PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C12Q 1/68, G06F 17/30 // 159:00

A1

(11) International Publication Number: **WO 99/05324**

(43) International Publication Date: 4 February 1999 (04.02.99)

(21) International Application Number: PCT/US98/15458

(22) International Filing Date: 24 July 1998 (24.07.98)

(30) Priority Data:

60/053,842	25 July 1997 (25.07.97)	US
60/069,198	11 December 1997 (11.12.97)	US
60/069,436	11 December 1997 (11.12.97)	US

(81) Designated States: JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(71) Applicant: AFFYMETRIX, INC. [US/US]; 3380 Central Expressway, Santa Clara, CA 95051 (US).

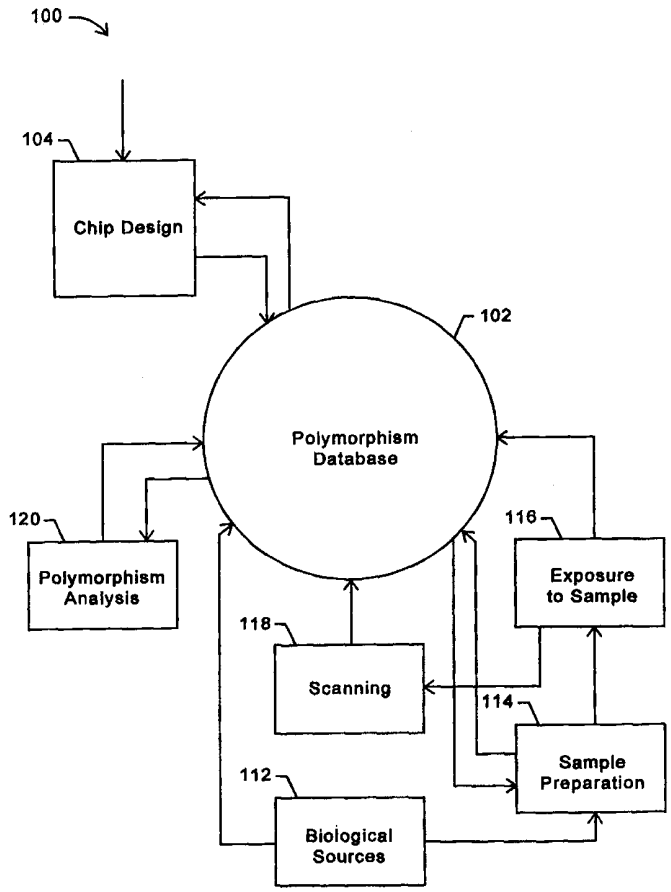
(72) Inventors: BALABAN, David, J.; 37 Bret Harte Road, San Rafael, CA 94901 (US). BAID, Joyti; 3330 Estates Drive, San Jose, CA 95148 (US). BERNO, Anthony; 570 South 12th Street, San Jose, CA 95112 (US).

(74) Agents: LANG, Dan, H. et al.; Townsend and Townsend and Crew LLP, 8th floor, Two Embarcadero Center, San Francisco, CA 94111-3834 (US).

(54) Title: SYSTEM FOR PROVIDING A POLYMORPHISM DATABASE

(57) Abstract

Systems and methods for organising information relating to a study of polymorphisms. A database model (102) is provided which interralates information about one or more of, e.g, subjects (112) from whom samples (114) are extracted, primers used in extracting the DNA from the subjects, about the samples themselves, about experiments done on samples, about particular oligonucleotide probe arrays used to perform experiments, about analysis procedures performed on the samples, and about analysis results. The model is readily translatable into database languages such as SQL. The database model scales to permit storage of information about large numbers of subjects, samples, experiments, chips, etc.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

SYSTEM FOR PROVIDING A POLYMORPHISM DATABASE

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims priority from U.S. Prov. App. No. 60/053,842 filed July 25, 1997, entitled COMPREHENSIVE BIO-INFORMATICS DATABASE, from U.S. Prov. App. No. 60/069,198 filed on December 11, 1997, entitled COMPREHENSIVE DATABASE FOR BIOINFORMATICS , and from U.S. Prov. App. No. 60/069,436, entitled GENE EXPRESSION AND EVALUATION SYSTEM, filed on December 11, 1997. The contents of all three provisional applications are herein incorporated by reference.

The subject matter of the present application is related to the subject matter of the following three co-assigned applications filed on the same day as the present application. GENE EXPRESSION AND EVALUATION SYSTEM (Attorney Docket No. 018547-035010), METHOD AND APPARATUS FOR PROVIDING A BIOINFORMATICS DATABASE (Attorney Docket No. 018547-033810), METHOD AND SYSTEM FOR PROVIDING A PROBE ARRAY CHIP DESIGN DATABASE (Attorney Docket No. 018547-033830). The contents of these three applications are herein incorporated by reference.

BACKGROUND OF THE INVENTION

The present invention relates to the collection and storage of information pertaining to chips for processing biological samples and thereby identifying polymorphisms.

The genomes of all organisms undergo spontaneous mutation in the course of their continuing evolution generating variant forms of progenitor sequences (Gusella, *Ann. Rev. Biochem.* 55, 831-854 (1986)). The variant form may confer an evolutionary advantage or disadvantage relative to a progenitor form or may be neutral. In some instances, a variant form confers a lethal disadvantage and is not transmitted to subsequent generations of the organism. In other instances, a variant form confers an

evolutionary advantage to the species and is eventually incorporated into the DNA of many or most members of the species and effectively becomes the progenitor form. In many instances, both progenitor and variant form(s) survive and co-exist in a species population. The coexistence of multiple forms of a sequence gives rise to polymorphisms.

Despite the increased amount of nucleotide sequence data being generated in recent years, only a minute proportion of the total repository of polymorphisms in humans and other organisms has so far been identified. The paucity of polymorphisms hitherto identified is due to the large amount of work required for their detection by conventional methods. For example, a conventional approach to identifying polymorphisms might be to sequence the same stretch of oligonucleotides in a population of individuals by dideoxy sequencing. In this type of approach, the amount of work increases in proportion to both the length of sequence and the number of individuals in a population and becomes impractical for large stretches of DNA or large numbers of persons.

Devices and computer systems for forming and using arrays of materials on a substrate have been developed. These devices and systems have been used for identifying polymorphisms. For example, PCT application WO92/10588, incorporated herein by reference for all purposes, describes techniques for sequencing or sequence checking nucleic acids and other materials. Arrays for performing these operations may be formed in arrays according to the methods of, for example, the pioneering techniques disclosed in U.S. Patent No. 5,143,854 and U.S. Patent No. 5,571,639, both incorporated herein by reference for all purposes.

According to one aspect of the techniques described therein, an array of nucleic acid probes is fabricated at known locations on a chip or substrate. A fluorescently labeled nucleic acid is then brought into contact with the chip and a scanner generates an image file indicating the locations where the labeled nucleic acids bound to the chip. Based upon the identities of the probes at these locations, it becomes possible to extract information such as the identity of polymorphic forms in of DNA or RNA. Such systems have been used to form, for example, arrays of DNA that may be used to study and detect mutations relevant to cystic fibrosis, the P53 gene (relevant to certain cancers), HIV, and other genetic characteristics.

It would be highly useful to apply such arrays to the study of polymorphisms on a large scale. For example, it would be useful to conduct large scale studies on the correlation between certain polymorphisms and individual characteristics such as susceptibility to diseases and effectiveness of drug treatments. To achieve these benefits, it is contemplated that the operations of chip design, construction, sample preparation, and analysis will occur on a very large scale. The quantity of information related to each of these steps to store and correlate is vast. For large scale polymorphism studies, it will be necessary to store this information in a way to facilitate later advantageous querying and retrieval. What is needed is a system and method suitable for storing and organizing large quantities of information used in conjunction with polymorphism studies.

