

Computational exploration of thermal field-flow fractionation as a technique for separating polymers and large biological molecules

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Abstract

Achieving the separation and purification of large or delicate molecules, such as polymers or DNA, can be difficult using conventional techniques, which may require introducing such compounds to extreme temperatures or pressures. Ergo, developing techniques to achieve high purity final products under mild conditions has obvious practical purposes. Micro thermal field-flow fractionation (TFFF) is a technique utilizing the interactive effects of temperature and concentration gradients on molecular diffusion, whereby large molecules can be separated with high purity by applying a very small temperature gradient (on a range of the order of 1 to 10 K cm⁻¹) to a fluid flowing through a very thin channel. These types of phenomena are extremely difficult to predict analytically – as such, in this paper we present an investigation into the potential use of computational techniques to model TFFF devices.

Objectives

The main objective of this project was to conduct an investigation into the ability of computational methods to model TFFF. As an extension of this goal, we intended to develop an application of TFFF by simulating actual separation models using experimentally derived values for the parameters defining how certain chemicals diffuse under thermal and concentration gradients. As a reach goal, we wanted to determine a way to estimate the Soret number (the ratio of the thermal and mass diffusivity

coefficients), since we need to know how each molecule will behave in a temperature and concentration gradient, and a method for estimating this number is not readily obvious.

Theory

Micro TFFF is a process whereby a thermal field or gradient is used to create differential flow displacement of large molecules in a stream of liquid flowing through a thin channel (see Fig. 1).

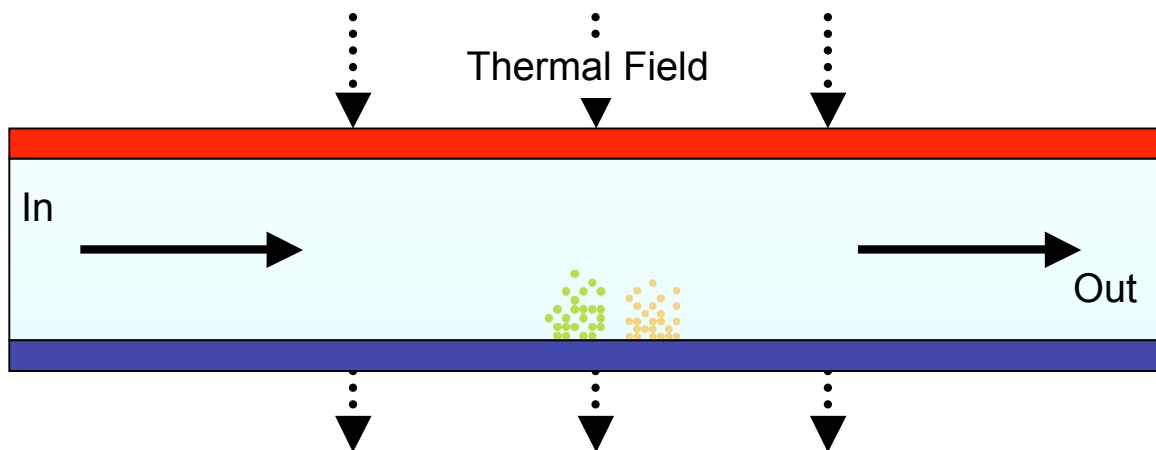


Figure 1: a cross sectional diagram of a typical thermal field-flow fractionation device. Two chemical species (one orange and one green) are injected at the inlet. The thermal field drives both species to the bottom plate but at different rates, resulting in different elution times for both species.

Consider a case where the top of the channel is kept at a constant high temperature, and the bottom of the channel is kept at a constant low temperature. Next, consider a solution composed of two different compounds (both compounds are made of large molecules, such as polymers), which is injected in a small pulse at the inlet of the TFFF channel. The thermal gradient of the channel drives the molecules of both compounds to the accumulation plate, but at different rates due to the different thermal diffusivity

properties of both compounds. The two compounds then travel through the channel at different rates, allowing for their separation. In this fashion, TFFF functions much in the same way as chromatography.

