A USER-FRIENDLY TOOL USING SYSTEMS BIOLOGY MODELS TO INFER CELL FUNCTIONS FROM OMICS

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The emergence of omic-technologies is driving the development of systems biology tools and targeted cell line engineering of robust industrial biomanufacturing platforms. However, despite the continual expansion of omics-driven data and available repositories, complex interdependencies between genes, proteins, and metabolites complicate the interpretation of omics experiments. While statistical methods have been invaluable for identifying sets of genes/proteins involved in a given phenotype, it remains difficult to obtain and quantify mechanisms underlying a cell's functions from only enriched ontology terms. Systems biology models now allow researchers to analyze genome-scale omics datasets, but they require specialized training and often require extensive effort and expertise to deploy.

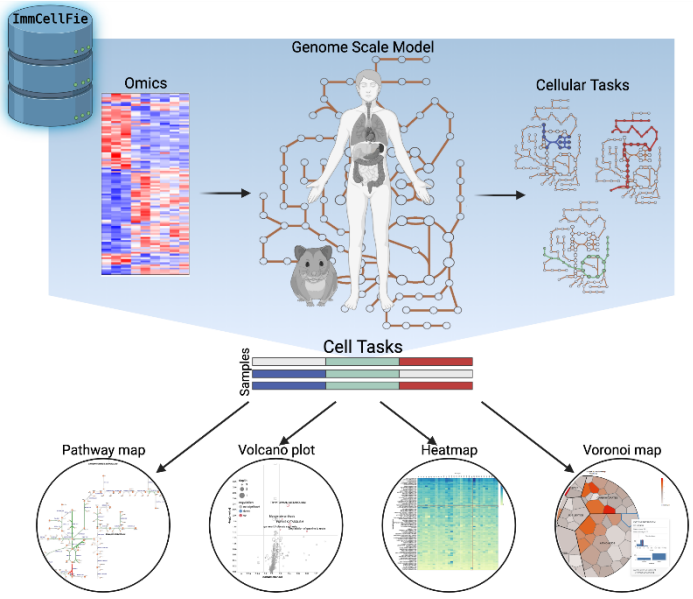

Figure 1 – The CellFie tool overlays transcriptomic and proteomic data onto genome scale models to quantify changes in pre-computed cellular tasks.

To increase accessibility of complex systems biology informatics to the broader scientific community, we built a computational toolbox called CellFie (Cell Function Inference)[1]. This tool overlays omics data onto genome scale models to quantify the activity of metabolic "tasks", defined by precomputed sets of genes that work together in metabolic models[2] (Figure 1). Currently, CellFie supports human, mouse, rat and CHO.

We further developed a web-based platform called ImmCellFie (immcellfie.renci.org). The simple point-and-click features of ImmCellFie enable users to create custom metabolic analyses, enabling any scientist, regardless of computational background, to directly predict, quantify, and visualize how changes in omics experiments correspond to the metabolic functions of cells or tissues.

Cellular metabolism, however, is just one key process that impacts growth, product yield, and product quality in biopharmaceutical production. Therefore our most recent work has focused on expanding the scope of CellFie beyond metabolism to include core tasks involved in protein secretion. Here we are leveraging our lab's reconstruction of mammalian protein secretion[3] to integrate core secretory tasks with the CellFie toolbox. This expansion of the CellFie toolbox enables mechanistic-based inference of metabolic and secretory cell functions, which could be used to guide the rational design of mammalian cell factory systems.

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