Steffan et al.5 studied detecting signaling pathways in protein interaction networks as guided by expression data. They listed all pathway candidates in a protein interaction network using exhaustive search. They scored each candidate based on how similar are the expression profiles of its genes. The drawback of this method is that exhaustive graph search is highly inefficient.

Kelly et al.6 detected conserved signaling pathways between related organisms by performing global alignment between their protein interaction networks. They score each pathway in terms of probability of true homology between aligned pair of proteins, as well as probability of true interactions between pairs of proteins along the pathway. This approach detects conserved pathways only and requires coupling between two datasets.

Bebek et al.7 presented a method called PathFinder for finding new signaling pathways using association rules of known ones. The method starts with mining association rules for known pathways, guided by the knowledge of functional annotations of their proteins. The method then performs an exhaustive search for candidate pathways and outputs the candidates that have at least a certain number of the known association rules and an average interaction weight above a given threshold. Again, the drawback of this method is that exhaustive graph search is generally inefficient.

Gitter et al.8 presented a method for discovering signaling pathways by adding edge orientation to protein interaction networks. They select an optimal orientation of all edges in the network that maximizes the weights of all satisfied length-bound paths. A path is satisfied if it follows the same direction along its edges from a source node to a destination node. They prove that this problem is NP-hard. They provide two approximation algorithms for it based on available solution methods for weighted Boolean satisfiability, and a third algorithm based on probabilistic selection. The drawback of these methods is that they do not scale well with increasing the number of source and destination nodes and the required path length.