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BIOPARTICLE SEPERATION IN NON-NEWTONIAN FLUID USING PULSED FLOW IN MICRO-CHANNELS

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ABSTRACT

Micro Total Analysis System (μ TAS) devices frequently need to deal with bio-particle suspensions in solution and separation of certain bio-particles is often desirable. Separation of plasma from the whole blood has become increasingly popular in clinical diagnostics.

Using a finite volume method, Volume of Fluid (VOF) and Discrete Phase (DP) governing equations for multiphase flow are used to delineate the effect of non-Newtonian shear-thinning viscosity of blood from Newtonian viscosity of water. It is observed that the Red Blood Cells (RBC) accumulate at the front of the blood column due to the effect of non-Newtonian viscosity, while the opposite is observed in water. For the selected parameters, 20% of the plasma is observed to be separated from the whole blood, while, in contrast, for a 98% diluted blood 45% of the plasma can be separated. Increase in the particle density and size has resulted in a better separation of the beads from the water for a given magnitude of pressure and number of pulses.

For a given pressure, increasing the number of pressure pulses provides more separation and with a low number of applied pulses, higher pressures provide better separation. The present calculations can be adopted to design the flow parameters necessary for the instantaneous separation of plasma from the whole and the diluted blood for μ TAS; thus reducing the number of experimental studies. The present method can also be used for calculating the separation of other bio-particles in aqueous solutions.

Key words: Blood, bead, separation, non-Newtonian, pulse, RBC.

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CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

Microelectromechanical systems (MEMS) technology for miniaturization was the most significant enabling technology of the 20th century. MEMS have many everyday applications such as telecommunications, life sciences (blood analysis and forensic applications) automobiles (accelerometers, pressure sensors) [Cao et al., 2001; Grodzinski et al., 2001; Ehrnstrom et al., 2002; Vespoorte et al., 2002]. Significant research has been focused over the past decade towards development of micro-fluidic devices. Since the introduction [Manz et al., 1990 and 1991; Glavina et al., 1993], the field has witnessed rapid development in the early 90's, implying that life sciences and chemistry are the main application fields of micro-fluidics.

1.2 MOTIVATION

Micro Total Analysis Systems (μ TAS) offer the advantage of low sample reagent volume, faster processing and low sample wastage, leading to low-cost efficient operation [Figeys et al., 2000; Vinet et al., 2002]. μ TAS systems frequently need to deal with biological fluids that are a complex mixture of proteins, minerals, electrolytes and cells etc. [Lin et al., 2000], where separation of certain components from the rest is often desirable. Techniques such as crystallization and distillation have been widely applied

Figure 1: RBC and the plasma in whole blood

[Melville et al., 1975] when separations of cells or fragments of cells from aqueous solutions or suspensions are required. These techniques become more complicated as the quantity to be separated becomes smaller.

Blood (fig.1), an analyte frequently used for various diagnoses, is a non-Newtonian fluid transporting oxygen, carbon dioxide, nutrients, salts, hormones, metabolites and various other components [Bitsch et al., 2002] to all parts of human body. The most important components from a rheological point of view are plasma and RBC. RBC takes up about 45% volume of whole blood and significantly impact the flow characteristics of blood.

1.3 PREVIOUS WORK

The process of separation of the cellular components of blood from the plasma is called *Plasmapheresis* [Siami et al., 2001]. This is routinely carried out for preparative, analytical and therapeutic purposes. There are a number of techniques in use for the separation of plasma from whole blood by physical means. Membrane separation and centrifugation have been the two most well known methods of blood-plasma separation over the last couple of decades [Dorn et al., 1978]. Other methods are separation by ultrasound [Cousins et al., 2000], and separation by magnetic means [Richards et al., 1996; Kovacs et al., 1998; Svoboda et al., 2000]. In membrane separation, the filtration of blood to separate RBC from the rest of the blood is done by passing whole blood through a ‘filter’ having pores of sizes smaller than red blood cells. The continuous flow

membrane filtration for therapeutic plasma exchange was first introduced by Soloman et al. [1978].

