Journal of Neurological Sciences [Turkish] **24:(1)**# 10;45-55, 2007
http://www.jns.dergisi.org/text.php3?id=141

Research Article

Neuroinformatics Literature System Oriented to Knowledge Discovery: Design and Preliminary Implementation

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Abstract

Neuroscience research has brought on enormous amounts of diverse data, this has led to the difficulty for the neuroscientists to grasp all userful information and conduct the comprehensive brain research independently. In addition, many barriers exist to the querying of multiple databases, including mismatches in query language, access mechanisms, data models and semantic deduction. In order to solve the neuroscientific information integration and database interoperability, we have been developing an internet-accessible Neuroinformatics Literature System(NILS) for neuroimaging and brain function research. NILS is designed for knowledge discovery and NILS consists of 8 main function modules: System Maintenance, Literature Renewal, Literature Retrieval, Result Display/Output, Literature Information Analysis, Neuroimaging Integration, Neuroinformation Text Mining and Nerve Ontology Prototype Construction. It makes possible to semiautomatic gather, coordinate, analyze and store data from multiple underlying sources into a single high-performance environment operating from a local server, provides multi-disciplinary and multi-level integrative retrieval service, helps us to establish a network of comprehensive neuroscientific knowledge for fully understanding the brain principle of work. NILS will not only serve as a foundation platform for the future study pattern driven by hypothesis, but also reveal a great variety of implication relations in the literature, which was previously rarely-known.

Keywords: Neuroinformatics; neuroimaging; brain function; literature; ontology; knowledge base; text mining; knowledge discovery

Bilgi Buluşuna Yönlendirilmiş Sinirbilim-Bilgi Kaynak Sistemi: Tasarım ve İlk Uygulama

Özet

Nörolojik bilimler araştırmaları önemli ölçüde bilgi birikimine neden olmuştur, bu nedenle sinir bilimci bütün bu bilgileri güçlükle sindirebilmekte ve ayrıntılı bir araştırmayı bağımsız olarak yönetebilmekte güçlüklerle baş etme durumundadır. Buna ek olarak çoklu veri tabanlarında sorgulamada, anlambilim, veri modelleri, ulaşım mekanizmaları ve sorgulama dili gibi uyumsuzluğa yol açan birçok engeller mevcuttur. Sinirbilim ile ilgili veri kaynaştırma ve veri tabanlarının işlerliğini sağlama yönünde sorunu çözmek üzere internet üzerinden ulaşılabilen NILS (Neuroinformatics Literature System=Sinirbilim-Bilgi Kaynak Sistemi) ile nörolojik görüntüleme ve beyin işlevleri araştırmalarında kullanıcıya çoklu ortamdan sonuç çıkartıcı, koordine edici, analiz eden ve bilgiyi kayıtlayan yarı-otomatik, yerel, hızlı çalışan bir ortama nakile çalışmaktayız ve bu sistemi geliştirmekteyiz. NILS bilgi buluşu için tasarlandı ve 8 ana işlev modülünden oluşmaktadır: Bunlar sistem bakımı, kaynak yenileme, kaynak düzeltme, sonuç sunumu, kaynak bilgi analizi, sinir görüntüleme bütünleşmesi, metin bulmada nöroinformasyon ve sinir ontoloji prototip yapımıdır. Bilgiyi yarı-otomatik anlam çıkarma, koordine etme, analiz ve depolamayı olası kılar. Beyinin çalışma prensibini tamamıyla anlama açısından ayrıntılı nörobilimsel bilginin ağını oluşturmada yardımcı olur. Multidisipliner ve çok katmanlı bütünleştiren ve düzelten servis olarak yüksek performanslı tek bir yerel şebekeye bağlar. NILS sadece hipotezle oluşacak gelecekteki çalışma modellerinin kaynağı olmakla kalmayacak, aynı zamanda daha önceleri ender olarak bilinen literatürdeki çeşitli anlamsal ilişkileri, dikkatten kaçan bağlantıların ve ilişkilerin tanınmasını da ortaya çıkaracaktır.

