International Tables for Crystallography (2006). Vol. F, Section 24.1.3, pp. 650–654.

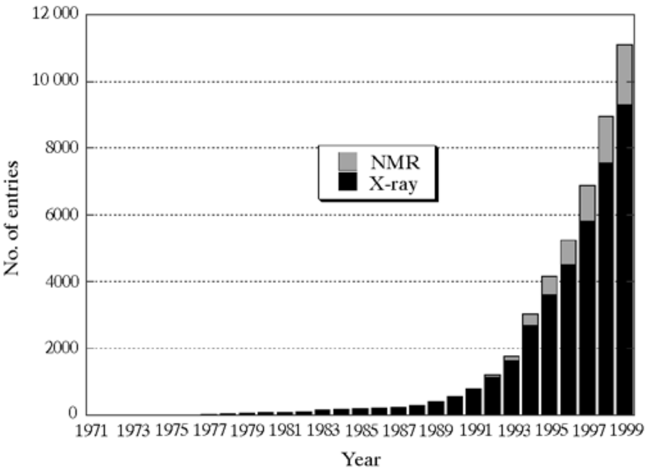


Fig. 24.1.2.1. PDB coordinate entries available per year.

Table 24.1.3.1. *PDB archive contents as of May 1999*

9862	Atomic coordinate entries
2768	Structure-factor files
560	NMR restraint files
Molecule type:	
8754	Proteins, peptides and viruses
415	Protein/nucleic acid complexes
681	Nucleic acids
12	Carbohydrates
Experimental technique:	
8103	Diffraction
1544	NMR
215	Theoretical modelling

PDB before 1987 to a rapid exponential growth reaching the current rate of about ten submissions per day (see Fig. 24.1.2.1).

In the same period, the proliferation and increasing power of computers, the introduction of relatively inexpensive interactive graphics, and the growth of computer networks greatly increased the demand for access to PDB data in many diverse ways. The requirements of molecular biologists, rational drug designers and others in academia and industry are often fundamentally different from those of the crystallographers and computational chemists who have been the major PDB users since the 1970s. This presents a challenge for the PDB and has been addressed in a number of ways (see below).

24.1.3. The PDB in 1999

24.1.3.1. *Contents and access to the PDB archives*

The archives contain atomic coordinates, bibliographic citations, primary- and secondary-structure information, crystallographic structure factors, and NMR experimental data. Annotations in the structure entries include amino-acid or nucleotide sequences (with notes of any conflicts between the structure in the PDB and sequence databases), source organisms from which the biological materials were derived, descriptions of the experiments, secondary structures, complexes with small molecules included within the structures, references to papers *etc*. Third-party annotations include images and movies of structures; pointers to specialized databases (maintained by others), such as the Protein Kinase Resource (http://www.sdsc.edu/Kinases/pk_home.html) and ESTHER (ESTerases and α/β Hydrolase Enzymes and Relatives) (http://www.ensam.inra.fr/cholinesterase/), and pointers to databases that provide additional experimental information, such as the BioMagResBank (BMRB) NMR structural database (http://www.bmrb.wisc.edu/). Table 24.1.3.1 gives a summary of the contents of the PDB archives.

PDB entries are available on CD-ROM, which PC users can search using the *PDB-SHELL* browser included (Abola, 1994). UNIX users can also search the CD-ROM if they download a copy of the browser software. The entries are also available over the WWW from Brookhaven and 17 mirror sites worldwide (Table 24.1.3.2). They can be searched and retrieved *via* the PDB's 3*DB Browser* (Sussman, 1997), which is interfaced through web browsers such as Netscape Communicator and Internet Explorer. Probably the best way to get a feeling for 3*DB Browser* is just to try it. A simple example of its use is illustrated in Fig. 24.1.3.1 in a search for a structure related to recent papers in *Nature* (Kwong *et al*., 1998) and *Science* (Rizzuto *et al*., 1998).

