New and Notable

How to Assemble the Parts: Structures of Protein Complexes from their Components

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X-ray crystallography and nuclear magnetic resonance have been utilized to determine the atomic resolution structures of many proteins and protein domains. It has proven more challenging to apply these same techniques to determine the structures of large protein complexes. This is an important problem since the formation of protein complexes is often critical to regulating protein function. One way to make progress toward determining structural features of an assembly of proteins is to solve the structure of each member and then dock these individual structures together. Toward this goal, computational docking algorithms have been developed and employed with great success to predict important structural features in a wide range of protein-protein interactions. Recent work on the bacterial chemotaxis proteins CheA and CheW (reviewed in (1)) has demonstrated how long-range interprobe distance constraints between spin-labeled side chains can be obtained by modern pulsed electron paramagnetic resonance (EPR) methods and then utilized to guide the docking process.

The work by Hilger et al. in the article on page 3675 utilizes a similar site-directed spin-labeling approach to determine the structure for the functional Na^+/H^+ antiporter dimer in a liposome starting from the known atomic resolution structure of the monomer. The authors describe a new scheme to account for the dimensions and flexibility of the spin-labeled side chains in the structure refinement process. As pointed out in several recent publications and as referenced in the article, this is an important step forward in using EPR-derived interprobe distances to build structural models since it is the distance between the unpaired electrons of the two interacting spin labels that is measured and not the distances between Cα carbons of the protein backbone. This work also points out that it is possible to utilize other methods including molecular dynamics to model the conformationally accessible space for the spin labels during the refinement process. Such work is being pursued in many laboratories around the world at this time. It is anticipated that continuing efforts along these lines will lead to the development of even more robust structure refinement tools in the future. However, the current work by Hilger et al., and references cited therein, demonstrate that site-directed spin labeling and modern EPR provides an important new capability for structural studies on large protein assemblies.

REFERENCES

1. Borbat, P. P., J. H. Freed, M. Simon, B. R. Crane, and A. B. Crane. 2007. Measuring distances by pulsed dipolar ESR spectroscopy: spin-labeled histidine kinases in two-component signaling systems. *Methods Enzymol*. In press.

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