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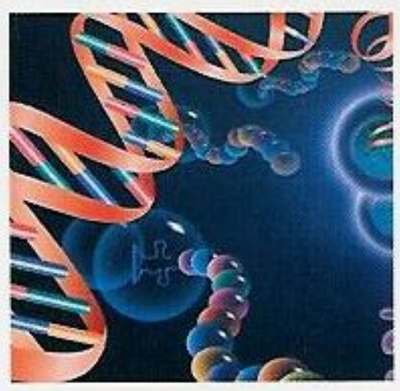

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A Personalized Data Management System for Heterogeneous Biological Data Editing

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ABSTRACT: The biological sequences in the biological laboratories have been produced since the techniques to get the sequences of genomes or proteins in HGP(Human Genome Project) have been improved. Unfortunately, there are scarcely the software packages to deal with the sequential data in most of biological laboratories and they are just stored in file formats. The integrated management system of biological data is required to manage the sequence data taken from other open databases to improve the analysis of the sequence data in our biological labs. We therefore suggest the system to edit, store, search biological information, and convert the formats of the sequence data, as well as to integrate and manage the data.

1 INTRODUCION

The biological Sequences have been made in many laboratories since the techniques to get the sequences of genomes or proteins in HGP(Human Genome Project) have been improved. The biologists connect the public biological Databases[1-4] and retrieve sequences which is similar with what they have, then this work is utilized in homology research, functional analysis and prediction. Unfortunately, there are scarcely the software packages to deal with the sequence data in most of biological laboratories and they are just stored in file formats

The integration and management technique of heterogeneous sequence data from public sequence databases is widely used to make diverse information and prediction. Thus the database management technique that is suitable for a sequence data is required. Especially, an integrated data model which handles the modification of program and data is needed for analysis on the various programs.

In this work, we support editing and converting among heterogeneous public biological database flat files as well as own sequences in laboratories. The BSML(Bioinformatic Sequence Mark up Language)[5] based on XML is utilized for representing the complex and hierarchical biological data. The biologists easily analyze their accumulated biological data using our system and apply the results of biological data analysis to medical science and pharmacy.

2 RELATED WORKS

2.1 BSML

The BSML is one of open standard of XML data in bioinformatics research. BSML represents good bio-physical features as well as visualization of biological sequence data comparing with other languages such as abstract annotations. It also supports converting formats among biological flat files base on flat-form independence. In this point, BSML is more complete and specifiable than other XML formats in bioinformatics. BSML which our system supports is used in the area of representing gene research results and biological molecules, and exchanging them, hence many laboratories and company choose BSML as new standard.

2.2 Genomic Workspace

The Recent tools for converting formats among standards are implemented by JAVA or Perl module. One of these worthy converting softwares is Genomic Workspace[6]. It converts Genbank[1] flat file into BSML format and includes Genomic Viewer for a good graphic visualization of biological information.

2.3 Staden Package

The Staden Package[7] is developed for managing and analyzing the sequence from sequencing machine by Medical Research Council Laboratory in U.K. It constitutes several tools as following. *Trev* represents raw experimental file from sequencing machine. *Trace_diff* describes the mutation information of reference and Trace data. *GAP4* edits contigs and assembly of sequences. Pregap4 is used for pre-processing the assembly data. Spin analyzes the result sequence such as retrieving similar sequences and some other operations.

The Staden Package analyzes and simply manages sequences in sequence experimental files but doesn't store sequences into database and retrieve. It can't process a mass of sequences.

2.4 Sequence Data Formats

Each flat file from public biological database has different format. Genbank[1], Swiss-Prot [2], PIR-Codata[3] and PDB[4] flat files are generally used. Also, each sequence analyzing software uses different format but FASTA[8] established by Pearson is the most common format.

```
> SQ2002060300001
GGTACCTTCTGAGGCGGAAAGAACCAG
CCGGATCCCTCGAGGGATCCAGACATG
CTTACCGGATACCTG
```

Figure 1: An example of FASTA format

The problems of biological formats I mentioned above are following. The formats can be modified when they are released. To understand the range of field and field value are difficult and data types in the same field in each format can be different. The conversion for different formats needs different parsers to extract the interesting field.

