Protein Corona Formation on Surface-modified SPIO Nanoparticles: Effects of pH, Coating and Incubation Time

Abdulrahman Ahmed Mahmood [a], Ahmed Abdullah Omar [a], Ali Mohammed Salih [b*], Mohammed Jamal Ahmed [c], Sadat Abdulla Aziz [d] and Mardin Mohammed Obaid [e]

[a] *College of Health and Medical Techniques, Northern Technical University, Kirkuk, Iraq.*
[b] *Technical College of Engineering, Sulaimani Polytechnic University, Sulaimani, Iraq.*
[c] *Hawler Medical University, Hawler, Iraq.*
[d] *College of Health Sciences, Cihan University, Sulaimaniya, Iraq.*
[e] *Kirkuk Second Sector for Primary Health Care / Kirkuk Directorate of Health, Ministry of Health, Iraq.*

Authors' contributions

This work was carried out in collaboration among all authors. Author AAM conceived and designed the study. Authors AAO and MJA collected the data and conducted the experiments. Author AMS analyzed the results and all authors reviewed and approved the final version.

Review Article

ABSTRACT

Aims: The goal of this review is to look into how the protein corona forms and affects superparamagnetic iron oxide nanoparticles (SPIO NPs). It will focus on how changes to the surface, pH levels, and incubation time affect their biological identity and biomedical performance.

_____

Corresponding author: E-mail: shwangeology@yahoo.com, ali.salih@spu.edu.iq;

Study Design: This is a narrative review of recent studies on biological fluids, protein corona, nanoparticles, and SPIO NP.

Place and Duration of Study: The review took place at the Department of Dialysis Technique at Northern Technical University from January to May 2025.

Methodology: The scientific literature was collected from ScienceDirect, PubMed, and Scopus. The review concentrated on protein corona formation and was grounded in theoretical and applied research on SPIO NPs and biological fluids. We assessed the effects of surface chemistry, pH, and incubation time on nanoparticle behaviour. They were analysed to demonstrate how recent developments in computer modelling and imaging aid in our comprehension of corona dynamics.

Results: SPIO NPs rapidly form a protein corona in biological fluids, which alters their physicochemical characteristics and conceals their surface features. These alterations affect how well they work as medications, how long they remain in the body, how the immune system responds, and how well cells absorb them. Protein binding was impacted by surface modifications such as polyethylene glycol (PEG) coating, charge, and targeted ligands. The corona layers were able to shift form as a result of pH changes over longer incubation periods. The design of SPIO NPs for biomedical applications, such as targeted drug delivery and hyperthermia therapy, has been made simpler by experimental findings and predictive computer models.

Conclusion: Designing SPIO NPs can be improved by knowing how protein corona formation works. Clinical outcomes, immunogenicity, and nanoparticle targeting are all enhanced by regulating surface characteristics, environmental factors, and exposure duration.

1. INTRODUCTION

The advancement of biomedical technologies depends heavily on nanoparticles which serve as fundamental components for imaging techniques and therapeutic applications (Al-Khayyat, Ameen, & Hamid, 2025). Superparamagnetic iron oxide nanoparticles (SPIO NPs) have gained significant interest because they possess unique magnetic properties together with excellent biocompatibility and wide-ranging functionalization capabilities (Attiah et al., 2023; Mahendra Kumar et al., 2023; Mahmood et al., 2019; Wei et al., 2017). The medical applications of SPIO NPs include magnetic resonance imaging (MRI) and hyperthermia treatment as well as targeted drug delivery systems (Avasthi et al., 2020; Del Pino et al., 2024). When nanoparticles enter biological environments they immediately react with multiple biomolecules especially proteins to form the "protein corona" structure. The biological coating that nanoparticles acquire after entering biological systems transforms their original synthetic characteristics while affecting their stability in solution and their distribution patterns and cellular absorption and immune response (Hajipour et al., 2023). The protein corona formation occurs through active competitive mechanisms which depend on multiple intrinsic and extrinsic elements (Tomak et al., 2021). The intrinsic properties of nanoparticles including size, shape, surface charge, hydrophobicity and surface coating characteristics determine their behavior (Mahendra Kumar et al., 2023). The composition and stability of the corona depends heavily on extrinsic factors which include surrounding pH levels, ionic strength, protein concentration and incubation duration. The interactions between nanoparticles and their environment determine their in vivo fate which affects both therapeutic outcomes and safety (Campagna, 2025).

The biological environment interacts with SPIO nanoparticles through surface modifications that control their behavior (Parida & Kar, 2025). The stealth properties of nanoparticles receive their stealth capabilities from surface coatings made of polyethylene glycol (PEG), dextran, silica and various biopolymers which also enhance stability and enable targeted delivery (Fig. 1) (Ghazi et al., 2025). The entry of nanoparticles into physiological systems always results in protein adsorption despite surface engineering strategies. The surface properties of nanoparticles require further investigation to understand their effects on protein selection and binding dynamics because they affect both specificity and predictability of nanoparticle behavior (Docter et al., 2015). The structural conformation of adsorbed proteins and the resultant corona gets affected by environmental pH conditions (Docter et al., 2015; Wheeler et al., 2021). The human body contains different pH levels that range from near-neutral blood
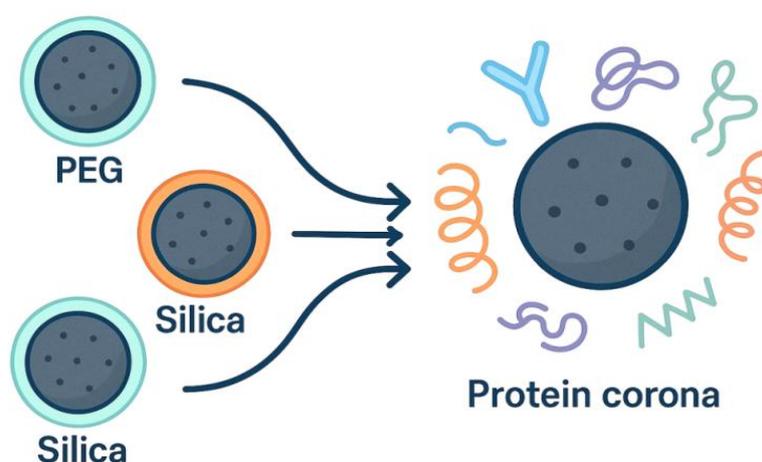
Fig. 1. Surface coatings on SPIONPs and their influence on protein Corona

