

# Investigation of Bio-Physical Interaction and Electrophoretic Properties of Fe<sub>3</sub>O<sub>4</sub>/DNA Nanocomposite and Colloids for Biomedical Application

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## Abstract

*In recent years, research on magnetic nanoparticles has gained significant attention. The core concept behind their physics lies in their interaction with biomolecules such as hemoglobin, DNA, and RNA. This study examines the fundamental forces involved in these interactions, including van der Waals attractions, electrostatic repulsion, thermal effects, and magnetic coupling between nanoparticles and biological molecules. To describe these interactions quantitatively, parameters such as zeta potential, magnetic moment density, and Gibbs free energy are analyzed using the DLVO (Derjaguin-Landau-Verwey-Overbeek) theory and DNA origami principles. These theoretical frameworks provide effective tools for understanding how nanoparticles interact with biomolecules. Furthermore, DLVO theory helps determine the aggregation and agglomeration behavior of nanoparticles and colloids, offering insights into their colloidal stability. Although DLVO theory primarily addresses electrostatic and van der Waals interactions, it is also used to approximate adhesive, steric, and magnetic interactions among nanoparticles. This makes it suitable for evaluating the stability of colloidal dispersions. On the other hand, the DNA origami model describes the systematic folding of a long single-stranded DNA molecule into well-defined structures using complementary short strands. By considering spherical interaction sites, relationships between key physical parameters, such as particle radius, surface area, zeta potential, and the distance between Helmholtz planes, can be established. Additionally, this research emphasizes the influence of surface and interfacial engineering on the binding behavior of Fe<sub>3</sub>O<sub>4</sub> nanoparticles with DNA.*

**Keywords:** Biomolecules, colloids, DNA origami, DLVO theory, magnetic nanocomposite, zeta potential

## INTRODUCTION

Advancement in physics reveals four fundamental interactions, namely gravitational interactions, electromagnetic interactions, weak nuclear interactions, and strong nuclear interactions. However, in

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the interaction between magnetic nanoparticles and biomolecules, only weak nuclear interactions, i.e., van der Waals interaction, become significantly important. Rarely, electrostatic, magnetic, and thermal interactions contribute to the overall interactions in extremely small amounts. However, the search for bio-physical interaction enables unleashing more interactions in micro-microcanonical ensemble. Experimentally, Zolghadri *et al.* had demonstrated the interaction of Fe<sub>2</sub>O<sub>3</sub> nanoparticles with human hemoglobin (Hb) by fluorescence, circular Dichroism, and UV/Vis spectroscopes [1]. Compared to macro molecules and micromolecules, nanomaterials can be easily

stretched, compressed, and exhibit size-dependent physicochemical properties. For example, unlike macro ceramics, nano-crystalline ceramics have a high elastic modulus, are tougher, wear resistant, and exhibit improved thermal and superior soft magnetic properties. These properties make them advantageous in flexible material processing and nanotechnology. Murthy *et al.* noted that the techniques of nanotechnology can be segregated into wet, dry, and computational engineering [2]. This technique paves the way to analyze and determine the type, nature, strength, and range of interaction at the particulate level.

Nowadays, the advancement of Physics and technology toward nanocomposite materials enables leveraging, analyzing, and computing more easily. Parameterizing the bio-physical interactions of nanoparticles and biomolecules enables to investigation of the properties of hybrid nanomaterials. It also enables investigating important properties of hybrid nano biomaterials such as bio compatibility, biodegradation, stability, surface absorption, and sensitivity.

Nanocomposites and nanoparticles have a size of 1–20 nm. Nanoparticles and colloids are also an active area of research and development. Among the dominant nanoparticles and composites, magnetic  $\text{Fe}_2\text{O}_3$  nanoparticles and their hybrids, such as  $\text{Fe}_2\text{O}_3$ -DNA,  $\text{Fe}_2\text{O}_3$ -Hb, and  $\text{Fe}_2\text{O}_3$ , are the focus of this study. As Zubairu *et al.* stated, the optical band gap of  $\text{Fe}_2\text{O}_3$ /DNA is 3.2 eV, which corresponds to the wide band gap semiconductors [3]. Magnetic  $\text{Fe}_2\text{O}_3$  nanoparticles can interact with DNA, RNA, Hemoglobin (Hb), and protein, but the degree of interaction varies. The degree of interaction is strongest in the case of Hemoglobin due to its iron-binding at the center of the heme.

The biophysical interaction between magnetic nanoparticles and biomolecules can be unleashed for biomedical applications. Particularly, the analysis of such interactions has greater prospects in molecular medicine and disease modeling. Some technologies, such as magnetic and molecular biosensors, inculcate the use of Zn-doped iron oxide nanoparticles for tissue imaging and drug delivery. As Pourmadadi *et al.* revealed, the nanocomposite of iron oxide with various polymers is widely used in biomedical applications, including drug delivery, tissue regeneration, and wound healing [4].  $\text{Fe}_2\text{O}_3$  nanoparticles conjugated with Aptamers are active in detecting and diagnosing DNA damage. Aptamers are artificial DNA, RNA, or peptide chains that bind a specific target molecule. Analyzing these interactions enables us to determine the effectiveness of Immuno-absorbents. The efficiency of Immuno-absorbent can be improved by forming MNP-DNA or MNPs-Hb composites.

