Nucleic Acids Research, 2006, Vol. 34, Database issue ***D195–D198***
doi:10.1093/nar/gkj017

PINT: Protein–protein Interactions Thermodynamic Database

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Received August 15, 2005; Revised and Accepted September 17, 2005

ABSTRACT

The first release of Protein–protein Interactions Thermodynamic Database (PINT) contains >1500 data of several thermodynamic parameters along with sequence and structural information, experimental conditions and literature information. Each entry contains numerical data for the free energy change, dissociation constant, association constant, enthalpy change, heat capacity change and so on of the interacting proteins upon binding, which are important for understanding the mechanism of protein–protein interactions. PINT also includes the name and source of the proteins involved in binding, their Protein Information Resource, SWISS-PROT and Protein Data Bank (PDB) codes, secondary structure and solvent accessibility of residues at mutant positions, measuring methods, experimental conditions, such as buffers, ions and additives, and literature information. A WWW interface facilitates users to search data based on various conditions, feasibility to select the terms for output and different sorting options. Further, PINT is cross-linked with other related databases, PIR, SWISS-PROT, PDB and NCBI PUBMED literature database. The database is freely available at http://www.bioinfodatabase.com/pint/index.html

INTRODUCTION

Protein–protein interactions play a key role in many biological processes such as signal transduction, gene expression and control, antibody–antigen complex and so on. Deciphering the details of interactions between the residues at protein–protein interface and the identification of binding sites are challenging problems in Computational Biology/Bioinformatics (1–3). The integration of structural data and thermodynamic parameters of protein–protein complexes would improve our knowledge and pave a way to understand their binding specificity and functions. Although the structural data of protein–protein complexes have been accumulated in Protein Data Bank (PDB) (4) the thermodynamic data, such as binding free energy change, association/dissociation constant, heat capacity change and so on are not yet well documented. We have developed a database, Protein–protein Interactions Thermodynamic Database, PINT, which contains experimental data of several thermodynamic parameters along with sequence and structural information, measuring methods, experimental conditions and literature information. This database has potential applications for understanding the relationship between binding specificity and the factors that are influencing protein–protein interactions. We have developed a WWW interface to facilitate searching the database and sorting outputs.

CONTENTS OF THE DATABASE

Each entry in the database is identified by a PINT database code and includes the following information.

Protein and peptide details. Protein/peptide name, source, domain, respective PIR (5), SWISS-PROT (6) and PDB (4) codes, information about wild-type and nature of mutations (single, double and multiple), secondary structure and solvent accessibility of residues at mutant positions. The solvent accessible surface area of all the residues was calculated and the secondary structure assignments of each mutant were made using the program DSSP (7). We have also provided the PDB code for the protein–protein complex. In PINT, the protein/peptide assignment was made based on the experiments, and not according to the size of the interacting protein/peptide. For example, for isothermal titration calorimetry (ITC) experiments, we have assigned the reactant inside the reaction cell as protein and the reactant getting injected as peptide.

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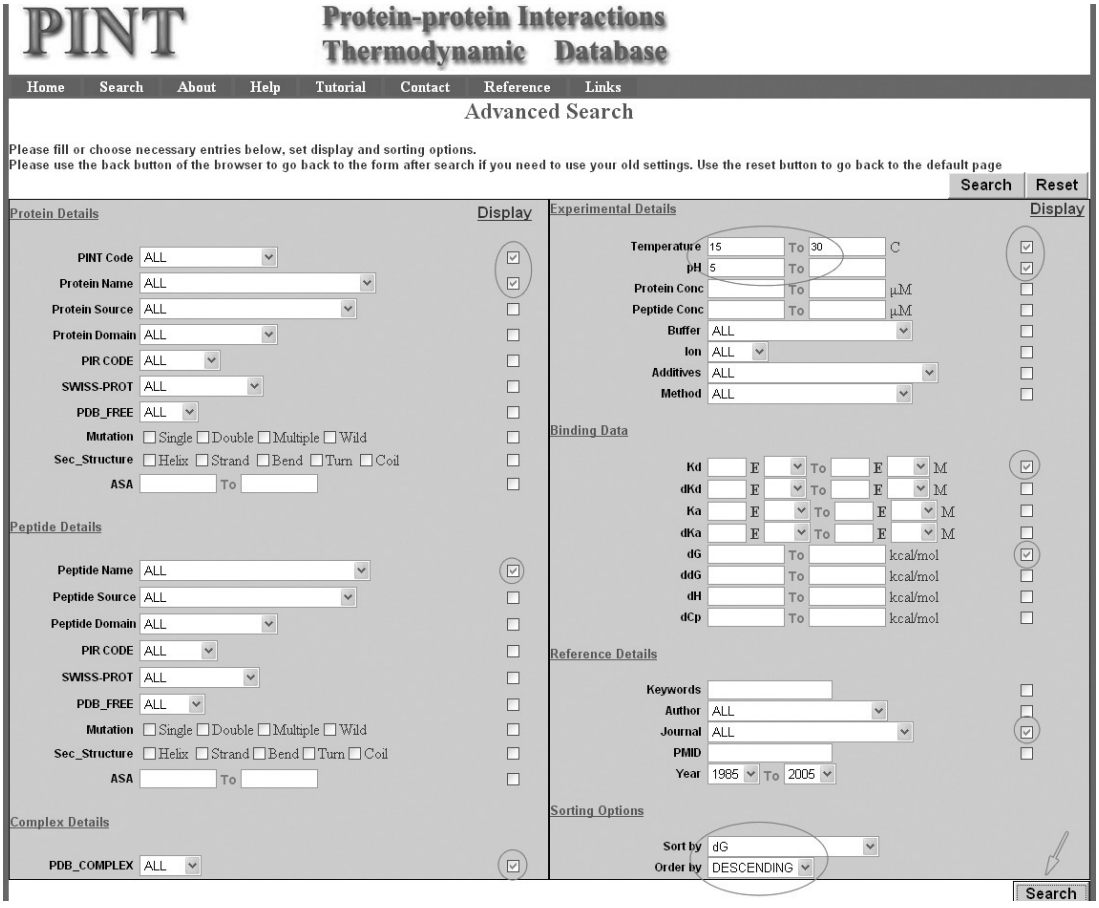
(a)



