Introduction of Supercomputer System for DNA Data Bank of Japan

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The Center for Information Biology and DNA Data Bank of Japan (CIB-DDBJ) at the National Institute of Genetics (NIG) has joined forces with GenBank (USA) and EMBL (Europe) to form the International Nucleotide Sequence Database Collaboration (INSDC) and make their databases accessible to researchers over the Internet. In parallel with advances made in the life sciences, the INSDC databases are increasing rapidly in size by 30–50% annually. Moreover, a large-scale computer system for constructing and releasing them and providing search and analysis services has become necessary. Important requirements of such a system will include ongoing enhancements to system performance and capacity and support for software evolution. This paper describes a new supercomputer system that went into operation in March 2007. It meets a variety of difficult requirements including support for a rapidly growing database, provision of high-speed and stable search/analysis services, smooth migration from the old system, compatibility with existing user assets, high reliability, and support for security. This paper also introduces the contributions that this new system is making to life sciences research both inside and outside Japan.

1. Introduction

In February 2007, the National Institute of Genetics (NIG) of the Research Organization of Information and Systems introduced a super-computer system consisting of large-scale servers, clusters of personal computers (PCs), large-capacity storage, keyword search systems, and other components. It has been in operation since March 2007. This supercomputer system aims to provide data collection, database construction, data release, and search and analysis services for the DNA Data Bank of Japan (DDBJ)[1)-3)] operated by the Center for Information Biology and DNA Data Bank of Japan (CIB-DDBJ) at NIG. It is provided for both NIG and research institutions inside and outside Japan for research purposes.

In this paper, we describe how this super-computer system has solved a number of difficult issues and how it is contributing to Japanese and international research in the life sciences.

2. DDBJ overview

CIB-DDBJ is working with EBI/EMBL[4)] in Europe and NCBI/GenBank[5)] in the USA as part of the DDBJ/EMBL/GenBank International Nucleotide Sequence Database Collaboration (INSDC).[6)] The INSDC databases consist of deoxyribonucleic acid (DNA) (or ribonucleic acid [RNA]) nucleotide sequences experimentally determined by researchers around the world and collected and edited by three international databanks—DDBJ, EMBL, and GenBank—according to a data construction scheme established by these three parties. To the user, this data is provided in the form of a unified computer file. The databases are prepared by editing DNA nucleotide sequence data received

directly from researchers, but they also include DNA data processed by the Japan Patent Office, European Patent Office, and United States Patent and Trademark Office.

The nucleotide sequence database is a set of data units called "entries". In addition to the nucleotide sequence itself, each entry includes information about the researcher who determined the sequence plus related references, organism, and gene function and features. Data collected by each databank is exchanged daily among the three databanks so that the same information will be provided by them. DDBJ collects and edits about 20% of the data released by these three international databases.

When DDBJ first released its nucleotide sequence database in July 1987, it consisted of only 66 entries and 108 970 base pairs. In recent years, however, the INSDC databases have been increasing at an annual rate of 130–150%. In September 2007, about 20 years after the initial release, they had reached 76 273 345 entries and 79 706 204 461 base pairs. The growth in data registered in INSDC is shown in **Figure 1**.

In addition, genome sequencers that can operate several tens to a hundred times as fast as conventional sequencers are now being introduced, and this should only accelerate the growth

in data from here on.

Each of the INSDC databanks (DDBJ, EMBL, and GenBank) makes its data accessible over the Internet and provides keyword search and homology search services (discussed in more detail later). These databanks have, as a result, come to be used by researchers throughout the world. The database provided by each databank may be copied and used by anyone in the world. However, the ongoing increase in the amount of data makes it difficult for a user to keep a copy up to date. For this reason, these search services, which enable a user to use a personal computer to search for data in a database that is always maintained with current data from around the world, are increasing in value, and they have been in great demand by researchers.

3. New computer system supporting DDBJ operations

To provide a dependable database that continues to grow at an explosive rate, as described in the previous section, it is important that the performance and capacity of the computer system be continuously upgraded and that software be allowed to evolve. Six years after the launch of the old system, it became difficult to support the rapid increase in data and the demand for new services. Plans for upgrading to a new system were drawn up in 2005–2006, culminating in the delivery of a new supercomputer system from Fujitsu. This section summarizes the requirements of this new supercomputer system and explains how those requirements were met.

