EXPERIMENT 12: STRUCTURE VALIDATION

Dr. Zhiyi Wei
SUSTC

nature International weekly journal of science

comments on this story

Stories by subject

Cell and molecular biology
Health and medicine
Lab life

Published online 22 December 2009 | *Nature* **462**, 970 (2009) | doi:10.1038/462970a

News

Fraud rocks protein community

University finds that researcher falsified data supporting 11 protein structures.

Brendan Borrell

All of the disputed structures had been deposited in the Protein Data Bank (PBD). So far, only the dengue virus NS3 serine protease has been both removed from the PDB and retracted by *The Journal of Biological Chemistry*, where it was first published in 1999 (ref. 1). The results in that paper sent the hunt for drugs against this protease down a blind alley. Stanley Watowich, a virus expert at the University of Texas Medical Branch in Galveston, says that two of Murthy's structures[1,3,4] were among 14 included in a virtual dengue drug-screening project run over the past year. This modelled how candidate molecules would interact with dengue proteins, using IBM's World Community Grid — a public computing network set up to harness unused computer time for projects of benefit to humanity. "Screening against the Murthy structures took about two months," says Watowich, "and it is unfortunate that this time could not have been more productively spent."

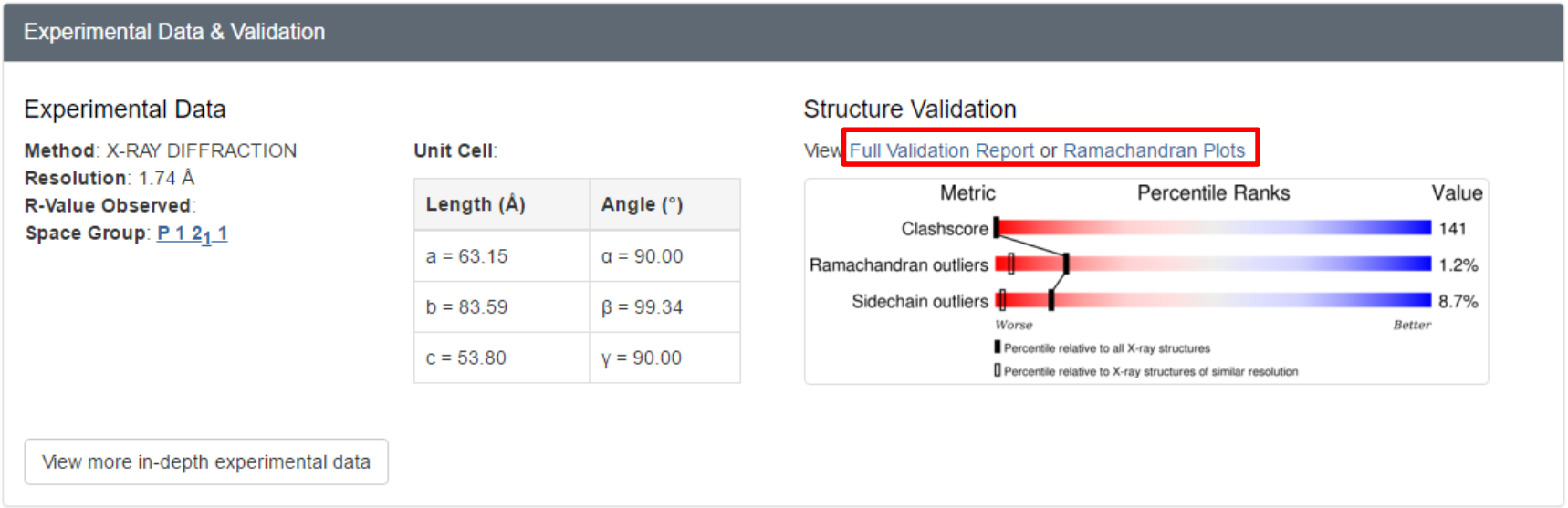
UAB Statement on Protein Data Bank Issues
https://www.uab.edu/reporterarchive/71570-uab-statement-on-protein-data-bank-issues

1BEF, 1CMW, 1DF9/2QID, 1G40, 1G44,
1L6L, 2OU1, 1RID, 1Y8E, 2A01, and 2HR0

Method

- Model validation
  - Geometry
  - Dihedral angels: Ramachandran plot
  - Sterics and packing: all atom clash
  - B-factor
- Deposited model quality check with PDB database