3*DB Browser* has a number of features that make it easy to access information found in PDB entries. Users can search according to any combination of fields, such as compound name, experiment title, authors (depositors), biological source, journal references, date of deposition and nature of small molecules (ligands and heterogens) complexed with the structure. Boolean operators allow highly complex search strings. Entries selected can be retrieved automatically, and the molecular structures can be displayed using the public-domain molecular viewer *RasMol* (Sayle & Milner-White, 1995), MDL's *Chemscape Chime* plug-in, or a similar viewer. The entries also include HyperText links to the SwissProt protein-sequence database (Bairoch & Boeckmann, 1994), the BioMagResBank (BMRB) NMR structural database (Seavey *et al*., 1991), the Enzyme Commission Database (Bairoch, 1994), PubMed access to the Medline database, and several other

Table 24.1.3.2. *PDB mirror sites as of May 1999*

Official PDB mirror sites
Argentina: University of San Luis
Australia: Australian National Genomic Information Service, Sydney; The Walter and Eliza Hall Institute of Medical Research, Melbourne
Brazil: ICB-UFMG, Inst. de Ciencias Biologicas, Univ. Federal de Minas Gerais
China: Institute of Physical Chemistry, Peking University, Beijing
France: Institut de Génétique Humaine, Montpellier
Germany: GMD, German National Research Center for Information Technology, Sankt Augustin
India: Bioinformatics Centre, University of Pune
Israel: Weizmann Institute of Science, Rehovot
Japan: Institute of Protein Research, Osaka University
Poland: ICM - Interdisciplinary Centre for Modelling, Warsaw University
Taiwan: National Tsing Hua University, HsinChu
United Kingdom: Cambridge Crystallographic Data Centre, Cambridge; EMBL Outstation, EBI, Hinxton
United States: Bio Molecular Engineering Research Center, Boston University; North Carolina Supercomputing Center, Research Triangle Park; University of Georgia, Athens, Georgia; PDB at Brookhaven National Laboratory

databases (see Table 24.1.3.3 for a list of linked external data sources).

The main source of information for the 3*DB Browser* is the data from the PDB. These data are highly structured, and most crystallographers usually consider a datum from a PDB entry as belonging to a particular 'record' or 'field'. It makes sense to use these fields to constrain the search. Searching for 'rich' as a keyword has a different meaning from searching for the author Rich.

The simplest operation with the browser is to enter one or more words in the 'Text query' field and press the 'Search' button. The browser engine will come back with those entries from the database that contain or are related to the words provided.

The symbol '*' can be used as a wild card to denote a sequence of any number (including 0) of arbitrary characters. Just add an asterisk, '*', at the beginning or end of a word (or both) to 'extend' the search. For example, enter '*tox*' in the keyword field to retrieve those entries containing keywords like neurotoxic and toxin. Wild cards have no meaning in number-only fields, like Resolution and Date.

The Boolean operator AND is the default for 3*DB Browser* and is mandatory (it cannot be changed) between fields (see Table 24.1.3.4). If 'ATP' is entered in the Associated group field and 'kinase' in the Keyword field, only those entries matching both constraints are returned. Inside a given field, Boolean logical operators may be applied at will to the words entered. The available Boolean logical operators are AND, OR and NOT. The case is unimportant. The operator AND can be represented by '+' and the operator NOT can be represented by '−'.

For example, 'zinc and (torpedo or snake)' in the Text query field will return those entries that contain either the word torpedo or the word snake, but only if the word zinc is also present. In addition, many specific records can be searched for regular expressions or numerical limits, as shown in Table 24.1.3.4 [see *Protein Data Bank Quarterly Newsletter* (1998), **83**, pp. 3–5, *The 'Intelligent' Search Engine Behind the 3DB Browser*^{TM}, and *Protein Data Bank Quarterly Newsletter* (1998), **84**, pp. 3–4, *3DB Browser*^{TM}*: Tips, Questions and Answers* at http://www.rcsb.org/pdb/newsletter.html).

One of the main concerns for us, as database-interface developers, is the 'false negative', that is, the failure to return data after a query even when the data are available in the database. Frequently, this happens because the user was unable to express the query in a way compatible with the search engine or used words or keywords unknown to the search engine.