Magnetic nanocomposite is designed for the purpose of diagnostics, therapeutics, drug kinetics, drug delivery, and nanobiosensors. Magnetic nanocomposite including  $\text{Fe}_2\text{O}_3$ /DNA can be designed for cancer cell, gene, and immunotherapy. Moreover, nanotechnology-based medical procedures are needed for rapid diagnosis of diseases such as cardiovascular disease and infectious diseases. It can also be engineered for nanozymes. Spekowiu and Wendler stated that enzyme-linked immunosorbent assays (ELISA) are used for protein diagnosis [5]. Taking these advantages into consideration, this research is aimed at investigating the nature, type, strength, and range of interactions of magnetic  $\text{Fe}_2\text{O}_3$ /DNA nanocomposite. It is then intended to describe the electrophoretic properties of  $\text{Fe}_2\text{O}_3$ /DNA nanocomposite and colloids. It also presents the risk effects of particle agglomeration and aggregation on human health.

### The DLVO Theory

Different computational techniques have been developed to model nanomaterials interaction. However, the type of models and theory developed may vary depending on the nature, type, and dimension of materials. For the case of nanoparticles and colloid interactions, DLVO and DNA Origami theory are used to describe the particle aggregations, particle agglomeration, and particle segregation. As the research of Hotze *et al.* stated, nanoparticle aggregation plays an important role in determining reactivity, toxicity, transport, risk, and fate of the environment [6]. Although Monte Carlo (MC) simulation, molecular dynamics (MD), force method, and tight banding density functional theory (TB-DFT) are predicted to generate accurate data, DLVO theory is more suitable for zeta potential

calculation. This is because DLVO theory enables analysis of all molecular interactions, weak interactions, magnetic interactions, as well as thermal interactions. As Kozlikova *et al.* [7] and Feiwei Qin *et al.* [8] verified, density functional theory, multi-scale Greens theory, and DLVO theorem are used to perform these tasks. However, at the molecular level, such as Fe<sub>2</sub>O<sub>3</sub>-DNA hybrids, collides have a significant role in controlling the physicochemical properties of the system. The electron dipole moment results from the higher electron density near the nucleus of an atom with higher electronegativity. Undoubtedly, as Mariagrazia *et al.* realized, the DLVO (Derjaguin and Landau 1941; Verwey and Over-bake 1948) theory can be extended to the adhesion, steric acid, and magnetic interactions between nanoparticles [9]. This theory is therefore suitable to determine the stability of colloidal dispersion. It is a good approximation to estimate interactions and zeta potentials. As Jiang reported, a central insertion scheme (CIS) had been developed by many scientific groups [10]. CIS is used to calculate the electronic structure of 1D, 2D, and 3D nanomaterials. Later, this theory is known as hybrid density functional theory. Tight banding Density functional theory (TBDFT) enables the determination of magnetic properties, electronic structures, and shape difference in Fe<sub>2</sub>O<sub>3</sub> magnetic anisotropy. It originates from the Kohn-Sham equations and is applicable to determine self-consistent energy and fields. It is also used for calculating the electronic band structures of long conjugated polymers, single-walled carbon nanotubes, DNA base pairs, nano Diamondoids, and Si nanoparticles. Oliveira *et al.* revealed that DFTB is used for determining the electronic structure of large systems, London dispersion, and molecular dynamics simulations [11]. As Spiegel *et al.* discussed, developments of the DFTB model are useful in describing non-covalent forces, electrostatic interaction, electronic excited states, large-scale simulations, small molecules, biomolecules, clusters, embedded systems, and nanoparticles [12].

However, in this research DLVO theory is found suitable for determining the Van der Waals interaction between the surface and molecule. Furthermore, Taboada-Serrano *et al.* revealed that many processes include the interplay of other forces, such as magnetic fields, which enhance aggregations besides the electrostatic and Van der Waals interaction [13]. These forces can be resolved by the extended DLVO theory. Hence, the DLVO theorem is preferred since magnetic nanoparticles can interact with biomolecules through electrostatic, magnetic, and thermal interactions. The DLVO theorem has a potential to solve problems involving such interaction. It can be applied to describe the aggregations and agglomeration of Fe<sub>2</sub>O<sub>3</sub> nanoparticles or nanofluid. Liu and Neretnieks had discussed the possibility of determining the maximum Gibbs energy of nanoparticles, colloids, and aggregates using DLVO theory [14]. Researchers Adamczyk and Weronki argued that the classical form of the DLVO theory is adequate to describe colloid systems [15]. However, colloid interactions are rather complicated and need an assessment of quantum computing. For this reason, extended DLVO theory has been developed because it takes an account the magnetic dipole interactions, electrostatic dipole interaction, and canonical ensemble. In addition, the crystal structures, shape, and DNA conformation can also affect the Van der Waals interaction.

The Vander Waals dispersion energy ( $G_{\max}$ ) of particle interaction with biomolecules is:

$$G_{\max} = 51.24 \frac{CRT}{K} \tanh^2 \left( \frac{Zy^d}{4} \right) \exp(2kd) \quad (1)$$

Where, C is heat capacity, R is the universal gas constant, and T is temperature (K). The Vander Waals dispersion energy ( $G_{\max}$ ) per unit area per unit parallel plate is:

$$G_{\max} = -\frac{A}{12\pi S^2} \quad (2)$$

Where, A is the Hamaker constant, which describes all van der Waals forces involved in the molecular interactions. The Hamaker constant, A, can also be determined by using Lifshitz theory to describe the dielectric and optical characteristics. As the research of Takagishi *et al.* indicates, the Hamaker constant is related to dipole-dipole moment, product of electron number density,  $n_i n_j$  for heterogeneous species, and dielectric constant [16]. In the discussion of DLVO theory, the electrical double layers are

continuously situated at equilibrium. Hence, the potential difference  $V_{vdw}$  between such layers is:

$$\frac{V_{vdw}}{K_B T} = \frac{-A}{6K_B T} \left( 2a^2 \left( \frac{1}{s(4a+s)} + \frac{1}{(2a+s)^2} \right) + \ln \left( \frac{4a+s}{(2a+s)^2} \right) \right) \quad (3)$$

