 Nucleic Acids Research, 2000, Vol. 28, No. 1 **283–285**

ProTherm, version 2.0: thermodynamic database for proteins and mutants

M. Michael Gromiha, Jianghong An, Hidetoshi Kono, Motohisa Oobatake, Hatsuho Uedaira, P. Prabakaran and Akinori Sarai*

Tsukuba Life Science Center, The Institute of Physical and Chemical Research (RIKEN), 3-1-1 Koyadai, Tsukuba, Ibaraki 305-0074, Japan

Received September 20, 1999; Revised and Accepted September 22, 1999

ABSTRACT

ProTherm 2.0 is the second release of the Thermodynamic Database for Proteins and Mutants that includes numerical data for several thermodynamic parameters, structural information, experimental methods and conditions, functional and literature information. The present release contains >5500 entries, an ~67% increase over the previous version. In addition, we have included information about reversibility of data, details about buffer and ion concentrations and the surrounding residues in space for all mutants. A WWW interface enables users to search data based on various conditions with different sorting options for outputs. Further, ProTherm has links with other structural and literature databases, and the mutation sites and surrounding residues are automatically mapped on the structures and can be directly viewed through 3DinSight developed in our laboratory. The ProTherm database is freely available through the WWW at http://www.rtc.riken.go.jp/protherm.html

INTRODUCTION

Thermodynamic data for proteins are important to understand the mechanism of protein folding and stability. In recent years, the accumulation of thermodynamic data has been steadily increasing. Pfeil (1) collected a set of data for several thermodynamic parameters from experimental studies that had been published up to 1996. Kawabata *et al*. (2) constructed a Protein Mutant Database (PMD) for literature information, which covers natural and artificial mutants of proteins. Recently, we have developed an electronically accessible database, ProTherm (3), which includes several aspects of thermodynamic data (unfolding Gibbs free energy change, enthalpy change, heat capacity change, transition temperature, activity etc.), structural information (secondary structure, accessibility etc.), measuring methods, experimental conditions and literature information. The current release 2.0 of ProTherm contains over 5500 entries that cover the up-to-date experimental data. We have developed a WWW interface to facilitate searching the database and sorting outputs.

MAIN DEVELOPMENTS IN VERSION 2.0

- Release 2.0 contains 5542 entries, 67% more than release 1.0 (Table 1).

Table 1. Increase of entries in ProTherm for different datasets

Dataset	Release 1.0	Release 2.0	% Increase
Total	3317	5542	67.1
Solvent accessibility[a]			
Buried	1317	1854	40.8
Partially buried	918	1105	20.4
Exposed	826	1098	32.9
Mutation type			
Wild type	429	1599	272.7
Single	2434	3312	36.1
Double	353	480	36.0
Multiple	101	151	49.5
Secondary structure			
Helix	1241	1594	28.4
Strand	789	1071	35.7
Turn	242	402	66.1
Coil	846	1078	27.4
Measurement			
Circular dichroism	1709	2450	43.4
Fluorescence	1052	1455	38.3
Calorimetry (DSC)	489	1397	185.7
Method			
Thermal	1628	2869	76.2
GdnHCl	1094	1697	55.1
Urea	573	942	64.4
Literature			
Number of proteins	61	194	218.0
Number of articles	245	599	144.5

[a]Buried: ASA <20%; partially buried: 20% < ASA < 50%; exposed: ASA >50%.