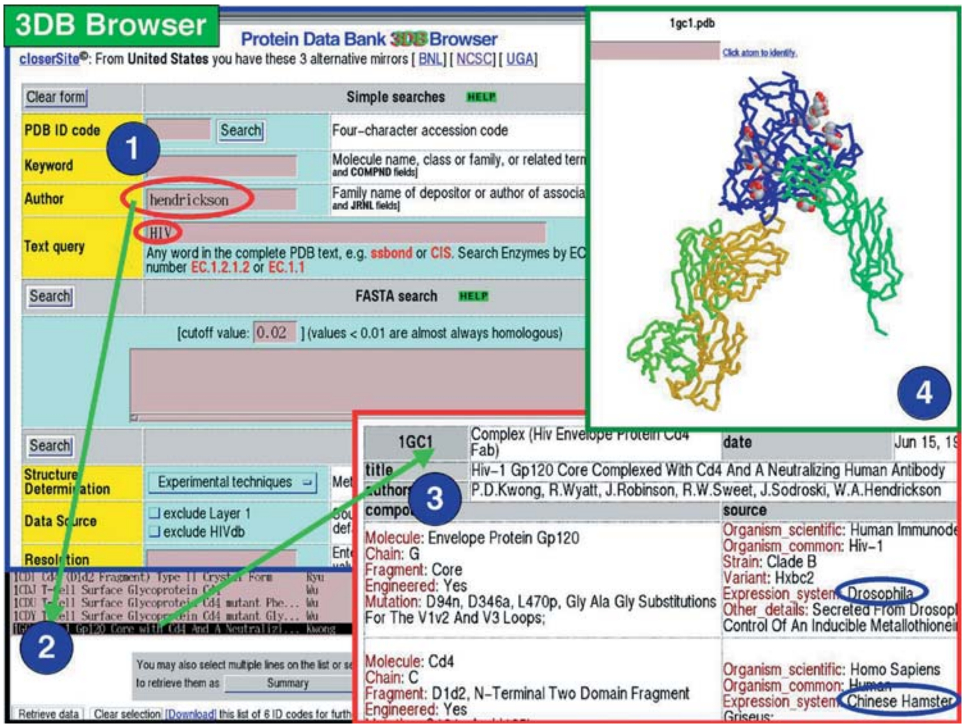
3*DB Browser* deals with this problem by incorporating several automatic and semi-automatic mechanisms to help the user retrieve the requested data. The request from the user gets filtered and transformed by one or more engines. At the end, the resulting query is the one used for the search (see Table 24.1.3.5).

A search in 3*DB Browser* brings up a rich Atlas page, summarizing additional information about the entry of interest. The links in this Atlas page carry one to the original sources of information. The number of external sources that 3*DB Browser* searches and dynamically incorporates into the Atlas pages increases daily (Table 24.1.3.3).

The PDB's WWW server is the major tool used to access the three-dimensional macromolecular structural information archived at the PDB. Thousands of times a day, scientists, students and other users around the world visit the PDB to browse through and access these data. In order to meet the need for rapid access worldwide, a global network of 17 official mirror sites has been established. To help orient the user, 3*DB Browser* incorporates *CloserSite* (see http://pdb.weizmann.ac.il/pdb-docs/closerSite.html), an automatic script that detects one's location and offers closer alternative sites (in the network sense).

The information on the PDB's web server changes frequently. New information is generated on a daily basis. Synchronizing the PDB and its mirror sites to provide exactly the same services while requiring minimum human involvement is a necessary but nontrivial task.

A protocol for the automatic mirroring of the web sites was developed at BNL based on ftp mirroring technology. This protocol has been used successfully by PDB and its mirror sites for approximately two years.



closerSite©: From United States you have these 3 alternative mirrors [BNL] [NCSC] [UGA]

PDB ID code: Four-character accession code

Keyword: Molecule name, class or family, or related term … and COMPND fields]

Author: hendrickson — Family name of depositor or author of associa… and JRNL fields]

Text query: HIV — Any word in the complete PDB text, e.g. ssbond or CIS. Search Enzymes by EC number EC.1.2.1.2 or EC.1.1

[cutoff value: 0.02] (values < 0.01 are almost always homologous)