Where,  $K_B$  is Boltzmann constant,  $s$  is the distance between particles, which is equated with the size of nanoparticles involved in the interaction,  $h$ -is the distance between two outer Helmholtz planes, and  $d$  is the Stern layer thickness in electrolytic solution. For the values,  $h=3.2$  nm,  $d=0.2$  nm,  $S=3.4$  nm.

$$V_{vdw} = \frac{-A}{6} \left( 2a^2 \left( \frac{1}{s(4a+s)} + \frac{1}{(2a+s)^2} \right) + \ln \left( \frac{4a+s}{(2a+s)^2} \right) \right)$$

$$V_{vdw} = \frac{-A}{6} (0.037 \text{ nm} + \ln(0.28)) \quad (4)$$

$$\frac{V_{vdw}}{A} = 0.178 \quad (5)$$

The origin of this equation is the interactions of electrons with biomolecules. On the other hand, the electrostatic attraction between double layers (P-n interface) is:

$$\frac{V_{vdw}}{K_B T} = \frac{201nKT}{\sigma} \frac{(a+\delta)^2}{(s+2a)} \left[ \tanh \left( \frac{Ze\Psi_d}{4kT} \right) \right]^2 e^{-\sigma(s-2\delta)} \quad (6)$$

Where,  $\Psi_d$  is surface potential,  $\sigma$  is surface charge density, and  $\alpha$  is the radius of the sphere. In addition, due to the alignment of electrons' spin:

$$V_m = - \frac{8\pi\mu_o M_s^2 a^3}{g \left( \frac{s}{a} + 2 \right)^3} \quad (7)$$

$$V_m = \beta M_s^2$$

Where,  $\mu_o$  is magnetic permeability,  $g$  is the landee factor,  $M_s$  is a spontaneous magnetization, and  $\beta = -1.84 \times 10^{-11} \text{ s/c}$ , is another constant describing the relation between electric, magnetic, and mechanical parameters. This constant is an electrical equivalent of Newton's law of Universal gravitational constant except with the sign reversed. As the Universal gravitational constant describes the weak force, this constant also describes weak interaction between nanocomposite and colloids at the interface. In the subsequent sections, the DNA Origami theory is discussed for demystifying the DNA structures and nanocomposites.

### DNA Origami Theory

DNA origami technology and origami structures have various applications in nanoscience and Technology. It is a good theoretical tool in molecular physics, biophysics, molecular imaging, and advanced solid-state physics. DNA nanostructures can be visualized as a 2D and 3D crystal lattice. As the DLVO theory suggests, DNA is the 3D extension of RNA. It is represented as A-DNA and B-DNA. However, Liu *et al.* revealed a series of symmetric DNA patterns such as squares and stars [17]. These patterns can be constructed by periodically folding the long strand of natural DNA single strand and fixing it with the short strand. DNA origami combines a long single strand of DNA with a series of designed short DNA fragments by complementary base pairs. This action enables the creation of highly complicated  $\text{Fe}_2\text{O}_3$ -DNA nanostructures. These structures can be remotely controlled and monitored. As Ali *et al.* revealed, a highly sensitive DNA electrochemical biosensor can be developed by using dendritic gold NPs [18]. These electrochemical biosensors have recognition ability up to 1 fm.

The fundamental symmetry operations that are undoubtedly applicable in crystal mapping and transformations are also applicable to Origami theory. Most importantly, reflections, rotations, and translations are performed at a finite angle. In this regard, the DNA origami theory can be carried out by fixing a non-organic  $\text{Fe}_2\text{O}_3$  nanostructure with a DNA strand. As Han and Zhu revealed, DNA computing undergoes three stages, namely, encoding information, molecular operation, and extracting a solution [19]. Moreover, the process may involve three pathways in the electrical signal generation,

namely the test tube stage, a transition stage, and the DNA chip maturity stage. At the transition state ( $\text{Fe}_2\text{O}_3$ -DNA) double layer, DNA molecules are fixed to a solid  $\text{Fe}_2\text{O}_3$  surface to overcome operational difficulties. DNA Origami models have a variety of applications. As Hong *et al.* presented, researchers can control how the DNA folds, creating designer nanoscale structures like biosensors, making it an integral part of molecular electronics and drug-delivery vehicles [20]. As Dey *et al.* explained, Origami structures are applicable in nanofabrication, nanoelectronics, catalysis, computation, molecular machines, bio-imaging, and drug delivery [21].

## DISCUSSION

### Interaction of $\text{Zn}_x\text{Fe}_{2-x}\text{O}_3$ With Body Fluids

The physics of colloids and nanoparticles delves into piecewise analysis of interatomic and biomolecular interactions. It also enables *in vivo* and *in vitro* study of interatomic and intermolecular interactions at the quantum mechanical level. In this regard, the extended DLVO theory is adapted to analyze the particle interaction in the  $\text{Fe}_2\text{O}_3$ -Organic interface layer. This theorem enables computing the Van der Waals interaction, electrostatic interaction, magnetic interaction, and thermal interaction. However, at the molecular and particulate level, the effect of gravitational interaction is almost negligible since it is very long ranged and extremely weak. Atoms executing interaction produce measurable crystal vibrations. In this manuscript, emphasis is given to  $\text{Fe}_2\text{O}_3$ -Hemoglobin (Hb) interactions or  $\text{Fe}_2\text{O}_3$ -DNA interactions. Tailoring these interactions enables engineering of nanocomposites such as  $\text{Fe}_2\text{O}_3$ -Hb and  $\text{Fe}_2\text{O}_3$ -DNA for desired pharmaceutical, biomedicine, and targeted drug delivery.

