Dried Reagent Resuspension for Point of Care Testing (Analysis at the Patient Bedside)

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Abstract

A microfluidic component was designed to collect blood from a finger prick and perform biological analysis [Ref 1,2]. To run a test, a reagent should be mixed with the collected blood. The reagent could be added prior to deposit of the blood in the component for convenient research procedure. However point of care philosophy fits better with embedded reagent [Ref 3], either lyophilized or dried, resulting in simpler use of the product, but it is more challenging to achieve, requiring the right formulation and process.

Valuable information can be obtained from simulating the kinetics of biological processes at the basis of an analysis, for example enzymatic reaction [Ref 4] or aggregation. In the case of dried reagent, the common hypothesis of a uniform concentration of chemical species at any time is easily questionable. This issue is addressed by creating a model, supported by experimental results, of the resuspension of the reagent. This model consists in the first step to the simulation of the whole biological analysis in the microfluidic component. The experimental work consists in the resuspension, in human blood plasma, of dried reagent containing fluorescein for monitoring.

The component is a 2D rectangle representing the 150µm thick portion of the microfluidic channel (xy plane in Figure 1) with the same dimension. The physics used is transport of diluted species applied to the fluorescein with a measured diffusion coefficient of 3x10^-9 m²/s. Initial condition is 0 mol/m^3 everywhere. A "no flow" condition was applied at top and right borders. Dried reagent is located at left and bottom borders (Figure 2). Its solvation is modeled by a flow expressed as N/τ e^((-t)/τ) with N the quantity of fluorescein in the deposited solution that was dried. Temporal solver is run from t=0s to t=120s, the typical duration of a biological analysis performed in this microfluidic component before blood starts to dry.

The experimental results are obtained by filming the resuspension with a RGB camera and by taking the green channel, minus the blue channel, and enhancing the contrast by a linear operation on the histogram. Figure 3 and 4 are respectively the experimental and the simulation results for t=100s. The diffusion speed is similar in experiment and simulation. However getting a similar look for simulation and experiment required an adjustment: figure 4 is log of the fluorescein concentration with a manual color scale. It is justified by the fact that the gray level in experiment is not a linear function of the concentration either.

The simulation reproduced the behavior of experimental dried fluorescein in a reagent resuspension. The concentration field of biological molecule involved in the analysis can be deduced from that of the fluorescein by changing the diffusion coefficient. This work is part of a broader simulation project that will involve simulation of biological processes in analysis, like enzymatic reactions [Ref 4] or even antigen/antibody coupling for immunological tests.

Reference

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P. Pouteau, et. al. , Dispositif de prélèvement d'un échantillon de liquide par capillarite et procédé d'analyse associé. WO2014135652 A1 (2014).

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J. Berthier, et. al. , Determination of the bi-substrate kinetic coefficients for the β-D-glucose-NAD-GDH enzymatic reaction. Proceedings of the 2015 NSTI-Nanotech Conference, June 14-18, 2015, Washington DC, USA.

Figures used in the abstract

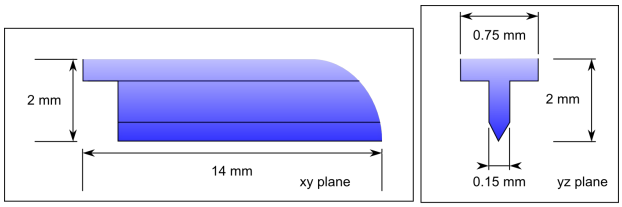

Figure 1: Geometry of the microchannel

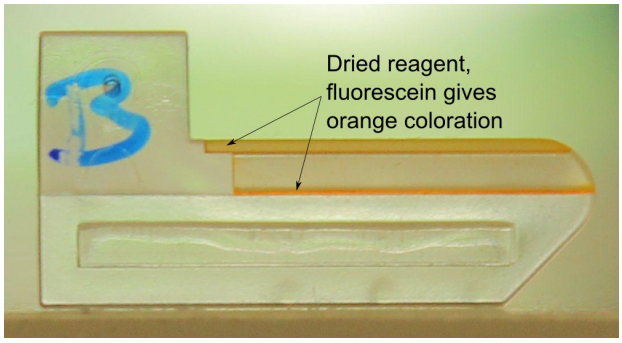

Figure 2: Photo of the microfluidic component with dried reagent

Figure 3: Experimental results at t = 100s

Figure 4: COMSOL results concentration at t = 100s