(b) **PINT Database: Search Results**

Your query resulted in 1174 data.

If you want to modify your query, please use the "back" button of your browser. If you want to try another new query, please go to the search page.

NUMBER	PINT_CODE	PROT_NAME	PEPT_NAME	PDB_COMPLEX	T (°C)	pH	Kd (M)	dG (kcal/mol)	REFERENCE
1021	PINT_CYCP_ISO1	Cytochrome C peroxidase	Cytochrome C iso-1	2PCC	25.0	6.0	4.05e-2	-1.90	Biochemistry. 2001 Jan 16;40 (2):422-8
1042	PINT_CALM_RS20	Calmodulin	RS20 peptide	NULL	25.0	7.5	8.33e-4	-4.21	J Biol Chem. 1999 Jun 25;274 (26):18161-4
733	PINT_CYCP_CYCC	Cytochrome C peroxidase	Cytochrome C	2PCB	26.0	6.0	5.00e-4	-4.52	Biochemistry. 1995 Jul 4;34 (26):8398-405
1182	PINT_GFB2_SOSA	Growth factor receptor-bound protein 2	SOS-A peptide	NULL	30.0	7.0	4.55e-4	-4.60	Biochemistry. 1994 Nov 22;33 (46):13531-9
725	PINT_GFR2_Y317	Growth factor receptor protein 2	pY317 peptide	1QG1	20.0	7.5	3.59e-4	-4.62	Biochemistry. 1997 Aug 19;36 (33):10006-14
1279	PINT_PCAF_ACKP	Histone acetyltransferase PCAF	ACK peptide	NULL	25.0	7.4	3.46e-4	-4.72	Nature. 1999 Jun 3;399 (6735):491-6
1043	PINT_CALM_RS20	Calmodulin	RS20 peptide	NULL	25.0	7.5	2.78e-4	-4.85	J Biol Chem. 1999 Jun 25;274 (26):18161-4
1041	PINT_CALM_RS20	Calmodulin	RS20 peptide	NULL	25.0	7.5	2.38e-4	-4.95	J Biol Chem. 1999 Jun 25;274 (26):18161-4
1264	PINT_TCD2_CD48	T-cell surface antigen CD2	CD48 antigen	NULL	25.0	7.4	2.32e-4	-4.96	Proc Natl Acad Sci U S A. 1998 May 12;95(10):5490-4
633	PINT_TSRC_HMTP	Tyrosine-protein kinase Src	hmT peptide	1SPS	25.0	7.5	2.27e-4	-5.00	J Mol Biol. 2002 Feb 15;316 (2):291-304
1269	PINT_TCD2_CD48	T-cell surface antigen CD2	CD48 antigen	NULL	25.0	7.4	1.92e-4	-5.07	Proc Natl Acad Sci U S A. 1998 May 12;95(10):5490-4
1267	PINT_TCD2_CD48	T-cell surface antigen CD2	CD48 antigen	NULL	25.0	7.4	1.84e-4	-5.10	Proc Natl Acad Sci U S A. 1998 May 12;95(10):5490-4
1265	PINT_TCD2_CD48	T-cell surface antigen CD2	CD48 antigen	NULL	25.0	7.4	1.76e-4	-5.12	Proc Natl Acad Sci U S A. 1998 May 12;95(10):5490-4
1268	PINT_TCD2_CD48	T-cell surface antigen CD2	CD48 antigen	NULL	25.0	7.4	1.68e-4	-5.15	Proc Natl Acad Sci U S A. 1998 May 12;95(10):5490-4

Figure 1. An example of searching conditions, display and sorting options, and the results of PINT search. (**a**) Search, display and sorting options: the search is performed for obtaining K_d and ΔG for protein–protein complexes obtained in the temperature range of 15–30° and pH >5. All these search items were selected to display in the output along with PINT code, protein name, peptide name, PDB complex and journal name. The data are sorted with ΔG in descending order. (**b**) Partial results obtained from PINT under the conditions specified in Figure 1a.