Centrifugation involves subjecting a liquid suspension with particles of different weights and densities to a centrifugal acceleration. The components in the liquid are separated according to their specific body forces. Another technique to efficiently separate blood cells from plasma is to cause aggregation of blood cells by exposure of whole blood to an ultrasonic standing wave [Cousins et al., 2000]. These techniques might cause damage to the live RBC when it comes to point of care testing (POCT) lab-on-a-chip.

Yang et al. [2005] have developed a technique of separating RBC from plasma in blood by controlling flow rate in micro-channels. Here the whole blood is sent through a micro-channel and the RBC's are collected through smaller diameter micro-channels, nearly 25% of the plasma is successfully separated from the whole blood. This technique is quite expensive and takes longer time for the separation. Jain et al. [2003] have demonstrated the separation of micro-spheres suspended in DI water by applying a series of high-pressure, short-duration pulses (fig. 2) to the suspension solution in micro-channels on a plastic device. About 60% of the fluid volume is successfully separated from particles.

Figure 2: Dynamic Pressure pulse

Han et al. [2005] have used the same technique and implemented it on whole blood, and are able to obtain 20% of plasma free from RBC, and separate cell / plasma from the whole blood in less than 7 seconds. This technique is considered to be one of the fastest plasma separations from human whole blood on a chip, suitable for POCT lab-on-a-chip. For better understanding of this new technique, a study on the effect of different parameters, like density of particles, viscosity of medium (Newtonian and non-Newtonian), and particle volume fraction is more than necessary. Considering the cost and the complications involved in the experimental methods, a numerical approach is very much desired.

Patankar et al. [2001] have studied numerically on the equilibrium position for a particle in a Poiseuille flow of a shear-thinning viscous fluid like blood for different Reynolds numbers. Feng et al. [2003] have studied on the equilibrium position for a particle in a horizontal shear flow for a Newtonian fluid. Cho et al. [2005] have studied on the numerical simulation of fluid flow laden with a maximum of 5120 particles. They showed the distribution of particles in the channel, the effect of different volume fractions and ratios of channel height to particle diameter.

1.4 OBJECTIVE OF THE RESEARCH

The present work is *unique* as it deals with large concentrations of particles (particle number of the order of millions). The effect of non-Newtonian viscosity and the different particle concentrations are also considered in the present work. Carreau model

[Cho et al., 1991] is adopted for the blood viscosity, and the two-way coupling between the particles and the fluid is also considered.

1.6 OUTLINE OF THESIS

The next chapter, chapter 2, discusses about the geometry used for the computations. Following that is the explanation of the formulation used to discretize the governing equations. The boundary conditions, the material properties are explained in detail. Finally the finite volume method and the techniques used for the pulsatile pressure are explained.

Chapter 3 describes the effect of pressure, particle density, particle size and particle concentration on the particle and fluid separation.

Chapter 4 gives the conclusion for this work. A brief summary of the research is given. Some suggestions for future work are mentioned.

CHAPTER 2

MATHEMATICAL FORMULATION

2.1 GEOMETRY & FORMULATION

A three-dimensional rectangular channel, having a fluid column, laden with particles, as schematically shown in Fig.3, is considered. The 3D channel is 250 μm in width, 100 μm in height, and 50 cm long. A 500 nl of water (2 cm long) and a 350 nl of whole blood (1.5 cm long) are considered for the computations.

The computations consist of two major sub-models: Volume of Fluid model (VOF) dealing with the motion of the continuous phase (fluids with particles inside); Discrete Phase model dealing with the suspended solid particles taking into account the action of external forces.