Anahtar Kelimeler: Sinirbilim-bilgisi, sinir-görüntüleme, beyin işlevi, kaynak, ontoloji, bilgi tabanı, metin tarama, bilgi buluşu

INTRODUCTION

Neuroscience research has brought on enormous amounts of diverse data, moreover the experimental technology progress of neuroscience causes the new neural information data type to increase unceasingly, this has led to the difficulty for the neuroscientists to grasp all userful information and conduct the comprehensive brain correlation research independently[6,15]. As a response to this predicament, the Human Brain Project (HBP)[7,10] was launched in 1993. HBP hopes to apply informatics tools and techniques to integrate the fragmented neuroscience data and knowledge, then making it possible to regain a sense of wholeness from the ever-diversifying parts. The collaborative research effort that results from these and similar goals is called Neuroinformatics[9]. The major goal of the neuroinformatics platform is to organize neuroscience databases and knowledge storage systems, which will facilitate the development of computational models and tools, and further international interdisciplinary cooperation[6].

Neuroscience collects many kinds of data from different human individual, different level (gene, molecular, ultrastructure, cell, nerve network, the entire brain) and different style (sequence, based on imaging, electrophysiology, behavior). In order to understand the nervous system structure and function, neuroinformatics database and tools are required to manage and integrate the massive multiple data. We also need a basic organizational skeleton to test the relationships between data that are derived from different experiments, to study different aspects of the brain, on different subjects, from different laboratories, with different methods. The fast approval and widespread application of neuroimaging to the research of brain structure and function provides an extraordinary opportunity to take advantage of databases to organize, query and share raw and processed data. Although important progress has been made in the aspect of neuroimaging databases development, many problems still need to be solved before these databases reach their full potential and become the invaluable assets in neuroscience research[21].

Database interoperability is an urgent issue within the field of Neuroinformatics[14]. With the strong request from the whole neuroscience community, the number and variety of repositories of neuroscientific information is rapidly expanding, for example, the SenseLab Project (http://senselab.med.yale.edu/senselab/), IBVD (Internet Brain Volume Database, http://www.cma.mgh.harvard.edu/ibvd/), Neuroinformatics Research in Vision (http://www.neuroinformatics.gr.jp), NIDS (Neuroinformatics Database System for Disease-Oriented Neuroimaging Research)[22]. However, many barriers exist to the querying of multiple databases, including mismatches in query language, access mechanisms, data models, and semantic deduction. The associated integration problems can be sorted as follows: system integration (software/hardware platforms, transport protocols, interface), structural integration (relational, object-oriented, semi-structured data) and semantic integration (common vocabularies, glossary, ontologies).

Therefore it is extremely significant to integrate the neuroscientific information resources. In order to solve the above problem, we have been developing an internet-accessible Neuroinformatics Literature System(NILS) for neuroimaging and brain function research, which will enable the user to gather, coordinate, analyze and store data from multiple underlying sources. This system also enables scientists to combine data which they have produced locally with data from public bioinformatics databases; it will serve as a foundation for future hypothesis-driven experiments. We look forward to

working with those who build such data archives to create a network of neuroscientific knowledge that might help us to attain a more complete understanding about how the brain works.

METHODS

System design

NILS is designed for knowledge discovery, it includes main function(Fig. 1) and expansive function(Fig. 2). The main function part is the system base frame, including the System Maintenance, Literature Renewal, Literature Retrieval and Result Display/Output 4 modules, its function is the prompt collection, reorganization and storage of related literature data for neuroscience research, to provide multi-disciplinary and multi-level integrative retrieval service, and it has the retrieval result demonstration and output for reference quotation with many kinds of ways to select. The expansive function provides high-level service oriented to neuroinformatics research, including the Literature Information Analysis, Neuroimaging Integration, Neuroinformation Text Mining and Nerve Ontology Prototype Construction 4 modules, it can statistically analyze literature publication information with related distribution, integrate multi-level neuroimaging data, extract knowledge from the literature, and provide the primary data for the nerve ontology prototype construction. Although these modules function is relatively independent, this integrated system is much easier to maintain, and it facilitates future database expansion.