Thus applying XML is essential to visualize and exchange the sequence data and the bio-molecules because XML has high level format conversion technology and re-usability. There are a lot of markup languages for representing the genome data such as BSML, BioML(Biopolymer Markup Language)[9]. The public biological databases[1-4] are also trying to produce the XML based formats for representing biological information.

3 SYSTEM ARCHITECTURE

Figure 2 shows the system architecture we suggest. We briefly explain each component of our system.

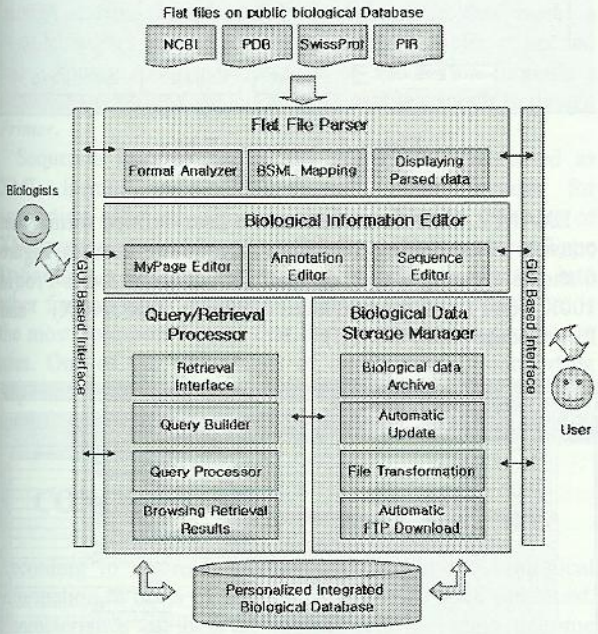

Figure 2: System Architecture

3.1 Flat File Parser

The Flat File Parser extracts meaningful data fields from each flat file in order to integrate heterogeneous formats from the various public biological databases. The Flat File Parser which is suitable for each flat file is developed for extracting the interesting fields from divergent biological flat files, then the integrated BSML model is created using extracted data. We developed Flat File Parsers per each flat file such as Genbank, Swiss-Prot, PIR-Codata, FASTA, BSML and so on. Figure 3 shows the mapping information between the parsed interesting fields and BSML elements(attributes) for loading on the system.

3.2 Biological Information Editor

Biological Information Editor edits annotation and sequence data. Our Editor consists of MyPage Editor, Annotation Editor and Sequence Editor.

MyPage Editor supports to make user defined formats that constitute the interesting fields extracted from various flat files such as Genbank, Swiss-Prot, PDB, PIR-Codata, BSML, FASTA, data on the local database and so on. Once MyPage format is made by user, Modification, insertion and deletion of the field in the format are also performed by MyPage Editor. The user defined format through MyPage Editor is stored as an XML format on the disk or local database.

