Behavior of multi-component magnetic colloidal systems in tunable magnetic fields and applications in biosensing

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Abstract. A system consisting of multiple-component beads, such as superparamagnetic beads, nonmagnetic beads and magnetorheological (MR) fluid, can display some very amazing and special properties when subjected to an external magnetic field because the MR fluid can act on both types of beads synchronously as a magnetic medium. Some novel structures and phenomena were discovered and are discussed in our work, including ‘ring-structures’, ‘small-ring’ and ‘ring-chains’ in static or rotational magnetic fields. If both probe and target molecules are attached consisting of functionalized superparamagnetic beads and non-magnetic beads, respectively, the ring-structure could be maintained due to biomolecular bonding, even after removing the external magnetic field. Using these remnant rings, we raised two protocols for biosensing: a two-dimensional biosensor using a magnetic self-assembled colloidal ring-structure, and an improved magneto-optical transmittance (MT) method. In the former protocol, we define the small nonmagnetic particles as “petals” because the whole structure looks like a flower. It was proved that the number of remnant ring petals was a function of the concentration of the target molecules’, with a concentration range from 0.0768 ng/mL ~ 3.8419 ng/mL, making it a promising technology for applications involving biosensing. In the latter protocol, the use of larger individual units made the magnetic particle chain longer, which was considered to be a promising way of improving the sensitivity of the MT method.
1. Introduction

The concept of micro total analysis systems was introduced into science in 1990. Parallel to the boom in microfluidic systems, nanomaterials and nanoparticles have become a hot topic in research. Magnetic micro/nano-particles can display several special properties involving magnetic actuation, which forms the theoretical basis for a wide range of research work. Therefore, there are a series of new biomedical applications such as MRI contrast enhancement, hyperthermia, drug targeting, magnetic separation, magnetic washing, magneto-optical biosensing, cell biophysics, and biological engineering. Almost all of these applications are based on the phenomenon whereby the particles can be magnetically probed and manipulated using permanent magnets or electromagnets. Because of this, three of the most important advantages of using these beads for analytical applications are known to be: (1) the possibility to reduce sample sizes and reagents to minute quantities; (2) relatively fast reaction times; (3) a large surface-to-volume ratio, which is considered to be one of the most effective ways to obtain high sensitivity. Specifically, applications of magnetic nanoparticles for point-of-care medical treatments include functionalized fluorescent magnetic beads for ultrafast medical diagnosis, biosensing using Hall biosensors, the detection of sub-200 nm magnetic particles by magneto-induced self-assembly, and label-less homogeneous biosensing by magneto-optical scattering.

A system consisting of paramagnetic and nonmagnetic particles in a magnetorheological (MR) fluid can display some very amazing and special properties. Because the MR fluid acts as a magnetic medium, it acts on both types of beads synchronously. Using such a multiple-component system, colloidal superstructures with multi-pole symmetry can be manufactured, such as "Saturn’s rings", flowers, linear quadrupoles (poles) and mixed multipole arrangements (‘two tone’). Kwan H. Li and Benjamin B. Yellen also conducted some research into the relationship between the ferrofluid concentration and the separation distance of particles within the ring structure.

In our study, some novel phenomena were observed in the kinds of multiple-component magnetic colloidal systems that exist in a tunable magnetic field, such as the formation of rings, small-rings, ring-chains, and we observed their behavior in a rotating magnetic field. These dynamical studies are expected to become the basis for much relevant research in the future.

Also, in our work, superparamagnetic beads and nonmagnetic beads were attached to probe molecules (streptavidin) and target molecules (biotin) respectively, and the ring-structures could be maintained even after removing the external magnetic field because of bio-interactions.

Since the shape of the ring-structure that we created is just like a flower, we define the small nonmagnetic beads around it as “petals”. We proved that the average number of petals in the ring was a function (a linear function at low concentration) of the concentration of biotin, which means that this procedure can be applied in biosensing. Since the whole procedure was carried out in a two-dimensional system, this approach offers a means of cutting down reagent consumption and waste generation, which is important for biosensing. Furthermore, the driving force generated by the external magnetic field enables the whole procedure to only take a few minutes, which makes this method very promising for applications requiring rapid diagnosis.

In addition, these remnant rings were also used to improve the sensitivity of the magneto-optical transmittance (MT) technique. With paramagnetic particles replaced by rings as the basic unit, the
magnetic chains became longer. Combined with the working principle of the MT method, this change is expected to lead to promising improvements.

