

# Protein Modeling Tools

The School of Theoretical Modeling

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# Protein modeling for every lab

## Everyday lab life

- Experiment design
- Protein Structure determination
- Structural modeling of the experimental results

## Pictures Movies

- Preparation of illustrations for manuscripts and presentations
- Visualization of large protein molecules and their ligands

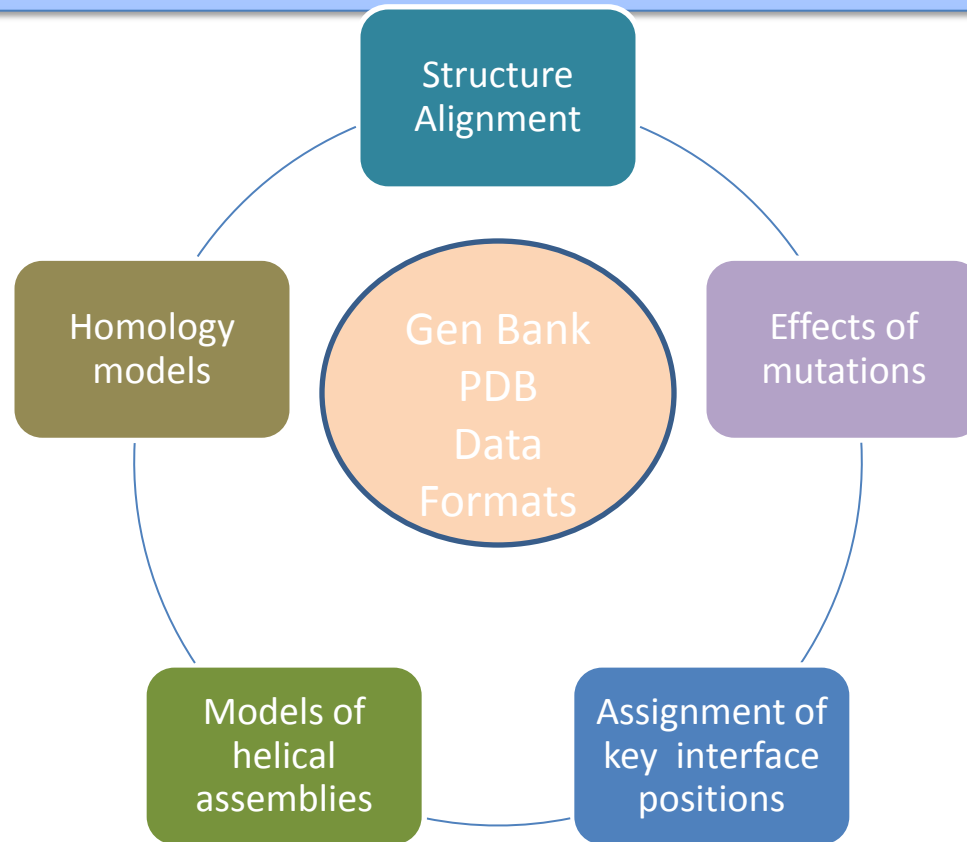
## Organizing data

- Produce and share structural data
- Share models of peptides and proteins
- Plan collaborative research

# New Protein Modeling Tools

- Structure alignment of proteins
- Secondary structure interfaces: Assignment of key interface positions (Leucine Zipper Nomenclature)
- Sequence and structure similarities in 3D
- Prediction of the effects of mutations on protein structure
- Modeling of homologous proteins
- Structure of helical assemblies