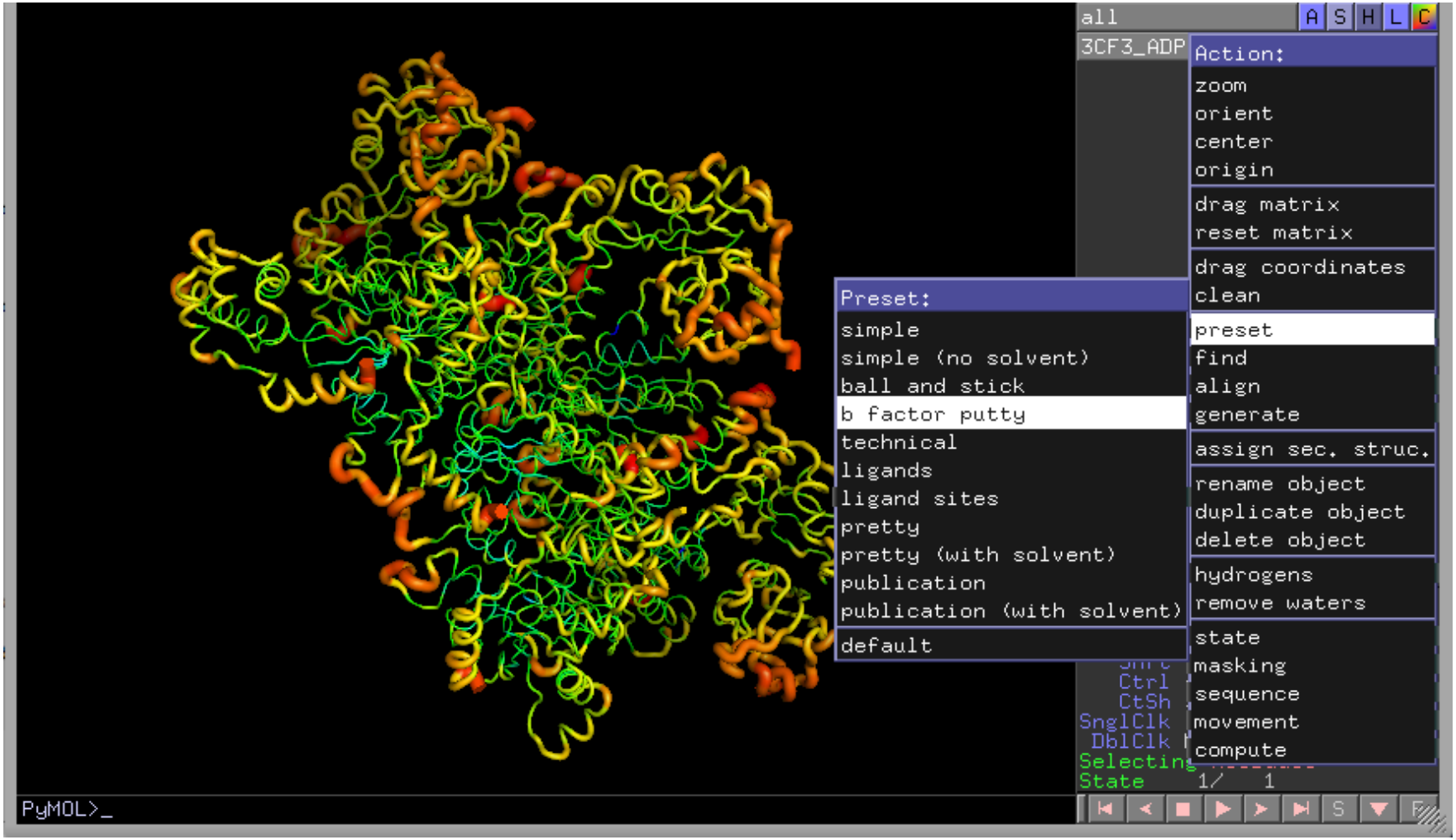
Validation reports in PDB



A structure with

- good quality
  - Ramachandran outliers 0%
  - Ramachandran favored >95%
- reasonable quality
  - Ramachandran outliers <1%
  - Ramachandran favored >90%

B-factor analysis in PyMOL



Tasks

1. Analyze the two Hemoglobin structures (4HHB and 2HHB) in PDB
   - Which one is better? Why?
2. Analyze the 2HHB structure in PyMOL considering the effects of B-factor
   - Which region is more flexible? Which region is more stable and reliable?
3. Investigate the Murthy's faked structure (1BEF) using MolProbity sever (http://molprobity.biochem.duke.edu/)
   - Why this structure is faked?
   - You can do it @home

Lab report format

- Title
- Your name and student No.
- Introduction
- Methods
- Results
- Conclusions