3.1 Requirements of new supercomputer system

1) Support explosive growth in data
- Support a massive amount of nucleotide sequence data that increases by 1.5 times annually, making for about 400 million entries in five years time
- Shorten the update interval for all data
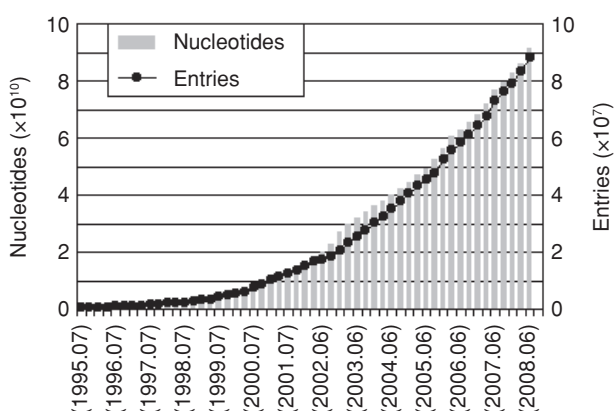
Source: DDBJ: DDBJ/EMBL/GenBank database growth.[7]

Figure 1
INSDC database growth.

(from 3 to 2 months)

2) Provide high-speed and stable search/analysis services

- Achieve high-speed response and high throughput in homology search services
- Achieve high-speed and stable response in keyword search services regardless of search conditions for data that is continuously growing

3) Achieve smooth migration from the old system and provide user-asset inheritance and compatibility

- Achieve smooth and rapid migration of the large number of existing application programs used for diverse services

4) Achieve high reliability and provide security measures

- Achieve a safe and secure system that supports data exchange among the three international databases and the provision of services to researchers inside and outside Japan

3.2 Features of the new supercomputer system

The new supercomputer system was developed to satisfy the above requirements. Its features are summarized below.

1) Resource allocation and system design supporting explosive growth of data

- For core data processing, the system combines large-scale symmetric multi-processing (SMP) servers, large-capacity storage, backup equipment, and the latest relational database management system (RDBMS) software to achieve high-speed processing of large volumes of data.
- For homology searches and analysis processing, it uses a new PC-cluster system, achieving high-speed response and high throughput through distributed processing.
- For keyword searches, it uses a large-scale extensible markup language (XML)

database server, achieving high-speed and stable response.

2) Provision of high-speed and stable search/analysis services

- For keyword searches, it achieves a stable response within ten seconds for 30 million entries of complex data, even for complicated search conditions.
- For homology searches, it achieves improved standalone performance five to eight times the old level and high-throughput performance by parallel processing.

3) Smooth migration from the old system and user-asset inheritance and compatibility

- For core data processing, it uses the Solaris operating system (OS), the same as the old system.
- For homology search processing, it uses Linux as the de facto standard OS.
- For analysis processing, it uses both Solaris and Linux to provide optimal processing according to the characteristics of the analysis program.

4) High reliability and security measures

- It supports active maintenance and a redundant configuration and detects faults in advance through a diagnostics monitoring function.
- It uses Symfoware and HiRDB, which are domestically developed RDBMS software.

3.3 Configuration and performance of new supercomputer system

The main items of equipment making up the newly introduced supercomputer system are listed below and shown in **Figure 2**.

1) Database construction/release servers
Large-scale SMP server: PRIMEPOWER2500 (28 CPUs)
Large-capacity storage: ETERNUS8000 (125 TB)
Blade server: BladeSymphony

2) Homology search server
PC cluster: PRIMERGY RX200 S3 (66 nodes)

3) Keyword search server
Large-scale XML database server:
ShunsakuEngine (2520 CPUs)

4) Analysis servers
Large-scale SMP server: PRIMEPOWER2500
(32 CPUs)
PC cluster: PRIMERGY RX200 S3 (66 nodes)

5) Backup equipment
Tape library: VD800 (750 TB)

6) Other servers/network equipment
Network server: PRIMERGY
RX200 S3/RX300 S3
Switches/routers:
Catalyst6506/IPCOM S2400, etc.

The performances of the new supercomputer system and the old system are compared in terms of major components in **Table 1**.