Volume of Fluid model (VOF): The interface between the liquid and the gas phases is tracked using VOF method. The governing equations for the fluid are given by

$$\frac{\partial \varepsilon_f}{\partial t} + (\nabla \cdot \varepsilon_f \bar{u}) = 0 \quad (1)$$

$$\rho \left[\frac{\partial}{\partial t} (\varepsilon_f \bar{u}) + (\nabla \cdot \varepsilon_f \bar{u} \bar{u}) \right] = -\varepsilon_f \nabla p + \rho \bar{g} + (\nabla \cdot \varepsilon_f \mu [(\nabla \bar{u}) + (\nabla \bar{u})^T]) + \bar{F}_\sigma - \bar{F}_{f \rightarrow s} \quad (2)$$

where, the source terms, $\bar{F}_\sigma$ and $\bar{F}_{f \rightarrow s}$, account for the forces due to surface tension and two-way coupling due to the presence of the suspended solid particles, respectively. Here, ‘-’ over the character signifies the vector quantity. Furthermore ε_f, u, p , and μ

Figure 3 : Geometry and boundary conditions

represent the volume fraction, the velocity of the continuous liquid phase, the pressure, and the coefficient of viscosity, respectively. For the local average density, ρ , linear weighing of the densities of the liquid (f) and discrete phase (p) is used:

$$\rho = \varepsilon_f \rho_f + (1 - \varepsilon_f) \rho_p \quad (3)$$

Discrete Phase model: The motion of the suspended solid particles is given by Newton's second law. The following expression, accounts for the action of gravity, far-field pressure, drag, and lift.

$$\frac{d}{dt}(m_p \bar{v}) = \bar{F}_g + \bar{F}_{f-p} + \bar{F}_d + \bar{F}_L \quad (4)$$

Where m_p , v , F_g , F_{f-p} , F_d , and F_L , denote the mass of the particle, velocity of the particle, force due to gravity, force due to far-field pressure, drag force and lift force, respectively. The action of gravity and the far field pressure is neglected as the channel is flat and is very long. Hence, the particle acceleration is given by

$$\frac{d\bar{v}}{dt} = \frac{18\mu}{\rho_p d_p^2} \frac{C_D \text{Re}}{24} (\bar{u} - \bar{v}) \quad (5)$$

where C_D is the coefficient of drag and is given by,

$$C_D = a_1 + \frac{a_2}{\text{Re}} + \frac{a_3}{\text{Re}^2}, \text{ the values of } a_1, a_2, \text{ and } a_3 \text{ are taken from Morsi et al.}$$

[1972] and Re is the relative Reynolds number.

$$\text{Re} = \frac{\rho_f d_p |\bar{v} - \bar{u}|}{\mu} \quad (6)$$

The momentum response time is given by [Crowe et al., 1997]

$$\tau_d = \frac{m_p |\bar{u} - \bar{v}|}{|\bar{F}_d|} = \frac{\rho_p d_p^2}{18\mu} \quad (7)$$

The peak Re in the present problem is found to be less than 5, and τ_d is found to be of the order of 10^{-6} , which implies that the time taken by the discrete phase (particles) to reach the continuous phase (medium) velocities is almost negligible.

2.2 BOUNDARY CONDITIONS

Specific boundary conditions are applied to complete the formulation of the problem. Flow Boundary Conditions are as follows:

- 1) No slip boundary condition is considered on the walls of the channel.
- 2) Pressure boundary condition is used for the inlet of the channel.
- 3) The boundary condition for outlet is given as atmospheric pressure.

2.3 MATERIAL PROPERTIES

Computations and the conditions are classified based on character of the medium used, water or blood. Bead size of $4.1 \mu\text{m}$, density of 1050 kg/m^3 is chosen [Jain et al., 2003]. The size and the density of the RBC are taken as $8 \mu\text{m}$, and 1050 kg/m^3 , respectively [Fujita et al., 1997]. The density, viscosity, surface tension and contact angle of water are 998 kg/m^3 , 0.001003 kg/m-s , 0.072 N/m and 92 degrees, respectively. A 500 nl of water and a 350 nl of whole blood are considered for the computations. The density, surface tension and contact angle of whole blood are 1050 kg/m^3 , 0.056 N/m and

92 degrees, respectively. The formulation for the non-Newtonian viscosity of the blood is discussed below.

