A high-throughput, multiplexed microfluidic method utilizing an optically barcoded drop library

The power of drop-based microfluidics promises reduced biological assaying times and greater sample throughput; however, current drop-based microfluidic methods focus on single-input single-output techniques to provide these benefits. In order to achieve truly high-throughput analysis of biological assays, a multiple-input approach must be taken. This thesis is focused on developing and validating a drop-based microfluidic method that is capable of encapsulating, in parallel, 96 assay samples in drops and optically tracking them in a barcoded drop library. The advantage of the method presented here is its ability to be integrated with current biological assays performed on a 384-well plate. The first step was to fabricate a three-dimensional microfluidic device capable of accepting 96 sample inputs. Second, formation of drops within the device was characterized by creating a state diagram using Capillary and Weber numbers of the two phase flow. Finally, the use of fluorescent microbeads was investigated for the purpose of optically barcoding drops. A barcoding scheme was developed to allow for fluorescent and spatial labeling of 96 wells of a 384-well plate. The three-dimensional microfluidic device was successfully used to encapsulate 50 μm diameter drops from 24 wells barcoded with fluorescent microbeads at a drop formation rate of 3 kHz per well. Fluorescent detection of the barcoded drop mixture was performed at a rate of 200 Hz and density-based clustering algorithm DBSCAN was used to identify barcoded drop clusters from the fluorescent signal data. Validation of this method was achieved by adding known concentrations of fluorescent blue microbeads to barcoded wells and detecting for their presence in barcoded drop clusters. The barcoding method can be expanded to fully incorporate the 96 inputs of the microfluidic device by adding a spatial barcoding component to each quadrant of 24 optically barcoded wells. The results presented here show the microfluidic platform has the potential to be a useful tool in biological assays involved with tracking a large number of samples in a well plate format.

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