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Microfluidic separation process by the Soret effect in biological fluids

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ABSTRACT

In this article the thermophysical and transport properties of mixtures composed of glucose and sucrose in dimethylsulfoxide (DMSO) are determined. The studied mass concentrations are 5%, 10%, 15%, 20% and 25% of glucose or sucrose in DMSO at an average temperature of 25 °C. The properties studied experimentally are the dynamic viscosity, density, mass and thermal expansion coefficient and thermodiffusion coefficient. The thermogravitational technique in flat configuration is used in order to obtain the thermodiffusion coefficients. Once these properties are known, the work is focused on the numerical study of applying a temperature gradient in microdevices in order to optimize the extraction of DMSO using the CFD Ansys Fluent software. The results show an improvement even of 35% on microfluidic separation techniques that are based on a purely diffusive regime.

1. Introduction

For over a decade, numerous studies have demonstrated the importance of miniaturization in biotechnology [1], since it can perform multiple assays simultaneously in a short period of time and uses less sample and reagent, among others. To this end, microfluidic platforms are used, where the flows are laminar. Because of this, the mix of components, in many cases, is limited by molecular diffusion. This makes the analysis of transport properties essential to determine the efficiency of the mixture.

Within this context, one of the applications that have been attributed to microfluidic devices is the cleaning of cryopreserved cells, removing the cryoprotectant by molecular diffusion [2–4]. However, the microdevices submitted for this purpose are too large or too complicated geometrically. This article presents the possibility of improving the efficiency of these microdevices by the application of temperature gradients. These temperature gradients increase the separation through the Soret effect [5].

One of the cryoprotectants employed is DMSO, which is used to cryopreserve cells, tissues or organs [6]. Some studies have shown that its power of cryopreservation, is improved by adding sugars such as glucose [7]. Although DMSO provides a protective benefit to cells during freezing, a long-term exposure can result in cell death because of its toxicity [4]. Therefore, before implanting the cells it is necessary to clean them. The usual technique is the centrifugation cleaning, however, this technique can damage up to 30% of the cells [8].

This article demonstrates the importance of determining the transport properties in biological mixtures in order to improve on a microscopic scale the separation process without damaging the cells. To determine the transport properties, specifically the thermodiffusion coefficient, the thermogravitational column technique is used [9]. The experimental results are used in the numerical software Ansys Fluent, where the benefits of the Soret effect at the micro-scale is observed, optimizing the microdevices for DMSO extraction.

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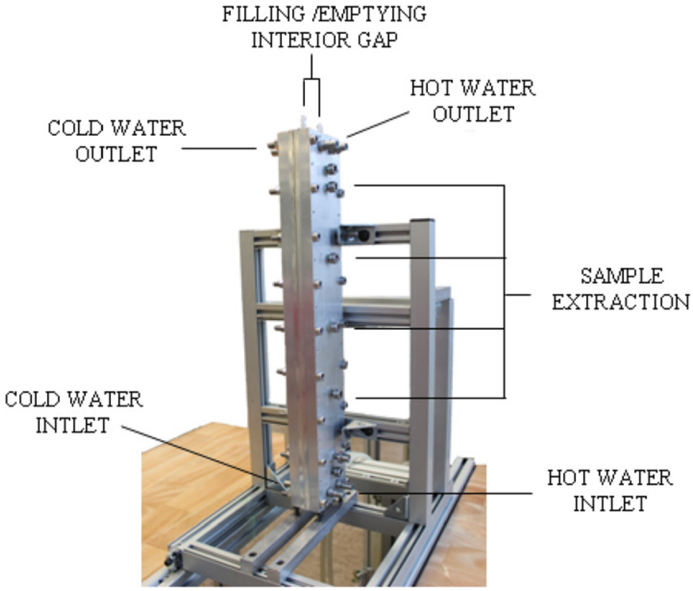

Fig. 1. Thermogravitational column configuration.

