

Crosstalk analysis of biological networks for improved pathway annotation

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Researchers at Stockholm University and Science for Life Laboratory have developed a new computer algorithm for analysing gene function called BinoX, which was e-published in *Nucleic Acids Research* on September 22 (Ogris et al., 2016a). The method, developed by Professor Erik Sonnhammer's research group, associates experimentally derived gene lists and known pathways. It does this in a new way, by employing a large gene network and determining if a gene list and a pathway has more network links than expected, using the binomial distribution. This is a significant advance over previous methods, and as a result BinoX yields substantially better accuracy. In particular, the improvement compared to the commonly used gene overlap enrichment method is massive; the sensitivity was benchmarked to increase by more than 60 times at the same time as the false positive rate was reduced to zero.

The paper demonstrates how BinoX can be used to find many biologically meaningful pathway annotations for gene sets from cancer and other diseases, which are not found by other methods.

"We believe that our new method will revolutionise the way researchers do pathway analysis and yield many new functional insights. The tools commonly used today are based on the gene overlap method which is very limited and unreliable. It often fails to find activated pathways, yet it often finds incorrect pathways. The reason for this is that it applies a statistical method to very sparse data that violate its statistical assumptions." says Erik Sonnhammer.

To make BinoX directly usable for other researchers, a public web server PathwaX.sbc.su.se (Ogris et al., 2016b) was set up for on-line pathway analysis of single gene sets, which applies the BinoX algorithm to all KEGG pathways and FunCoup networks. The FunCoup network database (FunCoup.sbc.su.se) of functional couplings between genes and gene products was also developed by Erik Sonnhammer's group. It currently contains comprehensive networks for human and 10 model organisms. For instance, the human network consists of over 18000 genes/proteins connected to each other with over 4 million links.

"BinoX works so well thanks to the high density of the FunCoup networks, which makes it possible to find many functional network links between [gene sets](#), even if they have no shared genes. This gives statistical power and makes it possible to find statistically significant enrichment of crosstalk." says Erik Sonnhammer.

More information: Christoph Ogris et al. A novel method for crosstalk analysis of biological networks: improving accuracy of pathway annotation, *Nucleic Acids Research* (2016). [DOI: 10.1093/nar/gkw849](https://doi.org/10.1093/nar/gkw849)

Provided by Stockholm University

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