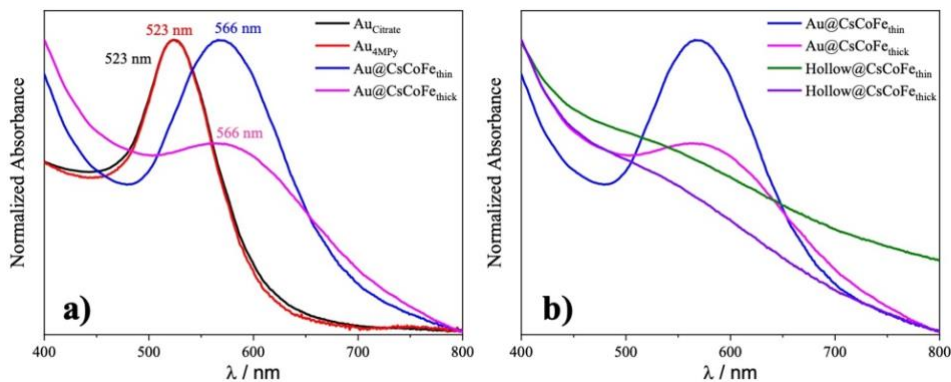
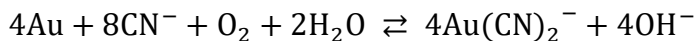


Figure 3.2: a) UV-Vis absorbance spectra of functionalized Au and core@shell NPs (b) Comparison of absorbance spectra between core@shell and hollow Au@CoFe NPs, highlighting the impact of core dissolution.

From the previous core@shells, hollow CsCoFe NPs were prepared by using a diluted KCN aqueous solution to etch the Au cores. In the presence of oxygen and thanks to the porosity of the PBA,^{180,183,184} the Au cores are dissolved mediated by CN^- through the reaction¹⁸⁵:



Again, the color change of the solution clearly indicates that core etching is occurring, while the UV-Vis spectrum shows a gradual decrease in the plasmon band, as shown in Figure 3.2 (b).

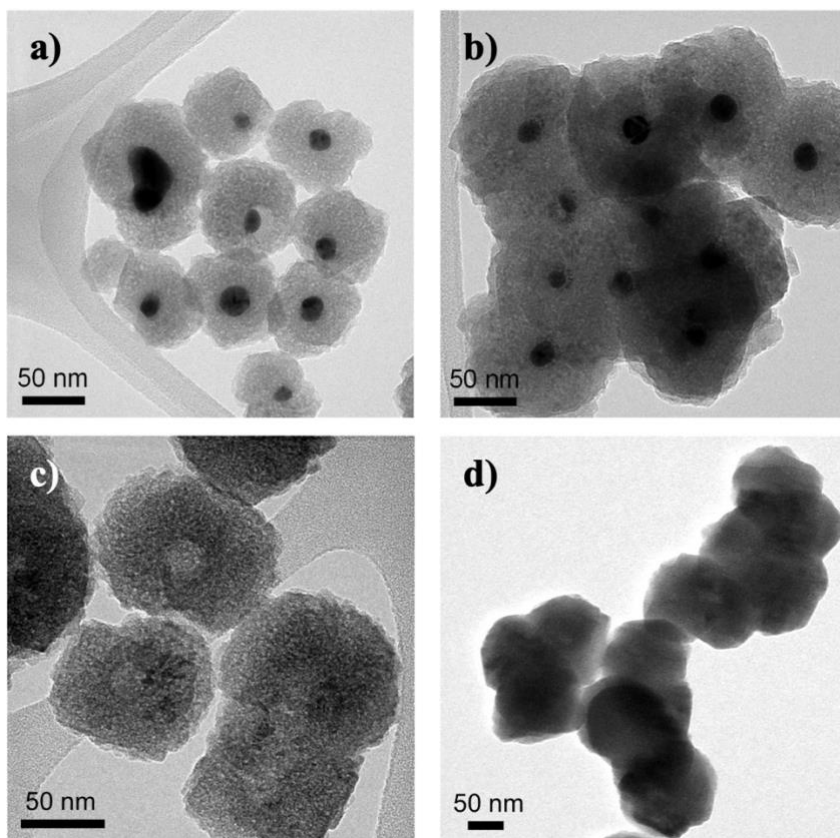


Figure 3.3: HR-TEM images of core@shell NPs: (a) Au core with thin CoFe shell (b) Au core with thick CoFe shell (c) Thin CoFe shell, and (d) Thick CoFe shell after dissolution of Au using KCN.

The core@shell and hollow nanostructures were observed by high resolution transmission electron microscopy (HR-TEM) and transmission electron microscopy (TEM) followed by elemental mapping of the metallic components present in the samples. HR-TEM images are displayed in Figure 3.3. As can be observed, the core@shells in Figures (a) and (b) have evident morphologies, with discrete cores corresponding to Au NPs and homogeneous CsCoFe PBA shells. In contrast, images (c) and (d) demonstrate the successful dissolution of Au cores resulting in CsCoFe PBA structures with a hollow in the center. Notably, the thin and thick-shell NPs

retain their overall structural integrity post etching. These images demonstrate effective control over shell thickness and the successful fabrication of hollow structures using a precision etching method. Furthermore, the samples were subjected to elemental mapping to observe the distribution of elements in the core@shell structures. The presence of Au, Co, Fe, and Cs was observed as seen in Figure 3.4 (a – b).

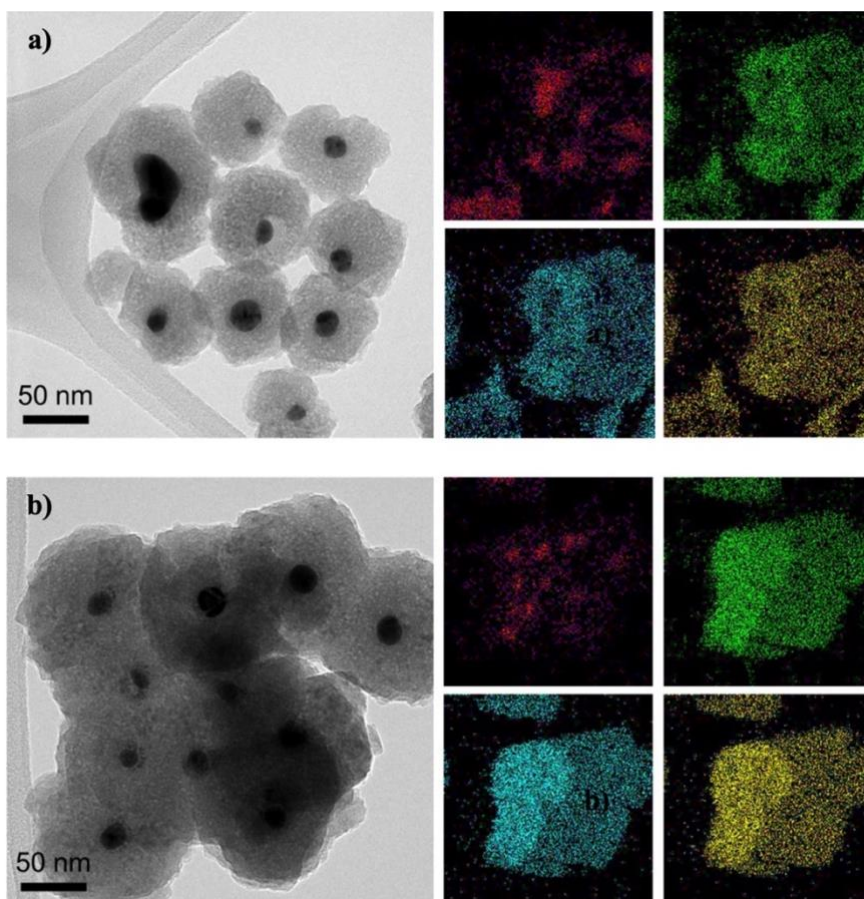


Figure 3.4: HR-TEM images and elemental mapping of core@shell NPs: Au core with (a) thin CoFe shell and (b) thick CoFe shell, showing the distribution of elements (Red: Au, Green: Co, Cyan: Fe, and combined elements) across the NPs.

The histograms were calculated from TEM images (a), (b), (c) and (d) in Figure 3.6 for the hybrids while for the pristine CsCoFe PBA histograms were calculated from Figure 3.5. The size distributions of the NPs were plotted and analyzed as shown in corresponding graphs. These plots indicate a relatively narrow particle size distribution for the samples, suggesting uniformity. The shell size for thin and thick is calculated to be approximately 20 nm and 45 nm while the hollow particles show an approximate mean size of 70 nm and 120 nm, proving that the overall structural integrity of the NPs stay intact even after the dissolution of Au NPs by cyanides.

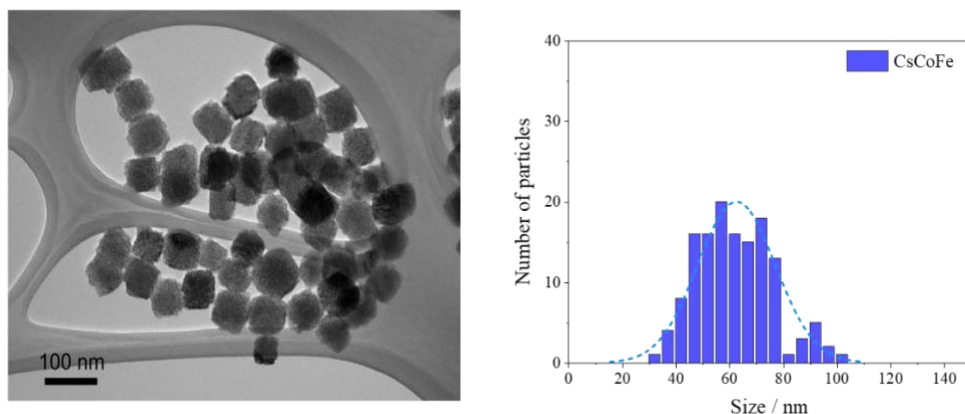


Figure 3.5: CsCoFe NPs showing detailed structural morphology at a scale of 100 nm with size distribution.

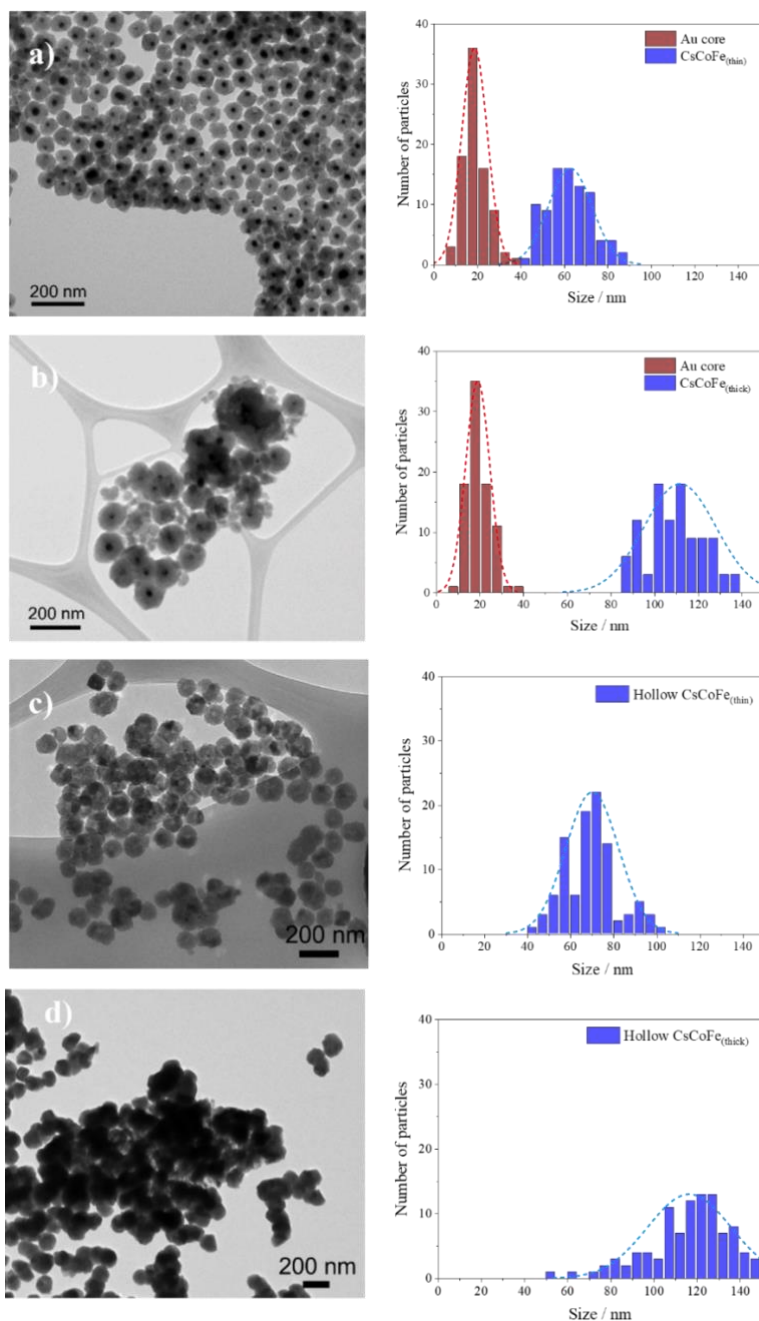


Figure 3.6: TEM images and size distribution of core@shell NPs, Au core with (a) thin CsCoFe shell, (b) thick CsCoFe shell, (c) hollow CsCoFe NPs after Au dissolution from (c) thin shell NP, and (d) thick shell NP,

After preparing the different nanostructures, their structure and composition were analyzed and compared to photomagnetic 70 nm CsCoFe NPs displayed in Figure 3.5 by means of different techniques including powder X-ray diffraction (PXRD), attenuated total reflectance Fourier-transform infrared (ATR-FTIR), X-ray photoelectron spectrometry (XPS) and energy-dispersive X-ray spectroscopy (EDX). In PXRD spectra, it can be observed in all samples the characteristic FCC cubic structure (Figure 3.7 a) of the cyanide-based coordination polymer. In core@shell structures, Au peaks were detected at ca. 38° and 44°.

Infrared spectra in the 2300-1900 cm^{-1} region show the vibration of the cyanide group (Figure 3.7 b), which is dominated in all cases by a band located at ca. 2100 cm^{-1} and a shoulder at 2060 cm^{-1} attributed to non-bridging cyanides that are on the surface of the particles. The predominant band comprises $\text{Co}^{\text{II}}\text{Fe}^{\text{II}}$ species, located at 2092 cm^{-1} , and $\text{Co}^{\text{III}}\text{Fe}^{\text{II}}$ species appearing at 2119 cm^{-1} . Thus, the closer is the peak to the former or the latter, the larger is the amount of the corresponding species. In this regard, CsCoFe NPs exhibit a maximum peak at 2114 cm^{-1} , which indicates the presence of mainly diamagnetic $\text{Co}^{\text{III}}\text{Fe}^{\text{II}}$ pairs. On the other hand, for the core@shell NPs with thin and thick shells, the main band can be found at 2098 and 2109 cm^{-1} , respectively. Thus, the thick shell contains more species capable of exhibiting photoinduced charge transfer than the thin heterostructure. This could be a consequence of: i) the smaller $\text{Co}^{\text{II}}\text{Fe}^{\text{III}}\text{-Co}^{\text{II}}\text{Fe}^{\text{II}}$ shell–core ratio in the PBA thin shell, which favors a higher proportion of photoactive diamagnetic $\text{Co}^{\text{III}}\text{Fe}^{\text{II}}$ species for the thicker heterostructure,^{169,186} and ii) the Co-Fe species at the Au/PBA interface, likely not photoactive due to the structural mismatch, which can cause strain in the PBA structure, in particular, in the thinner heterostructure. After removing the Au cores (case

of hollow NPs), the peak appears at 2095 and 2104 cm^{-1} , for the thin and thick structures, significantly shifted in comparison to the initial core@shells, possibly due to modifications in the PBA chemical composition during the etching process.

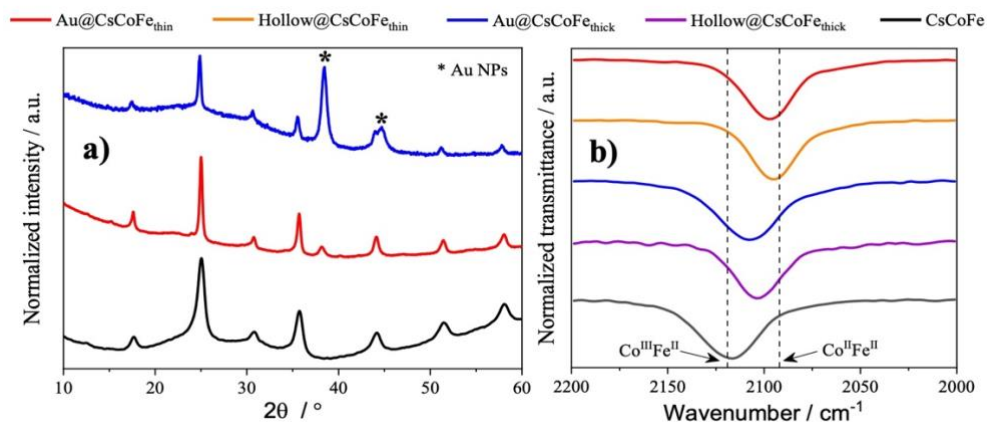


Figure 3.7: (a) PXRD spectra of Au@CsCoFe NPs with varying shell thicknesses. (b) ATR-FTIR spectra showing the characteristic Co^{III}Fe^{II} and Co^{II}Fe^{III} CN vibrations in core@shell and hollow samples.

To confirm these results, XPS was performed on a powder of the prepared NPs to gather more information about the oxidation state of the contained metals (Figures 3.8 a-b). The deconvolution of the Fe2p spectra reveals in all cases two main peaks located at 708.8 and 721.7 eV, characteristic of the diamagnetic Fe^{II}.¹⁶⁹ On the other hand, the Co2p region shows complex spectra with many different peaks due to the multiple splitting and satellite peaks typical of Co compounds. The peaks at 781.5, 785.2, and 789.0 eV are associated with the main 2p_{3/2} band of Co^{II} species and their satellites, while the one at 783.0 eV corresponds to the 2p_{3/2} orbital of Co^{III}.^{187,188} By comparing all these peaks for the different samples, it can be noticed that the Co^{III}/Co^{II} ratio is smaller for the core@shell NPs, in particular

when the PBA shell is thinner. In this regard, the ratio decreases from 3.2 to 0.6 and thus, less photoactivity is expected for the thinner CsCoFe shell. It should be noted that XPS is a superficial technique and given the shell thicknesses (greater than 20 nm), it does not represent the whole compound. As a result, for the core@shells, the amount of Co^{III} species is higher than what would be expected based on ATR-FTIR results, indicating that most of the non-photoactive centers are close to the gold core. In the case of hollow NPs, they exhibit a $\text{Co}^{\text{III}}/\text{Co}^{\text{II}}$ ratio of 0.4 for the thin and 1.3 for the thick, which is considerably lower than prior to the etching process, suggesting that cyanides and/or potassium ions are affecting the PBA.