1.1 Formation of Ring-structure

Randall M. Erb et al. used a theoretical model to describe the formation of these multi-component superstructures.\textsuperscript{[19]} Their physical model employs a continuum approach to approximate the local fluid magnetization, which is considered to be justifiable when the ferrofluid particles are much smaller than the other colloidal particles in the fluid. In our experiments, the MR fluid consisted of a colloid of nanoparticles mixed with micro-sized superparamagnetic and nonmagnetic beads. The effective dipole moment of a linearly-magnetizable spherical particle immersed in a magnetizable carrier fluid is given by

\[ \mathbf{m}_i = 4\pi a^3 \frac{\chi_i - \chi_f}{\chi_f + 2\chi_i + 3} \mathbf{H}_{\text{ext}} \]  

where \( a \) is the radius of the particle, \( \mathbf{H}_{\text{ext}} \) is the magnetic field at the location of the particle center, and \( \chi_f \) and \( \chi_i \) are the magnetic susceptibilities of the ferrofluid and the particle, respectively. If we can control the susceptibility of the ferrofluid to satisfy the relationship \( \chi_{NM} < \chi_f < \chi_{PM} \), then, according to the above equation, we can predict that paramagnetic particles for which \( \chi_i = \chi_{PM} > \chi_f \) will behave as point dipoles aligned parallel to the applied field, whereas the non-magnetic particles with \( \chi_i = \chi_{NM} \approx 0 \) will behave as point dipoles aligned antiparallel to the field. Here, in addition, compared with a ferrofluid with a typical susceptibility value of between 0.1-1.0, the susceptibility of non-magnetic beads is only on the order of \( 10^{-6} \), so the approximation \( \chi_{NM} \approx 0 \) is reasonable.

Equilibrium particle configurations can be explained from the expression for the magnetostatic potential energy of a dipole \( m \) in a locally-applied field \( \mathbf{H} \), given by

\[ U_i(r) = -2\pi a^3 \mu_0 \frac{\chi_i - \chi_f}{\chi_f + 2\chi_i + 3} |\mathbf{H}(r)|^2 \]  

where \( \mu_0 \) is the magnetic permeability of free space. For a non-magnetic particle (\( \chi_{NM} < \chi_f \)), according to (2), its potential energy must be strictly positive, which causes the particle to move towards regions of minimum magnetic field, \( |\mathbf{H}(r)| = |\mathbf{H}_{\text{min}}| \). In contrast to non-magnetic particles, for paramagnetic particles, with \( \chi_{PM} > \chi_f \), the potential energy is strictly negative, which causes the particle to move towards regions of maximum magnetic field, \( |\mathbf{H}(r)| = |\mathbf{H}_{\text{max}}| \). Hence, in mixed suspensions of two types of particles, the magnetic force drives non-magnetic particle towards the ‘equator’ of the paramagnetic particle, where the total magnetic field is equal to the dipolar field of the paramagnetic particle subtracted from the total magnetic field, which is a minimum according to equation (2), so the magnetic force drives nonmagnetic particles to this area.
external field. In a similar way, the paramagnetic particles move towards the equator of the non-magnetic particles, where the total magnetic field equals the dipolar field of the non-magnetic particle added to the external field. Fig.1 shows a schematic diagram for this principle.

In fact, the size-ratio between the paramagnetic particles and the non-magnetic particles is a very important parameter to determine the configuration of the ring-structure. When the system consists of large paramagnetic particles and small non-magnetic particles, the larger paramagnetic particles will act as a core and will be surrounded by pairs of smaller non-magnetic particles around their equatorial areas. When the non-magnetic particles are larger than the paramagnetic ones, the situation will be just the opposite.

1.2 Streptavidin-Biotin interaction

Streptavidin is a tetrameric protein that binds very tightly to the small molecule, biotin. The biotin-streptavidin system is the strongest noncovalent biological interaction known, having a dissociation constant $K(d)$ of about $\sim 10^{-15}$mol/L, and the complexes are also extremely stable over a wide range of temperature and pH. The strength and specificity of the interaction has led to it being one of the most widely used affinity pairs in molecular, immunological, and cellular assays.

![Figure 2 Structural formula (a) and 3D molecule model (b) of Biotin. The gray, white, blue, red and yellow balls represent C, H, N, O and S atoms respectively.](image)

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The molecular structure of Biotin is shown in Fig. 2, both in a structural formula and a 3D model. Fig. 3 shows how streptavidin and biotin connect with each other.

