NUMERICAL PROTOTYPING OF MICROFLUIDIC CHIPS FOR MULTIDIMENSIONAL ELECTROPHORETIC SEPARATIONS

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ABSTRACT
This work presents the numerical simulation of multidimensional electrophoretic separations in microfluidic devices. Calculations are performed by using the finite element method (FEM). A numerical prototype for free flow isoelectric focusing and capillary zone electrophoresis is studied. The separation of ten amphoteric species is successfully performed. It is shown that FEM with high performance parallel computing is a useful tool for the design and optimization of µTAS.

KEYWORDS: Electrophoresis, Numerical Prototyping, µTAS, FEM

INTRODUCTION
Multidimensional electrophoretic separations consist of two or more independent mechanisms that are employed sequentially, such as capillary zone electrophoresis (CZE), isoelectric focusing (IEF), isochromatography and free flow electrophoresis. These analytical techniques have been miniaturized in the last years and now represent one of the most important applications of the µTAS technology [1]. As µTAS are becoming increasingly complex, simulation tools are required to numerically prototype the devices [2]. In fact, computational simulations allow one to test successive prototypes, as well as to perform a series of pseudo-experimental runs, thus reducing costs and time in the path from concept to chip.

Numerical simulations of electrophoretic separations in microfluidic chips represent a challenging problem from the computational point of view [3]. Both the large difference among the relevant length scales involved and the multiphysics nature of the problem lead to numerical difficulties: multiple nonlinear problems (each field requires a nonlinear calculation), excessive number of degrees of freedom, and ill-conditioning global matrices due to the high aspect ratios. Therefore, the implementation of parallel computations and advanced preconditioning is crucial for the achievement of accurate numerical results and the diminution of calculation times. 3D simulations of electrophoretic processes employing parallel calculations were performed by Chau et al. [4] for FFE using finite difference method, and by Kler et al. [3,5] for different electrophoresis on chips using the finite element method (FEM).

In this paper we present the numerical prototyping of a two dimensional electrophoresis (2DE) that represents the state-of-the-art in electrophoretic chips. The mathematical model is based on the set of equations that governs electrical phenomena, fluid dynamics, mass transport and chemical reactions [5]. This model includes 3D domains, time-dependent reaction schemes, coupling between buffer composition and electroosmotic behavior, and full treatment of high conductivity gradients. All of these items are advantages in comparison to previous proposals [6].

SOFTWARE
All numerical simulations presented were performed with PETSc-FEM (Portable Extensible Toolkit for Scientific Computation – FEM), a parallel multiphysics code primarily targeted to 2D and 3D finite elements computations on general unstructured grids. PETSc-FEM provides a core library in charge of managing parallel data distribution and assembly of residual vectors and Jacobian matrices, as well as facilities for general tensor algebra computations at the level of problem-specific finite element routines. Additionally, PETSc-FEM provides a set of specialized application programs built on top of the core library and targeted to several engineering problems. Fluid flow computations presented in this article were carried out with the Navier—Stokes module, which provides the required capabilities for simulating mass transport (e.g. electrophoresis) and incompressible fluid flow through a monolithic SUPG/PSPG stabilized formulation for linear finite elements. Electric field calculations were carried out with the Charge Conservation module (see [3,5] for additional information).

NUMERICAL PROTOTYPING
The 2DE considered involves FFIEF (Free Flow IEF) and CZE, and is aimed to separate ten amphoteric analytes. The geometry of the fluid dynamic problem is presented in Fig. 1. FFIEF is carried out in the first section (10x3500x7000µm³), where the pH gradient is generated across the channel. This section is inspired on a FFIEF device recently published [7]. CZE is performed in the five channels (10x150x16000µm³) on the right (Fig. 1), which where designed in this work. The applied electric potentials (also shown Fig. 1) are fixed to provide the system with transversal electric field in the FFIEF section and, simultaneously, axial electric field in CZE channels.

The pH gradient for FFIEF is established by focusing twenty ampholytes (0.1 mM, 4.9 < pI < 8.03) between two sheath flows of anolyte and catolyte, at pH 4.8 and 8.2, respectively. A concentrated buffer (20 mM, pH 10) is continuously injected from the inlet at the right of the ECZ channels. When steady conditions are reached, a linear-like pH gradient is formed, as illustrated in Fig. 2.
The separation of a mixture of 10 amphoteric compounds (Table 1) was simulated. Analytes are injected on the left side of the FFIEF section. Concentration distributions at different times during the process are shown in Figs. 3a and 3b. When analytes reach the right side of the FFIEF channel they enter the CZE channels, where the second separation takes place, as shown in Figs. 3c and 3d. Finally a two-dimensional map of the separation is obtained (Fig. 4), which is the graphic format customarily used in experiments of two-dimensional electrophoresis [1] (further details on building this map from numerical data are given in ref. [5]). Complete separation is achieved after 120 s (real time). The computational time taken to complete the whole simulation is 60 hours.

Table 1. Physicochemical properties of analytes (pKa and pKb are acid and basic dissociation constants, respectively).

<table>
<thead>
<tr>
<th>Analytes</th>
<th>pKa</th>
<th>pKb</th>
<th>Mobility (x10^8 m²/Vs)</th>
<th>Diffusivity (x10^-10 m²/s)</th>
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<tr>
<td>1</td>
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<td>6.92</td>
<td>2.24</td>
<td>5.79</td>
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<td>2</td>
<td>2.27</td>
<td>7.37</td>
<td>3.84</td>
<td>9.92</td>
</tr>
<tr>
<td>3</td>
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<td>7.70</td>
<td>2.17</td>
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<tr>
<td>4</td>
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<td>8.05</td>
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<td>10.01</td>
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</table>

CONCLUSION
Numerical prototyping of complex 2DE on chips is successfully accomplished by a computational model previously reported. One may conclude that the use of PETSc-FEM with high performance parallel computing is a useful tool for future developments of µTAS.

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Figure 3: Total sample distribution for a) 20, b) 35, c) 50 and d) 65 seconds after the injection.

Figure 4: Two dimensional map for the separation of analytes (numbers refer to Table 1).

REFERENCES

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