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**Research/Technical Note**

# Plausible Approach for Rapid Detection of SARS-CoV-2 Virus by Magnetic Nanoparticle Based Biosensors

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**Abstract:** A new pandemic named as COVID-2019 (coronavirus disease 2019) has stunned the world. This pandemic situation arises due to an enormous death toll of human lives across the world by the infection of SARS-CoV-2 that results in pneumonia-associated respiratory syndrome. It is repentantly observed to speedy spread over the world day by day because of need in rapid detection, proper medication, and proven treatment. Since it's evolved in November 2019, scientists were engaged to find its genome code. However, the current efforts of the scientist (both physical and biological) in the world is to invent specific antiviral drugs and physical therapeutic against COVID-19 and rapid detection method. Hence we have tried to discuss in this report rapid detection system of the viral genome like +ssRNA, and S (spike) - protein containing into SARS-CoV-2 by magnetic nanoparticles (MNPs). To detect SARS-CoV-2 pathogens, giant magnetoresistive (GMR) biosensor along with MNPs may play a significant role. We expect that this detection system will be an effective challenge to control the outbreak of COVID-19.

**Keywords:** COVID-19, Magnetic Nanoparticle, GMR

## 1. Introduction

In recent years, researchers across the world have paid much attention to the synthesis of different kinds of MNPs and strive hard to enhance electrical and magnetic properties, and also to the structural correlation and tunability in them for their diversified applications in the fields of biotechnology, biomedical, material science, engineering, and environmental aspects [1-8]. In the biomedical section, biosynthesized such as bio-coated and biofunctionalized MNPs have already been extensively and effectively used in the multiferous applications like drug delivery, hyperthermia, magnetic resonance imaging (MRI), tissue engineering, and repair, biosensing, biochemical separation, and bioassay, etc. [9]. Recently, biofunctionalized MNPs are effectively used in the detection of bio pathogens such as bacteria and viruses [4, 10] across the world because of their small size, good mono-dispersity, superparamagnetic behavior, high coercivity, low Curie temperature, and high magnetic susceptibility etc. Besides, MNPs are presently found to be widely used to detect the deadly respiratory viral pathogens [11-14]. These bio-synthesized MNPs are used because most of them with good mono-dispersity and excellent magnetic properties are oil-soluble, which greatly restricts at the time of bio-detection [15-17]. Another reason for bio-synthesis is the divergence of control in size, shape, stability, and dispersibility of MNPs in desired bio-solvents. From December 2019 a new viral disease named coronavirus disease (COVID-19) has become at the apex of discussion across the globe that stunned the world [18]. The pathogen of COVID-19 is severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) [18] against which no vaccination, drugs, therapeutics, and effective and prompt detection kit are developed. That leads to a challenging issue for scientists and clinicians still to date. However, detection by MNPs or any other NPs is expected to be a promising one to face the aforesaid challenges in the near

future [14, 19]. In the present study, we have discussed how MNPs may play a vital role in biomedical applications such as testing of severe acute respiratory syndrome 2 or other viral pathogens and treatment of virus-infected patients, especially present pandemic COVID-19 patients.

# 2. Materials and Methods

### *2.1. Genome of SARS-CoV-2*

The SARS-CoV-2 is a β-type positive-sense (+ss) RNA virus with a size of ~29.9 kb [20]. Its genome structure is approximately similar to SARS-CoV and MERS-CoV having positive-sense RNA genomes of 27.9 kb and 30.1 kb, respectively [21]. This type of RNA genome is 50 capped and 30 polyadenylated, which contains a 5′ cap structure along with a 3′ poly (A) tail, allowing it to act as an mRNA for translation of the replicasepolyproteins [22]. Approximately 70% of viral RNA encodes 16 non-structural proteins (NSP) and the rest part of virus genome encodes four essential structural proteins, including spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein [23]. There are two types of SARS-CoV-2 such as L type (~ 70%) and S type (~ 30%). The strains in L type are more aggressive and contagious derived from S type [24]. Based on the genomic analysis it is clear that SARS-CoV-2 could use angiotensin-converting enzyme 2 (ACE2), as similar to SARS-CoV [25], to infect the human body. To detect +ssRNA and S-protein in the said virus is required to know the synthesis process, and surface functionalization of MNPs.

### *2.2. Magnetic Nanoparticle Synthesis*

Magnetic nanoparticles (MNPs) can be synthesized in a variety of ways like wet chemical [26], template-directed [27], microemulsion [28], thermal decomposition [29], solvothermal method [30], solid-state [31], deposition method [32], spray pyrolysis [33], self-assembly [34], physical and lithographic [35] methods. Some of these methods have some drawbacks due to irregular shape, and the possibility of contamination at the time of synthesis. However, co-precipitation, thermal decomposition, hydrothermal, laser ablation, microemulsion, and chemical vapor deposition or arc discharge [36] are considered to be suitable methods for biomedical applications by MNPs to date. Here in this section, we have discussed a short description of thermal decomposition and hydrothermal methods due to their approaching better results in magnetic nanostructures, size, and morphology in comparison with other synthetic routes [37] for the purpose.