Viscosity: The relation between the shear stress and the shear rate is given by,

$$\tau = \mu \frac{\partial u_f}{\partial y} \quad (8)$$

where τ is the shear stress and, for a Newtonian fluid the coefficient of viscosity μ is constant. The shear thinning non-Newtonian viscosity of blood is modeled using Carreau model. Carreau fluid is a type of Generalized Newtonian fluid, where viscosity depends upon shear rate by the following equation:

$$\mu_{eff}(\dot{\gamma}) = \mu_{\infty} + (\mu_0 - \mu_{\infty}) \left(1 + (\lambda \dot{\gamma})^2 \right)^{\frac{n-1}{2}} \quad (9)$$

where $\mu_{eff}(\dot{\gamma})$ is viscosity as a function of shear rate, $\mu_{\infty} = 0.0345$, $\mu_0 = 0.56$, $\lambda = 3.313$ and $n = 0.3568$ are coefficients [Cho et al., 1991]. At very high shear rates, the viscosity of blood is nearly three to four times higher than that of water.

2.4 FINITE VOLUME METHOD

A finite volume method [FLUENT] is used to solve for the governing equations of the multiphase flow. The 3D channel is modeled using finite volume mesh of about 500,000 cells. The finite volume mesh is developed with hexahedral elements. The governing equations for fluid flow are discretized and solved iteratively using the finite-volume method. An implicit linearization scheme is employed to discretize the non

linear governing equations. The coupling of pressure and velocity equations is achieved using the PRESTO (Pressure Staggering Option) algorithm, to derive pressure from the discrete continuity equation. A second-order upwind scheme is adapted to stabilize the governing equations. The pulsatile profile for the pressure is achieved using a user defined function (UDF). A sample of the code is given below.

```
#include "udf.h"

DEFINE_PROFILE(unsteady_pressure, thread, position)
{
    face_t f;

    real t = CURRENT_TIME;

    begin_f_loop(f, thread)
    {
        if (t<=0.05)
            F_PROFILE(f, thread, position) = 27300*sin(3.14285714*t/.05);
        else if (0.055>=t&t>0.05)
            F_PROFILE(f, thread, position) = 0;
        else if (0.055<t&t<=0.105)
            F_PROFILE(f, thread, position) = 27300*sin(3.14285714*(t-0.055)/.05);
        else if (0.11>=t&t>0.105)
            F_PROFILE(f, thread, position) = 0;
        else if (0.11<t&t<=0.16)
            F_PROFILE(f, thread, position) = 27300*sin(3.14285714*(t-0.11)/.05);
        .....
        .....
        F_PROFILE(f, thread, position) = 27300*sin(3.14285714*(t-2.09)/.05);
    }
}
```

```

    else if (2.145>=t&t>2.14)
F_PROFILE(f, thread, position) = 0;
    else if (2.145<t&t<=2.195)
F_PROFILE(f, thread, position) = 27300*sin(3.14285714*(t-2.145)/.05);
    else
F_PROFILE(f, thread, position) = 0;
}
end_f_loop(f, thread)
}

```

CHAPTER 3

RESULTS & DISCUSSION

3.1 RESULTS & DISCUSSION:

The effects of time dependent pressure pulse and magnitude as well as particle concentration on separation of bead in aqueous solution and RBC in blood are discussed.

