Implementation of an Intelligent Agent-Based Chromosome Database Using WWW

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Abstract

The task for chromosome karyotyping and diagnosis is requiring repetitive, time consuming job and high cost even it is done by well-experienced cytogenetists.

For that reason, an intelligent agent-based chromosome database using WWW has been established to be able to analyze chromosomes and obtain necessary advises from the database instead of human experts and the database is including 2 divisions with database and agent.

The completed database provides variously morphological information by analysis of normal or abnormal chromosomes and it also makes users enable to control and search the information in a short period with learning of high amount of knowledge.

Keywords :
chromosome, karyotyping, intelligent agent

Introduction

Since Tjio and Levan proved that the human metaphase chromosomes had been composed of 46 at 1956[1], the task for chromosome abnormalities by experienced cytogenetists is being concerned as some of important that can be divided into two major groups as clinical investigations in the pediatrics area including the differential diagnosis of congenital anomalies and in the Obstetrics & Gynecology including studies of mutagens and carcinogens and their effects on cells[2].

Especially, the karyotyping and diagnosis task for patient chromosomes in cytogenetic laboratory is based on general informations such as features of normal and abnormal chromosomes with related syndromes, chromosome banding techniques, ISCN(An International System for Human Cytogenetic Nomenclature) nomenclature[3] as well as particular informations such as chromosome images, family history, pregnancy experiences of a patient[4]-[6].

However above task is requiring repetitive, time consuming job and high cost even it is done by well-experienced cytogenetists.

Also, the decision making necessary for chromosome karyotyping and diagnosis is demand of cytogenetic expertise and knowledge by practically operational experience to the complex structures and natural diversities of the chromosome patterns exhibited.

For that reason, it is valuable to create an intelligent agent-based chromosome database using www that contains an integrated search function, graphic user interface, a knowledge base system, agent and relational database.

This intelligent agent-based database has been established to analyze chromosomes and obtain necessary advises from the database instead of human experts and independent agent with the inference by knowledge base entered the inference data into the database.

Implemented database is flexible and active then makes us possible to replace experts when they are out of the position. The completed database is capable to create interaction between users and system, and the agent can deduct conclusions from knowledge base even the communications are not perfect or crashed. Then it provides variously morphological information by analysis of normal or abnormal chromosomes and it also makes users enable to control and search the information in a short period with learning of high amount of knowledge.

Preliminaries

Chromosome karyotyping

Figure 1. Human metaphase chromosomes at the 350 to 400 band stage, GTG-banding

Human GTG-banding metaphase chromosomes consist of 46 as shown in Figure 1. Karyotyping using this metaphase chromosomes is usually done by well-experienced cytogenetists or auto analysis system with computers using chromosome features such as centromeric index($c.i.$), relative size(size), banding pattern that have higher significant relationship than others.
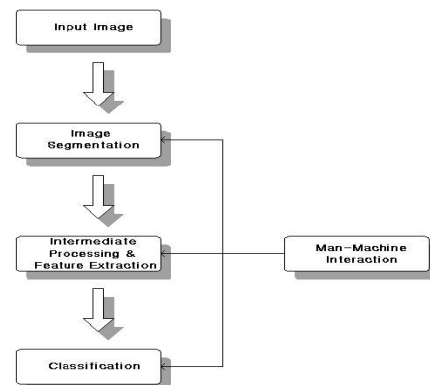

Figure 2. Flow diagram for automatic karyotyping

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As shown in Figure 2, it is necessary for exact chromosome karyotyping to intervene in interactive error correcting operations by well-experienced cytogenetists. Also, it demands of cytogenetic expertise and knowledge by practically operational experience to the complex structures and natural diversities of the patterns exhibited in the chromosome karyotyping and diagnosis.

Modeling of chromosome karyotyping and diagnosis

Modeling is that task behaviors and demands of users corresponding to virtual environment of computer with one to one.
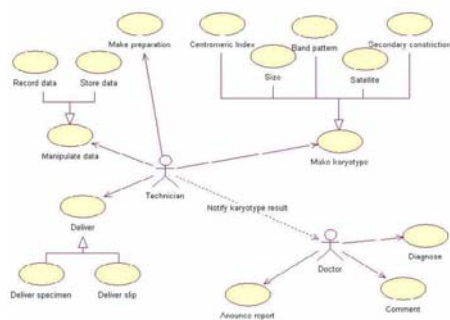

Figure 3. A use-case diagram showing behaviors of technician and doctor in cytogenetic laboratory

Task behaviors of technicians as receiving, delivering and culturing of specimen, reporting, making preparation, karyotyping, and notifying the result and task behaviors of doctors as diagnosis, comment, announcing the report for analysis and diagnosis of chromosome have been showed as shown in Figure 3 using use-case diagrams.of UML(Unified Modeling Language)[7]-[8].
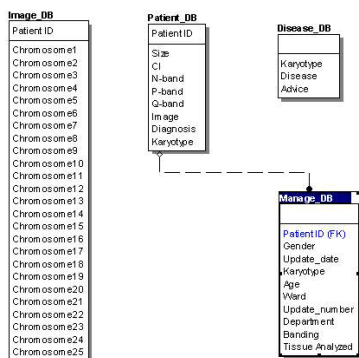

Figure 4. Database model for the implemented database

As shown in Figure 4, database model for the implemented database was constructed with relational database consisting of Patient_DB, Image_DB, Disease_DB, and Manage_DB according to configurations or objects of the database. Also, knowledge base was constructed with IF THEN production rule to support proper decision making using intelligent agent could deduct conclusions from knowledge base even the communications was not perfect or crashed.

