Figure 1. A schematic to illustrate the complex network of interconnections in the cell between gene space, protein space and metabolic space. In gene space numbers represent distinct genes with arrows representing connections to other genes or transcription to proteins. In protein space the currency symbols represent unique proteins with arrows representing reactions catalyzed or protein-protein interactions. In metabolic space letters represent molecules which are substrates or metabolites with arrows representing reactions or effects on proteins.

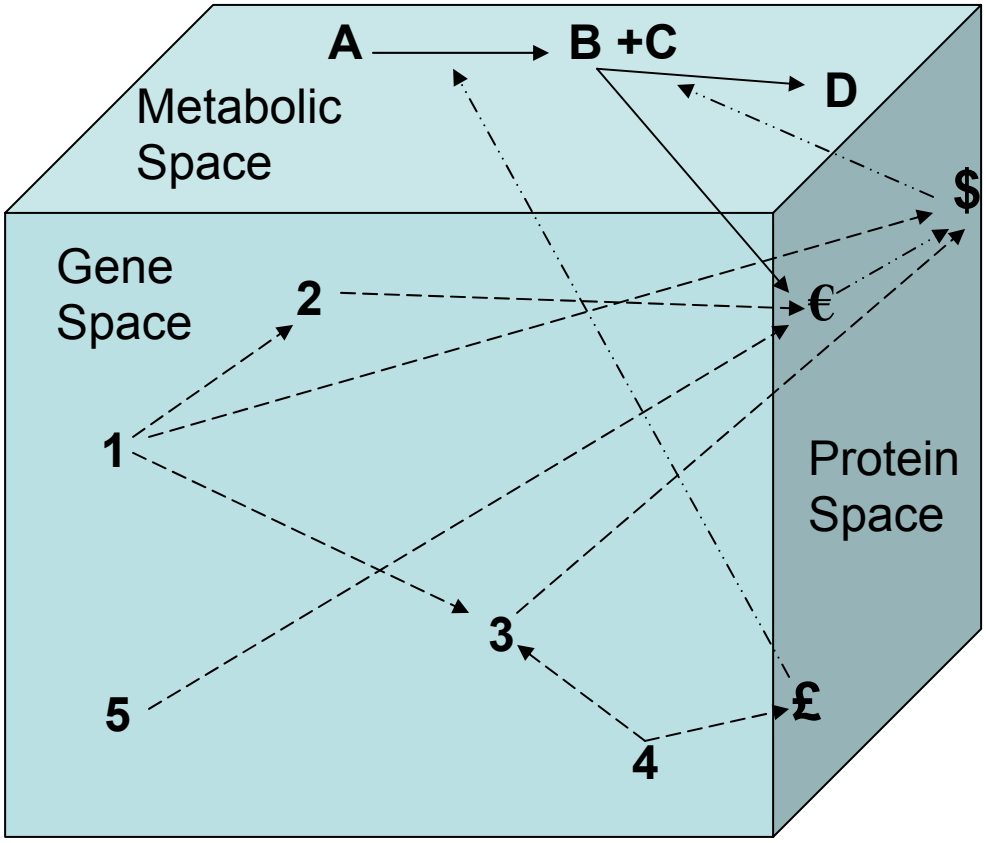


Figure 2. The utility of high throughput data for providing information on the functional blocks and use for systems level analysis. Nine levels of regulation of protein activity in a human cell can be summarized: 1. Gene transcription, 2. mRNA processing and editing, 3. mRNA transport from nucleus, 4. mRNA stabilization, 5. protein translation, 6. protein transport, 7. folding and protein stabilization. 8. allosteric modulation, 9. covalent modification