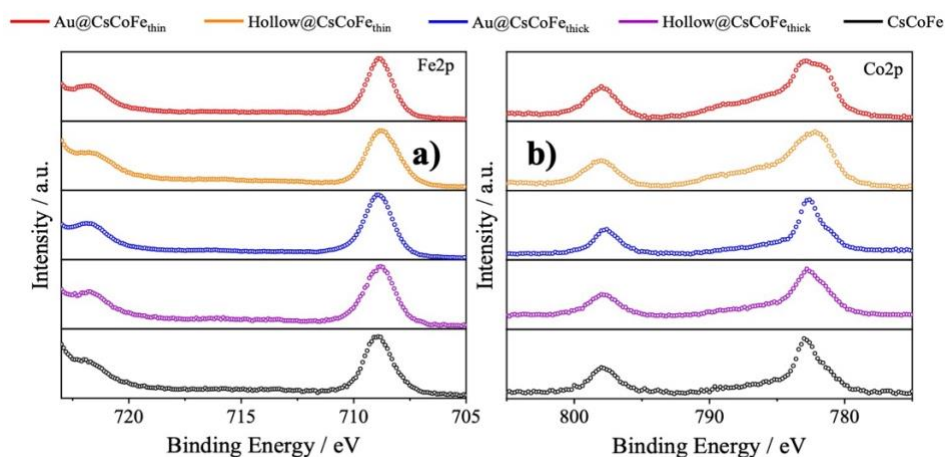


Figure 3.8: XPS spectra of (a) Fe 2p and (b) Co 2p binding energies for Au@CsCoFe and hollow CsCoFe NPs with varying shell thicknesses.

We determined the chemical formula for all the samples using EDX. The ratio of Fe/Co was determined to be between 0.84-0.90 indicating apparently a comparable number of vacancies in all the samples as seen in Table 2.1. However, the amount of Cs varied in all the nanostructures with core@shells and hollow NPs having higher number of $\text{Co}^{\text{II}}\text{Fe}^{\text{II}}$ contained

more Cs to compensate the lower positive charges. Moreover, K was detected in the hollow NPs, indicating that this cation was introduced during the etching process without replacing Cs. As observed by ATR-FTIR and XPS, this K inclusion is accompanied by a reduction of Co^{III} to Co^{II} , leading to a possible diminished photoactivity in case of the hollow NPs.

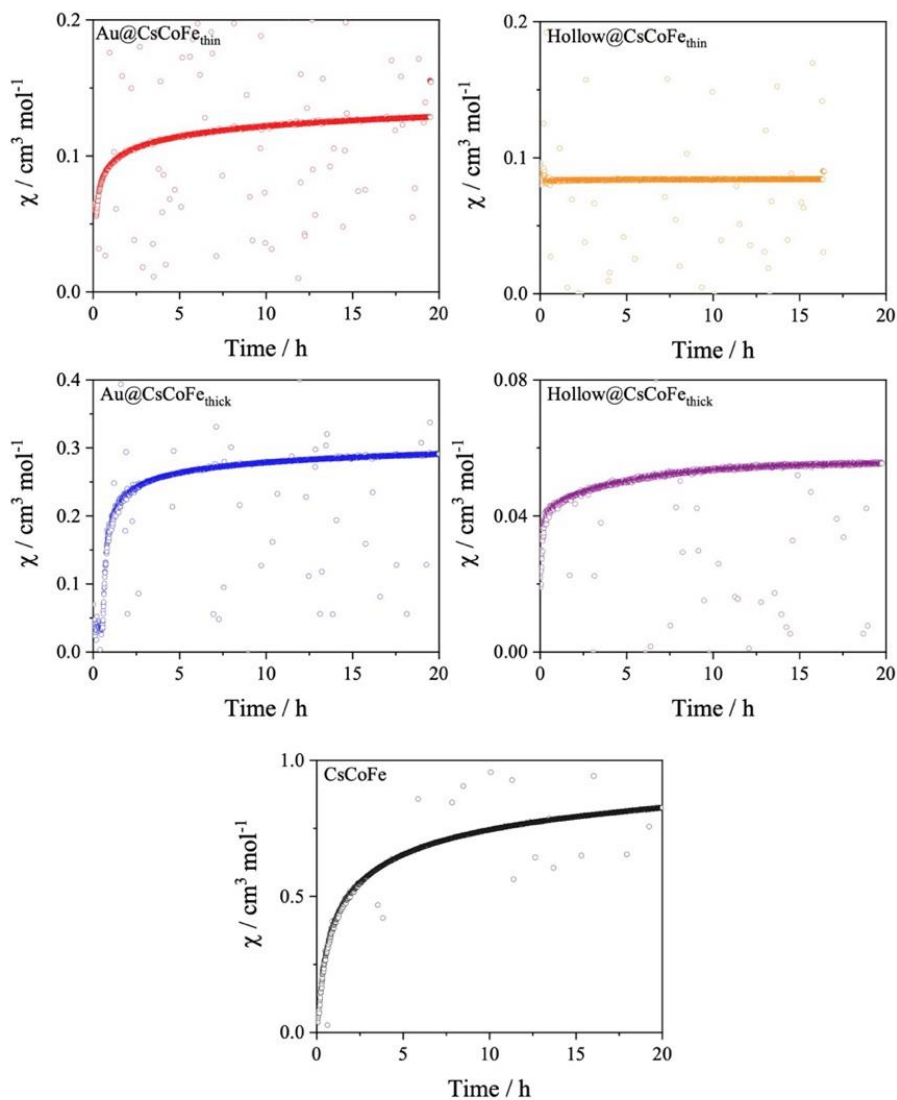


Figure 3.9: Magnetic susceptibility (χ) as a function of time for core@shell and hollow NPs with varying shell thicknesses, compared to pristine CsCoFe,

After characterizing the nanostructures, their photomagnetic behavior was studied. Magnetization was measured as a function of temperature in field-cooled mode (FCM) using a SQUID magnetometer. To promote charge transfer, the samples were irradiated at 10 K for 20 hours using a 633 nm laser as shown in Figure 3.9. The samples reached near-complete excitation to the metastable state after just 3 hours of irradiation, but the process was extended to 20 hours to ensure higher conversion and optimize the photomagnetic effects. Before irradiation, the FCM curve (Figure 3.10) evidenced a significant magnetization increase below 20 K as a consequence of the paramagnetic species $\text{Co}^{\text{II}}\text{Fe}^{\text{II}}$. This increase is more pronounced for the thin core@shell and even more for the corresponding hollow NPs due to the higher content of paramagnetic species compared to the other samples. Yet, for the thin core@shell sample it is still possible to induce by light the charge transfer of $\text{Co}^{\text{III}}\text{Fe}^{\text{II}} \rightarrow \text{Co}^{\text{II}}\text{Fe}^{\text{III}}$ (Figures 3.9 and 3.10). In the case of the corresponding hollow NPs, no photo magnetism was observed. This lack of response can be attributed to changes in the chemical composition that occurred during the etching process, also observed by EDX, which altered the properties and makes it harder for charge transfer to occur.

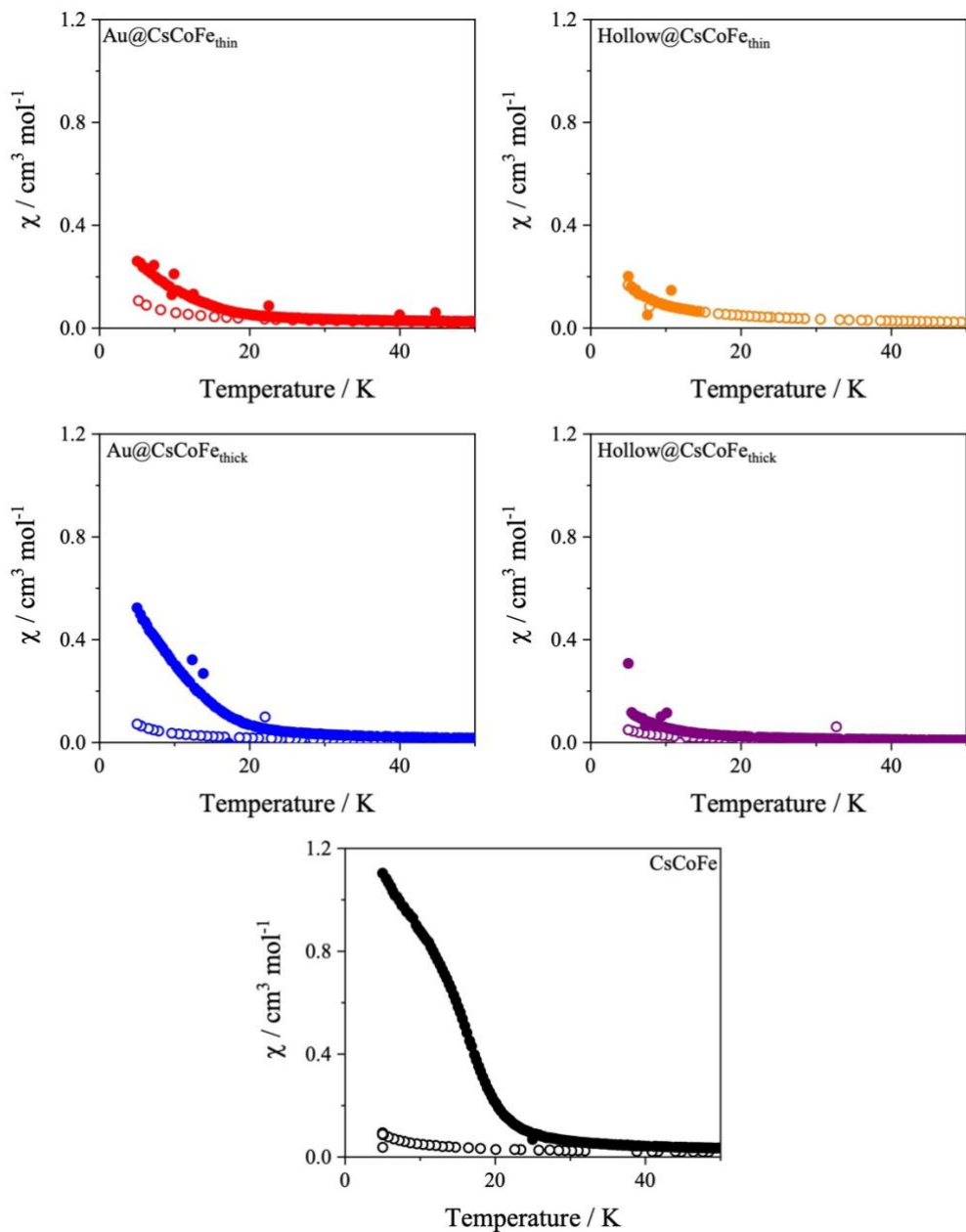


Figure 3.10: Temperature dependence of χ for core@shell and hollow NPs with varying shell thicknesses, compared to pure CsCoFe.

As the CsCoFe shell becomes thicker, more diamagnetic species $\text{Co}^{\text{III}}\text{Fe}^{\text{II}}$ leads to higher overall magnetization values. In the same manner, as the shell thickness increased, the On/Off ratio at 5 K improved. The ratio for core@shell structures increased from 2.4 in the thinner shell to 7.3 in the particle with thicker shell. This enhanced ratio reflects the improved stability and magnetic switching capabilities of thicker-shell NPs as shown in Fig 3.10. It is important to note that these values are significantly lower than those obtained in pristine CsCoFe, whose On/Off ratio is around 12.3.

Table 2.1: Molecular formulas and On/Off ratios at 5K for various PBA and Au@PBA nanostructures with thin and thick shells.

Samples	Molecular Formula	On/Off ratio (5K)
PBA	$\text{K}_{0.04}\text{Cs}_{0.69}\text{Co}[\text{Fe}(\text{CN})_6]_{0.90}$	12.3
Au@PBA (Thin Shell)	$\text{Au}_{0.31}\text{K}_{0.06}\text{Cs}_{0.96}\text{Co}[\text{Fe}(\text{CN})_6]_{0.84}$	2.4
Hollow PBA (Thin)	$\text{K}_{0.24}\text{Cs}_{0.93}\text{Co}[\text{Fe}(\text{CN})_6]_{0.84}$	1.0
Au@PBA (Thick Shell)	$\text{Au}_{0.10}\text{K}_{0.01}\text{Cs}_{0.68}\text{Co}[\text{Fe}(\text{CN})_6]_{0.86}$	7.3
Hollow PBA (Thick)	$\text{K}_{0.18}\text{Cs}_{0.72}\text{Co}[\text{Fe}(\text{CN})_6]_{0.84}$	2.7

Last but not least, in an attempt to detect the charge transfer mediated by light through electrical measurements, as was previously done in spherical Au NPs surrounded by a SCO shell,¹⁷⁴ we drop casted Au@CsCoFe(thin) NPs on commercial fingerprint electrodes with a gap of 2.5 μm . These NPs were chosen because they were expected to be the most conductive due to the thinner CsCoFe shell. I-V curves were collected at room temperature (Figure

3.11), showing a resistance of 140 M Ω and was compared with the CsCoFe pristine compound where a very low signal was recorded due to the insulating character of the sample. Thus, the core@shell system evidences an improvement in the conductance which is attributed to the presence of the Au cores. As observed in the Au@CsCoFe (thin) heterostructure, Au facilitates the charge transport through the device.

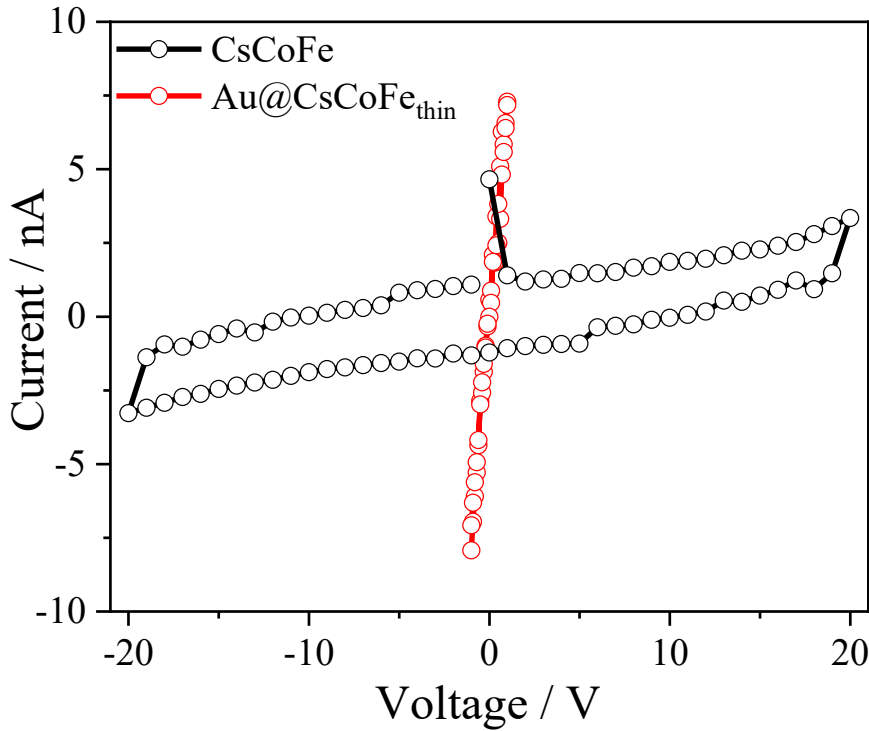


Figure 3.11: (*I-V*) characteristics of CsCoFe and Au@CsCoFe thin core@shell nanostructures at room temperature.

To reduce the resistance of the CsCoFe shells in our core@shell nanostructures, we must focus on making the shells thin while preserving their photomagnetic activity. This may be achieved by optimizing the synthetic protocol, such as adjusting precursor concentrations and addition

rates, to enhance the cooperativity of the PBA compound even at reduced thickness. Given that we need to conduct measurements at 10K (where CsCoFe PBA NPs are not conductive), using electrodes with smaller gaps will enhance the charge transfer efficiency and lower the resistance. Additionally, nanostructuring the electrodes may provide a better contact with the NPs and improve the electrical performance. On the other hand, it is also essential to continue fine-tuning the shell thickness to achieve a balance: thinner shells reduce resistance, while thicker shells enhance the photomagnetic properties of the CsCoFe shell. Our goal is to find an optimal shell thickness that achieves both low resistance and strong photomagnetic activity.

3.3 Conclusions

In this work, we have successfully synthesized core@shell Nps which consists of an Au spherical core and a CsCoFe photomagnetic PBA shell with different shell thicknesses, followed by the preparation of hollow PBAs of CsCoFe by etching the Au cores using KCN. Our results reveal the differences in photomagnetic activity because of the different shell sizes of core@shell NPs and chemical structural modification in hollow NPs induced because of the etching. Core@shell NPs with thicker shell exhibit a significant increase in the photomagnetic behavior as they contain greater number of diamagnetic $\text{Co}^{\text{III}}\text{Fe}^{\text{II}}$ species. In contrast, the core@shell NPs with thinner shell have more paramagnetic $\text{Co}^{\text{II}}\text{Fe}^{\text{II}}$ species which are responsible for a lower photomagnetic response as compared to the response coming from the thicker shell. As a result, we observe an increase in the On/Off ratio for NPs with thicker shell.

On the other hand, the hollow CsCoFe Nps exhibit no detectable photomagnetic response, which is attributed to the chemical changes that occur during the etching process, introduction of K ions altering the structure, leading to the formation of more Co^{II} paramagnetic species, resulting in decrease in photomagnetic activity. These findings underscore the role of shell thickness in influencing the photomagnetic properties of core@shell NPs. Furthermore, these hybrids could benefit from the enhanced electrical conductivity provided by the Au core, which may enable the magnetic PBA to be electrically readable at low temperatures.

3.4 Experimental Details

3.4.1 Materials

All chemical reagents were purchased and used without further purification. Silver nitrate was purchased from Alfa Aesar. Chloroauric acid, sodium citrate tribasic dihydrate, 4-mercaptopyridine 95%, cesium chloride, cobalt (II) chloride, potassium hexacyanoferrate and potassium cyanide were purchased from Sigma-Aldrich. Ultrapure water (18.2 M Ω) was used in the following syntheses.