The determined properties correspond to biological mixtures of sucrose–DMSO and glucose–DMSO at mass concentrations of 5%, 10%, 15%, 20% and 25% of sucrose and glucose. Similarly, the thermophysical and transport properties for a mass concentration of 10% of DMSO in phosphate buffered saline (PBS) is determined, to discuss the results of work [3] and demonstrate the effectiveness of the Soret effect in separation microdevices in biological mixtures.

2. Experimental procedure

To determine the thermodiffusion coefficient, the thermogravitational column (TC) technique is used. In this case a flat configuration with four-point sample extraction is used (Fig. 1). For more details around the experimental procedure of this technique the reader is invited to consult [10] where is fully explained.

The thermodiffusion coefficient can be determined by measuring the change in the density of samples at steady state along the column, as shown in Eq. (1) [11]:

$$D_T = -\frac{gL_X^4}{504}\frac{\alpha}{c_0(1-c_0)\beta\eta}\frac{\partial\rho}{\partial z} \tag{1}$$

where L_x is the gap of the TC, c_0 the initial mass fraction of the reference component in the initial homogeneous mixture, $\alpha = -\frac{1}{\rho}\frac{\partial\rho}{\partial T}$ the thermal expansion coefficient, $\beta = \frac{1}{\rho}\frac{\partial\rho}{\partial c}$ the mass expansion coefficient, ρ the density of the mixture, $\frac{\partial\rho}{\partial z}$ the density gradient along TC, υ the kinetic viscosity, g the gravitational acceleration and η the dynamic viscosity.

3. Experimental results

All experiments are performed at an average temperature of 25 °C. All measurements were repeated at least 4 times. In all cases the deviation was less than 4%. Table 1 shows the thermophysical and transport properties determined for mixtures of sucrose–DMSO, glucose–DMSO and DMSO–PBS at different mass concentrations at an average temperature of 25 °C. Fig. 2 shows the thermal diffusion coefficient versus the mass concentration of sucrose (Fig. 2a) and glucose.

Fig. 2 shows how the thermodiffusion coefficient decreases linearly as the solute concentration increases. At solute concentrations on the order of 30% of sucrose and glucose it is expected that the thermal diffusion coefficient changes sign, i.e. in these concentrations the denser component is directed toward the warmest wall. Therefore, at higher concentration of sugars in DMSO, the thermodiffusion coefficient is negative which will mean readjusting the sense of the temperature gradient depending on the range of solute concentration in the mixture in order to optimize the separation.

4. Numerical simulation

Through numerical studies performed in a finite volume method (FVM) based fluid flow solver [12], the possibility of optimizing the separation process in the microdevices by Soret effect is analyzed [13]. To this purpose, the geometry proposed by other researchers is used [3], which separates the DMSO only by molecular diffusion. This device shown in Fig. 3 is composed mainly of a central cavity of constant rectangular section where the separation occurs by diffusion of

Table 1
Thermophysic and transport properties of sucrose–DMSO, glucose–DMSO and DMSO–PBS mixtures at an average temperature of 25 °C.

% Sucrose	Density (kg/m^3)	α (°C^{-1}) (10^{-4})	β (10^{-1})	η (kg/m s) (10^{-3})
5	1113.85	8.87	3.404	2.73
10	1132.89	8.57	3.41	4.05
15	1152.37	8.28	3.438	6.4
20	1172.38	8.03	3.449	10.95
25	1192.70	7.72	3.532	20.59
% Sucrose	Density (kg/m^3)	α (°C^{-1}) (10^{-4})	β (10^{-1})	η (kg/m s) (10^{-3})
5	1114.08	8.86	3.405	2.93
10	1133.12	8.56	3.402	4.06
15	1152.62	8.30	3.4	6.34
20	1172.36	8.01	3.399	10.55
25	1192.41	7.69	3.386	18.73
% PBS	Density (kg/m^3)	α (°C^{-1}) (10^{-4})	β (10^{-1})	η (kg/m s) (10^{-3})
10	1070.64	3.97	0.706	1.345