SUMMARY OF THE INVENTION

The present invention provides systems and methods for organizing information relating to study of polymorphisms. A database model is provided which interrelates information about one or more of, e.g, subjects from whom samples are extracted, primers used in extracting the DNA from the subjects, about the samples themselves, about experiments done on samples, about particular oligonucleotide probe arrays used to perform experiments, about analysis procedures performed on the samples, and about analysis results . The model is readily translatable into database languages such as SQL. The database model scales to permit storage of information about large numbers of subjects, samples, experiments, chips, etc.

Applications include linkage studies to determine resistance to drugs, susceptibility to diseases, and study of every characteristic of humans and other organisms that is related genetic variability. Another application of a database constructed according to this model is quality control of the various steps of performing a polymorphism study. By preserving information about every step of a polymorphism study, one can assess the reliability of the results or use the preserved information as feedback to improve procedures.

A further understanding of the nature and advantages of the inventions herein may be realized by reference to the remaining portions of the specification and the attached drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 illustrates an overall system and process for forming and analyzing arrays of biological materials such as DNA or RNA.

Fig. 2A illustrates a computer system suitable for use in conjunction with the overall system of Fig. 1.

Fig. 2B illustrates a computer network suitable for use in conjunction with the overall system of Fig. 1.

Fig. 3 illustrates a key for interpreting a database model.

Figs. 4A-4H illustrate a database model for maintaining information for the system and process of Fig. 1 according to one embodiment of the present invention.

DESCRIPTION OF SPECIFIC EMBODIMENTS

Investigation of Polymorphisms

A. Preparation of Samples

Polymorphisms are detected in a target nucleic acid from an individual being analyzed. For assay of genomic DNA, virtually any biological sample (other than pure red blood cells) is suitable. For example, convenient tissue samples include whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin and hair. For assay of cDNA or mRNA, the tissue sample must be obtained from an organ in which the target nucleic acid is expressed. For example, if the target nucleic acid is a cytochrome P450, the liver is a suitable source.

Many of the methods described below require amplification of DNA from target samples. This can be accomplished by e.g., PCR. *See generally PCR Technology: Principles and Applications for DNA Amplification* (ed. H.A. Erlich, Freeman Press, NY, NY, 1992); *PCR Protocols: A Guide to Methods and Applications* (eds. Innis, et al., Academic Press, San Diego, CA, 1990); Mattila et al., *Nucleic Acids Res.* 19, 4967 (1991); Eckert et al., *PCR Methods and Applications* 1, 17 (1991); *PCR* (eds. McPherson et al., IRL Press, Oxford); and U.S. Patent 4,683,202 (each of which is incorporated by reference for all purposes).

Other suitable amplification methods include the ligase chain reaction (LCR) (see Wu and Wallace, *Genomics* 4, 560 (1989), Landegren et al., *Science* 241, 1077 (1988), transcription amplification (Kwoh et al., *Proc. Natl. Acad. Sci. USA* 86, 1173 (1989)), and self-sustained sequence replication (Guatelli et al., *Proc. Nat. Acad.*

Sci. USA, 87, 1874 (1990)) and nucleic acid based sequence amplification (NASBA). The latter two amplification methods involve isothermal reactions based on isothermal transcription, which produce both single stranded RNA (ssRNA) and double stranded DNA (dsDNA) as the amplification products in a ratio of about 30 or 100 to 1, respectively.

B. Detection of Polymorphisms in Target DNA

There are two distinct types of analysis depending whether a polymorphism in question has already been characterized. The first type of analysis is sometimes referred to as de novo characterization. This analysis compares target sequences in different individuals to identify points of variation, i.e., polymorphic sites. By analyzing groups of individuals representing the greatest ethnic diversity among humans and greatest breed and species variety in plants and animals, patterns characteristic of the most common alleles/haplotypes of the locus can be identified, and the frequencies of such populations in the population determined. Additional allelic frequencies can be determined for subpopulations characterized by criteria such as geography, race, or gender. The second type of analysis is determining which form(s) of a characterized polymorphism are present in individuals under test. There are a variety of suitable procedures, which are discussed in turn.

1. Allele-Specific Probes

The design and use of allele-specific probes for analyzing polymorphisms is described by e.g., Saiki et al., *Nature* 324, 163-166 (1986); Dattagupta, EP 235,726, Saiki, WO 89/11548. Allele-specific probes can be designed that hybridize to a segment of target DNA from one individual but do not hybridize to the corresponding segment from another individual due to the presence of different polymorphic forms in the respective segments from the two individuals. Hybridization conditions should be sufficiently stringent that there is a significant difference in hybridization intensity between alleles, and preferably an essentially binary response, whereby a probe hybridizes to only one of the alleles. Some probes are designed to hybridize to a segment of target DNA such that the polymorphic site aligns with a central position (e.g., in a 15 mer at the 7 position; in a 16 mer, at either the 8 or 9 position) of the

probe. This design of probe achieves good discrimination in hybridization between different allelic forms.

Allele-specific probes are often used in pairs, one member of a pair showing a perfect match to a reference form of a target sequence and the other member showing a perfect match to a variant form. Several pairs of probes can then be immobilized on the same support for simultaneous analysis of multiple polymorphisms within the same target sequence.

2. Tiling Arrays

The polymorphisms can also be identified by hybridization to nucleic acid arrays, some example of which are described by WO 95/11995 (incorporated by reference in its entirety for all purposes). WO 95/11995 also describes subarrays that are optimized for detection of a variant forms of a precharacterized polymorphism. Such a subarray contains probes designed to be complementary to a second reference sequence, which is an allelic variant of the first reference sequence. The second group of probes is designed by the same principles as described in the Examples except that the probes exhibit complementarily to the second reference sequence. The inclusion of a second group (or further groups) can be particular useful for analyzing short subsequences of the primary reference sequence in which multiple mutations are expected to occur within a short distance commensurate with the length of the probes (*i.e.*, two or more mutations within 9 to 21 bases).

3. Allele-Specific Primers

An allele-specific primer hybridizes to a site on target DNA overlapping a polymorphism and only primes amplification of an allelic form to which the primer exhibits perfect complementarily. See Gibbs, *Nucleic Acid Res.* 17, 2427-2448 (1989). This primer is used in conjunction with a second primer which hybridizes at a distal site. Amplification proceeds from the two primers leading to a detectable product signifying the particular allelic form is present. A control is usually performed with a second pair of primers, one of which shows a single base mismatch at the polymorphic site and the other of which exhibits perfect complementarily to a distal site. The single-base mismatch prevents amplification and no detectable product is formed. The method works best when the mismatch is included in the 3'-most position of the oligonucleotide aligned with the polymorphism because this position is most destabilizing to elongation from the primer. *See, e.g.*, WO 93/22456.

4. Direct-Sequencing

The direct analysis of the sequence of polymorphisms of the present invention can be accomplished using either the dideoxy chain termination method or the Maxam Gilbert method (see Sambrook et al., *Molecular Cloning, A Laboratory Manual* (2nd Ed., CSHP, New York 1989); Zyskind et al., *Recombinant DNA Laboratory Manual*, (Acad. Press, 1988)).

5. Denaturing Gradient Gel Electrophoresis

Amplification products generated using the polymerase chain reaction can be analyzed by the use of denaturing gradient gel electrophoresis. Different alleles can be identified based on the different sequence-dependent melting properties and electrophoretic migration of DNA in solution. Erlich, ed., *PCR Technology, Principles and Applications for DNA Amplification*, (W.H. Freeman and Co, New York, 1992), Chapter 7.

6. Single-Strand Conformation Polymorphism Analysis

Alleles of target sequences can be differentiated using single-strand conformation polymorphism analysis, which identifies base differences by alteration in electrophoretic migration of single stranded PCR products, as described in Orita et al., *Proc. Nat. Acad. Sci.* 86, 2766-2770 (1989). Amplified PCR products can be generated as described above, and heated or otherwise denatured, to form single stranded amplification products. Single-stranded nucleic acids may refold or form secondary structures which are partially dependent on the base sequence. The different electrophoretic mobilities of single-stranded amplification products can be related to base-sequence difference between alleles of target sequences.