Structure Determination: Experimental techniques

Data Source: □ exclude Layer 1 □ exclude HIVdb

Resolution

1CDI Cd4 (D1d2 Fragment) Type II Crystal Form … Ryu
1CDJ T-Cell Surface Glycoprotein Cd4 … Wu
1CDU T-Cell Surface Glycoprotein Cd4 mutant Phe... Wu
1CDY T-Cell Surface Glycoprotein Cd4 mutant Gly... Wu
1GC1 … Gp120 Core with Cd4 And A Neutralizi... Kwong

You may also select multiple lines on the list or se… to retrieve them as Summary

[Download] this list of 6 ID codes for furth…

1GC1	Complex (Hiv Envelope Protein Cd4 Fab)	date	Jun 15, 19…
title	Hiv-1 Gp120 Core Complexed With Cd4 And A Neutralizing Human Antibody		
authors	P.D.Kwong, R.Wyatt, J.Robinson, R.W.Sweet, J.Sodroski, W.A.Hendrickson		
compo…		source	
Molecule: Envelope Protein Gp120 Chain: G Fragment: Core Engineered: Yes Mutation: D94n, D346a, L470p, Gly Ala Gly Substitutions For The V1v2 And V3 Loops;		Organism_scientific: Human Immunode… Organism_common: Hiv-1 Strain: Clade B Variant: Hxbc2 Expression_system: Drosophila Other_details: Secreted From Drosop… Control Of An Inducible Metallothionei…	
Molecule: Cd4 Chain: C Fragment: D1d2, N-Terminal Two Domain Fragment Engineered: Yes		Organism_scientific: Homo Sapiens Organism_common: Human Expression_system: Chinese Hamster Griseus;	

Fig. 24.1.3.1. 3*DB Browser* as a tool to visualize recently published structures. (1) Search for author: Hendrickson; text query: HIV. (2) Six hits obtained, PDB ID Code 1GC1 highlighted. (3) 3*DB Browser* Atlas page. Ovals highlight the expression systems used for the different components in the multicomponent system. (4) Structure as visualized with MDL's *Chemscape Chime* plug-in.

Fig. 24.1.3.2 outlines the web mirroring protocol, which consists of the following five steps.

(1) Develop and test HTML pages and common-gateway-interface (CGI) codes on the development server in a special source-code control area.

(2) Copy the working code and HTML pages to a read-only area.

(3) Mirror the updated information onto an internal test server that uses its own directory tree, distinct from that used for development. This internal server simulates the production environment under controlled conditions. For example, we verify that updated files are mirrored properly and that relative HTML links work.

(4) Copy the files outside the firewall to an account accessible only to the mirror sites.

(5) Activate the mirror software to transfer the updated files to the PDB web server. Official mirror-site servers are updated automatically by their own mirroring procedures.

Table 24.1.3.3. *3DB Browser's linked external data sources*

Source name	Short description
BioMagResBank	Relational database for sequence-specific protein NMR data
BLOCKS	Database of conserved regions in groups of proteins
CATH	Protein structure classification
DALI/FSSP	Families of structurally similar proteins
EMBL	European Molecular Biology Laboratory sequence database
Entrez	NCBI's documentation database
ENZYME	Enzyme nomenclature database
ESTHER	Esterases and alpha/beta hydrolase enzymes and relatives database
GenBank	NIH genetic sequence database
GDB	Genome Data Base
Kinase	Protein Kinase Database Project
KineMage	Protein Science's *Kinemage* server
LPFC	Library of Protein Family Cores
MacroMolecule	Crystal MacroMolecule files at the EBI
MMDB	Molecular Modelling Database
NDB	Nucleic Acid Database
OLDERADO	Core, domain and representative structure database
PDBObs	Archive of obsolete PDB entries at SDSC
PDBREPORT	Structure verification reports for X-ray structures
PIR	Protein Information Resource
PROSITE	Dictionary of protein sites and patterns
ProtMotDB	Protein Motions Database
PubMed	Medline bibliographic database
SCOP	Structural classification of proteins
Swiss 3D-Image	3D images of proteins and other biological macromolecules
SwissProt	Annotated protein sequence database
TREMBL	Translation from EMBL sequence database