3.4.2 Synthesis of Nanoparticles

3.4.2.1 Au NPs:

The synthesis of nanospheres (NSp) was carried out using typical Turkevich's method.^{189,190} To reduce a 0.25 mM HAuCl₄ solution (100 ml), 2.5 mM of sodium citrate was added to the boiling solution while stirring constantly to maintain homogeneity. After about a minute, the solution turned mild grey, then darkened to a deep red color over the next 20 minutes. The color change is a strong visual indication that colloidal Au is being formed.

3.4.2.2 Au@CsCoFe (thin shell) NPs:

In 10 ml of 0.5mM gold nanospheres, 10 μ L of 1 mM 4-mercaptopyridine (4-MPy) was added, the solution was agitated for 20 minutes to allow it to interact with the Au NSp surface. The solution was then rinsed with water at 8000 rpm for 20 minutes to remove any excess citrate and 4-MPy. To grow the PBA shell, the following precursor solutions were prepared:

- i) 50 ml solution containing 1×10^{-3} mol of CoCl_2 .
- ii) ii) 50 ml solution containing 1×10^{-3} mol mM of $\text{K}_3[\text{Fe}(\text{CN})_6]$ and 2×10^{-3} mol of CsCl

A total of 100 μL of each solution was added slowly into the colloidal Au@4-MPy NP solution under moderate stirring and at an addition rate of 10 μL per 20 seconds. The final solution was left to stir overnight and centrifuged at 13000 rpm for 15 minutes thrice (using water).

3.4.2.3 Au@CsCoFe (thick shell) NPs:

The obtained precipitate was then redispersed in 100 ml of H_2O while stirring. Then, 2 ml of each precursor solution was added dropwise to the redispersed solution and stirred overnight. The resulting solution was centrifuged and rinsed twice at 13000 rpm for 15 minutes.

3.4.2.4 Hollow@CsCoFe NPs:

5 mg of core@shell NPs were redispersed in 10 mL of an aqueous solution containing 1 mM KCN and stirred for 24 hours. The resulting solution was centrifuged and rinsed twice at 13000 rpm for 15 minutes.

3.4.2.5 CsCoFe NPs:

11 nm NPs were prepared by using a procedure similar to one already reported.¹⁰ After 24 hours the solution was centrifuged at 13000 rpm for 15 minutes twice to clean the final particles. 5 mg of the dried sample was redispersed in 100 ml of H_2O while stirring. Then, 2 ml of each precursor solution was added dropwise to the redispersed solution and stirred overnight. The resulting solution was centrifuged and rinsed twice at 13000 rpm for 15 minutes.

3.5 Physical Characterization

3.5.1 UV/Vis Spectroscopy:

UV-vis absorption spectra were recorded on Thermofischer multiskan skyhigh microplate spectrophotometer from 300 to 900 nm range, using Thermoscientific clear flat-bottom immune nonsterile 96-well plates. 300 μ L of the sample was collected in the well plates for these measurements.

3.5.2 Transmission Electron Microscopy:

TEM studies were carried Hitachi HT7800 120 kV, and a Technai G2 F20 microscope operating at 200 kV. Samples were prepared by dropping suspensions on lacey formvar/carbon copper grids (300 mesh).

3.5.3 Powder X-Ray Diffraction:

PXRD patterns were collected in a PANalytical Empyrean diffractometer using copper radiation ($\text{Cu K } \alpha \lambda = 1.5418 \text{ \AA}$) with an PIXcel detector, operating at 40 mA and 45 kV at room temperature.

3.5.4 Attenuated total reflectance Fourier-transform Infrared Spectroscopy:

Spectra were collected in an Agilent Cary 630 FTIR spectrometer in the $4000\text{--}500 \text{ cm}^{-1}$ range in the absence of KBr pellets.

3.5.5 X-ray Photoelectron Spectroscopy:

Samples were analyzed using a KALPHA Thermo Scientific spectrometer. All spectra were collected using $\text{Al K } \alpha$ radiation (1486.6 eV), monochromatized by a twin crystal monochromator, yielding a focused X-ray spot (elliptical in shape with a major axis length of 400 μm) at 30 mA and

2 kV. The alpha hemispherical analyzer was operated in the constant energy mode with survey scan pass energies of 200 eV to measure the whole energy band and 50 eV in a narrow scan to selectively measure the particular elements. XPS data were analyzed with Advantage software. A background function was used to approximate the experimental backgrounds. Charge compensation was achieved with the system flood gun that provides low-energy electrons and low-energy argon ions from a single source.

3.5.6 Magnetic Measurements:

Magnetic data were collected with a Quantum Design MPMS XL-5 susceptometer equipped with a SQUID sensor. DC FC magnetization measurements were performed under an applied magnetic field of 1000 Oe. The isothermal Magnetization at 2 K were performed between -7 and +7 T. A laser of wavelength 633 nm was used for the photomagnetic studies by irradiating the sample for 20 hours at 10 K.

3.5.7 Electrical Measurements:

Au@CoFe and CoFe transport measurements have been performed inside a glovebox under N₂ atmosphere at room temperature, using a Keithley 4200-SCS as voltage source and electrometer. The measurements were carried out in a two-probe configuration using commercial fingerprinted electrodes, with a gap of 2.5 μm . The NPs were organized in the electrodes gap by drop-casting a suspension of the material.

Chapter

4

Chemical Design of Au@MnFe PBA Nanostructures for pH and NIR Responsive Drug Release

4.1 Introduction

Cancer is a complex disease characterized by uncontrolled cell growth, resistance to treatment, and the potential to spread throughout the body. Its complexity has resulted in a demand for new treatments that selectively target cancer cells while minimizing damage to surrounding healthy tissues.^{191–193} Consequently, more attention has been paid to developing innovative treatment strategies that improve therapeutic effectiveness, minimize side effects and overcome drug resistance.^{193,194} This need for improved treatments has driven research toward advanced nanomaterials that offer new possibilities in cancer therapy.¹⁹⁵ These include drug delivery nano systems that enhance targeted treatment while decreasing systemic toxicity, and photothermal therapy (PTT), which utilizes light-absorbing nanomaterials to selectively destroy cancer cells with reduced harm to healthy tissues.

In this context, gold nanoparticles (Au NPs) and Prussian Blue Analogues (PBAs) are two prominent nanomaterials with increasing interest in biomedicine.^{196–199} Au NPs have been attracting considerable attention in cancer research because of their remarkable optical properties originating from localized surface plasmon resonances (LSPR). This phenomenon allows the conduction electrons to resonate with an incident light, enabling Au NPs to absorb light across various wavelengths.^{197,198} As a result, they become capable of performing PTT, where absorbed light is converted into heat to selectively eliminate cancer cells. In addition, the large and continuous surface area of Au NPs makes them suitable as a drug delivery platform, permitting an efficient loading of chemotherapeutics, antibodies or nucleic acids, etc. Besides, Au NPs can act as imaging agents, making them valuable for theragnostic, which encompasses diagnosis and therapy within the same

platform. Also, they can be functionalized with ligands like aptamers or peptides to target cancer cells.^{198,200,201} Nevertheless, Au NPs have a relatively low drug-loading capacity. In addition, although they are highly efficient in localized PTT, their ability to deliver drugs across more extensive areas of a tumor is limited.²⁰² To address these challenges, hybrid systems combining optical advantages with improved drug delivery efficiency are being explored

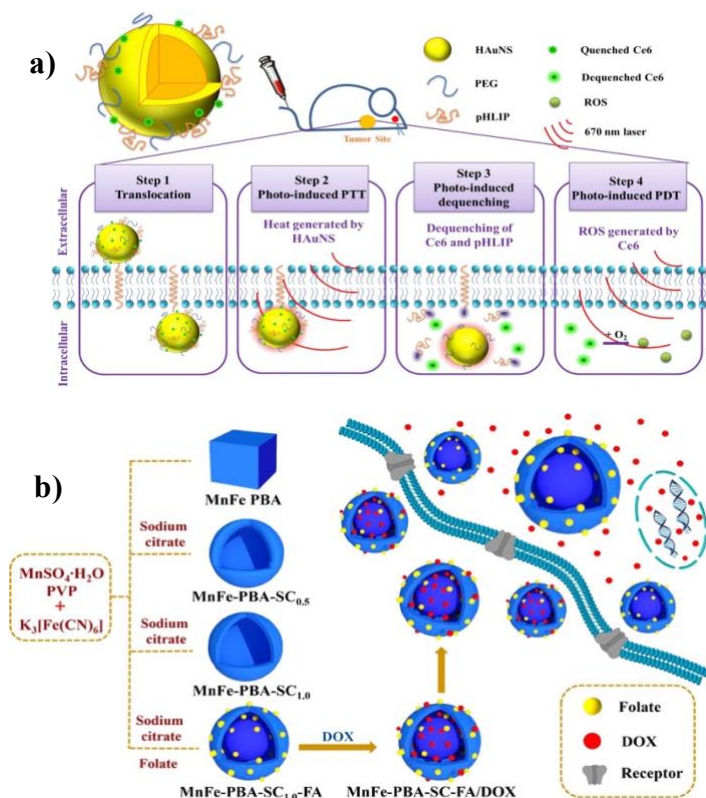


Figure 4.1: (a) Scheme of a multifunctional nanoplatform based on PEGylated hollow gold nano shells (HAuNS) for cancer therapy reprinted from 203. (b) MnFe-PBA-based nanocarriers for targeted drug delivery, reprinted with permission from 12.

On the other hand, PBAs are coordination polymers with the chemical formula $A_nM^{II}_x[M'^{III}(\text{CN})_6]_y \cdot n\text{H}_2\text{O}$, exhibiting physical properties that make

them suitable for certain biomedical fields.^{198,204,205} Among them MnFe are one class of these PBAs, that has shown potential in drug release systems due to their pH-responsive properties. Their hollow structure allows for loading large amounts of therapeutic agents, like doxorubicin (DOX), enabling controlled release depending on the presence or absence of an acidic environment.²⁰⁶

Given their complementary properties, the combination of Au NPs and PBAs in a core@shell nanostructure presents a highly promising approach for biomedical applications. While Au NPs offer tunable plasmonic properties ideal for imaging and PTT, PBAs can contribute with structural stability, functional versatility for drug loading, and pH-responsive behavior for controlled drug release. This synergistic integration can lead to the development of advanced nanomaterials with enhanced biological performance, including applications in *in vivo* computed tomography and PTT, providing precise diagnostic guidance, excellent therapeutic efficiency, and high biological stability.^{207,208} Despite these advantages, the process of synthesizing Au@MnFe heterostructures remains a significant challenge. The complexity lies in achieving a well-defined PBA shell strongly attached to an Au NP core without compromising the core and the properties of the shell.^{209,210}

Thus, in this study, it is reported the synthesis and characterization of core@shell and yolk@shell Au@MnFe nanostructures, consisting in a gold nanoparticle core encapsulated by a MnFe PBA shell. Core@shell NPs were initially synthesized to develop a drug delivery system; however, poor drug loading and low biocompatibility was observed. To address these issues, a modified synthetic protocol was developed, resulting in a novel and

previously undescribed nanostructure with a yolk@shell morphology. In addition, we employed a modified growth strategy that mitigates gold etching while ensuring controlled shell formation. Structural and spectroscopic analyses revealed that yolk@shell NPs exhibit a hollow cavity, attributed to Fe^{3+} leaching. This novel hybrid system takes advantage of plasmonic properties of gold and the structural and intrinsic drug-like functionality of MnFe PBAs, creating a multifunctional platform for enhanced drug delivery. For controlling their colloidal stability and drug-loading capability, the Au@MnFe nanostructures were functionalized with thiolate polyethylene glycol carboxylic acid (PEG). Moreover, the PEG on the NPs surface provide functional groups that can be used for the conjugation of additional drugs and biomolecules, such as antibodies, making this system an attractive platform for drug delivery applications. To test the drug-loading and release behavior, DOX was used as a model drug. DOX was loaded into the synthesized hybrid Au@MnFe NPs. The yolk@shell NPs exhibited a higher loading efficiency of 50%, as compared to 19% for core@shell NPs. On the other hand, drug release studies demonstrated a pH-sensitive mechanism, with a continuous release of 40% at pH 5 over 24 hours, which was further accelerated upon near-infrared (NIR) laser irradiation. This acceleration was attributed to the plasmonic properties of Au that facilitated a photothermal effect which contributed to a local temperature increase. Furthermore, TEM images confirmed the efficient internalization of NPs in A549 and HeLa cells. These findings highlight two remarkable conclusions: 1) Au@MnFe NPs are hybrid NPs that can function as a drug delivery system and potentially serve as a contrast agent; 2) the Au@MnFe yolk@shell demonstrated promising results for controlled drug delivery and PTT.

4.2 Results and discussion

Core@shell Au@MnFe PBA NPs: Synthesis and Characterization.

To obtain Au@MnFe NPs, we adjusted the protocol presented in Chapter 2 consisting in anchoring a 4-mercaptopyridine (4-MPy) molecule on the surface of ca. 20 nm Au NPs to facilitate the growth of the PBA shell, while minimizing Au etching by the cyanide species. In this manner, CsMnFe shell was grown by simultaneously adding the PBA precursors ($\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, CsCl and $\text{K}_3\text{Fe}(\text{CN})_6$) to the colloidal solution containing 4-MPy-modified Au NPs. Cs was selected as the counter cation since its presence inside the PBA structure helps stabilize it and enhances its potential as a contrast agent.^{211,212} Notably, without Cs, the PBA structure can quickly dissolve, leading to an uncontrolled drug release.

As expected, during the synthesis, a noticeable color change in the solution occurs during the shell formation. The maximum absorbance displays a red shift in the case of core@shell NPs as seen in Figure 4.2. This change indicates the existence of an interaction between the Au NPs and the PBA. Specifically, the red shift happens because of two primary factors, the change in the dielectric environment and refractive index.^{179–181} As the LSPR of Au NPs is highly sensitive to the refractive index of the surrounding medium, this tends to cause an increase in the dielectric constant which red shifts the plasmon peak.^{209,210,213,214}

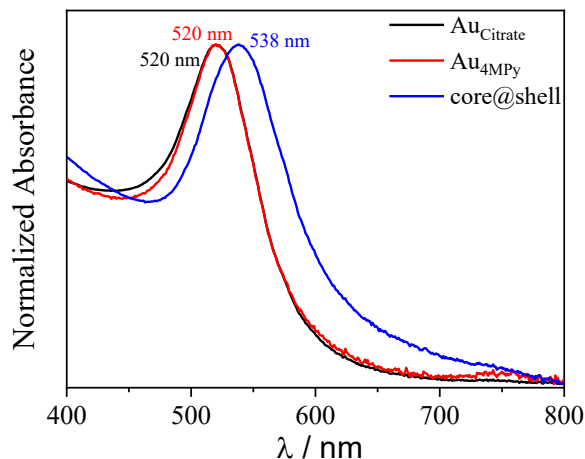


Figure 4.2: UV-Vis absorbance spectra of functionalized core@shell NPs.

Following the UV-Vis study, further characterization was conducted through TEM. A clear core@shell structure with a narrow size distribution was distinguished as observed in Figure 4.3 (a). The acquired TEM images demonstrate the successful synthesis of the NPs, with Au cores surrounded by MnFe shells. The size distribution histogram provides further evidence, showing a distinct Au core of around 20 nm and a complete particle size of ca. 70 nm. The narrow size distribution evidences uniform growth of the MnFe shell around the Au core, with minimal aggregation, indicating the stability and homogeneity of the NPs.

Furthermore, EDX mapping of core@shells was carried out to analyze the elemental distribution as displayed in Figure 4.3 (b). As expected, Au (red) is located within the core, whereas manganese (Mn, blue) and iron (Fe, yellow) are concentrated in the surrounding shell. In addition to this, EDX allowed us to determine the chemical formula for the core@shell NPs as $\text{Au}_{0.71}@\text{Cs}_{1.56}\text{Mn}_1[\text{Fe}(\text{CN})_6]_{0.97}$.

After visual confirmation of the core@shell structure of the obtained NPs by TEM, the NPs were redispersed in an aqueous solution of HS-PEG-COOH to functionalize the PBA surface through the formation of covalent bonds thanks to the thiol groups and as well to improve the colloidal stability of the NPs and the biocompatibility for use in further studies.^{215–218} An aliquot was taken to perform UV-Vis to monitor the absorbance, ATR-FTIR to see the cyanide peaks and dynamic light scattering (DLS) to measure the hydrodynamic size and as well the colloidal stability.

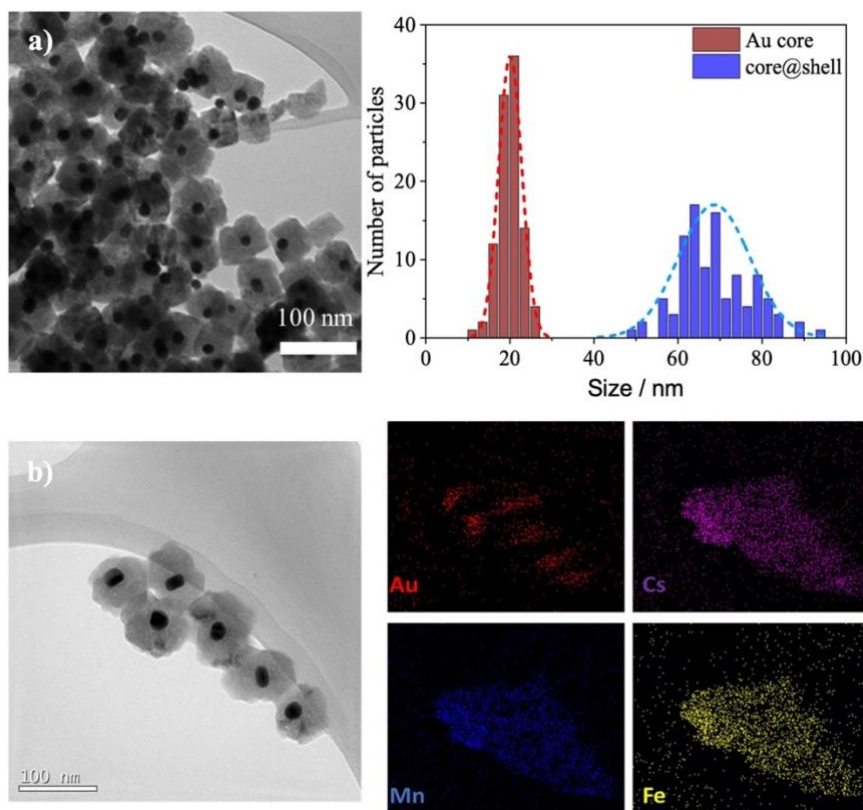


Figure 4.3: (a) TEM image of obtained core@shell NPs (b) Energy-dispersive X-ray spectroscopy (EDX) mapping of the Au (red), Cs (purple), Mn (blue), and Fe (yellow) present in the core@shell NPs.