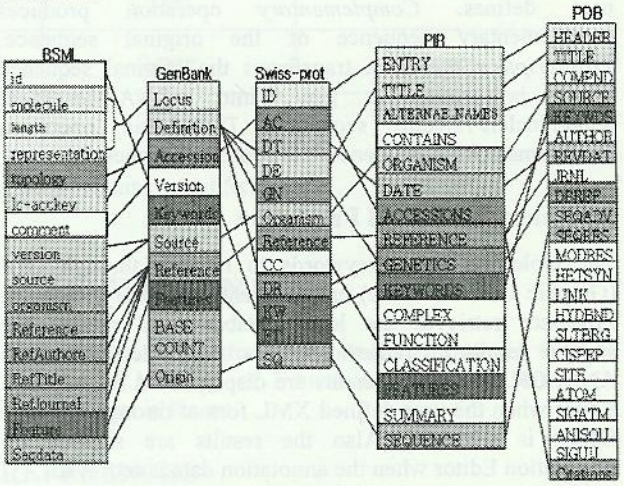

Figure 3: Mapping Information among biological Formats

While MyPage Editor creates user-defined formats and performs insertion, modification and deletion of the interesting field extracted from each format, Annotation Editor performs the same operations for annotation data in each format. Therefore original source(flat file) is maintained their own frame. The modified original source stored as BSML format on the disk and local database if the user wants. Annotation Editor mainly handles annotation data of interesting sequence such as types, taxonomic information, citations, reference data, authors, specific sites of sequences and so on.

The original Sequence:

```
0123456789012345678901234567890123456789012345678901234567
atgttctacgtggttatatgcatactggaagcctacgacgtcatctaa
            10        20        30        40
```

(a) Base composition

A: 13 bp T: 15 bp G: 10 bp C: 10 bp

(b) Set-Subsequence

```
0123456789012345678901234567890123456789012345678901234567
tctacgtggttatatgcatactggaagcctacgacgtcatc
5        15        25        35        45
```

(c) Complementary

```
0123456789012345678901234567890123456789012345678901234567
ttagatgacgtcgtaggcttccagtatgcatataaccacgtagaacat
            10        20        30        40
```

(d) Transcription

```
0123456789012345678901234567890123456789012345678901234567
auguucuacgugguuauaugcauacuggaagccuacgacgucaucuaa
            10        20        30        40
```

(e) Translation

```
0123456789012345678901234567890123456789012345678901234567
Mfyvvicileaydvi
10        20
```

Figure 4: Sequence operations

Sequence Editor[10] supports the useful operations handling sequence, so it produces a new sequence from original sequence. We will briefly introduce several operations on Figure 4. *Base Composition* operation calculates the composition of DNA(Deoxyribo-Nucleic Acid) and shows us the percentage and the numbers of each Nucleotide(Adenine, Guanine, Cytosine and Thymine). *Set-Subsequence* operation makes a new sequence from original sequence using starting and ending index which the user defines. *Complementary* operation produces complementary sequence of the original sequence. *Transcription* operation transforms the original sequence which is proven as gene, into mRNA(Messenger Ribo-Nucleic Acid) sequence. *Translation* operation transforms mRNA sequence into Protein sequence.

3.3 Query/Retrieval Processor

The biologists input keywords to retrieve through GUI (Graphic User Interface) environment and Query/Retrieval Processor retrieves the local database and returns the suitable results for retrieval options users selected such as AND, OR. The query results are displayed on the MyPage Editor when the user defined XML format through MyPage Editor is retrieved. Also the results are showed on Annotation Editor when the annotation data is retrieved.

The query results on the MyPage and Annotation Editor is also modified by adequate Editors if user wants.

3.4 Biological Data Storage Manager

Sequence data and annotation data for sequence is separately stored because the fast accession to biological data and retrieval are needed in order to analyze data. When biologist wants to make other format from the database, for example FASTA format, the necessary biological data on the database for making a new format is retrieved.

Our database maintains up-to-date biological information through automatic FTP (File Transfer Protocol) download and update. Users can monitor new release information of public biological database on the web using our system. Users store the absolute FTP path in our FTP lists. When the biological databases release a new version, what the users have to do is just choosing appropriate FTP path in FTP lists.

A new flat file from FTP downloading is compared with existing entry in the database to be updated. In the procedure, the system asks whether the database is updated as a new flat file or not.

4 IMPLEMENTATION AND EVALUATION

4.1 Example queries and results

The implementation environments are following. MySQL 4.0.17 is used to store genome sequence and annotation data. JAVA from Sun Mirco System is used to implement major interface and JAXP(JAVA API for XML Processing) v1.2 for parsing XML documents. Our system is distributed on the web[11] and archive contains install files of MySQL 4.0.17 and our implements. We have two examples to show our implementation.