### Interaction of $\text{Fe}_2\text{O}_3$ with hemoglobin

Hemoglobin is a globular protein that is folded into a compact spherical shape. It is a biomolecule that contains heme with a centered Fe that forms a bond with neighboring nitrogen. It consists of four subunits, namely oxyhemoglobin, deoxyhemoglobin, meta-hemoglobin, and hemichromes. The existence of hemichrome produces suitable conditions for biomolecular- $\text{Fe}_2\text{O}_3$  nanoparticle interactions. The adult human red blood contains Hemoglobin A, which is a heterotetramer composed of two  $\alpha$ -globins and two  $\beta$ -globins polypeptides. Each  $\alpha$ -globins and  $\beta$ -globins polypeptide has Hb as a central unit. The focus of this research is hemichrome, a form of low-spin hemoglobin that contains  $\text{Fe}^{3+}$ . The heme molecule contains an iron atom (Fe) in the ferrous or  $\text{Fe}^{+2}$  oxidation state. In the oxidation state, Zn can exist in  $\text{Zn}^{+2}$ , which can replace iron in the ferrous state,  $\text{Fe}^{+2}$  Heme.

Computationally, DNA can be modeled by Monte Carlo Simulation, molecular dynamics, and force methods. These methods can inevitably generate free energy and self-energy. Besides, the energy states can also be determined by *ab initio* first-principles density functional theory. DNA-grafted 3D super lattice can be assembled in conjunction with  $\text{Fe}_2\text{O}_3$  core and DNA shell. Most red blood cells are rich in hemoglobin, which is enriched with iron bonded with oxygen, which performs the transport process. As Atkins and Paula discussed, with the aid of the NMI technique, the role of blood flow in the brain can be monitored [22]. Magnetic nanoparticles, including Zn-doped  $\text{Fe}_2\text{O}_3$ , can efficiently interact with body fluids such as red blood (hemoglobin). On the other hand, the existence of Fe in the heme of Hemoglobin makes the possibility of designing  $\text{Zn}_x\text{Fe}_{2-x}\text{O}_3$ -based nanosensor, which exhibits high detection efficiency.

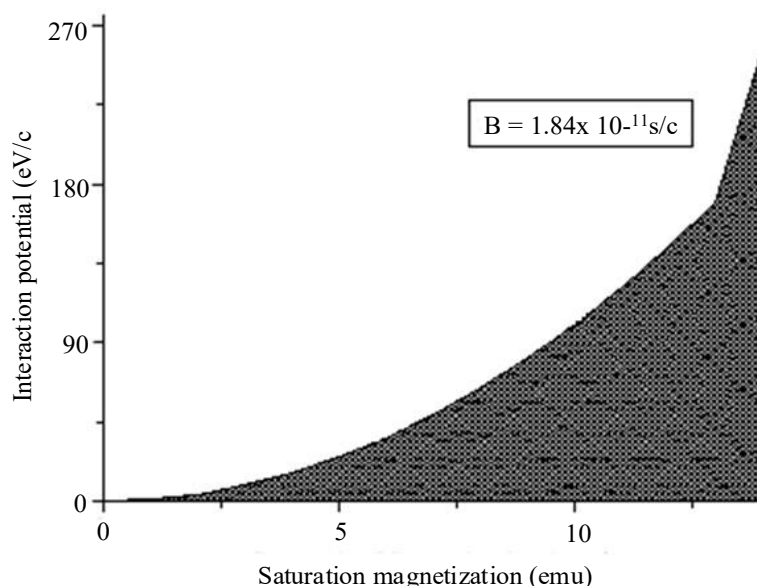
The structure can be characterized by X-ray diffraction, Neutron diffraction, and magnetic resonance imaging. In this interaction, the DLVO theorem can be expressed in terms of the repulsive electrostatic Zeta Potential between double layers and the van der Waals force. The electrostatic Zeta potential between double layers stabilized the particle and colloid suspension, while the Van der Waals force describes coagulation. As Di Marco *et al.* noticed, metal oxide,  $\text{Fe}_2\text{O}_3$ , can build up a surface charge when in contact with water and induce electrostatic repulsion with neighborhood charge [23]. This effect develops Zeta Potential at the interface. Zeta potential helps in determining surface charge density and stability.

In this interaction, magnetic and thermal interaction is considered since the ferrofluid of  $\text{Fe}_2\text{O}_3$  can experience spontaneous magnetization and generate heat in proportion to temperature. It also exhibits electro-mechanical, electrostatic, and magnetic interactions.  $\text{Fe}_2\text{O}_3$  nanoparticles also experience Van der Waals Interaction. This interaction is a weak interaction between the nanoparticles and genetic matter. It gives rise to resonant dispersion. The research of Nikiforovon *et al.* indicates that the magnetic properties of DNA can be demonstrated by a Magnetic SQUID magnetometer [24].

