Techniques: Application of systems biology to absorption, distribution, metabolism, excretion and toxicity

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Techniques: Application of systems biology to absorption, distribution, metabolism, excretion and toxicity

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It is widely recognized that either predicting or determining the absorption, distribution, metabolism, excretion and toxicity (ADME/Tox) properties of molecules helps to prevent the failure of some compounds before they reach the clinic. Consequently, there has been considerable research into developing better *in silico*, *in vitro* and *in vivo* methods and models. Toxicogenomics, proteomics, metabonomics and pharmacogenomics represent the latest experimental approaches that can be combined with high-throughput molecular screening of targets to provide a view of the complete biological system that is modulated by a compound. The functional interpretation and relevance of these complex multidimensional data to the phenotype observed in humans is the focus of current research in toxicology. Multiple content databases, data mining and predictive modeling algorithms, visualization tools, and high-throughput data-analysis solutions are being integrated to form systems-ADME/Tox. In this review, we focus on the most recent advances and applications in this area.

Glossary

Monte Carlo optimization:
Random generation of values for uncertain variables to simulate a model. In the context of networks this method is used to find highly connected nodes in networks.

Nodes:
An object (genes and molecules) connected in a network.

Probabilistic graphical models:
A combination of graph theory and probability theory. They represent multivariate joint probability distributions via a product of terms, each of which involves only a few variables. The structure is represented by a graph that relates variables that appear in a common term.

Simulated annealing:
A technique to find a good solution to an optimization problem by trying random variations of the current solution. A worse variation is accepted as the new solution with a probability that decreases as the computation proceeds. The slower the cooling

schedule or rate of decrease, the more likely the algorithm is to find an optimal or near-optimal solution.

Superparamagnetic clustering:

This method assigns a ‘spin’ to each node and spins in a highly connected cluster fluctuate in a correlated fashion, which is used to identify these nodes.

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