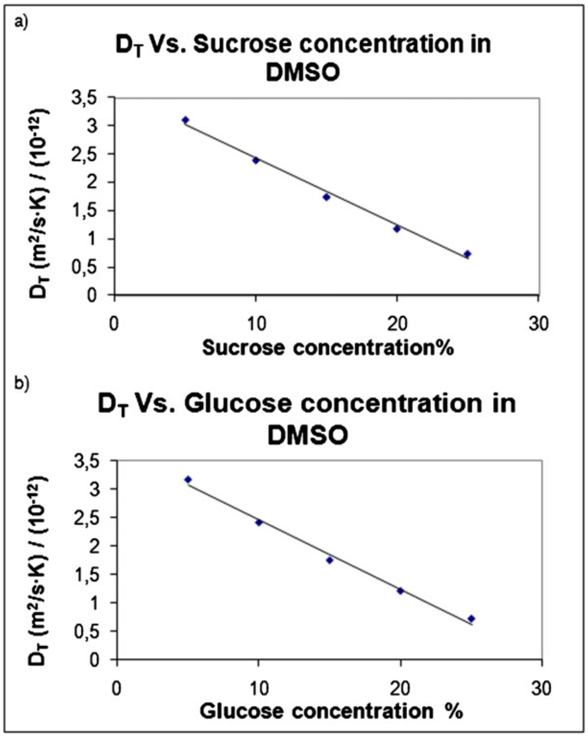

Fig. 2. Variation of the thermal diffusion coefficient in mixtures of a) sucrose–DMSO, b) glucose–DMSO versus the mass concentration and at a temperature of 25 °C.

DMSO. The flows are introduced through two opposing inlets. These two flows are separated by a splitter plate that redirects the flow and prevents the mixing between them, so that they flow in parallel to the central cavity. The flow extraction is performed by two outputs identical to the inlet design. From the top entry cleaning liquid is introduced, which in this case is PBS, while from the bottom entry a mixture of 10% DMSO in PBS is introduced.

The model used in the numerical simulation represents the main parts of the device, i.e. the central cavity and the transition to outlets. The central cavity consists of two flat plates that generate a constant rectangular cavity. The dimensions of it are exactly those used in [3], 25 mm wide, 500 μm high and 75 mm long. Downstream of this section, constant area geometry is used as transition to outlets. The overall length from the beginning of the central cavity to the outlets, is $L = 111$ mm. In Fig. 4a can be appreciated the two inputs coupled to the central cavity in order to achieve fully developed flow in the cavity. In Fig. 4b the whole geometry can be seen, where the transition from the central cavity to the outlets is shown.

A 3-D incompressible implicit numerical method is used. For higher accurate results double precision option is used and to avoid instabilities second order discretization for pressure, density, momentum, mass flux and energy is used too.

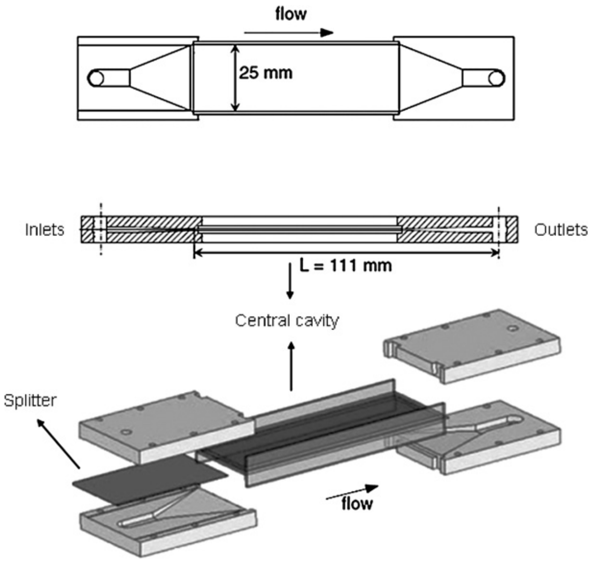

Fig. 3. Diagram of the experimental device used in [3].

