

CS597A Structural Bioinformatics

Thomas Funkhouser
Princeton University
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Outline

Overview of structural bioinformatics

- Goals
- Challenges
- Applications

Overview of course

- Goals
- Lectures
- Coursework
- Projects

Bioinformatics

Definition:

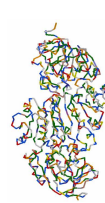
- "The collection, archiving, organization, and interpretation of biological data." [Orengo, 2003]

Generally speaking:

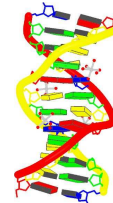
- Large biological data sets
- Computer representations and algorithms
- Storage, analysis, visualization, prediction, and design

Structural Bioinformatics

Focus on data sets with molecular structure



Proteins
[RCSB]



DNA
[NDB]

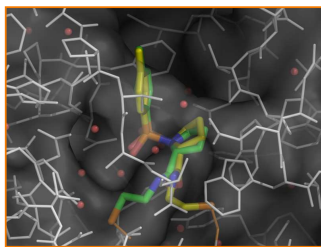


Small Molecules
[CCDC]

Structural Bioinformatics

Motivation 1:

- Detailed understanding of molecular interactions

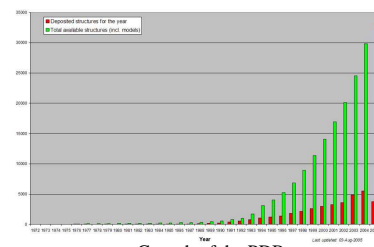


[pymol.sourceforge.net]

Structural Bioinformatics

Motivation 2:

- Lots of structural data is becoming available



Growth of the PDB
[RCSB]

Structural Bioinformatics



Goals:

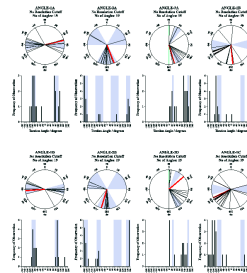
- Analysis
- Visualization
- Comparison
- Prediction
- Design

Structural Bioinformatics



Goals:

- ∅ Analysis
- Visualization
- Comparison
- Prediction
- Design



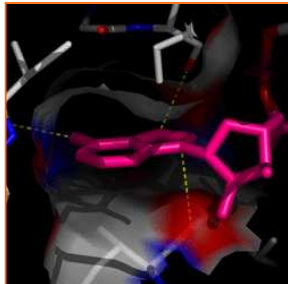
Geometrical and conformational analysis of Haem Ligand (7cat)
[Karmirantzou and Thornton]

Structural Bioinformatics



Goals:

- Analysis
- ∅ Visualization
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- Design



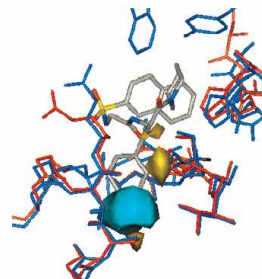
Adenine ring from FAD bound to Luxy
[Stockwell05]

Structural Bioinformatics



Goals:

- Analysis
- Visualization
- ∅ Comparison
- Prediction
- Design



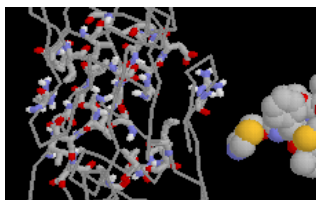
Comparison of S1 binding pockets of thrombin (blue) and trypsin (red).
Cyan (yellow) regions are more favorable for trypsin (thrombin) when binding NAPAP (gray).
[Katzenholtz00]

Structural Bioinformatics



Goals:

- Analysis
- Visualization
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- ∅ Prediction
- Design



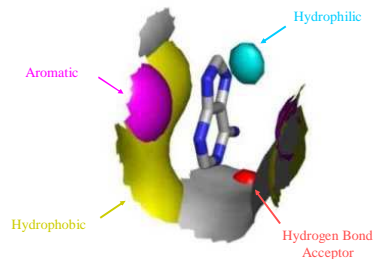
Simulation of inhibitor Ritonavir binding to HIV protease
[Protein Explorer]