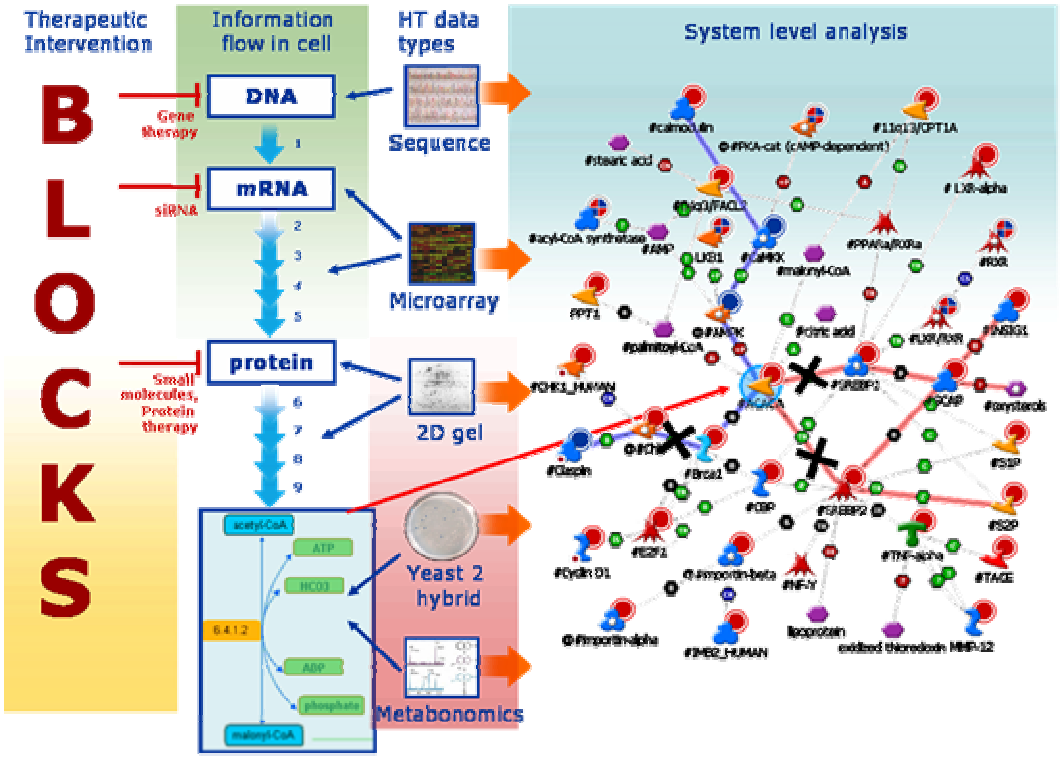


Figure 3. An interactive map for human purine metabolism from MetaCore™. Metabolic pathways are shown as rectangular icons; the enzymes are tagged with EC numbers. The differentially expressed genes are uploaded directly from a microarray experiment and are marked next to the pathways as thermometer objects.