No significant difference was observed by the UV-Vis measurement in Figure 4.4 (a). Moreover, by ATR-FTIR spectroscopy we analyzed the vibrational properties and coordination environments of the synthesized NPs. The cyanide (CN) band at around 2080 cm^{-1} corresponds to $\text{Mn}^{\text{II}}\text{Fe}^{\text{II}}$. These vibrations remain consistent, even after the PEG addition confirming the stability of the shell, as shown in Figure 4.4 (b). On the other hand, no peaks associated with PEG were observed in the fingerprint region ($400\text{--}1600\text{ cm}^{-1}$). This probably reflects a moderate amount of PEG present on the NPs.

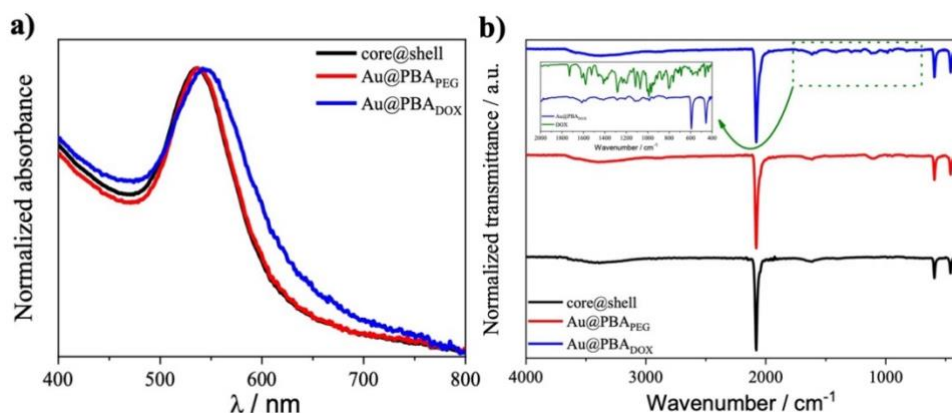


Figure 4.4: (a) Normalized UV-Vis absorbance and (b) ATR-FTIR spectra of core@shell NPs with surface modifications and DOX loading.

To verify the colloidal stability of the NPs, dynamic light scattering (DLS) measurements were performed. Hydrodynamic size of Au@PBA core@shell functionalized with SH-PEG-COOH over time (48 hours) was as well observed. As shown in Figure 4.5. The hydrodynamic diameter of the core@shell NPs remains stable over a time span of 48 hours as compared to the NPs without PEG which tends to aggregate within 24 hours that could be seen in the mother solution. This indicates good colloidal stability for 48

hours for the NPs with PEG. Thus, DLS results shows the effectiveness of the surface functionalization in maintaining colloidal stability.

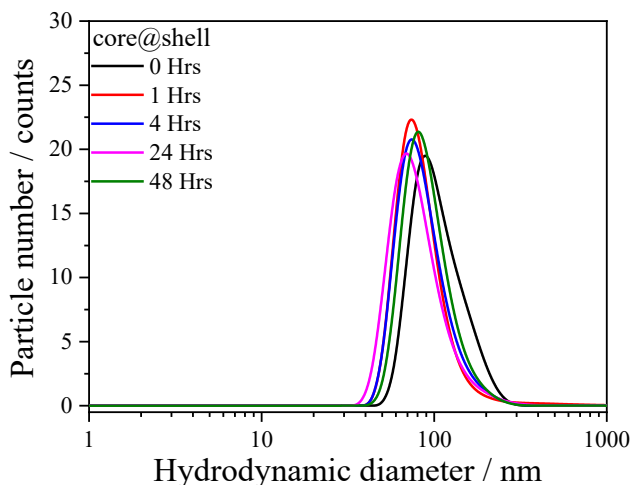


Figure 4.5: DLS graph of core@shell NPs after functionalization with SH-PEG-COOH displaying over time colloidal stability.

Core@shell NPs: DOX loading.

After functionalizing the NPs, drug loading was carried out by redispersing them in a DOX solution. Specifically, 1 mg/ml of DOX was added in a 1 mg/ml solution containing the nanostructures and stirred at a moderate speed for 24h. After washing the NPs to remove DOX excess, UV-VIS spectra were recorded. The third spectrum (blue) in Figure 4.4 (a) shows the DOX-loaded core@shell NPs. For the core@shell NPs, DOX peak (at around 480 nm) was not detected, indicating a minimal presence of DOX.

Subsequently the UV-VIS measurements, ATR-FTIR analysis was conducted to qualitatively confirm the presence of DOX, focusing on the fingerprint region ($400\text{--}1600\text{ cm}^{-1}$) as shown in Figure 4.4 (b). Characteristic

DOX peaks were observed, albeit with low intensity suggesting the possible presence of DOX

In order to confirm the presence and quantify the amount of DOX within the NPs, further characterization techniques such as UV-Vis spectroscopy were used. Owing to the intense absorption of DOX Figure 4.6 (a), its loading was estimated by measuring the maximum absorbance at 480 nm of the supernatant obtained after centrifuging the DOX-loaded NPs.

By using the absorbance value collected at 480 nm from the DOX supernatant obtained from core@shells as displayed in Figure 4.6 (c) and the calibration curve displayed in Figure 4.6 (b), we determined the amount of unloaded DOX in the supernatant. This allowed us to calculate the amount of DOX loaded into the nanostructures. Indeed, a higher absorbance value in the supernatant indicates a lower amount of loaded DOX.

The drug loading efficiency was then calculated using the following formula.

$$\text{Drug loading efficiency (\%)} = \frac{\text{weight of DOX in nanocomposites}}{\text{weight of feeding DOX}} \times 100\%$$

The drug loading was estimated to be around 19% for Au@PBA core@shell. Furthermore, Figure 4.6 (d) illustrates the in-vitro cumulative release of DOX from core@shell NPs under pH 7 and pH 5 environment over 24 hours. DOX release is enhanced in acidic condition as compared to physiological conditions. A maximum of ~28% DOX release is observed after 24 hours at

pH 5 while at pH 7 maximum release is ~10%. This difference is attributed to the destabilization of the MnFe shell structure in acidic environments.²¹⁹

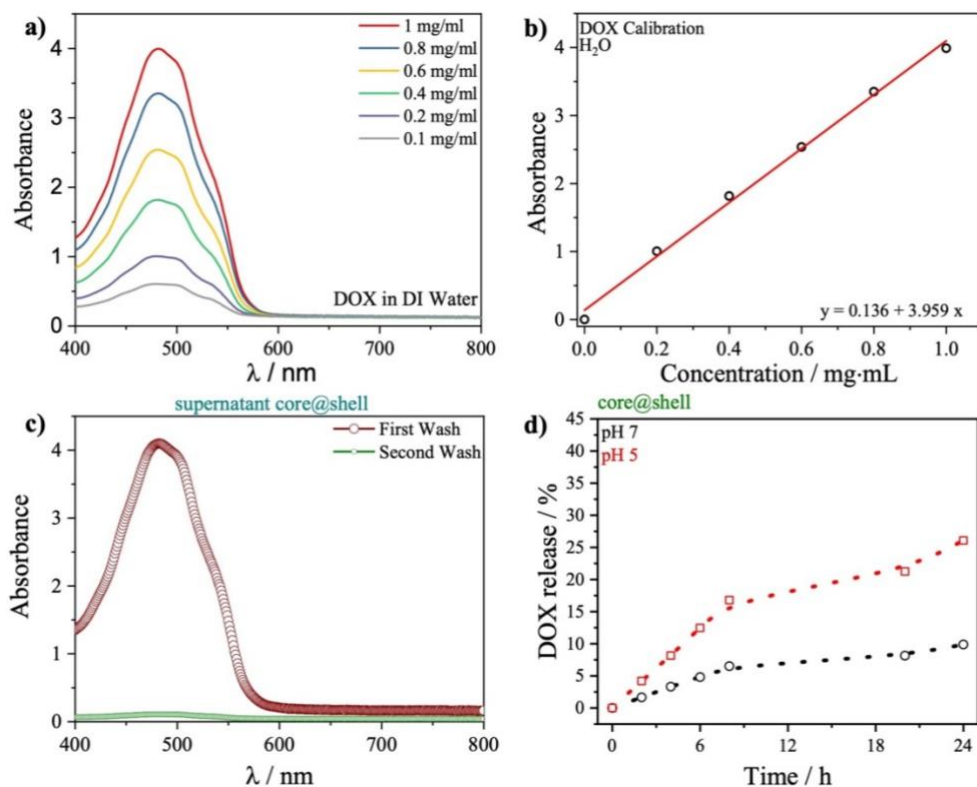


Figure 4.6: (a) UV-Vis absorbance (b) Calibration curve of different concentration of DOX in DI water, (c) UV-Vis absorbance of DOX supernatant collected from core@shell. (d) Cumulative release over 24 hours of DOX from core@shell NPs over time at pH 7 and pH 5.

Core@shell NPs: Cytotoxicity Assay

To investigate the effect of DOX loaded NPs, a cell viability experiment was performed. The original plan was to add the NPs to a cell culture, allowing their internalization by the cells, followed by the release of DOX, which

would induce cell death. The cell line A549 was chosen due to its relevance in lung cancer research, well-characterized properties, and ease of culture. A549 cells, derived from human lung adenocarcinoma, serve as a representative model for lung cancer and respiratory diseases, making them suitable for evaluating NP-based therapies for lung cancer. Cellular uptake studies were conducted in order to understand the internalization of the NPs. As represented in the graph of Figure 4.7 (a) cellular uptake of the NPs increases with both dose and time. Therefore, an uptake time of 4 hours was chosen for the cell viability experiments. 24 hours after the uptake, MTT assay was performed to evaluate the cytotoxicity of the NPs (see Figure 4.7 b) Regrettably, The NPs without DOX exhibited cytotoxicity toward the cells at higher concentrations, which may limit the biological applications of these hybrid NPs, particularly for in vivo anti-cancer therapy.²¹⁹

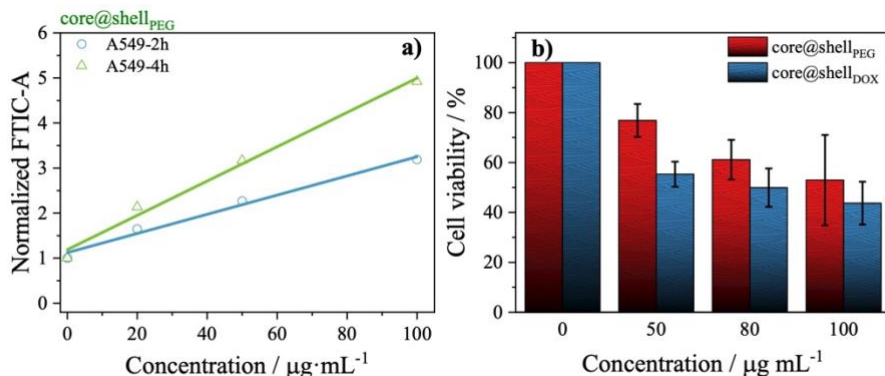


Figure 4.7: Cytotoxicity assay. (a) Cellular uptake of NPs by A549 cells at 2 and 4 hours.

(b) Cell viability of A549 cells after 24-hour treatment with varying concentrations core@shell with PEG and DOX.

Yolk@shell Au@MnFe PBA NPs: Synthesis and Characterization.

In an attempt to reduce the toxicity and poor DOX loading observed in core@shell NPs, we modified the synthesis protocol in a second batch of experiments. As the presence of high concentrations of Cs (80 mM), can lead to cytotoxicity by potentially disrupting mitochondrial and cytoskeletal function.²²⁰ Thus, Cs was reduced during the synthesis of the core@shell NPs to maintain a balance between PBA structural stabilization and biocompatibility.

During the preparation of the precursor solution the concentration of $K_3[Fe(CN)_6]$ and $MnCl_2 \cdot 4H_2O$ were kept the same, while the concentration of CsCl was reduced by half. Then, the previous synthesis protocol was followed for the growth of the PBA shell. After synthesis, UV-Vis spectroscopy was performed, revealing a plasmon redshift beyond that of the core@shell NPs, along with a change in absorbance intensity. This redshift was attributed to the change in refractive index caused by the PBA shell, leading to a variation in the dielectric constant. Additionally, the decrease in the intensity was attributed to the increase in distance of Au surface to the PBA shell.^{209,210,213,221}

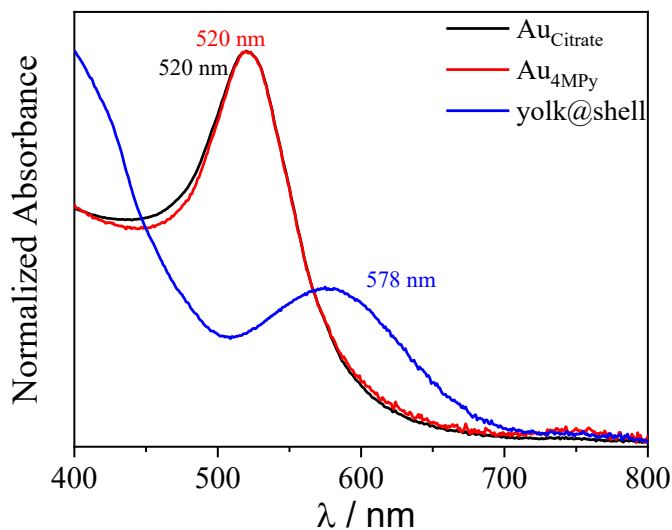


Figure 4.8: absorbance spectra of functionalized yolk@shell NPs.

TEM images in Figure 4.9 (a) revealed that our modified synthesis resulted in the formation of nanostructures in the form of yolk@shells, with the presence of Au enclosed in a cavity surrounded by a shell. The narrow size distribution in the histogram indicates the homogeneity of the NPs, showing an Au core of approximately 20 nm and complete particle size of 105 nm. Interestingly, traces of Au were also observed in the shell for the yolk@shell NPs by the EDX mapping as shown in Figure 4.9 (b). The chemical formula was found to be $\text{Au}_{0.18} @ \text{Cs}_{1.27} \text{Mn}_1 [\text{Fe} (\text{CN})_6]_{0.90}$.

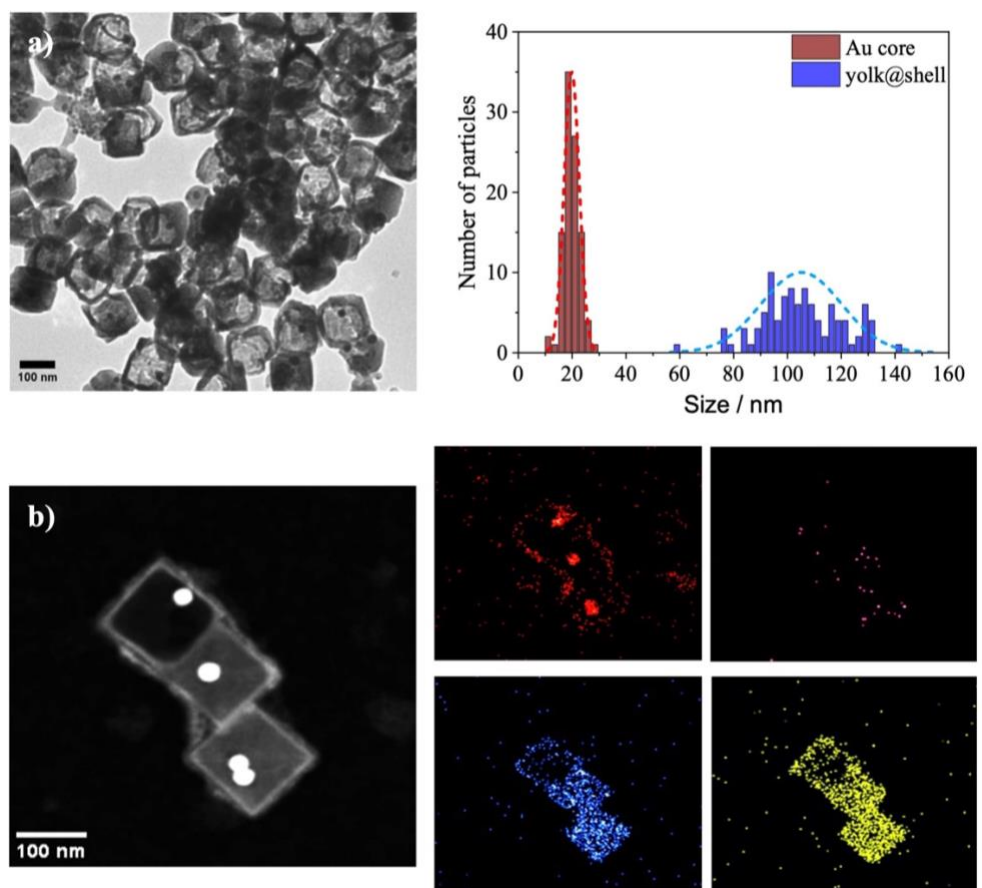


Figure 4.9: (a) TEM image of obtained with corresponding size distributions. (b) EDX mapping of the Au (red), Cs (purple), Mn (blue), and Fe (yellow) present in the yolk@shell NPs.

This significant result, revealed through the TEM images and the presence of Au in the shell, prompted a further and detailed investigation of the formation of yolk@shell NPs. Therefore, we studied by ATR-FTIR and TEM the formation of the yolk@shell. To this aim, aliquots of the sample were taken at different time intervals a 24-hour reaction period. TEM images in Figure 4.10 (a-c) revealed that in the first minute of the reaction, core@shells NPs are formed with uniform size distribution as seen in Figure

4.10 (a). After six hours, the morphology remains consistent, as observed in Figure 4.10 (b), with a slight increase in overall particle size. Up to this point, no yolk@shell structure is detected, indicating a gradual progression in shell development. However, in Figure 4.10 (c), after 24 hours of the reaction a yolk@shell structure can be seen. As it has been reported, it could be that Fe^{3+} ions in the PBA structure undergo partial hydrolysis, forming soluble iron species that leach from the PBA framework, weakening the shell structure and promoting hollowing.^{222,223}

To validate this phenomenon, ATR-FTIR analysis was performed to detect potential variations in the $\text{Mn}^{\text{II}}\text{-Fe}^{\text{III}}$ cyanide coordination. As illustrated in Figure 4.10 (d), the characteristic signals corresponding to $\text{Mn}^{\text{II}}\text{-Fe}^{\text{III}}$ species at wavenumber of 2149 cm^{-1} progressively weakens over time, indicating the continuous leaching of Fe^{III} . Although no change is observed for the cyanide peak at 2079 cm^{-1} but we can see the appearance of the shoulder at around 2060 cm^{-1} that is related to uncoordinated cyanides. The presence of the uncoordinated cyanides further provides evidence supporting the leaching of Fe^{III} and dissolution of Mn^{II} from $\text{Mn}^{\text{II}}\text{-CN-Fe}^{\text{III}}$ species. This gradual depletion ultimately drives the formation of the yolk structure.