It is shown that DNA and doped DNA exhibit a paramagnetic and spin-glass state. Particularly, doping of DNA with transition metals such as Cd, Cr, Gd, Mn, and V will produce a spin glass state. These elements can potentially produce magnetically frustrated states and defects. Hence, they induce a spin-glass paramagnetic state that can be determined by the 2D-Ising model. The origin of this magnetism is the intrinsic and induced charge flow along the DNA helix. We can mention the paramagnetic and superparamagnetic states. This state makes suitable conditions for interaction between  $\text{Zn}_x\text{Fe}_{2-x}\text{O}_3$  nanoparticles and human blood, particularly hemoglobin via Heme easily. The helical magnetic field induced in this way is directed orthogonal to the current density. As Lee *et al.* noted, DNA can exhibit ferromagnetic properties in liquid Helium [25]. Heme plays a central role during the interaction of magnetic nanoparticles with protein interactions.

Moreover, Dehghan *et al.* suggested that SPIONs@DA-Chr binds to DNA via groove binding mode [26]. In this regard, Paramagnetism is attributed to the charge carrier, specifically electrons, producing helical fields along the transverse direction of the charge carrier. Moreover, a moment is induced when exposed to an external magnetic field. This idea is useful in describing the interaction between  $\text{Fe}_2\text{O}_3$  nanoparticles with biomolecules such as DNA. It must also be noted that for the ferrofluid, temperature is inversely proportional to magnetization as governed by Weis-Curie's law. Figure 1 demonstrates the relation between interaction potentials and spontaneous magnetization (Ms).

As the calculation of this research indicates, the Vander Waals Potential is directly proportional to the square of spontaneous magnetizations. Hence, the constant of proportionality,  $\beta$ , illustrated in the figure, has the same form as Newton's Universal Gravitation constant, except its unit and magnitude are less by the factor of 3.65. Although the Vander Waals interaction is dominating most interactions in  $\text{Fe}_2\text{O}_3/\text{DNA}$ , the Value of constant  $\beta$  is very low, showing that it is a weak interaction. It is also investigated that Van der Waals interactions are attractive as expected since positive charge of  $\text{Fe}_2\text{O}_3$  is attracted by the negative charge of DNA. It is long-range and gives rise to an electrophoretic property due to unlike charges appearing in two species.



**Figure 1.** The relation between the interaction potential and magnetizations.

Zn has the capacity to increase the oxygen affinity of both normal and sickle red blood cells due to a Zn-hemoglobin binding mechanism. In this context, the Coagulation process describes the change of blood from the liquid phase to the gel phase, leading to blood clotting. This process has a risk effect on human health, including hypertension, anemia, leukemia, etc. In theoretical settings, DLVO theory can help to model such problems.

All Zn, Fe, and O<sub>2</sub> are highly abundant in the human body. Zn figure is a piece of protein structure motif that stabilizes protein folding. Zn and Fe can exist in the same oxidation state, which is analogous to ferrous iron. Zn is used to read DNA sequence while Fe controls metabolic activities such as blood transmission, enzymatic activity, DNA repair, and biomarker. The deficiency of these elements in the body causes various risks and effects on health, such as anemia, oxidative stress, and DNA damage.

Enumerating the interaction of Magnetic Fe<sub>3</sub>O<sub>4</sub> nanoparticles with hemoglobin at the interface of Fe<sub>3</sub>O<sub>4</sub>/Hb is an in-depth investigation of the electrophoresis process. Hemoglobin's electrophoresis is a red blood test for identifying and visualizing specific types and functions of hemoglobin. It is used to detect Thalassemia, sickle cell disease, and hemoglobin C. In the electrophoresis process, the membrane is a supporting matrix or chamber through which the electric current passes. The gene, Polyacrylamide or nitrocellulose, serves as a separating medium of Fe<sub>3</sub>O<sub>4</sub>/DNA double layer.

As Jeng and Chen revealed, the deficiency of zinc (Zn) is an indication of the deficiency of iron, which is responsible for anemia [27]. Common human diseases such as sickle cell, anemia, and Thalassemia are caused by abnormalities in Hemoglobin. This indicates that Thalassemia can be treated by leveraging the interaction of Zn<sub>x</sub>Fe<sub>2-x</sub>O<sub>3</sub> nanoparticles with red blood cells seamlessly. Moreover, Thalassemia can be treated by chelation therapy. Chelation therapy can also efficiently remove poison heavy metals and enable new cell growth.

#### ***Interaction of Fe<sub>2</sub>O<sub>3</sub> NPs with DNA and Gene***

The knowledge of DNA nanotechnology enables insights into microscopic and nanoscale interactions of particles. In this section, the major interaction between Fe<sub>2</sub>O<sub>3</sub> nanoparticles with DNA, genes, and the underlying principles is explored. Analyzing and modeling these interactions enables the detection, diagnosis, and control of epidemic diseases such as cancers and infectious diseases such as cardiovascular disease. It also provides efficient treatment, like genome editing/CRISPR. DNA Nanotechnology also enables detecting and controlling the transmission of epidemic diseases such as TB, Ebola, Gonorrhea, HIV-AIDS, and coronavirus. It studies the phenomenon of nanoparticles' interactions with human body fluids at the chromosomal level, such as DNA and genes. DNA is studied because all viruses contain DNA, which carries genetic information. In order to fully understand the response of Fe<sub>2</sub>O<sub>3</sub> nanoparticles to the epidemic, it is important to explore the interaction of these nanoparticles with genetic matter. As Gomes and Ashley revealed, mass spectroscopy can be used for proteomic and metabolomic studies [28]. Hence, the mass spectroscopy enables the generation of ions by bombarding either Fe<sub>2</sub>O<sub>3</sub> or the Organic component (DNA, RNA, or Hemoglobin).