Structural Bioinformatics



Goals:

- Analysis
- Visualization
- Comparison
- Prediction
- ∅ Design



Model derived from all adenine binding sites in PDB
[Stockwell05]

Structural Bioinformatics



Research challenges:

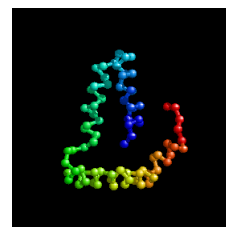
- Structure determination
- Binding site detection
- Binding site modeling
- Binding site matching
- Binding prediction
- Molecular design
- etc.

Structural Bioinformatics



Research challenges:

- Structure determination
- Binding site detection
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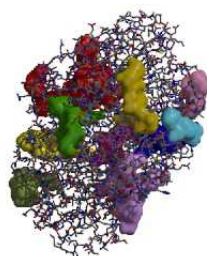
Protein Folding Simulation
[David Jones]

Structural Bioinformatics



Research challenges:

- Structure determination
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- etc.



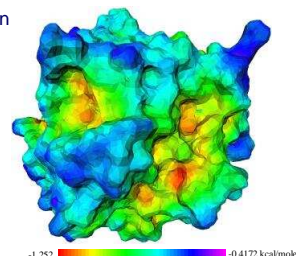
Surface Clefts detected in 1b14
[Surfnet]

Structural Bioinformatics



Research challenges:

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- etc.



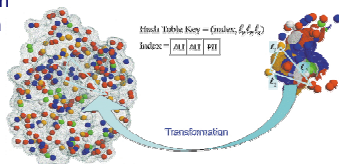
Surface potential for the Carboxypeptidase A
[Continuum Dynamics]

Structural Bioinformatics



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- etc.



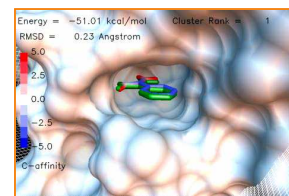
[Shulman-Peleg04]

Structural Bioinformatics



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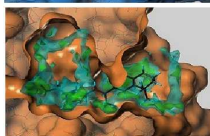
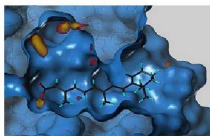
Benzamidine binding to beta-Trypsin (3ptb)
[AutoDock]

Structural Bioinformatics



Research challenges:

- Structure determination
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- Binding site matching
- Binding prediction
- Molecular design
- etc.



Superpose 1H33 maps for the binding site of the protein-ligand complex 1L218. The ligand is red (rod ends), blue (binding site where map for substrate) (orange) probe. Amber (binding site where map for substrate) (orange) probe. [CCDC]

Structural Bioinformatics



Applications:

- Biology
- Medicine
- Agriculture
- Industry
- etc.

Outline



Overview of structural bioinformatics

- Goals
- Challenges
- Applications

Overview of course ←

- Goals
- Lectures
- Coursework
- Projects

CS597A



Goals

- Survey current methods in structural bioinformatics
- Investigate specific research problems in depth
- Build shared infrastructure for research
- Build links across disciplines

Lectures



Class meetings:

- One topic per meeting
- 50% lecture
- 50% discussion

Speakers:

