

Integrative modeling techniques applied to resolving ambiguous sequence assignment in DNAPKcs.

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Integrative modeling ideally represents information from multiple different sources and of varying quality as simple models that can be widely interpreted. In structural biology, we generally use these approaches to condense complex biophysical data and information into the 3D coordinates of a biomolecule or complex; however, they can also be applied to other representations, such as the assignment of sequence to low resolution structure. The recent crystal structure of the DNA-dependent protein kinase catalytic subunit (DNAPKcs) from Tom Blundell's group was solved at 4.3 angstroms and contains areas of structure where the amino acid identity cannot be assigned. We have developed a scoring function based on restraints derived from chemical cross-linking, selenomethionine anomalous scattering and statistical potential information that is systematically applied to the space of threading solutions using a Gibbs sampling scheme. Preliminary results are able to localize the unassigned structural helices within a few residues in sequence space and provides validation of the initial sequence assignment in structured areas.