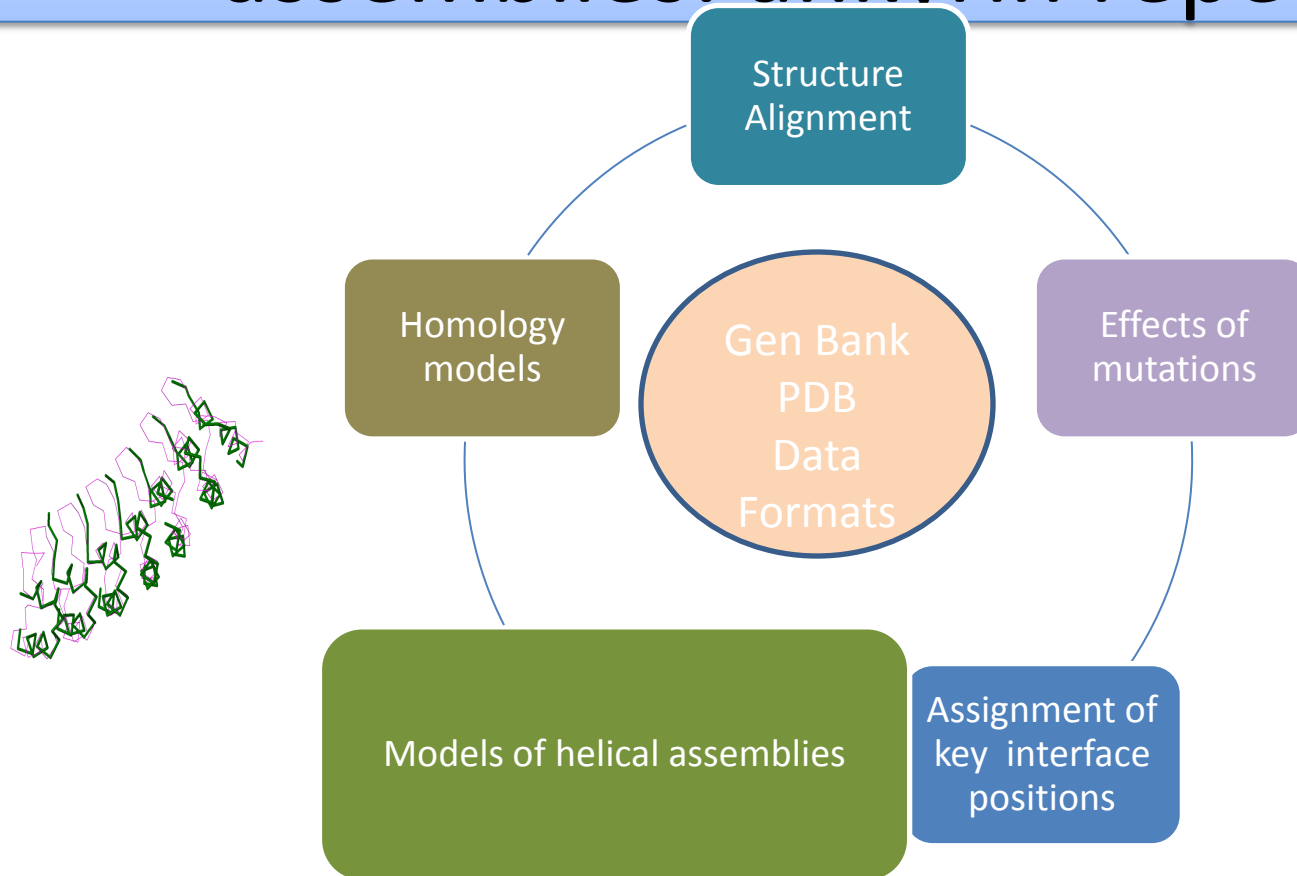
# Technology Corner



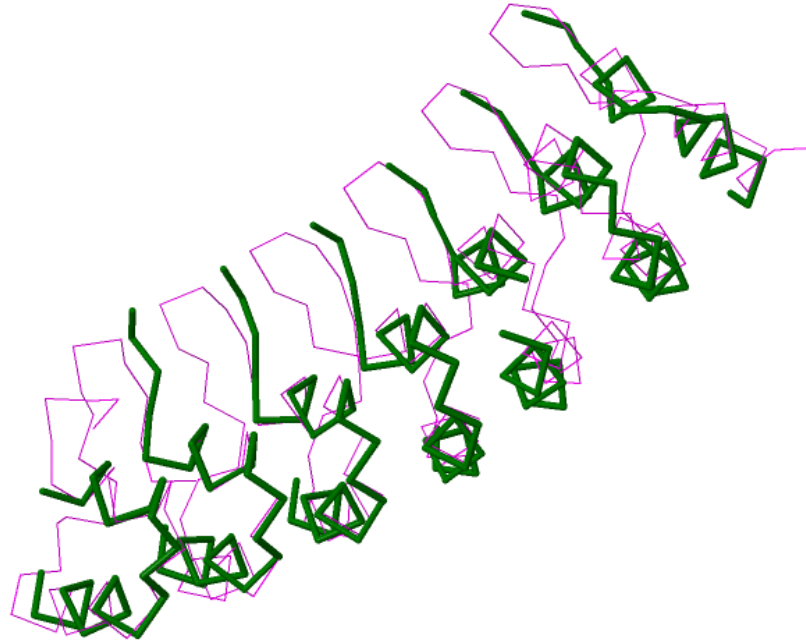
# Structure alignment of proteins

Amino acid sequence alignment and structure alignment are widely used to analyze differences in protein specificity and affinity toward ligands, introduce mutations and predict effect of the mutations on protein structure and behavior. Two proteins with similar fold when aligned (or superimposed) show structurally equivalent positions. If two proteins are not similar in amino acid sequence but are similar in three-dimensional structure, structure similarity is used to improve the amino acid sequence alignment.

# Structure modeling of helical assemblies: ankyrin repeats



# Predicted structure of gankyrin



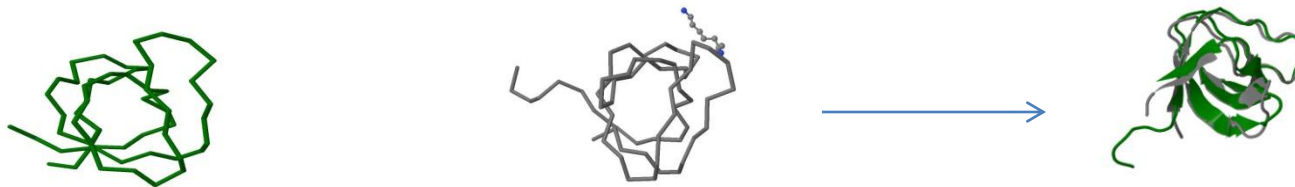
# Structure alignment of proteins

## *G. gallus* $\alpha$ -spectrin and *M. musculus* myosin 1E

### Amino acid sequence alignment

- SpecA 963 -----MDETGKE----LVLAL-YDYQ---EK--SPREVT-----
- M1E 1018 KVPDQGVAGVRRQTSSRPPPAGGRPKPQPKPKPQVP-----QCKAL-YAYD---AQ--DTDELSFN--
- 
- SpecA 988 MKKGDILTLLNS-TN----KDW-WKTEVN--GR-QGFVPAAYVKKLD----- /1uue/
- M1E 1071 --ANDIIDIIKED-P----SGW-WTGRLR--GK-QGLFPNNYVTKI----- /2xmf/

### Structure alignment



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# New Topics in Protein Modeling

The School of Theoretical Modeling teaches course “**Protein Modeling**” for people who work in the field of structure of biological macromolecules. New topics are constantly added to the course.

