Improvement Design of Biochip Towards High Stable Bioparticle Detection Utilizing Dielectrophoresis Impedance Measurement

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Abstract：Dielectrophoresis impedance measurement（DEPIM）is a powerful tool for bioparticle detection due to its advantages of high efficiency，label-free and low costs. However，the strong electric field may decrease the viability of the bioparticle，thus leading to instability of impedance measurement. A new design of biochip is presented with high stable bioparticle detection capabilities by using both negative dielectrophoresis（nDEP）and traveling wave dielectrophoresis（twDEP）. In the biochip，a spiral electrode is arranged on the top of channel，while a detector is arranged on the bottom of the channel. The influence factors on the DEP force and twDEP force are investigated by using the basic principle of DEP，based on which，the relationship between Clausius-Mossotti（CM）factor and the frequency of electric field is obtained. The two-dimensional model of the biochip is built by using Comsol Multiphysics. Electric potential distribution，force distribution and particle trajectory in the channel are then obtained by using the simulation model. Finally，both the simulations and experiments are performed to demonstrate that the new biochip can enhance the detection efficiency and reduce the negative effects of electric field on the bioparticles.

Key words：dielectrophoresis；impedance measurement；detection；biosensor

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0 Introduction

Impedance measurement is a powerful tool for analysis and characterization of bioparticles. It is widely used in bioparticle detection，e.g. bacterial content，but the traditional impedance measurement techniques suffer time-consuming and low sensitivity. An effective strategy to enhance sensitivity and reduce the testing time is to integrate with a dielectrophoresis（DEP）chip into the impedance measurement system. The integrated dielectrophoresis impedance measurement（DEPIM）has advantages of high efficiency，label-free and low costs.

Suehiro designed a DEPIM chip for real-time bacteria monitoring[1]，in which the antibodies-antigens technique was adopted to increase the enrichment efficiency. The antibodies were fixed on the electrode surface，and the bacteria were attracted to the electrode by the DEP force. Then，bacteria could combine with the antibodies by adjusting DEP force and Stokes force properly. As a result，the target bacteria were trapped on the surface of chip，meanwhile，the non-target bacteria are taken to the outlet under the Stokes force. Yang[2] proposed a biochip design for foodborne bacteria detection. The experiment demonstrated that the biochip，which integrated with DEP chip，was more effective than the one without DEP chip. Higginbotham et al.[3] developed a biochip for bioparticle detection，which used traveling wave dielectrophoresis（twDEP）force to

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drive bioparticles to detection area for detecting. Hamada et al. [4] designed the bacteria detection chip with both positive dielectrophoresis (pDEP) and negative dielectrophoresis (nDEP). Two working areas are designed in this chip: the concentration area and the detection area. When the bacteria passed through the concentration area, they were driven to the bottom of the channel under the nDEP force. After entering the detection area, the bacteria were captured at detector by the pDEP force. Compared with the detector with pDEP, the nDEP concentrator could further improve the DEP trapping efficiency.

However, there are still some disadvantages in the biochips above. Bioparticles are captured at detector by pDEP force, and they are very close to the electrode. The electric field strength is very strong near the electrode, which has some negative effects on bioparticle viability. Kang et al. [5] found that live cancer cells died soon when they were exposed in a very high electric field. Furthermore, Donato et al. [6] found that the cell metabolism was affected by the electric field after 10 min of exposure, cells no longer produce green fluorescent protein (GFP) after 15 min of exposure and the most of the cells being dead. In addition, Joule heating effect was obvious near the electrode, and it was harmful for the cell activity[7]. Due to the negative effects of electric field on bioparticles viability, the concentration of the living bioparticles in the detection area was low, which significantly enlarged the detection time costs. Therefore, the biochips above are still inefficient and unstable.

A novel biochip design is proposed for bioparticle detection with both nDEP and twDEP, which can significantly enhance the detection efficiency, meanwhile reduce the negative effects caused by the electric field. The schematic diagram of the proposed bioparticle detection chip is shown in Fig. 1, and the biochip is made up of microelectrode, microchannel and detector. The spiral electrode is arranged on the top of the channel, while the detector is arranged on the bottom of the channel. Bioparticles in the channel are pushed to the bottom of the channel under nDEP force and gravity. Meanwhile, they are driven to the centre of the detector under the twDEP force. As a result, the bioparticles are captured on the detector.

