Multi-omics data integration into computational models to unveil the many facets of metabolic heterogeneity

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Abstract:

Understanding human metabolism represents a crucial opportunity for coping with complex human diseases, such as cancer. However, metabolic therapies are challenged by the high heterogeneity of metabolic programs across individuals and among cells in time and space.

For this reason, the use of patient-specific omics data, at bulk or single-cell level, has a pivotal role in the understanding of the regulatory mechanisms of several metabolic phenomena and to achieve personalized medicine. Transcriptomics, proteomics, and metabolomics datasets are increasingly available but provide static profiles of a cell's metabolic state. Fluxomics data could represent a key factor to unveil the dynamic profiles of cells, but such data are far from being high-throughput, especially at the single-cell level.
Computational methods allow to reconstruct metabolic fluxes from omics data by integrating them into an appropriately constrained metabolic network at steady-state conditions. More in detail, transcriptional and/or proteomics data can be used to set specific constraints on the fluxes at which a given reaction can occur. Metabolomics data enable to discriminate fluxes regulated at the substrate level only from fluxes controlled by transcriptomics expression.

Efficient metabolic network models must be developed and studied, which must properly deal with the intrinsic complexity related to the simulation of human metabolism. To this aim, we developed a new core metabolic network, named ENGRO2, which is a constraint-based core model about central carbon and essential amino acids metabolism. The use of such a model combined with single-cell/bulk omics data allows us to perform in silico experiments with the aim of studying single-cell metabolism and unveil new possible regulatory levels at which a given reaction is controlled.