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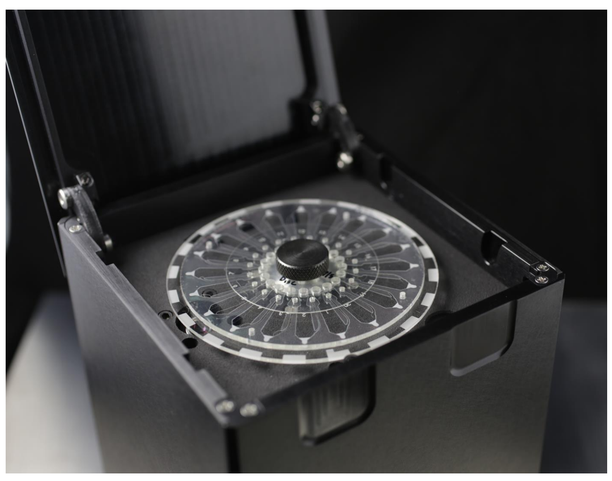
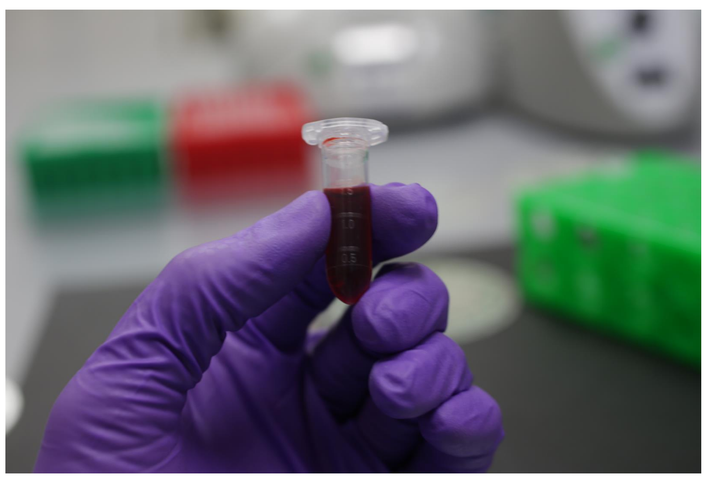
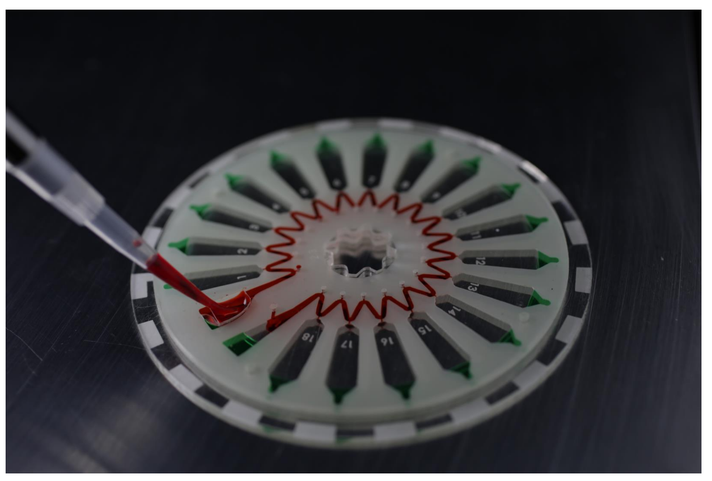
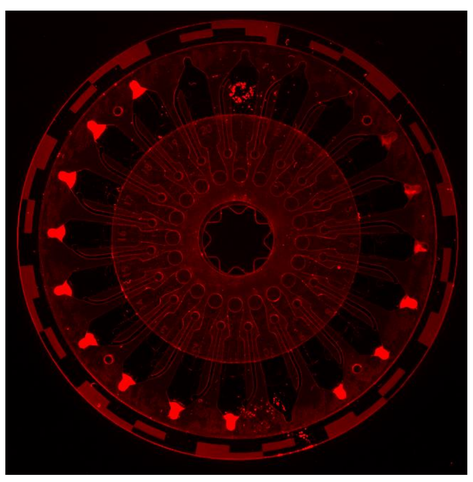

# Passive On-Disk Aliquoting Structure and Reliability Testing for Centrifugal Microfluidic Diagnostic Platform

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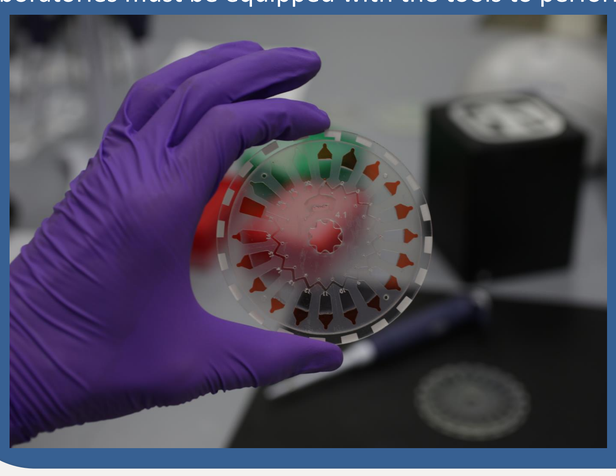
## Abstract

Infectious disease outbreaks and bioterrorist attacks pose serious concerns which stretch the capabilities of public health facilities. SpinDx is a centrifugal microfluidic platform intended as a quick and reliable diagnostic tool for testing of clinical and environmental samples in the case of such an event. Immunoassay tests have demonstrated the ability of SpinDx to deliver consistent results with minimal to zero user-dependence. A passive aliquoting structure was developed and optimized for use within the current platform which enables the splitting of a single sample into defined sub-volumes for subsequent release into separate reaction chambers. This enables rapid multiplexed analysis of small volumes with minimal user training, manual intervention, and existing equipment.

