

CUSTOMER STORY

A Theoretical Chemist Builds Biological Networks



EXECUTIVE SUMMARY

Coming from a different perspective is often helpful for discovering novel answers to difficult research questions, as Dr. Danail Bonchev from Virginia Commonwealth University can attest. Trained as a theoretical chemist, Dr. Bonchev has found Elsevier's Pathway Studio an invaluable tool in applying a systems biology approach to the study of a wide range of disorders, from cancers, to wound healing, and neurodegenerative diseases, looking for commonalities in the biological processes that underly these diverse diseases.

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At Virginia Commonwealth University’s Center for Study of Biological Complexity, theoretical chemist Danail Bonchev has been using Pathway Studio to create network views of the common genetic mechanisms of Parkinson’s, Alzheimer’s and Huntington’s disease.

How did a theoretician come to research these widespread neurodegenerative diseases? “Systems biology,” says Bonchev. “It started for me 13 years ago. I was not in life sciences, but I was dealing with small molecules. Chemical reactions are like small networks, and their analysis is very similar to that of biological networks. The difference is mainly in the scale, and in the more complex nature of biological networks.”

Excited by the new field of systems biology, Bonchev headed to VCU from Texas A&M to work on unraveling the complexity in biological networks. Since then, his research in network biology has been diverse, ranging from investigating lung adenocarcinoma, to searching for options to accelerate wound healing, to examining neurodegenerative diseases and studying longevity in model organisms. He has also explored the idea that a common pool of genes might be responsible for many types of cancer.

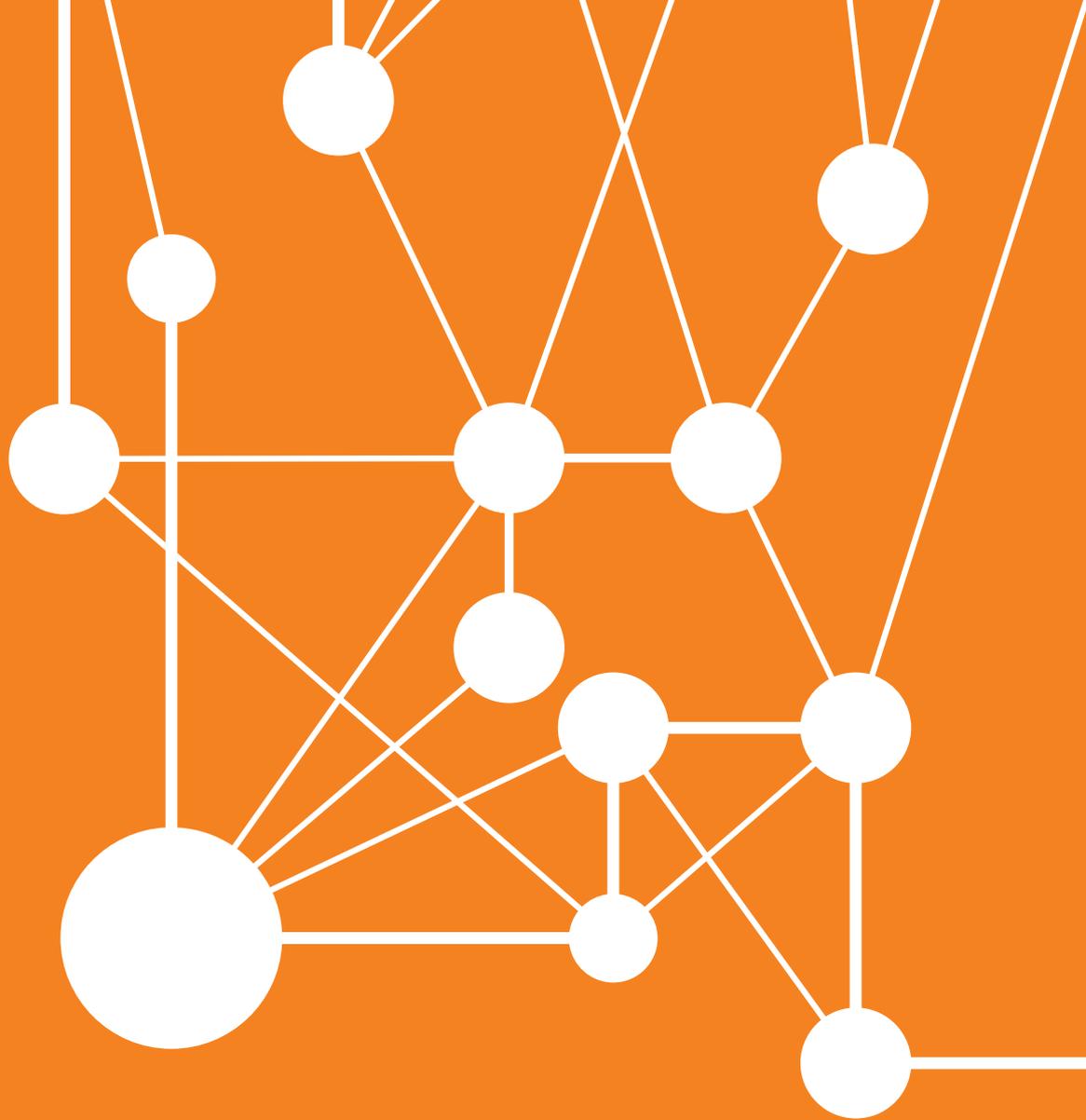
Across all of this work, he calls Pathway Studio his essential analytical tool for understanding biological processes. He also uses Pathway Studio in the graduate level classes he teaches, encouraging students to use the software in their own biological research. He believes that understanding network biology is critical to success in life sciences today, and he notes that students who learn to use Pathway Studio in classroom and research settings to make predictive models and understand the biological processes of diseases are more marketable to employers when they leave the university.

One of Bonchev’s early findings using Pathway Studio to build network maps, was that about half of the proteins in a living cell are specialized—associated with a single biological function- and conditions—while the other half have more generalized function and condition, and are active participants in many diseases. “If you build a network to show how these significant genes are involved in a disease, associations to other diseases start popping up,” he says. For instance, a protein-protein interaction network describing one type of cancer can often include links to as many as 10 other kinds of cancers, as well as other diseases like heart diseases, diabetes, obesity and other seemingly unrelated conditions. These networks can also help predict how therapeutics designed to target one disease pathway can have negative interactions with other pathways, leading to undesired off-target effects.

In January, Bonchev presented a webinar about recent work done with one of his former PhD students, Dr. Sreedevi Chandrasekaran, to summarize network views on several common neurodegenerative diseases. “Better understanding of the molecular mechanisms of these diseases will help identify new potentially effective drug candidates, as well as molecular markers that may help predict an increased chance for such disorders,” he explained.

Their study identified three routes for triggering the molecular mechanisms underlying Parkinson’s disease, 17 genes of interest from a Parkinson’s disease-associated microRNA regulatory network and 28 genes with close relationships to known Parkinson’s disease genes. “That ‘shortest-path’ algorithm in Pathway Studio is very, very useful for predicting key interactions when building relevant biological networks.” he says.

From their study, Bonchev and Chandrasekaran identified four genes present in both predicted Parkinson’s-related sets that are prime candidates for further experimental studies. Appropriately, Bonchev, the theoretician notes, “Our results so far are based on computational work and that type of work needs experimental verification to validate the predictions made.”



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