Figure 4 shows the qualitative images of the bead concentration at the rear, mid and the leading locations of the fluid column inside the micro-channel for water after 5, 10 and 15 pulses for a pressure magnitude of 5 psi. The concentration of beads at the rear end of the fluid column increases, whereas the concentration decreases at the front or leading end of the fluid column for increasing number of pulses. The interface motion is dynamic (dynamic contact angle) during the duration of pulse; hence, to accommodate the movement of the interface there is a gap between the beads and the interface. The pulse effect decreases as the number of pulses increase; thus a decreasing gap between the rear interface and the beads can be observed.

Figure 4: Numerical images of rear, middle and leading locations of water column for 5, 15 and 30 pulses respectively for a 5 psi pressure, 1% particle volume fraction and particle diameter of $4.1\mu\text{m}$.

Figure 5: RBC concentration in the blood plasma for different number of pulses with a 5 psi pressure and bead concentration in the fluid column for different number of pulses with a 5 psi pressure.

Figure 5 shows the percentage of total particles in the fluid column along the flow direction in the medium, after 10, 20 and 30 pulses for a pressure magnitude of 5 psi. The figure shows the result for both fluid mediums: water and blood, and the details are explained individually for each medium below.

Water: The bead volume fraction is 1% (total number of 132,000 particles), and the concentration (percentage of total number of beads in the fluid column in the axial direction) present initially inside the channel is constant and is about 0.022% (28 beads per $4.1\mu\text{m}$ along the column) along the flow direction. The concentration increases at the rear end and decreases at the leading end, with increase in number of pulses applied to the fluid column. The increase in accumulation at the rear interface compared to the initial concentration is nearly 4 times greater after 30 pulses as shown in Fig. 5. The drag [Jain et al., 2003] and the movement of the beads to the corners [Feng et al., 2003] cause the beads to lag the fluid, and the beads get accumulated at the rear end of the fluid column.

Blood: Carreau model [Cho et al., 1991] is used to account for the shear thinning non-Newtonian viscosity of whole blood. The concentration present initially inside the channel is constant and is about 0.0571% (~ 150 RBC per $8\mu\text{m}$ along the column) along the flow direction. The increase in accumulation at the leading interface is twice when compared to the initial concentration after 30 pulses as shown in Fig. 5. The RBC-RBC interaction is damped due to the high shear thinning property of the blood viscosity; hence, RBC stay in the center and as the velocity in the center is much greater than the

velocity at the walls, the RBC move to the front end resulting in accumulation at the leading interface. The accumulation at the leading interface for blood is just the opposite of what is seen for water.

Figure 6: Bead concentration along the width of the channel in water, with a particle volume fraction of 1% and for a 5 psi pressure.

Figure 6 shows the percentage of total beads in the water column along the width of the channel ($\pm y$ -direction) after 10, 20 and 30 pulses for a pressure magnitude of 5 psi for water. The results discussed here are for 1% bead volume fraction. Initially, the concentration of beads present along the width of the channel is about 1.64%. Feng et al. [2003] have shown that in a horizontal shear flow, when the density ratio (ρ_p / ρ_f) is about 1.05 for Re_p less than 5, the equilibrium position for the beads is very near to the channel wall, i.e. y_E (distance from the walls) is less than 0.6 times bead diameter. Figure 6 shows the results of Feng et al. [2003] and it is found that majority of the beads move near to the walls. Nearly 3% of the total beads are observed to be present at the corners after 5 pulses and the concentration near the walls decrease after 5 pulses. At the center a very low amount, 0.1% of the beads, are observed to be present after 5 pulses, and the percentage of the beads keep increasing to 1.1% after 30 pulse. The wall boundary layer thickness is of the order of bead diameter; hence, the beads get trapped inside the boundary layers and, as the velocity of the fluid is comparatively lower than the center, the beads accumulate at the rear end.

Figure 7: RBC concentration along the width of the channel in whole blood for a 5 psi pressure.