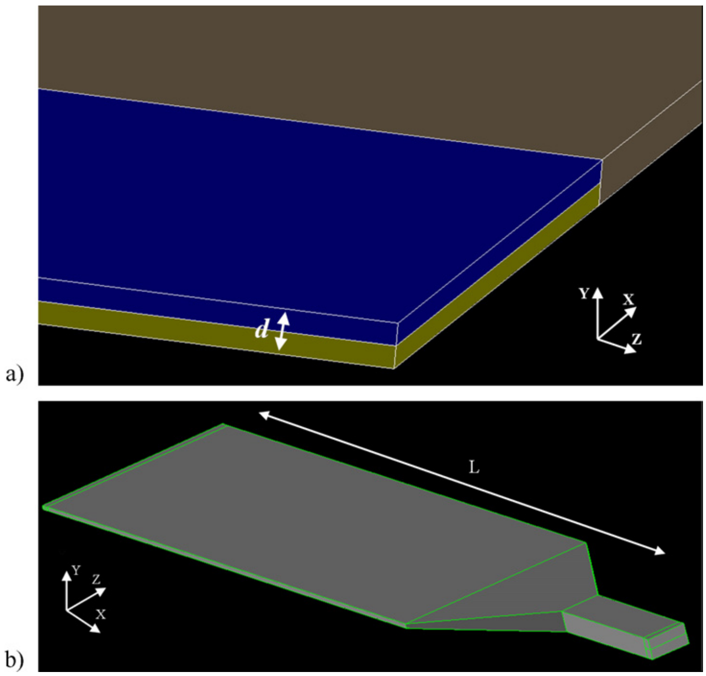

Fig. 4. Model used. a) Detail of the entrance area of the flow, b) general view of the device model.

A fourteen order of magnitude residual level drop is selected to convergence in this study to be sure that the system reaches the steady state. The final mesh configuration consists of 416 000 hexahedral cells.

4.1. Governing equations

The fully developed flow in a microchannel is governed by the Navier–Stokes equations (Eq. (2)) for the geometrical model of the channel depicted in Fig. 4:

$$\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2} = \frac{1}{\eta}\frac{\mathrm{d}p}{\mathrm{d}x}$$

Table 2
Comparison of the separation ratio with and without Soret effect for DMSO–PBS mixture with a mass fraction of 10% DMSO at $T = 25\,^{\circ}\mathrm{C}$.

f_q	q_t ($\mathrm{m^3/min}$) (10^{-8})	c_c/c_0 [3]	c_c/c_0 (Soret)	Improvement (%)
0.1	3.3	0.13	0.08	35.84
0.1	5.4	0.17	0.13	25.12
0.1	7.5	0.20	0.17	17.20
0.1	13.3	0.26	0.24	8.13
0.15	3.3	0.20	0.15	26.40
0.15	5.4	0.25	0.21	15.92
0.15	7.5	0.29	0.26	10.72
0.15	13.3	0.37	0.35	5.68
0.23	3.3	0.30	0.25	15.63
0.23	5.4	0.36	0.33	7.72
0.23	7.5	0.41	0.39	4.22
0.23	13.3	0.52	0.50	3.85
0.37	3.3	0.46	0.42	9.61
0.37	5.4	0.53	0.50	5.23
0.37	7.5	0.59	0.57	3.39
0.37	13.3	0.69	0.67	2.62

$$\begin{aligned}
&\frac{\partial^2 v}{\partial x^2}+\frac{\partial^2 v}{\partial y^2}+\frac{\partial^2 u}{\partial z^2}=\frac{1}{\eta}\frac{\mathrm{d}p}{\mathrm{d}y}\\
&\frac{\partial^2 \omega}{\partial x^2}+\frac{\partial^2 \omega}{\partial y^2}+\frac{\partial^2 \omega}{\partial z^2}=\frac{1}{\eta}\frac{\mathrm{d}p}{\mathrm{d}z}
\end{aligned}\tag{2}$$

where u, v and ω are the velocity components and p is the pressure. To study the molecular diffusion between streams "Species Transport" model is necessary. To know the contribution of the temperature gradient the "thermodiffusion" option is enabled too. Mass transport is formulated in Eq. (3) [14]:

$$\vec{J} = -\rho D\nabla c_0 - \rho D_T c_0(1-c_0)\nabla T \tag{3}$$

where D is the molecular diffusion coefficient and T is the temperature. For molecular diffusion, not having this property the value of order $\sim 10^{-9}\ \mathrm{m^2/s}$ used also in [3] has been chosen. To analyze the effect of thermodiffusion, the properties of the mixture determined experimentally are used. Jointly a temperature difference is imposed between the top and the bottom walls of the dispositive. As the DMSO is the heaviest component and the mixture of 10% of DMSO in PBS has a positive Soret effect, the bottom wall is heated and the top wall cooled. This will boost the DMSO to the washing stream (PBS) enhancing the separation. The chosen working temperature difference is 10 K.