EXAM 1. User wants to make *Complementary, Transcription, Translation, Set-Subsequence* operated Sequence of original sequence in Genbank locus name 'DRONCX' with base composition. The upper window on Figure 5 shows the original sequence and the lower one shows the derived sequences from operations.

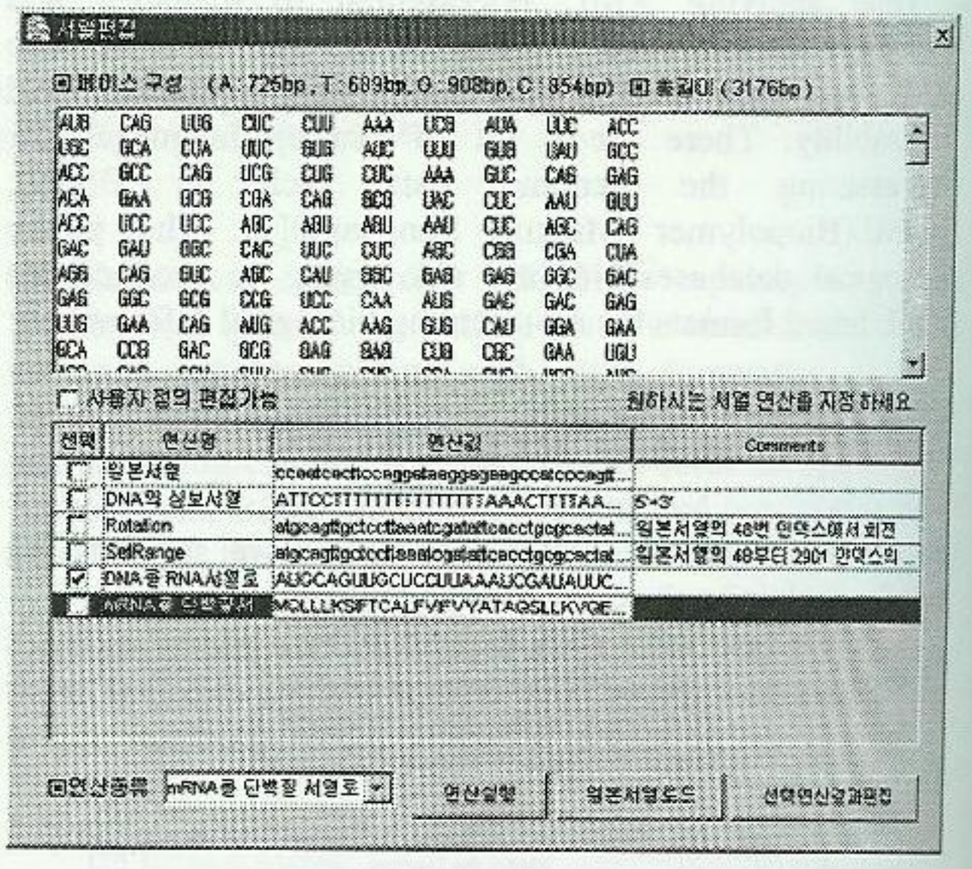

Figure 5: Sequence Editor

EXAM 2. User wants to create a user defined format that consists of interesting field from various file formats. Figure 6 shows creating a user defined format from Swiss-Prot(id 100K_RAT), Genbank(locus name DRONCX) and PIR-Codata (entry CCHU).