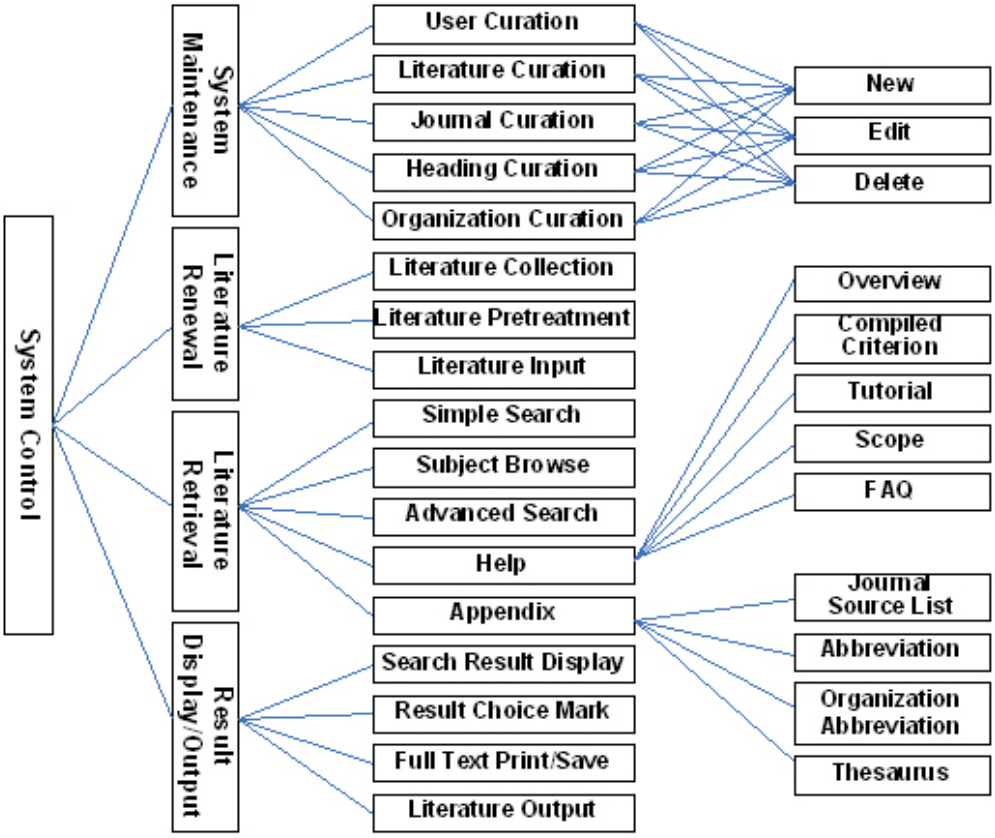

Figure 1: *System principal function structure schematic drawing. Each pane shows different function module, and these modules, function is relatively independent, so it facilitates database maintenance and expansion in future.*

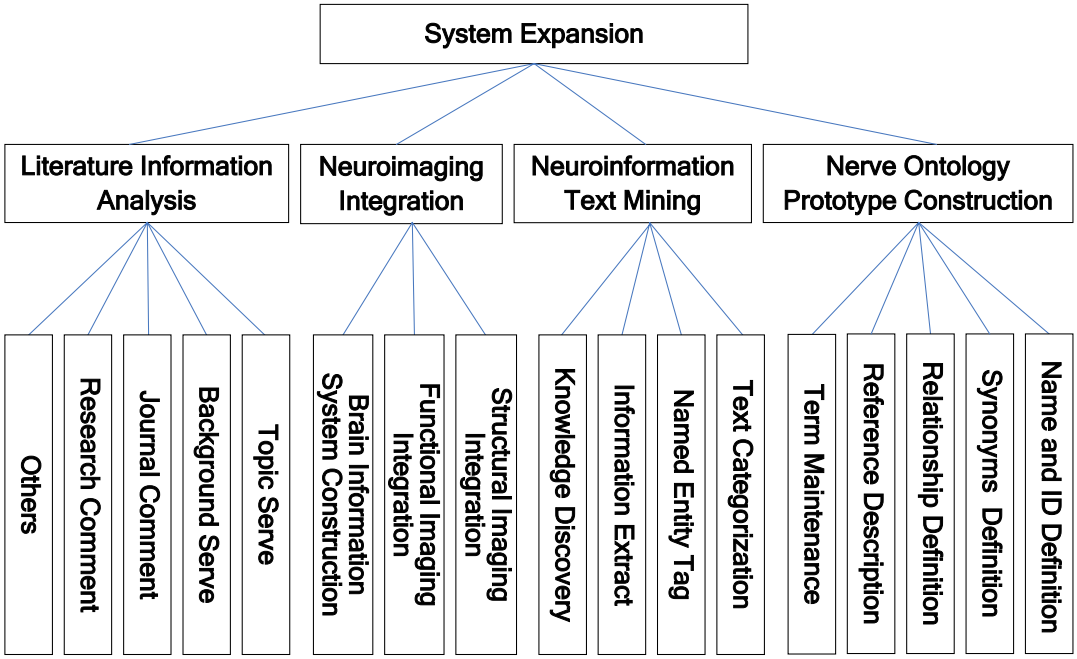

Figure 2: *System expansive function structure schematic drawing. Each pane shows different function module, and every lengthwise function modules includes various sub-modules as well.*

System configuration

We use the cluster system of TS10000 in our laboratory as the database hardware platform. This server has 17 double pathway computation nodes (computational ability achieves 100G flops at peak value) and 11 high speed optical fibers in a hard disk array(capacity achieves 1.5T), and can provide formidable parallel computational ability and large-scale, high-speed, reliable digital data service. The object-oriented relational database Oracle 9i (operating system is Linux 7.3) act as the database management system. Oracle 9i leads the field in many aspects, such as system usability, stability, program development environment and so on.