1.3 Working principle of the MT technique

As we know, paramagnetic beads tend to form chains in an external magnetic field, and if the external magnetic field rotates, the chains will rotate as the magnetic field rotates in a stationary frequency. Sang Yoon Park et al. [13, 14, 21] applied this phenomenon in biosensing combined with a light scattering technique.
A rotating external field (H\textsubscript{ex}) applied to an aqueous solution containing biotinylated superparamagnetic beads (SBs) produced linear chains of SBs rotating in phase with H\textsubscript{ex} due to magnetically induced self-assembly. At constant H\textsubscript{ex}, the addition of avidin to the solution led to the formation of longer SB-chains than those formed without the presence of avidin. This change in length of the SB-chains was revealed by increases in the amplitude of the oscillating optical transmittance signal of the magnetic colloid solution. Monitoring changes in the amplitude of the optical transmittance of the solution enabled quantitative determination of the concentration of avidin that was added to the solution. The rotating chains acted as biomolecular probes and micromagnetic mixers, enabling the detection of biomolecular recognition in a very short time.

Fig. 4 shows a schematic diagram of the MT measurement set-ups that were utilized. In this figure, the angle between the incident beam and the direction of the external magnetic field is defined. Fig. 5 shows how the MT technique can be used for biosensing. First of all, the light that is incident on the SBSs is scattered, and the intensity of the transmitted light depends on the angle (0) between the SBC direction and the light propagation path, which we refer to as the ‘magneto-optical transmittance (MT) effect’. As for the rotation of the external magnetic field, the optical transmittance signal curve is sinusoidal. When \(\theta=0^\circ\), the value of the optical transmittance signal reaches a maximum (peak value); while when \(\theta=90^\circ\), the value of this signal reaches a minimum (valley value). The average length of a rotating SBC at a given hydrodynamics force (FH) depends only on the magnetic dipolar force (F\textsubscript{m}). After the attachment of a biomolecule, a new avidin biotin conjugation force (F\textsubscript{ABC}) is introduced, which results in stronger and longer biotinylated SBCs. Furthermore, this leads to a greater amplitude of the oscillating signal of the MT effect. The longer the chains, the larger the peak-to-valley ratio of the signal we can obtain.

![Figure 4](image1.png)

**Figure 4** \[21\] Schematic illustration of the measurement setups utilizing (a) rotatable permanent magnet and (b) Helmholtz magnet. The size of SPBs and the wavelength of incident light were 1.5 \(\mu\)m and 630 nm, respectively.

![Figure 5](image2.png)

**Figure 5** \[14\] Schematic illustration of the process of magneto-optical biomolecular detection by rotating superparamagnetic bead chains in solution. (a) Different transmission situation with different \(\theta\). (b) Addition of biomolecule change the length of the SBs-chain.
2. Results and Analysis

2.1 Behavior of a multiple-component magnetic colloid system in a tunable field

2.1.1 Formation of a ring-structure

Superparamagnetic beads with diameters of 2.8-μm 35μL (Invitrogen Dynal AS, Oslo, Norway), nonmagnetic beads with diameters of 1.0-μm 20μL (Micromod Partikel Technologie GmbH), and MR fluid (Sigma-hc. Co.) with a volume fraction of 1.2% 50μL were mixed to form a solution. The initial concentrations of superparamagnetic beads and nonmagnetic beads were 6.7×10^8 particles/mL and 9.3×10^10 particles/mL respectively. The sample was treated with supersonic vibration for 3 min to cause the different components to mix sufficiently. An external magnetic field was then applied using an electric solenoid, and the magnetic field intensity could be adjusted by changing the current through the solenoid.

The configuration of the ring structure depends not only on the concentration of the MR fluid, [19] but also on the magnetic field intensity and the concentration ratio between the individual components.

We also monitored the ring-structure formation process for different concentrations of MR fluid while slowly increasing the intensity of the magnetic field.

Fig. 6 shows a perfect ring structure. In this case, the magnetic field was generated by a permanent magnet at a magnetic field of ~260Oe. In this structure, paramagnetic beads with larger sizes act as cores, and are surrounded by nonmagnetic beads. Every “flower” has 8-12 petals.

We also monitor the ring-structure formation process by varying the concentration of the MR fluid and slowly increasing the intensity of the magnetic field. Four different stages are defined: incompact, semi-formed, integral and uniformity. A schematic diagram is shown in Fig. 7.