Methods

We used three equation systems to model this process. The first governed the fluid dynamics of the model, and was represented by the incompressible Navier-Stokes equation, shown in Eq. 1.

$$\rho \frac{\partial u}{\partial t} + \rho u \cdot \nabla u = \mu \nabla^2 \cdot u - \nabla p + \rho g \quad (1)$$

The second equation we used governed thermal convection and conduction, and is shown in Eq. 2

$$\rho C_p \frac{\partial T}{\partial t} + \nabla \cdot (-\kappa \nabla T) = Q - \rho C_p u \cdot \nabla T \quad (2)$$

The third and final equation shown in Eq. 3 was given by deGroot and Mazur, and governs the convection and diffusion of the large molecules in question as a result of the fluid flow, thermal gradient, and concentration gradient.

$$\nabla \cdot [cD_T \nabla T + D \nabla c - uc] = 0 \quad (3)$$

These three equations were solved simultaneously using Comsol Multiphysics ©. The geometry of the channel was based on dimensions found in literature for actual TFFF devices. This geometry is shown in Fig. 2.

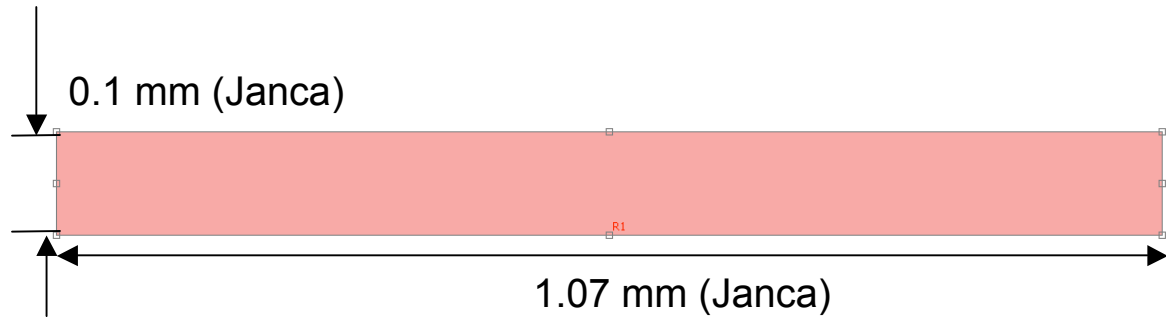


Figure 2: geometry of the TFFF device modeled; dimensions are based on those reported in literature (Janca)

For each solution, all three equations were evaluated for 4,736 finite mesh elements, resulting in 41,557 degrees of freedom. The mesh and boundary labels are depicted in Fig. 3.

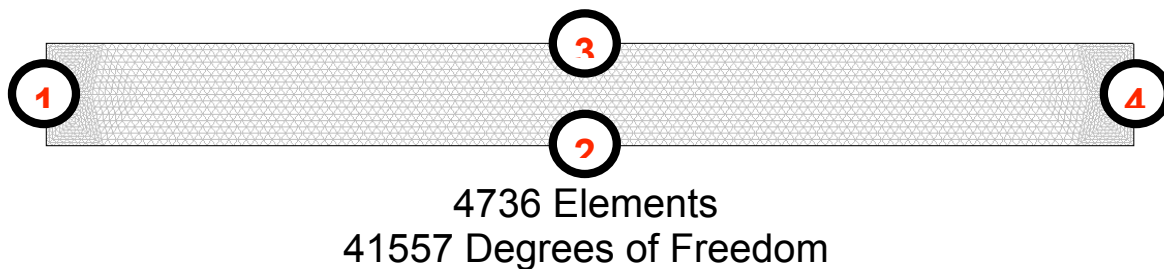


Figure 3: mesh and boundary condition labels for the TFFF model.

We then defined the boundary conditions for all three equations. In the list below, we report the values for each boundary condition for the fluid dynamics (FD) model, the thermal convection and conduction model (TCC) and the deGroot and Mazur model (DGM):

- BC 1 (inlet)
 - FD: inlet velocity of 0.13 m/s (value taken from literature).