Biological Material Analysis System

One embodiment of the present invention operates in the context of a system for analyzing biological or other materials using arrays that themselves include probes that may be made of biological materials such as RNA or DNA. The VLSIPS™ and GeneChip™ technologies provide methods of making and using very large arrays of polymers, such as nucleic acids, on chips. *See* U.S. Patent No. 5,143,854 and PCT Patent Publication Nos. WO 90/15070 and 92/10092, each of which is hereby incorporated by reference for all purposes. Nucleic acid probes on the chip are used to

detect complementary nucleic acid sequences in a sample nucleic acid of interest (the "target" nucleic acid).

Fig. 1 illustrates an overall system 100 for forming and analyzing arrays of biological materials such as RNA or DNA. A part of system 100 is a polymorphism database 102. Polymorphism database 102 includes information about, e.g., biological sources, preparation of samples, design of arrays, raw data obtained from applying experiments to chips, analysis procedures applied, and analysis results, etc. Polymorphism database 102 facilitates large scale study of polymorphisms.

A chip design system 104 is used to design arrays of polymers such as biological polymers such as RNA or DNA. Chip design system 104 may be, for example, an appropriately programmed Sun Workstation or personal computer or workstation, such as an IBM PC equivalent, including appropriate memory and a CPU. Chip design system 104 obtains inputs from a user regarding chip design objectives including polymorphisms of interest, and other inputs regarding the desired features of the array. Optionally, chip design system 104 from external databases such as GenBank. The output of chip design system 104 is a set of chip design computer files in the form of, for example, a switch matrix, as described in PCT application WO 92/10092, and other associated computer files. The chip design computer files form a part of polymorphism database 102. Systems for designing chips for study of polymorphisms are disclosed in U.S. Patent No. 5,571,639 and in PCT application WO 95/11995, the contents of which are herein incorporated by reference.

The chip design files are input to a mask design system (not shown) that designs the lithographic masks used in the fabrication of arrays of molecules such as DNA. The mask design system designs the lithographic masks used in the fabrication of probe arrays. The mask design system generates mask design files that are then used by a mask construction system (not shown) to construct masks or other synthesis patterns such as chrome-on-glass masks for use in the fabrication of polymer arrays.

The masks are used in a synthesis system (not shown). The synthesis system includes the necessary hardware and software used to fabricate arrays of polymers on a substrate or chip. The synthesis system includes a light source and a chemical flow cell on which the substrate or chip is placed. A mask is placed between the light source and the substrate/chip, and the two are translated relative to each other at appropriate times for deprotection of selected regions of the chip. Selected chemical reagents are

directed through the flow cell for coupling to deprotected regions, as well as for washing and other operations. The substrates fabricated by the synthesis system are optionally diced into smaller chips. The output of the synthesis system is a chip ready for application of a target sample.

Information about the mask design, mask construction, and probe array synthesis is presented by way of background. A biological source 112 is, for example, tissue from a plant or animal. Various processing steps are applied to material from biological source 112 by a sample preparation system 114. Operation of sample preparation system 114 in the context of a polymorphism study is discussed below in further detail.

The prepared samples include nucleic acid sequences such as DNA. When the sample is applied to the chip by a sample exposure system 116, the nucleic acids may or may not bond to the probes. The nucleic acids can be tagged with fluoroscein labels to determine which probes have bonded to nucleotide sequences from the sample. The prepared samples will be placed in a scanning system 118. Scanning system 118 includes a detection device such as a confocal microscope or CCD (charge-coupled device) that is used to detect the location where labeled receptors have bound to the substrate. The output of scanning system 118 is an image file(s) indicating, in the case of fluorescein labeled receptor, the fluorescence intensity (photon counts or other related measurements, such as voltage) as a function of position on the substrate. These image files may also form a part of polymorphism database 102. Since higher photon counts will be observed where the labeled nucleic acid(s) has bound more strongly to the array of probes, and since the monomer sequence of the probes on the substrate is known as a function of position, it becomes possible to analize the sequence(s) of the nucleic acid(s) that are complementary to the probes.

The image files and the design of the chips are input to an analysis system 120 that, e.g., calls bases. Such analysis techniques are described in EPO Pub. No. 0717113A, the contents of which are herein incorporated by reference.

Chip design system 104, analysis system 120 and control portions of exposure system 116, sample preparation system 114, and scanning system 118 may be appropriately programmed computers such as a Sun workstation or IBM-compatible PC. An independent computer for each system may perform the computer-implemented functions of these systems or one computer may combine the computerized functions of

two or more systems. One or more computers may maintain chip design database 102 independent of the computers operating the systems of Fig. 1 or chip design database 102 may be fully or partially maintained by these computers.

Fig. 2A depicts a block diagram of a host computer system 10 suitable for implementing the present invention. Host computer system 210 includes a bus 212 which interconnects major subsystems such as a central processor 214, a system memory 216 (typically RAM), an input/output (I/O) adapter 218, an external device such as a display screen 224 via a display adapter 226, a keyboard 232 and a mouse 234 via an I/O adapter 218, a SCSI host adapter 236, and a floppy disk drive 238 operative to receive a floppy disk 240. SCSI host adapter 236 may act as a storage interface to a fixed disk drive 242 or a CD-ROM player 244 operative to receive a CD-ROM 246. Fixed disk 244 may be a part of host computer system 210 or may be separate and accessed through other interface systems. A network interface 248 may provide a direct connection to a remote server via a telephone link or to the Internet. Network interface 248 may also connect to a local area network (LAN) or other network interconnecting many computer systems. Many other devices or subsystems (not shown) may be connected in a similar manner.

Also, it is not necessary for all of the devices shown in Fig. 2A to be present to practice the present invention, as discussed below. The devices and subsystems may be interconnected in different ways from that shown in Fig. 2A. The operation of a computer system such as that shown in Fig. 2A is readily known in the art and is not discussed in detail in this application. Code to implement the present invention, may be operably disposed or stored in computer-readable storage media such as system memory 216, fixed disk 242, CD-ROM 246, or floppy disk 240.

Fig. 2B depicts a network 260 interconnecting multiple computer systems 210. Network 260 may be a local area network (LAN), wide area network (WAN), etc. Bioinformatics database 102 and the computer-related operations of the other elements of Fig. 2B may be divided amongst computer systems 210 in any way with network 260 being used to communicate information among the various computers. Portable storage media such as floppy disks may be used to carry information between computers instead of network 260.

Overall Description of Database

Polymorphism database 102 is preferably a relational database with a complex internal structure. The structure and contents of chip design database 102 will be described with reference to a logical model depicted in Figs. 4A-4H that describes the contents of tables of the database as well as interrelationships among the tables. A visual depiction of this model will be an Entity Relationship Diagram (ERD) which includes entities, relationships, and attributes. A detailed discussion of ERDs is found in "ERwin version 3.0 Methods Guide" available from Logic Works, Inc. of Princeton, NJ, the contents of which are herein incorporated by reference. Those of skill in the art will appreciate that automated tools such as Developer 2000 available from Oracle will convert the ERD from Figs. 4A-4H directly into executable code such as SQL code for creating and operating the database.

Fig. 3 is a key to the ERD that will be used to describe the contents of chip design database 102. A representative table 302 includes one or more key attributes 304 and one or more non-key attributes 306. Representative table 302 includes one or more records where each record includes fields corresponding to the listed attributes. The contents of the key fields taken together identify an individual record. In the ERD, each table is represented by a rectangle divided by a horizontal line. The fields or attributes above the line are key while the fields or attributes below the line are non-key. An identifying relationship 308 signifies that the key attribute of a parent table 310 is also a key attribute of a child table 312. A non-identifying relationship 314 signifies that the key attribute of a parent table 316 is also a non-key attribute of a child table 318. Where (FK) appears in parenthesis, it indicates that an attribute of one table is a key attribute of another table. Both the depicted non-identifying and identifying relationship are one to one-or-more relationships where one record in the parent table corresponds to one or more records in the child table. An alternative non-identifying relationship 324 is a one to zero-or-more relationship where one record in a parent table 320 corresponds to zero or more records in a child table 322.