Data model and implementation

For this system we have adopted a 3-tier structure: the permanent level, the control level and the display level. A major part of the effort involved in developing a database is spent in modeling the type of information which is to be included in the database and how it is to be queried. The database model and optimized table relations design are shown in Fig. 3. Data models were devised to classify, organize and represent classes of different text and images to support information retrieval.

The overall system uses the B/S paradigm: the back-end application program was developed on the basis of Java, the front-end mainly uses JSP, JavaBean and other Java web application technology to implement the database inquiry safeguarding and so on. At present, we use Apache Tomcat 5.0 for the web server and have installed J2SDK1.4 of Sun to cooperate with Tomcat. Tomcat 5.0 provides not only the web service, but also web containment, through responsibility for compiling the JSP file.

Firstly we designed a flow chart (Fig. 4) of the overall system showing how the user makes a query, then this query is linked to the database using the JDBC driver, and finally Java is utilized to code various modules. After finishing the code, then it is tested for functionality. This is a cyclical process until our requirements are met completely.

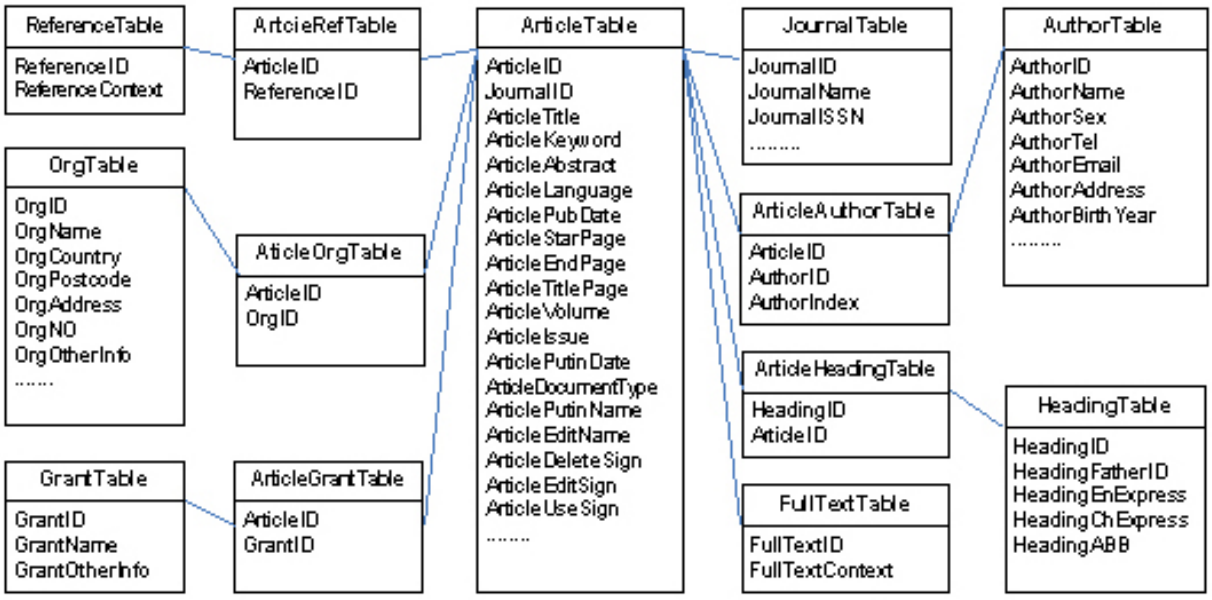

Figure 3: *Table fields mapping relations of journal literature. The database tables are designed according to the optimized E-R model. Each pane represents an object entity. Above the horizontal line is the table name in the box; below the line is the object attribute.*