Table 24.1.3.4. *Search fields of 3DB Browser*

Search field	PDB entry
Entry ID code	Four-character accession code
Keyword	Molecule name, class or family, or related term (HEADER, TITLE, KEYWDS and COMPND fields)
Author	Family name of depositor or author of associated publication (AUTHOR and JRNL fields)
Text query	Any word in the complete PDB text, excluding most field names
Experiment	Method of structure determination
FASTA Search	FASTA search of the sequence
Resolution	A unique value or range of values, in Å (REMARK 2 field)
Space group	Both extended and standard Hermann–Mauguin symbols (CRYST1 field)
Organism	Trivial name, systematic name or expression system (SOURCE field)
Date (lower)	Date entry was deposited or released
Date (upper)	Date entry was deposited or released
Associated group	Prosthetic group, metal ion, ligand, substrate, or its three-letter PDB abbreviation (HET and HETNAM fields)
Chain size	A unique value or range of values

Table 24.1.3.5. *Search engines used by 3DB Browser*

Engine	Example
American–British	‘Amoeba’ and ‘ameba’ are equivalent
Synonyms	‘Protease’ is equivalent to ‘proteinase’
Spelling search	Based on a dictionary built from the current PDB data, the spelling engine will produce words that are close to the entered one. As an example, entering ‘imune’ will offer ‘immune’ as a valid alternative.
Soundex search	Based on the soundex algorithm that approximates the sound of the word when spoken by an English speaker. Looking for author ‘Weich’ will offer as alternatives Weiss, Wess and Wyss

Special steps are taken to isolate files, thus obviating problems associated with the existence of files and directories not related to PDB web activities. HTML documents are stored under the directory /pdb-docs/, and executables are stored under the directory /pdb-bin/. In addition, index files and local configuration files are stored in the directory /PDB-support/.

Specific areas on the http server are dedicated to PDB web activities. All the HTML pages and CGI scripts are in the /pdb-docs/ and /pdb-bin/ directories, respectively. There are also index files and local configuration files in /PDB-support/. This avoids confusing PDB applications with other applications on the same server, which would complicate the mirror procedure.

Relative links are used in all the HTML pages and the HTML pages generated by the scripts. For example, to create a hyperlink to 3*DB Browser* in the file named index.html, <a href=“/pdb-bin/pdbmain”>3DB Browser</a> is used instead of <a href=“http://

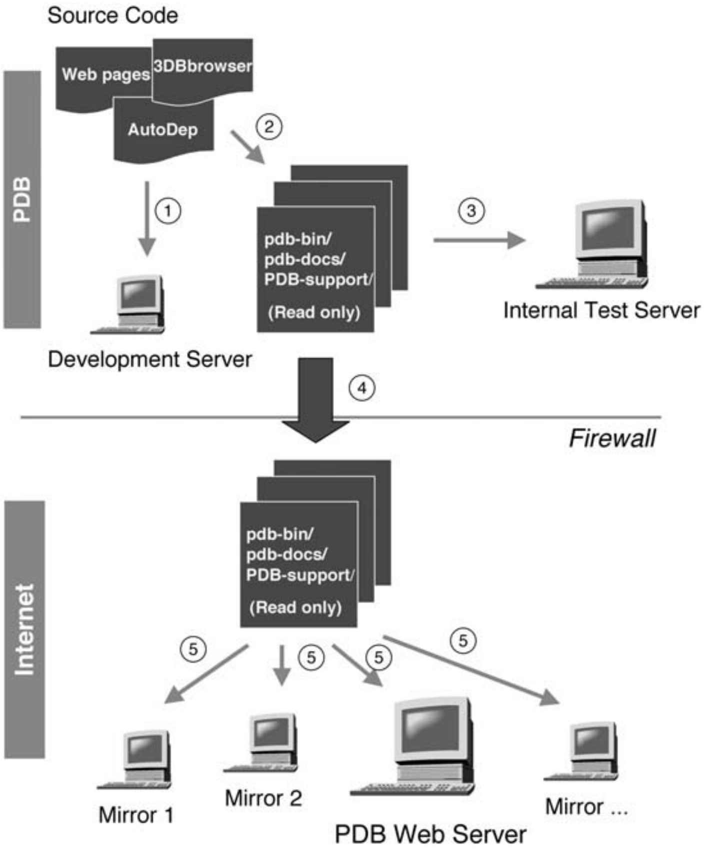


Fig. 24.1.3.2. Schematic diagram of the PDB WWW mirror system.