and extracellular fluids at pH 7.4 to acidic tumor microenvironment and intracellular compartments such as endosomes and lysosomes at pH 5.0–6.8 (Shen et al., 2008; Hameed et al., 2025; Hamasalih et al., 2025). The binding affinities and kinetics of protein-nanoparticle interactions get affected when pH changes cause protein denaturation or unfolding. The nanoparticle surface binds proteins more strongly and irreversibly when exposed to acidic pH conditions that are typical of tumors and intracellular vesicles (Ghosh & Panicker, 2021; Aziz et al., 2025). The pharmacokinetics and intracellular trafficking of SPIO NPs get significantly affected by this phenomenon which leads to changes in therapeutic outcomes.

The study of protein corona formation remains essential because of multiple important reasons. The process reveals how nanoparticles interact with the mononuclear phagocyte system (MPS) through opsonization mechanisms (Panico et al., 2022). The corona affects active targeting strategies by either concealing targeting ligands or displaying endogenous recognition motifs (Li et al., 2025). Nanoparticle immunogenicity and toxicity profiles depend on the corona formation because these factors determine regulatory approval and clinical translation possibilities (Zaccariotto et al., 2025; Ali et al.,2025). The structure and dynamics of the protein corona have been studied through multiple advanced analytical methods (Kopac, 2021). The characterization of corona size and composition and binding kinetics has been achieved through dynamic light scattering (DLS), zeta potential measurements, transmission electron microscopy (TEM), liquid chromatography–mass

spectrometry (LC-MS) and surface plasmon resonance (SPR) (Fu et al., 2024). The recent development of isothermal titration calorimetry (ITC) and quartz crystal microbalance with dissipation monitoring (QCM-D) provides real-time observations of corona evolution across different environmental conditions (Fu et al., 2024; Zhang et al., 2024). The field continues to face multiple ongoing obstacles. The clinical prediction of nanoparticle behavior faces challenges because of individual differences in protein corona formation and pathological conditions that alter corona composition and the absence of standardized corona characterization methods (Corbo et al., 2017). The protein corona in vivo experiences additional complexity because it exists in a dynamic state which is affected by blood flow and cellular barriers (Mahmoudi et al., 2011; Ahmed et al., 2025).

The review examines three essential parameters which include SPIO nanoparticle surface modifications and environmental pH conditions and incubation time. The study combines experimental data with theoretical knowledge to explain how these variables affect the structure and composition and biological effects of the protein corona. The rational design of SPIO NPs with predictable in vivo behavior requires this understanding to advance their application in precision nanomedicine.

2. SURFACE COATING AND ITS INFLUENCE

Surface modification serves as an optimal method to manage how nanoparticles interact with biological systems. The selection of surface

coating determines the level of protein adsorption which controls how nanoparticles behave biologically. The use of organic polymers and inorganic shells together with biomimetic molecules serves to improve nanoparticle stability while extending circulation time and decreasing immunogenicity. Table 1 illustrates different types of surface modification. The use of polyethylene glycol (PEG) as an organic coating is widespread because it creates steric stabilization while reducing protein adsorption and extending blood circulation times(Owens & Peppas, 2006). The PEGylation process creates a hydrophilic brush layer that surrounds nanoparticles to prevent protein attachment and minimize opsonization. Research indicates that PEGylated nanoparticles still develop a protein corona but the amount and nature of adsorbed proteins differ from non-PEGylated nanoparticles (Owens & Peppas, 2006). The natural polymers dextran together with chitosan and hyaluronic acid provide benefits through their biocompatible and biodegradable nature and their ability to receive additional functionalization (Mahmoudi et al., 2011). SPIO nanoparticles coated with dextran have received FDA approval for medical use as MRI contrast agents under the brand name Feridex (Avasthi et al., 2020). The protein adsorption resistance of dextran coatings is limited because they tend to bind particular plasma proteins including immunoglobulins and fibrinogen which could affect nanoparticle distribution and immune response (Karmali & Simberg, 2011).

The surface functionalization of inorganic coatings such as silica and gold shells enables robustness and allows multiple ligand attachments. Silica-coated SPIO nanoparticles serve as a flexible system which enables researchers to bond targeting ligands and fluorescent dyes and therapeutic molecules through covalent reactions (Aljarjary et al., 2023; Comanescu, 2023). The chemical inertness of silica does not prevent protein adsorption from occurring which results in a well-defined hard corona layer (Comanescu, 2023). The surface charge characteristics play a vital role in determining the outcome. The adsorption of albumin and immunoglobulins which are negatively charged serum proteins occurs more frequently on positively charged nanoparticles than on neutral or negatively charged particles (Ghareeb, 2023; Lundqvist et al., 2008). The electrostatic attraction between positively charged nanoparticles and negatively charged cell membranes leads to better cellular uptake but simultaneously increases the chances of immune system detection. The degree of surface roughness together with heterogeneity acts as additional factors that affect protein binding. The numerous binding sites on nanoparticles with rough or textured surfaces result in increased formation of corona. The protein adsorption rate remains low when surfaces appear smooth and uniform. The formation and evolution of the protein corona gets influenced by surface coatings but biomolecular adsorption remains impossible to fully prevent (Yu et al., 2022). The combination of surface chemistry with charge properties and hydrophobicity and roughness elements determines how proteins bind to nanoparticles which affects their performance in biological systems.