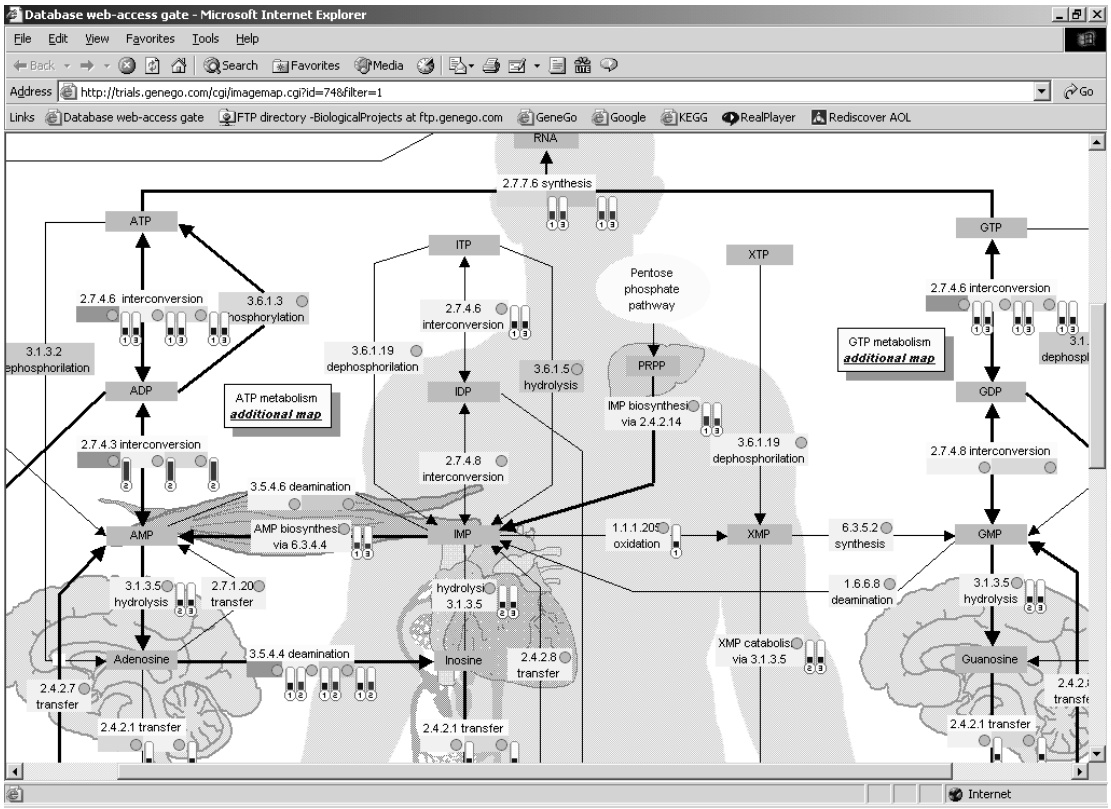


Figure. 4. Some possible causes of initial insult to the optic nerve head in different glaucoma patients [1]. While increased intraocular pressure (IOP) is the most significant risk factor for glaucoma, RGCs cell death caused by optic nerve deformation may provide an explanation for a mechanical cause of glaucoma. While elevated IOP definitely plays role in structural displacement of the ONH causing cytosceletal alteration, loss of microtubules in RGC axons and impedes retrograde axonal transport [2-4], it is conceivable that it also provides indirect insults via reduced blood flow and reactivation of microglia [5]. The role of vascular factors also is thought to be of significance to optic nerve and RGCs injury [6-9].

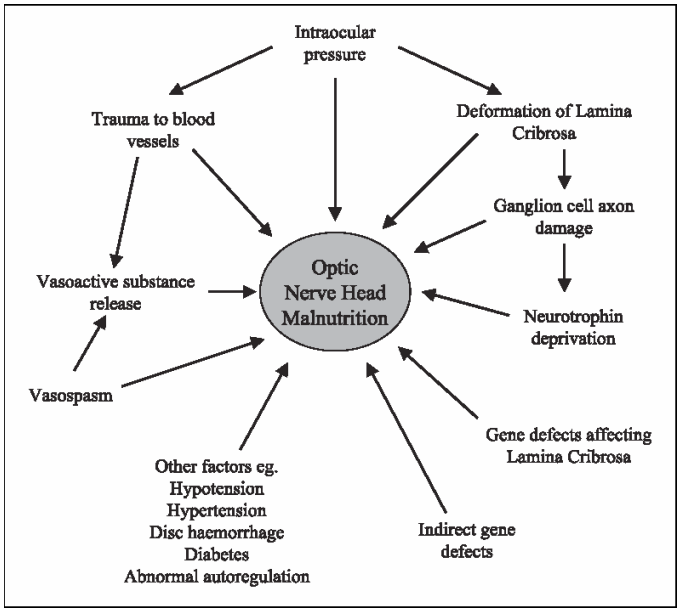


Figure. 5. A functional network for differential gene expression in glaucoma. Pathways marked in blue are down-regulated; pathways in red up-regulated. Blue and red circles on the nodes mark the differentially expressed genes. The expression ratios and the page with gene/protein/interaction annotations are hyperlinked with nodes.