www.pdb.bnl.gov/pdb-bin/pdbmain">3DB Browser</a>. The advantage of relative links is that pages copied to the mirror sites' machines will point to local resources without having to be edited locally. This is one of the key points in automating the web mirror procedure. To make relative links work properly, the mirror sites maintain a local configuration file. The configuration file reflects the local directory tree and available resources. The PDB provides a generic template, and mirror sites modify it according to their setup. This configuration file is excluded from the automatic mirroring procedure to avoid being overwritten by the original template file. Changes to the configuration files are sent to mirrors by e-mail one week in advance, to be included manually.

To avoid duplication and allow easy maintenance of the resources, PDB's web and ftp servers share some files. All mirror sites support both web and ftp servers. When a hyperlink points to a file on the ftp server, a server side include (SSI) script is used to access the local ftp server of each mirror site. Its function is to use configuration variables to generate a path to the local file dynamically.

HTML pages and CGI scripts are put into a read-only account available to official mirror sites. Mirror sites use the ftp mirror tool mirror.pl (ftp://sunsite.org.uk/packages/mirror/) to mirror the updated information from this account. For security reasons, this account is not an anonymous ftp account, but requires a password for access. In addition, this account can only be accessed by ftp. This process can be made as a cron job to automate the update procedures fully. Although the procedure is automatic, an e-mail message is sent to mirror sites for update verification. For details on the PDB mirror system, see *Protein Data Bank Quarterly Newsletter* (1999), **87**, pp. 3–5, *PDB World Wide Web Mirroring System* at http://www.rcsb.org/pdb/newsletter.html).

Web access to the archives has become the primary mode of retrieving entries from the PDB. However, the PDB continues to receive a considerable number of orders for our CD-ROM product. The PDB anticipates that this will continue to be so for a variety of reasons. For example, network performance still remains poor in a number of locations, and these disks, released quarterly, provide local access to the contents of the archive. PDB files may first be copied from the CD-ROM to a local disk, and then incremental updates can easily be made using mirroring software.

24.1.3.2. *Data deposition*

Since its inception in 1971, the method followed by the PDB for entering and distributing information has paralleled the review and edit mode used by scientific journals. Currently, the author submits their data to the PDB, in mmCIF (http://ndbserver.rutgers.edu/NDB/mmcif/) or PDB format, *via* the PDB's web-based *AutoDep* facility (Lin *et al.*, 2000; http://autodep.ebi.ac.uk) (see Fig. 24.1.3.3). *AutoDep* then calls a suite of validation programs, whose output is returned *via* the web to the depositor within minutes of sending the data to the PDB. This has made it possible for authors to request that their data be 'released on publication' and has reduced the number of authors requesting that their data be held to less than 22%, compared to over 75% just a year ago (Sussman, 1998).

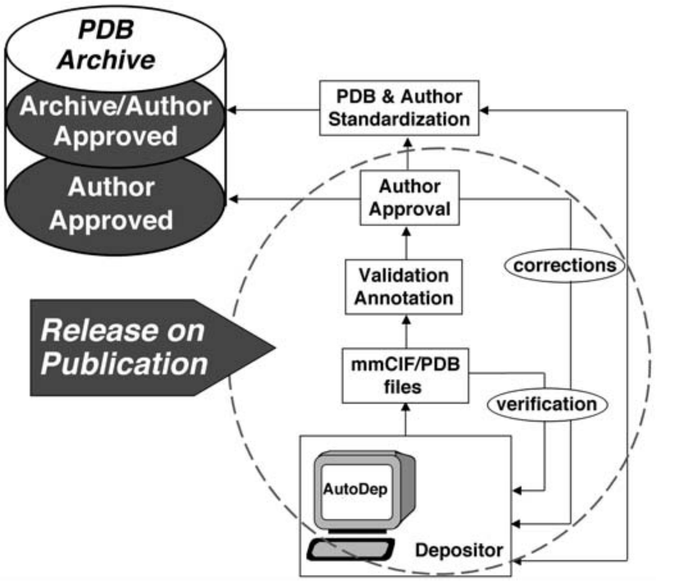


Fig. 24.1.3.3. PDB WWW-based submission *via AutoDep* facilitates releasing the entries *via* a layered approach, making it possible to release entries automatically on publication, as indicated in the portion of the figure enclosed in a dashed circle.