Table 1. Surface coatings on SPIO nanoparticles and their influence on protein corona formation

Coating Material	Key Features	Effect on Protein Corona	References
PEG (Polyethylene glycol)	Hydrophilic, flexible polymer; "stealth" effect	Reduces nonspecific adsorption but does not completely prevent corona formation	(Gupta et al., 2023)
Dextran	Natural polysaccharide; biocompatible	Preferential adsorption of immunoglobulins and fibrinogen; potential immune recognition	(Erensoy et al., 2024)
Silica Shell	Chemically inert, easily functionalized	Stable hard corona; suitable for ligand attachment	(Phumsathan et al., 2025)
Gold Coating	Biocompatible, photothermal properties	Strong binding of albumin and complement proteins	(Chae et al., 2025)
Zwitterionic Polymers	Charge-balanced hydrophilic surfaces	Minimizes protein adsorption and immune activation	(Singh et al., 2025)

3. EFFECT OF pH ON PROTEIN CORONA FORMATION

Environmental pH serves as a crucial factor which controls the formation process and stability maintenance and composition development of protein coronas on SPIO nanoparticles. The changes in pH values modify both the surface properties of nanoparticles and the binding proteins which leads to major differences in corona structure and function (Fig. 2). Table 2 illustrates the effect of environmental pH on the formation of protein corona on SPIO nanoparticles. Biological environments maintain various pH levels which include blood and interstitial fluids at neutral pH 7.4 while tumor tissues have slightly acidic pH 6.5–6.8 and intracellular organelles like lysosomes maintain pH values between 4.5–5.5 (Peppicelli et al., 2014). The adsorption of proteins onto nanoparticle surfaces at physiological pH occurs mainly through electrostatic, hydrophobic and van der Waals interactions because proteins maintain their native conformations. Acidic conditions trigger protein conformational changes that result in partial unfolding and hydrophobic domain exposure and increased positive charge through acidic residue protonation (Tenzer et al., 2011; Salih et al., 2019). Protein surfaces show increased binding to nanoparticles when their structure changes because of which protein coronas become more stable and less flexible (Corbo et al., 2017).

The surface charge and aggregation behavior of SPIO nanoparticles become affected by pH changes which modify their corona formation process. The interaction profile of proteins with dextran and PEG coatings changes when these coatings undergo protonation or deprotonation due to different pH conditions. The aggregation behavior of SPIO NPs increases when exposed to acidic conditions because electrostatic repulsion weakens which affects both corona composition and nanoparticle stability in biological fluids (Mirshafiee et al., 2013). The slightly acidic tumor microenvironment promotes the binding of particular plasma proteins which maintain stability better at these pH levels thus improving EPR-mediated passive tumor targeting. The formation of corona at acidic pH conditions enables the exposure of targeting ligands and generates new epitopes that tumor-specific receptors can recognize thus enabling the development of pH-responsive nanocarriers (Shen et al., 2008; Wei et al., 2017).
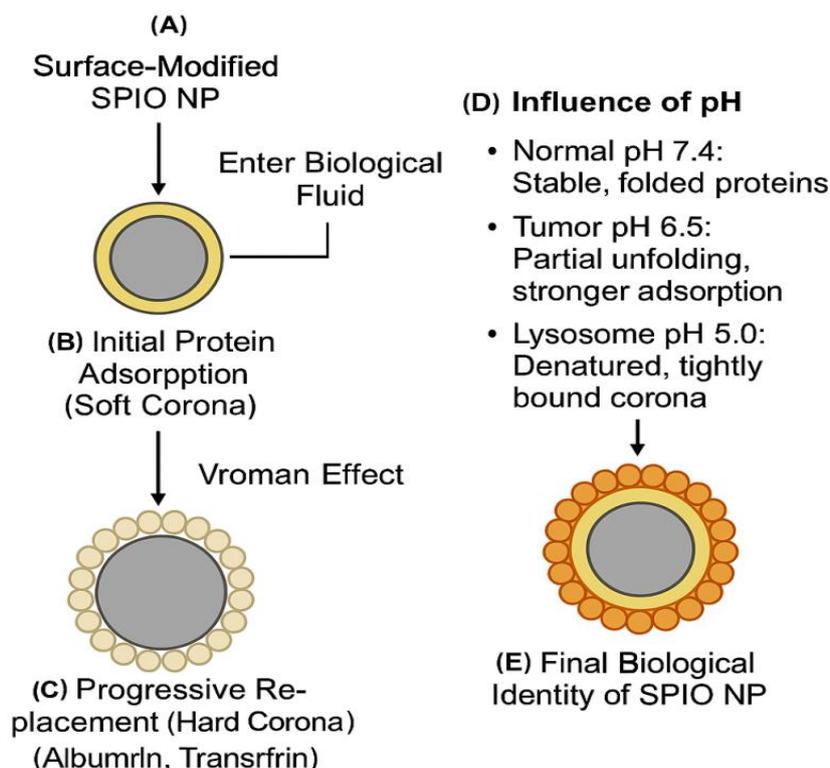

Fig. 2. Dynamic evolution of the protein corona on surface-modified SPIO nanoparticles under different pH and incubation conditions

Table 2. Effects of environmental pH on protein corona formation on SPIO nanoparticles

pH Environment	Protein Behavior	Nanoparticle Surface Changes	Biological Implications	References
Neutral (pH ~7.4)	Proteins maintain native conformation; reversible adsorption	Stable surface properties	Prolonged circulation; moderate uptake by target cells	(Tenzer et al., 2011)
Slightly acidic (pH 6.5-6.8)	Partial protein unfolding; exposure of hydrophobic domains	Surface charge may shift, increased protein binding	Enhanced tumor targeting through EPR effect	(Mirshafiee et al., 2013)
Acidic (pH 5.0-6.0)	Significant conformational changes; stronger binding	Surface aggregation, potential coating degradation	Promotes lysosomal accumulation; potential cytotoxicity mitigation	(Albanese et al., 2012)
Highly acidic (pH <5.0)	Protein denaturation; irreversible adsorption	Loss of stealth functionality; core exposure	Accelerated degradation; inflammatory responses possible	(Debnath et al., 2025)