Database Model

Figs. 4A-4H are entity relationship diagrams (ERDs) showing elements of polymorphism database 102 according to one embodiment of the present invention. Each

rectangle in the diagram corresponds to a table in database 102. First, the relationships and general contents of the various tables will be described.

The interrelationships and general contents of the tables of database 102 will be described first. Then a chart will be presented listing and describing all of the fields of the various tables.

Fig. 4A illustrates core elements of database 102 according to one embodiment of the present invention. A subject table 402 lists organisms from which samples have been extracted for polymorphism analysis or other tissue sources. Samples may also be obtained from tissue collections not associated with any one identified organism. Information stored within subject table 402 includes the name, gender, family, position with family, (e.g., father , mother, etc.), and ethnic group. For human subjects, the name and family will preferably be represented in coded form to assure privacy. Associated with each subject is a species as listed in a species table 404. Also, a relationship may be defined among subjects a subject relationship table 406 which includes records corresponding to related subjects. These relationships may be father-mother, sibling, twins, etc. Subjects may be part of a group that is being studied, e.g., a group with a congenital disease, or a toxic reaction to a particular drug. The groups are listed in a subject group table 408. Participation of subjects in groups is defined by a subject participation table 410 which lists all group memberships.

Samples and their attributes are listed in a sample table 412. Each sample has an associated sample type. The sample types are listed in a sample type table 414. Possible sample types include blood, urine, etc. Companies or institutions that provide samples are listed in a sample source table 416.

Database 102 provides an item table 418 that includes records for items. There are various types of items that correspond to different stages of the sample preparation process. An "item derivation" transforms an item of one type into an item of another type. The following table lists various item types and item derivation types for a representative embodiment.

Item Type	Derived from	by Item Derivation Type
Sample	other samples	pooling
Sample	other sample	splitting

Extracted DNA	Sample	DNA Extraction
Target (Sequences of interest amplified)	Extracted DNA	PCR
Fluorescently Labeled Target	Target	Labeling
Hybridized Chip	Labeled Target	Hybridization (application of target to chip)
Stained Hybridized Chip	Hybridized Chip	Staining

Item derivations are listed in an item derivation table 420. It should be noted that derivations need not produce a change between item types. Each item derivation occurs in accordance with a protocol that characterizes the step or steps in the derivation. Protocols are listed in a protocol table 428. Each item derivation is performed by an employee listed in employee table 432.

Unused chips are listed in a chip table 422. Hybridized chips (i.e., chips that have had target applied) are listed in a hybridized chip table 424. A hybridized sample map table 426 lists the relationships between hybridized chips and the samples that have been applied to them.

Stained hybridized chips are scanned in a process referred to here as a scan experiment. Scan experiments are listed in a scan experiment table 430. The scan experiment occurs in accordance with a protocol listed in protocol table 428. The scan experiment is performed by an employee listed in employee table 432.

Fig. 4B depicts further details of the data model for items and item derivations. The various item types are listed in an item type table 434 and the various item derivation types are listed in an item derivation type table 436. The relationships between successive item types, e.g., sample and target are defined in an item type derivation table 438. An item has associated attributes. For example, for a target, database 102 may store the concentration, volume, location and/or remaining amount. All item attributes are stored in an item attribute table 440. Item attributes may be shared among multiple items. For example, a series of targets may all share a preparation date. An item attribute item map table 442 implements a many-to-many

relationship between item attributes and items. The various types of item attributes such as preparer, preparation date, etc. are listed in an item attribute type table 444. Each item type has corresponding attribute types. Some attribute types are, however, shared among various item types. Accordingly, there is a many-to-many relationship among item attribute types and item types that is implemented by an item type map table 446.

The tables of Fig. 4B represent a powerfully general model of the sample preparation process. Changes in process steps that require changes in the type of information that should be stored may be implemented by changing and adding table contents rather than providing new tables or changing relationships among tables.

Fig. 4C depicts a detailed data model for storing information about protocols according to the present invention. Protocols as stored in protocol table 428 represent information about particular processes that have been performed including item derivations, analyses, and scan experiments. Each protocol has an associated protocol template. Protocol templates identify protocol types. For example, one protocol template may be a PCR template. All protocols associated with the PCR template identify parameters for performing a PCR procedure. Protocol templates are listed in a protocol template table 448. A parameter table 450 lists all the parameters and their values for all the protocols listed in protocol table 428. A parameter template table 452 lists the various parameter types along with default values. An examples of a parameter template would be a PCR reaction temperature. The parameter template would include a default value for this parameter. Parameter table 450 might then list many different PCR reaction temperature values that would be used by many different protocols. If a parameter value has not been modified by the user, it inherits the standard value of the associated parameter template. A parameter template set is a set of parameter templates that are used for a particular purpose, e.g., in association with protocols according to one or more protocol templates. Parameter template sets are listed in a parameter template set table 454. There are different types of parameter template set and these are listed in a parameter template set table 456. A mapping between parameter template sets and protocol templates is defined by a protocol template set map table 458.

Protocol templates may have associated lengthy verbal information about how to perform protocol steps. A protocol template document table 460 stores references to documents that include instructions for performing protocols.

As with the items, the data model for protocols defined by Fig. 4C is highly general and allows significant changes in the way item derivations, analyses, and experiments are performed without changing the underlying data model.

Referring again to Fig. 4A, there are tables to record information concerning the use of primers in PCR. A fragment table 462 lists all the sequence fragments investigated in conjunction with database 102. Associated with each fragment are one or more primer pairs used to amplify the fragment in a PCR process. A primer pair table 464 lists all the primer pairs including information about whether the primer pair actually worked to amplify the fragment. In order to develop the information about the effectiveness of primer pairs, there is a PCR table 466 that lists records identifying the outcome of multiple PCR operations. The individual PCR operations are identified by reference to item derivation table 420.

A single PCR operation may be used to amplify many different fragments and thus employ many different primer pairs. Of course, a single primer pair may be used in multiple PCR operations. There is therefore a many-to-many relationship between PCR operations and primer pairs that is recorded by a primer pair PCR map table 468. Information about individual primers is stored in a primer table 470. Also, each primer has an associated protocol in protocol table 428 that characterizes the primer preparation process. Information about primer orders is listed in a primer order table 472. Each primer order is to a vendor and the vendors are listed in a vendor table 474. Each primer order is made by an employee listed in employee table 432. A primer order design map table 476 implements a many-to-many relationship between primer orders and primers.

The data model described here thus preserves information about primers used in PCR reactions. One can improve results by using primers that have successfully amplified a given fragment in the past. Sometimes particular groups of primer pairs cannot be multiplexed together in the same PCR process. The information preserved here thus permits experimenters to make optimal use of expensive and time consuming PCR procedures.

It is also useful to preserve information about the chip production process and the origin of individual chips. A wafer table 478 lists wafers. When chips are produced, many chips are produced at the same time as part of a single wafer. Chip

table 422 stores references to wafer table 478 for each chip and the location of each chip on its wafer at production time. Sometimes there is analytic significance associated with the location of a chip on the wafer. Each wafer is produced as part of a lot and the identify of the lot for each wafer is recorded by wafer table 478 as a reference to a lot table 480 that lists each lot.

Fig. 4D depicts further details of tables pertaining to chip design that are preferably maintained within polymorphism database 102 according to one embodiment of the present invention. A tiling design table 482 lists tiling designs. Each tiling design represents the application of a particular tiling format to a sequence to be investigated. Tiling formats indicate probe orientation, probe length, and the position within a probe of a single nucleotide polymorphism being investigated. In a preferred embodiment, there may be very few tiling formats and they are listed in a tiling format table 484.