Based on these checks, authors may decide to give permission to release the entry immediately, to release it after up to a maximum one-year hold, or to go back and re-examine the structure in light of the output diagnostics before completing the submission procedure. The PDB ID code is issued only after the author gives release approval. The submitted data must include all mandatory information [see *Protein Data Bank Quarterly Newsletter* (1987), **82**, pp. 2–3, *Proposed Mandatory Items* at http://www.rcsb.org/pdb/newsletter.html and in the *List of Items Mandatory for a Complete PDB Submission* at http://pdb.rutgers.edu/~adbnl/pdb-docs/mandatory_items.html). The data must also pass certain validation criteria (see *Validation for Layered Release* at http://pdb.rutgers.edu/~adbnl/pdb-docs/validation.html). Entries passing the validation criteria are released clearly identified as 'LAYER-1'. An associated file containing output diagnostics is also released.

Following this, PDB staff process the entry. The entry and the output of the validation suite are evaluated by a PDB scientific staff

Table 24.1.3.6. *PDB data-validation checks*

Class	What is checked
Stereochemistry	Bond distances and angles, Ramachandran plot (dihedral angles), planarity of groups, chirality
Bonded/non-bonded interactions	Crystal packing, unspecified inter- and intraresidue links
Crystallographic information	Matthews' coefficient, *Z* value, cell-transformation matrices
Noncrystallographic transformation	Validity of noncrystallographic symmetry
Primary sequence data	Discrepancies with sequence databases
Secondary structure	Generated automatically or visually checked
Heterogen groups	Identification, geometry and nomenclature
Miscellaneous checks	Solvent molecules outside the hydration sphere, syntax checks, internal data consistency checks

Table 24.1.3.7. *PDB structure-factor submissions, as of November 1998*

Year	No. of X-ray structure submissions	No. of structure-factor submissions (%)
1994	804	205 (25.0)
1995	963	343 (36.0)
1996	1124	546 (49.0)
1997	1484	932 (62.8)
1998	1616	868 (53.7)
Total	5991	2894 (48.3)

member, who completes the annotations and returns the entry to the author for comment and approval. Table 24.1.3.6 summarizes the checks included in our current data-validation suite. Corrections from the author are incorporated into the entry, which is reanalysed and validated before being archived and released. Most of this work covers issues not now fully delegated to automatic software. The resulting entry, after author approval, replaces the LAYER-1 entry in the archive. We strongly believe that such thorough checking and annotation is essential for ensuring the long-term value of the data.

The PDB has long made available the experimental data that were used to determine the three-dimensional structures in the database. In recent years, more and more depositors and users of the PDB have come to appreciate the importance of reliable access to such fundamental data. The deposition of the experimental data, along with the coordinates, is essential for the following reasons.

(1) Rigorous validation of the structure-determination results can only be carried out using both atomic parameters and experimental structure-factor amplitudes.

(2) Archiving of these data will ensure their preservation and continued accessibility.

Whether or not to require that the experimental data be deposited concomitantly with the structure data has recently been hotly discussed in the scientific press (Baker *et al.*, 1996) and on the internet (*EBI/MSD Draft Consultative Document for Deposition of Structure Factors*, http://msd.ebi.ac.uk/sf/sf.html).

At present, more than 50% of the X-ray diffraction submissions are being deposited with their associated structure factors (see Table 24.1.3.7), compared with 25% four years ago. This increase is probably partly due to the ease of uploading the files *via* our web-based submission tool, *AutoDep*, which is available at the EBI (http://autodep.ebi.ac.uk). The PDB strongly encourages all researchers to deposit their structure factors at the time of coordinate submission. Furthermore, we actively encourage journals to require their submission as a prerequisite for publication [see *Protein Data Bank Quarterly Newsletter* (1996), **75**, p. 1, *What's New at the PDB* at http://www.rcsb.org/pdb/newsletter.html).