![Figure 6](image)

**Figure 6** Photo of ring-structure taken by microscope.

| Volume fraction of MR Fluid | Magnetic field intensity needed (Oe) |
|----------------------------|------------------------------------|
|               | Incompact | Semi-formed | Integral | Uniformity |
| 0.3%          | 29        | 34          | 50       | 53         |
| 1.2%          | 13        | 18          | 26       | 47         |
| 2.2%          | 8-10      | 13          | 18       | 34         |
Table 1 shows the magnetic field intensities that are needed to form the different stages with different MR fluid concentrations. As the concentration of the MR fluid increases, lower magnetic field intensity is required to form every stage.

2.1.2 Formation of a small-ring

Figure 7 As the intensity of the magnetic field gradually increases, the ring-structure formation process goes through four main stages. This schematic diagram shows these in order. (1) With no magnetic field, the system is totally orderless; (2) Incompact stage: small nonmagnetic beads start to approach core paramagnetic beads; (3) Semi-formed: some (but not fully, about 3–4) small beads have attached onto the surfaces of the core beads; (4) Integral: perfect individual ring-structures form, every core particle is fully surrounded by small particles; (5) Uniformity: the distribution of individual ring-structures in the whole solution system becomes uniform.

Figure 8 Photo of small-ring. There are many basic units for the formation of small-ring in this photo. A magnified schematic diagram is shown on the right side.
We made a solution with nonmagnetic-1.0μm beads 20μL and MR fluid (with a volume fraction Cv=1.2%) 100μL. Then we exposed this sample in an external vertical magnetic field, obtaining structures as in the following pictures. Fig. 8 shows the basic unit for the formation of a small-ring. The small dark spots that surround the nonmagnetic beads are actually the chain-like clusters of MR nanoparticles. (We cannot see discrete MR nanoparticles with an optical microscope because of the limitation of the amplification factor.) And as Fig. 8 shows, every basic unit for the small-ring structure is composed of one nonmagnetic bead as a core that is surrounded by 3-5 MR nanoparticle-chains.

![Image](image.jpg)

**Figure 9** Photo of small-ring. Every small-ring is composed of 3-5 nonmagnetic particles and a ‘pistil’ made of several MR nanoparticle-chains.

Fig. 9 emphatically shows small-ring structures. Every small-ring is composed of 3-5 nonmagnetic particles and a ‘pistil’ made of several MR nanoparticle-chains.

Based on our observation, we raised a theory conjecture to explain the formation of small-ring. As we mentioned above, the dark spots in this system are actually MR nanoparticle chains seen from a top view. These MR-chains infibulate nonmagnetic particles just like we use chopsticks to infibulate dishes. In the next, because of the lateral attraction between the MR-chains, these chains tend to bring nonmagnetic particles together. Fig. 10 is a schematic diagram of this process.

2.1.3 Formation of ring-chains

We all know paramagnetic beads form chains in a horizontal magnetic field (that is, relative to the observation angle) and a multiple-component system forms ring-structures in a magnetic field perpendicular to that in the former statement. What would happen if there are magnetic field components in both directions? We carried out an experiment in an aligned magnetic field using a multiple-component system consisting of paramagnetic beads, nonmagnetic beads and MR fluid.
A simple device that can offer an aligned magnetic field was set up as shown in Fig. 11. The angle of inclination $\alpha$ is defined as the angle between the sample plane and the plane of the magnet. In this part, our study is non-quantitative, so $\alpha$ is just for a qualitative description.

It turns out that with an aligned magnetic field, chain-structure and the ring-structure form at the same time, which we call ‘ring-chains’. Two experiments were carried out with $\alpha=30^\circ$ and $\alpha=70^\circ$ respectively. Photos of these are shown in Fig. 12 (a) and (b).
We can see from the photos that the shape of a ‘ring-chain’ is like a scolopendra. On one hand, paramagnetic beads align in a row according to the direction of the total external magnetic field; on the other hand, nonmagnetic particles revolve around the core particles on the equator plane which is vertical to the total external magnetic field. When α becomes larger, the horizontal component of the external magnetic field becomes higher. Furthermore, the chains become longer.

2.1.4 Ring-chain in a rotating magnetic field

The magnet in this experiment is aligned such that it will generate a relatively large horizontal magnetic field component. In this way, from the visual angle of the microscope, we observe something really interesting, which is the axial rotation of a ring-chain.
Video 1 shows this phenomenon which is considered to be the first such discovery in this field of study. We were very surprised to see the ring structure rotate on its axis.