## Introduction

Recent infectious disease outbreaks have exposed an urgent unmet need for quick, simple, and readily available diagnostic methods in limited-resource areas. In order to facilitate effective handling of such outbreaks as well as potential bioterrorism threats, public health facilities and field laboratories must be equipped with the tools to perform rapid sample-to-answer patient screenings on demand. SpinDx is a centrifugal microfluidic immunoassay platform capable of ultrasensitive point-of-care detection. This simple-to-use device can perform direct analysis of samples such as whole blood and food without any sample preparation, in under 30 minutes, and with sample sizes smaller than a single drop of blood (~20µL). In order for the SpinDx to meet the current needs, reliability and ease of use must be essential characteristics.

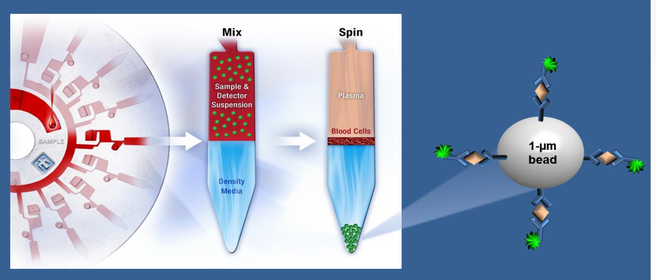


## Reliability Testing Methods

The following protocol was repeated 10 times for each of the 20 current SpinDX devices. Special care was taken to ensure identical and repeatable conditions for each of the 200 runs.

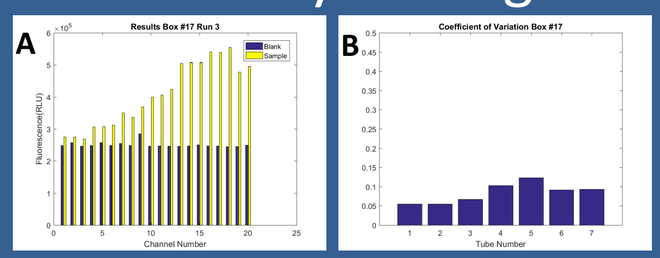
**Immunoassay Protocol**

- Serial dilutions of IL-6 antigen were mixed with capture beads and a fluorescent detection antibody
- Assay mixture was loaded into each channel of a SpinDX disk
- Disk was inserted into the SpinDX device and centrifuged through density medium to sediment the beads
- Automated analysis by quantification of laser-induced fluorescence




Schematic illustrating the centrifugal microfluidic immunoassay approach

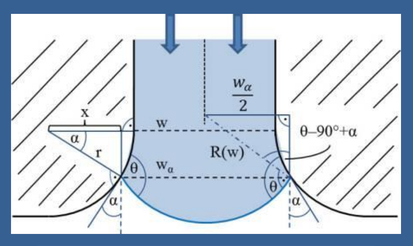
## Reliability Testing Results & Discussion




Plots displaying (a) typical results of a SpinDx immunoassay analysis and (b) coefficient of variation for a selected device

- Comparison of data sets shows assay results to be user-independent despite minimal prior laboratory experience
- Coefficient of variation between runs ranges from 5-15% on well-functioning boxes
- Primary source of variation is due to "dead well" readings, likely caused by indexing motor imprecision

## Microfluidic Theory




$$R(w) = \frac{w_\alpha}{2\sin(\theta - 90^\circ + \alpha)} = \frac{w_\alpha}{-2\cos(\theta + \alpha)}$$

$$\Delta p_{burst} = max\left(-\gamma\left(\frac{2\cos(\theta)}{h} + \frac{2\cos(\theta+\alpha)}{w_\alpha}\right)\right), \quad 0 \le \alpha \le 90^\circ$$

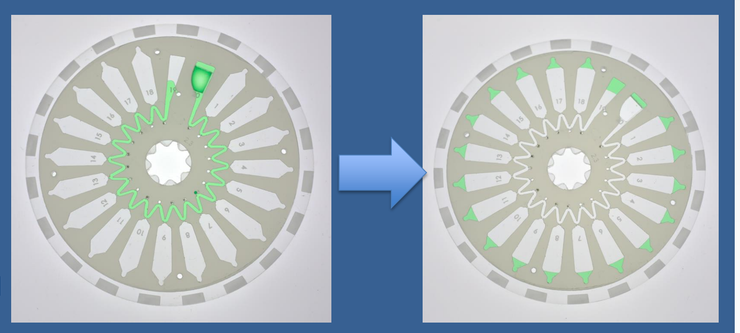
Description of parameters w, x, α, r, θ, and $w_\alpha$ and equations for calculation of the radius of curvature R(w) of filling liquid with surface tension γ advancing in a gradually opening microfluidic channel , as well as the burst pressure $\Delta p_{burst}$ required inside the liquid to overcome a capillary stop valve [1]

## Disk Fabrication

Disks consist of a pressure sensitive adhesive sandwiched between two clear polymer layers. Disk layers were modeled in AutoCAD, then etched/cut using a laser engraver before alignment/joining

## Aliquoting Structure Design & Optimization

- Points of focus: slow capillary filling times (8+ min), pre-spin valve leakage
- Implemented changes: varied capillary valve dimensions, adhesive thickness, radial position of valve, aliquoting channel shape and dimensions
- Inlet position to facilitate low-speed forced filling



**References: [1]** Hagmeyer B., Zechnall F., and Stelzle M., Biomicrofluidics 8, 056501 (2014).10.1063/1.4896063

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