Intelligent agent

Basic concepts of intelligent agent

Agents are autonomous or semi-autonomous hardware or software systems that perform tasks in complex, dynamically changing environment.

This agent is used to characterize very different kinds of systems, starting from primitive biological systems as cells, bees, and ants to systems that simulate or describe whole human societies or organizations.

Also, agent is called the intelligent agent[9] that carries out delegated task instead of user, communicates to user for interactions, and does the task autonomously within delegated fields. In order to cope with these difficult tasks, agents need basic capabilities: firstly, they should be reactive, i.e., react timely and appropriately to unforeseen events and to changes in the environment. Secondly, they should be capable of deliberation to perform their tasks in a goal-directed manner. Thirdly, they should solve their tasks efficiently by making use of hard-wired procedures in routine situations. Fourthly, they have to deal with positive and negative interactions with other agents. Fifthly, agents need to be adaptable to changing environmental conditions.

Most agent models are based on BDI architectures that started in 1987 with Bratman[10]-[11].

The basic idea of the BDI architectures is to describe the internal processing state of an agent by means of a set of mental categories, and to define a control architecture by which the agent rationally selects its course of action based on their representation. The mental categories are beliefs, desires, and intentions.

Intelligent agent model

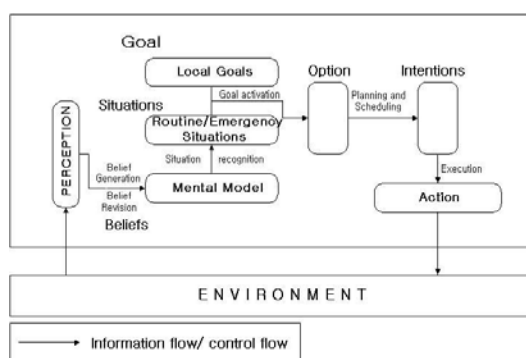Intelligent agent consists of mind state and environment as shown in Figure 5.

Figure 5. The conceptional agent model for chromosome analysis and diagnosis

The arrows in Figure 5 denote functional relationships between the components of the mental model of an agent. Mind state divides into cognition, belief, situation, goal, and intention, and action starts as soon as trigging specific events.

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Cognition, belief, and condition change according to intelligent agent that surrounds with environment caused by action.

Agent has the ability to recognize certain classes of situations, to drive goals from these situations, and to perform actions in order to achieve these goals.

For example, in circumstances of a chromosome is given, agent infers chromosome from cognition for numbers of chromosome, belief for doing chromosome karyotyping, intention for determining chromosome number with goal of karyotyping in scheduled conditions.

If we apply these circumstances to all chromosomes of a patient, belief, condition goal and intention are changed by the change of environment.

That is to say, agent infers karyotyping and diagnosis of chromosomes from belief that does chromosomes karyotyping of a patient, goal that diagnose to be with karyotyping result in scheduled conditions, and intention for determining disease by the karyotyping result.

This means that after intelligent agent triggers the knowledge base instead of user, it begin to notify the karyotyping result and disease to database.

Because intelligent agent can react to considering actions such as the latest usage frequency of karyotyping and diagnosis, the present state of saved data, the event of mouse click or keyboard key in, it can forecast related information by intention of it. And non-skilled user can learn to karyotyping and diagnosis of chromosome spontaneously. Also, because chromosome evolves by the influence of environment, agent can do modification or deletion of changed information.

Because agent can extract and integrate related information from constructed database before user query, user can get query result from database effectively and easily.

Result

As shown in Table 1, experimental data were composed of two kinds. The first was CPR dataset regarding as benchmark of chromosome karyotyping[12]-[13]. CPR dataset were composed of normal chromosomes of 2,535 patients' cases and abnormal chromosomes of 68 patients' cases that have been obtained from GTG-banding metaphase amniotic fluid samples from 1988 to 1990 using Magiscan Interactive Cytogenetic Analysis System.

The second was cytogenetic laboratory dataset of domestic hospitals. This dataset were composed of normal chromosomes of 201 patients' cases and abnormal chromosomes of 191 patients' cases that have been obtained from GTG-banding metaphase peripheral blood and amniotic fluid samples from 1988 to 1998.

	No of Cases	%
Normal Chromosomes	2736	91.4
Abnormal Chromosomes	259	8.6
- Numerical Abnormalities	169	5.6
- Structural Abnormalities	73	2.4
- Combined Abnormalities	17	0.6
Total	2995	100

Table 1. Distribution of the analyzed chromosomes

Construction tools

Presented database was implemented in the environment of Windows NT for server and Windows 98 for client.

