

Automated
homology modeling

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MODELER for QUANTA

MODELER uses a comparative modeling methodology to rapidly build structural models for protein sequences without a known structure. Currently, the sequences of over a million proteins have been discovered with developing techniques in molecular biology. Experimental structure determination from X-ray crystallography and NMR spectroscopy has determined approximately 30,000 structures, a fraction of the known sequences. With the current emphasis on genome mapping projects, this gap between numbers of known sequences and experimentally solved structures continues to grow with no end in sight. MODELER aids this research process.

MODELER's unique methodology builds a structure by simultaneously satisfying spatial restraints and local molecular geometry. Structural models for a sequence can be constructed from structures of one or more homologous proteins in the same family. With about one third of known sequences related by homology to one or more known structures, homology modeling can provide useful



This model of Fatty acid-binding protein homolog 1 (EgFABP1) (EgDfi) from E. granulosus was generated with MODELER using multiple template modeling.

models that guide biochemical experiments far beyond the range of experimentally determined structures. In addition, these models can speed the process of experimental structure determination by molecular replacement phasing in X-ray crystallography. As more and more structures are experimentally determined, homology models can be constructed for an increasing variety of sequences.

Automated Homology Modeling

With a sequence alignment of the unknown protein and at least one other known structure, MODELER automatically creates a complete model for your protein using a network of empirically-derived spatial restraints. Because it optimizes both restraints and stereochemical geometry, MODELER provides an extremely accurate modeling method. With 40% sequence homology or more, MODELER can produce a 3D model in many respects equivalent to a medium resolution X-ray structure.

QUANTA and MODELER are integrated to give a complete homology modeling solution that contains sequence searching, multiple sequence alignment, and structure evaluation with the most extensive protein analysis tools available in one package. MODELER identifies problematic regions in the model that can be visualized on the model and plotted. With this powerful combination of functionality, accurate sequence alignment (which is critical to successful homology modeling) is optimized through cyclic realignment based on results of initial MODELER computations, especially for sequences with less than 40% sequence homology. The result is an accurate structural model for your sequence obtained quickly and with minimal effort.

The combination of MODELER with QUANTA's powerful protein structural analysis tools, allows you to develop an accurate working model for your structure more rapidly than ever before. Now, a model structure for your sequence is accessible

in a matter of hours, giving you new ideas and intuitive understanding of your target.

Required Software

- QUANTA 3D graphic program

Complementary Software

- Protein Health, Protein Modeling (includes Protein Health & Protein Design), and CHARMM

References

1. Fiser, A., Sali, A., *Methods in Enzymology*, **2003**, 374, 463-493.
2. Sánchez, R., Sali, A., *Protein Structure Prediction: Methods and Protocols*, **2000**, 97-129.

System Requirements:

QUANTA runs on Linux and SGI work stations.

Dial Box is supported for QUANTA on both the Linux and SGI IRIX platforms.

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