Dielectrophoretic separation of biological particles

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We present a numerical study of biological particles separation, we have proposed earlier, by making use of the force that arises because of particle polarization in an alternating inhomogeneous electric field, when a cell suspension moves along a separating channel. Since particle polarizability depends on the physical and biological properties of particles, dielectrophoresis allows biological particles to be separated from particles of other nature or intact cells from the damaged ones. Electric fields, particle trajectories, and threshold values of the cell polarizability, which serves a criterion for particle separation, are calculated for different values of channel parameters and particle size. A dimensionless criterion of similarity that relates the parameters mentioned above is proposed. This criterion can be used for selecting optimal parameters of the separating channel.

Introduction

The possibility of making biological particles to move, attract, or repulse is very important in solving many medical and biological problems, such as separation and identification of biological particles, detection of cancerous cells, concentration of cells in diluted suspensions, and separation of cells in accordance with their specific properties. The effect of dielectrophoresis (DEP) is very promising for solution of the above problems. The main idea of the effect is as follows.

A particle in a dielectric medium becomes polarized under the action of an alternating electric field. If the electric field is inhomogeneous, then the polarized particle undergoes the action of the DEP force. Depending on the frequency of the electric field and dielectric properties of the cells and medium, the force can be directed along the field gradient or opposite to it. These cases correspond to positive and negative dielectrophoresis.[1,2]

Dielectrophoresis allows separation of biological particles from particles of other nature or intact cells from the damaged ones.[1,3] References 4–6 describe the application of DEP to separation of cancerous cells of different types in blood. Moreover, the sensitivity of the method allows the first stages of the virus–cell interaction to be studied.[7,8]

A device for separation of particles with the help of dielectrophoresis[3,4] includes a channel with a rectangular-shaped cross section formed by two glass plates. A number of parallel electrodes are located on the inner surface of one of the plates. The liquid with suspended particles flows along the channel normally to electrodes, to which the alternating voltage with the frequency of 50–250 kHz is applied. In this case the cancerous cells are affected by the DEP force directed toward electrodes. Thus, they are caught and can be removed after the voltage is turned off. In such a way, particles are separated into two fractions in accordance with their physical and biological properties affecting the polarizability.

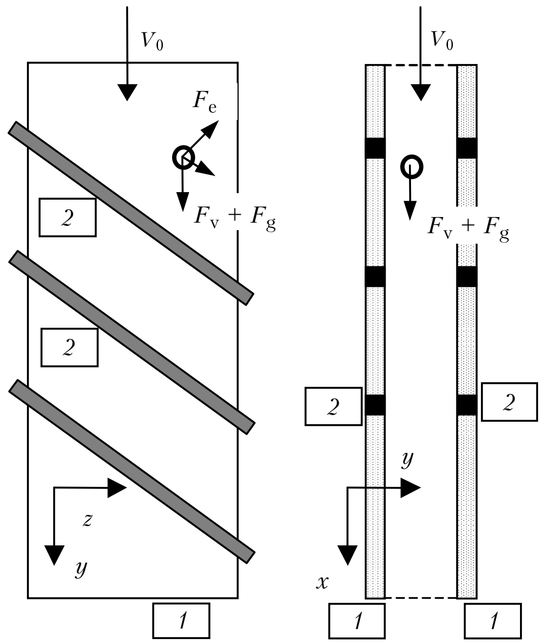

Fig. 1. Channel for separation of particles with the help of dielectrophoresis: plates *1* and electrodes *2*.

Figure 1 shows the new separating channel,[9] which differs from that described above by the arrangement of electrodes. The electrodes are on both plates that face each other while at some angle to the suspension flow vector. The frequency of the electric field corresponds to negative DEP, i.e., particles are repulsed from electrodes. If the DEP force compensates for the component of the force of viscous friction that is normal to the electrode, then the particle moves along this electrode toward a device for cell counting.

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Otherwise, the particle moves along with the flow toward the next electrode. The more downstream is the electrode, the higher is the voltage applied. Thus, particles with lower polarizability can be affected. The described separating channel allows operation in a continuous mode with the number of separated fractions equal to the number of electrodes.