The SPIO NPs experience increasingly acidic environments during their endocytic uptake into endosomes and lysosomes inside cells. The acidification process triggers changes in the protein corona structure. The acidic environment causes weak protein bindings at neutral pH to break while strong protein bindings become more stable. The modifications affect how endosomes escape and how quickly they degrade as well as which intracellular pathways they follow (Albanese et al., 2012; Omar et al., 2025). The acidic pH of lysosomes triggers the breakdown of biodegradable coatings such as dextran and chitosan which reveals the SPIO core and may boost its imaging or therapeutic capabilities. The direct exposure of bare iron oxide surfaces to cells through this process could trigger oxidative stress responses. The modifications of the protein corona that occur based on pH levels directly affect the pharmacokinetic behavior and therapeutic outcomes of SPIO NPs (Rasul et al., 2025). A thorough comprehension of these processes allows scientists to create smart nanoparticles that use environmental pH gradients to improve targeting capabilities and enhance drug release profiles and reduce off-target effects (Rennie et al., 2025; Salih et al., 2021).

4. INFLUENCE OF INCUBATION TIME

The incubation time functions as a crucial factor which determines the protein corona composition and structure and biological behavior of SPIO nanoparticles. The protein adsorption process develops through fast initial protein binding followed by protein reorganization and exchange and maturation of the corona. The protein corona's temporal evolution determines how nanoparticles behave regarding stability and cellular uptake and biodistribution and immune recognition. SPIO nanoparticles experience an intricate protein competition for surface adsorption sites when they first encounter biological fluids. The "soft corona" emerges during the first minutes to seconds of exposure and contains proteins that bind weakly to the surface. The initial soft corona transforms into the hard corona through time as proteins with stronger binding properties and slower exchange rates become dominant (Kelle et al., 2025; Abdul et al., 2025).

Short incubation periods of less than 30 minutes result in a corona that contains abundant plasma proteins including albumin, immunoglobulins and fibrinogen. The high concentration and fast diffusion rates of these proteins enable them to rapidly form a surface coating on the nanoparticles. The proteins do not necessarily exhibit the strongest binding properties to the nanoparticle surface. The initial proteins that adsorb to the surface will be displaced by proteins with stronger surface binding properties but lower bulk concentrations including apolipoproteins and complement factors and coagulation proteins (Sun et al., 2024; Mohammed et al., 2025). The biological identity of nanoparticles becomes determined by a highly stable and resilient hard corona that develops after incubation times spanning from several hours to days. The matured hard corona covers up the original surface functionalities of the nanoparticle which disrupts active targeting strategies that depend on ligand-receptor interactions. The extended incubation period leads to structural modifications of surface-bound proteins which reveals previously concealed epitopes that might trigger immune responses or modify cellular uptake mechanisms (Sun et al., 2024).

Several factors control the rate at which corona evolves including nanoparticle surface chemistry and size and shape and biological medium composition. Tables 3 illustrate the impact of incubation duration on protein corona on SPIO nanoparticle. PEGylated SPIO nanoparticles show reduced protein adsorption rates and decreased total protein binding when compared to non-PEGylated nanoparticles. The exchange of proteins in the system depends on environmental factors including temperature and ionic strength and pH. The therapeutic field requires knowledge of protein corona temporal evolution patterns for proper control. The engineered surface properties of nanoparticles require minimal exposure to plasma before cell targeting because they need to reach their target cells quickly. Nanoparticles that need to stay in circulation for extended periods would gain advantage from forming a hard corona that maintains their biological identity (Ashkarran et al., 2024).

The recent developments in proteomics and bioinformatics have made it possible to conduct detailed temporal analysis of protein corona composition. Mass spectrometry combined with label-free quantification techniques in time-resolved studies have shown that particular proteins function as exchange catalysts which enable the replacement of initial protein adsorbates with higher-affinity proteins.

Table 3. Influence of incubation time on protein corona formation on SPIO nanoparticles

Incubation phase	Time frame	Dominant proteins	Biological impact	References
Early Phase	Seconds to Minutes	Abundant plasma proteins (e.g., albumin, immunoglobulins)	Rapid soft corona formation; reversible binding	(Gupta et al., 2023)
Intermediate Phase	Minutes to Hours	High-affinity proteins (e.g., complement proteins, apolipoproteins)	Vroman effect; dynamic protein exchange	(Mao et al., 2022)
Late Phase	Hours to Days	Stable hard corona proteins	Defines long-term biological identity and immune interactions	(N. Zhao & Yuan, 2023)
In Vivo Evolution	Variable, under flow conditions	Dynamic reshaping due to environmental stimuli	Alters targeting efficiency and clearance pathways	(Sun et al., 2024)

The gained knowledge enables rational nanoparticle design through pre-coating methods which expose nanoparticles to chosen proteins before systemic administration to create predetermined coronas (Salih et al., 2021). The protein corona composition on SPIO nanoparticles undergoes significant changes based on the duration of incubation. The complete comprehension of temporal protein corona evolution remains crucial for predicting nanoparticle behavior in living organisms and designing them for particular biomedical uses.