A particular tiling design includes many atom designs specifying the design of a single atom. In one embodiment, an atom is a group of typically four probes used to investigate a single base position with each probe hybridizing to a sequence including a different base at that position. Atom designs are listed in an atom design table 486. Records identifying the designs of individual probes are listed in a probe design table 488. A probe design role table 490 indicates the roles of probes listed in probe design table 488 in the atom designs of atom design table 486. For combinations of probe design and atom design, probe design role table 490 indicates which base the probe hybridizes to at the substitution position and whether the probe represents a match or a mismatch to the wild type.

A probe data table 492 gives the hybridization intensity values for particular probes designs as determined in particular scan experiments. Each record of the table also gives the number of pixels used to determine the intensity value and the standard deviation of intensity as measured among the pixels.

Figs. 4E-4G depict aspects of polymorphism database 102 related to analysis procedures and their results according to one embodiment of the present invention. An analysis table 494 lists analyses performed. An analysis generally refers to a non-trivial transformation of data. Records of analysis table 494 include references to protocol table 428 to specify parameters used for each analysis. Analyses may take as their input raw data or the results of previous analyses. An analysis dependency table

496 lists dependencies among analyses where one analysis depends on the data developed by another analysis. An analysis input table 498 lists inputs for analyses listed in analysis table 494.

On the right side of Fig. 4E are various tables used to support analyses. A chip design sequence map table 500 correlates particular fragments with chip designs. A sequence position table 502 lists investigated sequence positions indicating their positions on a fragment. Records of sequence position table 502 reference a genomic sequence position table 504 which gives sequence positions in the genome rather than within individual fragments.

A scan experiment set table 506 lists sets of scan experiments. This allows for groupings of experiments for individuals or populations to serve as the basis for polymorphism analysis. A scan experiment used table 508 lists records indicating memberships of a scan experiment in a scan experiment set.

A tiling data table 510 lists records identifying tiling designs as implemented in particular chips measured by particular scan experiments. An atom data table 512 lists the intensities measured for particular sequence positions as measured in scan experiments identified by the tiling data records. A subject sequence position data table 514 lists combinations of sequence position and scan experiment.

A series of tables in Figs. 4E-4G correspond to different types of analysis that occur during the course of a polymorphism investigation. The types presented here are merely representative. A parallel series of tables provide the analysis results. A polymorphism analysis table 516 lists references to analysis table 494. The results of the performed polymorphism analyses are listed in a polymorphism position result table 518. A record of this table gives a result for a polymorphism analysis for a particular position as determined based on a particular set of scan experiments. In one embodiment the result is whether a particular mutation is certain, likely, possible, or not possible at the position. The result may also be that the reference is wrong.

A user polymorphism analysis table 520 lists user interpretations of results as listed in polymorphism position result table 518. The records of user polymorphism analysis table 520 are references to analysis table 494. The user interpretations themselves are stored in a user polymorphism analysis result table 522. Each result is a

likelihood of a particular mutation at a position as considered by a user plus an accompanying user comment.

A P-Hat analysis estimates the relative concentrations of wild type sequence and sequence having a particular mutation as determined in a particular scan experiment. A P-Hat analysis table 524 lists references to analysis table 494. An atom result table 526 gives estimates of the relative concentration along with upper and lower bounds and a maximum intensity. For heterozygous mutations, the estimates of relative concentration will cluster around 0.5 For homozygous mutations, the estimates should cluster around 1.0.

Base call analyses are determinations of the base at a particular position for a particular individual that may be based on more than one experiments. A base call analysis table 528 lists references to analysis table 494. A base call result table 530 lists the called bases for particular combinations of sequence position and subject.

A P-Hat grouping analysis determines a measure of likelihood that data in a set of scan experiments results from separate genotypes. P-hat grouping analyses are listed in a p-hat grouping analysis table 532 by reference to analysis table 494. P-hat grouping analysis results are listed in a mutation fraction result table 534. A group separation is given for various combinations of sequence position and scan experiment set.

A clustering analysis determines an alternative measure of likelihood that data in a set of scan experiments results from separate genotypes. Clustering analyses are listed in a clustering analysis table 536 by reference to analysis table 494. Clustering analysis results are listed in a clustering result table 538. A clustering factor is given for various combinations of sequence position and scan experiment set.

Fig. 4F shows tables which support normalization and footprint finding operations that support the analyses referred to in Fig. 4E. Hybridization intensity measurements made in scan experiments should be normalized over a set of scan experiments. The normalization should take into account differences in amplification level produced by different PCR processes.

Normalization is done by region of sequence. A normalization region analysis determines the boundaries of a region to be normalized. The determination of boundaries takes into account that different fragments of sequence are amplified by

different PCR procedures. A normalization region analysis table 540 lists normalization region analyses by reference to analysis table 494. A normalization region result table 542 lists the boundaries for each determined normalization region.

Normalization values for identified normalization regions are themselves determined by normalization analyses. Normalization analyses are listed in a normalization analysis table 544 by reference to analysis table 494. A normalization result table 546 lists the normalization values for regions.

A footprint analysis determines regions of sequence for which the hybridization intensity is elevated for the purposes of quality control. Footprint analyses are listed in a footprint analysis table 548 by reference to analysis table 494. Footprints are identified by sequence starting point and ending point in a particular scan experiment in a footprint table 550.

Fig. 4G depicts tables pertaining to measurement quality according to one embodiment of the present invention. A tiling data quality analysis determines the quality of results from a scan experiment. These analyses are listed in a tiling data quality analysis table 552 by reference to analysis table 494. Tiling data quality analysis results are listed in a tiling data quality result table 554. The results include an average hybridization intensity value for perfect match or mismatch probes. A wild type call rate gives the fraction of atom data where the probe corresponding to the reference base has the highest hybridization intensity. A wild type call rate of around 1.0 indicates good quality. Where the call rate is less than 0.75, the scan experiment should be rejected. An accept data field indicates whether the analysis indicates rejection or acceptance.

Where scan experiment measurements indicate two or more non-wild type bases within a probe length, this indicates a measurement problem for the affected region of sequence. These regions are identified by difficult region analyses listed in a difficult region analysis table 556 by reference to analysis table 494. A difficult region result table 558 lists the regions identified as being difficult.

Analysis dependency table 496 indicates interrelationships among the various analyses of Figs. 4E-4G. A footprint analysis may depend on a normalization analysis which may in turn depend on a normalization region analysis. A basecall analysis or PHatGrouping analysis may depend on an atom analysis. A polymorphism

analysis may depend on any of these analyses and/or a user polymorphism analysis and/or a clustering analysis.

Another aspect of the investigation of polymorphisms is seeking patent protection for identified polymorphisms. Fig. 4H shows tables of polymorphism database 102 related to efforts to seek patent protection according to one embodiment of the present invention. A polymorphism patent sequence table 560 lists sequences for which patent protection is sought. A patent application table 562 lists patent applications directed toward the protection of polymorphisms. A polymer patent application sequence map table 564 implements a many-to-many relationship between patent applications and sequences. A prior application table 566 lists relationships between patent applications and prior related patent applications. An attorney table 568 lists attorneys responsible for preparing patent applications listed in patent application table 562. A law firm table 570 lists the law firms to which the attorneys listed in attorney table 568 belong.

An employee group table 572 lists groups of inventors for the patent applications listed in table 562. Individual inventors are listed in employee table 432. An employee group map table 574 implements a many-to-many relationship between inventors and groups of inventors.

The data model of Fig. 4H greatly facilitates the process of securing patent protection for polymorphisms and thereby increases the commercial incentive for investigation of polymorphisms.

Database Contents

The contents of the tables introduced above will now be presented in greater detail in the following chart.

TABLE	FIELD	COMMENT
tblSubject		

TABLE	FIELD	COMMENT
	SubjectId:INTEGER	Identifies biological source of sample.
	SpeciesID:INTEGER	Species of subject.
	Name:VARCHAR2(20)	Name of subject (anonimized for human subjects).
	Gender:VARCHAR2(10)	Gender of subject.
	Family:VARCHAR2(20)	Family of subject (anonimized for human subjects).
	Member:SMALLINT	Position in family (father, mother, etc.).
	Group_:VARCHAR2(20)	Ethnic group.
	CellLineID:VARCHAR2(20)	Identifier for sample source not associated with particular organism.