Recent new topics and introductory movies (Youtube and LabTube.tv) :

“**Structure Alignment of Proteins**” <http://youtu.be/TIH0NqqDkPI>

“**Helix-helix interfaces: Key positions**” <http://youtu.be/SR-SiK23o9Q>  
<http://www.labtube.tv/playVideo.aspx?vid=156804>

“**Sequence Similarities in 3D**” <http://youtu.be/ec5LMiGVTLc>  
<http://www.labtube.tv/playVideo.aspx?vid=160933>

“**Prediction of the tertiary structure of Helical Assemblies**”  
[http://lnkd.in/d\\_qUCf3](http://lnkd.in/d_qUCf3)

“**Prediction of the effect of mutations on protein structure**”  
“**Homology Modeling**”

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Youtube:

<http://youtu.be/oBIOL3UXaS0> <http://youtu.be/SR-SiK23o9Q>

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- One day Course
- Semester Course
- Summer Course

Registration: [www.schtm.org](http://www.schtm.org)

E-mail: [info@schtm.org](mailto:info@schtm.org)

Phone: (240) 381-2383

Fax: (202) 508-3799

- Cost
  - \$370 per person – One-day
  - 1,400 per person – Semester or Summer Course
- Course is also available on-line

# Technology Corner

- Program Library - a collection of tools for Protein Modeling
- Input and output data: in standard GenBank and PDB formats
- Visualization of protein models - JMol

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# Methods

- **Coordinate system of the layer** (Kurochkina, 2008) allows to find the best superimposition of two proteins and generate a list of amino acid residues located at equivalent positions.
- **Specific sequence combinations** at parallel and antiparallel helix-helix interfaces. (Kurochkina, 2007, 2008) are used to model proteins and their interactions with ligands, predict protein conformation and effects of mutations on protein structure
- **Helical edges** involved in protein-protein interactions contribute to understanding and prediction of shapes of the assemblies (Kurochkina, 2010)
- **Chirality of noncovalent interactions/assemblies** is a determinant of specificity of protein-protein interactions (Kurochkina & Iadarola, 2015)

# Publications

- Barbara KE, Willis KA, Haley TM, Demino SJ, Santangelo VGM 2007 Coiled coil structures and transcription: an analysis of the *S. cerevisiae* coilome. *Mol Genet Genomics* (2007) **278**, 135
- Gernert KM, Surles MC, Labean TH, Richardson JS, Richardson DC 1(995) Alacoil: a very tight, antiparallel coiled-coil of helices. *Protein Sci.* 4, 2252
- Harbury PB, Zhang T, Kim PS, Alber T (1993). A switch between two-, three- and four-stranded coiled coils in GCN4 leucine zipper mutants. *Science* **262**, 1401
- Krylov D, Mikhailenko I, Vinson C (1994). A thermodynamic scale for leucine zipper stability and dimerization specificity: e and g interhelical interactions. *EMBO J.* **13**, 2849
- Kurochkina N (2007) Amino acid composition of parallel helix-helix interfaces. *J. Theoretical Biology* **247**, 110
- Kurochkina N (2008) Specific sequence combinations at parallel and antiparallel helix-helix interfaces. *J. Theoretical Biology* **255**, 188
- Kurochkina N, Choekyi T (2011) Helix-helix interfaces and ligand binding. *J. Theoretical Biology* **283**, 92
- N. Kurochkina, (2010) Helix-helix interactions and their impact on protein motifs and assemblies. *J. Theoretical Biology* **284**, 585 (2010).
- O'Shea EK, Klemm JD, Kim PS, Alber T (1991). Crystal structure of GCN4 leucine zipper, a two-stranded parallel coiled coil. *Science* **254**, 539
- Parry DAD, Fraser RDB, Squire JM (2008) Fifty years of coiled-coils and  $\alpha$ -helical bundles: A close relationship between sequence and structure. *J Struct Biol* **163**, 258
- **Kurochkina, N.**, Iadarola, M. (2015) Helical assemblies: Structure determinants. *Journal of Theoretical Biology*. 369C 80-84  
<http://dx.doi.org/10.1016/j.jtbi.2015.01.012>
- **Kurochkina, N.**, Guha, U., Lu, Z. (2015) SH Domains and Epidermal Growth Factor Receptors. In: SH Domains. Structure, mechanisms, and applications. Ed: Kurochkina. Springer, 2015.
- **Kurochkina, N.**, Iadarola M. (2015) SH Domains and Helical Assemblies. In: SH Domains. Structure, mechanisms, and applications. Ed: Kurochkina. Springer, 2015.
- SH Domains. Structure, mechanisms, and applications. Ed: **Kurochkina**. Springer, 2015.