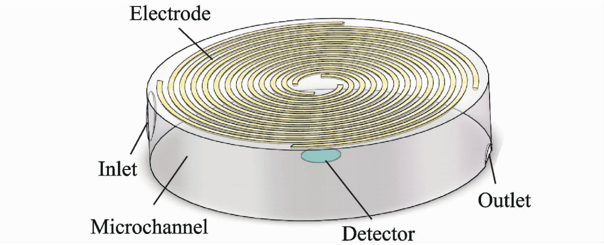


Fig. 1 Schematic diagram of bioparticle detection chip based on nDEP and twDEP

1 Theoretical Analysis

1.1 DEP force

The dielectrophoresis force on the spherical particle which immersed in a solution can be formulated as[8]

$$\boldsymbol{F}=2\pi r^3\varepsilon_{\mathrm{m}}\{\mathrm{Re}[K_{\mathrm{CM}}]\nabla E^2+\mathrm{Im}[K_{\mathrm{CM}}](E_x^2\nabla\varphi_x+E_y^2\nabla\varphi_y+E_z^2\nabla\varphi_z)\} \tag{1}$$

where r denotes the radius of the spherical particle, ε_{m} the permittivity of the media, E^2 the RMS value of the electric field, φ_i the phase angle component in Cartesian coordinate, $\mathrm{Re}[K_{\mathrm{CM}}]$ the real part of Clausius-Mossotti factor which refers to pDEP and nDEP, $\mathrm{Im}[K_{\mathrm{CM}}]$ the imaginary part of Clausius-Mossotti factor, and K_{CM} is formulated as

$$K_{\mathrm{CM}}=\frac{\varepsilon_{\mathrm{p}}^*-\varepsilon_{\mathrm{m}}^*}{\varepsilon_{\mathrm{p}}^*+2\varepsilon_{\mathrm{m}}^*} \tag{2}$$

where $\varepsilon_{\mathrm{m}}^*$ and $\varepsilon_{\mathrm{p}}^*$ denote the complex permittivities of the medium and the particle, respectively, which are related to the conductivity σ and the angular frequency of the electric field ω.

In the paper, the polystyrene beads with radius 1 μm are used to simulate the bioparticles. Tables 1 lists the related parameters of polystyrene beads and solution.

Table 1 The related parameters of polystyrene beads and solution

r/μm	ε_{m}	ε_{p}	σ_{m} /(mS · m^{-1})	σ_{p} /(mS · m^{-1})
1	80	2.5	1	5

1.2 Gravity

The gravity of the immersed particle can be formulated as

$$\boldsymbol{F}_g = V(\rho_p - \rho_m)\boldsymbol{g} \tag{3}$$

where V and ρ_p denote the volume and density of the particle, respectively, and ρ_m is the density of solution.

1.3 Stokes force

The Stokes force of the particle is formulated as follows

$$\boldsymbol{F}_s = -6\pi\eta r\boldsymbol{v} \tag{4}$$

where η denotes the dynamic viscosity of the solution, and $\boldsymbol{v}$ the relative velocity of the particle and the solution.

As shown in Fig. 2, particles in the channel are pushed to the bottom of the channel driven by the nDEP force and gravity. Meanwhile, they are driven toward the centre of the detector with the twDEP force. As a result, the bioparticles are captured by the detector and detected with the impedance measurement method.

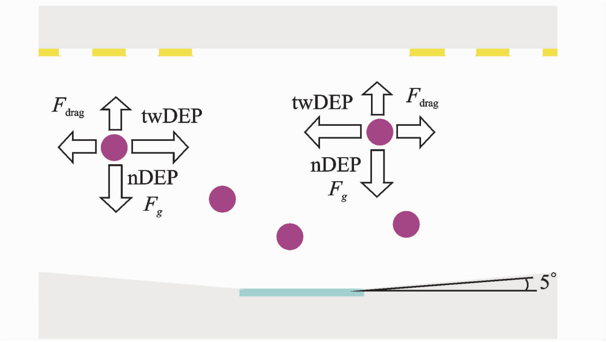
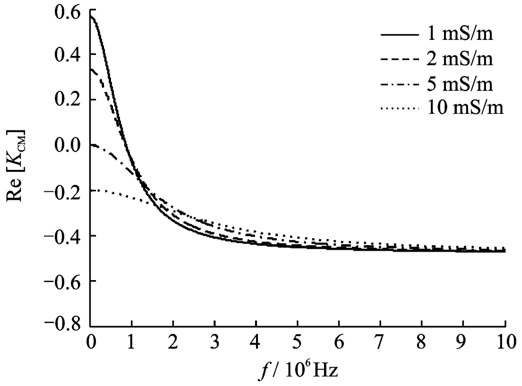


