BIOLOGICALLY CONSISTENT ANNOTATION OF CHO CELL CULTURE METABOLOMICS DATA

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Metabolomics represents the effort to understand the role of metabolites in a biological system. Unfortunately, unambiguous metabolite identification represents a major bottleneck in liquid chromatography-mass spectrometry (LC-MS) based untargeted metabolomics. A widely used approach is to search spectral (MS/MS) libraries in reference databases for matching metabolites; however, this approach is limited by incomplete coverage. An alternative approach is to match detected features to candidate chemical structures based on their mass and computationally predicted fragmentation pattern. Both approaches often return too many possible matches; moreover, the results from different annotation tools rarely agree. This presentation describes a novel annotation tool that combines search results from several MS/MS libraries and computational fragmentation tools, and evaluates these results based on the content of a metabolic model. This captures the relevant biological context to determine the most likely identity for a given LC-MS data feature. This workflow, termed Biologically Consistent Annotation (BioCAn), improves on other publicly available annotation tools, achieving superior accuracy and sensitivity, while reducing the false discovery rate. The utility of this tool for investigating metabolic inefficiencies in cell culture processes is demonstrated by identifying novel CHO cell metabolites associated with enhanced or reduced cell growth and monoclonal antibody production. The function of these metabolites was evaluated in shake flask and controlled bioreactor experiments.