The results shown in Fig. 7 are for the whole blood, where the RBC concentration is about 45%. The initial concentration present along the width of the channel is about 3.2%. Patankar et al. [2001] have showed that the equilibrium position for a particle in a Poiseuille flow of a shear thinning non-Newtonian fluid is greater than $4 d_p$ for Re less than 5. In Fig. 7, it can be seen that the majority of the RBC are in the center, which is in agreement with Patankar et al. [2001]. A maximum of 12% of the total RBC are observed to accumulate at the center of the channel after 20 pulses and the concentration decreases to about 11% after 30 pulses. The RBC concentration near the walls decreases with increase in pulses and the fluid near the walls are observed to be almost free from RBC after 20 pulses.

Figure 8 : Effect of pressure and the number of pulses on the bead separation in water and RBC separation in whole blood.

3.2 EFFECT OF PRESSURE

Figure 8 shows the percentage volume of liquid free from beads inside the medium with variation of pulses. The validation of this numerical study is done for the experimental data for the water from Jain et al. [2003]. The maximum error between the numerical data and the experimental data is about 3.3% at 25 pulses. About 60% of the volume of fluid is separated from the beads after 30 pulses. A 12% increase in the bead separation is observed after 15 pulses for 5 psi pressure when compared to 3 psi pressure. A pressure of 3 psi applied for 15 pulses gives the same separation as that of 5 psi applied for 11 pulses.

Figure 8 also discusses the separation of RBC inside blood, the results obtained are compared with Han et al. [2005] and it is found that the results are in accordance with the experimental data. The maximum error between the numerical data and the experimental data is about 3.3% at 15 pulses. A maximum of 20% of plasma separation is obtained for a 5 psi pressure after 30 pulses for the whole blood.

Figure 9: Effect of particle density on the bead separation in water.

3.3 EFFECT OF PARTICLE DENSITY

Figure 9 shows the comparison for bio-particles with different densities: 1050, 1500 and 2000 kg/m³. A maximum of 63% separation is observed with a particle density of 2000 kg/m³. 45% increase in density leads to a 5.5% more separation for 15 pulses of 5psi pressure, and about 90% increase in the density resulted in 9% more separation. Hence, an increased separation can be achieved for denser bio-particles with a lower number of pulses for a fixed pressure.

3.4 EFFECT OF PARTICLE CONCENTRATION

Figure 10: Effect of particle concentration on the bead separation in water and the effect of dilution on the RBC separation in blood.

The effect of particle volume fraction is also discussed in Fig. 6 for both water and blood for 5 psi pressure. For the bead separation in water, the effect of 1%, 5% and 10% bead volume fraction is discussed. A 3.3% reduction is observed in the total volume free from beads after 30 pulses for a 10% bead volume fraction when compared to a 1% bead volume fraction. In the case of blood, the effect of RBC concentration of 1% (98% dilution), 25% (45% dilution) and 45% (whole blood) of RBC on the separation is discussed. A maximum of 45% of the total volume of liquid is observed to be free from RBC for the 98% diluted blood whereas a 30% of the total volume of liquid is observed to be free from RBC for the 45% diluted blood. The whole blood has about 45% RBC by volume and, because of this large volume fraction, the percentage of liquid volume that can be free from RBC is 20% less than that for 98% diluted blood, where the RBC volume fraction is 1%. A 20% of the total volume of liquid is observed to be free from RBC for the whole blood for 5 psi pressure.

Figure 11: Effect of particle size on the bead separation in water.

3.5 EFFECT OF PARTICLE SIZE

Figure 11 shows the percentage volume of liquid free from particles with variation of pulses for a Newtonian medium for 5 psi pressure and for different particle diameters, namely 1, 4.1 and 10 μm . A maximum of 62% volume of liquid is observed to be free from particles for with a particle diameter of 10 μm . An increase in particle size from 4.1 to 10 μm resulted in a 3.4% increase in the total volume of liquid free from particles for a fixed pressure and pulses. A 11.4% reduction in the total volume of liquid free from particles is observed when the particle size is 1 μm , whereas a 8.5% increase in the total volume of liquid free from particles was observed when the particle size is 10 μm , for 5 pulses.