Zn<sub>x</sub>Fe<sub>2-x</sub>O<sub>3</sub> nanoparticles can also interact with DNA, genes, and proteins. The physicochemical process takes place at the interface between biomolecules-nanoparticles (B-N). It should also be noted that by surface and interfacial engineering, Fe<sub>3</sub>O<sub>4</sub> can be resized and shaped for DNA binding. Surface effects, including surface absorption, pH values, and contact angle, can be modulated for effective drug delivery, surface Plasmon resonance, and imaging. Particularly, the contact angle can influence the biocompatibility, bacterial adhesion, and cell interaction of Fe<sub>3</sub>O<sub>4</sub>/DNA nanocomposite, and enhance CGT therapy, drug delivery, and surface engineering. This action enables rapid DNA deletions, particularly when infected with cancers, and helps in drug delivery.

An immunological function includes the circulation of white blood cells and the detection of foreign material by antibodies. Particularly, Fe<sub>2</sub>O<sub>3</sub> nanoparticles have immunogenic properties. As Udriște *et al.* realized, iron may accumulate in the infarcted myocardium for more than six months [29]. This property makes iron-containing oxides more preferable in treating cardiovascular disease and cancer

therapy. Metal oxide NPs have been identified as therapeutic agents with an extended half-life and therapeutic index.

Analysis of nanoparticles' interactions with DNA is very important since nanotechnology-oriented drug delivery systems, such as Nanosyrinx, involve the use of nano syringes based on genes or proteins. Nanosyrinx is a cutting-edge synthetic Biology Company aimed at fabricating the next-generation drug delivery systems with painless injection. An example of such devices includes nano-needles and Nanozymes.

Hydrogen bonding is a critical mechanism responsible for linking biological molecules (DNA) and polymers. It is formed by the sharing of a proton between two atoms and creates linkages between the turns of the helix. The bases of the DNA double helix are paired through hydrogen bonds (H-bonds), forming base pairs (bp). There are two hydrogen bonds between Adenine and Thymine, which form electric polarization. On the other hand, there are three hydrogen bonds between Guanine and Cytosine. However, one of the third hydrogen can be removed from the bond by the tautomerization effect. This fact is important to harness nuclear energy through the process of nuclear emissions or positron emissions. As Seeman and Sleiman revealed, the ability to conjugate numerous photonic and electronic materials to DNA enables next-generation personal medicine [30]. This action can enable efficient photon interaction with an external organism, such as a smartphone.

Nucleotides are the monomeric units of DNA and contain genetic information. This information is useful in digital and microelectronics. Like a Computer's central processing unit (CPU), a nucleotide is the central functional unit of DNA. As discussed by Huang *et al.*, it is possible to design a stimulus-responsive DNA reaction network in order to integrate sensing, translation, and decision-making operations [31]. The research of Herrer *et al.* indicates that Proteins are building blocks of bioelectronics, protein-based transistors, and nanobiosensors [32]. As Vasudevan *et al.* explain, the side chains of peptides are free to rotate through Ramachandran angles on either side of the peptide bond [33]. This rotation determines the spatial orientation of the peptide chain. According to Allen, Green fluorescent proteins provide a suitable condition to probe gene expression, protein trafficking, and signal response [34].

DNA conformation and structures have significant impacts on the biomedical function of  $\text{Fe}_2\text{O}_3$  nanoparticles and chemotherapy application. For example, Wu *et al.* have noted the significance of the DNA double helix for drug delivery, transfection, and chemotherapy with the same role as platinum nanoparticles [35]. As presented by Miao *et al.*, molecular dynamics simulations (MDS) provide a detailed picture of the biomolecular dynamics in an atomistic view [36].

We can mention the paramagnetic and superparamagnetic states. This state makes suitable conditions for interaction between  $\text{Zn}_x\text{Fe}_{2-x}\text{O}_3$  nanoparticles and human blood, particularly hemoglobin via Heme, easily. As per Krukemeyer *et al.*, in a magnetic drug targeting system, a positively charged nanoparticles containing iron are loaded with negatively charged nucleic acids, which are brought to the target cells by the magnetic field [37]. Sometimes,  $\text{Fe}_2\text{O}_3$  nanocomposite may damage DNA. We overcome such a severe problem by controlled substitution of  $\text{Fe}^{2+}$  with  $\text{Zn}^{2+}$  ion. As Oelshlegel *et al.* noted, Zn can also bind to more than one amino acid residue due to the oxygen affinity [38].

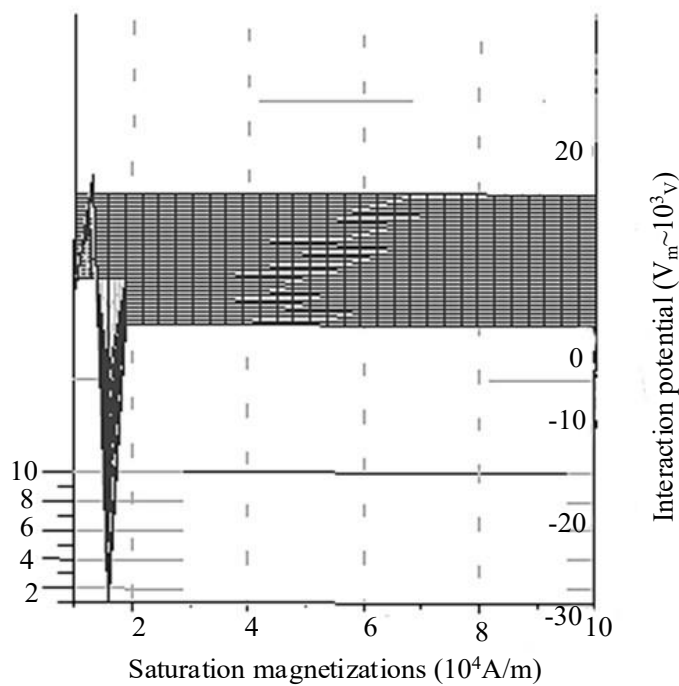
Nanoscience encompasses the interaction of  $\text{Fe}_2\text{O}_3$  with DNA, which is a fundamental specification of the biomedical characteristics of  $\text{Fe}_2\text{O}_3$  nanoparticles. Most nanotechnologies and nanodevices incorporate DNA. The DNA nanosystems can also serve as an electrode and electrolyte material in an analytical biosensor. In the electric DNA- $\text{Fe}_3\text{O}_4$  double layer, the electric charge and electrolytic interaction take place (Table 1). This interaction is responsible for the evolution of Helmholtz's height in Grahame's model. Moreover, free energy is calculated by using the equations stated by Fu *et al.* [39].

