Abstract

The progress of genomic science and technology has propelled a fundamentally new vision in medicine, agriculture, marine and other sectors of biotechnology. The immense data generated in the genomic era offer endless opportunities for technological innovations. In order to capitalize the advances created by the current biological revolution and to harness its benefit to advance metabolic engineering, drug discovery and other biotechnological applications, novel approaches of computational and experimental research need to be initiated and integrated with existing biochemical, genetic and physiological research tools.

In my research work, a novel bioinformatic approach has been used to establish an integrated genomic-biochemical pathway database from annotated genomic information along with biochemical, physiological and strain-specific information for the yeast Saccharomyces cerevisiae. The metabolic genotype was then determined to reconstruct cellular metabolic networks. The resulting computation-experimentation platform (CEP) is the basis for systematic study of the genotype-phenotype relationship under given environmental conditions using flux balance analysis (FBA). CEP is a new generation of integrated research tools that enables us to investigate cellular processes in following aspects: 1) cell physiology; 2) metabolism/enzymatic activity; 3) genomics/proteomics; 4) gene deletion, and 5) gene transfer. A multi-fermentor system consisting of up to 17 fermentors was established for growth, screening and gene expression experiments. The results from simulation and experiments on CEP can be compared at the genomic, biochemical, and physiological levels at the same time. Integration of computation and experimentation for investigation of whole cells can thus be conducted for the understanding of well-orchestrated cellular responses to the genetic variation and environmental stimuli.

Other applications of CEP include genomic comparison of different microbial or marine organisms, development of antibacterial strategy and prediction of new pathway insertion. CEP can also be used for educating next generation of bioengineering students in process control, optimization, multidimensional data analysis, genomics, proteomics, and bioinformatics.