- TCC: $10,000y + 298$ K. Here, where y is the dimension representing the height of the channel, we assume that the inlet temperature gradient is fully developed. Hence, this linear gradient is used, where the slope is based on the temperature of the top and bottom plates.
- DGM: $c = 1$ unit of concentration.
- BC 2 (bottom plate)
 - FD: no slip.
 - TCC: 298 K (this was chosen because ambient temperature is a reasonable assumption).
 - DGM: no mass flux.
- BC 3 (top plate)
 - FD: no slip.
 - TCC: 299 K. Based on information reported in existing literature, many TFFF devices used for this purpose have a temperature gradient of approximately 10^2 K per cm of height. Based on the height of the channel, this corresponds to 1 K difference between the top and bottom plates. For subsequent experimental runs, this value was varied to observe the effects of temperature gradient.
 - DGM: no mass flux.
- BC 4 (channel exit)
 - FD: outlet pressure of 101.3 kPa.
 - TCC: convective flux.
 - DGM: convective flux.

Results and Discussion

Here we show the results for a steady-state solution where only one compound is added to the TFFF device. While the following solutions do not simulate a separation process, they do demonstrate the effects of the thermal and concentration gradients on the molecules that pass through the channel. All experimental values for the diffusivity coefficients for each type of compound were taken from existing literature.

We first present a simulation of Polystyrene in a solvent stream of Tetrahydrofuran (Fig. 4).

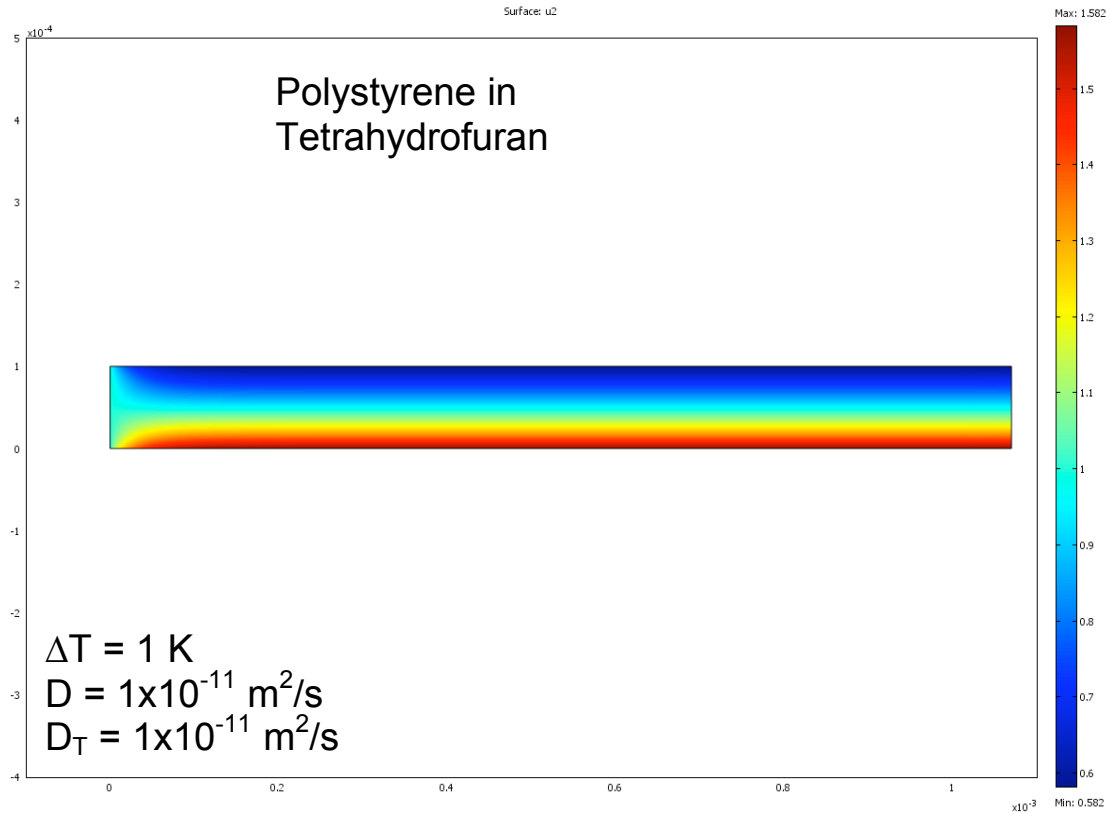


Figure 4: steady state solution for Polystyrene in Tetrahydrofuran

Note that in Fig. 4, the Polystyrene has collected on the bottom plate, such that the concentration at the top of the channel is ~ 0.6 while the concentration at the bottom is ~ 1.5 . To emphasize the effect of the temperature gradient, we present Fig. 5, where our solution is identical to that shown in Fig. 4, except that the temperature gradient has been increased from 1 K to 10 K.

