Increased throughput in the techniques used to engineer new metabolic pathways in unicellular organisms demands similarly high throughput tools for measuring the effects of these pathways on phenotype. For example, the metabolic engineer is often faced with the challenge of selecting the one genomic perturbation that produces a desired result out of tens of thousands of possibilities [1]. We propose a separation method – iso-dielectric separation, or IDS – which separates microorganisms continuously based on their intrinsic dielectric properties [2-3]. Because IDS is an equilibrium method, sorting cells according to their unique equilibrium positions in an energy landscape, it offers enhanced specificity over other label-free separation methods [4]. This technology would enable high throughput screening of cells based upon electrically distinguishable phenotypes.

Iso-dielectric separation uses dielectrophoresis (DEP) and media with spatially varying conductivity to create the energy landscape in which cells are separated according to their effective conductivity (Figure 1). It is similar to iso-electric focusing, except that it uses DEP instead of electrophoresis, and is thus applicable to uncharged particles, such as cells [5]. The IDS leverages many of the advantages of microfluidics and equilibrium gradient separation methods to create a device that is continuous-flow, capable of parallel separations of multiple (>2) subpopulations from a heterogeneous background and label-free. We demonstrate the simultaneous separation of three types of polystyrene beads based upon surface conductance as well as sorting non-viable from viable cells of the budding yeast Saccharomyces cerevisiae (Figure 2). Current efforts are focused on the separation of Escherichia coli based upon the amount of the intracellular polymer poly(hydroxybutyrate) each cell contains.

REFERENCES