

# Concentrating on LOC

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Lab-on-a-chip (LOC) technologies combine a sequence of chemical and/or biological analyses on a miniaturized platform (a "chip") to perform a task or series of tasks. LOC applications include chemical/biological agent detection, drug discovery, and point-of-care testing, to name only a few. The various analytical tasks are performed in a network of micro-channels etched into a glass or plastic plate. The characteristic length-scale of the channels is between 10  $\mu\text{m}$  and 1 mm; and the chip itself typically has a footprint of a few square centimeters.

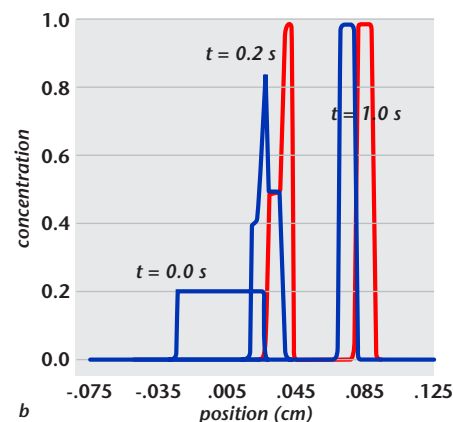
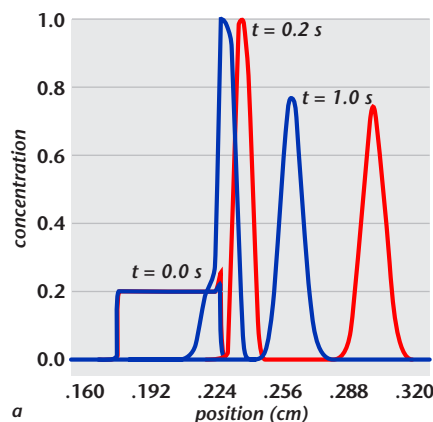
Two critical issues in an LOC analysis are separation and detection of a target species. Mobility-based separations take advantage of differences in the migration speed of charged molecules (ions) to separate and even pre-concentrate sample species. The latter is especially critical when working with small sample volumes. The speed of an ion in an electric field is  $v = bE$ , where  $E$  is the electric field and  $b$  is the electrophoretic mobility (migration speed per unit electric field). FIDAP's electrohydrodynamic modeling capability was used to model two common mobility-based separations: sample stacking and isotachopheresis (ITP).

In sample stacking, sample species are suspended in a low conductivity buffer ( $k_{\text{low}}$ ), which is sandwiched between zones of high conductivity ( $k_{\text{high}}$ ). The low conductivity buffer has a higher resistance to passing the electric field, so there is a steeper voltage gradient across it, relative to the high conductivity zone. Thus, the sample species rapidly "stack" at the interface between the low and high conductivity zones. The concentrated bands then migrate electrophoretically in the high conductivity zone. Sample stacking produces relative increases in concentration that correspond to the ratio of the conductivity of each zone ( $= k_{\text{high}}/k_{\text{low}}$ ). The drawback of this technique is that the subsequent electrophoretic migration is subject to diffusive dispersion.

ITP also uses a discontinuous buffer system. In this case, the species concentrations are high enough that the conductivity of each zone is proportional to the local species concentration. At steady-state, the ITP results in a series of constant mobility bands that migrate at the same speed. The electric field is constant within each



The micro-channel is initially divided into three regions: a leading, sample, and trailing zone. In sample stacking, a high conductivity buffer solution is present in the leading and trailing zones, and a low conductivity buffer is present in the sample zone. In ITP, a high mobility buffer is in the leading zone and a low mobility buffer is in the trailing zone. The two species in the sample are of intermediate mobility, i.e.  $\mu_T < \mu_2 < \mu_1 < \mu_L$



Distribution of the two sample species with time in (a) sample stacking and (b) ITP. The degree of concentration is 5x for each example. Diffusive spreading decreases the maximum concentration in (a) even after 1 s, while the self-correction mechanism in ITP (b) maintains a narrow sample band for the same separation time

sample zone, resulting in a self-correction mechanism that maintains the separation of solutes into individual bands in spite of diffusive spreading [1]. This makes ITP a very powerful preconcentration technique. The FIDAP results for this type of separation show that the bands maintain a very narrow distribution, even at a time when the sample stacking method exhibits signs of diffusive spreading. In ITP, the increase in sample concentration is proportional to  $\mu_L/\mu_p$ , where  $\mu_L$  is the mobility of the leading electrolyte and  $\mu_p$  is the mobility of the species of interest.

The modeling provided an analysis of these separations without ever manufacturing a proto-

type chip. Other factors such as channel filling, electro-osmosis, and Joule heating could also be evaluated numerically before ordering a single chip, drastically reducing development costs and time to market. ■

## reference:

- 1 F. M. Everaerts, J. L. Beckers, and T. P. E. M. Verheggen, *Isotachopheresis, Theory, Instrumentation and Applications*, New York, Elsevier Scientific Publishing Company, 1976.