5. BIOLOGICAL IMPLICATIONS AND APPLICATIONS

The biodistribution patterns of nanoparticles along with their clearance rates depend heavily on the characteristics of their protein corona (Ali, Obaid, & Jassim, 2024). The presence of opsonins including immunoglobulins and complement proteins in hard coronas leads to fast recognition by mononuclear phagocyte system cells which results in nanoparticle accumulation within liver and spleen organs (Jassim, Ali, & Tawfeeq, 2025; Salih et al., 2025). Nanoparticles that have dysopsonin-enriched coronas such as albumin or clusterin remain hidden from immune surveillance which enables them to stay in circulation for longer periods. The optimization of nanoparticle delivery to specific tissues requires knowledge of these interactions which can be engineered for better results (Lopez-Mitjavila et al., 2025). The composition of corona determines how cells will take up nanoparticles and their targeting precision. Nanoparticles with apolipoprotein-enriched coronas show better uptake by liver hepatocytes and brain endothelial cells which enables liver targeting and blood-brain barrier penetration. The uptake of nanoparticles by macrophages together with inflammatory responses occurs

when coronas contain fibrinogen or vitronectin (Ashkarran et al., 2024; Rahman et al., 2021). Advanced theranostic applications become possible through rational preconditioning of nanoparticles with specific proteins or ligands to achieve controlled targeting of cancer cells neurons or immune cells. The recent findings on protein corona on SPIO nanoparticle show in Table 4.

The immune system identifies nanoparticle-protein complexes in a manner that either intensifies or decreases inflammatory reactions. The exposure of hidden epitopes through protein adsorption leads to complement pathway activation and cytokine production and hypersensitivity reactions. Stealth coronas made from non-immunogenic proteins work to decrease immune activation while improving biocompatibility. The outcome between these processes remains sensitive and needs thorough preclinical testing to validate both safety and effectiveness (Sharma et al., 2025). The corona's in vivo reshaping dynamics makes it difficult to predict how immune responses will evolve throughout time. The field of utilizing coronas for therapeutic and diagnostic applications continues to emerge as a new frontier. The addition of tumor-homing peptides or antibody fragments or small molecules to functionalized coronas enables active targeting of malignancies with enhanced effectiveness. Engineered coronas show potential to enhance MRI contrast enhancement as well as photothermal conversion in hyperthermia therapy and stimulus-responsive drug release (Mahmood et al., 2019). Smart coronas that adjust their behavior based on environmental signals such as pH levels and enzymatic activity and redox conditions show potential to develop advanced nanoparticle platforms for precision medicine.

Table 4. Recent findings on protein corona effects on SPIO nanoparticles

Surface Modification	Key Findings	Biological Outcome	References
PEGylation	Reduced nonspecific protein adsorption, enhanced circulation time	Prolonged systemic circulation, reduced liver uptake	(Lopez-Mitjavila et al., 2025)
Dextran coating	Increased binding of complement proteins	Enhanced clearance by MPS, reduced tumor targeting	(Psarrou et al., 2025)
Silica shell with RGD peptides	Selective enrichment of fibrinogen and vitronectin	Improved targeting to tumor vasculature	(He & Zhong, 2025)
Zwitterionic coating	Minimal protein corona formation	Low immunogenicity, improved biocompatibility	(C. Zhao et al., 2025)
Chitosan modification	pH-sensitive protein adsorption in tumor environments	Enhanced tumor penetration and retention	(Sharma et al., 2025)

6. CONCLUSION

The biological identity and fate of SPIO nanoparticles along with their efficacy depends heavily on how the protein corona forms and evolves. The composition structure and dynamics of the corona develop through the combined effects of surface coatings environmental pH and incubation time to determine nanoparticle performance in clinical applications. A comprehensive understanding of these parameters allows researchers to create SPIO NPs that achieve better biocompatibility and precise targeting while reducing immunogenicity and delivering improved therapeutic results. Future research should focus on creating personalized nanomedicine approaches and using dynamic environmental triggers such as pH gradients and developing advanced computational models to design optimal protein coronas. The vision of intelligent corona-optimized nanoparticles for precision diagnostics and therapy is becoming increasingly real through ongoing interdisciplinary research between nanotechnology and proteomics and bioinformatics and clinical research.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

ETHICAL APPROVAL

The authors of this article have not conducted any research involving humans or animals; rather, it is a review of previously published literature. Consequently, ethical clearance was not necessary.

CONSENT

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Abdul, N. A., Saeed, M. W. M., Salih, A. M., Talb, S. S., Ali, R. A., Sdiq, S. J. M., & Abdulrahman, A. B. M. (2025). Enhancing dough quality: The effects of transglutaminase and glucose oxidase on stability and mixing resistance. *International Journal of Scientific Research in Modern Science and Technology, 4*(4), 07–20.

Ahmed, K. M., Salih, A. M., Raoof, B. K., Ahmed, T. N., Ahmed, T. N., Mohammed, B. A., ... Omer, Z. O. (2025). Economic burden of air pollution and healthcare costs for respiratory diseases in the United States of

America. *International Journal of Scientific Research and Modern Technology, 4*(3), 64–75. https://doi.org/10.38124/ijsrmt.v4i3.389

Albanese, A., Tang, P. S., & Chan, W. C. W. (2012). The effect of nanoparticle size, shape, and surface chemistry on biological systems. *Annual Review of Biomedical Engineering, 14*, 1–16.

Ali, G. H., Obaid, S. S., & Jassim, W. M. (2024). Prevalence and antibiotic sensitivity profile of *Pseudomonas aeruginosa* isolated from patients with otitis media in Kirkuk City. *NTU Journal of Pure Sciences, 3*(1), 1–7.

Ali, R. A., Sdiq, S. J. M., Salih, A. M., Ahmed, A., Mahmood, Z. O. O., Yaqub, K. Q., ... & Sirwan, K. (2025). Quality assessment of commercial tomato paste in Kurdistan region of Iraq: Implications for agripreneurship and market standards.

Aljarjary, N., Al-Dulaimi, F. K. Y., & Saeed, H. A. (2023). Investigation of the role of *Brassica* roots & *Fusarium* mycelium in accumulation of gold particles. *NTU Journal of Agriculture and Veterinary Science, 3*(2), Article 2.