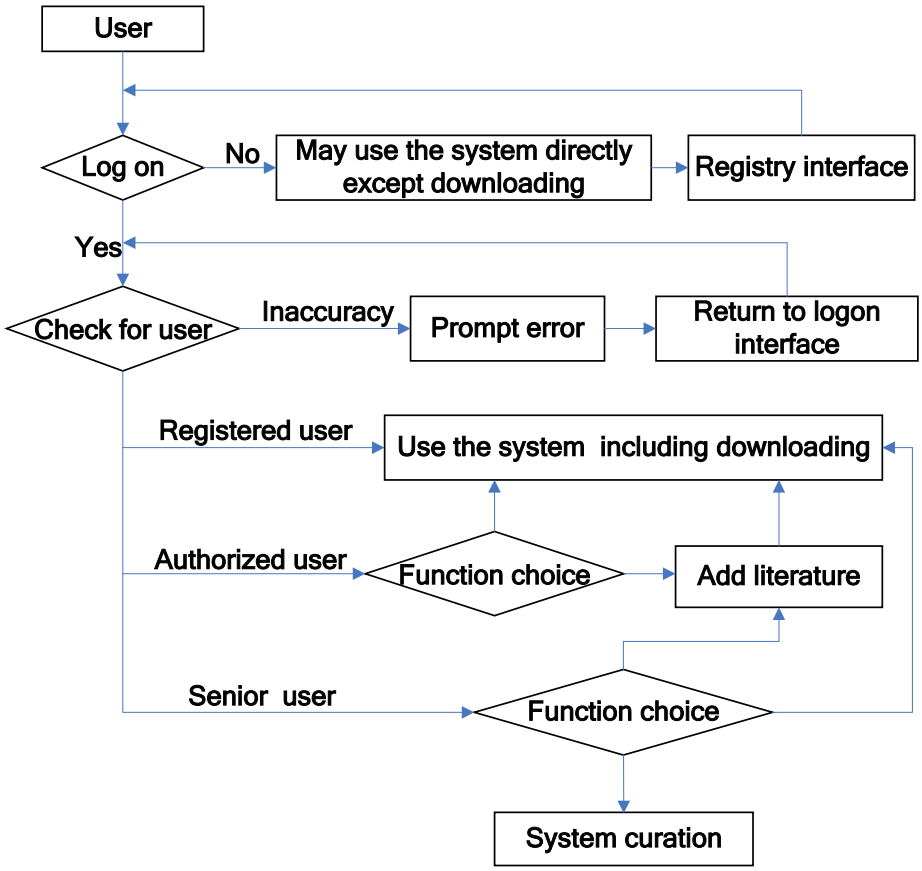

Figure 4: *Client flow chart. After logging on the system, the user interface could provide different services according to the user's permission level.*

Our goal is to provide easy access to the database for researchers with little or no knowledge of how the database operates, so we have designed and built a web-accessible interface, which allows users to interact with the database using commonly available web browser software. A primary challenge in the user interface design was determining in advance which subset of queries would satisfy the needs of most users, while still providing a simple interface. We chose this approach, rather than providing a more powerful, but cumbersome, standard query language (SQL) interface.

PERFORMANCE

NILS is a multi-purpose academic periodical full-text literature platform; it safeguards the literature involving Neuroscience, Bioinformatics, Proteomics, Biomedical Photonics, Medical Imaging and so on, and can carry on the input, retrieval and maintenance of the literature data (Fig. 5). Besides the complete information retrieval function, this platform also has secure and reliable use conditions, and consequently may be available for information sharing and data exchange on campus networks or the Internet.

User jurisdiction

NILS has set the network user jurisdiction graduation at four levels: (1) the general non-registered user can retrieve and examine the abstract page, but cannot download the full text; (2) the ordinary registered user may retrieve and download the full text; (3) the authorized user can retrieve, download and populate the literature; (4) In addition to the above functions, the senior user can also modify and delete the literature, and view inquiry processing records for literature.

Literature renewal

The system can store and maintain all kinds of files, such as PDFs of literature, image files and experimental data. All users can utilize the database operations to retrieve and curate the data at any time on any networking computer according to their usage rights. While importing the literature to the database, the program will first check for duplication. If the author, title, year and publication type are the same, it would be recognized as a duplicate and then discarded; if the database does not have the present literature source, it would complete all the information needed in the literature populating page, and submit it for the first time. This initial submission is saved in a primary folder, in holding until personnel are able to check it against the authoritative text, at which point it can be submitted officially to the database and made available for user retrieval. When submitting new literature to the database, the software automatically takes account of literature processing and quantity, which boosts the guarantee of accurate and reliable literature data.