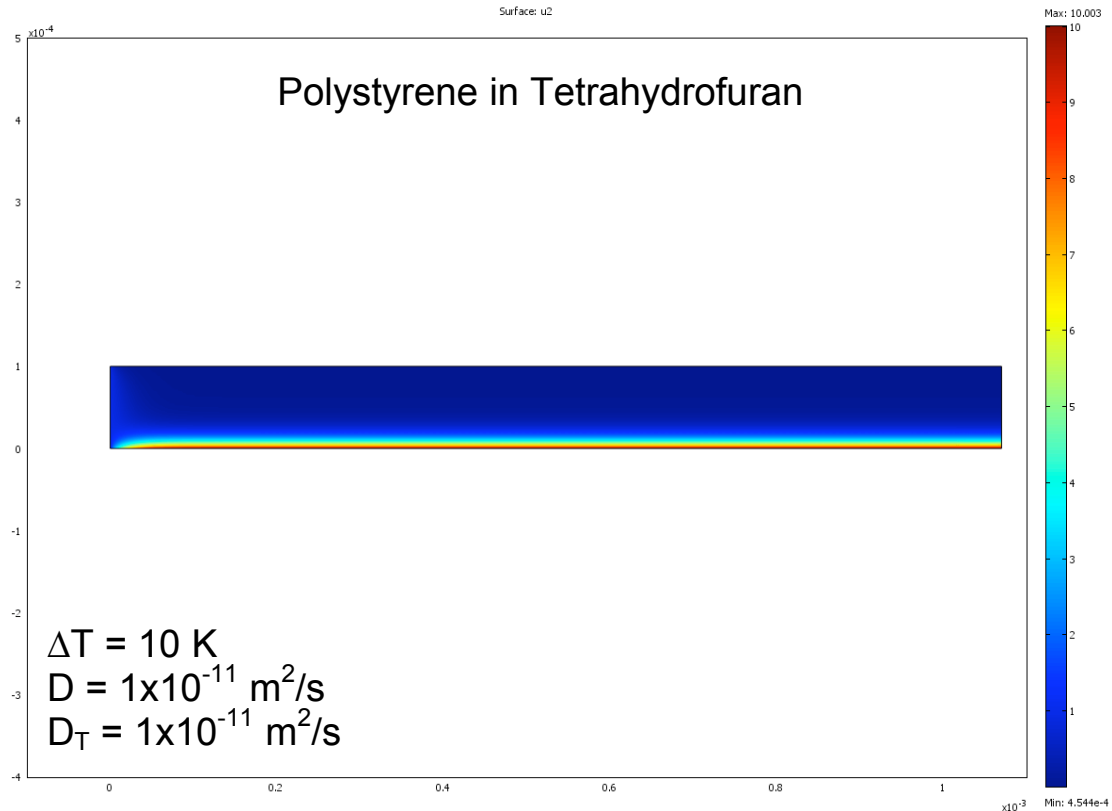


Figure 5: steady state solution for Polystyrene in Tetrahydrofuran for a temperature difference of 10K.

Note that the Polystyrene has a much higher concentration on the bottom of the channel, and that the concentration at the top of the channel is significantly lower. We can conclude, then, that for this specific scenario, the temperature gradient has a dramatic effect on the degree of accumulation on the bottom of the channel.

Next we present Fig. 6, corresponding to DNA in Water with a temperature gradient of 1 K. We observe that, compared to the case presented in Fig. 4, we predict a much smaller degree of accumulation. This is due to the smaller value of the thermal diffusivity coefficient.

