

Navigating through disease maps

Joaquín Dopazo

Clinical Bioinformatics Area, Fundacion Progreso y Salud, Seville, Spain

Despite the increasing availability of genomic and transcriptomic data, there is still a gap between the detection of perturbations in gene expression and the understanding of their contribution to the molecular mechanisms that ultimately account for the phenotype studied. Disease maps (<http://disease-maps.org/projects>) and other generic maps that recapitulate cell signaling, metabolism and functionality (e.g. KEGG, WikiPathways, etc.) offer a detailed picture on the complex network of interrelationships among genes that result in cell activity decisions.

Alterations in the in the functioning of such networks are behind the initiation and progression of many diseases, including cancer. The wealth of available knowledge on biological networks can therefore be used to derive mechanistic models that link gene expression perturbations to changes in metabolic, signaling, etc. activities that provide relevant clues on molecular mechanisms of disease and drug modes of action (MoA).

Here we present simple mechanistic models of signaling (hipathia) and metabolic (Metabolizer) activity based on modules defined as functionally substantiated circuits within pathways. The models have been implemented as web-based applications, which offer intuitive, easy-to-use interactive interfaces to analyze differences in pathway activities that can also be used for class prediction and in silico prediction of Knock-Out (KO) effects. We provide different types of validations of some of the predictions made by the models.

Metabolizer can be found at: <http://metabolizer.babelomics.org>

Hipathia can be found at: <http://hipathia.babelomics.org> A Bioconductor/R package can be found at: <http://bioconductor.org/packages/devel/bioc/html/hipathia.html>