Fig. 2 Force analysis of particles in channel

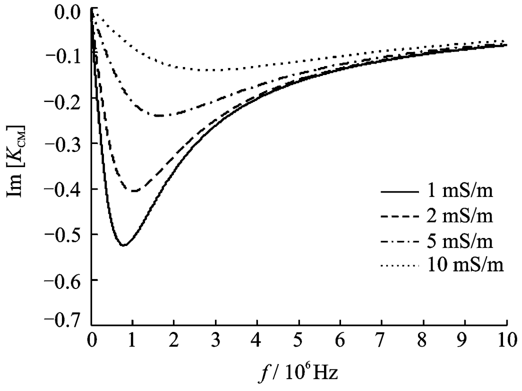
1.4 Influence factor

The velocity of the particle determines the detection efficiency. From Eq. (1), it is known that the velocity of the particle relates to three parameters: Re[$K_{\rm CM}$], Im[$K_{\rm CM}$] and electric field intensity. Increasing the voltage applied to the electrode can enhance the strength of the electric field. However, excessive voltage is not conducive to the experimental operation. Hence, we only consider the influence of Clausius-Mossotti (CM) factor on the velocity. As shown in Eq. (2), Re[$K_{\rm CM}$] and Im[$K_{\rm CM}$] are related to the frequency of the electric field, permittivity and conductivity of the particle and solution. Permittivity and conductivity remain unchanged for specific configuration of particles and solution. Therefore, the velocity of the particle is controlled by controlling the frequency of the electric field and conductivity of the solution.

Fig. 3 illustrates the relationship between CM factor and the frequency of the electric field when the polystyrene beads with conductivity of 5 mS/m are immersed in a solution of different conductivity. It is seen that Re[$K_{\rm CM}$] is always negative in the solution of conductivity 5 mS/m and 10 mS/m, and its variation range is small. Meanwhile, the variation range is larger in the solution of conductivity 1 mS/m than in the solution of conductivity 2,5 and 10 mS/m. As shown in Fig. 3(b), Im[$K_{\rm CM}$] can attains larger values in the solution of conductivity 1 mS/m than in the solution of conductivity 2, 5 and 10 mS/m, which implies a larger twDEP force generation. As a result, the solution of conductivity is set at 1 mS/m in the paper.



(a) Re[$K_{\rm CM}$]



(b) Im[$K_{\rm CM}$]

Fig. 3 Relationship between CM factor and frequency of electric field

The polystyrene beads of conductivity 5 mS/m are immersed in the solution of conductivity 1 mS/m, the relationship between CM factor and the frequency of the electric field is shown in Fig. 4.

In order to speed up the collection rate in the

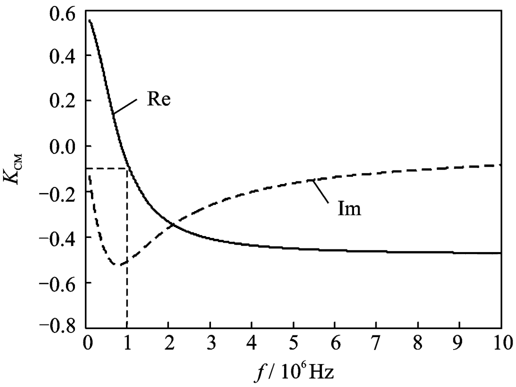


Fig. 4 CM factor in solution of conductivity 1 mS/m

horizontal plane, Im[K_{CM}] should be minimized to its maximum. However, when the frequency of the electric field is 0.8 MHz, Re[K_{CM}] = 0, nDEP force has no effect on the particle motion. Therefore, the frequency of the electric field is set at 1 MHz so that Re[K_{CM}] = 0.08, which can well meet the requirements of the experiment.

2 Numerical Simulation

Comsol Multiphysics 4.3 is used to study the electric field distribution and particle trajectory. The microchannel is designed a cylindrical area with radius 330 μm and 150 μm high. In order to collect particles better, a tilt angle with 5° is designed at the bottom of the channel, as shown in Fig. 2. The spiral electrode is arranged on the top of the channel, both the width and spacing of the electrodes are 40 μm. The other simulation parameters are listed in Table 2.

Table 2 Simulation parameters

V_0/V	f/MHz	ρ_p / (kg • m^{-3})	ρ_m / (kg • m^{-3})	η/ (Pa • s)
5	1	1 080	1 030	10^{-3}

Since the cylindrical area is symmetric, its physical model can be simplified as a plane model. Electric potential distribution in the channel can be obtained by solving Laplace equation in the simulation area, as shown in Fig. 5. The electrode potential is very high near the electrode on the top side of the channel, while it is low in the detection area at the bottom of the channel. Thus, the particles captured at the detection area are less affected by the electric field. The force distribution is illustrated in Fig. 5, and it can be seen that the composite forces point to the detection area. The particle trajectory is shown in Fig. 6, and it is seen that particles move towards the detection area under composite forces successfully as we expected.