Literature retrieval

Users may obtain a listing of existing database entries for a given field prior to launching a query; in addition, the NILS provides three ways of retrieving information, simple search, advanced search and subject browse, as well as fourteen different retrieval fields, including title, author, key word, abstract, journal name, year, organization, classified subject and so on. In addition, the system is equipped with logical coordinate retrieval ("AND", "OR", "NOT") and secondary circulation retrieval, to enhance the retrieval hit probability. Subject Browse is provided along with the novel tree-structure index system in the field of neuroimaging and brain function. This index is based on important targets in neuroscience, such as neuroanatomy, neurophysiology, neurogenesis, cognitive function and clinical diseases. The overview of the field it offers will benefit students and beginners especially.

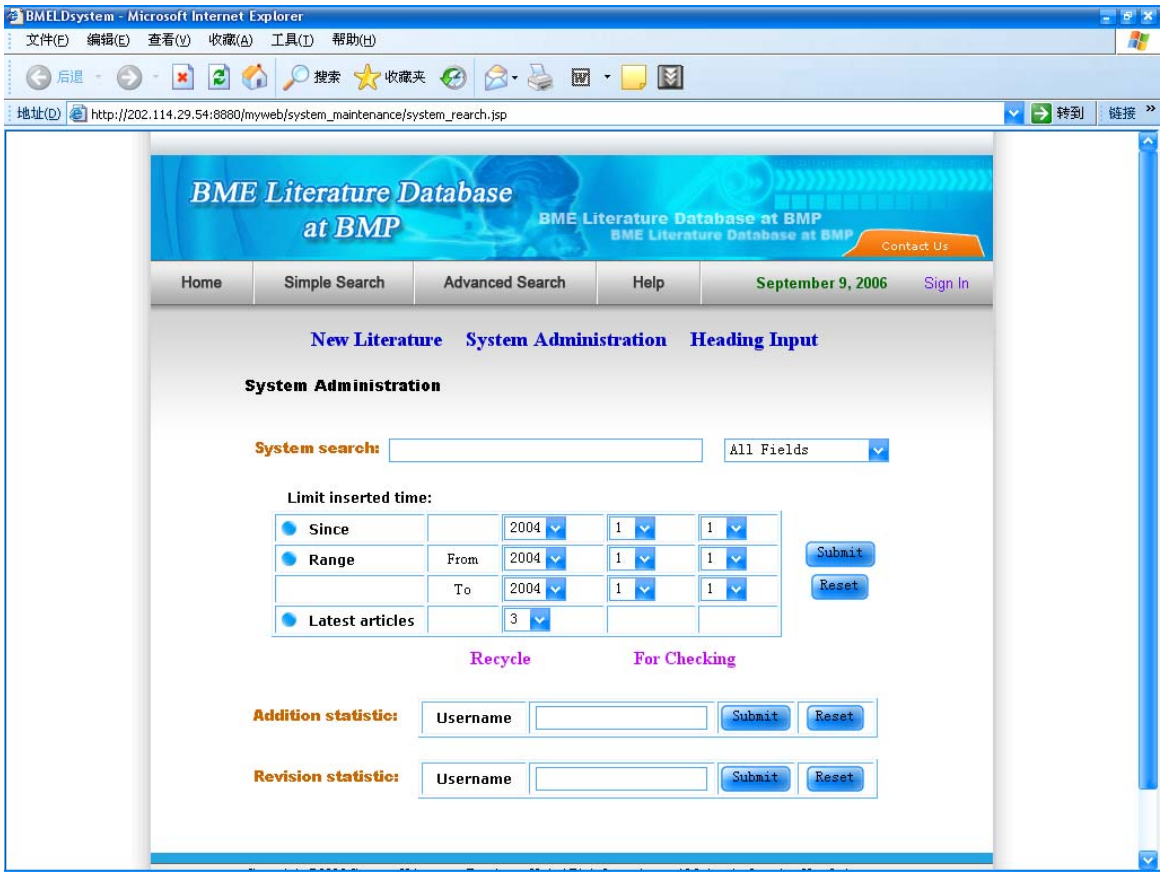

Figure 5: *System administration interface. All users can access the database operations to retrieve and curate data at any time on any networking computer according to their different levels of authorization.*

Result display and output

The retrieval result output mode is equipped with data item selection, and the records display may sort according to correlation, year, title and so on; the amount on each page may be freely chosen also. Besides such functions as tagging and saving retrieval results, printing and saving full texts, or examining and outputting selected records, the database retrieval software can simply export results to the program EndNote (a literature management tool, produced by Thomson ISI ResearchSoft, which is famous for SCI), so that the user may conveniently consult, refer and quote the text while composing a paper.