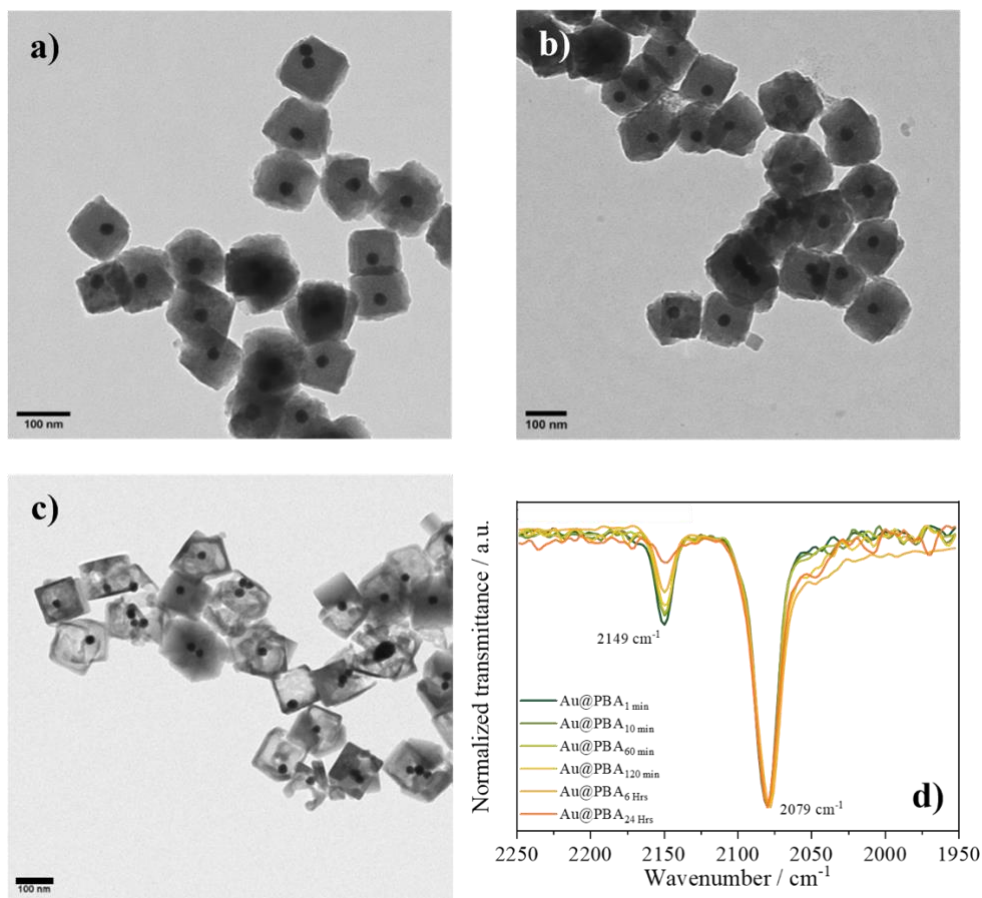


Figure 4.10: TEM images of *yolk@shell* NPs performed over different time intervals for a time span of 24 hours (a) 1 minute (b) 6 hours (c) 24 hours (d) ATR-FTIR spectra of *yolk@shell* NPs performed over different time intervals.

Considering that the formation of *yolk* structures involves the leaching of the Fe^{III} and dissolution of Mn^{II}, we hypothesize that some gold may be etched by free Fe(CN)₆ species and redeposited onto the shell during the formation of the heterostructure. The presence of Au on the surface of PBA may also lead to exciting novel properties that are not observed in *core@shell* structures.

Furthermore, the structure of the yolk@shell was analyzed and compared with core@shell and as well pristine PBA. As illustrated in the diffraction patterns in Figure 4.11 the black curve correlates with the CsMnFe structure, exhibiting distinct peaks that validate its distinctive fcc structure. The red pattern represents the core@shell NPs while the blue curve shows the yolk@shell NPs. The successful incorporation of the Au core can be seen in the two heterostructures, maintaining the overall crystallinity of the shell structure. The core@shell structure exhibits sharper and more intense peaks in the overall diffraction profile, indicative of higher crystallinity. In contrast, the yolk@shell structure shows slightly broader peaks, possibly indicating a smaller crystallite size due to the leaching process during its formation. Additionally, a slight shift in the peaks can be observed in both cases (as shown in the right panel). This shift could suggest the presence of lattice strain or structural distortions. In the core@shell structure, this shift is more pronounced than in the yolk@shell, possibly due to the PBA being closer to the Au/PBA interface, which is, as analyzed in Chapter 2, more strained.

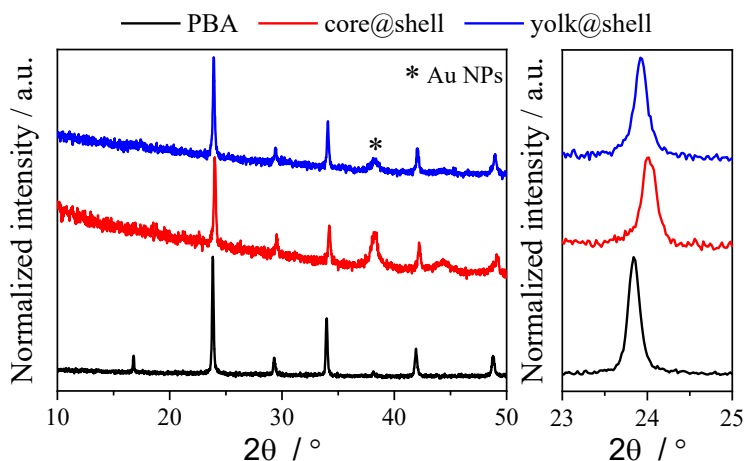


Figure 4.11: PXRD displaying the structural comparison of the obtained yolk@shell, core@shell and pristine MnFe NPs.

After understanding the formation of the yolk@shell NPs, surface functionalization with SH-PEG-COOH was performed, as previously done for core@shell NPs. Figure 4.12 (a) shows a blue shift upon PEG functionalization. This blue shift can be attributed to interaction of PEG with Au present in both the yolk and the shell, as well as interaction of PEG with the PBA shell. As a result, the local dielectric constant is altered, leading to a blue shift and a reduction in the refractive index at the Au surface.²²⁴ On the other hand, no peaks associated with PEG were observed in the fingerprint region (400–1600 cm^{-1}) for yolk@shell NPs as well. This probably reflects the moderate amount of PEG present on the NPs. These findings suggest that, although surface modifications are present, their quantities are insufficient to cause significant changes in the FTIR spectra in the lower wavenumber regions.

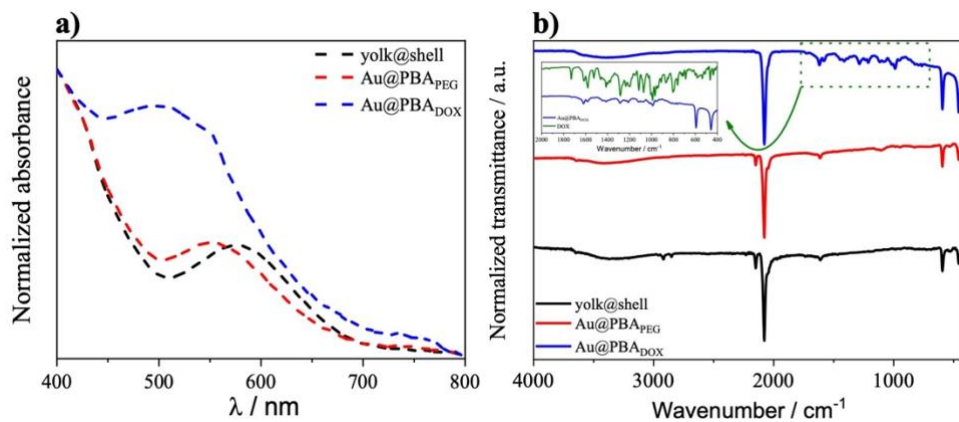


Figure 4.12: (a) Normalized UV-Vis absorbance and (b) ATR-FTIR spectra of yolk@shell NPs with surface modifications and DOX loading.

In addition, to verify the colloidal stability of the NPs, DLS measurements were performed to study the size distribution of yolk@shell NPs functionalized with SH-PEG-COOH over time span of 48 hours. As

shown in Figure 4.13, the *yolk@shell* NPs also maintains stable hydrodynamic diameters and narrow size distributions over 48 hours.

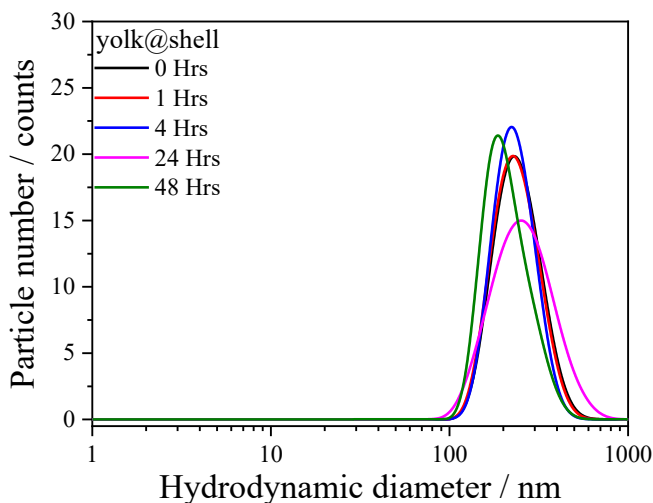


Figure 4.13: DLS graph of *yolk@shell* NPs after functionalization with SH-PEG-COOH displaying over time colloidal stability.

Yolk@shell: DOX loading.

After functionalizing the NPs, drug loading was carried out by redispersing them in a DOX solution as previously performed for the *core@shell* NPs. After successful loading of DOX, UV-VIS spectra were recorded. The third spectrum (blue) in Figure 4.12 (a-b) shows the DOX-loaded *yolk@shell* NPs. A noticeable peak was observed, confirming a higher amount of DOX in the NPs. Subsequently the UV-VIS measurements, ATR-FTIR analysis was conducted to qualitatively confirm the presence of DOX, focusing on the fingerprint region ($400\text{--}1600\text{ cm}^{-1}$). Characteristic DOX peaks were observed, with a stronger presence in the NPs. This indicated that

the yolk@shell NPs have a higher DOX loading efficiency, Likely due to either enhanced surface interactions, a larger surface area, or the presence of a unique cavity compared to the core@shell NPs.^{225,226}

As before, DOX loading of yolk@shell NPs was estimated by measuring the maximum absorbance at 480 nm of the supernatant obtained after centrifugation of the DOX-loaded NPs. The loading efficiency was calculated to be 50%.

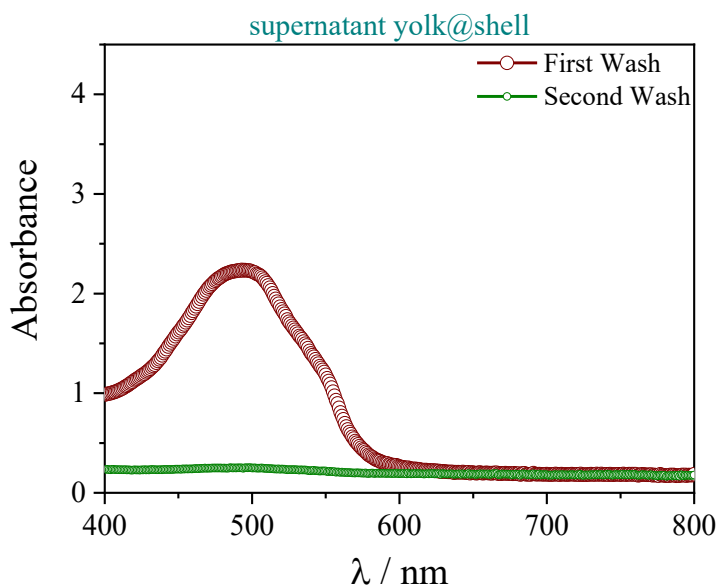


Figure 4.14: UV-Vis spectra of DOX supernatant collected from yolk@shell NPs.

Interestingly, yolk@shell exhibited an excellent loading of 50%. This loading efficiency was further validated by breaking down the nanostructures using DMSO. Au@PBA yolk@shell containing DOX was dispersed in DMSO and sonicated at 37°C for 1 h. Afterward, the mixture was centrifuged, and the absorbance of the supernatant was measured (see Figure 4.15). Using the DOX calibration curve, the DOX content in the NPs was estimated to be

47%, which is consistent with the value obtained in the supernatant after the loading.

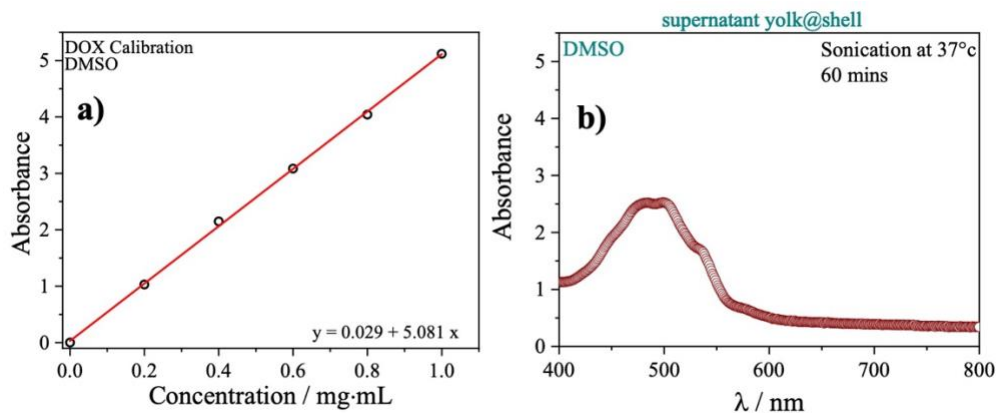


Figure 4.15: (a) Calibration curve of DOX concentration vs absorbance in DMSO. (b) UV-Vis absorbance spectra of the DOX supernatant following the complete degradation of yolk@shell NPs in DMSO.

Considering that yolk@shell NPs contains more amount of DOX after the loading as compared to the core@shell NPs, they were selected as the better structure to use as nanocarrier. Furthermore, as previously seen in Figure 4.9 (b), since traces of Au were observed in the shell, taking in to account that thin Au shells with a cavity can result in NIR plasmonic properties,²²⁷ we checked the NIR region in the UV-Vis of a solution containing 50 μg , 100 μg , 250 μg and 500 $\mu\text{g}/\text{ml}$ of yolk@shell NPs and compared them with same concentrations of core@shell, pristine $\text{Mn}^{\text{II}}\text{Fe}^{\text{II}}$ and $\text{Mn}^{\text{II}}\text{Fe}^{\text{III}}$ PBA NPs. As displayed in Figure 4.16 (a-d), we observed a slight absorbance peak at 808 nm for the yolk@shell NPs, which could potentially generate photothermal heat. The presence of this absorbance peak can be attributed to the Au deposited in the shell, as a thicker shell surrounding a cavity can enhance absorbance.²²⁷ On the other hand, no significant NIR absorbance was noticed for either core@shell or the pristine PBAs.

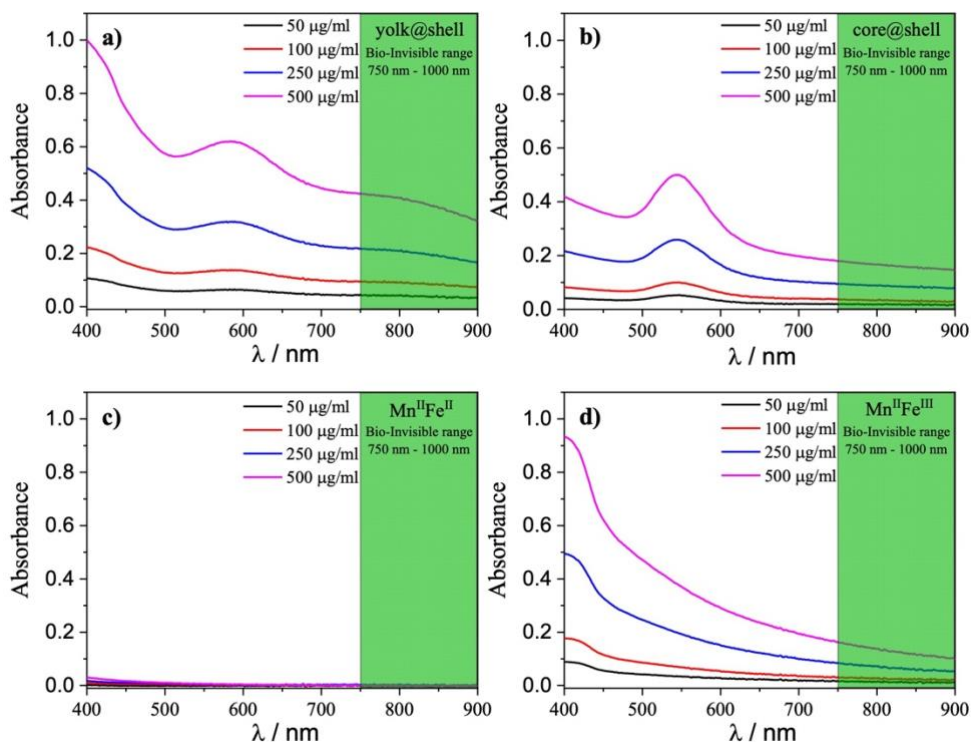


Figure 4.16: UV-Vis absorbance spectra at varying concentrations, highlighting absorbance in NIR region for (a) yolk@shell (b) core@shell (c) $\text{Mn}^{\text{II}}\text{Fe}^{\text{II}}$ and (d) $\text{Mn}^{\text{II}}\text{Fe}^{\text{III}}$ PBA NPs.

Yolk@shell: Photothermal Effect.