In order to facilitate the use of deposited structure factors, we at the PDB, together with a number of macromolecular crystallographers and the IUCr Working Group on Macromolecular CIF, developed a standard interchange format for structure factors [*PDB Structure Factor mmCIF* at http://ndb-mirror-2.rutgers.edu/NDB/ftp/PDB/structure_factors/cifSF_dictionary; *Protein Data Bank Quarterly Newsletter* (1995), **74**, p. 1, *What's New at the PDB* at http://www.rcsb.org/pdb/newsletter.html]. This standard is the mmCIF format, *i.e.*, the IUCr-developed macromolecular Crystallographic Information File. It was chosen for its simplicity of design and for being clearly self-defining. The format is also easy to expand as new crystallographic experimental methods or concepts are developed, by simply adding additional tokens. The entire mmCIF crystallographic dictionary (http://ndb.rutgers.edu/NDB/mmcif) has recently been ratified by the IUCr's Committee for the Maintenance of the CIF Standard (COMCIFS).

The PDB has written a program to quickly and easily convert structure factors, as output by the most frequently used crystallographic programs, into mmCIF format. This tool, which also converts binary CCP4 MTZ files, will be accessible through the *AutoDep* program following final testing. MTZ files, which are useful in individual laboratories, are not appropriate for archival purposes. This is because particular groups arbitrarily attach different labels to the MTZ columns.

During the past year, the PDB has converted virtually all the old structure-factor files to this standard format and is keeping up-to-date on all new submissions. As of November 1998, there are about 2000 structure-factor files released in structure-factor mmCIF format (Jiang *et al.*, 1999; PDB mmCIF structure-factor files can be found at ftp://ftp.rcsb.org/pub/data/structures/divided/structure_factors/), with about an additional 1300 'on hold'. The current IUCr policy states that 'The IUCr also urges crystallographers to use their influence to ensure that all journals that publish articles on macromolecular three-dimensional structure require the deposition of both atomic parameters and structure-factor amplitudes.' and 'Authors are urged to release the atomic parameters and structure-factor amplitudes immediately after the publication date. This should be the normal practice. They can, however, request a delay of up to six months in the release of the atomic parameter data and the structure-factor amplitudes.' (Commission on Biological Macromolecules, 2000). The structure factors are also available *via 3DB Browser* (http://pdb-browsers.ebi.ac.uk/pdb-bin/pdbmain or http://bioinfo.weizmann.ac.il:8500/oca-bin/ocamain). This can be seen on the browser's Atlas page for each structure.

The ready availability of structure-factor files in a standard format has made it possible for any scientist to validate a structure in the PDB *versus* its experimentally observed data. There are now some excellent tools available for this, such as the Uppsala Electron Density Server (http://alpha2.bmc.uu.se/valid/density/form1.html) and the program *SFCHECK* (http://www.iucr.org/iucr-top/comm/ccom/School96/pdf/sw.pdf). The PDB has also observed that one of the most popular uses for these stored structure factors is for the crystallographer who did the experiment to be able to retrieve their own misplaced data.

24.1.4. Examples of the impact of the PDB

There are numerous examples in molecular biology, medicine and drug discovery where the PDB is playing an increasingly important role, as can be seen in the many sites related to the PDB (see Table 24.1.4.1).

One key example is the impact that structural information is having on the design of new drugs to combat diseases such as AIDS. At present, the three-dimensional structures of eight HIV proteins have been determined, one of which is illustrated in Fig. 24.1.3.1. These three-dimensional structures have aided researchers in the design of several drugs that have one of these proteins as their targets. Other examples can be seen in our basic understanding of the immune system (Madden *et al.*, 1993), Fig. 24.1.4.1, and the interaction between proteins and DNA (Schultz *et al.*, 1991), Fig. 24.1.4.2.

The PDB is a major international resource used by scientists, educators and students throughout the world. During the past few years, we at the PDB, in collaboration with many others, have greatly enhanced this resource into a powerful user-friendly tool for bridging the gap between the three-dimensional structure and the genome worlds (Sussman, 1997). Some examples follow.

(1) The PDB's *AutoDep* procedure (Lin *et al.*, 2000) has made

references