- Professors
- Guests
- Students

Date	Topic	Speaker	Book	Papers	Resources	Notes
Jan 10	Chemical structure	Ch 1	1001			
Jan 17	Protein structure determination	Ch 2	1001			
Jan 24	Protein structure prediction	Ch 19	1001			
Jan 31	Protein-protein alignment	Ch 16	1001			
Feb 7	Binding site detection (primary)	-	1001			
Feb 14	Binding site detection (tertiary)	-	1001			
Feb 21	Binding site matching (primary)	-	1001			
Feb 28	Binding site matching (tertiary)	-	1001			
Mar 7	Protein-protein docking I	Ch 22	1001			
Mar 14	Protein-protein docking II	-	1001			
Mar 21	Protein-protein docking III	-	1001			
Mar 28	Protein-protein docking IV	-	1001			
Apr 4	Protein-protein docking V	-	1001			
Apr 11	Protein-protein docking VI	-	1001			
Apr 18	Protein-protein docking VII	-	1001			
Apr 25	Protein-protein docking VIII	-	1001			
May 2	Protein-protein docking IX	-	1001			
May 9	Protein-protein docking X	-	1001			
May 16	Protein-protein docking XI	-	1001			
May 23	Protein-protein docking XII	-	1001			
May 30	Protein-protein docking XIII	-	1001			
Jun 6	Protein-protein docking XIV	-	1001			
Jun 13	Protein-protein docking XV	-	1001			
Jun 20	Protein-protein docking XVI	-	1001			
Jun 27	Protein-protein docking XVII	-	1001			
Jul 4	Protein-protein docking XVIII	-	1001			
Jul 11	Protein-protein docking XIX	-	1001			
Jul 18	Protein-protein docking XX	-	1001			
Jul 25	Protein-protein docking XXI	-	1001			
Aug 1	Protein-protein docking XXII	-	1001			
Aug 8	Protein-protein docking XXIII	-	1001			
Aug 15	Protein-protein docking XXIV	-	1001			
Aug 22	Protein-protein docking XXV	-	1001			
Aug 29	Protein-protein docking XXVI	-	1001			
Sep 5	Protein-protein docking XXVII	-	1001			
Sep 12	Protein-protein docking XXVIII	-	1001			
Sep 19	Protein-protein docking XXIX	-	1001			
Sep 26	Protein-protein docking XXX	-	1001			
Oct 3	Protein-protein docking XXXI	-	1001			
Oct 10	Protein-protein docking XXXII	-	1001			
Oct 17	Protein-protein docking XXXIII	-	1001			
Oct 24	Protein-protein docking XXXIV	-	1001			
Oct 31	Protein-protein docking XXXV	-	1001			
Nov 7	Protein-protein docking XXXVI	-	1001			
Nov 14	Protein-protein docking XXXVII	-	1001			
Nov 21	Protein-protein docking XXXVIII	-	1001			
Nov 28	Protein-protein docking XXXIX	-	1001			
Dec 5	Protein-protein docking XL	-	1001			
Dec 12	Protein-protein docking XLI	-	1001			
Dec 19	Protein-protein docking XLII	-	1001			
Dec 26	Protein-protein docking XLIII	-	1001			
Jan 2, 2008	Protein-protein docking XLIV	-	1001			

Lectures



Student presentations:

- Choose topic from schedule
- Submit list of relevant papers/resources
- 15-20 minute presentation
- Lead discussion afterwards

Readings



Book

- P.E. Bourne, H. Weissig, "Structural Bioinformatics," Wiley-Liss, 2003.

Papers

- Read ~1 paper for each lecture
- Be prepared for class discussion



Course Projects



Description

- Investigate research problem
- Any problem(s) related to course
- Multi-disciplinary teams (if possible)

Dates

- Proposal (Oct 19)
- Presentation I (Nov 16)
- Presentation II (Dec 14)
- Presentation III (~Jan 15)
- Written report (~Jan 15)

Course Projects

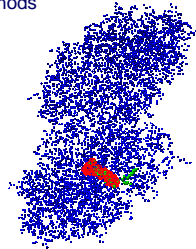


Example projects

- Develop new method
- Evaluate/compare existing methods
- Combine methods in system
- Apply method

Key elements

- Investigation
- Evaluation



Wrap Up



Students' to do list:

- Hand in survey questionnaire
- Send me a picture of yourself by email
- Sign up for in-class presentations
- Start thinking about project topics