The efficiency of particle separation into fractions and the threshold values of particle polarizability depend on the width of a gap between the plates, the distance between the electrodes and their width, the voltage applied to the electrodes, the liquid flow rate, and the particle size. To choose an optimal design of the device, we should know the relation between these parameters. Toward this end, it is worth using mathematical simulation, since it allows estimating the characteristics of different versions of the device to be done without making them and without time-consuming experiments. In this paper, we study numerically the separation of particles by their polarizability in the device described above.

Methods of calculation

The potential φ of the electric field was calculated in the 2D region shown in Fig. 2 by numerical solution of the Laplace's equation

$$\Delta\varphi = 0 \tag{1}$$

using the Libman finite-difference iteration method.[10] The boundary conditions were determined by the geometry of the separating channel and the voltage across the electrodes. Figure 2 shows the equipotential lines calculated for the following parameters of the channel: the gap between the plates $H = 100$ µm, the width of an electrode and the distance between the electrodes $D = 100$ µm, the voltage across the electrodes $U = \pm 20$, ± 40, and ± 60 V.

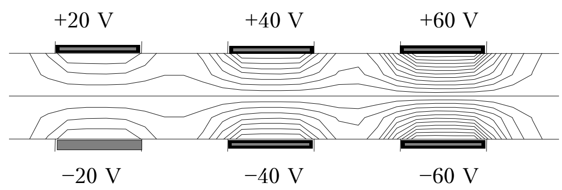

Fig. 2. Equipotential lines of the electric field in the separating channel ($H = 100$ µm, $D = 100$ µm; $U = \pm 20$, ± 40, ± 60 V).

A particle undergoes polarization in the electric field, i.e., acquires a dipole moment:

$$\mathbf{p} = \varepsilon_0\, \varepsilon\, \alpha_p\, \mathbf{E}, \tag{2}$$

where ε_0 is the electric constant; ε is the dielectric constant of the medium; α_p is the polarizability of a particle; $\mathbf{E} = -\operatorname{grad}\varphi$ is the electric field strength. The force of the inhomogeneous electric field acting on a polarized particle is proportional to the gradient of the potential energy of a dipole:

$$\mathbf{F} = \operatorname{grad}(\mathbf{pE}) = \varepsilon_0\, \varepsilon\, \alpha_p \operatorname{grad}(\mathbf{E}\cdot\mathbf{E}). \tag{3}$$

The resulting DEP force acting on a particle submerged in water can be written as

$$\mathbf{F} = \varepsilon_0\, \varepsilon\, (\alpha_p - \alpha_w\, n) \operatorname{grad}(\mathbf{E}\cdot\mathbf{E}) = \varepsilon_0\, \varepsilon\, \alpha_e \operatorname{grad}(\mathbf{E}\cdot\mathbf{E}), \tag{4}$$

where α_w is polarizability of water molecules; n is the number of water molecules displaced by the particle; α_e is the effective polarizability of the particle.

The liquid acts on the particle with the Stokes force of viscous friction

$$F_v = 3\pi\eta d_p (V_w - V_p), \tag{5}$$

where η is the viscosity of water; d_p is the particle diameter; V_p is the particle speed; V_w is the water flow rate.

We should also take into account the gravity

$$F_g = \frac{\pi}{6}\, d_p^3 g (\rho_p - \rho_w), \tag{6}$$

where g is the acceleration of free fall; ρ_p is the particle density; ρ_w is the density of water.

Inertia of particles in water can be neglected, because the relaxation time of particles at characteristic values of the particle size, flow rate, and viscosity is much less than the characteristic time of particle motion in the device.

If the direction of the gravity coincides with the direction of flow in the device and the direction of the axis x, then the equations of particle motion can be written in the following form:

$$\frac{dx}{dt} = \frac{\alpha_e \operatorname{grad}_x(\mathbf{E}\cdot\mathbf{E}) + \pi d_p^3 g(\rho_p - \rho_w)/6}{3\pi\eta d_p} + V_w, \tag{7}$$

$$\frac{dy}{dt} = \frac{\alpha_e \operatorname{grad}_y(\mathbf{E}\cdot\mathbf{E})}{3\pi\eta d_p}; \tag{8}$$

$$V_w = 1.5\, V_0 \left\{1 - [(2y - H)/H]^2\right\}, \tag{9}$$

where V_w is the rate of the laminar viscous flow, V_0 is the mean flow rate in the device.