*To whom correspondence should be addressed. Tel: +81 298 36 9082; Fax: +81 298 36 9080; Email: sarai@rtc.riken.go.jp
Present addresses:
Hidetoshi Kono, Department of Chemistry, Pennsylvania University, 231S 34 Street, PA 19104, USA
Motohisa Oobatake, Faculty of Science and Technology, Meijo University, 1-501 Shiogamaguchi, Tenpaku-ku, Nagoya 468-8502, Japan

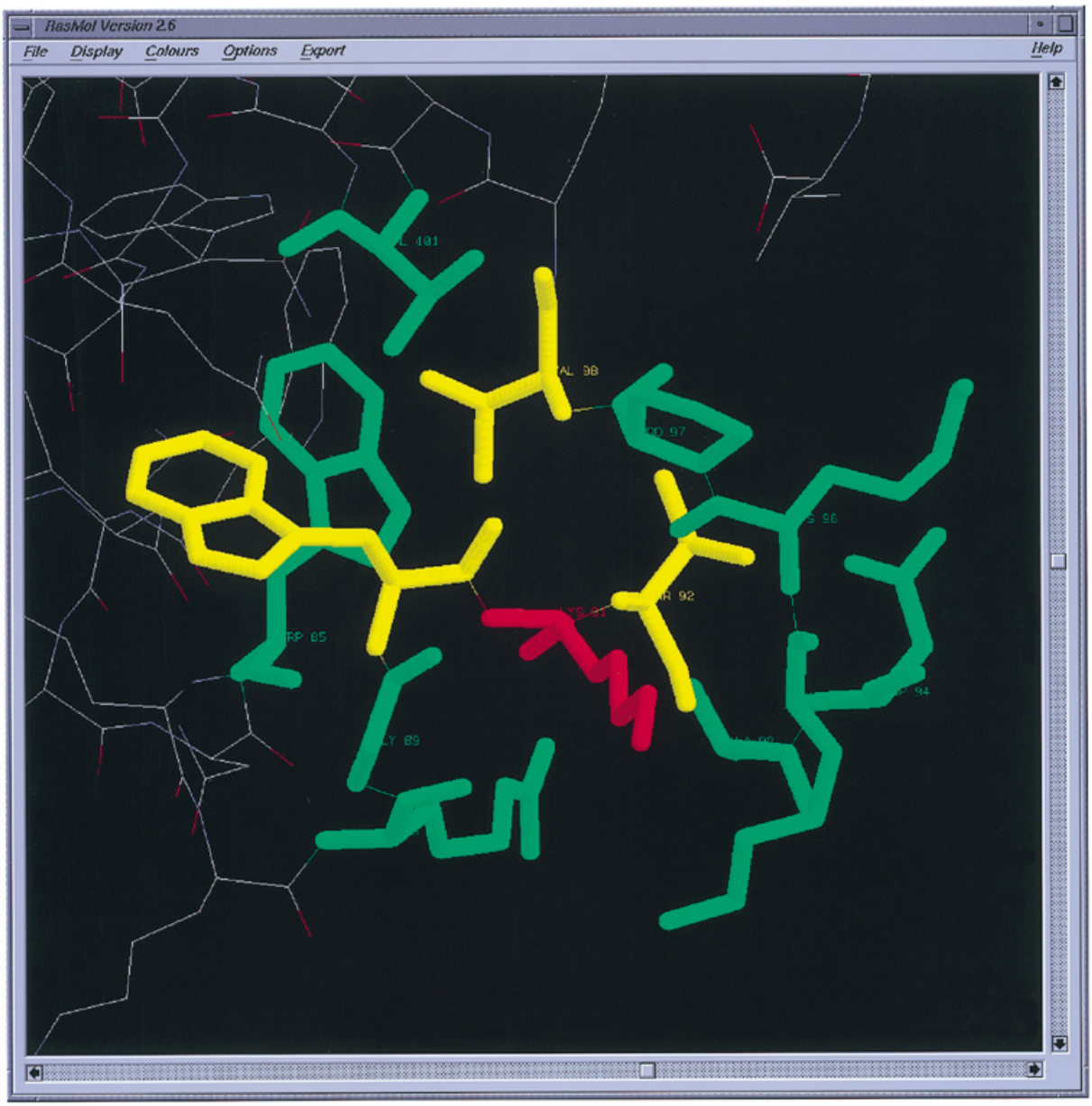

Figure 1. Display of protein mutants and surrounding residues by RasMol. As an example, we show the surrounding residues of Lys 91 in Ribonuclease H (2RN2). The central residue, surrounding residues within 4 Å and surrounding residues between 4 and 8 Å are shown in red, yellow and green, respectively.