Al-Khayyat, M. Z., Ameen, A. G., & Hamid, N. T. (2025). Insights on the antibacterial activities of nanoparticles. *NTU Journal of Pure Sciences, 4*(1), 26–30.

Ashkarran, A. A., Gharibi, H., Sadeghi, S. A., Modaresi, S. M., Wang, Q., Lin, T.-J., Yerima, G., Tamadon, A., Sayadi, M., Jafari, M., Lin, Z., Ritz, D., Kakhniashvili, D., Guha, A., Mofrad, M. R. K., Sun, L., Landry, M. P., Saei, A. A., & Mahmoudi, M. (2024). Deep plasma proteome profiling by modulating single nanoparticle protein corona with small molecules. *bioRxiv*. https://doi.org/10.1101/2024.03.06.582595

Attiah, B. H., Obaid, H. M., & Al-Salihi, S. S. (2023). Assessment the Ag and ZnO biosynthesized nanoparticles effects on *Giardia lamblia* trophozoites which grown in HSP-1 culture media. *NTU Journal of Pure Sciences, 2*(1), Article 1.

Avasthi, A., Caro, C., Pozo-Torres, E., Leal, M. P., & García-Martín, M. L. (2020). Magnetic nanoparticles as MRI contrast agents. *Topics in Current Chemistry, 378*(3), 40.

Aziz, C. H., Abdul, N. A., Ali, R. A., Salih, A. M., Rasul, H. I., Raheem, S. M., & Yaqub, K. Q. (2025). From farm to fallout: Agriculture's role in America's environmental crisis. *Asian Journal of Advances in Agricultural Research, 25*(6), 16–29.

Campagna, M. (2025). *Structural analysis of low-density lipoprotein interactions with proteins and corona formation* [Laurea thesis, Politecnico di Torino].

Chae, W. R., Song, Y.-J., & Lee, N. Y. (2025). Polydopamine-mediated gold nanoparticle coating strategy and its application in photothermal polymerase chain reaction. *Lab on a Chip, 25*(6), 1429–1438.

Comanescu, C. (2023). Recent advances in surface functionalization of magnetic nanoparticles. *Coatings, 13*(10), Article 10.

Corbo, C., Molinaro, R., Tabatabaei, M., Farokhzad, O. C., & Mahmoudi, M. (2017). Personalized protein corona on nanoparticles and its clinical implications. *Biomaterials Science, 5*(3), 378–387.

Debnath, M., Malhotra, M., & Kulkarni, A. (2025). Protein corona formation on supramolecular polymer nanoparticles causes differential endosomal sorting resulting in an attenuated NLRP3 inflammasome activation. *Biomaterials Science, 13*(11), 3030–3047.

Del Pino, P., Pelaz, B., Zhang, Q., Maffre, P., Nienhaus, G. U., & Parak, W. J. (2024, February 27). Protein corona formation around nanoparticles—From the past to the future. *Bio-Nano Interfaces, 2024*, 515–545.

Docter, D., Westmeier, D., Markiewicz, M., Stolte, S., Knauer, S. K., & Stauber, R. H. (2015). The nanoparticle biomolecule corona: Lessons learned – challenge accepted? *Chemical Society Reviews, 44*(17), 6094–6121.

Erensoy, G., Råberg, L., von Mentzer, U., Menges, L. D., Bardhi, E., Hultgård Ekwall, A.-K., & Stubelius, A. (2024). Dynamic release from acetalated dextran nanoparticles for precision therapy of inflammation. *ACS Applied Bio Materials, 7*(6), 3810–3820.

Fu, F., Crespy, D., Landfester, K., & Jiang, S. (2024). In situ characterization techniques of protein corona around nanomaterials. *Chemical Society Reviews, 53*(22), 10827–10851.

Ghareeb, O. (2023). Adverse impact of titanium dioxide nanoparticles on hepato-renal functions and improved role of *Rosmarinus officinalis*. *Journal of Natural Science Biology and Medicine, 14*, 33–38.

Ghazi, R., Ibrahim, T. K., Abdul Nasir, J., Gai, S., Ali, G., Boukhris, I., & Rehman, Z. (2025).

Iron oxide based magnetic nanoparticles for hyperthermia, MRI and drug delivery applications: A review. *RSC Advances, 15*(15), 11587–11616.

Ghosh, G., & Panicker, L. (2021). Protein–nanoparticle interactions and a new insight. *Soft Matter, 17*(14), 3855–3875.

Gupta, A., Verma, J., & Kumar, D. (2023). Mitigation of erosion and corrosion of steel using nano-composite coating: Polyurethane reinforced with SiO_2-ZnO core-shell nanoparticles. *Progress in Organic Coatings, 183*, 107733.

Hajipour, M. J., Safavi-Sohi, R., Sharifi, S., Mahmoud, N., Ashkarran, A. A., Voke, E., Serpooshan, V., Ramezankhani, M., Milani, A. S., Landry, M. P., & Mahmoudi, M. (2023). An overview of nanoparticle protein corona literature. *Small (Weinheim an Der Bergstrasse, Germany), 19*(36), e2301838.

Hamasalih, I. K., Salih, A. M., Mohammed, B. A., Yaqub, K. Q., Ahmed, Y. A., & Palani, P. M. (2025). Attracting foreign direct investment is central to successful economic development and balance with environmental protection. *International Journal of Scientific Research in Technology, 2*(3).

Hamasalih, I. K., Salih, A. M., Sdiq, S. J. M., Yaqub, K. Q., Raheem, S. M., & Latif, A. D. (2025). Tanjaro River pollution and its impact on the aquatic food chain. *Science and Education, 5*(3), 235–244.