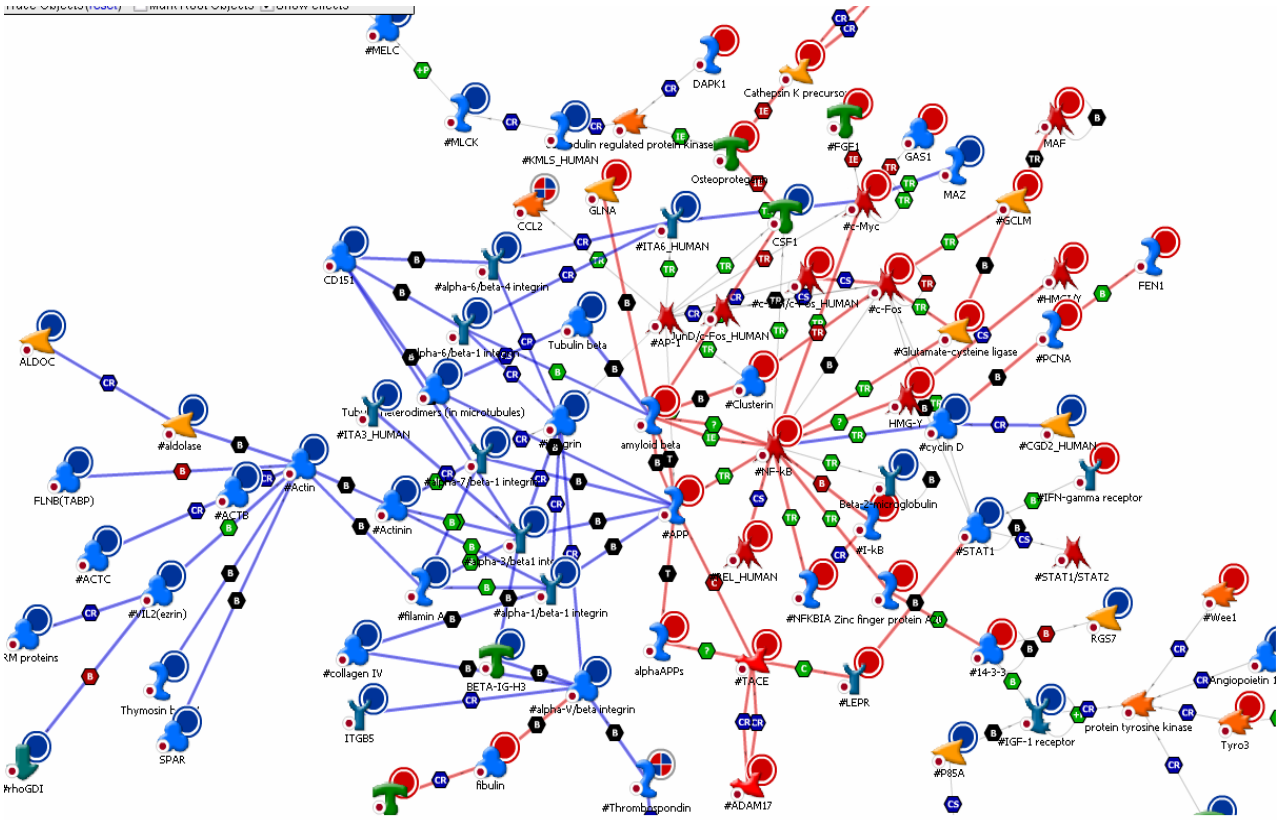
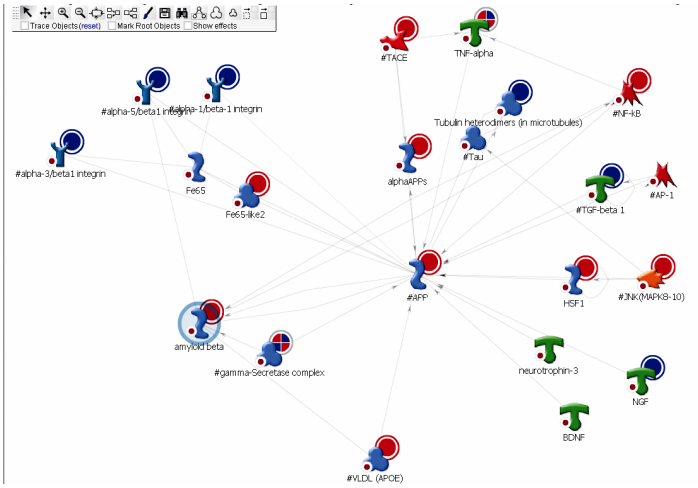
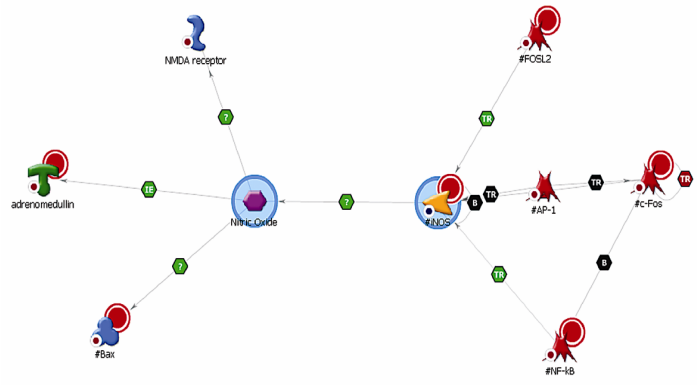