DISCUSSION

We have completed NILS system design and realized the main functions. With the future work, we will firstly focus on the work about statistical analysis and neuroimaging information integration module, and then design/integrate text mining tools, and complete the construction for knowledge base and imaging repository finally.

Neuroimaging integration

The NILS is just one effort among many to create web-accessible data resources for all types of imaging, from whole organs to molecules. Neuroinformatics is particularly focused towards understanding the brain in all its aspects – anatomy, pathology, and function (including behavior). Thus, images and anatomy are important components of neuroinformatics research, but they are not the only ones. Our neuroimaging integration will be organized into three basic sections: structural imaging integration, functional imaging integration, and image-based brain information system construction[6,15]. Our efforts will contribute to the development of a new

biomedical information system for better understanding of integrative brain function.

Text mining

All neuroscientists are busy with inquiring into how the brain works, but they only spent a part of time in the laboratory or clinic for the new knowledge discovery actually. Learning what has already been reported in the literature is becoming an increasingly larger task, they either appraise a hypothesis and plan to confirm it by adopting the optimal means, either understand the new research trends and maintain the synchronization, or simply avoid the repetition discovery in the scientific research work. As more and more scientists archive their primary research results in databases, and as data sharing becomes more and more common[13,16,20], data mining across different databases will become an increasingly important endeavor[1,7,17]. As more and more biomedical literature is published electronically, it is not only an opportunity, but also a pressing need, to automatically summarize the literature in a customized way. The process of fact extraction can be automated and optimized to keep literature pointers up-to-date or to filter relevant information from the literature[8]. We plan to develop an information extraction system to allow for automatic updates of information that describes certain aspects of neuroimaging, as well as to mine potentially relevant literature from neuroscience resources to help populate the NILS.

Literature-based discovery

Mikhail V. Blagosklonny et al. propose the new term - conceptual biology on Nature in 2002, they consider: 'The conceptual review should take its place as an essential component of scientific research'[3]. Millions of easily retrievable research results are agglomerated in databases, which they come from a variety of sources in seemingly unrelated fields, and from thousands of different periodicals. 'Reviewing' these accumulated results in a concept-driven manner, linking them into testable chains and networks, can generate new knowledge. With the rapidly growing body of scientific knowledge and increasing specialization, it is possible that the research of one group might solve an important problem of another, without the two groups being aware of each other's work. In the field of biomedicine, a great deal of knowledge is recorded at least in secondary form in bibliographic databases such as Medline, as well as in various specialized molecular biology databases. These resources provide both an opportunity and a need for developing advanced methods and tools to discovery new knowledge supported by computers.

The goal of literature-based discovery, in general, is to discover new, potentially meaningful relationships between a given starting concept of interest and other concepts, by mining bibliographic databases such as Medline. The idea of discovering new relationships from a literature database was recommended by Swanson[18] who, together with collaborator, made a lot of medical discoveries that have been published in relevant medical and informative journals. The main idea is first to find all the phenomena B related to the starting concept A (e.g. if A is a disease then B might be pathological symptoms, effects, etc.). Then all the phenomena C related to B are discovered (e.g. if B is a pathological symptom, C might be a gene, structurally or functionally, related to the pathophysiology of B). At the last process we examine whether A and C appear together in the same literature. If they do not appear together, we have discovered a potentially new association between A and C. This association should be corroborated or denied using human judgment, laboratory methods or clinical investigations, depending on the nature of A and C. We are engaged in an ongoing project to devise an interactive biomedical discovery support system, similar to

BITOLA[11] for the field of neuroimaging, brain function and disease.

Nerve ontology prototype construction

These days, the term 'bio-ontologies' spreads throughout discussions of scientific data integration and exploration[2, 4, 12]. Beyond dictionaries or thesauri, bio-ontologies formally delineate relationships between defined biological concepts, consequently the glossaries can be used both by humans and by computers to exchange and explore information. Bio-ontologies for the obvious knowledge domains are ready and are engaged in widespred use. Now the attention is beginning to be focused on ontologies that describe *in vivo* cell imaging, molecular interactions and data that are linked to space rather than text. In addition to general-purpose controlled vocabularies such as the Unified Medical Language System (UMLS) and Gene Ontology[5,19], a large number of more specialized vocabularies are being created (http: //obo.sourceforge.net, Open Biological Ontologies,). Despite this growth, it has been observed that many of the publicly available ontologies are simply controlled vocabularies, and do not satisfy the primary requirements of formal ontologies that can be used for purposes like automated logical interpretation. Hence, they cannot be easily integrated into larger information management systems. We aim to construct a consolidated, extensible biomedical ontology system in an effort to understand the basic mechanism of the brain function and diseases, by combining information from existing public ontologies and developing them further with new information from relevant research literature. We have devised hundreds of ontological terms and mapped their relationships, and look forward to building a comprehensive ontology for neuroimaging.