- Includes additional information on reversibility for all data.
- Details about buffers and ions and their concentrations for each entry.
- Information about the surrounding residues around each mutant in space for a specific radius (e.g. 0–4 and 4–8 Å).
- Display option to view all mutants and surrounding residues through RasMol (4). An example is shown in Figure 1.

FEATURES AVAILABLE AT THE ProTherm SITE

All details about search options, tutorials and database statistics may be accessed by clicking the text links of the home page.

Each entry in the database contains: (i) structural information, (ii) thermodynamic data obtained from thermal and denaturant denaturation experiments, (iii) experimental methods and conditions, (iv) functional and (v) literature information.

The solvent accessibilities of all residues were computed using the program ASC (5,6) as described in our earlier article (7).

DATABASE STATISTICS

Details about the increase of data in release 2.0 for secondary structures, mutation types, various regions of solvent accessibility (ASA), different experimental measurements and methods are

presented in Table 1. We observed a substantial increase of data in most of the classified groups.

ACCESS TO ProTherm USING THE WWW

The ProTherm database can be directly accessed online using the WWW server at http://www.rtc.riken.go.jp/protherm.html . At present, cross references to Enzyme Code, EC (http://www.expasy.ch/sprot/enzyme.html); Protein Mutant Database, PMD (ftp://ftp.nig.ac.jp/pub/db/mutant/) (2); Protein Data Bank, PDB (http://www.tcsb.org/pdb/) (8); 3DinSight, integrated database for structure, function and property of biomolecules (http://www.rtc.riken.go.jp/3DinSight.html) (9) and MEDLINE PUBMED (http://www.ncbi.nlm.nih.gov/Entrez/medline.html) can be directly accessed through the WWW server.

CITATION OF ProTherm

Users of ProTherm are asked to cite this article in their publication, including the URL, http://www.rtc.riken.go.jp/protherm.html . Suggestions and other materials for inclusion in the database are welcome and should be sent to the corresponding author.

ACKNOWLEDGEMENTS

MMG wishes to thank JISTEC for providing financial support in the form of an STA fellowship and RIKEN for local hospitality to develop and maintain the database.

REFERENCES

1. Pfeil,W. (1998) *Protein Stability and Folding: A Collection of Thermodynamic Data.* Springer, NY.
2. Kawabata,T., Ota,M. and Nishikawa,K. (1999) *Nucleic Acids Res.*, **27**, 355–357.
3. Gromiha,M.M., An,J., Kono,H., Oobatake,M., Uedaira,H. and Sarai,A. (1999) *Nucleic Acids Res.*, **27**, 286–288.
4. Sayle,R.A. and Milner-White,E.J. (1995) *Trends Biochem. Sci.*, **20**, 374–376.
5. Eisenhaber,F. and Argos,P. (1993) *J. Comp. Chem.*, **14**, 1272–1280.
6. Eisenhaber,F., Lijnzaad,P., Argos,P., Sander,C. and Scharf,M. (1995) *J. Comp. Chem.*, **16**, 273–284.
7. Gromiha,M.M., Oobatake,M., Kono,H., Uedaira,H. and Sarai,A. (1999) *Protein Eng.*, **12**, 549–555.
8. Bernstein,F.C., Koetzle,T.F., Williams,G.J., Meyer,E.E.,Jr, Brice,M.D., Rodgers,J.R., Kennard,O., Shimanouchi,T. and Tasumi,M. (1977) *J. Mol. Biol.*, **112**, 535–542.
9. An,J., Nakama,T., Kubota,Y. and Sarai,A. (1998) *Bioinformatics*, **14**, 188–195.