Figure. 6. Smaller networks for glaucoma microarray data. A. The APP protein node and its immediate interaction space. B. iNOS cross-activation network in glaucomatous astrocytes, C. Potential role of clusterin in glaucoma pathology of astrocytes. The arrows indicate direction of protein interactions.

A.



B.



C

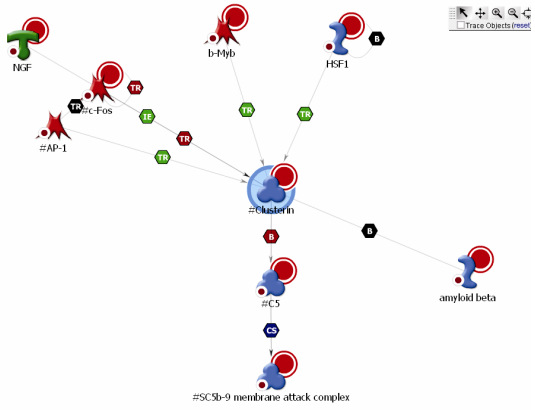


Figure 7. Clusters of highly responsive genes for the treatment of MC-7 breast cancer cells with 4-hydroxytamoxifen (A) and estrogen (B) after 24hr. Both treatments induce similar sets of cell-cycle related genes, but the topology of the networks is different, correlating with the unique impact of these treatments on cell proliferation. Gene towards the exterior possess fewer interactions than those located centrally.