Hameed, K., Sirwan, K., Omar, Z. O., Mohammed, E. F., Sourkan, S., Salih, A. M., & Yaqub, K. Q. (2025). Addressing the issue of poverty, economic growth, health matters, and environmental challenges. *International Journal of Scientific Research in Modern Science and Technology, 4*(3), 18–32.

He, S., & Zhong, Z. (2025). Application research of hollow mesoporous silica nanoparticles in targeted thrombolysis for deep vein thrombosis of the lower extremities. *Discover Applied Sciences, 7*(4), 281.

Jassim, A. K., Ali, A. A., & Tawfeeq, A. A. (2025). A comparison between microscopic and conventional PCR in the diagnosis of *Giardia lamblia* among children in Kirkuk. *NTU Journal of Pure Sciences, 4*(1), 9–16.

Karmali, P. P., & Simberg, D. (2011). Interactions of nanoparticles with plasma proteins: Implication on clearance and toxicity of drug delivery systems. *Expert Opinion on Drug Delivery.*

Kelle, D., Speth, K. R., Martínez-Negro, M., Mailänder, V., Landfester, K., & Iyisan, B. (2025). Effect of protein corona on drug release behavior of PLGA nanoparticles. *European Journal of Pharmaceutics and Biopharmaceutics, 207*, 114611.

Kopac, T. (2021). Protein corona, understanding the nanoparticle–protein interactions and future perspectives: A critical review. *International Journal of Biological Macromolecules, 169*, 290–301.

Li, Y., Sun, H., Cao, D., Guo, Y., Wu, D., Yang, M., Wang, H., Shao, X., Li, Y., & Liang, Y. (2025). Overcoming biological barriers in cancer therapy: Cell membrane-based nanocarrier strategies for precision delivery. *International Journal of Nanomedicine.*

Lopez-Mitjavila, J. J., Palma-Florez, S., Lagunas, A., Mir, M., Samitier, J., Rodriguez-Abreu, C., & Grijalvo, S. (2025). PEGylated PLGA nanoparticles prepared from nano-emulsion templates as versatile platforms to cross blood-brain barrier models. *Journal of Drug Delivery Science and Technology, 110*, 107057.

Lundqvist, M., Stigler, J., Elia, G., Lynch, I., Cedervall, T., & Dawson, K. A. (2008). Nanoparticle size and surface properties determine the protein corona with possible implications for biological impacts. *Proceedings of the National Academy of Sciences, 105*(38), 14265–14270.

Mahendra Kumar, S., Rajni, Y., & Sandeep Prasad, T. (2023). Recent advances in nanotechnology. *International Journal of Nanomaterials, Nanotechnology and Nanomedicine, 9*(2), 015–023.

Mahmood, A. A., Zhang, J., Liao, R., Pan, X., Xu, D., Xu, H., & Zhou, Q. (2019). Evaluation of non-targeting, C- or N-pH (low) insertion peptide modified superparamagnetic iron oxide nanoclusters for selective MRI of liver tumors and their potential toxicity in cirrhosis. *RSC Advances, 9*(25), 14051–14059.

Mahmoudi, M., Sant, S., Wang, B., Laurent, S., & Sen, T. (2011). Superparamagnetic iron oxide nanoparticles (SPIONs): Development, surface modification and applications in chemotherapy. *Advanced Drug Delivery Reviews, 63*(1), 24–46.

Mao, L., Russell, A. J., & Carmali, S. (2022). Moving protein PEGylation from an art to a data science. *Bioconjugate Chemistry, 33*(9), 1643–1653.

Mirshafiee, V., Mahmoudi, M., Lou, K., Cheng, J., & Kraft, M. L. (2013). Protein corona significantly reduces active targeting yield. *Chemical Communications, 49*(25), 2557–2559.

Mohammed, A., Salih, A., & Raof, H. (2020). Vipulanandan constitutive models to predict the rheological properties and stress–strain behavior of cement grouts modified with metakaolin. *Journal of Testing and Evaluation, 48*(5), 3925–3945.

Omar, Z. O., Hamasalih, I. K., Salih, A. M., Mohammed, K. S., Sdiq, S. J. M., Ali, S., ... & Ahmed, A. (2025). Gypsum calcination in order to clear impurities and to use phosphogypsum at its entire cycle microbial bioremediation. *International Journal of Scientific Research in Technology, 2*(3).

Owens, D. E., & Peppas, N. A. (2006). Opsonization, biodistribution, and pharmacokinetics of polymeric nanoparticles. *International Journal of Pharmaceutics, 307*(1), 93–102.

Panico, S., Capolla, S., Bozzer, S., Toffoli, G., Dal Bo, M., & Macor, P. (2022). Biological features of nanoparticles: Protein corona formation and interaction with the immune system. *Pharmaceutics, 14*(12), Article 12.

Parida, S. K., & Kar, N. R. (2025). Exploring magnetic nanoparticles in oncology: Synthesis to therapeutic applications. *Journal of Bio-X Research, 8.*

Peppicelli, S., Bianchini, F., & Calorini, L. (2014). Extracellular acidity, a "reappreciated" trait of tumor environment driving malignancy: Perspectives in diagnosis and therapy. *Cancer and Metastasis Reviews, 33*(2), 823–832.

Phumsathan, P., Kalasin, S., Somasundrum, M., Ngamchana, S., Rijiravanich, P., Surareungchai, W., & Khownarumit, P. (2025). Electrochemical detection of paraquat using Fe_3O_4 nanoparticles coated with silica shells and modeling of its adsorption by molecular dynamics. *ACS Applied Nano Materials, 8*(1), 780–792.

Psarrou, M., Vamvakaki, M., Karatasos, K., & Rissanou, A. N. (2025). Interfacial interactions between DNA and polysaccharide-coated magnetic nanoparticles: Insight from simulations and experiments. *Colloids and Surfaces B: Biointerfaces, 246*, 114386.