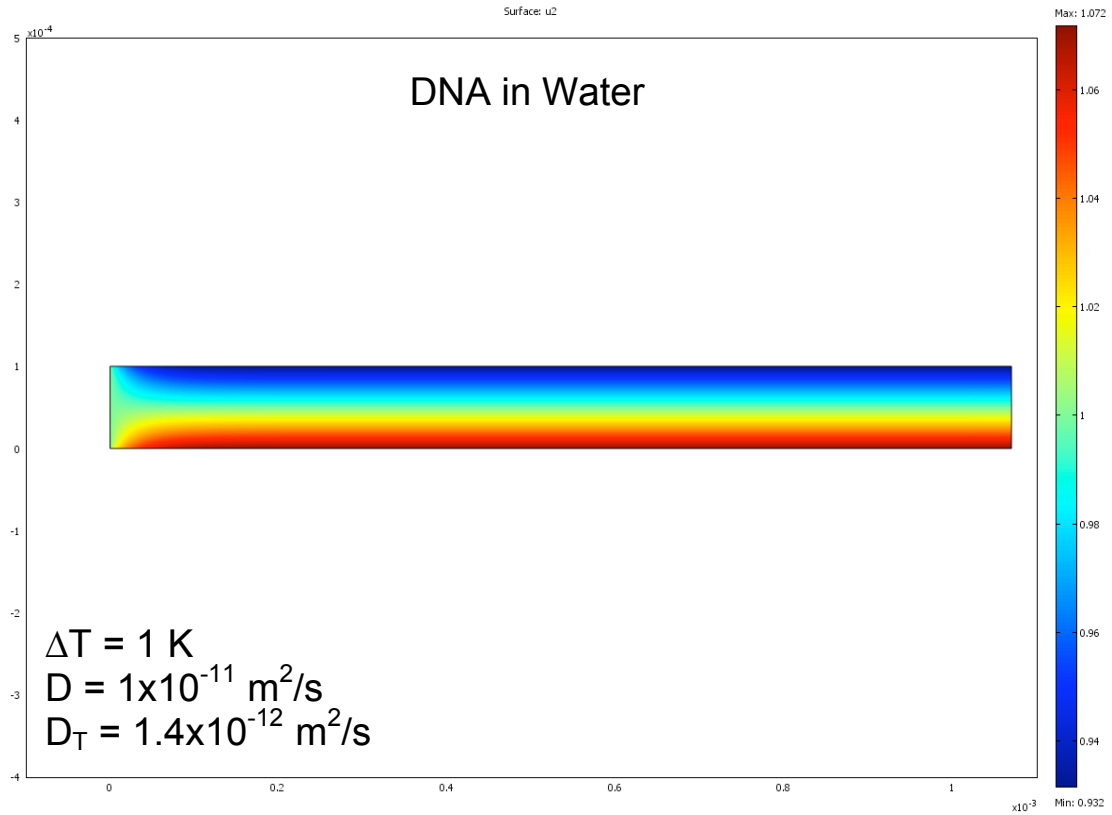


Figure 6: steady state solution for DNA in water.

Finally, we present a case for DNA in Water with a temperature gradient of 10 K. We note that in Fig. 7, we again see an increased degree of accumulation on the bottom plate due to the higher temperature gradient.