Indeed, the localized heating of the NPs may enhance DOX release through structural destabilization and causing hyperthermia.^{228,229} To investigate this, a series of experiments were conducted using an NIR laser with an 808 nm wavelength. Firstly, different concentrations of yolk@shell NPs were irradiated using a NIR laser for 10 minutes with a power of 0.7 W (2 W/cm^2) and compared with same concentrations of core@shell, pristine $\text{Mn}^{\text{II}}\text{Fe}^{\text{II}}$ and $\text{Mn}^{\text{II}}\text{Fe}^{\text{III}}$ PBA NPs. The findings displayed in Figure 4.17 (a-d) are in agreement with the UV-Vis absorbance measurements of the NPs. A

significant temperature increase was observed by the yolk@shell NPs reaching a maximum ΔT of $\sim 21^\circ\text{C}$ at a concentration of $500\ \mu\text{g/mL}$ within 10 minutes. Conversely, core@shell, the pristine $\text{Mn}^{\text{II}}\text{Fe}^{\text{II}}$ and $\text{Mn}^{\text{II}}\text{Fe}^{\text{III}}$ PBA NPs exhibited negligible temperature increases (less than 8) across all tested concentrations.

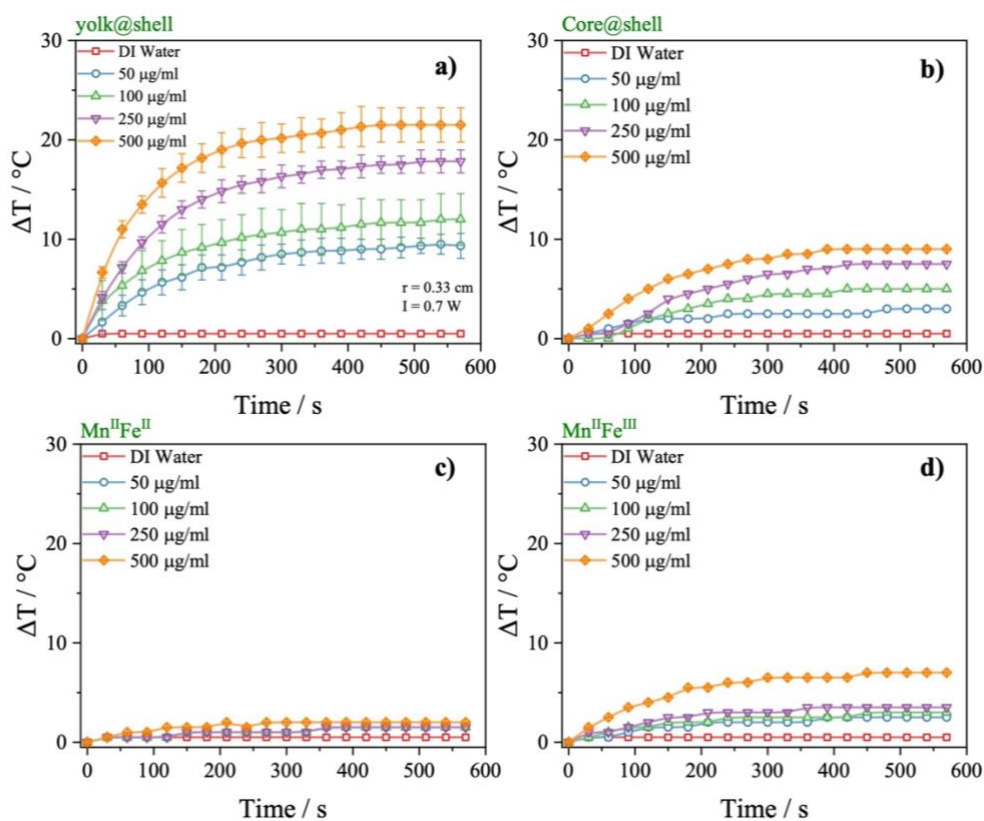


Figure 4.17: Photothermal heating profiles at varying concentrations under NIR laser irradiation at power of $0.7\ \text{W}$ for (a) yolk@shell compared with (b) core@shell (c) $\text{Mn}^{\text{II}}\text{Fe}^{\text{II}}$ and (d) $\text{Mn}^{\text{II}}\text{Fe}^{\text{III}}$ PBA NPs.

In parallel, yolk@shell solution with concentration of $50\ \mu\text{g/mL}$ was irradiated for a time span of 10 min with varying power (400 mW, 500 mW, 700 mW, 850 mW and 1.36 W) to observe how the laser power affects the heat generated by the NPs. A pronounced power dependent increase in

temperature was observed, with the highest power (1.36 W) resulting in a substantial temperature rise up to $\sim 30^\circ\text{C}$. At powers of 400 mW and 500 mW moderate temperature increase was observed, which demonstrated a clear correlation between laser power and photothermal efficiency.

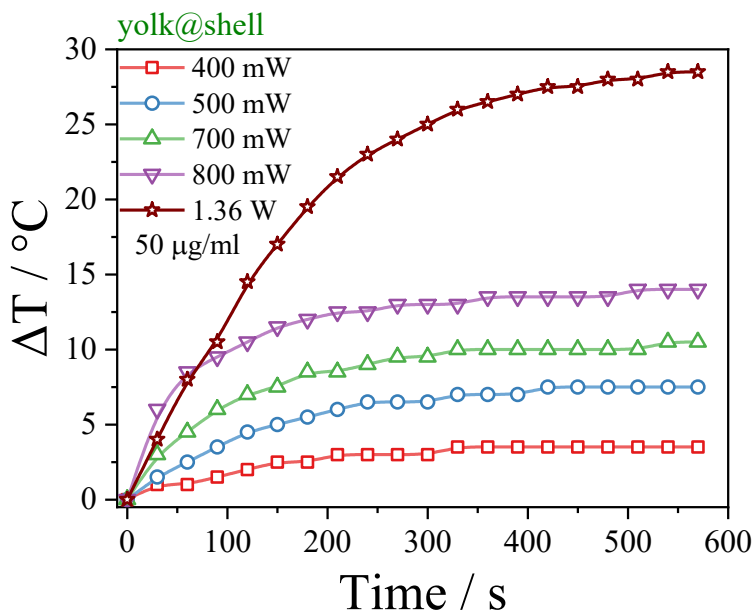


Figure 4.18: Photothermal heating profile at varying power for 50 $\mu\text{g/mL}$ yolk@shell NPs.

Furthermore, based on our data obtained we calculated the photothermal conversion efficiency of the yolk@shell NPs using the following equation.

$$\eta = \frac{hS(T_{\max} - T_{\text{surr}})}{I(1 - 10^{-A_{808}})}$$

Where η is the photothermal conversion efficiency, I is the incident laser power, $T_{\max}$ and T_{surr} are initial and final equilibrium temperature of the solution, A is the absorbance measured at 808 nm, and h is the heat transfer coefficient while S is the surface area of the container. hS can be derived according to the following equation.

$$hS = \frac{\sum m_i C_i}{\tau_s}$$

Where m represents the mass, and C represents the heat capacity of the solvent that is 4.2 Jg^{-1} in case of DI water. τ_s is the time constant obtained by the exponential decay fit of the data obtained while the cooling of the system displayed in Figure 4.19. For exponential decay the following equation is used.

$$\Delta T(t) = \Delta T_{\max} e^{-\frac{t}{\tau_s}}$$

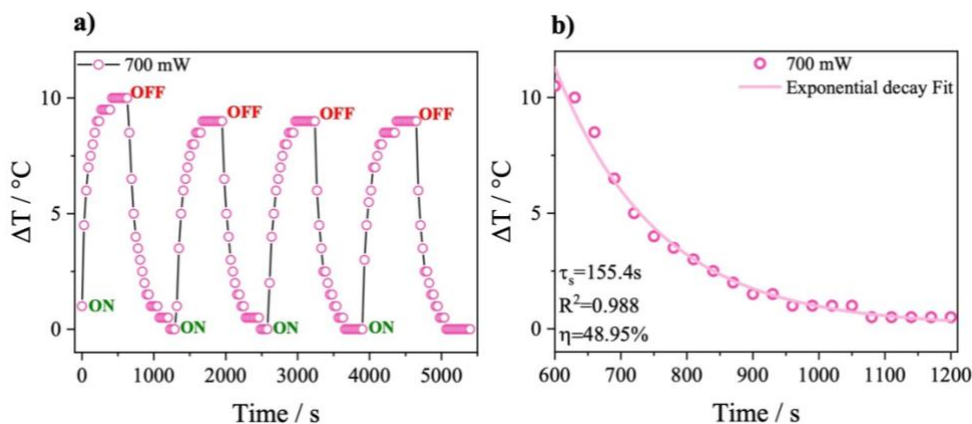


Figure 4.19: (a) Cyclic heating and cooling curves demonstrating the photothermal stability. (b) Exponential decay fit of cooling curve.

Finally, the η was calculated using the formula defined earlier to be 48.95%. The obtained efficiency indicates the material's effective conversion of absorbed NIR light into thermal energy.

Yolk@shell: DOX Release.

Furthermore, we investigated the *in-vitro* release behavior of our novel nanocarrier, 1 mg of the NPs was immersed in a 1 ml of PBS solution

of pH 7 and pH 5 at 37°C. The absorbance values were collected at different time intervals for 24 h to monitor the release behavior. Additionally, a different set of NPs in PBS buffer solution of pH 7 and pH 5 at 37°C with same concentration was irradiated for 10 min using a power of 0.7 W each and the absorbance values were collected at different time intervals. Prior to each absorbance measurement, the NP solutions were centrifuged at 13,000 rpm for 2 minutes, and the supernatants were collected. Fresh PBS buffer solution was then added to the NPs, and the solutions were maintained at 37°C. This process was repeated before each absorbance measurement. PBS buffer solution of pH 7 and pH 5 were used to simulate physiological and mildly acidic tumor microenvironments, respectively. While pH 7 represents normal physiological conditions, pH 5 mimics the acidic conditions found in tumor tissues and intracellular compartments such as lysosomes. These conditions enable the evaluation of the pH-responsive release of DOX from the NPs.

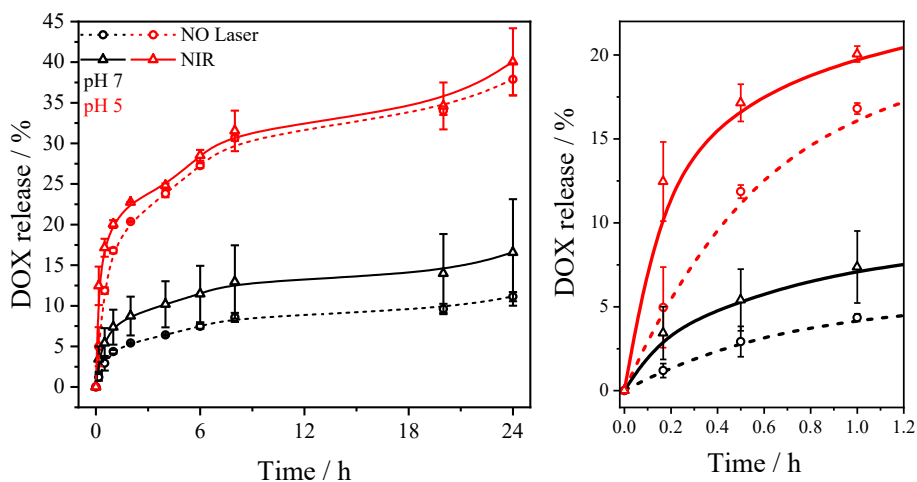


Figure 4.20: (left) cumulative release over 24 hours of DOX from yolk@shell NPs over time at pH 7 and pH 5, with 10 minutes of NIR laser irradiation and without. (right) the release behavior within the first hour.

Figure 4.20 illustrates the in-vitro release of DOX from *yolk@shell* NPs under varying conditions, including pH 7 and pH 5, with 10 minutes of NIR laser irradiation and without. Figure 4.20 (left) depicts the cumulative release over 24 hours. DOX release is significantly enhanced in acidic condition as compared to physiological conditions. A maximum of 40% DOX release is observed after 24 hours at pH 5 while at pH 7 the maximum release is ~10 – 15%. This difference is attributed to the destabilization of the MnFe shell structure in acidic environments. On the other hand, Figure 4.20 (right) shows the initial release within the first hour. After 10 min of NIR irradiation at pH 5, a rapid release of ca. 20% was observed, which is 150% more than without irradiation. This rapid initial release is associated with the temperature increase induced by photothermal activation, which accelerates the destabilization of the *yolk@shell* structure.^{228,229} However, by the end of the 24-hour period, the release values under both conditions (with and without irradiation) become quite similar. This suggests that photothermal activation plays a critical role in the early stages. This rapid and sustained release behavior underscores the dual stimuli-responsive nature of the NPs. In addition, these results highlight the effectiveness of combining pH sensitivity and photothermal activation for controlled and efficient drug release.

Yolk@shell: Cytotoxicity Assays.

As mentioned previously, the synthesis of *yolk@shell* NPs was developed to address the low drug loading of *core@shell* NPs and to avoid cell toxicity caused by the counterion Cs. Since these NPs demonstrated good colloidal stability, efficient DOX loading and 20% DOX release after just 10 minutes of photothermal activation, they emerged as strong candidates for

further testing. Therefore, the next phase of the study focused on evaluating their effects on cancer cells. For this purpose, A549 and HeLa cell lines were chosen. HeLa cells (from human cervical cancer) are known for their rapid proliferation and robust growth. They are widely used in drug efficacy studies and provide a reliable model for assessing cancer cell responses to treatment.

TEM was used to assess the intracellular localization of a 50 $\mu\text{g/mL}$ *yolk@shell* NPs in A549 and HeLa cells after incubation for 4 hours. In Figure 4.21 (a) a well distribution of *yolk@shell* NPs can be observed within the cytoplasm of A549 cells, showing predominant localization in vesicular structures such as endosomes or lysosomes. On the other hand, the nucleus appears to be intact with no observable penetration of NPs, while mitochondria remain dispersed and structurally preserved, indicating no significant disruption of cellular organelles. Similarly, the high magnification image confirms the presence of *yolk@shell* NPs within vesicles of A549 cell, which exhibits strong contrast suggesting efficient cellular uptake via endocytosis. Similarly, in HeLa cells, *yolk@shell* NPs were successfully internalized and confined to vesicular compartments as can be seen in Figure 4.21 (b). The nucleus and mitochondria of HeLa cell are also seen to remain undisturbed, which indicates no apparent cytotoxic effects or structural interference within the first hours of internalization.

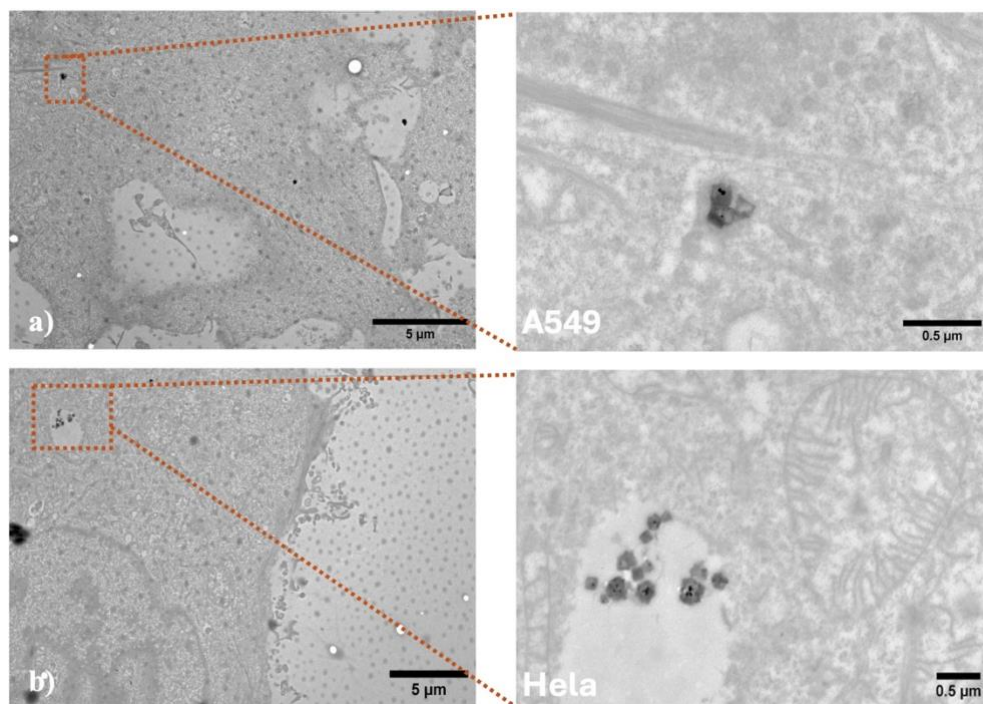


Figure 4.21: TEM images of yolk@shell NPs in (a) A549 and (b) HeLa cells after 4 hours of incubation.

As internalization was confirmed by TEM images, we further evaluated the toxicity of the NPs and the effect of DOX. A549 and HeLa cells were treated with different concentrations of yolk@shell NPs, both with PEG and with DOX. Cell viability was measured after 24 hours. As shown in Figure 4.23, the red bars represent the Au@PBA yolk@shell PEG NPs without DOX while blue bars correspond to the same NPs but loaded with DOX. For A549 cells, the cytotoxicity of the NPs without DOX was not significant, as cell viability remained above 80% even at high concentrations (100 $\mu\text{g/mL}$). However, for HeLa cells, the toxicity was more pronounced, with cell viability dropping below 70% when the NP concentration exceeded 50 $\mu\text{g/mL}$. On the other hand, when the NPs were loaded with DOX, a significant decrease in cell viability was observed for both cell lines. The

difference in cytotoxicity compared to the unloaded NPs was most noticeable at a concentration of 50 $\mu\text{g}/\text{mL}$. For A549 cells, the difference in viability was almost 30%, and for HeLa cells, it was also around 30%.

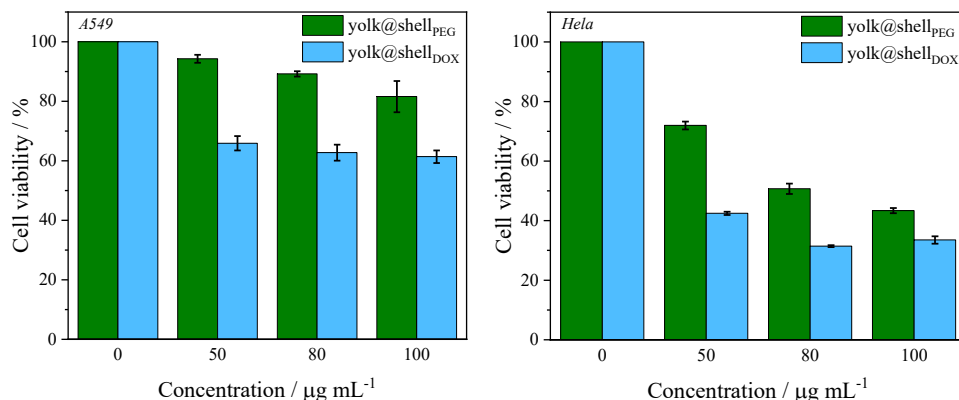


Figure 4.22: Cytotoxicity assays. Cell viability of A549 (left) and HeLa (right) cells after 24-hour treatment with varying concentrations of yolk@shell_{PEG} and yolk@shell_{DOX}.

