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Automated construction of genetic networks from mutant data

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Geneticists use mutations to investigate biological phenomena. Mutations cause changes of organism's phenotype and may reveal which genes participate in a certain biological process and how. To represent these functional interactions between genes, a gene regulatory network is an often used formalism.

We have developed a system called GenePath (*1*) for automated construction of genetic networks from mutant data. GenePath considers classical genetic data where a phenotype is observed for a set of single or double mutants. Prior knowledge, expressed through relations between genes (possibly extracted from the relevant literature) can also be included. GenePath employs a set of logical patterns of the type "IF there exist a set of experiments that involves genes A, B, … THEN a certain relation between these genes can be inferred". These relations are then used to propose genetic networks. An important feature of GenePath is the ability to explain each relation from the constructed network by reporting on the logic that was used to infer it together with the corresponding experiments.

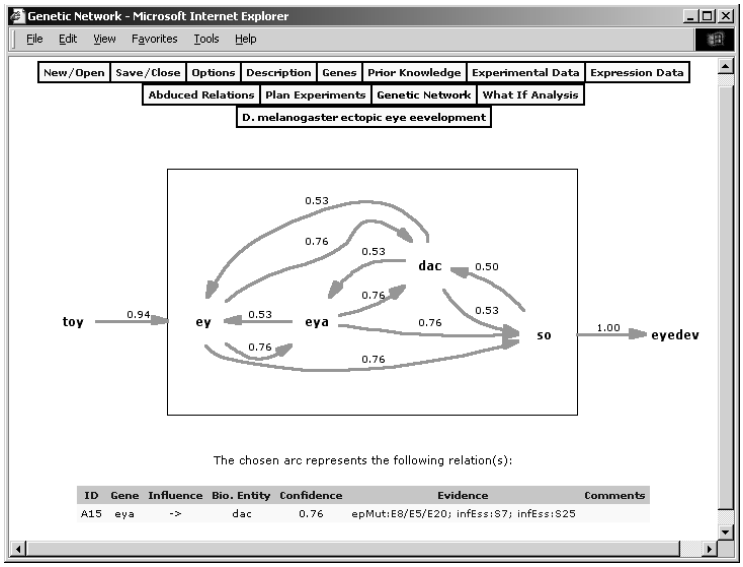

Figure 1: An example snapshot of GenePath (http://genepath.org) showing a regulatory network for *D. melanogaster* ectopic eye development and experimental evidence for epistasis of dac to eya genes (eya→dac).

GenePath thus formalizes genetic data analysis, facilitates the consideration of all the available data in a consistent manner, and allows for the examination of the large number of possible consequences of planned experiments. At the meeting we will report on recent extensions of GenePath that include (1) handling of uncertainties in genetic data by allowing a geneticist to assign confidence to experiments and background knowledge, (2) assistance in experiment planning, where GenePath can propose the set of the "cheapest" experiments to assert some new gene-to-gene relation, (3) inclusion of expression data, (4) interactive what if analysis, which eneables the user to on-the-fly test alternative hypothesis about the organism's regulatory mechanisms, and (5) handling of cyclic pathways through detection of genes that are involved in such network and approapriate visualizations.

1. Zupan, B., Demsar, J., Bratko, I., Juvan, P., Halter, J. A., Kuspa, A., and Shaulsky, G. (2003) *Bioinformatics 19*, 383-389.