Chemical Gradients, Carryover And Mixing In Fluidic Diagnostic Systems

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Abstract

Recent events underscore the importance of rapid diagnostic tests for detecting viruses such as the SARS-CoV-2 coronavirus or for screening cancer biomarkers. Many fluidic-based diagnostics applications require careful control of chemical and biological species concentrations. In this talk, we discuss three such examples: chemical concentration gradients in microchannels, chemical carryover in microchannels, and mixing in a microwell.

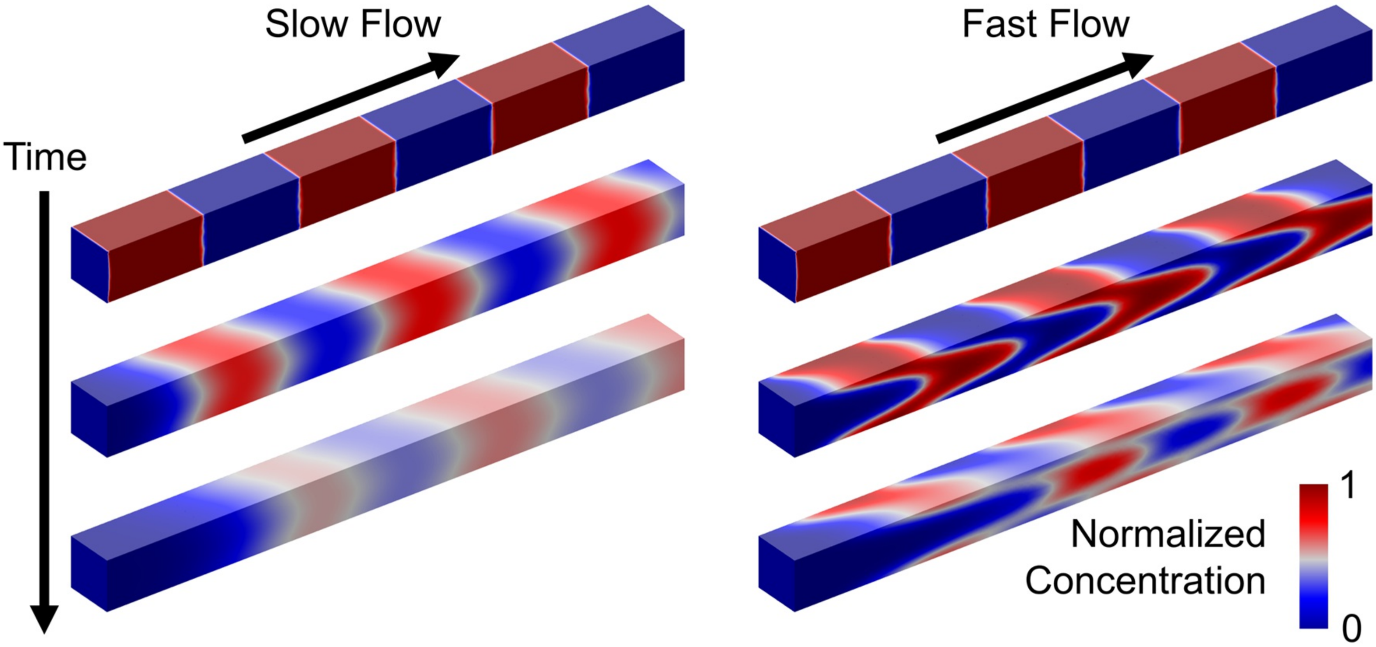
Many diagnostic systems involve flowing successive segments of different reagent solutions through a channel, resulting in reagent dispersion and concentration gradients between solution segments (Figure 1). Dispersion and gradient growth increase with the Peclet number, defined as (channel height) × (avg. flow speed) / (molecular diffusivity). In this example, COMSOL's Laminar Flow and Dilute Species Transport interfaces are used to tune operating parameters (e.g. flow rate) to control gradient growth.

Removing reagents or sample from a previous processing step via a wash cycle is another challenge in diagnostic assays. In straight channels, reagent removal improves by increasing wash buffer volume and flow time (Figure 2). In corners, recirculation zones develop and increase in size as the flow rate and Reynolds number increase (Figure 3). COMSOL's Laminar Flow and Dilute Species Transport interfaces are used to understand and optimize the wash strategy based on channel geometry and tradeoffs between operating time and wash buffer volume. In Figure 3, the same wash buffer volume flows through each channel. Flow field streamlines are shown as white lines to visualize the recirculation.

Mixing reagent solutions is a common step in diagnostic systems. One such example involves mixing two solutions in a microwell by repeatedly dispensing and withdrawing solution from a pipette (Figure 4). This is an advection-diffusion problem involving a moving air/liquid interface and chemical gradients. COMSOL's Two-Phase Flow and Dilute Species Transport interfaces are used to model the mixing process and assess the effects of flow rate and cycled volume. Figure 4 shows the flow field and concentration profile at different times as solution is dispensed and withdrawn according to the schedule shown in the lower right plot.