TABLE	FIELD	COMMENT
	IsReference:SMALLINT	Whether or not subject is in a group.
tblSpecies		
	SpeciesId:INTEGER	Species identifier.
	Name:VARCHAR2(30)	Name of species.
SubjectRelationship		
	Subject1:INTEGER	First subject in relationship.
	Subject2:INTEGER	Second subject in relationship.
	Position:VARCHAR2(2)	Nature of relationship.
tblSubjectGroup		
	GroupId:INTEGER	Identifier of group of subjects (not same as ethnic group).
	GroupCode:VARCHAR2(20)	Code identifier for group.
	Comments:LONG VARCHAR	User comments on group.

TABLE	FIELD	COMMENT
	upsize_ts:DATE	Creation date for group.
tblSubjectParticipation		
	SubjectId:INTEGER	Reference to subject table.
	GroupId:INTEGER	Reference to subject group table.
tblSample		
	SampleId:INTEGER	Sample identifier.
	SubjectID:INTEGER	Reference to subject table.
	SampleSourceId:CHAR(18)	Institutional source of sample.
	Code:VARCHAR2(20)	Code representing individual subject.
	Recipient:VARCHAR2(20)	Person accepting sample.
	Provider:VARCHAR2(20)	Person or institution providing sample.

TABLE	FIELD	COMMENT
	DateReceived:DATE	Date sample received.
	ProtocolId:INTEGER	Reference to protocol table.
	SampleTypeId:INTEGER	Reference to sample type table.
tblSampleType		
	SampleTypeId:INTEGER	Sample type identifier.
	Description:VARCHAR2(50)	Description of sample type.
tblSample Source		
	SampleSourceId:CHAR(18)	Identifier of institutional sample source.
	ProviderName:VARCHAR2(20)	Name of individual or institutional sample provider.
Item		
	ItemId:INTEGER	Item identifier.
	ItemTypeId:INTEGER	Item type identifier.
	ItemName:VARCHAR2(50)	Name of item.

TABLE	FIELD	COMMENT
ItemDerivation		
	Item1Id:INTEGER	Derivation source.
	Item2Id:INTEGER	Derivation result.
	EmployeeId:INTEGER	Employee responsible for derivation.
	DerivationTypeId:INTEGER	Derivation type identifier.
	Protocolid:VARCHAR2(18)	Reference to protocol table.
	Date:DATE	Date of derivation.
tblChip		
	ChipId:INTEGER	Rename reference to item table.
	ChipDesignPlacementId:INTEGER	Placement on wafer.
	LocationId:INTEGER	Location of chip.
	WaferId:INTEGER	Wafer the chip was on.
tblHybedChip		

TABLE	FIELD	COMMENT
	HybedChipId:INTEGER	Rename reference to item table.
	SubjectID:INTEGER	Reference to subject table.
	ProtocolId:INTEGER	Reference to protocol table.
	Repetition:SMALLINT	Refers to number of times chip has been washed and reused.
tblHybSampleMap		
	ItemId:INTEGER	Reference to item table.
Protocol		
	ProtocolId:INTEGER	Protocol identifier.
	ProtocolTemplateId:INTEGER	Protocol template identifier.
	Name:VARCHAR2(100)	Name of protocol.
tblScanExperiment		

TABLE	FIELD	COMMENT
	ScanExptId:INTEGER	Scan experiment identifier.
	ItemId:INTEGER	Reference to item table.
	ScanCode:VARCHAR2(25)	File for scan results.
	ProtocolId:INTEGERP	Reference to protocol table.
	ScanRatingId:INTEGER	Assessment of scan quality.
	ExperimenterId:INTEGER	Experimenter identifier.
	Date:DATE	Date of experiment.
	ConversionTool:VARCHAR2(50)	Program used to convert from scan image to intensities.
	ConversionDate:DATE	Date of conversion.
	ScanStatus:VARCHAR2(50)	whether or not scan image has been converted to intensities
	Comments:LONG VARCHAR	Comments.

TABLE	FIELD	COMMENT
Employee		
	EmployeeId:INTEGER	Employee identifier.
	EmployeeCode:VARCHAR2(5)	Code for employee
	FName:VARCHAR2(20)	First name of employee.
	MName:VARCHAR2(20)	Middle name of employee.
	LName:VARCHAR2(20)	Last name of employee.
ItemType		
	ItemId:INTEGER	Item type identifier.
	ItemTypeName:VARCHAR2(30)	Name of item type.
	FormName:VARCHAR2(100)	Reference to user interface form for item type.
ItemDerivationType		
	DerivationTypeId:INTEGER	Derivation type identifier.

TABLE	FIELD	COMMENT
	DerivationType:VARCHAR2(50)	Description of derivation type.
ItemTypeDerivation		
	NextItemTypeId:INTEGER	Result type of derivation.
	ItemTypeId:INTEGER	Source type of derivation.
ItemAttribute		
	itemAttributeId:INTEGER	Item attribute identifier.
	ItemAttributeTypeId:INTEGER	Reference to item attribute type table.
	Attribute:VARCHAR2(50)	Attribute value.
ItemAttributeItemMap		
	ItemAttributeId:INGEGER	Reference to item attribute table.
	ItemId:INTEGER	Reference to item table.
ItemAttributeType		
	ItemAttributetypeId:INTEGER	Item attribute identifier.

TABLE	FIELD	COMMENT
	ItemAttributeName:VARCHAR2(30)	Name of item attribute type.
ItemTypeMap		
	ItemAttributeTypeId:INTEGER	Reference to item attribute type table.
	ItemTypeId:INTEGER	Reference to item type table.
ProtocolTemplate		
	ProtocolTemplateId:INTEGER	Protocol template identifier.
	Name:VARCHAR2(100)	Name of protocol template.
	DateCreated:DATE	Date protocol template created.
	FormName:VARCHAR2(50)	Name of the electronic form used for protocol template.
Parameter		
	ParameterId:INTEGER	Parameter identifier.

TABLE	FIELD	COMMENT
	ParameterTemplateId:INTEGER	Reference to parameter template table.
	Value:VARCHAR2(20)	Value of parameter.
	ProtocolID:INTEGER	Reference to protocol table.
ParameterTemplate		
	ParameterTemplateId:INTEGER	Parameter template identifier.
	Name:VARCHAR2(100)	Name of parameter template.
	ParamTemplateSetId:INTEGER	Reference to parameter template set table.
	StandardValue:VARCHAR2(100)	Default value for parameter.
ParamTemplateSet		
	ParamTemplateSetId:INTEGER	Parameter template set identifier.

TABLE	FIELD	COMMENT
	TypeId:INTEGER	Renamed reference to parameter template set type table.
	Name:VARCHAR2(20)	Name of parameter template set.
ParamTemplateSetType		
	ParamTempSetTypeId:INTEGER	Parameter template set type identifier.
	Description:VARCHAR2(50)	Description of parameter template set type.
ParameterTemplateSetMap		
	ProtocolTemplateId:INTEGER	Reference to protocol template table.
	ParamTemplateSetId:INTEGER	Reference to parameter template set table.
ProtocolTemplateDoc		

TABLE	FIELD	COMMENT
	ProtocolDocId:INTEGER	Protocol Template document identifier.
	ProtocolTemplateId:INTEGER	Reference to protcol template table.
	Name:VARCHAR2(100)	Name of protocol template.
	PathAndFileName:VARCHAR2(50)	File name for protocol template document.
	AuthorName:INTEGER	Author of protocol template document.
	CreationDate:DATE	Creation Date of protocol template document.
tbFragment		
	FragmentId:INTEGER	Fragment identifier.
	ChipSequence:LONG VARCHAR	Sequence of fragment.