As we analyze different density fluid streams and due to diffusion the density varies, the Boussinesq approximation (Eq. (4)) to account those changes in density is used:

$$\rho = \rho_0\big(1-\alpha(T-T_0)-\beta(c-c_0)\big) \tag{4}$$

where ρ_0 is the density for 10% of DMSO in PBS. User defined function (UDFs) are written in C++ programming language and are successfully incorporated into the present model to account for the changes in density.

4.2. Boundary conditions

No-slip boundary conditions are imposed at walls, which mean: $u = v = \omega = 0$. Outflow 0.5 outlet condition is applied at both outlets in order to have same volumetric flow rate conditions at the outlets.

4.3. Numerical results

Table 2 provides a comparison of results obtained in [3] and those obtained in this study using the Soret effect. Sixteen different cases were analyzed in total. At Table 2 the dimensionless variable dependent on the concentration of the bottom plate is represented c_c/c_0, where c_0 is the initial mass concentration of DMSO (10%) and c_c the mass concentration of DMSO in the output. In the same way it is represented a fraction of the inflows, defined in Eq. (5):

$$f_q = \frac{q_c}{q_t} \tag{5}$$

where q_c is the flow of the mixture DMSO–PBS and q_t the total input flow. The inlet flow of PBS is q_w and therefore $q_t = q_c + q_w$.

As can be seen, the results of Table 2 show a clear improvement in the separation process by the Soret effect, which can reach up to 35% for a total volumetric flow of $3{,}33 \times 10^{-8}\ \mathrm{m^3/s}$. In the same way the results are shown in a neutral diagram (Fig. 5) of the dimensionless variable dependent c_c/c_0 as a function of $(1/P_e) \times (L/d)$, where P_e is the Peclet number, and

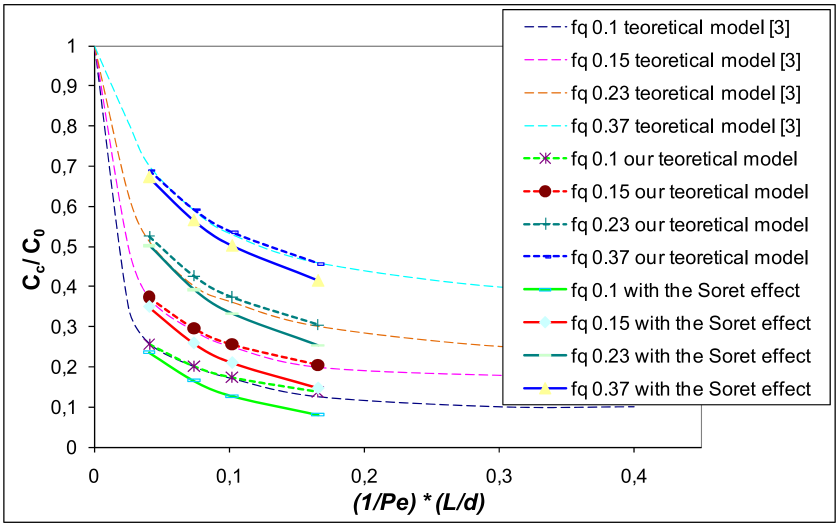

Fig. 5. DMSO extraction fraction c_c/c_0 as a function of $(1/P_e) \times (L/d)$.

L and d are the length and height of the diffusion zone, respectively. The Peclet number is represented as $P_e = U \cdot d/D$, where U is the characteristic velocity. These variables are parameterized by f_q, where the results of [3] are compared with this work diffusion and Soret effect model.