As illustrated in Figures 2 and 3, the interaction of  $\text{Fe}_2\text{O}_3$  nanoparticles with biomolecules such as DNA and RNA generates charge carriers that propagate between electrodes. The stream of these charge carriers produces an electric signal at the signal generators. In this work, data for the zeta Potential is generated by first computing it in terms of thermal, mechanical, and electrical parameters. Then, it is graphed by using the origin-pro 8.

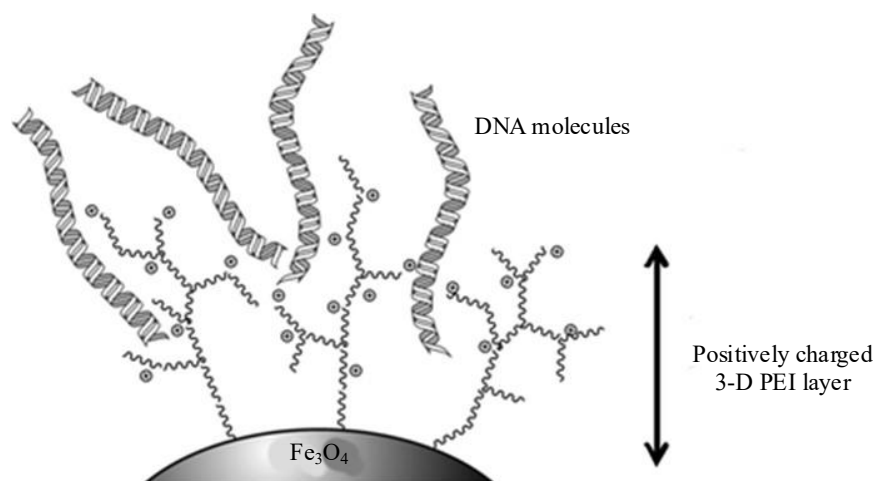
The repulsive potential decreases as the distance between nearest neighbors diverge from above the symmetric axis. This interaction is equated with the Pauli repulsive potential. However, the Coulomb potential or attractive potential shows the same fluctuation below the symmetric x-axis.

**Table 1.** The values of different parameters.

a	S	T	$V_z/A$	$V_z$
0.4 nm	0.56 nm	25°C=298 K	-1.078	565 $\mu\text{V}$



**Figure 2.** Change in interaction potential with the square of saturation magnetizations.



**Figure 3.**  $\text{Fe}_3\text{O}_4$ -DNA interaction [40].

Fe<sub>3</sub>O<sub>4</sub>/hemoglobin (Hb) composites can be used for signal amplification in biosensors. The magnetic Fe<sub>3</sub>O<sub>4</sub> nanoparticles are used as a signal amplification element, while hemoglobin serves as an electron immobilizer or catalyst. By connecting the charge reservoir with Amplifiers such as MOSFETs integrated biosensors, we can improve its signal amplification and moderate the gain factor. The result is then displayed on the screen, which is helpful in decision-making and establishing a concluding remark. The signal generators rectify, amplify, and direct them to the fluorescent screen where the signal display emerges.

The study also revealed that the interaction of ferric oxide (Fe<sub>2</sub>O<sub>3</sub>) with hemoglobin results in fluorescence quenching of Hb by Fe<sub>2</sub>O<sub>3</sub> nanoparticles. This forms a Fe<sub>2</sub>O<sub>3</sub>-Hb nanocomposite, forming electrostatic double layers.

Cryogenic study of thermal properties reveals that Fe<sub>2</sub>O<sub>3</sub>-Fe<sub>2</sub>O<sub>3</sub>, Fe<sub>2</sub>O<sub>3</sub>-DNA, and Fe<sub>2</sub>O<sub>3</sub>-Hb are thermally stable. This property is significantly important in bioelectronics and biomedicine. For biomedical and pharmaceutical applications, the Colloidal stability of magnetic nanoparticles must be in aqueous suspension states.

The challenge is particle aggregation and agglomeration, which cause surface charge instability. However, these effects can be reduced or prevented by coating with carbon films, gradually changing the concentrations of magnetic ions such as Fe<sup>2+</sup>, and remotely controlling with magnetic fields. As the DLVO theory suggests, controlling the relations between interaction potential, spontaneous magnetization, and temperature of nanocolloids reduces particle aggregation and agglomeration.