The equations of particle motion (7) and (8) were integrated numerically using the fourth-order Runge–Kutta method.

Results

Typical trajectories of particles are shown in Fig. 3. The calculations were made for the following values of the parameters: the gap between the plates $H = 100$ µm; the width of the electrode and the distance between the electrodes $D = 100$ µm; the voltage across the electrodes $U = \pm 20$ V; the mean flow rate in the device $V_0 = 20$ µm/s; the particle diameter $d_p = 7.2$ µm; the particle density $\rho_p = 1.05$ g/cm^3.

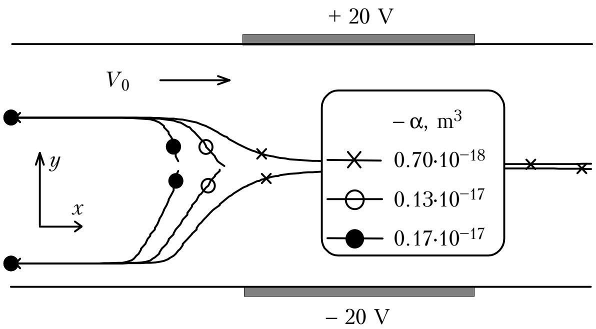

Fig. 3. Trajectories of particles near the electrodes ($U = \pm$ 20 V).

It is easy to see that under the effect of DEP forces the particles move to the central plane of the channel regardless of their initial position. Near the electrode edge, where the repulsive force is maximum the particle stops, if the DEP force is equal to the sum of the gravity and viscous friction forces. Extrusion of particles to the central plate by the electric field provides high quality of separation into fractions, because all particles near the electrode find themselves in roughly the same position (in the coordinate y) regardless of their initial coordinate at the entrance cross section of the channel.

Figure 4 shows the calculated trajectories of particles at the voltage of 20, 40, and 60 V across the electrodes and different values of the polarizability. It is easy to notice that particles with the effective polarizability $\alpha_e = -1.19 \cdot 10^{-18}$ m^3 stop before the electrode with the voltage of 20 V, the particles with $\alpha_e = -0.697 \cdot 10^{-18}$ and $-0.349 \cdot 10^{-18}$ m^3 are caught near the electrode with the voltage of 40 V, etc. It is also seen that the particles stop just at the electrode edges (in the coordinate x). If a particle does not stop here, it moves along with the flow to the next electrode.

#	1	2	3	4	5	6	7
$-\alpha \cdot 10^{-18}$, m^3	1.19	0.697	0.349	0.279	0.209	0.139	0.07

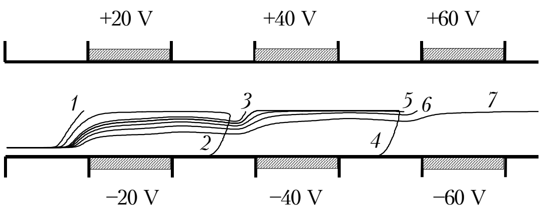

Fig. 4. Trajectories of particles in the separating channel.

The threshold value of the effective polarizability α_{EC} can be determined in the following way. The particles with $\alpha_e \le \alpha_{EC}$ are kept at an electrode by the DEP force, whereas the particles with $\alpha_e \ge \alpha_{EC}$ continue to move with the flow. The threshold values of the effective polarization were calculated by the method of bisection for different values of the voltage U, channel height H, particle diameter d_p, mean flow rate V_0, and the electrode width and interelectrode distance D. Besides, for every set of parameters the dimensionless parameter EV was calculated. This parameter is the ratio of the characteristic DEP force acting on a particle to the force of viscous friction

$$EV = \frac{\alpha_{EC}\, U^2/(H^2 D)}{3\pi\eta d_p V_0}\,. \qquad (10)$$

As an illustration, the Table presents some calculated results for different sets of the initial parameters.