In order to explain this phenomenon, we have to start with force and torque analyses of the ring-chain (See schematic diagram Fig. 13). As we know, the magnetic field generated by a magnet can be deconvolved into two parts: an x-y plane component and a z-component. For simplicity, we just pre-digest the x-y component as the x-component. $H_{x-mag}$ offers a force moment in the x-direction, which tends to force the chain to align parallel to the x-direction, and its magnitude can be described as:

$$M_{x-mag} \propto H_{x-mag} \cdot l \cdot \sin \theta$$

At the same time, the rotating magnetic field $H_{rot}$ offers a torque to the chain, the magnitude of which can be described as:

$$M_{rot} \propto H_{rot} \cdot l$$

When $\theta=0^\circ$, only $M_{rot}$ acts on the ring-chain, so the chain rotates along the direction of the rotating magnetic field. As $\theta$ increases, $M_{x-mag}$ becomes larger and tends to “drag” the chain harder. When it comes to $M_{x-mag}=M_{rot}$, the chain is dragged back to its horizontal station. With further increases in $\theta$ (when $\theta>90^\circ$), $|\sin \theta|$ becomes smaller and the ring-chain swings to the other side. So far, we can explain the swing movement of the ring-chains that were shown in Video 1.

Considering the magnetic field generated by a magnet in the z direction $H_{z-mag}$, the ring-chain cannot lie on the x-y plane, as discussed above, so the ring-chains will ‘cock up’. To sum up all the

![Video 1](image-url) Rotation and swing movement of ring-chains.

![Figure 13](image-url) Schematic diagram (x-y plane) to explain swing movement of ring-chains.
factors, the ring-chains tend to describe an ‘egg-whisk-like’ movement. Hence, a hydrodynamical hindrance acts on the nonmagnetic particles, and this situation can be compared with the situation when a windmill rotates; the nonmagnetic particles are just like the blades of a windmill.

In the video, it is very clear that in one ring-chain, the ring-structure in the center almost doesn’t rotate at all, while the ring-structure at the end of the ring-chain rotates most vigorously. This is because every ring-chain swings around its center; if we define the linear velocity as $v$, the angular velocity as $\omega$ and the distance between a ring-structure and the center as $r$, we have

$$v = \omega \cdot r$$

From this equation, we can see that, the further a ring-structure is from the center, the larger linear velocity it can obtain. Furthermore, according to related hydromechanics theory, the hydrodynamical hindrance is in direct proportion to the linear velocity of movement.

### 2.2 Protocols for biosensing

#### 2.2.1 Two dimensional detection system using a magnetically self-assembled ‘ring’

This protocol consists of two parts: the experimental group and the reference group. The experimental procedure goes as follows: (1) Immobilize the target molecules onto the surfaces of the nonmagnetic beads. (2) Mix together paramagnetic particles with probe molecules attached to their surfaces, the former non-magnetic particles, and the MR fluid to obtain a multi-component suspension in solution. (3) Transfer a droplet from the mixture solution onto a glass slide and cover it with a coverslip. (4) Apply an external vertical magnetic field to the two-dimensional plane for a couple of minutes. (5) Remove the external magnetic field and leave it to stand for a while. (6) Take photos of the remnant structure, then count and calculate the statistical average number of ring petals. The entire procedure is shown in Fig. 14.

![Reference Sample](image1)

![Detect Sample](image2)

**Figure 14** In both the reference and the detection samples, five steps are taken: (1) Immobilize target molecules (the first two pictures); (2) Mix multiple components; (3) Apply external magnetic field; (4) Remove external magnetic field; (5) Observe remnant structures.
For the reference group, there are no target molecules in the initial solution in step (1). The remaining manipulations are the same as those in the experimental group. Under ideal circumstances, the average number for the reference group should be zero because there are no bio-interactions at all.

By varying the concentration of the target molecules in step (2), we can obtain a series of statistical results and generalize the rule.

![Graph: Average number of ring petals is a function of Biotin concentration](image)

Figure 15 Average number of ring petals is a function of Biotin concentration

Looking into the statistical results, it turns out that the average number of ring petals is a function of the concentration of Biotin (shown as Fig. 15). As the concentration of the biotin increases, the average number of petals on the ring increases monotonously. In the ‘low-concentration’ region, the function is linear (as shown by the purple line). Because of observations such as these, this protocol is considered to be a promising approach for biosensing.