Fe<sub>3</sub>O<sub>4</sub>/DNA can be a choice of magnetic field-induced therapy, magnetic fluid hyperthermia, and superparamagnetic resonance imaging (SPRIM). Besides, Fe<sub>3</sub>O<sub>4</sub>/DNA can serve as a constituent material in biosensors where electrophoretic separation is a part of the detection method. Leveraging surface properties, surface absorption, and electrophoretic properties of Fe<sub>3</sub>O<sub>4</sub>/DNA enhances its biomolecular separation and biomedical application. Fe<sub>3</sub>O<sub>4</sub>/DNA facilitates biomolecular separation and purification through diagnosis, magnetic separation, and streamlining biomedical assays.

## ELECTROPHORETIC PROPERTIES

The next step after magnetic separation is the electrophoresis process. This process can be used to separate and visualize the DNA based on its size and charge, help to purify, and confirm its existence. Electrophoresis is the movement of charged biomolecules, including DNA, RNA, or hemoglobin, via a medium such as gels. This movement is usually assisted by an external agent such as an electric field. The electric field enables the migration of positive charges from a non-organic molecule toward the negatively charged organic layer. In Fe<sub>3</sub>O<sub>4</sub>/DNA nanocomposite, this movement is from positively charged Fe<sub>3</sub>O<sub>4</sub> toward negatively charged DNA. Hence, Fe<sub>3</sub>O<sub>4</sub>/DNA exhibits electrophoretic properties due to the dipolar moment formed by the separation of opposite charges.

The electrophoretic properties of Fe<sub>3</sub>O<sub>4</sub>/DNA double layer are impacted by several factors. Most dominantly, it is determined by the Zeta potential ( $V_z$ ) of Fe<sub>3</sub>O<sub>4</sub>, and the Van der Waals interaction between Fe<sub>3</sub>O<sub>4</sub> and DNA. DNA is attracted to the anode in gel electrophoresis. This process can enhance the interaction of magnetic Fe<sub>3</sub>O<sub>4</sub> nanoparticles with DNA molecules. As Shen *et al.* explained, Fe<sub>3</sub>O<sub>4</sub> possesses high surface energy, leading to aggregation, which minimizes the surface energy [41]. Lallman *et al.* revealed gel electrophoresis to determine overall mobility (includes contributions from electrophoretic and electroosmotic forces) in ionic conditions [42].

The electrophoresis process is quite important in forensics and gene fingerprinting, biomedicine, and Pharmacognosy. Fe<sub>3</sub>O<sub>4</sub>/DNA can be used for electrophoretic devices, primarily for magnetic separation and DNA purification. Therefore, electrophoresis of Fe<sub>3</sub>O<sub>4</sub>/DNA facilitates magnetic gene delivery by inducing a magnetic field and guiding Fe<sub>3</sub>O<sub>4</sub> nanoparticles. It also enables DNA purifications, drug delivery, and enhances Pharmaco-medical applications of Fe<sub>3</sub>O<sub>4</sub>/DNA nanocomposite.

As Dourado described, the electrical double layer (EDL) is the point where the effect of interfacial pH is stated [43]. This interaction is promising for designing a nanobiosensor. By leveraging these interactions, Fe<sub>2</sub>O<sub>3</sub> nanoparticles can be engineered for immunosensors, immunoassays, magnetic resonance imaging, Gene therapy, and drug delivery. These interactions are also responsible for magnetic fluid hyperthermia.

Overall, parameterizing the bio-physical interactions of nanoparticles and biomolecules enables to investigation of the biocompatibility, sensitivity, and reactivity of Fe<sub>3</sub>O<sub>4</sub>/DNA nanocomposite. Leveraging these properties enables tailoring the biomedical and pharmacological application of Fe<sub>3</sub>O<sub>4</sub>/DNA composites.

## CONCLUSION

The interaction of magnetic nanoparticles, including Fe<sub>3</sub>O<sub>4</sub> and Zn<sub>x</sub>Fe<sub>2-x</sub>O<sub>3</sub>, with biomolecules such as DNA, RNA, lipids, or proteins exhibits fascinating biophysical properties. More importantly, it exhibits a hydrophobic and hydrophilic group. As the study reveals, such biophysical interactions are dominated by Vander Waals interaction, thermal interaction, and magnetic interaction to a minimum extent. The molecular interactions between Fe<sub>3</sub>O<sub>4</sub>, DNA, and Hb are explored by DLVO theory and DNA-Origami theory. The theorems summarize the relationships among electrical, mechanical, magnetic, and thermodynamic parameters. The result shows that these parameters are directly impacting the functional properties of hybrid Fe<sub>2</sub>O<sub>3</sub>- Organic molecules. As the DLVO theory suggested, the Vander Waals interaction potential is directly proportional to the Hamaker parameter and the square of spontaneous magnetization. As shown on the graph of potential surface, the repulsive potential decreases as the distance between nearest neighbors diverges from above the symmetric axis, while the Coulomb potential shows the same fluctuation below the symmetric x-axis. Moreover, adjustments in electrical, magnetic, and thermal quantities, such as repulsive and zeta potential, magnetizations, and temperature, enable Fe<sub>2</sub>O<sub>3</sub>/DNA or Fe<sub>2</sub>O<sub>3</sub>/Hb hybrids for efficient electrodes. This enables the hybrid nanocomposite to be quite useful in desired, flexible, and non-volatile bioelectronics. Both electrophoretic and magnetic properties of Fe<sub>3</sub>O<sub>4</sub>/DNA and Fe<sub>3</sub>O<sub>4</sub>/Hb are associated with Van der Waal interactions and Zeta Potential. These properties make both Fe<sub>3</sub>O<sub>4</sub>/DNA and Fe<sub>3</sub>O<sub>4</sub>/Hb bilayer important in biomedical engineering, molecular medicine, pharmaceuticals, cancer therapy, and treatment for Thalassemia.

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