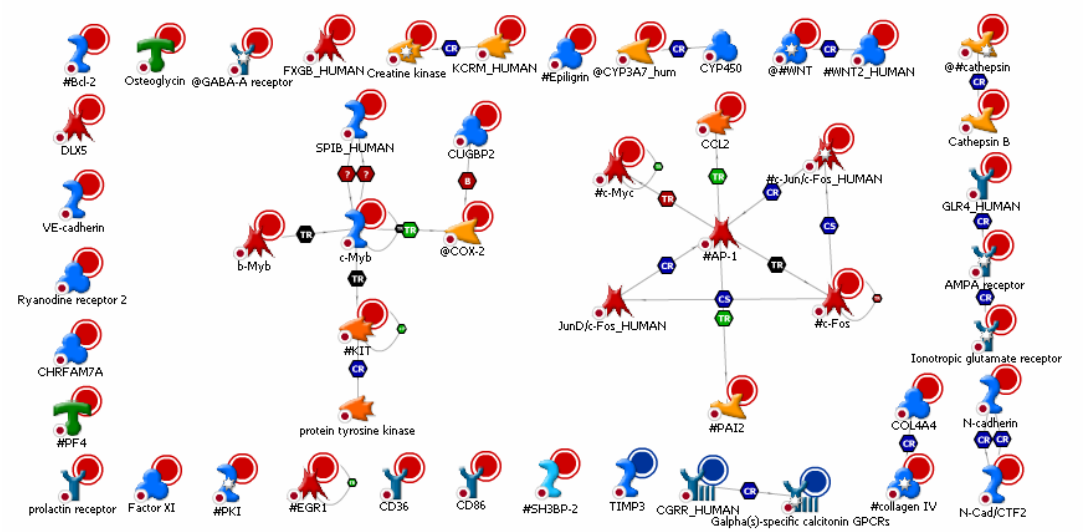


Figure 8. MetaDrug interaction map of key proteins and ligands linked to theophylline (red circle) The network of cell signaling interactions built from the list of genes. This network has been automatically reconstructed, based on the interactions contained in the database. The genes from the original list are encircled.