4. Details of new genome sequence database system

4.1 Database construction/release servers

The database construction/access servers constitute a system for uniformly managing DDBJ data and creating data for release purpos-es. This system consists of ETERNUS8000 125 TB high-capacity storage equipment and a BladeSymphony blade server centered on a PRIMEPOWER2500 (featuring 28 CPUs and 88 GB of memory) large-scale SMP server running the Solaris OS, which has a proven record of stable operation of large-scale database systems. Two types of database management software are used for different applications: HiRDB is used for the database construction system and Symfoware is used for the database release system. Both the database and release data are stored in the ETERNUS8000 high-capacity storage equipment, and in addition to performing periodic backups to VD800 backup equipment, the system can perform remote backups of especially important data to disk drives connected to servers belonging to the National Institute of Informatics.

The database construction system stores nucleotide sequence analysis data submitted mainly by researchers in Japan using either the SAKURA[8] nucleotide sequence submission system or a mass submission system. This data is checked and edited by specialists called
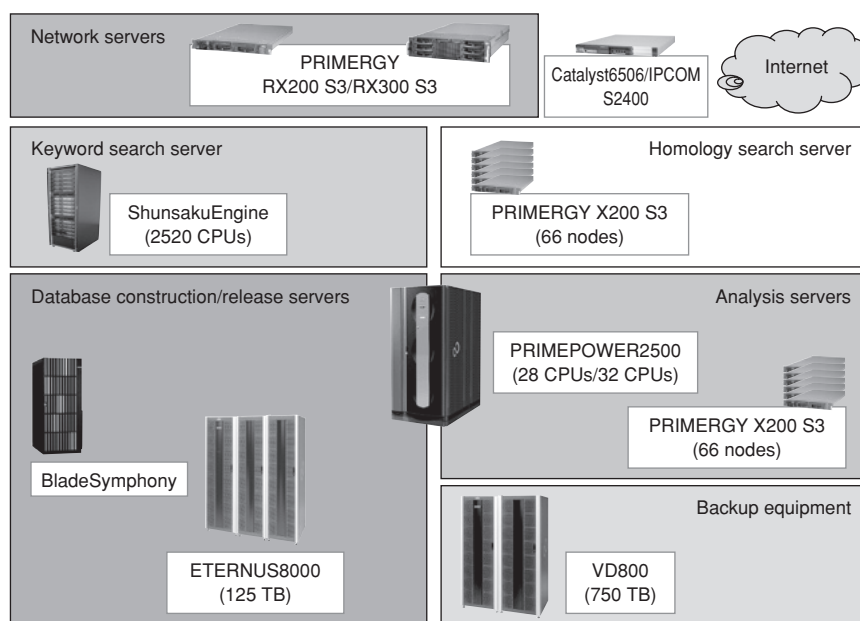

Figure 2
New supercomputer system.

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"annotators" at NIG. Checked data is edited into units of entries and passed on to the database release system on a daily basis.

In addition to data received from the database construction system, the database release system edits updated data received from EMBL/GenBank also on a daily basis and converts it to DDBJ format. The system releases all daily edited data of the three international databases. The entire database is released in entry (flat-file) format, DDBJ-XML format, INSDC-XML format, or FASTA format. Users may download data from a DDBJ anonymous FTP site[9] and may retrieve data using the getentry[10] search system (in units of entries) or by the homology/keyword search systems described below.

4.2 Homology search server

A homology search searches for biological similarity among DNA, RNA, and amino-acid sequences. In life sciences research, it is widely used for estimating genetic function, evolutionary analysis, etc. There are various types of software for conducting homology searches depending on the type of data targeted for retrieval and the algorithm used to conduct the search. At present, researchers are making much use of BLAST, PSI-BLAST, FASTA, SSEARCH, and HMMPFAM, for example. Life sciences researchers are also

making extensive use of multiple-alignment analysis based on biological similarities among nucleotide sequences and amino acid sequences.

The DDBJ provides Web-based services[11] for conducting homology searches by the above software or multiple-alignment analysis (by CLUSTALW) of the INSDC database and other databases having more than 70 million entries (as of November 2007), including a key-protein database. Search requests can be made by E-mail or from programs using a Web application programming interface. Search results may be viewed on a Web browser or received by E-mail.

The homology search server uses a PC cluster consisting of 66 nodes (2 of which are management nodes) of PRIMERGY RX200 S3 servers. Each node has two 3.0-GHz dual-core CPUs, 8 GB of memory, and 140 GB of hard disk storage (RAID1) and runs 64-bit-mode Linux for the OS.