Table. Threshold values of the effective polarization and the dimensionless parameter of similarity *EV*

α_{EC}, m^3	U, V	$H \cdot 10^6$, m	$D \cdot 10^6$, m	$d_p \cdot 10^6$, m	$V_0 \cdot 10^6$, m/s	EV
ρ_p = 1 g/cm^3, ρ_w = 1 g/cm^3						
$-4.87 \cdot 10^{-20}$	80	100	50	10	20	−0.237
$-4.33 \cdot 10^{-20}$	60	100	50	5	20	−0.237
$-4.88 \cdot 10^{-19}$	40	100	50	10	20	−0.238
$-1.56 \cdot 10^{-17}$	20	200	100	10	50	−0.237
ρ_p = 1.05 g/cm^3, ρ_w =1 g/cm^3						
$-1.06 \cdot 10^{-19}$	80	100	100	10	20	−0.258
$-2.49 \cdot 10^{-20}$	80	100	50	5	20	−0.242
$-1.69 \cdot 10^{-18}$	20	100	100	10	20	−0.259
$-3.98 \cdot 10^{-19}$	20	100	50	5	20	−0.242

The calculated results have shown that the threshold value of the effective polarization at constant parameters of the separating channel H, D, and V_0 depends only on the voltage across the electrodes U and particle size. The threshold value of the effective polarization α_{EC} for particles of the same size can be obtained by applying the corresponding voltage U. The calculated results (in particular, those given in the Table) show that if the particle density coincides with the density of water (no effect of the gravity), then the parameter $EV \cong -0.24$ is independent of H, D, U, and V_0, i.e., it is the parameter of similarity for the separating channel of this type. The values of EV calculated for particles with the density 1.05 g/cm^3 depend on the particle diameter, but only slightly (the values of EV calculated at d_p = 5 and 10 μm differ roughly by 6%). Consequently, the value of the dimensionless parameter $EV \cong -0.24$ can be used for estimating the threshold value of the effective polarization α_{EC} at different geometrical parameters of the separating channel and electrodes, voltage, and particle size.

Conclusion

Thus, we have developed a mathematical model of separation of particles in an inhomogeneous electric field. The dimensionless parameter of similarity EV has been proposed that allows estimating the geometrical parameters of the separating channel, flow rate of the cell suspension, and voltage across the electrodes that are needed for separation of particles at a given threshold value of the effective polarization.

It should be noted that the DEP force manifests itself in various non-conducting media. So, this method can be used for separation and identification of particles in air (aerosols) or space.[9,11] Since the number of displaced molecules in air is much less than that in water, the DEP force in air depends practically on the particle polarizability only. As a result, the particles are always attracted to the nearest electrode. In this case, the ratio of the dielectric and viscous forces acting on a particle can be characterized by the parameter of similarity EV with the allowance made for the viscosity, density, and polarizability of air.

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References

1. T.S. Bakirov, V.M. Generalov, and V.S. Toporkov, Biotekhnologiya, No. 2, 73–82 (1998).

2. X. Wang, X.-B. Wang, and P.R.C. Gascoyne, J. Electrostat. **39**, 277–295 (1997).

3. Y. Huang, X.-B. Wang, F.F. Becker, and P.R.C. Gascoyne, Biophys. J. **73**, 1118–1129 (1997).

4. P.R.C. Gascoyne, X.-B. Wang, Y. Huang, and F.F. Becker, IEEE Transactions on Industry Applications **33**, No. 3, 670–678 (1997).

5. F.F. Becker, X.-B. Wang, Y. Huang, R. Pathig, J. Vykoukal, and P.R.C. Gascoyne, J. Phys. D: Appl. Phys. **27**, 2659–2662 (1994).

6. F.F. Becker, X.-B. Wang, Y. Huang, R. Pathig, J. Vykoukal, and P.R.C. Gascoyne, Proc. Natl. Acad. Sci. USA **92**, 860–864 (1995).

7. T.S. Bakirov, A.A. Chepurnov, G.I. Tyunnikov, and V.M. Generalov, Biotekhnologiya, No. 4, 47–54 (1997).

8. T.S. Bakirov, V.M. Generalov, A.A. Chepurnov, G.I. Tyunnikov, and V.D. Poryvaev, Dokl. Akad. Nauk **363**, No. 2, 258–259 (1998).

9. V.S. Toporkov, S. Bakirov, V.M. Generalov, and A.S. Safatov, Atmos. Oceanic Opt. **12**, No. 6, 530–533 (1999).

10. D. Anderson, J. Tannehill, and R. Platcher, *Computational Hydromechanics and Heat Exchange* [Russian translation] (Mir, Moscow, 1990), Vol. 1, 384 pp.

11. Patent No. 2105815 RF, MKI6, C12Q1/00.