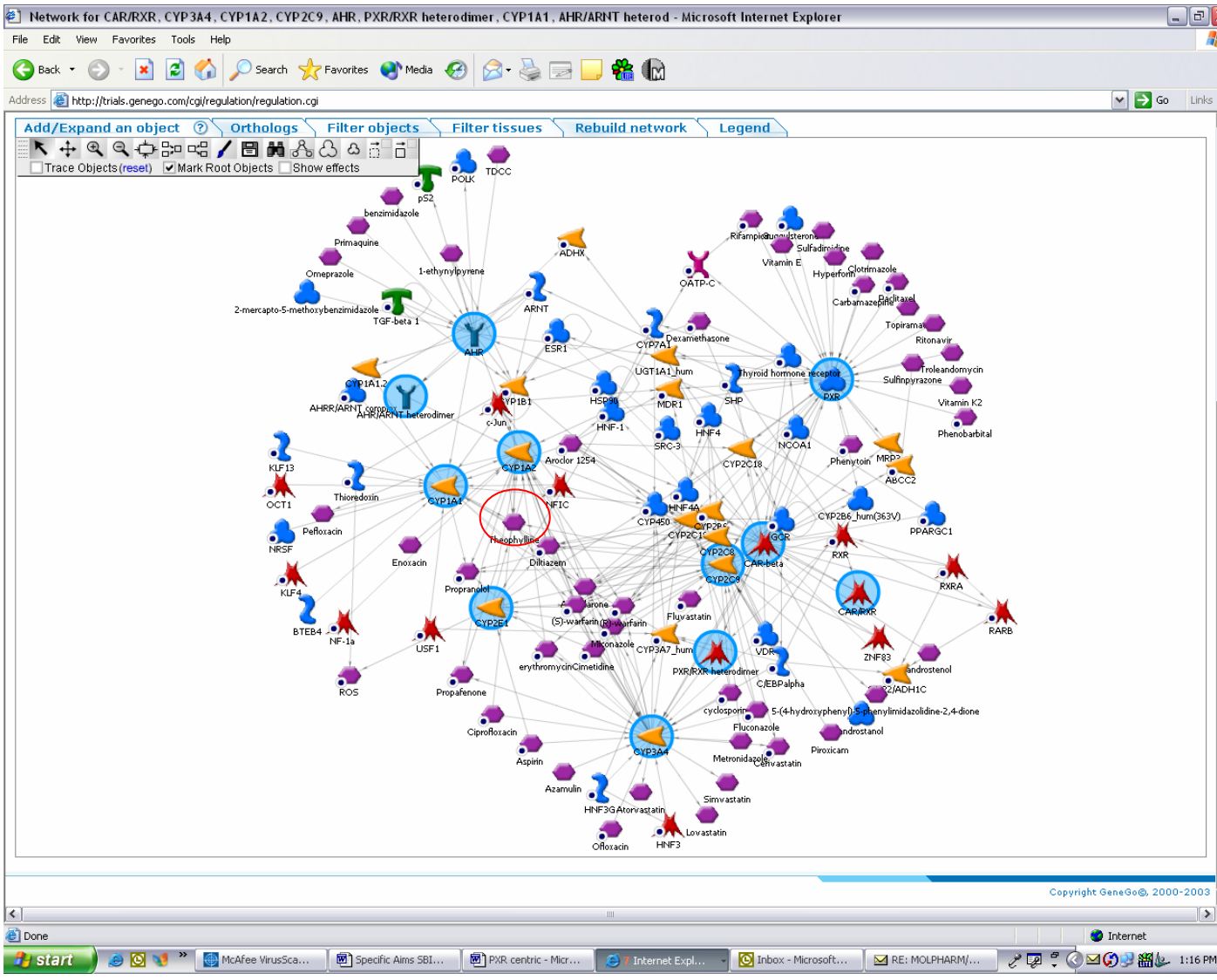


Figure 9. A proposed future database model. Borders enclose the database entities related to core functional entities: dotted border – entities related to the component; dashed line – entities related to the transformation; solid border – entities related to the functional block.

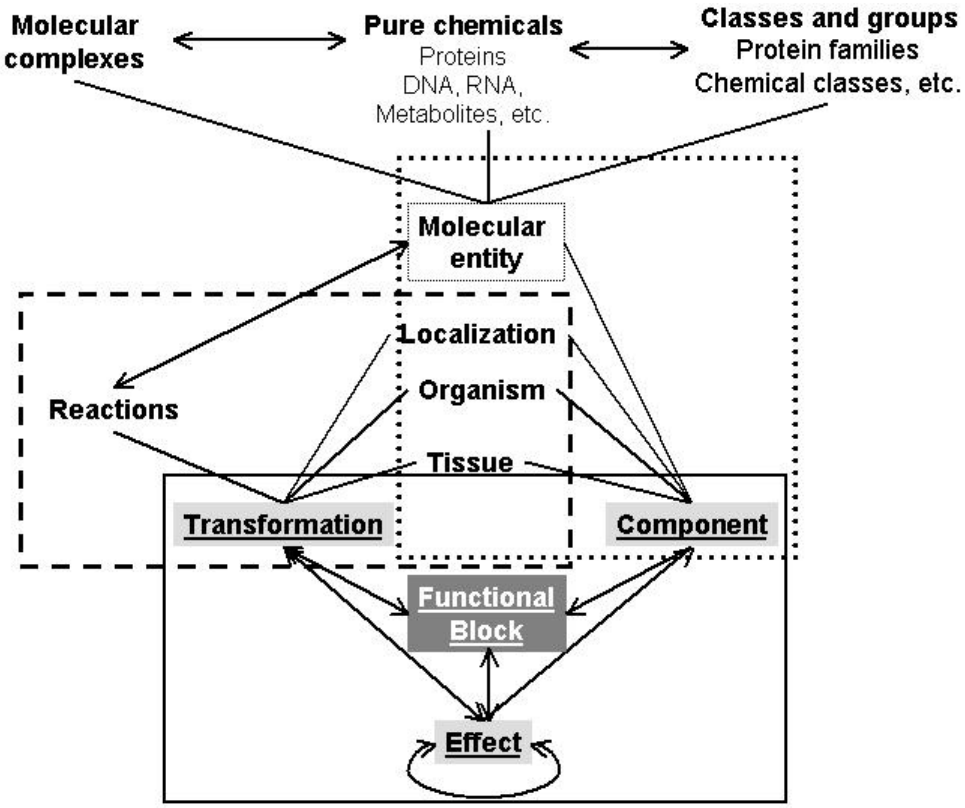


Figure 10. A schematic to demonstrate two graphs with identical topology but different directionality of edges. Graph A is more likely to represent a functional module as it contains longer directed paths than graph B.