Therefore, based on the previous findings, a concentration of 50 μg of yolk@shell_{PEG} and yolk@shell_{DOX} were selected for further experiments that involve irradiation with a NIR laser. Before using the NIR laser on cells treated with NPs, we evaluated the cell viability of A549 and HeLa cells by irradiating them with an 808 nm NIR laser at different power, with a maximum power of 1.36 W (4 W/cm²) for 5 minutes. As shown in Figure 4.23, cell viability remained high, with only slight effects at higher power densities. Therefore, we selected a power of 700 mW (2 W/cm²) as the optimal condition for further studies.

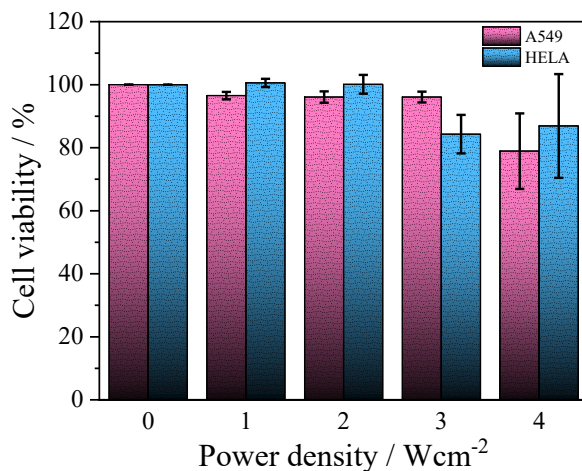


Figure 4.23: Effects of NIR 808 nm laser power densities on A549 and HeLa cell viability.

After treating the cells with yolk@shell NPs containing DOX, they were irradiated for 5 minutes using an 808 nm NIR laser at a power of 700 mW (2 W/cm²) (Figure 4.24). As previously observed, minimal damage was detected in untreated cells under irradiation, while cells treated with unloaded NPs exhibited higher toxicity when exposed to the NIR laser. This pronounced cell death was attributed to the localized heat generated by the NPs due to the excitation of the plasmon resonance band in the NIR region, caused by the gold deposited in the shell during the synthesis of the yolk@shell NPs.

Furthermore, cells treated with DOX-loaded NPs showed a drastic reduction in viability in both A549 and HeLa cells after irradiation. This outcome highlights the synergistic effect of localized heat generation by the NPs and the chemotherapeutic action of DOX, whose release was further facilitated by the photothermal effect, as previously demonstrated in vitro.

Thus, these findings demonstrate the strong potential of yolk@shell Au@MnFe PBA NPs for the development of nanostructures with high stability and low toxicity, capable of acting simultaneously as drug-delivery nanocarriers for chemotherapy and as PTT agents upon NIR irradiation.

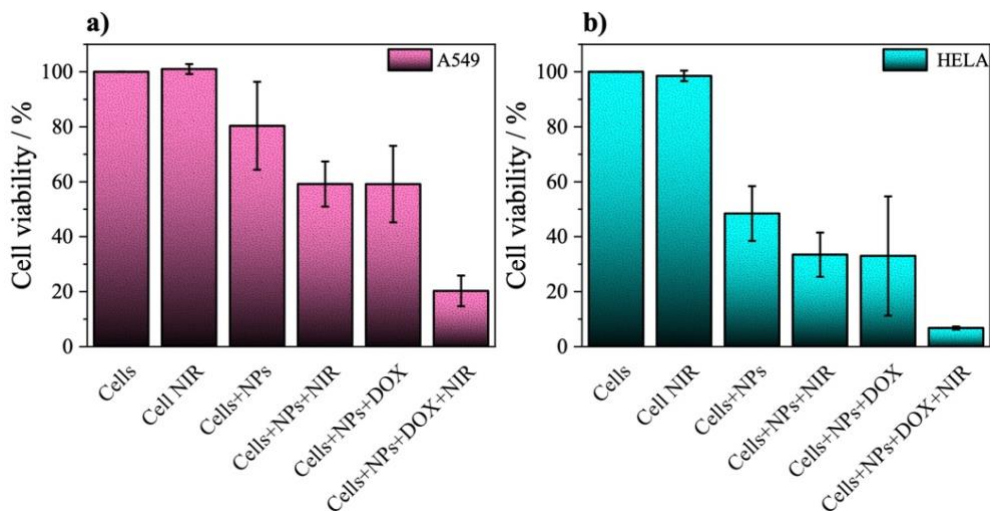


Figure 4.24: Cytotoxicity assays. Cell viability of (a) A549 and (b) HeLa cells under different treatment conditions with respect to yolk@shell NPs.

4.3 Conclusions

In this work, the synthesis, characterization, and application of Au@MnFe PBA nanostructures were explored for pH and NIR laser-responsive drug release. The development of both core@shell and yolk@shell nanostructures was achieved, with yolk@shell NPs demonstrating superior drug-loading capacity, enhanced colloidal stability, and improved release behavior. The formation of the yolk@shell structure was attributed to the leaching of Fe³⁺ species, leading to the creation of a hollow cavity, which ultimately contributed to a higher DOX loading efficiency (50%) compared to core@shell NPs (19%). UV-Vis spectroscopy and TEM imaging successfully validated the synthesis of yolk@shell NPs, while ATR-FTIR and PXRD provided insights into their chemical composition. Drug release studies revealed a pH-dependent release profile, with further acceleration under NIR laser irradiation, underscoring the potential for controlled and stimuli-responsive therapy. In vitro studies in A549 and HeLa cells demonstrated efficient NP internalization and cytotoxic effects. Yolk@shell NPs exhibited lower intrinsic toxicity compared to core@shell NPs. However, a significant reduction in cell viability was observed upon treatment with DOX-loaded yolk@shell NPs. Moreover, a synergistic effect between photothermal therapy and chemotherapy was evident, resulting in enhanced cell death.

These findings highlight the potential of yolk@shell Au@MnFe PBA nanostructures as multifunctional platforms for cancer therapy. Their combination of pH-responsive drug release, photothermal therapy, and high drug-loading capacity makes them promising candidates for future biomedical studies.

4.4 Experimental section

4.4.1 Materials

All chemical reagents were purchased and used without further purification. Chloroauric acid, sodium citrate tribasic dihydrate, 4-mercapto pyridine 95%, cesium chloride, manganese (II) chloride tetrahydrate, potassium hexacyanoferrate, Doxorubicin hydrochloride (pharmaceutical secondary standard), Phosphate buffered saline (PBS), Sodium Citrate and HS-PEG3500-COOH were purchased from Sigma-Aldrich. Ultrapure water (18.2 M Ω) was used in the following syntheses.

4.4.2 Synthesis of NPs

4.4.2.1 Au NPs:

The synthesis was performed following the standard Turkevich's method²³⁰, with a slight modification. A 0.25 mM HAuCl₄ solution (100 mL) was reduced by adding 2.5 mM of sodium citrate to the boiling solution with constant stirring to maintain a homogenous solution. A faint grey color was observed in the solution for approximately one minute, the solution was left for 20 minutes with heating on the stirring plate. As the deep wine color was noticed, the solution was kept aside until cooled to room temperature. Note that the color change indicates that the colloidal Au is being produced.

4.4.2.2 Au@4-MPy NPs:

In 100 mL of Au spheres (concentration of 0.25 mM), 60 μ L of 1 mM 4-MPy was added and stirred for 20 minutes to allow the 4-MPy to interact

with the surface of Au NSp. Then, the solution was washed with water (8000 rpm, 20 minutes) to remove the excess citrate and 4-MPy.

4.4.2.3 core@shell NPs:

For the growth of the core@shell NPs, the following precursor solutions were prepared: i) 40 ml solution containing 1×10^{-3} mol of $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, and ii) 40 ml solution containing 1×10^{-3} mol of $\text{K}_3[\text{Fe}(\text{CN})_6]$ and 2×10^{-3} mol of CsCl . A total of 1 mL of solution (i) was added slowly into the colloidal Au@4-MPy NP solution under stirring and at an addition rate of 100 μL per 20 seconds, after 10 minutes of moderate stirring 1 mL of sol (ii) was then added with the same addition rate as sol (i). The final solution was left to stir overnight and centrifuged at 9500 rpm for 20 minutes thrice (using DI water).

4.4.2.4 yolk@shell NPs:

For the growth of the yolk@shell NPs, the following precursor solutions were prepared: i) 40 ml solution containing 1×10^{-3} mol of $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, and ii) 40 ml solution containing 1×10^{-3} mol of $\text{K}_3[\text{Fe}(\text{CN})_6]$ and 1×10^{-3} mol of CsCl . A total of 1 mL of solution (i) was added slowly into the colloidal Au@4-MPy NP solution under stirring and at an addition rate of 100 μL per 20 seconds, after 10 minutes of moderate stirring 1 mL of sol (ii) was then added with the same addition rate as sol (i). The final solution was left to stir for 24 hours. The final solution was centrifuged at 9500 rpm for 20 minutes thrice (using DI water). Aliquots were collected at different time intervals for characterization

4.4.2.5 Surface functionalization of core@shell and yolk@shell NPs:

The collected precipitates collected from core@shell and yolk@shell were further dried under vacuum. 1 mg of both were separately redispersed in 2 ml of DI water containing 7.64×10^{-3} mol and 5.41×10^{-3} mol of SH-PEG3500-COOH respectively. Then, the solution was kept overnight under moderate stirring followed by centrifugation twice at 9500 rpm for 10 min for the removal of excess or unbounded PEG.

4.4.2.6 DOX Loading:

The collected precipitate was dried in order to obtain the powder form for weighing the material. DOX loading was achieved by adding 1mg/1ml of DOX in H₂O to an equal weight/volume of the precipitate of core@shell_{PEG} and yolk@shell_{PEG} (1mg/1ml). Since DOX·HCl contains equimolar ratios of DOX and HCl, the amount of HCl in 1 mg of DOX·HCl was calculated to be 1.72×10^{-6} moles. To neutralize the HCl, 1.72 μ L of 1 M NaOH was added to the solution. The solution was kept in a thermomixer by Thermo Fischer at 2000 RPM for 24 hours under dark. After 24 hours the solution was centrifuged twice at 13000 RPM to remove the unloaded DOX. The supernatant containing unloaded DOX was kept and subjected to UV-Vis for the calculation of loaded DOX.

An aliquot of the precipitate from each stage was kept for further characterization.

4.4.2.7 DOX-Release:

The release of DOX in yolk@shell was investigated through four experiments at pH 7 and pH 5, both with and without laser treatment. The DOX precipitate was evenly divided into four vials, each containing 1 mg of

the compound. Each vial was supplemented with 1 ml of PBS solution: two vials at pH 7 and two at pH 5. An initial aliquot of the PBS solution was measured at time zero to establish a baseline for DOX release. Vial A and Vial B containing yolk@shellDOX at pH 7 were subjected to DOX release experiments with and without NIR laser treatment for 10 minutes, respectively. At different time intervals the solutions were followed by centrifugation at 13,500 RPM for 2 minutes. The collected supernatant was analyzed using a UV-Vis spectrometer to determine the absorbance value and quantify the DOX release. While each time the supernatant was redispersed in fresh PBS for further release.

The absorbance of each supernatant after centrifugation was measured at 480 nm using a UV-vis spectrophotometer and cumulative graph was plotted against time.

4.4.3 Cell culture conditions

4.4.3.1 Cytotoxicity Assay:

Toxicity in A549 and Hela was measured at different samples and controlled concentrations using an MTT assay. Firstly, cells were trypsinized, counted, and resuspended in complete medium to achieve 1×10^5 cells/ml concentration. Using a multichannel pipette, 100 μ l of this cell suspension containing 10 000 cells was dispensed into each well of a 96-well plate. The plates were incubated at 37°C in a humidified atmosphere containing 5% CO₂ for 24 hours to facilitate cell attachment and growth. After 24 hours a positive control, dimethyl sulfoxide (DMSO), and various concentrations of the test samples were prepared and distributed into a multi-well reservoir to facilitate the subsequent plate dispensing, followed by aspiration of the existing cell

medium from 96-well plates. 50 ml of the prepared samples and control were added to the respective wells. The plates were then incubated at 37°C in a 5% CO₂ atmosphere for the three desired periods of exposure (2 hours, 4 hours and 24 hours). The MTT stock solution (5 mg/ml) was prepared in PBS, vortexed, sonicated for 5 minutes, and sterilized by filtration through a 0.22 µm filter. It was stored at -20°C protected from light. By diluting the stock solution in the complete medium with a ratio of 1:10, the MTT working solution was prepared, followed by aspiration of the medium from the wells at designated time points, with the addition of 50 µl of MTT working solution. Then, plates were incubated for 2 hours at 37°C in a 5% CO₂ atmosphere. Following incubation, the MTT solution was aspirated, and 100 µl of isopropanol was added to each well to dissolve the formazan crystals. The plates were gently shaken to ensure complete stabilization. Absorbance was measured at 570 nm using a microplate reader, with a reference wavelength of 650 nm recorded to correct for any background absorbance.

4.5 Physical characterization

4.5.1 UV/Vis Spectroscopy:

UV-vis absorption spectra were recorded on Thermofischer multiskan skyhigh microplate spectrophotometer from 300 to 900 nm range, using Thermoscientific clear flat-bottom immune nonsterile 96-well plates. 300 μ L of the sample was collected in the well plates for these measurements.

4.5.2 Dynamic Light Scattering:

Dynamic Light Scattering (DLS) were performed with a Zetasizer Nano ZS instrument (Malvern Instruments Ltd.).

4.5.3 Transmission Electron Microscopy:

TEM studies were carried Hitachi HT7800 120 kV and a Technai G2 F20 microscope operating at 200 kV. Samples were prepared by dropping suspensions on lacey formvar/carbon copper grids (300 mesh).

4.5.4 Attenuated total reflectance Fourier-transform Infrared Spectroscopy:

Spectra were collected in an Agilent Cary 630 FTIR spectrometer in the 4000–500 cm^{-1} range in the absence of KBr pellets.

4.5.5 Powder X-Ray Diffraction:

PXRD patterns were collected in a PANalytical Empyrean diffractometer using copper radiation ($\text{Cu K } \alpha \lambda = 1.5418 \text{ \AA}$) with an PIXcel detector, operating at 40 mA and 45 kV at room temperature.

4.5.6 *In Vitro* Laser Irradiation:

For *in vitro* laser irradiation, an MDL-H-808/5W infrared diode laser with a central wavelength of 808 nm was used. The laser operated in a continuous wave mode, with a delivered output power of maximum 1.35 W (4 W/cm^2). The laser output was coupled into a Thorlabs FT038 optical fiber to ensure precise and uniform light delivery to the NPs.

4.5.7 *In Vitro* Photothermal detection:

Photothermal heating profiles were collected using the lascar EI-USB-TC-LCD thermocouple USB data logger connected to a type K thermocouple.

5 General Conclusions

This thesis explores the development of hybrid core@shell nanoparticles (NPs) with a gold core and a Prussian Blue Analogue (PBA) shell, designed to enhance the interactions between both components and achieve novel or improved properties. These heterostructures were obtained by partially functionalizing Au NPs with 4-MPy to enable the subsequent growth of the PBA shell. In particular, the research conducted in this work examines these heterostructures from three key perspectives: catalysis, magnetism, and biomedicine.

The most relevant overall conclusions that can be extracted are the following:

- The developed synthetic protocol enables the preparation of Au@PBA core@shell NPs with different gold morphologies and tunable PBA composition and thickness. This versatility allows for optimizing their properties depending on the application. In this regard, three different PBA shells were prepared: CsNiFe for catalysis, CsCoFe for magnetism and CsMnFe for biomedicine.
- The presence of an Au core induces structural distortions and polycrystallinity within the PBA shell, with both effects becoming more pronounced as the anisotropy of the gold core increases. These changes enhance the electrocatalytic properties of the PBA shell of CsNiFe, enabling tunable catalytic activity based on the core morphology.
- The thickness of the CsCoFe PBA shell directly influences photomagnetic activity, with thicker shells exhibiting enhanced

photomagnetic behavior due to a higher concentration of photo-switchable species. This correlation underscores the importance of precise thickness control in optimizing photomagnetic performance.

- By modifying the synthesis, it was possible to create an internal cavity between the Au core and the CsMnFe shell resulting in yolk@shell NPs. Thanks to this internal cavity, yolks@shell NPs can load a larger drug amount (and thus, higher drug release) compared to core@shell NPs. These findings highlight the potential of yolk@shell NPs as a theragnostic nanoplatform.

6 Resumen de la Tesis

Los nanomateriales híbridos son materiales a escala nanométrica que combinan dos o más componentes distintos para integrar o mejorar propiedades físicas, químicas o biológicas. Entre ellos, las nanopartículas híbridas formadas por oro y por materiales análogos al Azul de Prusia (PBAs) han demostrado un enorme potencial en una gran variedad de aplicaciones. Esto se debe a que esta combinación aprovecha la sinergia entre la alta estabilidad química, conductividad y propiedades ópticas del oro, junto con la versatilidad estructural, capacidad de ajuste químico y características catalíticas, magnéticas y biológicas de los PBAs. Además de mejorar propiedades individuales, la interacción entre ambos materiales puede dar lugar a nuevas funcionalidades emergentes, ampliando su aplicación en sensores, catálisis, fotomagnetismo y biomedicina.

Por tanto, en esta tesis hemos desarrollado un protocolo sintético basado en la química coloidal para combinar estos materiales en heteroestructuras de tipo núcleo@recubrimiento (core@shell), permitiendo modular tanto la morfología del núcleo de oro como la composición y el tamaño del recubrimiento de PBA. Hemos estudiado las propiedades emergentes de estas nanoestructuras y su potencial en aplicaciones catalíticas, magnéticas y biomédicas.

Introducción

El diseño de nanomateriales híbridos ha abierto nuevas oportunidades en campos como la catálisis, el magnetismo y la administración de fármacos. En particular, los PBAs han despertado un gran interés debido a su versatilidad estructural, propiedades ajustables y facilidad para integrarse con otros materiales a escala nanométrica. Su estructura de red abierta permite modificar su composición química, lo que posibilita el ajuste de sus propiedades magnéticas, catalíticas y electroquímicas. Además, su capacidad para alojar iones y moléculas los hace atractivos en almacenamiento energético, sensores y biomedicina.