#### *2.2.1. Thermal Decomposition*

Thermal decomposition is one of the nanoparticle synthesis methods wherein the nature of metallic ion and the force of reaction with the ligands in coordination compounds have effects at elevated temperature and pressure that resulting in the breaking of the chemical bond [38, 39]. In this method, no particular stabilizing agent (stabilizer) is required/used for thermodynamic or kinetic stability in coordinated compounds [40]. However, according to Maity et al., to control the size, morphology and magnetic structure some organometallic compounds (such as oleylamine, oleic acid, phenyl ether, benzyl ether, 1-octadecene, and acetylacetonate) are used with magnetic oxide in this method [41]. Surprisingly, it is noted that the spherical and cubic shape nanoparticles are plausible to synthesis by this thermal decomposition method [42]. Wherein the spherical-shaped nanoparticles are usually obtained at the short decomposition duration (2-4 hrs) whereas longer duration (10 – 12hrs) resulted in cubic morphology [43].

#### *2.2.2. Hydrothermal Process*

The hydrothermal method is another important chemical route for the synthesis of nanoparticles where heterogeneous reactions occur in aqueous media above ambient temperature and pressure [44]. The MNPs of metal, metal oxide [46, 46], rare earth transition metal magnetic nanocrystals [47], semiconducting [48], dielectric, rare-earth fluorescent, and polymeric [49] can be fabricated by using this method. In this method, the aqueous solution of analytical graded associated chemical reagents has been prepared at a high boiling point and high pressure under the argon atmosphere. The MNPs can then be synthesized from that aqueous solution with controlled shape and size [50].

### *2.3. Functionalization of MNPs*

After synthesizing the MNPs, some defects remain on its surface, hence it needs to be functionalized its surface by grafting or organic/inorganic coating. The functionalization of MNPs is required because non-functionalized MNPs restrict bio-detection, bio-imaging, bio-sensing, and biomedicine. And the enhanced magnetic properties of MNPs are shown after the effect of surface functionalization. Hence in this section, we have discussed the surface functionalization by organic compounds, biomolecules, and inorganic materials.

#### *2.3.1. Surface Functionalization by Organic Materials*

In order to prevent or decrease the agglomeration of MNPs and increase the stability of MNPs, organic compounds such as carboxylate [16], glycine [51], dextran [16, 52, 53], polyvinylpyrrolidone (PVP) [54], acropolis [55], polyethyleneglycol (PEG) [56, 57], polyethyleneimine (PEI) [58], polyvinylalcohol (PVA) [59], oleic acid, lauric acid, dodecyl phosphonate, hexadecyl phosphate and so on often play an important role to passivate the surface of MNPs during or after their synthesis to avoid agglomeration [60]. To remove oil solubility and water-solubility of MNPs, the hydrophilic and hydrophobic chemical groups are used [60]. It is to be noted that organic compounds functionalized MNPs provide not only the basic magnetic properties but also possess good biocompatibility and biodegradability of the functional organic materials [61].

#### *2.3.2. Surface Functionalization by Biomolecules*

In order to expand the scopes of MNPs for the biological

application, some biomolecules such as protein [62, 63], polypeptide [64], antibody [65, 66], biotin and avidin [67], etc are usually employed to enhance its biocompatibility [68]. The biological molecules functionalized MNPs are very useful to assist an effective separation of proteins, DNA, cells, biochemical products, etc. The human serum albumin (HAS)-coated MNPs are more important for n-Vivo regional target therapy [69]. The water proton coated superparamagnetic MNPs are reported to act as magnetic switches by enhancing spin-spin relaxation times [70] and thus make them suitable to develop biocompatible magnetic nanosensors [71].

#### *2.3.3. Surface Functionalization by Inorganic Materials*

With all organic and biomolecules, inorganic compounds such as silica [72], metal [73], nonmetal [74], metal oxides [75-77], and sulfides [72, 78] have extensively used for surface functionalization of MNPs [68]. The inorganic compounds are used to enhance the antioxidation properties of MNPs, which have promising applications in catalysis, bio-labeling, and bioseparation [72]. The inorganic compound functionalized MNPs can control the structure and interface interaction with demonstrated physical and chemical properties that will be essential for future technological applications. With all inorganic compounds, optical-electronic material functionalized MNPs play an important role to enlarge the MNPs application scope. Novel water-soluble hybrid material consisting of quantum dots (QDs) and MNPs encapsulated in a silica shell exhibits a good luminescent and magnetic properties with broad excitation, and strong resistance to photobleaching, resulting in these materials are easy to apply for bio-detection and bio-sensing [99].