2.2.2 Improvement of the MT method

In Section 2.3, we have already introduced the working theory of the MT (magneto-optical transmittance) method used for biosensing. The most important parameter in this method is the difference in length between the chains in the initial sample system and that in the biomolecules decorating the detection system, because this length difference can be transferred to the vibration amplitude of the sinusoidal curve in the optical transmittance measurements. One of the most effective ways of improving the sensitivity of this method is to increase the length difference as much as possible under the same sample conditions.

Hence, we considered combining our ring-structure with the MT method to improve its sensitivity. According to the statement above, the essence of this protocol is to increase the length difference for the ‘ring-structure’ as a basic unit in a chain instead of a paramagnetic
Most of the basic manipulations in this experiment are the same with the steps in Section 3.2.1. After the remnant rings were formed, a rotating magnetic field was applied for MT detection. The expected result is shown in Fig. 16.

We carried out two experiments with a reference sample and a detection sample in a rotating magnetic field separately. Both the reference sample system and the detection system consisted of streptavidin-coated paramagnetic-2.8μm particles and MR fluid (Cv=1.2%); the difference lies in whether there is biotin molecules decorating the nonmagnetic particles, which determines whether there is a bio-interaction between the core-particles and the petal-particles. The formula for the two samples are given in Table 2.

![Reference Sample](image1)

![Detect Sample](image2)

$L_2>L_1$, so the “MT (magneto-optical transmittance) effect” will be stronger.

Figure 16 The quintessential idea for MT-improvement protocol: longer length difference results in stronger MT effect.

| Reference sample | Strep-para-2.8μm / μL | Non-1.0μm / μL | MR fluid (Cv=1.2%) / μL |
|------------------|----------------------|----------------|------------------------|
|                  | 10                   | 10             | 20                     |

| Detection sample | Strep-para-2.8μm /μL | Biotin-non-0.8μm / μL | MR fluid (Cv=1.2%) / μL |
|------------------|----------------------|----------------------|------------------------|
|                  | 10                   | 10                   | 20                     |

Table 2. Formula for reference sample and detect sample.

Fig. 17 shows the result of this pair of experiments.

Obviously, because the unit-cell of the chain changed from paramagnetic particles to the ring structure, the size of the units became larger, so the length of chains became longer. It is expected that this phenomenon can help to enhance the “MT effect” (magneto-optical transmittance) and improve its sensitivity.
3. Conclusion

We introduced our work concerning the study of the dynamics of colloidal solution consisting of multi-component magnetic beads in a magnetic field and its potential applications in biosensing.

The behavior of multiple-component systems built up from paramagnetic, ferromagnetic and nonmagnetic beads were investigated both theoretically and by experiments. Some novel behavior of new structures, such as the rotation of ‘ring-chains’ in a rotating magnetic field and the formation of ‘small-rings’ were observed for the first time. We also proposed a theory to explain these novel phenomena. These fundamental theoretical studies are expected to contribute to the industrial application of related fields in the future.

We also tried to exploit these basic studies in biosensing applications ourselves. Two protocols based on ring-structures were raised: a two-dimensional detecting system using magnetically self-assembled ‘rings’, and improvements in the MT (magneto-optical transmittance) method.

As a result, two-dimensional biosensing using a magnetic self-assembled colloidal ring-structure is considered to be the most promising method for use in biosensing. A suspension solution containing multiple-components including paramagnetic particles, non-magnetic particles and MR fluid was exposed under an external vertical magnetic field for a few minutes. Due to the magnetic force, a ring-structure was formed. If the particles are coated with functional molecules such as streptavidin or biotin, the rings can still remain, even after removing the magnetic field. The average number of remnant ring petals is a function of the concentration of target molecules (biotin). In this way, this technique can be applied to two-dimensional biosensing.

Randall M. Erb et al. (2009) calculated that the size limitation that can be manipulated
using this technique is on the order of 60 nm in diameter\cite{19}, which means that the use of a higher magnification microscope would allow this protocol to be used to detect smaller carrier particles.

Nowadays, the most commonly used biosensing methods include Enzyme Linked Immunosorbent Assay (ELISA), Gel-shift assay, Quartz crystal microbalance (QCM), Surface plasmon resonance (SPR) and so on. The former two are both time consuming, very cumbersome and require labeling; the latter two offer high quantification but are so expensive that they cannot be applied in portable point-of-care treatment systems. \cite{22}

Compared to these methods, our protocol is much cheaper, and with the support of pattern recognition and statistics software, the detection time can be cut down to just a few minutes. In addition, combined with a portable microscope of the type that can already be purchased on the market, this two-dimensional biosensing technique is expected to be a promising method for diagnosis in remote areas or in fieldwork.

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