Para potenciar la eficiencia de los PBAs en aplicaciones específicas, a menudo es necesario mejorar sus propiedades intrínsecas o incorporar nuevas funcionalidades. En este contexto, la combinación de PBAs con nanopartículas de oro (AuNPs) ha demostrado ser una estrategia altamente efectiva. Las AuNPs presentan una estabilidad química excepcional, propiedades ópticas únicas, control preciso de tamaño y forma, y una amplia gama de aplicaciones. En particular, su integración con PBAs no solo mejora la conductividad térmica y eléctrica, sino que también introduce efectos ópticos adicionales a través de la resonancia de plasmones superficiales localizados (LSPR), lo que amplía las posibles aplicaciones en sensores ópticos, fotocatalisis y liberación controlada de fármacos.

Entre las posibles heteroestructuras que pueden formarse al combinar estos materiales en la nano escala, las de tipo core@shell destacan por la intensa interacción entre los dos materiales, lo que puede generar nuevas propiedades o mejorar las ya existentes. El estrecho contacto existente entre el núcleo de oro y el recubrimiento de PBA favorece la aparición de efectos sinérgicos,

permitiendo el desarrollo de materiales híbridos con funcionalidades avanzadas y mejor rendimiento en diversas aplicaciones tecnológicas. Esta interacción entre el núcleo y el recubrimiento puede implicar acoplamientos electrónicos, estructurales y magnéticos, dando lugar a nuevas o mejores propiedades que van más allá de la simple suma de las propiedades individuales de cada material.

Sin embargo, la preparación de estructuras Au@PBA presenta desafíos sintéticos significativos. Uno de los principales problemas es que el cianuro utilizado en la síntesis de los PBAs puede atacar el oro (oxidándolo y disolviéndolo), lo que limita la estabilidad de las nanopartículas coloidales de oro y complica la formación de una cáscara uniforme de PBA. Aunque existen muchos protocolos sintéticos para la obtención de Au@PB (utilizando Azul de Prusia (PB)), la formación de Au@PBA sin reducir el estado de oxidación del mismo y sin utilizar condiciones agresivas sigue siendo poco explorada. Además, el uso de nanopartículas de oro anisotrópicas como núcleo añade una capa de complejidad, ya que las formas irregulares de los núcleos pueden ser atacadas fácilmente por estos compuestos basados en cianuros. Por lo tanto, es necesario desarrollar más métodos sintéticos para superar estos obstáculos y lograr una integración eficiente entre el oro y los PBAs.

Objetivos

El principal objetivo de esta tesis es la síntesis, caracterización y aplicación de nanopartículas híbridas de Au@PBA con el fin de optimizar sus propiedades y explorar su potencial en diferentes campos tecnológicos. Los objetivos específicos incluyen:

Objetivo del Capítulo 1: Introducir el contexto general de los nanomateriales híbridos y su importancia en aplicaciones avanzadas. Se describen los fundamentos de los PBAs y las nanopartículas de oro, explicando su relevancia en campos como la catálisis, el magnetismo y la biomedicina. Asimismo, se describen las heteroestructuras más relevantes y las síntesis de Au@PBA desarrolladas hasta la fecha.

Objetivo del Capítulo 2: Presentar la metodología empleada para la síntesis de nanopartículas core@shell de Au@PBA (con CsNiFe como el PBA). En este capítulo, se detallan las condiciones experimentales y los parámetros clave utilizados en la fabricación de estos nanomateriales, asegurando la reproducibilidad y estabilidad de las muestras. También se lleva a cabo una caracterización exhaustiva de las propiedades estructurales, ópticas, magnéticas y catalíticas de las nanopartículas híbridas. Además, se analiza la eficiencia catalítica de las nanopartículas Au@PBA en reacciones de evolución de oxígeno, comparando su desempeño con catalizadores convencionales.

Objetivo del Capítulo 3: Estudiar las propiedades fotomagnéticas de las nanopartículas híbridas Au@PBA. Se investiga los cambios estructurales y magnéticos inducidos al sobrecrecer un compuesto de CsCoFe (PBA) alrededor de nanopartículas de oro. Este capítulo se centra en el análisis de la

respuesta fotomagnética al modificar el espesor del recubrimiento de PBA y al disolver el core central del oro.

Objetivo del Capítulo 4: Explorar la aplicabilidad biomédica de las nanopartículas híbridas. En concreto, se estudia su capacidad para la administración controlada de fármacos y se investiga su potencial en terapia fototérmica mediante irradiación con luz infrarroja cercana (NIR). Este capítulo examina la interacción entre las nanopartículas Au@PBA (usando CsMnFe) y sistemas biológicos, evaluando su estabilidad en medios fisiológicos y su capacidad para liberar fármacos de manera controlada.

Metodología

Para la síntesis, caracterización y evaluación de las nanopartículas híbridas, se siguió un enfoque experimental en varias fases que garantizó la reproducibilidad y optimización de sus propiedades fisicoquímicas. La metodología incluyó:

Síntesis de nanopartículas híbridas Au@PBA: Los pasos seguidos para preparar estas heteroestructuras fueron:

1) Síntesis de nanopartículas de oro (AuNPs): Se sintetizaron nanopartículas de oro con diferentes morfologías (esferas, cilindros (nanorods) y estrellas (nanostars)) mediante reducción química controlada del tetracloruro de oro (III) (HAuCl₄). Se utilizó citrato de sodio como agente reductor y estabilizador para obtener nanopartículas esféricas de oro. Para las formas anisotrópicas, se siguió un método de crecimiento mediado por semillas. Para la formación de nanorods, la reducción de la sal de oro se da en una disolución conteniendo ácido ascórbico, nitrato de plata y bromuro de

cetiltrimetilamonio (CTAB). En el caso de las nanostars, se utilizó un método basado en la reducción de HAuCl_4 en presencia de nitrato de plata y ácido ascórbico, seguido de la estabilización de las estructuras formadas con CTAB.

2) Funcionalización del núcleo de oro: Para facilitar la interacción con la cáscara de PBA, se modificó la superficie de las AuNPs con 4-mercapto piridina (4-MPy). Esta molécula se une a la superficie del oro por medio del azufre del grupo tiol y, a través del nitrógeno de la piridina, permite la coordinación del oro con uno de los precursores del PBA, promoviendo un crecimiento homogéneo alrededor de cualquier forma de oro coloidal.

3) Crecimiento del recubrimiento de PBA alrededor de las nanopartículas de oro: Se llevó a cabo mediante coprecipitación controlada de los precursores del PBA (disoluciones conteniendo 1) NiCl_2 , CoCl_2 , o MnCl_2 y 2) $\text{K}_3\text{Fe}(\text{CN})_6$ y CsCl) en una disolución coloidal de oro. La concentración de reactivos se optimizó para lograr una cobertura uniforme sobre las AuNPs.

Caracterización de las nanopartículas Au@PBA

Para evaluar la estructura y propiedades de las nanopartículas obtenidas, se utilizaron diversas técnicas avanzadas:

- Microscopía Electrónica de Transmisión (TEM y HR-TEM): Se obtuvieron imágenes detalladas para estudiar la morfología, tamaño y espesor del recubrimiento de PBA.
- Espectroscopía de Absorción UV-Vis: Se analizaron los efectos plasmonicos y la absorción característica de los PBAs.
- Difracción de Rayos X en polvo (PXRD): Se utilizó para confirmar y analizar la estructura cristalina de los nanomateriales.

- Espectroscopía de Fotoelectrones de Rayos X (XPS): Se determinó la composición química y los estados de oxidación de los elementos.
- Mediciones Magnetométricas (SQUID): Se estudiaron las propiedades magnéticas bajo diferentes condiciones de temperatura y campo aplicado.
- Voltametría Cíclica: Se empleó para evaluar la eficiencia catalítica de los diferentes core@shells de Au@CsNiFe en la reacción de evolución de oxígeno.
- Medidas eléctricas: Las mediciones se realizaron en una configuración de dos electrodos utilizando electrodos comerciales, con una separación de 2,5 μm . Las nanopartículas se organizaron en el hueco de los electrodos mediante el método de “drop casting” de una suspensión del material.

Evaluación de las propiedades

- Catálisis Electroquímica: Se evaluó la actividad catalítica de las nanopartículas en la reacción de evolución de oxígeno en electrodos de carbono glasificado modificados con Au@CsNiFe, determinando el sobrepotencial y la estabilidad operativa a pH neutro.
- Foto magnetismo: Se estudió el efecto de la irradiación con luz (633 nm) en la respuesta magnética de las nanopartículas basadas en CsCoFe, midiendo cambios en la susceptibilidad.
- Liberación controlada de fármacos: Se encapsuló doxorubicina en la estructura de CsMnFe y se midió su liberación en medios con pH fisiológico y ácido.

- Terapia fototérmica: Se investigó la capacidad de las nanopartículas para generar calor mediante una fuente de irradiación de luz infrarroja cercana (NIR), analizando su eficacia en la conversión de luz en calor.

Resultados y Discusión

Los experimentos realizados confirmaron la formación exitosa de nanopartículas híbridas de tipo core@shell bien definidas, con tamaños controlables y propiedades plasmónicas mejoradas. Estas nanopartículas presentaron una excelente estabilidad coloidal, permitiendo un buen control en el espesor del recubrimiento de PBA. De esta manera, se pueden obtener propiedades ópticas y plasmónicas ajustables.

Además, se observaron los siguientes resultados clave:

Propiedades ópticas mejoradas: La resonancia de plasmones superficiales localizada del oro generó un desplazamiento en los picos de absorción de las nanopartículas híbridas, indicando una fuerte interacción entre el núcleo plasmónico y el recubrimiento de PBA. Se observó que la intensidad y la posición del pico plasmónico pueden ajustarse mediante la variación del espesor del PBA, permitiendo un cierto control de las propiedades ópticas del sistema. Además, el efecto de acoplamiento óptico entre el oro y el PBA sugiere que estas nanopartículas pueden ser utilizadas en aplicaciones magneto ópticas.

Influencia del tamaño y la forma del núcleo de oro: Se evidenció que la morfología de las AuNPs afecta significativamente la nucleación y el crecimiento del recubrimiento de PBA, influyendo en su estructura y, por tanto, en sus propiedades ópticas y catalíticas. En particular, se observó que

los núcleos generan una tensión en el PBA, y además hace que el recubrimiento crezca y se forme con mayor policristalinidad. Estos efectos se ven incrementados en las nanopartículas anisotrópicas (nanorods y nanostars). Estas diferencias estructurales también influyen en la actividad magnética y catalítica. En el caso del PBA de CsNiFe, se observó que, en las nanopartículas con forma de estrella, la actividad catalítica mejora hasta 10 veces en comparación con el PBA sin oro.

Eficiencia catalítica en la reacción de evolución de oxígeno: Se demostró que las nanopartículas Au@PBA tienen una mayor eficiencia en la evolución de oxígeno en comparación con PBAs puros, debido a la sinergia entre la conductividad del oro y las propiedades catalíticas del PBA. Se encontró que la incorporación de AuNPs mejora la transferencia de carga en la superficie del catalizador, reduciendo el sobrepotencial requerido para la reacción.

Influencia del espesor del recubrimiento de PBA en las propiedades fotomagnéticas: Se demostró que el grosor del recubrimiento de PBA tiene un impacto crucial en las propiedades fotomagnéticas de las nanopartículas core@shell. Las nanopartículas con un recubrimiento de PBA más grueso exhiben un aumento significativo en la actividad fotomagnética debido a la mayor cantidad de especies diamagnéticas presentes en el recubrimiento. En cambio, las nanopartículas con un recubrimiento más delgado muestran una menor respuesta fotomagnética, ya que contienen una mayor proporción de especies paramagnéticas. Estos resultados subrayan la importancia del espesor del recubrimiento de PBA en el comportamiento fotomagnético, destacando que un recubrimiento más grueso mejora la respuesta fotomagnética y aumenta la relación ON/OFF. Esto es debido a la mayor contribución de la interfase oro PBA al disminuir el espesor.

Aplicaciones biomédicas: En estas últimas, existe una cavidad entre el núcleo de oro y el recubrimiento, lo que permite incrementar su capacidad para almacenar moléculas en su interior. De este modo, se introdujo en las nanopartículas doxorubicina (DOX), lo que permitió su uso en sistemas de liberación controlada de fármacos y en terapia fototérmica mediada por irradiación con luz infrarroja cercana (NIR). Como esperábamos, en el caso de las nanopartículas tipo *yolk@shell*, la cantidad de DOX almacenada fue superior a la de las *core@shell*. Estudios de liberación en medios con diferente pH indicaron que la doxorubicina es liberada de manera más eficiente en medios ácidos que simulan las condiciones del microambiente tumoral. Por otro lado, la irradiación con NIR mostró un aumento significativo en la temperatura del medio, lo que confirma la capacidad de las nanopartículas híbridas para generar calor y potencialmente inducir la muerte celular por hipertermia. Este incremento en la temperatura también facilita la liberación del fármaco del material híbrido.

Conclusiones

Las principales conclusiones extraídas en esta tesis son:

1. Se ha establecido un protocolo sintético reproducible que permite la preparación de nanopartículas híbridas de tipo *core@shell* Au@PBA con control preciso sobre la composición y el espesor del recubrimiento, lo que posibilita la optimización de sus propiedades en función de la aplicación deseada. Se demostró que la variación de los parámetros de síntesis, como la concentración de los precursores y el tipo de nanopartícula de oro, permite ajustar las propiedades morfológicas y fisicoquímicas de los materiales obtenidos. Este nivel

de control ofrece una ventaja significativa en la producción de nanomateriales diseñados para aplicaciones específicas.

2. Se evidenció que el recubrimiento de PBA experimenta tensiones estructurales inducidas por la presencia del núcleo de oro, lo que influye en sus propiedades fisicoquímicas. Estas tensiones modifican significativamente el comportamiento magnético y catalítico de las nanopartículas híbridas, destacando la importancia de comprender y controlar estos efectos durante el diseño de heteroestructuras. Se determinó que la tensión interna en la estructura del PBA afecta la eficiencia en procesos catalíticos, lo que sugiere que la ingeniería de deformación en nanomateriales híbridos puede ser una herramienta clave para optimizar su desempeño.
3. Se encontró que la morfología del núcleo de oro tiene un impacto directo en la estructura y funcionalidad del recubrimiento de PBA. La anisotropía del núcleo de oro induce distorsiones estructurales y policristalinidad en el recubrimiento, mejorando notablemente su actividad catalítica. En particular, se evidenció que los núcleos de oro con formas de nanorods y nanostars proporcionan sitios activos adicionales y facilitan la transferencia electrónica, lo que explica su mayor eficiencia en la reacción de evolución de oxígeno (OER). Este hallazgo resalta la importancia de seleccionar adecuadamente la forma del núcleo de oro para aplicaciones catalíticas avanzadas.
4. En términos de fotomagnetismo, se demostró que la actividad fotomagnética de las nanopartículas híbridas está fuertemente influenciada por el espesor de la cáscara de PBA. Se confirmó que las cáscaras más gruesas presentan una mayor respuesta a la irradiación

por luz NIR, mientras que la eliminación del núcleo de oro mediante cianuración reduce significativamente esta respuesta debido a cambios estructurales inducidos por la incorporación de iones de potasio. Esto sugiere que el control del grosor de la cáscara y la composición química de los PBAs es fundamental para maximizar la respuesta fotomagnética, abriendo la posibilidad de desarrollar materiales con aplicaciones en almacenamiento de información magnética y espintrónica.

5. En el campo biomédico, se compararon estructuras de tipo core@shell con las de tipo yolk@shell para evaluar su eficiencia en la administración de fármacos. Se determinó que las nanopartículas de tipo yolk@shell, gracias a su cavidad interna generada por lixiviación de Fe^{3+} , tienen una capacidad de carga de fármacos superior, con una eficiencia del 50%. Esto supone una mejora considerable frente a las core@shell, cuya eficiencia de carga es solo del 20%. Se verificó que la liberación de doxorrubicina es sensible al pH y que puede potenciarse mediante irradiación NIR, lo que confirma su idoneidad para aplicaciones en terapia fototérmica y liberación controlada de fármacos. Estos hallazgos sugieren que los sistemas yolk@shell ofrecen ventajas significativas sobre las estructuras core@shell convencionales en términos de almacenamiento y liberación de agentes terapéuticos.
6. Se determinó que la interacción entre el núcleo de oro y el compuesto de PBA puede explotarse para el desarrollo de materiales multifuncionales. La combinación de efectos plasmonicos, catalíticos, magnéticos y biológicos en un solo material ofrece oportunidades

únicas para aplicaciones en conversión de energía, dispositivos magnéticos o electrónicos, y terapia combinada en biomedicina.

7. En términos generales, esta tesis contribuye al desarrollo de nanomateriales híbridos de tipo core@shell formado por oro y PBA, proporcionando una mejor comprensión de su síntesis y propiedades a nivel nanométrico. Los resultados obtenidos abren nuevas vías para la optimización de nanomateriales híbridos para diversas aplicaciones tecnológicas, desde el almacenamiento de energía hasta el tratamiento del cáncer.

Perspectivas Futuras

El trabajo realizado en esta tesis abre nuevas oportunidades para el diseño de nanomateriales híbridos con aplicaciones avanzadas. Algunas direcciones futuras incluyen:

- Optimización del diseño estructural: Cabría explorar la síntesis de nanopartículas de tipo core@shell con diferentes tamaños de oro para mejorar la respuesta catalítica y optimizar su rendimiento en procesos electroquímicos.
- Balance entre grosor del recubrimiento de PBA y las propiedades fotomagnéticas: Se continuará ajustando el espesor del PBA para encontrar un equilibrio que reduzca la resistencia eléctrica mientras se maximiza la actividad fotomagnética de las nanopartículas core@shell, para así poder detectar la transferencia de carga en dispositivos electrónicos.

- Evaluación de su biocompatibilidad: Se requieren estudios adicionales sobre la toxicidad y la respuesta inmune de las nanopartículas en modelos biológicos, con el fin de validar su seguridad para aplicaciones en biomedicina.
- Exploración de otras morfologías de oro: Se considerará el uso de nanopartículas de oro con núcleos anisotrópicos, como las estrellas, para aprovechar mejor sus propiedades plasmónicas, lo que podría mejorar la liberación controlada por luz de fármacos y la terapia fototérmica.
- Exploración de estrategias de escalabilidad: Se plantea la necesidad de optimizar los métodos de síntesis para facilitar la producción a gran escala y evaluar su aplicabilidad en procesos industriales.

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