Understanding and Improving Massively Parallel DNA Detectors for Biomedical Assays

BENJAMIN SMITH, RICHARD YEH, JASON CARPENTIER, STEVEN RODRIGUEZ, SHANNON GUILES, DAVID LIN, CARL FRANCK, Cornell University — Microarrays are highly parallel sequence specific DNA detectors used to quantitatively study genotypes and gene-expression levels. Commercial agitation systems aim to remove the coverslip diffusion bottleneck, but the efficiency increase provided by these devices is variable and occasionally even negative. The underlying causes of these variations are not well understood. We have investigated hybridization efficiency using liquid-on-liquid mixing, in which an impeller stirs a viscous oil phase covering a thin film of fluorescently labeled target solution, which lies on a glass microarray substrate. Absolute efficiency studies indicate the diffusion limit is generally well obeyed by static hybridizations, but stirring produces no significant improvement in efficiency. To check whether shear deformation of DNA is a limiting factor a pause cycle is added to the mixing procedure, but no further improvement is observed. Antibody delivery experiments with a comparable diffusion constant show a clear increase in efficiency due to mixing.