Chromosomes that had been completed the karyotyping were scanned and segmented with HP ScanJet 3c/T.

Chromosome features were extracted using IMAQ Vision Builder and Chromosome Image Processing program that we had programmed, and they were transplanted to SQL server.

Knowledge base was constructed with Visual Rule Studio 1.5 version, and intelligent agent was developed with Visual Basic 6.0 enterprise sp3, and related all programs were completed with Microsoft Visual Studio.

Also, ASP(Active Server Page) provides flexible, extensible easy to use, and it was interacted to ODBC supporting database server that could communicate with database server by ADO component.

The construction of an intelligent agent-based chromosome database
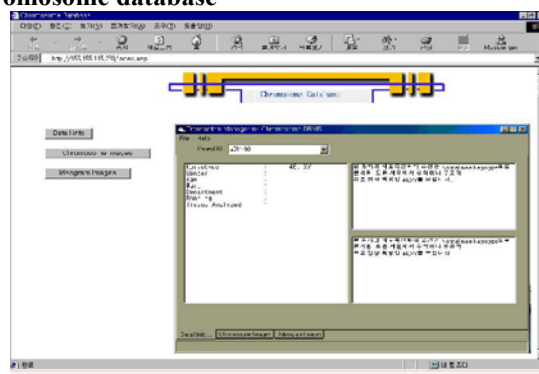

Figure 6. Detail information tab of transaction manager for chromosome DB

In case of selecting detail button and a patient ID located in the left as shown in Figure 6, Implemented database shows the result such as sex, age, ward, request department, banding, and analysis tissue of selected patient located in the left and shows diagnosis result and

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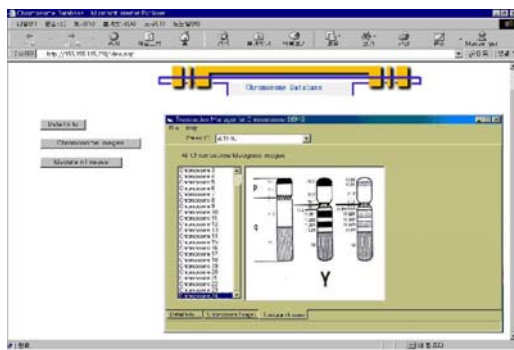related explanation of chromosome in the right.

Figure 7. Ideogram images tab of transaction manager for chromosome DB

In case of clicking chromosome image tab if necessary as shown in Figure 7, the database shows zooming chromosome images freely, and in case of double clicking chromosome image tab, it shows a standardized ideogram image of the chromosome.
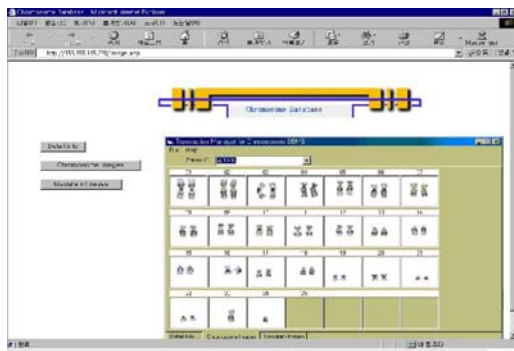

Figure 8. Chromosome images tab of transaction manager for chromosome DB

In case of clicking ideogram image tab as shown in Figure 8, it can make a comparison between practical chromosome image of a patient and standardized ideogram image.
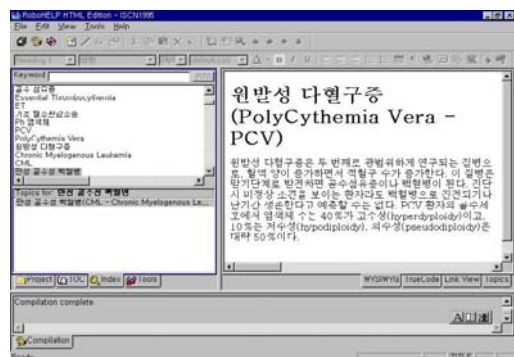

Figure 9. Handbook composed of ISCN 1995 and chromosome abnormal diagnosis

As shown in Figure 9, If user has questions about ISCN nomenclature or related questions about chromosomes, while using the database, user can search directly for

ISCN 1995 and Handbook of abnormal chromosome diagnosis or click Indexing keyword located in the left.

Conclusion

Implemented intelligent agent-based chromosome database is much more different from other passive databases that only keep the data, it is flexible and active then makes us possible to replace experts when they are out of the position. The completed database is capable to create interaction between users and system, and the intelligent agent can deduct conclusions from knowledge base even the communications are not perfect or crashed. Then it provides variously morphological information by analysis of normal or abnormal chromosomes and it also makes users enable to control and search the information in a short period with learning of high amount of knowledge.

In the future, intelligent agent must evolve toward multi intelligent agents such as knowledge acquisition agent, statistics analysis agent that are independent and maintained collaboration through the messages than competition.

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