TABLE	FIELD	COMMENT
	Code:VARCHAR2(50)	Code representing fragment.
tblPrimerPair		
	PrimerPairId:INTEGER	Identifier for primer pair.
	LeftPrimerId:INTEGER	Left primer identifier.
	RightPrimerId:INTEGER	Right primer identifier.
	PCRSize:INTEGER	length of amplified fragment
	Worked:SMALLINT	Whether or not pair successfully amplified fragment.
	FragmentId:INTEGER	Reference to fragment table.
tblPCR		
	Item1Id:INTEGER	First part of reference to item derivation table.

TABLE	FIELD	COMMENT
	Item2Id:INTEGER	Second part of reference to item derivation table.
	Reactionworked:SMALLINT	Whether or not PCR reaction worked.
PrimePairPCRMap		
	PrimerPairId:INTEGER	Reference to primer pair table.
	Item1ID:INTEGER	First part of referenced item derivation table.
	Item2Id:INTEGER	Second part of referenced item derivation table.
tblPrimer		
	PrimerId:INTEGER	Primer identifier.
	ProtocolId:INTEGER	Reference to protocol table.
	OligoSeq:VARCHAR2(35)	Sequence of primer.

TABLE	FIELD	COMMENT
	Position:INTEGER	Position of primer on fragment.
	Length:INTEGER	Length of primer.
	MeltingTemp:INTEGER	Melting temperature of primer.
	Direction:VARCHAR2(20)	Direction (forward or reverse).
tblPrimerOrder		
	OrderId:INTEGER	Order identifier.
	EmployeeId:INTEGER	Employee who made order.
	VendorId:INTEGER	Vendor for order.
	OrderDate:DATE	Date of order.
	Owner:VARCHAR2(50)	Name of employee making order.
	Vendor:VARCHAR2(50)	Name of vendor.
tblVendor		

TABLE	FIELD	COMMENT
	VendorId:INTEGER	Vendor identifier.
	Vendor:VARCHAR2(50)	Name of vendor.
	PhoneNumber:VARCHAR2(15)	Phone number of vendor.
	FaxNumber:VARCHAR2(15)	Fax Number of vendor.
	Address:VARCHAR2(50)	Address of vendor.
	City:VARCHAR2(50)	City of vendor.
	State:VARCHAR2(50)	State of vendor.
	Zip:VARCHAR2(50)	Zip code of vendor.
tblPrimerOrderDesignMap		
	PrimerId:INTEGER	Reference to primer table.
	OrderId:INTEGER	Reference to order table.
tblWafer		
	WaferId:INTEGER	Wafer identifier.
	LotId:INTEGER	Lot to which wafer belongs.

TABLE	FIELD	COMMENT
	Code:VARCHAR2(8)	Code for wafer.
	SynthesisDate_delete:DATE	Synthesis date for wafer.
	Released:DATE	Date wafer available.
	Done:SMALLINT	Whether wafer production is complete.
	ExpirationDate:DATE	Expiration date of wafer.
	ExpectedLife:CHAR(18)	Expected useful life of wafer.
tblLot		
	LotId:INTEGER	Lot identifier.
	WaferDesignId:INTEGER	Identifier for wafer design.
	LotNumber:VARCHAR2(12)	Lot number.
	WaferPN:VARCHAR2(50)	Part number for wafer.
tblTiling Design		
	TilingDesignID:INTEGER	Tiling design identifier.

TABLE	FIELD	COMMENT
	ChipDesignSequenceMapID:NUMBER	Reference to chip design sequence map.
	TilingFormatID:INTEGER	Reference to tiling format table.
	UnitNumber:INTEGER	1 for sense, 0 for antisense
	AtomOffset:INTEGER	# to add to translate atom position in tiling to atom position in chip design
tblTiling Format		
	TilingFormatID:INTEGER	Tiling format identifier
	Orientation:CHAR(18)	Orientation for tiling.
	ProbeLength:SMALLINT	Length of probes.
	SubstitutionPosition:SMALLINT	Substitution position for mutation base in probes.
tblAtomDesign		

TABLE	FIELD	COMMENT
	AtomDesignId:NUMBER	Atom design identifier.
	TilingDesignID:INTEGER	Reference to tiling design table.
	Position:INTEGER	Position of atom in sequence.
tblProbeDesign		
	ProbeDesignID:NUMBER	Probe design identifier.
	ChipDesignId:INTEGER	Reference to chip design.
	x:SMALLINT	x position of probe.
	y:SMALLINT	y position of probe.
tblProbeDesignRole		
	ProbeDesignID:NUMBER	Reference to probe design table.
	AtomDesignID:NUMBER	Reference to atom design table.

TABLE	FIELD	COMMENT
	Substitution:CHAR(18)	Substitution position in probe design.
	Mismatches:NUMBER	Whether probe is match or mismatch.
tblProbeData		
	ProbeDesignID:NUMBER	Reference to probe design table.
	ScanExptID:INTEGER	Reference to scan experiment table.
	Intensity:FLOAT	Measured hybridization intensity for probe.
	NPixels;NUMBER	Number of pixels used for intensity calculation.
	StDev:NUMBER	Standard deviation for pixels.
tblAnalysis		

TABLE	FIELD	COMMENT
	AnalysisId:INTEGER	Analysis identifier.
	AnalysisVersionID:INTEGER	Reference to version of analysis.
	ProtocolID:INTEGER	Reference to protocol table.
	DatePerformed:DATE	Date analysis performed.
	NeedsUpdate:NUMBER	Whether analysis is current.
tblAnalysisDependency		
	ParentAnalysisId:INTEGER	Analysis providing input.
	SubAnalysisId:INTEGER	Analysis receiving input.
	Role:VARCHAR2(20)	Role of data provided by parent analysis.
TblAnalysisInput		
	AnalysisinputID:INTEGER	Analysis input identifier.

TABLE	FIELD	COMMENT
	AnalysisId:INTEGER	Analysis receiving input.
	Inputtype:VARCHAR2(20)	Type of input.
	ObjectID:INTEGER	Reference to input data.
tblChipDesignSequenceMap		
	ChipDesignSequenceMapID:NUMBER	Chip design sequence map identifier.
	FragmentID:INTEGER	Reference to fragment table.
	ChipDesignId:INTEGER	Chip design identifier.
	AtomOffset:NUMBER	# to add to translate atom position in tiling to atom position in chip design
tblSequencePosition		
	SequencePositionID:NUMBER	Sequence position identifier.
	ChipDesignSequenceMapID:NUMBER	Reference to chip design sequence map table.

TABLE	FIELD	COMMENT
	Position:NUMBER	Position in fragment.
	GenomicSequencePositionID:INTEGER	Reference to genomic sequence position table.
	RefBase:INTEGER	Reference base.
tblGenomicSequencePosition		
	GenomicSequencePositionID:INTEGER	Genomic sequence position identifier.
tblScanExperimentSet		
	ScanExperimentSetID:NUMBER	Scan experiment set identifier.
tbsScanExperimentUsed		
	ScanExptID:INTEGER	Reference to scan experiment table.
	ScanExperimentSetID:NUMBER	Reference to scan experiment set table.
tblTilingData		
	TilingDataID:NUMBER	Tiling data identifier.
	ScanExptID:INTEGER	Reference to scan experiment table.
	TilingDesignID:INTEGER	Reference to tiling design table.
tblAtomData		

TABLE	FIELD	COMMENT
	AtomDataID:INTEGER	Atom data identifier.
	TilingDataID:NUMBER	Reference to tiling data table.
	SubjectSequencePositionID:INTEGER	Reference to subject sequence position table.
tblSubjectSequencePosition		
	SubjectSequencePositionID:INTEGER	Subject sequence position identifier.
	SubjectID:INTEGER	Reference to subject table.
	SequencePositionID:NUMBER	Reference to sequence position table.
tblPolymorphismAnalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tblPolyPositionResult		
	AnalysisId:INTEGER	Reference to analysis table.
	PolyPositionID:INTEGER	Polymorphism position identifier.
	ScanExperimentSetID:NUMBER	Reference to scan experiment set table.