We look forward to collecting and depositing as much literature data as possible, thus aiding neuroscientists in their research and promoting the development of neuroscience. Completion of this project will have several outcomes with vital significance for the field of neuroscience: (1) Dispersed biomedical research literature will be integrated through one database, making it easier to avoid repetition in scientific research; (2) Neuroscientists will be able to conduct background research for their current projects much more conveniently and accurately; (3) Decision-makers will be able to access comprehensive neuroscience information, promoting informed development in science and technology; (4) The database may serve as the foundation of a virtual biomedical engineering information centre, helping to realize the potential of resource sharing; (5) The ultimate objective of Neuroinformatics, integrated study of the brain, would be more fully realized; (6) The social and economic efficiency of neuroscience research will increase.

CONCLUSION

The modern neuroscience research technique progress, enables the integration analysis of different data from the gene to the behavior level. This involves two aspect: enormous data collection, reorganization and maintenance, as well as inhomogeneous nerve information data conformity, thus needs to design integrative data system conforms to the Neuroinformatics research demand, as well as reliable data analysis tool. In order to solve the database interoperability and neuroscientific information integration, we have been developing an internet-accessible Neuroinformatics Literature System for neuroimaging and brain function research. The NILS may retrench many data conversions for the researcher and promotes data sharing, and it can provide a unified inquiry connection, then partly works out the conformity with isomerized neuroinformatics database and forms a data platform to integrate the correlative information from different

database, thus it will be advantageous to the database information extraction and knowledge discovery.

Based on the cluster system of TS10000 and data processing technologies, a NILS with integration, expansibility and customization is constructed through the technology of object-oriented relational database. Our main work are as followed:

1)Designed the Neuroinformatics Literature System oriented to knowledge discovery. The system design includes 8 main function modules: System Maintenance, Literature Renewal, Literature Retrieval, Display/Output Result, Literature Information Analysis, Neuroimaging Integration, Neuroinformation Text Mining and Nerve Ontology Prototype Construction.

2) Realized the neuroinformatics literature system main function. NILS is a multi-purpose academic periodical full text literature platform related to neuroimaging and brain function topic, which maintains the multi-disciplinary and many kinds of forms of literature. The overall system uses the B/S frame, formulated the unique literature renewal flow to guarantee the literature quality, including the user jurisdiction graduation, checking for duplicate, first submission, second examination and verification, official storage, the responsibility signature and measurement statistics.

3) NILS provides three ways of retrieving information, as well as fourteen different retrieval fields. In addition, the system is equipped with the flexible retrieval result output way, may carry on the choice mark, preservation and printing the retrieval result. Moreover NILS integrated third party reference management software EndNote, it can fast import the retrieval result into EndNote.

4) Combining the neuroinformatics data characteristic, designed a tree structure index based on important nerve information research area, which has manifested the feature of neuroimaging and brain function research. This tree structure has been used in the neuroinformatics literature index and literature collection, has been regarded as the basis of classified subject browsing, and also has been applied in nerve ontology prototype construction. At present this tree structure includes eight kinds of subject heading altogether more than 350.

Acknowledgements

We would like to thank Guoqing Zhang and Pan Wang for many fruitful discussions during the preparation of database, and our colleagues who have provided suggestions and help with the beta testing. Thanks also to the databases that publish neuroscience-related articles and serve as our reference and resources.

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Received by: October 27 2006
Accepted : Febuary 05 2007

The Online Journal of Neurological Sciences (Turkish) 1984-2005
This e-journal is run by Ege University Faculty of Medicine,
Dept. of Neurological Surgery, Bornova, Izmir-35100TR
as part of the Ege Neurological Surgery World Wide Web service.
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E-mail: editor@jns.dergisi.org
URL: http://www.jns.dergisi.org
Journal of Neurological Sciences (Turkish)
Abbr: J. Neurol. Sci.[Turk]
ISSNe 1302-1664

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