Magnetically Labeled GMR Biosensor With a Single Immobilized Ferrimagnetic Particle Agent for the Detection of Extremely Low Concentration of Biomolecules

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***Abstract*—It was numerically and experimentally demonstrated that "one giant magnetoresistance (GMR) biosensor + single ferrimagnetic nanoparticle or micro particle sensor agent" architecture is more technically suitable for the detection of extremely low concentration of biomolecules than the "one GMR biosensor + single superparamagnetic nanoparticle sensor agent" architecture. The large remnant magnetization of a single immobilized ferrimagnetic nano or micro particle sensor agent that allows for, producing a sufficiently large stray magnetic field, maintaining negligibly small variation of interaction factor (IF) formed between the agent and the free layer (sensing layer) of the GMR biosensor, and a larger "effective sensing area" directly corresponding to a practically larger optimized sensor size, were found to be the main physical reasons for the technical promises.**

***Index Terms*—Extremely low concentration of biomolecules, ferrimagnetic particle agent, magnetically labeled giant magnetoresistance (GMR) biosensor, superparamagnetic nanoparticle agent.**

I. Introduction

THE magnetically labeled immunoassay-based giant magnetoresistance (GMR) biosensor system has been extensively investigated for the past ten years in the field of disease diagnosis, DNA genotyping, and molecular concentration measurement [1]–[14]. The main reason is that this sensory system shows several technical advantages such as higher sensitivity, lower power consumption, portable sensor size, and more economic compared to the commercial fluorescence-based bioassays. In particular, the technical feasibility to detect extremely low concentration of biomolecules or viruses ($<10^{-20}$ mol/L) using a single immobilized sensor agent implicitly makes it apply for virus-based disease diagnosis, biological warfare, and chemical terrorism [8]–[14].

The magnetically labeled GMR biosensors currently considered in lab-on-chip or point-of-care sensor technologies mostly use superparamagnetic nanoparticles (SPN) for a sensor agent [1]–[12]. The SPN sensor agents have a lot of technical advantages such as easy manipulation on the sensor surface, easy retrieval of stray magnetic field, and possible delivery of low concentration of biological entities below 10^{-18} mol/L [4], [16]. Accordingly, the GMR biosensor with SPN sensor agents have been and are intensively being considered for an *in-vitro* biosensor system to count biological entities and to diagnose diseases [9]–[11]. However, despite the huge biotechnical potential, the application to "single sensor agent + one GMR biosensor" architecture, which is expected to detect one single entity or small number of viruses as few as 10 viruses/μL [17]–[19], is severely limited by an extremely low signal-to-noise ratio (SNR) and a poor sensitivity due to the tiny stray magnetic field generated from a single SPN sensor agent. Therefore, in order to overcome these technical challenges, a great deal of technical efforts relevant to enhancing SNR and developing more effective GMR-based biosensor modalities are actively being made in the current magnetic biosensor technologies.

In this paper, we present the magnetic and electrical characteristics of "single ferrimagnetic nanoparticle (FN) or micro particle (FM) sensor agent + one GMR biosensor" architecture to explore its biotechnical feasibility for both the detection of extremely low concentration of biomolecules (or possibly extend to detect single biological entity) and the virus-based disease diagnosis. The main physical reason to consider single FN or FM for a sensor agent is that it has a large saturation or remnant magnetization, which can generate a sufficient stray magnetic field to stably rotate the free layer (FL) (or sensing layer) of the GMR biosensor allowing to achieve a higher SNR [13]–[15]. In addition, different from the GMR biosensor with multiple FN sensor agents, the agglomeration of FNs or FMs during introducing via a PolyDiMethlySiloxane (PDMS) channel does not have to be considered in this sensory system. Two different research approaches were attempted to evaluate the technical feasibility in this work. Prior to an experimental demonstration, the numerical analysis was first made to compare the sensing performance of GMR biosensors with single immobilized FN or SPN sensor agent. For this analysis, the experimentally determined magnetic parameters of $CoFe_2O_4$FNs (diameter, $D = 26$ nm) and $CoFe_2O_4$ SPNs ($D = 7$ nm) were considered and the "Stoner–Wohlfarth model" was employed to interpret the magnetization reversal behavior of FL caused by the stray magnetic field produced from the sensor agents. The sensing performance of the two GMR biosensors was estimated in terms of the relative change of magnetoresistance (δR), the variation

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