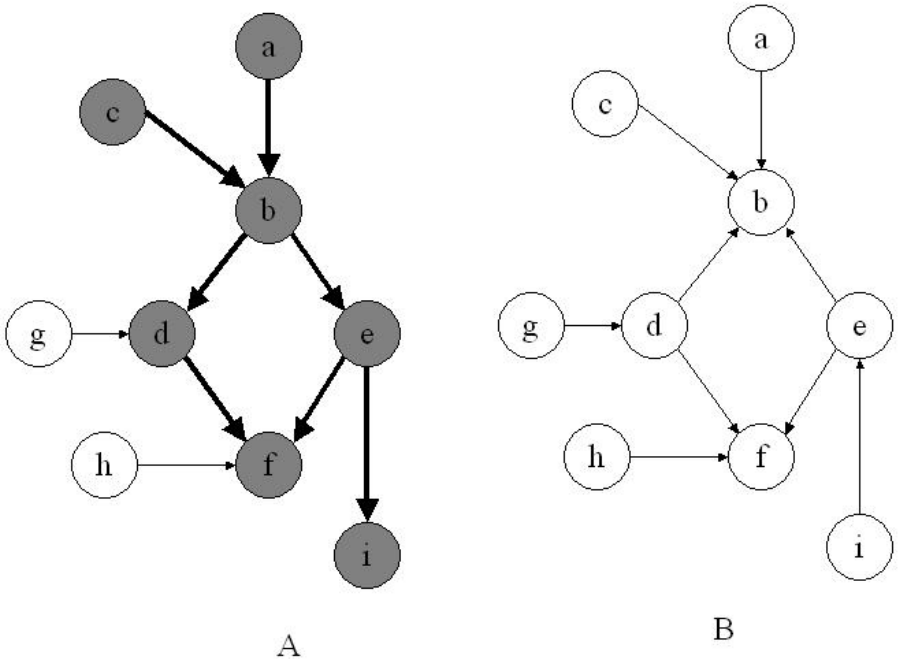


Figure 11. A schematic to illustrate how two network modules sharing 83% molecular composition can have significant topological differences. On network A the shortest distance between nodes A and E is 2, while on network B it is 4. The global connectivity of network A is also higher.

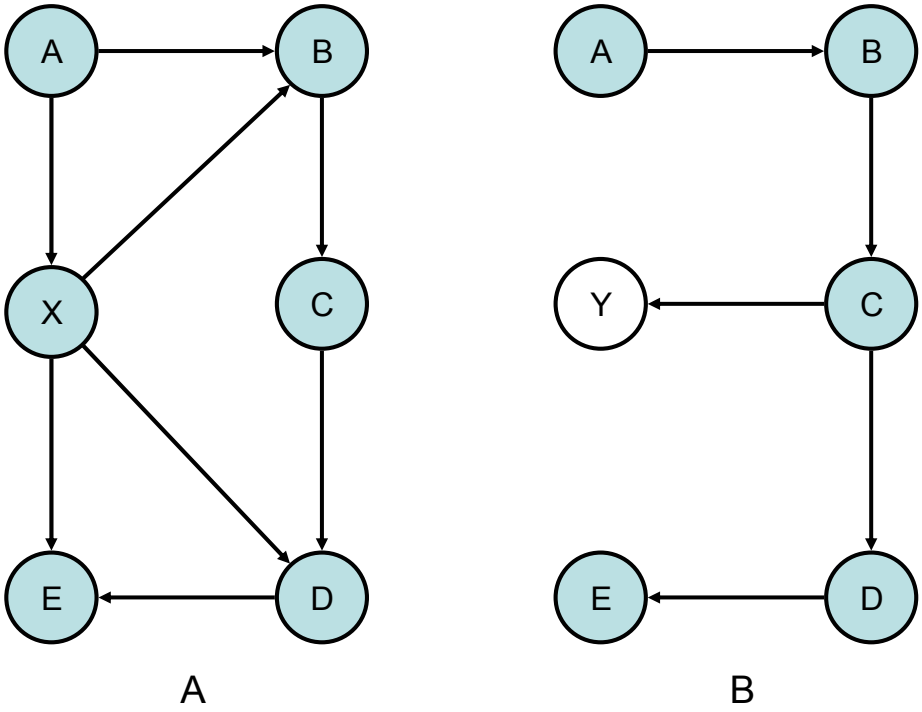


Figure 12. A schematic to show the identification of tight clusters from differentially expressed genes. Filled circles represent differentially expressed genes from the original set; open circles represent nearest neighbors; bold lines and circles represent genes and edges connecting genes into cluster.