As shown in Fig. 5, the results obtained for the diffusion model of this work are in well agree with those of [3]. Even the amount of DMSO diffused into the cleaning flow (PBS) is higher due to the temperature gradient applied. As shown in Table 2, the lower the difference between inflows best results are obtained. In the same way, the lower the flow velocity best results are obtained. Thus, for all tested flows an improvement in separation by the Soret effect is achieved.

5. Conclusions

This work has highlighted the importance of the transport properties in microfluidics, as well as its applications in biotechnological mixtures. Similarly, it has reflected the importance of experimental data in the numerical study. In this case, we have explored the possibility of the removal of DMSO by molecular diffusion and proposed an improvement by implementing the Soret effect. The results showed an improvement in the process of extracting up to 35%. In this way we can reduce the final size of the device and the extraction time. Therefore, we propose a more efficient and lower cost microdevice due to the decrease in extraction channel length and extraction time.

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References

[1] J. Köhler, M.T. Henkel, Chip devices for miniaturized biotechnology, Appl. Microbiol. Biotechno. 69 (2005) 113–125.
[2] K.K. Fleming, E.K. Longmire, A. Hubel, Numerical characterization of diffusion-based extraction in cell-laden flow through a microfluidic channel, Journal of Biomechanical Engineering 129 (2007) 703–711.
[3] C. Mata, E.K. Longmire, D.H. McKenna, K.K. Glass, A. Hubel, Experimental study of diffusion-based extraction from a cell suspension, Microfluid Nanofluid 5 (2008) 529–540.
[4] K.K. Fleming, E.K. Longmire, A. Hubel, Optimization of a microfluidic device for diffusion-based extraction of DMSO from a cell suspension, International Journal of Heat and Mass Transfer 51 (2008) 5749–5757.
[5] J.K. Platten, M.M. Bou-Ali, P. Blanco, J.A. Madariaga, C.J. Santamaria, Phys. Chem. B 111 (2007) 11524–11530.
[6] A. Torreggiani, M. Di Foggia, I. Manco, S.A. Markarian, S. Bonora, Effect of sulfoxides on the thermal denaturation of hen lysozyme: A calorimetric and Raman study, Journal of Molecular Structure 891 (2008) 115–122.
[7] N.H. Chao, C.P. Chiang, H.W. Hsu, C.T. Tsai, T.T. Lin, Toxicity tolerance of oyster embryos to selected cryoprotectants, Aquat. Living Resour. 7 (1994) 99–104.
[8] V. Antonenas, K. Bradstock, P. Shaw, Effect of washing procedures on unrelated cord blood units for transplantation in children and adults, Cytotherapy 4 (2002) 16.
[9] J.K. Platten, M.M. Bou-Ali, P. Costeseque, J.K. Dutrieux, W. Köhler, C. Leppla, S. Wiegand, G. Wittko, Benchmark values for the Soret, thermal diffusion and diffusion coefficients of three binary organic liquid mixtures, Philosophical Magazine 83 (2003) 1965–1971.
[10] M.M. Bou-Ali, J.J. Valenciaga, J.A. Madariaga, C. Santamaría, O. Ecenarro, J.K. Dutrieux, Determination of the thermodiffusion coefficient in three binary organic liquid mixtures by the thermogravitational method, Philosophical Magazine 83 (2003) 2011–2015.

[11] M.M. Bou-Ali, O. Ecenarro, J.A. Madariaga, C.M. Santamaría, J.J. Valencia, Thermogravitational measurement of the Soret coefficient of liquid mixtures, Journal of Physics 10 (1998) 3321–3331.
[12] Fluent, Fluent Inc., Version 6.3.26, 2006.
[13] H. Barrutia, A. Martin, A. Zebib, M.M. Bou-Ali, Thermal diffusion effects in T-shaped micromixers, in: 1st European Conference on Microfluidics, Bologna, 2008.
[14] S.R. De Groot, P. Mazur, Non-Equilibrium Thermodynamics, North-Holland Pub. Co., Amsterdam, 1962.