# Recent collaborations and joint publications with NHGRI and NCI laboratories, CC/NIH

- Yardeni, T., Choekyi, T., Jacobs, K., Ciccone, C., Patzel, K., Anikster, Y., Gahl, W. A., N. Kurochkina, Huizing, M. (2011) Identification, Tissue Distribution and Molecular Modeling of Novel Human Isoforms of the Key Enzyme in Sialic Acid Synthesis, UDP-GlcNAc 2-epimerase/ManNAc Kinase: *Biochemistry*, 50, 8914.
- N. Kurochkina, Guha, U. (2012) SH3 domains: modules of protein-protein interactions. *Biophysical Reviews* DOI: 10.1007/s12551-012-0081-z. On-line Edition.
- Yardeni, T., Jacobs, K., Niethamer, T. K., Ciccone, C., Anikster, Y., N. Kurochkina, Gahl, W. A., Huizing, M. (2012) Murine isoforms of UDP-GlcNAc 2-epimerase/ManNAc kinase: Secondary structures, expression profiles, and response to ManNAc therapy. *Glycoconj J.* 2013 6:609-18. doi: 10.1007/s10719-012-9459-1. Epub 2012 Dec 25.
- N. Kurochkina, Guha, U. (2013) SH3 domains: modules of protein-protein interactions. *Biophysical Reviews* 5 (1) 29-39.
- **Kurochkina, N.**, Iadarola, M. (2015) Helical assemblies: Structure determinants. *Journal of Theoretical Biology.* 369C 80-84 <http://dx.doi.org/10.1016/j.jtbi.2015.01.012>
- **Kurochkina, N.**, Guha, U., Lu, Z. (2015) SH Domains and Epidermal Growth Factor Receptors. In: *SH Domains. Structure, mechanisms, and applications.* Ed: Kurochkina. Springer, 2015.
- **Kurochkina, N.**, Iadarola M. (2015) SH Domains and Helical Assemblies. In: *SH Domains. Structure, mechanisms, and applications.* Ed: Kurochkina. Springer, 2015.
- *SH Domains. Structure, mechanisms, and applications.* Ed: **Kurochkina.** Springer, 2015.

# Modeling of GNE/MNK enzyme

Our collaborative on modeling of GNE/MNK enzyme with Dr. M. Huizing laboratory (NHGRI/NIH) was published in Glycobiology: [Molecular modeling of the bifunctional enzyme UDP-GlcNAc 2-epimerase/ManNAc kinase and predictions of structural effects of mutations associated with HIBM and sialuria.](#) **Kurochkina N, Yardeni T, Huizing M.** Glycobiology. 2010 Mar;20(3):322-37.

New crystallographic structures of MNK in complex with substrate, UDP and inhibitors were described in the Journal of Biological Chemistry: Crystal structures of N-acetylmannosamine kinase provide insights into enzyme activity and inhibition. **Martinez, J., Nguyen, L.D., Tauberger, E., Hinderlich, S., Reutter, W., Fan, H., Saenger, W., Moniot, S.** (2012) J.Biol.Chem.287: 13656 . (<http://www.jbc.org/content/287/17/13656.long> )

Good correspondence of the predicted model and experimental results.

# Links

- The School of Theoretical Modeling [www.schtm.org](http://www.schtm.org)
- Protein Data Bank (PDB) [www.rcsb.org](http://www.rcsb.org)
- Molecular graphics [www.jmol.org](http://www.jmol.org)