COMSOL Multiphysics® is a powerful tool to help understand, control, and optimize processes in fluidic diagnostics systems. We can use simulations to quickly test and optimize device geometries, parameters, and operation protocols before prototyping, thereby reducing costs and saving time.

Figures used in the abstract



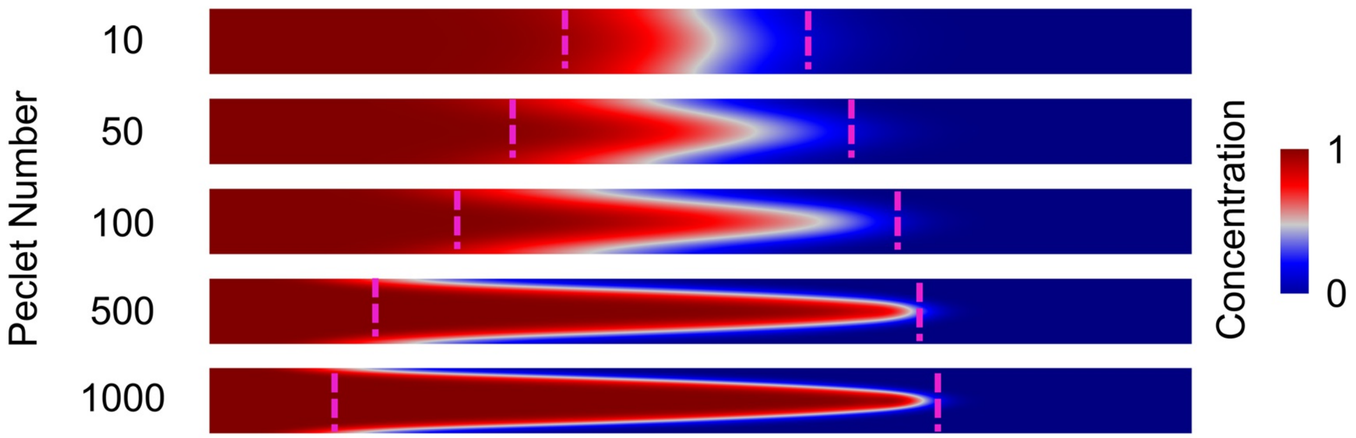


Figure 1 : Figure 1: Gradient growth in a microchannel at different Peclet numbers

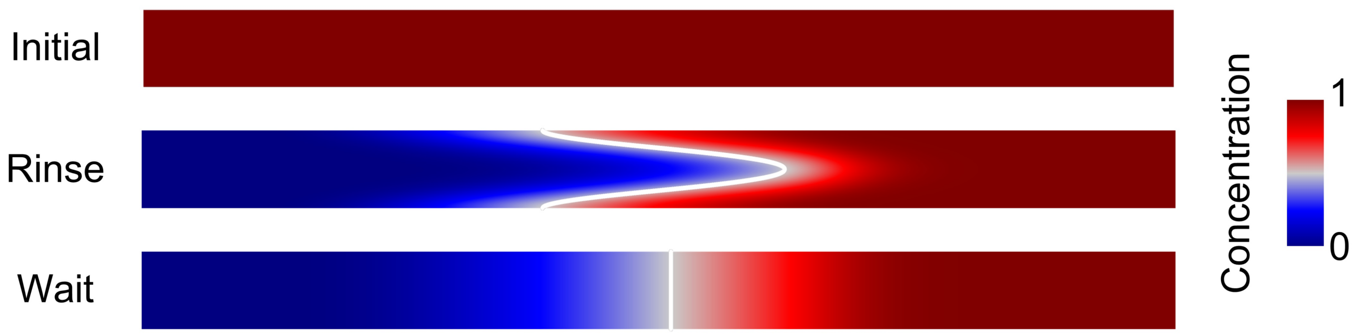


Figure 2 : Figure 2: A straight microchannel initially filled with a reagent solution (red) is washed with buffer (blue)