CHAPTER 4

CONCLUSIONS

4.1 SUMMARY:

The reasoning behind the RBC separation in blood and bead separation in water is discussed. The effect of particle concentration on bead separation in water and the effect of dilution on RBC separation in blood are discussed. From equation 7, it is observed that the reason for the bead separation in water is not only drag, but also due to the movement towards the walls as can be seen in Fig. 4. The cause behind the RBC separation from plasma is the restriction of RBC movement from the center to the wall as can be seen in Fig 5. For a given pressure, increasing the number of pressure pulses provides more separation. For higher input pressures, the maximum separation is achieved with a lower number of pulses, as compared to that for lower applied pressure. For a low number of applied pulses, the inlet pressure has a significant impact. However, for a very large number of pulses, the separation is essentially independent of pressure; thus maximum separation can also be achieved even at low pressure but requires more time. *A desired dynamic pressure characteristic can be applied by optimizing the inlet pressure and number of pulses to achieve maximum possible separation in a relatively short time.* The larger the particle density and size the higher and faster is the bead separation in water for a given pressure and pulses. For a given pressure, the lesser the particle concentration the higher and faster is the bead separation in water. Under similar

scenario, increasing the dilution of blood can significantly cause increase in the amount of plasma free from RBC.

4.2 FUTURE WORK

Further, the above technique can be used for particle-particle separations in fluid suspensions for a POCT lab-on-a-chip. The application of pressure and the pulses can be effectively optimized to obtain the particle-particle separation based on their difference in the particle density and size.

REFERENCES

- Anand, M., Rajagopal, K.R., 2004. A Shear-thinning viscoelastic fluid model for describing the flow of blood, *International Journal of Cardiovascular Medicine and Science* 4 (2), 59-68.
- Bitsch, L., 2002. Blood Flow in Microchannels, MS Thesis, Technical University of Denmark.
- Cao, L., Mantell, S., Polla, D., 2001. Design and Simulation of an Implantable Medical Drug Delivery System using Microelectromechanical Systems Technology, *Sensors and Actuators*, 94, 117-125.
- Cho, S.H., Choi, H.G., Yoo, J.Y., 2005. Direct numerical simulation of fluid flow laden with many particles, *International Journal of Multiphase flow* 31, 435-451.
- Cho, Y.I., Kensey, K.R., 1991. Effects of non-Newtonian viscosity of blood on flows in a diseased arterial vessel. Part 1: Steady flows, *Biorheology*, 28, 241-262.
- Cousins, C.M., Holownia, P., Hawkes, J.J., Price, C. P., Keay, P., Coakley, W. T., 2000. Clarification of plasma from whole human blood using ultrasound, *Ultrasonics* 38, 654-656.

Crowe, C., Sommerfeld, M., Tsuji, Y., 1997. Multiphase Flows with Droplets and Particles Interpharm/CRC, ISBN: 0849394694.

Dorn, G.L., Smith, K., 1978. New centrifugation blood culture device, Journal of clinical microbiology 7 (1).

Ehrnstrom, R., 2002. Miniaturization and Integration: Challenges and Breakthroughs in Microfluidics, Lab on a Chip, 2, 26-30.

Feng, Z., Michaelides, E.E., 2003. Equilibrium position for a particle in a horizontal shear flow, International Journal of Multiphase Flow 29, 943–957.

Figeys, D., Pinto, D., 2000. Lab-on-a-chip: a revolution in biological and medical sciences, Anal. Chem. 72, 330–335.

FLUENT, Fluent Inc, Lebanon, NH.

Fujita, H., 1997. A decade of MEMS and its future, IEEE Trans (1-8).

Glavina, P.G., Manz, A., 1993. Towards miniaturized electrophoresis and chemical analysis systems on silicon: an alternative to chemical sensors, Sensors and Actuators B (Chemical) 2,107-116.