In response to a search request from a user, the system automatically distributes the request to all the nodes using a network queuing system. This minimizes the waiting time and achieves a high-speed response and high throughput for the user. The HMMPFAM service, in particular, achieves ultrahigh-speed processing by using parallelization software developed by Fujitsu Laboratories.

As a result of these performance improvements, the usage rate of the popular BLAST/FASTA/CLUSTALW services increased by 10–30% in October 2007 over the same month a year earlier.

4.3 Keyword search server

The DDBJ provides the ARSA[12),13)] integrated keyword search service targeting INSDC and 24 other important databases in the life sciences. In past keyword search systems such as SRS,[14] the deterioration in response time accelerated as search conditions became more complex. Moreover, as the volume of data

Table 1
Performance comparison with old system.

Service/application	Equipment	Performance comparison
Database construction/release	UNIX server	About 10 times
	Blade server	
	Storage	
Keyword search	ShunsakuEngine	About 20 times
Homology search	PC cluster	About 15 times
Analysis	UNIX server	About 20 times
	PC cluster	
Storage	SAN storage	About 5 times
Backup equipment	Tape archive	

increased, a relatively long time was needed to create a keyword index. In the light of these problems, the ARSA keyword search service uses the ShunsakuEngine, a server dedicated to large-scale XML databases equipped with the Fujitsu-developed Shunsaku XML database engine loaded in dedicated hardware. This server provides a response time of less than 10 s (3 to 4 s on average) even for complex, compound search conditions for 24 databases with 30 million entries (as of November 2007). The ShunsakuEngine has 168 core CPUs and a total of 42 GB of memory in a 2 U chassis and includes a dedicated search algorithm for retrieving data in memory, resulting in short search response times in addition to a space-saving and power-saving configuration. The entire keyword search system uses 15 ShunsakuEngine units and 9 Linux servers mounted in two racks. As a result of the above deployment, the usage rate of the keyword search service increased by 10–20% in 2007 over the previous year.

4.4 Analysis servers

NIG operates—for joint research and analysis use—the PRIMEPOWER2500 SMP-type server featuring 32 CPUs, 128 GB of memory, the Solaris OS, which is applicable to large-scale memory jobs, and a Linux PC cluster system with 66 nodes (2 of which are management nodes), which is applicable to distributed memory jobs. Each node of the PC cluster system has two 3.0-GHz dual-core CPUs, 8 GB of memory, and 140 GB of hard disk storage (RAID1) using 64-bit-mode Linux for the OS. In addition to ordinary Gigabit Ethernet, the PC cluster is equipped with a high-speed InfiniBand interconnect, which achieves high-speed processing of distributed programs.

Researchers at NIG can make use of analysis servers by application, and outside researchers can do the same if they are involved in joint research with NIG.

4.5 Backup equipment

For backup purposes, the supercomputer system uses a VD800 tape library with a capacity of 750 TB. This equipment comes with 6.25 TB of hard disk storage for automatically backing up and restoring data to and from tape. By accessing these disk drives, a user can use the backup equipment as if it were a 750-TB disk system without been aware of the actual tape library. This backup equipment is normally used for backing up the DDBJ database, but it can also be used by NIG researchers on application.

4.6 Other network servers/equipment

The servers described above are separated from the Internet by a firewall at NIG. To provide robust security, Web servers, FTP servers, and mail servers for releasing data to the Internet are installed in a "demilitarized zone", and systems that store crucial data like the INSDC databases are separated in sub-networks.

5. Future outlook

This supercomputer system has been operating since March 2007 in a stable fashion without any major problems. The plan is to enhance system performance and capacity by about two times at the two-year mark after system introduction. The idea here is to upgrade the system after analyzing how it is being used while also giving sufficient consideration to usage trends in information systems in the field of life sciences research.

6. Conclusion

This paper described how a newly introduced supercomputer system has solved a number of key issues surrounding the operation of a very large nucleotide sequence database in life sciences research. We can expect the amount of life sciences data available to researchers to continue its dramatic growth in the years to come, but we also foresee a rapid move away from the separate databases and separate research

themes of the past to an interlinking of data and the pursuit of the "big picture" in biological phenomena. There will be a need to manage more complicated data in a more systematic way and provide user-friendly application services. Our goal is to operate this new supercomputer system as a cutting-edge information platform for life sciences research in Japan and throughout the world.

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