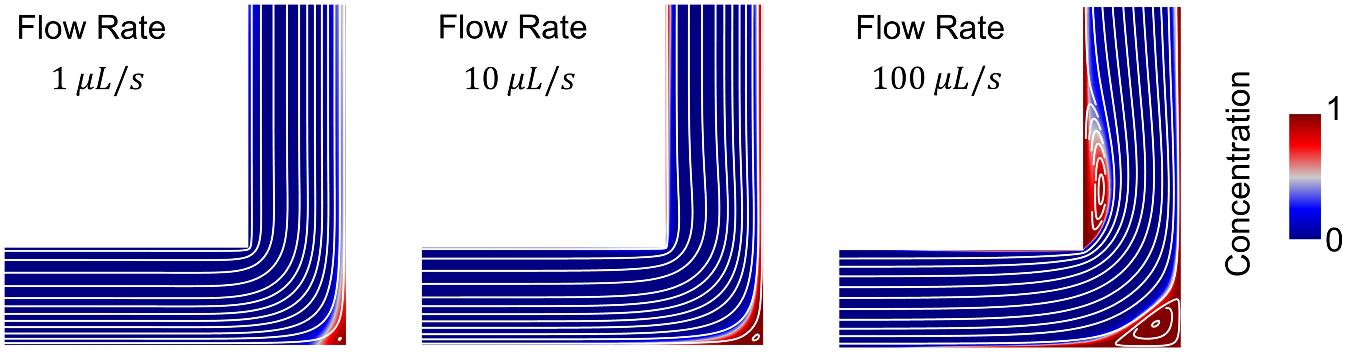


Figure 3 : Figure 3: A corner in a channel initially filled with a reagent solution (red) is washed with buffer (blue)

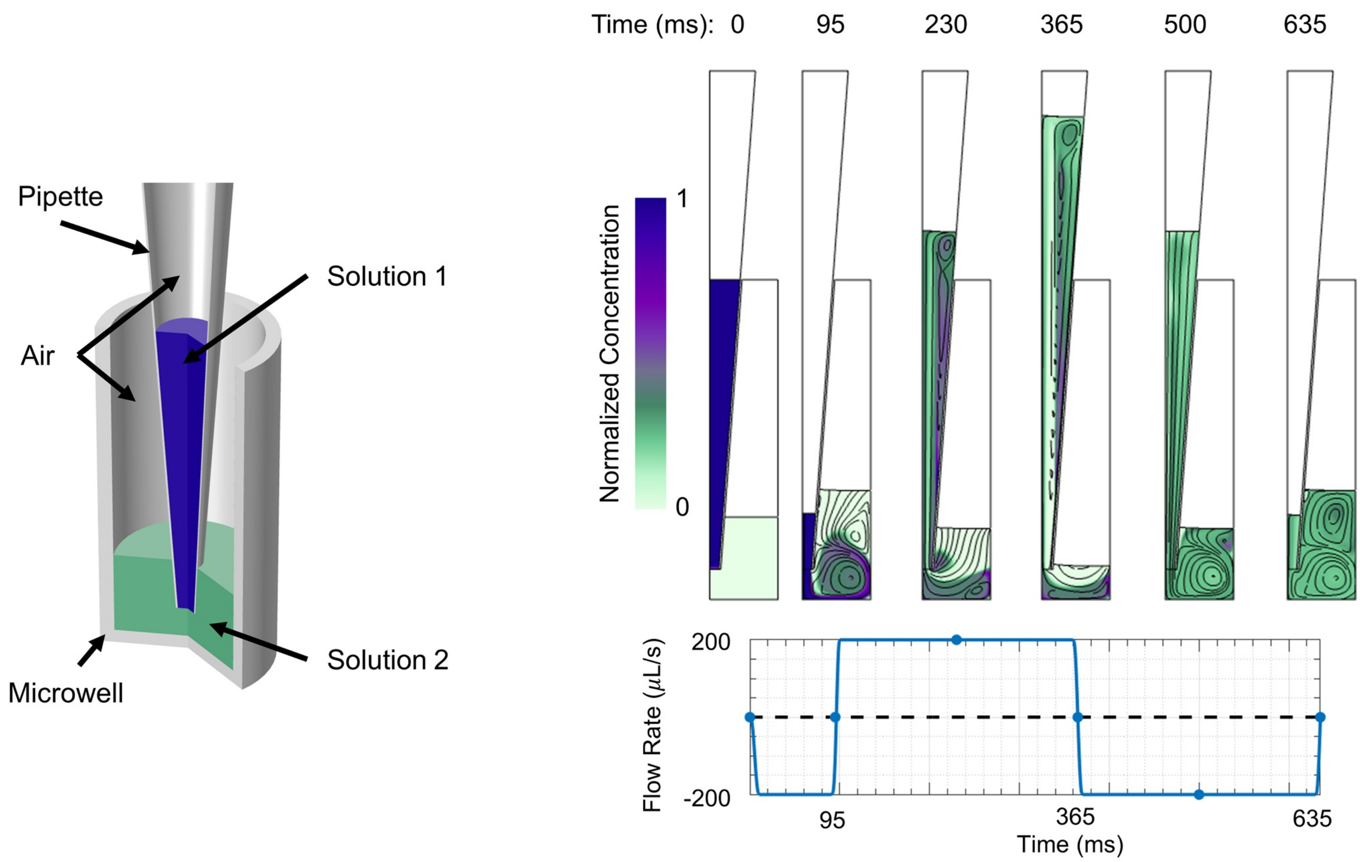


Figure 4 : Figure 4: Two solutions are mixed in a microwell by dispensing and withdrawing solution from a pipette