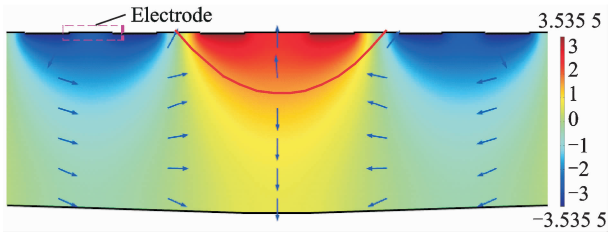


Fig. 5 Potential distribution and force distribution

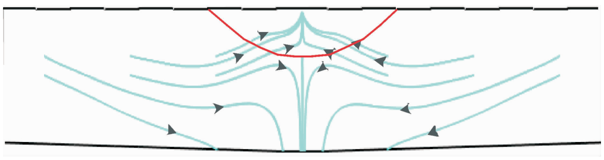


Fig. 6 Particle trajectory

Note that a whirlpool exists in the center of the spiral electrode, as shown in Fig. 5. the composite forces within area enclosed by the red curve points to the center of the spiral electrode, and the particles within the area are driven to the center of the spiral electrode, as illustrated in Fig. 6. Note that for improving the detection efficiency, the particles should be maintained outside the region enclosed by the red curve.

3 Experiment

An experiment is carried out with new biochip based on DEPIM, as shown in Fig. 7. The biochip is made up of DEP chip, microchannel and detector. The DEP chip is made of ITO glass, and the spiral electrode is etched on the glass. A cylindrical microchannel is designed at the center of the glass substrate. Micro holes are designed around each side of the glass substrate as the inlet and outlet of the microchannel. In the later research, the detector will be arranged on the bottom of the channel. The DEP chip is upside down on the glass substrate, the electrode and conductor are connected by conductive adhesives.

When the solution enter into the channel, the four electrodes are respectively applied an AC signal ($V_0 \sin(\omega t)$). It is seen that particles in the channel are pushed to the bottom of the channel under nDEP force and gravity. Meanwhile, they moves toward the centre of the detector under the twDEP force(see Figs. 8(a—c)). Finally, the particles are captured on the detector, as seen in Fig. 8 (d).

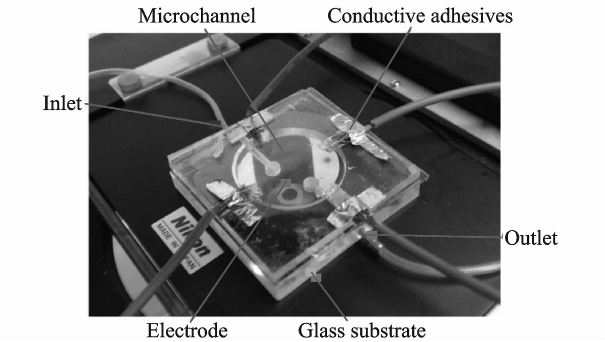


Fig. 7 High stable impedance measurement based on biosensor (without detector)

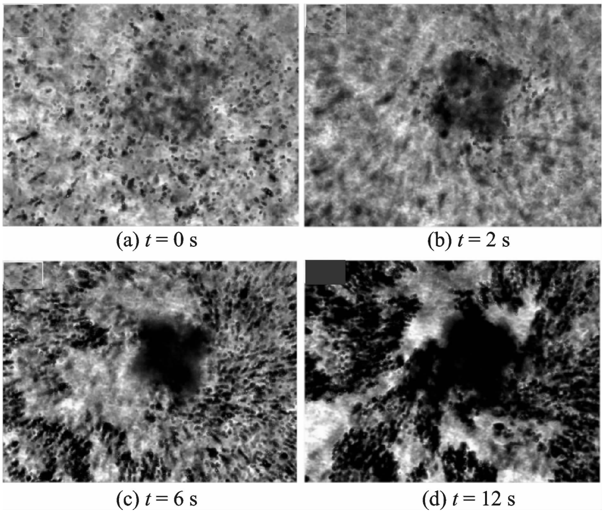


Fig. 8 Particle concentration under DEP force

4 Conclusions

The traditional impedance measurement technique is time-consuming and low sensitivity. By integrating a DEP chip into the design of the impedance measurement system, the detection efficiency can be enhanced significantly. However, due to the fact that strong electric field may cause unexpected negative effects on bioparticle viability, thus causing instability in the impedance measurement. In the paper, a novel biochip design improving the detection efficiency and decreasing the negative effects caused by the electric field is presented. By inverting a DEP chip at the top of the channel, particles are concentrated at the detector by nDEP force, twDEP force and gravity . Based on DEP principle analyzing , the relationship between CM factor and the frequency of the electric field is obtained, furthermore, optimal simulation and experimental parameters are obtained. The two-dimensional model of the biochip is built with the help of Comsol Multiphysics. Electric potential distribution, force distribution and particle trajectory in the channel are obtained by solving the simulation model. Finally, both simulation and experiment are performed to prove the efficiency of the proposed biochip design.

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