DEVELOPMENT OF A HANDHELD OPTOFLUIDIC IMMUNOSENSOR TO TRACK THE TRANSPORT AND DISTRIBUTION OF H1N1/2009 VIRUS IN A MOCK CLASSROOM

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ABSTRACT

A handheld lab-on-a-chip immunosensor was developed for rapid detection of H1N1/2009 virus inside a 1:10 scale mock classroom. The device detected Mie light scattering from immunoagglutination of antibody-conjugated submicron latex beads with H1N1/2009 target in a handheld optofluidic device. The lowest detectable amount was 55 pg of H1N1/2009 viruses in 0.1 m^3 of a room with 2 min sampling time. A 3-D computational fluid dynamics simulation was utilized to track the transport and distribution of H1N1/09 within a mock classroom, and corresponded very well with immunosensor readings. The device and 3-D CFD model could serve as a good model for monitoring the viral pathogen within a human environment.

KEYWORDS: Mie Scattering, Immuagglutination, Liquid-Core Waveguide, Computational Fluid Dynamics

INTRODUCTION

Influenza A H1N1/09 is a highly infectious disease that initiated a global pandemic in 2009. The spread of H1N1/2009 (and other airborne viral pathogens) inside a human environment has not been investigated in-depth using a network of real-time biosensors or computational fluid dynamics (CFD) studies. A surrogate molecule has been used to perform such experimental monitoring and/or CFD studies, including smoke and CO_2. The use of a near-real-time, handheld biosensor device as a networked system in a human environment is the key to monitoring the spread of dangerous viral pathogens.

In this work, the use of a handheld immunosensor which includes a liquid-core waveguide optofluidic device is demonstrated to detect H1N1/2009 from a mock human within a mock classroom in near-real time. A 3-D computational fluid dynamics (CFD) simulation is also attempted to track the transport and distribution of H1N1/2009 within a mock classroom (from the mouth of a mock human to the air outlet), and compared with the readings from a handheld device. This systematic investigation can potentially allow us to determine how many sensors should be installed in what specific locations to monitor such airborne pathogens and help prevent or reduce the resulting damages.

MATERIALS AND METHODS

The device uses integrated, liquid core, optical waveguides for measuring immunoagglutination-induced light scattering of submicron latex beads from a microfluidic channel [1-3], in a highly reproducible manner. The optical waveguides, or optofluidic channels, were constructed around the microfluidic channels but not touching each other. To minimize any optical noise, the mold for fabricating the PDMS device was made using deep reactive ion etching (DRIE) technology. The optical parameters, including the diameter of antibody-conjugated latex beads (d), the wavelength of incident light (λ), and the scattering angle (θ), were optimized through a series of Mie scattering simulations and experimentally validated. This optimization was conducted to maximize the scattering by immunoagglutination and minimize the scattering by the sample matrix (dust particles from air). The optimized parameters were $d = 920$ nm, $\lambda = 380$ nm and $\theta = 50°$ (forward scattering) for the detection of H1N1/2009 virus in the air samples. The disposable optofluidic device was placed on a “tray” that was inserted into the handheld device. The tray made a friction fitting to the ultraviolet light emitting diode (UV LED; light source) and the avalanche photodiode (APD; light detector), which were connected to the six-stage op-amp circuit. The analog voltage output was sent to the microcontroller board (Arduino) for time-averaging, noise filtering and displaying the results on a small liquid crystal display (LCD) panel. All components were integrated into a handheld device that was made by the Dimension 1200ES 3D printer. No external computer was required during the assays. Figure 1 shows the picture of the handheld device. The dimension of the device is 21 cm x 18 cm x 5 cm and its weight is 630 g.

The handheld optofluidic device was used to analyze the air samples collected from a mock classroom as shown in Figure 2. A 1:10 scale mock classroom was constructed with an air ventilation system and a mock human (a nebulizer that generated aerosol particles containing H1N1/2009 virus). Total volume of the mock classroom was about 0.1 m^3. The classroom was ventilated using two small computer fans with the ventilation rate of 1.02 CFM (= 0.0289 m^3/min), which is well above the ASHRAE requirement for minimum ventilation (0.14 CFM). Median diameter of the aerosol particles generated from the nebulizer was 5 µm. The aerosol particles were injected for 3 seconds with 11.2 m/s of velocity. The amount of injected virus was varied by changing the concentrations of viral solution in the nebulizer. These aerosol particles were collected at various locations as shown in Figure 2 using a commercial button aerosol sampler.

