

Wayne State University
Department of Physics and Astronomy

Colloquium

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Progress Toward Accurate 3D Structure Prediction of Nucleic Acids

Methods for macromolecular structure determination cannot keep pace with the exponential growth of biological sequence databases. Thus, there is a need to develop tools for structure prediction from sequence and constraint information. Our goal is to fill this need by developing homology modeling and de novo structure prediction methods for RNA and DNA from natural or artificial sources. Homology modeling uses the known coordinates one sequence (i.e. the “template”) and automatically and optimally accommodates the substitutions, deletions, and insertions a different but similar sequence (i.e. the “query”). We have developed a new alignment method that incorporates secondary structure constraints. We have also developed new methods for optimizing highly distorted initial geometries that include long bond lengths due to deletions and overlaps due to substitutions and insertions. The homology modeling project is important for converting biological sequence databases into 3D structure databases. Modeling of protein-RNA complexes as large as the bacterial ribosome have been done. For RNA and DNA molecules with new folds, de novo structure prediction is required. Our method of de novo structure prediction combines the strengths of dynamic programming algorithms for secondary structure prediction, a novel BUILDER algorithm, and modified classical molecular dynamics simulations. The BUILDER algorithm uses a motif database derived from fragments of known X-ray and NMR structures. The classical dynamics calculations allow for structural distortions to be resolved using a customized forcefield and optimization algorithms. These methods are also being used to automatically design new self-assembling DNA/RNA nano-structures.

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4:00-5:00 PM

Room 245