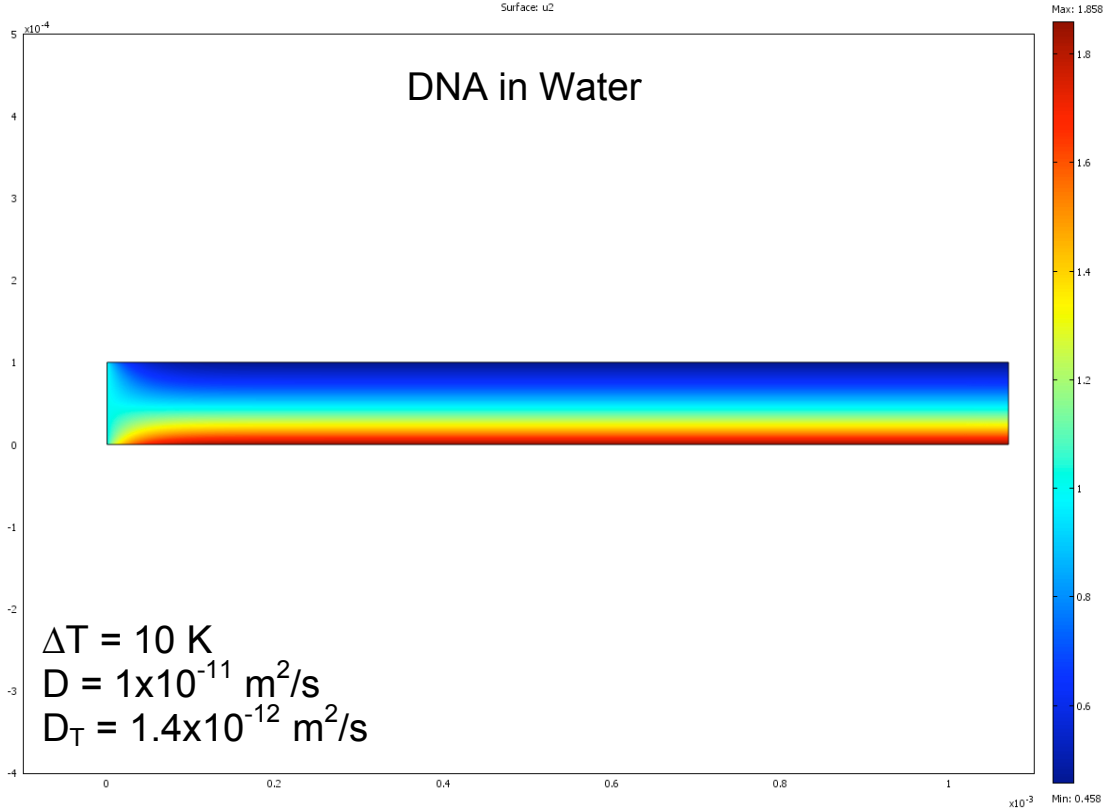


Figure 7: steady state solution for DNA in water with a temperature difference of 10K.

We were unable to determine a method which could be used to estimate the Soret number based on the computational analysis performed in this study. We did, however, find methods in existing literature which employ regression techniques in order to estimate the thermal diffusivity coefficient based on the conductivity, density, and activation energy of the particular solute in question. These are shown in Eq. 4 and 5 below.

$$D_T = 3.69 \times 10^{-2} \frac{(\kappa_p - \kappa_s)^{3.74}}{U_s^{0.623}} \quad (4)$$

$$D_T = 8.17 \times 10^6 \frac{\rho_p^{3.41}}{U_s^{1.28}} \quad (5)$$

While these equations may only provide reasonable estimations of the thermal diffusivity coefficient for a small sub-set of molecules (the reference in question dealt with polystyrene and compounds of similar size and chemical structure), if one knew the mass diffusion coefficient, one could use these equations to approximate the Soret Number.

While these results demonstrate clearly the effects of applying a temperature gradient to a liquid flowing through a small geometry, they can not demonstrate the separating abilities of TFFF. In order to clearly demonstrate these effects, one would have to construct a transient model and solve an additional equation system to handle the mass convection and diffusion of the second solute. While this was attempted, we have been unable to produce a convergent solution at this time. Often modeling transient processes is much more complicated. This is compounded by the fact that in a separation process, as opposed to having a constant non-zero concentration of both solutes at the channel inlet, we instead want to inject a pulse of the mixture. This means that in a transient model, the inlet boundary condition must change rather abruptly over time; often Comsol has difficulty in finding a convergent solution for these sorts of discontinuous boundary conditions.

Conclusions and Recommendations

We can conclude that computational methods can approximate the expected behavior of TFFF phenomena, at least in a qualitative sense. What remains is to demonstrate the ability for our computational models to predict the degree of separation of a particular

mixture of large molecules with accuracy and precision. This would require us to either find existing experimental data for a TFFF separation of two or more compounds, model the dimensions of the channel used in the experiment as well as the constants for the chemical species in question, and then to assess how close the experimental results compare with our predictions.

Literature Cited

Giddings, J. Calvin. "Science." Field-Flow Fractionation: Analysis of Macromolecular, Colloidal, and Particulate Materials 260(1993): 1456-1465.

Janca, Josef. "Micro-Thermal Field-Flow Fractionation in the Analysis of Polymers and Particles: A Review." International Journal of Polymer Anal. Charact. 11(2006): 57-70.

Schimpf, Martin E., J. Calvin Giddings. "Characterization of Thermal Diffusion in Polymer Solutions by Thermal Field-flow Fractionation: Dependence on Polymer and Solvent Parameters." Journal of Polymer Science: Part B: Polymer Physics 27(1989): 1317-1332.