Experimental conditions. Temperature, pH, protein and peptide concentrations, buffer, ion, additives and measuring method.

Thermodynamic data. Dissociation constant (K_d), association constant (K_a), free energy change (ΔG), enthalpy change (ΔH) and heat capacity change (ΔC_p) of the interacting proteins upon binding. The changes in K_d, K_a and ΔG have also been provided for mutants as ΔK_d, ΔK_a and $\Delta\Delta G$, respectively.

Literature information. Keywords, authors, reference and PMID.

DATABASE STATISTICS

The first release of PINT, version 1.0, contains 1513 entries from 72 original research articles. PINT has 129 protein–protein complexes and 33 of them have complete 3D structures, which are deposited in PDB. Majority of the data were obtained with ITC experiments (670) followed by surface plasmon resonance (SPR) (322) and Fluorescence (216).

ACCESS TO PINT

PINT can be accessed through World Wide Web at http://www.bioinfodatabase.com/pint/index.html. We have implemented both quick and advanced search options in PINT database. In the advanced search, various options are available in the interface, as shown in Figure 1, and are briefly explained below. (i) Retrieving data for a particular protein/peptide. For the convenience to the users, we have provided the complete list in a pull down menu. (ii) Specifying the codes, PIR (5), SWISS-PROT (6) and PDB (4). (iii) Searching the data based on secondary structure and solvent accessibility of protein/peptide mutants. (iv) Extracting the data for a particular measurement (ITC, Fluorescence, Electrophysiology, Spectrophotometry, SPR and so on). (v) Obtaining the data for specific range of T, pH, K_d, K_a, ΔG, ΔH and ΔC_p. (vi) Limiting the data to specific years or journals. (vii) Searching with keywords, journal, PMID and authors' names.

Detailed tutorials describing the usage of the present PINT are available at the home page. As an example, the necessary items to be filled/selected to search the thermodynamic data, dissociation constant and free energy change for protein–protein complexes obtained in the temperature range of 15–30° and pH >5 are shown in Figure 1a. In the same figure, we have shown the display items in the output by tick marks. In PINT, it is possible to sort the data by T, pH, K_d, ΔG and so on and we showed the sorting with ΔG in descending order. This search picked up 1174 data and a part of the results obtained with the search conditions and sorting option is shown in Figure 1b.

GUIDELINES

We have provided a detailed help page explaining about the contents of the database and different modes of search options. Further, we have given the lists of PINT codes, protein and peptide names, buffers, ions and additives, PIR, SWISS-PROT and PDB codes and authors. This will assist the users to obtain the relevant data quickly.

COMPARISON WITH OTHER RELATED DATABASES

Salwinski *et al*. (8) developed a Database of Interacting Proteins, which mainly contains the information about the relationship between protein structure and function and the thermodynamic data are minimal. The Biomolecular Interaction Network Database, archives biomolecular interaction, reaction, complex and pathway information (9). The Kinetic Data of Bio-molecular Interactions, aimed at providing experimentally determined kinetic data of protein–protein and other complexes (10). In the present work, we have developed a database, PINT, which mainly accumulates the thermodynamic data of interacting proteins upon binding. We have provided all the experimentally measured thermodynamic data (K_d, K_a, ΔG, ΔH and ΔC_p) for wild-type and mutant proteins. PINT differs from all other existing databases and it will be useful to understand the relationship among sequence, structure and binding specificities of protein–protein complexes.

LINKS TO OTHER DATABASES

Each data in PINT is linked to the sequence databases PIR (5) and SWISS-PROT (6), structure database, PDB (4), and the literature database, PUBMED (http://www.ncbi.nlm.nih.gov/entrez/). Further, general links are given to related protein–protein interaction and other databases (8–10).

AVAILABILITY AND CITATION OF PINT

The database is freely available for academic purpose at http://www.bioinfodatabase.com/pint/index.html. The users of PINT should cite this article, including the URL. Suggestions and other materials for inclusion in the database are welcome and should be sent to admin@bioinfodatabase.com.

ACKNOWLEDGEMENTS

Funding to pay the Open Access publication charges for this article were waived by Oxford University Press.

Conflict of interest statement. None declared.

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