### *2.4. Attaching Viruses to Magnetic Nanoparticles*

To know the viral genome detection mechanism by magnetic nanosensor it is required to know how viruses and MNPs attached to each other. Viruses and MNPs are attached as supramolecular architectural design with unique building blocks [79]. These supramolecular assemblies with the perfect ratio of viruses and MNPs change the optical and magnetic properties of pure MNPs [80]. These supermolecular structures are therefore very sensitive to the virus, which may allow designing magnetic nanosensors capable of detecting targets such as nucleic acid (DNA, RNA) and proteins [81], specially +ssRNA and S-proteins containing SARS-CoV-2 and thus ultimately to the rapid detection of the SARS-CoV-2 virus.

### *2.5. Magnetic Separation Technique*

A viral object often needs to be separated from its environment [82] for virus detection. Magnetic separation is indeed the mechanism of rapid virus detection by the MNPs. So, it is required to know about the magnetic separation technique to understand the mechanism of virus detection by MNPs. The magnetic separation of targeted biomolecules is caused by interacting with the surface ligand and receptor of functionalized MNPs [10]. This magnetic separation technique is comparatively simple, rapid, and capable of capturing specific proteins or other biological macromolecules efficiently [83] as compared to the centrifugation technique, which is much time-consuming, less efficient, and has a poor effect.

## 3. Discussion

### *3.1. Detecting Viruses*

The new virus SARS-CoV-2 is spreading out in the human body at an alarming rate. By the time, around 253 countries in the world have been severely affected because of a lack of ineffective and rapid detection kits due to a variety of transmutation nature of this virus. This fact necessitates to exploit/explore or discover such an effective and rapid and efficient detection device for the SARS-CoV-2 virus. As such, efforts are still continuing to invent such a rapid detection device among the scientific community across the world. Recently, Fluorescence, [84] light scattering [85] surface-enhanced Raman scattering (SERS) [86] electrochemical [87, 88] quartz crystal microbalance (QCM) [89, 90] microcantilevers (MCLs) [91], surface plasmon resonance (SPR) [92, 93] and magnetic [94] sensors have developed for virus or other viral genome detection. With all magnetic nanosensors such as giant magnetoresistive (GMR) sensors, magnetic tunnel junction (MTJ) sensors, and SQUID sensors play a vital role to detect viral pathogens. At present, the most-used MNPs are superparamagnetic NPs, which can be magnetized by applying the magnetic field. Then they redisperse in the solution with the removal of the magnetic field. Thus magnetic nanosensors with superparamagnetic NPs can be capable to detect the more complex target, such as intact viral particles in serum. [81]. As compared to SQUID sensors, GMR sensors are simpler and more portable, and they operate at room temperature. This is why we try to discuss +ssRNA and S-protein containing the SARS-CoV-2 detection technique by GMR sensors.

### *3.2. GMR Biosensor and Detection Principle*

GMR biosensors along with MNPs is a powerful tool for high sensitivity, real-time electrical readout, and rapid biomolecule detection which was first introduced by Baselt et al. in 1998 [95] and then have been developed by several research groups [96-101]. The basic principle of giant magnetoresistance-based immunoassay detection is the alternation of magnetization with changing the electrical resistance from high to low [102]. Because of spin collision at the interfaces between MNPs and non-magnetic biomolecules such as viral protein [103, 104]. This spin collision at the interface is the governing factor of changing the electrical resistance. Accordingly, when the spin collision increases then the electrical resistance decreases that ultimates to increase the magnetization in the interface between MNPs and protein, and thereby by proper calibration to the uninfected body this magnetic signal may be the measuring parameters in the said detection device in its operation. Since there is no

ferromagnetism property in S-protein and +ssRNA containing SARS-CoV-2, it may allow the detection of magnetic signals with less background noise, which is evident from the previously published report [105]. In the overall discussion, to detect respiratory viral pathogens like SARS-CoV-2, the MNPs play a vital aspect in the GMR biosensing technology. The GMR biosensor based device is more sensitive, less time consuming, low costing device than other conventional testing devices. GMR biosensors rely on a magnetic tag. that offers several key advantages over other sensing modalities [98]. First, the biological samples (blood, urine, serum, etc.) naturally lack any detectable magnetic content, providing a sensing platform with a very low background level and thus lower detection limit of analytes. Second, the sensors can be arrayed and multiplexed to perform analysis on a panel of proteins or nucleic acids in a single assay. Lastly, the sensors can be manufactured cheaply, in mass quantities, to be deployed in a one-time use disposable format. For these reasons, magnetic biosensors are an attractive and competitive alternative to optical techniques. Also, GMR biosensor is important because it is possible to integrate this assay into a portable, handheld device for on-site application.

# 4. Conclusion

During the COVID-19 pandemic, the rapid and reliable detection of the pathogens of SARS-CoV-2 to protect its spread has become an undeniable necessity for us. Magnetic biosensor especially the GMR biosensor along with MNPs may be a very sensitive and promising biosensing device to rapid detection of SARS-CoV-2 S-protein and +ssRNA from the biological samples (blood, urine, serum, etc.). This is focused as an alternative option to develop sooner for separating COVID-19 patients and thus protect the outbreak of COVID-19 to regain a normal pace in the world.

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