Rahman, A., Khazini, L., & Salih, A. M. (2021). Origins of water pollution in Tanjaro River.

Third National Congress of Chemistry and Nanochemistry from Research to National Development, 45–50.

Rasul, H. I., Salih, A. M., Raheem, S. M., Sirwan, K., Hameed, K., Yaqub, K. Q., ... & Abdul, N. A. (2025). Economic, environmental and management perspectives on soil pollution and sustainable remediation strategies. *Asian Journal of Soil Science and Plant Nutrition, 11*(2), 123–139.

Rennie, C., Morshed, N., Faria, M., Collins-Praino, L., & Care, A. (2025). Nanoparticle association with brain cells is augmented by protein coronas formed in cerebrospinal fluid. *Molecular Pharmaceutics, 22*(2), 940–957.

Salih, A. (2021). Conversion of natural bentonite into effective adsorbents for removing of Pb^{2+} ions from wastewater. *Journal of Zankoy Sulaimani-Part A, 23*(2), 107–119.

Salih, A. M. (2018). *The purification of industrial wastewater to remove heavy metals and investigation into the use of zeolite as a remediation tool* [Doctoral dissertation, University of Wolverhampton]. Wolverhampton Research Archive. https://wlv.openrepository.com/items/3300e578-bd9c-4b5e-841e-5cf3c1894280

Salih, A. M., Hamasalih, I. K., Sdiq, S. J. M., Yaqub, K. Q., Latif, A. D., Abdulrahman, R. R., & Muhamad, A. O. (2025). Batch absorption, regeneration studies of the natural zeolite and evaluate their performance of removal efficiency over multiple cycles. *Contemporary Research Analysis Journal, 2*(2), 103–109.

Salih, A. M., Williams, C., & Khanaqa, P. (2019). Synthesis of zeolite Na-LSX from Iraqi natural kaolin using alkaline fusion prior to hydrothermal synthesis technique. *UKH Journal of Science and Engineering, 3*(1), 10–17.

Salih, A., Williams, C., & Khanaqa, P. (2019). Heavy metal removals from industrial wastewater using modified zeolite: Study the effect of pre-treatment. *Journal of Garmian University, 6*(2), 406–416.

Sharma, S., Gauba, P., Tyagi, A., & Dang, S. (2025). Chitosan-modified polymeric nanoparticles for the nose-to-brain drug delivery of paroxetine: An in vitro and in vivo evaluation. *Nanoscale, 17*(3), 1687–1702.

Shen, Y., Tang, H., Radosz, M., Van Kirk, E., & Murdoch, W. J. (2008). pH-responsive nanoparticles for cancer drug delivery. In

K. K. Jain (Ed.), *Drug Delivery Systems* (pp. 183–216). Humana Press.

Singh, M., Srivastava, A., & Mandal, M. (2025). Unravelling the potential of zwitterionic polymers in molecular imprinting. *Langmuir, 41*(9), 5687–5704.

Sun, Y., Zhou, Y., Rehman, M., Wang, Y.-F., & Guo, S. (2024). Protein corona of nanoparticles: Isolation and analysis. *Chem & Bio Engineering, 1*(9), 757–772.

Tenzer, S., Docter, D., Rosfa, S., Wlodarski, A., Kuharev, J., Rekik, A., ... & Stauber, R. H. (2011). Nanoparticle size is a critical physicochemical determinant of the human blood plasma corona: A comprehensive quantitative proteomic analysis. *ACS Nano, 5*(9), 7155–7167.

Tomak, A., Cesmeli, S., Hanoglu, B. D., Winkler, D., & Oksel Karakus, C. (2021). Nanoparticle-protein corona complex: Understanding multiple interactions between environmental factors, corona formation, and biological activity. *Nanotoxicology, 15*(10), 1331–1357.

Wei, Y., Liao, R., Mahmood, A. A., Xu, H., & Zhou, Q. (2017). pH-responsive pHLIP (pH low insertion peptide) nanoclusters of superparamagnetic iron oxide nanoparticles as a tumor-selective MRI contrast agent. *Acta Biomaterialia, 55*, 194–203.

Wheeler, K. E., Chetwynd, A. J., Fahy, K. M., Hong, B. S., Tochihuitl, J. A., Foster, L. A., & Lynch, I. (2021). Environmental dimensions of the protein corona.

Nature Nanotechnology, 16(6), 617–629.

Yu, Y., Luan, Y., & Dai, W. (2022). Dynamic process, mechanisms, influencing factors and study methods of protein corona formation. *International Journal of Biological Macromolecules, 205*, 731–739.

Zaccariotto, G. de C., Bistaffa, M. J., Zapata, A. M. M., Rodero, C., Coelho, F., Quitiba, J. V. B., ... & Zucolotto, V. (2025). Cancer nanovaccines: Mechanisms, design principles, and clinical translation. *ACS Nano.*

Zhang, P., Cao, M., Chetwynd, A. J., Faserl, K., Abdolahpur Monikh, F., Zhang, W., ... & Lynch, I. (2024). Analysis of nanomaterial biocoronas in biological and environmental surroundings. *Nature Protocols, 19*(10), 3000–3047.

Zhao, C., Wen, S., Xu, R., Wang, K., Zhong, Y., Huang, D., ... & Chen, W. (2025). Oral delivery of ultra-small zwitterionic nanoparticles to overcome mucus and epithelial barriers for macrophage modulation and colitis therapy. *Acta Biomaterialia, 196*, 399–409.

Zhao, N., & Yuan, W. (2023). Antibacterial, conductive nanocomposite hydrogel based on dextran, carboxymethyl chitosan and chitosan oligosaccharide for diabetic wound therapy and health monitoring. *International Journal of Biological Macromolecules, 253*, 126625.

Peer-review history:
The peer review history for this paper can be accessed here:
https://pr.sdiarticle5.com/review-history/137760