A 3-D computational fluid dynamics (CFD) simulation [4] was utilized to track the transport and distribution of H1N1/2009 from the nebulizer to the air outlet within a mock classroom, and compared with the readings from the device.

The commercial software was used to build the computational domain and the models for the mock classroom by using the finite volume method (FVM). Turbulence analysis of the air flow in the mock classroom was performed with a realizable k-ε model. Discrete phase modeling was used to describe the movements of virus particles from the mock human's coughs, as it could describe the movement of particles injected from a mock human (nebulizer). The model predicted the trajectory of a discrete phase viral aerosol particles by integrating the force balance on the particle. The movements of injected particles were tracked until the particles finally trapped by any wall or escaped through the outlet or captured by air sampler. The percentage of captured viral aerosol particles by the air sampler was estimated for two different sampling locations.

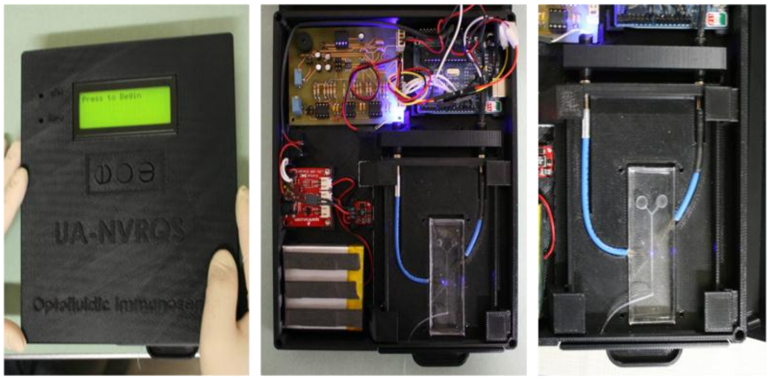

Figure 1: The handheld optofluidic immunosensor (left), with inside view (middle) and the optofluidic device view (right).

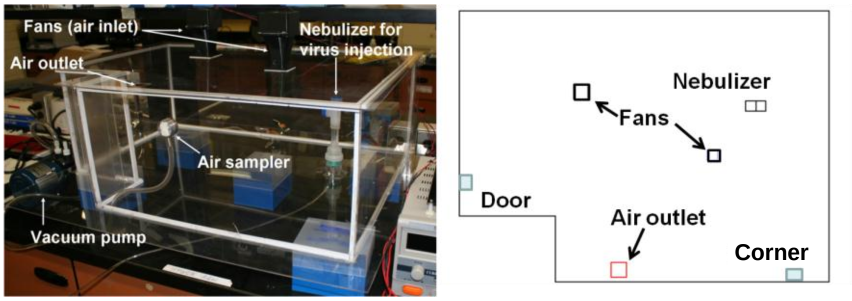

Figure 2: The 1:10 scale mock classroom, modeled after the actual classroom at the University of Arizona, shown with its top view (right) illustrating the sampling locations.

RESULT AND DISCUSSION

Figure 3 shows a standard curve made by the handheld immunosensor. All light scattering intensities were normalized to that of a blank sample. The detection limit was 1 pg/mL and the response was largely linear up to 1 µg/mL. The dips at 1 ng/mL and 10 µg/mL is characteristics of Mie scattering from immunoagglutinated latex beads [5].

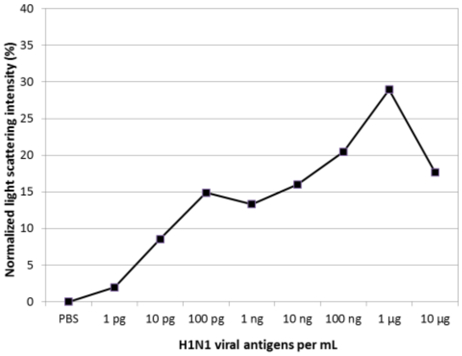

Figure 3. A standard curve made by the handheld immunosensor.

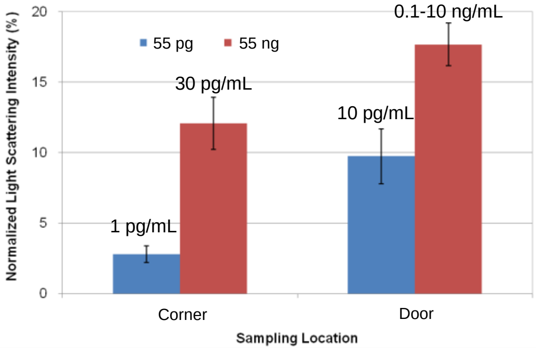

Figure 4: Immunosensor readings for the air samples captured at two different locations.