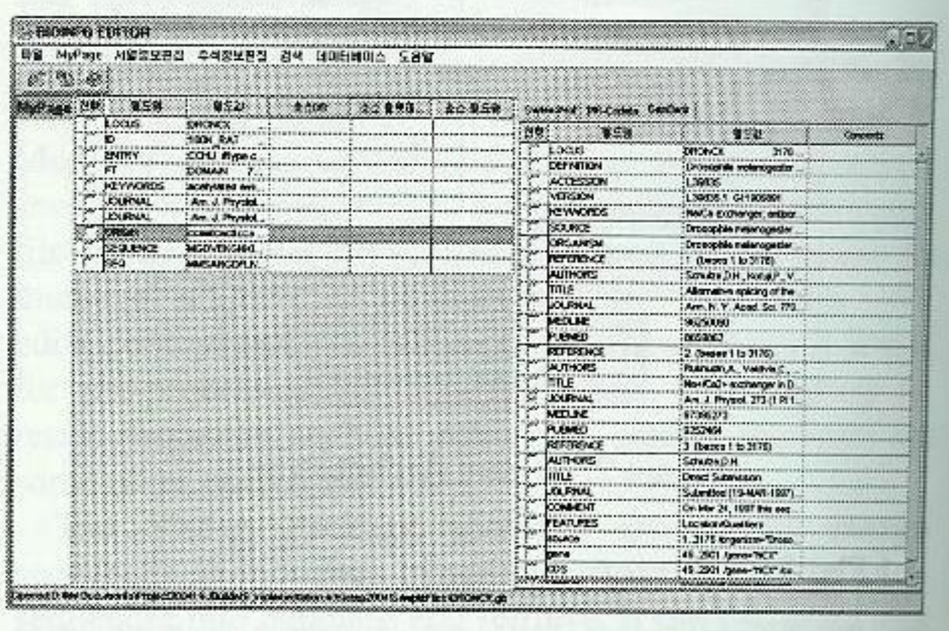

Figure 6: MyPage Editor

4.2 Evaluation

In this paper, we implement new issues that we mentioned in introduction with deep consideration. The evaluation of the proposed system is performed according to comparing with Staden Package, Genbank, Genomic Workspace and so on. Table 1 shows the result of comparing.

Storing the historical data of sequence release version is applied for analyzing the change of protein sequence, we expect that new useful protein and drug can be discovered based on analysis of version sequence.

Item	Staden Package	Genbank	Genomic Workspace	Proposed System
Sequence Manipulation	Support	None	None	Support
File Format	EMBL format	Genbank/ASN.1 /BSML	BSML	XML Format based on BSML DTD
Storing Sequence	File	DBMS	BSML Documents/ Text	DBMS
Sequence Versions	None	Support	None	Support
File Transformation	None	None	Support	Support

Table 1: Comparison with existing Sequence Management Systems

Creating and designing a new sequence for experiment and analysis through Sequence Editor is possible. The purpose of a PCR (Polymerase Chain Reaction) is to make a huge number of copies of a gene. This is necessary to have enough starting template for sequencing. In this work, a complementary sequence of one of double helix is needed and a known *Primer* is required to synthesize. Therefore sequence operations we suggest are usable enough to design *Primer*.

Sequence information in this system is represented as XML format and converted into other formats for supporting efficient sequence analysis. That is, because of XML representation based on BSML DTD(Document Type Definition), sequence information is easily converted into other formats used in various analysis program. FASTA is the most common format that the most analyzing software uses. One of the advantages of our system is converting sequence from database or various sources into FASTA format.

5 CONCLUSION

According to improving techniques to get the biological information, a mass of biological data have been produced. Characteristics of these biological data including genome sequences are heterogeneous and various. Although the need of management systems for genome sequencing which should reflect biological characteristics has been raised, the most current biological databases provide restricted function as repositories for biological data.

Therefore, this paper describes the management system of genome sequences and annotation data of those sequences for manipulating the formats in bioinformatics. It includes format transforming, editing, storing and retrieving for collected nucleotide sequences from public databases, and handles sequence produced by experiments. It uses BSML based on XML as a common format in order to extract data fields and transfer heterogeneous sequence formats. To manage sequences and their changes, version management system for originated DNA is required. This system automatically updates the information in local database using FTP. This research is widely used for a long term study of biology, medical science, pharmacy and helps to accumulate the own sequence information at the level of biological laboratories.

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