DELANO AWARD FOR COMPUTATIONAL BIOSCIENCES

Zhang takes the lead in protein modeling

By Courtney Chandler

The old adage "Function depends on structure" has been taught in protein biology courses for decades. Yet as some of the most complex and versatile biomolecules, proteins can be challenging to structurally define. Bioinformatics algorithms that predict 3D protein structure based on amino acid sequence are crucial for deducing the biological function of proteins that have not been structurally characterized by other methods.

Yang Zhang, a professor of biological chemistry and computational medicine and bioinformatics at the University of Michigan, has developed a repertoire of computational methods for predicting protein structure. For his work, Zhang is being awarded the American Society for Biochemistry and Molecular Biology's 2020 DeLano Award for Computational Biosciences.

After earning a Ph.D. in physics, Zhang began applying his background to translational science, partially because biomolecules were more tangible than the theoretical concepts of particle physics.

"As a scientist and human being, I want to understand how and why a protein that's coded from DNA can fold into a stable 3D structure," he said. "That is the secret of life."

His methods, including prediction algorithms I-TASSER and QUARK, have been listed consistently as top-tier based on fieldwide assessments. William Smith, a professor emeritus at the University of Michigan, described Zhang as "a worldwide leader in structural bioinformatics and protein structure modeling" in his letter nominating Zhang for the award.

For Zhang, the thrill of basic discovery goes hand-in-hand with translational impact. Both can be aided significantly by structural prediction and modeling algorithms.

"If we can computationally model protein shape, it will have a big impact on drug design and discovery, and on human health in general," he said. "But … it is also important for us to understand protein systems and the life science systems they are involved in outside of disease."

Zhang also has begun to harness the increased power that comes with machine learning, which enables computational systems to improve their function based on experience without explicit programming.

"Now you can tell a computer to learn the principles of a system even if you don't understand them, and the computer will generate a model," he said. "This will represent a big change for the field."

Yang Zhang

Enhancing protein structure prediction algorithms

Computation-based protein structural modeling provides a fast and inexpensive way to investigate protein-related scientific queries across many disciplines. However, partially due to the complicated nature of proteins and their folding patterns, the researchers behind computational programs have struggled to make protein structure prediction methods more accurate.

Using machine learning, Yang Zhang recently has leveraged big data from whole-genome sequencing studies to improve upon his existing computational models. This approach enables him to derive co-evolutionary relationships among proteins, which helps improve prediction of protein structure.

Zhang's award lecture, "Toward the solution of the protein structure prediction problem," will focus on the progress the field has made in improving protein prediction models and what the future will look like.

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