Figure 4 shows the immunosensor readings for the air samples captured at two different locations, "corner" and "door." The sampling time was 2 min. The concentrations of virus solutions in a nebulizer were 1 ng/mL (blue) and 1 µg/mL (red), which were injected into the classroom for 3 seconds. The corresponding amounts of injected viruses were calculated as 55 pg (blue) and 55 ng (red) for the 0.1 m^3 of the classroom. The normalized light scattering intensities were varied 3-18%, and the corresponding concentrations estimated from the standard curve (Figure 3) are shown within Figure 4. Note the concentration at “door” with higher amount of viruses could not be estimated precisely because of the dip at 1 ng/mL from the standard curve. The immunosensor reading with 55 pg of injected viruses corresponded to the detection limit of the device, 1 pg/mL, indicating the detection limit of the device with 2 min sampling time would be 55 pg per 0.1 m^3 volume. The estimated concentrations at “door” were about an order of magnitude higher than those at “corner.”

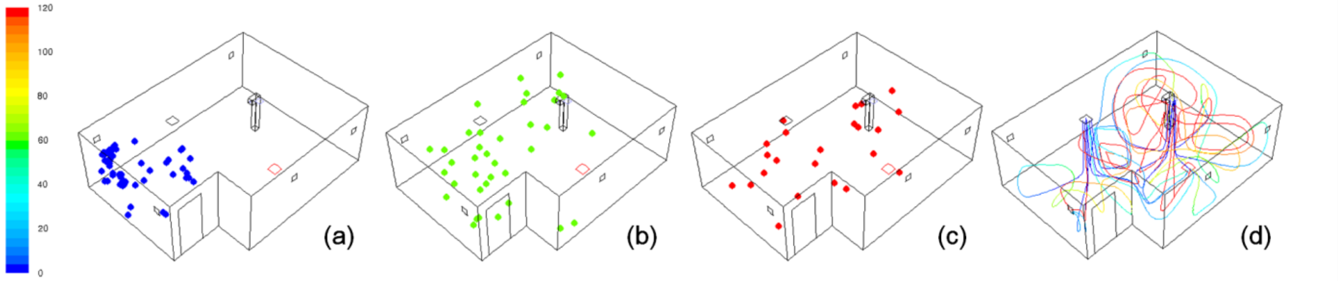

Figure 5: Predicted distribution of viral aerosol particles using CFD simulation: (a) 0 min, (b) 1 min, and (c) 2 min of sampling, with (d) their predicted pathways for 2 min sampling. The color represents residential time.

The distribution of the injected particles predicted by CFD simulation was shown in Figure 5. Median residence time of the particles was 2 min. Some particles were estimated to stay more than 15 min. Table 1 shows the percentile fractions of aerosol particles that were captured by the air sampler, escaped through the air outlet, or trapped by the walls. The captured amount at “door” was about an order of magnitude higher than that at “corner,” which corresponded very well with experimental data shown in Figure 4. Both immunosensor readings and CFD simulation results indicate that the virus amount could be varied by an order of magnitude by the location, despite the room was extremely well ventilated (ventilation rate was 7 times higher than the ASHRAE requirement and the air distribution was nearly homogeneous throughout the classroom). This non-uniformity can be explained by the different transport behavior of aerosol particles compared to that of air. The assumption that the pathogen-containing aerosol particles behave the same as air is thus not valid; the governmental regulations on ventilation systems may need to be revisited.

Table 1. % captured, escaped and trapped aerosol particles at two different sampling locations with varying sampling time.

Sampling time	**Door**			**Corner**		
	Captured (%)	Escaped (%)	Trapped (%)	Captured (%)	Escaped (%)	Trapped (%)
0.5 min	3	0	18	0	0	20
1 min	8	7	23	0	3	20
1.5 min	17	8	25	0	10	25
2 min	23	12	27	2	18	27

CONCLUSION

The developed handheld device can be miniaturized further towards a smoke-detector-like, unmanned monitoring device. The developed CFD model will help designing the better ventilation system to eliminate any dead zones for the viral pathogens to stay long term and/or pinpoint the installation location for the handheld immunosensor.

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