

Synchrotrons and Biological Complexity: "The Action Is in the Interaction"

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The recombinant DNA era has enabled us to examine the stereochemistry that underlies the mechanisms of a wide variety of macromolecular interactions. The mechanisms of gene regulation, immune response, protein synthesis, signal transduction, viral assembly and infection, and RNA catalysis are just a few exciting examples where the interfaces discovered by high-resolution crystallography have redefined how we think about the chemistry of life processes. While the "blast and saturate" approach of genomics provides a rich context of ground-state structures, it does not address the issues of combinatorial complementarity and the chemical nature of specific functional interfaces. As crystalline asymmetric units required to solve these problems grow in mass and complexity, the crystals themselves often diminish in size, but the bright and tunable synchrotron beam comes to our rescue.

What are the limits/challenges of the single crystal diffraction approach to our assault on the complex biological systems? Are we being lured away from central questions by the ever increasing capabilities of synchrotron-based crystallography to solve bigger but not better complexes?