- Grodzinski, P., Liu, R., Chen, B., Blackwell, J., Liu, Y., Rhine, D., Smekal, T., Rhine, D., Smekal, T., Ganser, D., Romero, C., Yu, H., Chan, T., Kroutchinina, N., 2001. Development of Plastic Microfluidic Devices for Sample Preparation, *Biomedical Microdevices*, 34, 275-283.
- Han, J., Ahn, C.H., 2005. An On-Chip Whole Blood Cell-Serum Separator Using Dynamic Pulsatile Pressure, *The 9th international Conference on Miniaturized System for Chemistry and Life Sciences (μ TAS)*, Boston, MA, USA, 1346-1348.
- Jain, A., Puntambekar, A., Ahn, C.H., 2003. A novel bioparticle separation technique using sequential pressure pulses, *7th international Conference on Miniaturized Chemical and Biochemical Analysts Systems* October 5-9, Squaw Valley, California USA, 1017-1020.
- Kovacs, G., 1998. *Micromachined Transducers Sourcebook*, Boston: WCB Mc-Graw Hill.
- Lin, L., Guthrie, J.T., 2000. Preparation and characterization of novel, blood-plasma separation membranes for use in biosensors, *Journal of Membrane Science* 173 (1), 73-85.
- Manz, A., Graber, N., Widmer, H.M., 1990. A novel concept for chemical sensing, *Miniaturized total chemical analysis systems*. B1, 244-248.

Manz, A., Harrison, D.J., Fettingner, J.C., Verpoorte, E., Ludi, H., Widmer, H.M., 1991. Integrated electroosmotic pumps and flow manifolds for total chemical analysis systems Proc. TRANSDUCERS . International Conference on Solid-State Sensors and Actuators, 939-41.

Melville, D., Paul, F., Roath, S., 1975. High gradient magnetic separation of red cells from whole blood, IEEE Trans. Magn. 11, 1701.

Morsi, S.A., Alexander, A.J., 1972. An Investigation of Particle Trajectories in Two-phase Flow Systems, J. Fluid Mech.55 (2), 193-208.

Patankar, N.A., Huang, P.Y., KO, T., Joseph, D.D., 2001. Lift-off a single particle in Newtonian and visco-elastic fluids by direct numerical simulation, J. Fluid Mech 438 (100), 67.

Richards, A.J., Roath, O.S., Smith, R.J.S., Watson, J.H.P., 1996. The mechanisms of high gradient magnetic separation of human blood and bone marrow, IEEE Trans. Magn. 32.

Siarni, G.A., Siarni, F.S., 2001. Membrane Plasmapheresis in the United States: A Review Over the Last 20 Years, Therapeutic Apheresis 5 (4), 315-320.

Soloman, B.A., Castino, F., Lysaght, M.J., Colton, C.K., Friedman, L.I., 1978.

Continuous flow membrane filtration of plasma from whole blood, ASAIO Trans
24, 6-21.

Svoboda, J., 2000. Separation of red blood cells by magnetic means, Journal of
Magnetism and Magnetic Materials 220 (2-3), 103-105.

Yang, S., Undar, A., Zahn, J.D., 2005. Blood plasma separation in micro-fluidic channels
using flow rate control, ASAIO Journal 51, 585 - 590.

Unni, H.N., Yang, C., 2005. Brownian dynamics simulation and experimental study of
colloidal particle deposition in a micro-channel flow, Journal of Colloid and
Interface Science 291, 28 – 36.

Vespoorte, E., 2002. Microfluidic Chips for Clinical and Forensic Analysis,
Electrophoresis 23, 677-712.

Vinet, F., Chaton, P., Fouillet, Y., 2002. Microarrays and Microfluidic Devices:
Miniaturized Systems for Biological Analysis, Microelectronic Engineering 61,
41-47.