Thermal-Optical Modeling of a Signal Enhancement Approach for Paper-Based Diagnostics

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Abstract

INTRODUCTION:
Point of care diagnostics aimed at low-resource settings need to be relatively simple, robust and low-cost. The most commonly-used diagnostic platform in these settings is the lateral flow assay (LFA). LFAs are paper-based immunoassays designed to perform on-strip binding with analytes in patient samples in order to generate a visual signal if disease-specific antigen is present. These tests are easy to administer, low-cost, require only small volumes of patient sample for operation, and can generate a visual result in less than 30 minutes. While LFAs have proven highly effective for Plasmodium falciparum case management, their relatively high limit of detection makes them unable to diagnose asymptomatic carriers [1]. Mechanistically, this means that while there are signal particles at the LFA test line, there are not enough of them to generate a signal visible to the human eye. To get around this limitation, a variety of LFA reader technologies have been developed to identify the presence of signal particles at the LFA test line at concentrations below the visual threshold of the human eye. One technology in particular exploits the optical absorption properties of LFA signal particles composed of colloidal gold by illuminating the particles at the test line with laser light emitted at the particles' plasmonic resonance frequency [2]. This approach has the potential to generate a signal distinguishable from the background signal when the concentration of colloidal gold particles at the LFA test line is significantly lower than the visual threshold concentration. In this presentation, we describe efforts to characterize the performance limitations and opportunities of this method using a model system that couples the output from optical Monte Carlo (OMC) simulations to a COMSOL Multiphysics® software finite element model for simulating the absorptive heating effects of the colloidal gold nanoparticles on an LFA strip during laser illumination.

USE OF COMSOL MULTIPHYSICS:
The transfer of optical energy to thermal energy within the LFA is a complex process due to the absorptive properties of the gold signal particles and the multilayered nature of LFA's, where each layer has unique optical absorption and scattering characteristics. A desire to understand the limits of performance of the laser illumination approach amongst this complexity motivated the creation of a first-principles computational model that couples and simulates optical and thermal phenomena. The model simulates light propagation and absorption within the LFA materials using an established Monte Carlo approach, and heat transfer due to optical absorption and thermal/convective transport using COMSOL Multiphysics (see Figure 3). The resulting model enables the efficient exploration of important questions about the performance capabilities of the

laser illumination approach, and enables the exploration of 'what if' scenarios that would otherwise take significant time to explore at the bench top.

RESULTS:
Model validation was performed, and the results are presented in Figure 1. Signal contrast results from OMC-FEM model with various material and geometry modifications to LFA are shown in Figure 2.

CONCLUSION:
- The model validation exercise demonstrated a high level of fit between OMC-FEM model and physical systems.
- Preliminary results from the validated model system provided guidance on the potential gains in signal over background for the laser illumination method for various LFA material and geometry parameters.

Reference

[1] "Malaria rapid diagnostic test performance: results of WHO product testing of malaria RDTs: round 5 (2013)," WHO, Geneva, 2014.

[2] Z. Qin, W. C. Chan, D. R. Boulware, T. Akkin, E. K. Butler and J. C. Bischof, "Significantly improved analytical sensitivity of lateral flow immunoassays by using thermal contrast," Angewandte Chemie, vol. 18, pp. 4434-4437, 2012.

Figures used in the abstract

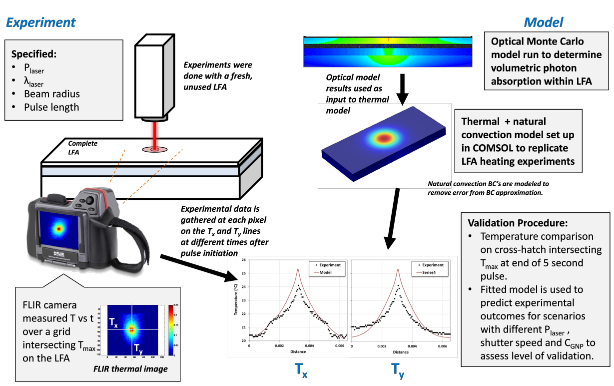

Figure 1: A schematic depicting the validation process for the laser illumination model.

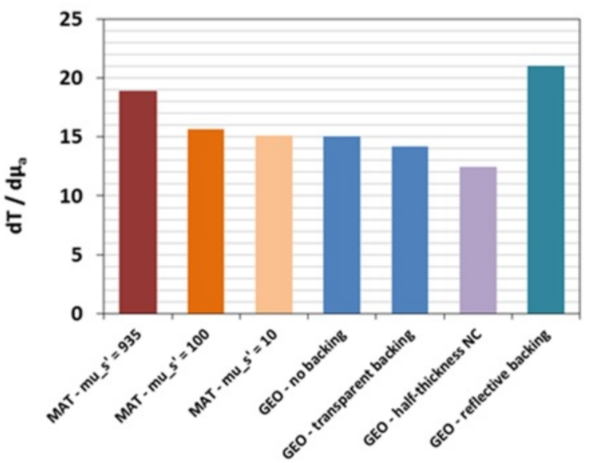

Figure 2: Results from steady-state simulations demonstrating the improvement in signal over background for different LFA material properties and geometries.

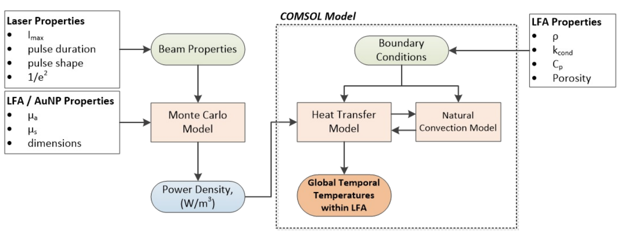

Figure 3: A schematic describing the model inputs, key modules (Monte Carlo, conductive heat transfer, and natural convection models), and transfer of information between key modules within the LFA thermal-optical model.