

Morphological Profiling for Targeting Diseases and Characterizing Compounds

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Abstract—Microscopy images contain rich information about the state of cells, tissues, and organisms. Our laboratory is extracting patterns of morphological perturbations (“signatures”) from images in order to identify similarities and differences between various chemical or genetic treatments, with the ultimate goal to identify the causes and potential cures of disease. Using model systems that are more and more physiologically relevant, yet still compatible with automated instrumentation, we are developing assays and accompanying algorithms to extract multiparametric morphological fingerprints of cell populations.

Our goals in these profiling experiments include identifying drug mechanisms of action, the impact of disease-related alleles, performance-diverse chemical libraries, mechanisms of liver toxicity, and diagnostics for bipolar disorder and schizophrenia.

Several data analysis problems need to be addressed to achieve these goals – what are the common sources of systematic noise? How do we transform a matrix of cellular measurements to a perturbation signature? What distance metrics are appropriate for these signatures? How can we make signatures that are interpretable by biologists? How do we integrate information across different assays? I will present approaches we have used in our own experiments to address these problems.

Overall, we aim to make perturbations in cell morphology as computable as other large-scale functional genomics data. I will share our results on one of our pilot projects – done in parallel with high-throughput gene expression data – that has helped move closer towards this goal.

Index Terms — image-based profiling; morphology; microscopy; high-content screening.

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