TABLE	FIELD	COMMENT
	PolyPositiontypeID:INTEGER	Refers to possibility of polymorphism at position, e.g., certain, likely, possible, mismatch (reference is wrong).
	WTBase:CHAR(18)	Wild type base at position.
	MuBase:INTEGER	Mutation base at position.
tblUserPolyanalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tblUserPolyanalysisResult		
	AnalysisId:INTEGER	Reference to analysis table.
	SequencePositionID:NUMBER	Reference to sequence position table.
	ScanExperimentSetID:NUMBER	Reference to scan experiment set table.
	PolyPositionTypeID:INTEGER	See polymorphism position result table.

TABLE	FIELD	COMMENT
	UserComment:VARCHAR2(256)	User comment done polymorphism analysis.
tblAtomanalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tblAtomResult		
	AnalysisId:INTEGER	Reference to analysis table.
	AtomDataID:INTEGER	Reference to atom data table.
	PHat:FLOAT	Relative concentration of mutant and wild type.
	PHatUpperbound:FLOAT	Upperbound for relative concentration.
	PHatLowerbound:FLOAT	Lowerbound for relative concentration.
	MaxIntensity:FLOAT	Maximum measured intensity for atom.
	WTIntensity:FLOAT	Measured wild type intensity.

TABLE	FIELD	COMMENT
	MutIntensity:FLOAT	Measured mutation intensity.
	LocalWTCallRate:FLOAT	rate at which atoms associated with surrounding sequence call reference base
	IntensityRatio:FLOAT	Ratio of intensity of wild type probe over intensity of mutation probe.
tblBaseCallAnalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tblBaseCallResult		
	AnalysisId:INTEGER	Reference to analysis table.
	SubjectSequencePositionID:INTEGER	Reference to sequence position table.
	ScanExperimentSetID:NUMBER	Reference to skin experiments set table.
	CalledBase:VARCHAR2(1)	Base called for subject based on experiment set.

TABLE	FIELD	COMMENT
	SuggestCheck:NUMBER	Used to indicate whether this sample should be used for resequencing
tblClusteringAnalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tblClusteringResult		
	AnalysisId:INTEGER	Reference to analysis table.
	SequencePositionID:NUMBER	Reference to sequence position table.
	ScanExperimentSetID:NUMBER	Reference to scan experiment set table.
	ClusteringFactor:FLOAT	Result of clustering analysis.
tblNormalizationRegionAnalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tblNormalizationRegion		
	NormalizationRegionID:INTEGER	Normalization region identifier.
	AnalysisId:INTEGER	Reference to analysis table.

TABLE	FIELD	COMMENT
	ChipDesignSequenceMapID:NUMBER	Reference to chip design sequence map table.
	NumberScanExpt.Set	Reference to scan experiment set table.
	RegionEnd:INTEGER	Indication of end of the normalization region.
	RegionStart:INTEGER	Indication of beginning of the normalization region.
tblNormalizationAnalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tblNormalizationResult		
	NormalizationResultID:INTEGER	Normalization result identifier.
	AnalysisId:INTEGER	Reference to analysis table.
	TilingDataID:INTEGER	Reference to tiling data table.
	NormalizationRegionResultID:INTEGER	Reference to normalization result.
	NormalizationValue:NUMBER	Value used for normalization.

TABLE	FIELD	COMMENT
	DataOK:NUMBER	Indication whether normalization result is usable.
tblFootprintAnalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tblFootprint		
	FootprintID:NUMBER	Footprint identifier.
	AnalysisId:INTEGER	Analysis identifier.
	ChipDesignSequenceMapID:NUMBER	Reference to chip design sequence map table.
	ScanExperimentSetID:NUMBER	Reference to scan experiment set table.
	FFStart:NUMBER	Start of footprint and sequence.
	FPEnd:NUMBER	End of footprint and sequence.
tblTilingDataQualityAnalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tbltilingDataQualityResult		
	TilingDataID:NUMBER	Reference to tiling data table.

TABLE	FIELD	COMMENT
	AnalysisId:INTEGER	Reference to analysis table.
	AvgWTIntensity:NUMBER	Average wild type intensity.
	WTCallRate:NUMBER	Fraction of atoms where brightest of probes is one with reference space.
	AcceptData:INTEGER	Whether data is of acceptable quality.
tblDifficult Regionanalysis		
	AnalysisId:INTEGER	Reference to analysis table.
tblDifficultRegionResult		
	ScanExptId:INTEGER	Reference to scan experiment table.
	AnalysisId:INTEGER	Reference to analysis table.
	ChipDesignSequenceMapID:NUMBER	Reference to chip design sequence map table.
	RgnStart:NUMBER	Beginning of difficult region in sequence.
	RgnEnd: NUMBER	End of difficult region in sequence.

TABLE	FIELD	COMMENT
	Reason:INTEGER	Code indicating reason for difficult region, e.g., two or more non-wild type bases and less than a probe length.q
tblPolyPatentSeq		
	PolyPatentSeqId:NUMBER	Polymorphism sequence identifier.
	Polyscreen:VARCHAR2(50)	reference to internal grouping of polymorphisms
	FragmentCode:VARCHAR2(50)	Fragment sequence found in
	Position:LONG	Position of polymorphism.
	RefAllel:CHAR(2)	Wild type base at position.
	FreqP:FLOAT	Frequency of wild type.
	AltAllele:CHAR(2)	Mutation base at position.
	FreqQ:FLOAT	Frequency of mutation base.
	Heterozygocity:FLOAT	Heterozygocity value.

TABLE	FIELD	COMMENT
	SequenceTag:VARCHAR2(50)	Sequence containing polymorphism including ambiguity code at polymorphism position.
	GeneName:VARCHAR2(50)	Name of gene.
	ChromosomeNum:VARCHAR2(20)	Chromosome number.
	ChromosomeLoc:VARCHAR2(20)	Location of gene on chromosome.
	ForwardPrimer:VARCHAR2(50)	Identifier for forward primer used to implement fragment.
	ReversePrimer:VARCHAR2(50)	Identifier of primer used to amplify fragment.
tblPatentApp		
	PatentAppId:NUMBER	Patent application identifier.
	GroupId:NUMBER	Reference to employee group table.
	AttorneyId:NUMBER	Reference to attorney table.
	DocketNum:VARCHAR2(30)	Docket number for patent application.

TABLE	FIELD	COMMENT
	FilingDate:DATE	Filing date for filing application.
	Classification:VARCHAR2(30)	Patent office classification for patent application.
	SerialNumber:VARCHAR2(50)	Serial number assigned by patent office.
	CountryCode:VARCHAR2(50)	Country in which patent application was filed.
	InventionTitle:VARCHAR2(100)	Title for patent application
tblPolyPatentSeqMap		
	PatentAppId:NUMBER	Reference to patent application table.
	PolyPatentSeqId:NUMBER	Reference to polymorphism patent sequence table.
tblPriorApp		
	PriorAppId:NUMBER	Reference to related prior patent application in patent application table.

TABLE	FIELD	COMMENT
	AppId:NUMBER	Reference to application to which prior application is related.
tblAttorney		
	AttorneyId:NUMBER	Attorney identifier.
	LawFirmId:NUMBER	Law firm where attorney works.
	FirstName:VARCHAR2(20)	First name of attorney.
	MiddleName:VARCHAR2(5)	Middle name of attorney.
	LastName:VARCHAR2(30)	Last name of attorney.
	RegistrationNum:VARCHAR2(25)	Patent office registration number of attorney.
tblLawFirm		
	LawFirmId:NUMBER	Law firm identifier.
	Company:VARCHAR2(100)	Name of law firm.
	Address:VARCHAR2(100)	Address of law firm.
	City:VARCHAR2(30)	City address of law firm.

TABLE	FIELD	COMMENT
	State:VARCHAR2(20)	State address of law firm.
	ZipCode:VARCHAR2(15)	Zip Code of law firm.
	Country:VARCHAR2(15)	Country of law firm.
	Telephone:VARCHAR2(30) Fax:VARCHAR2(30)	Telephone number of law firm.
	TELEX:VARCHAR2(20)	Facsimile number of law firm.
		Telex number of law firm.
tblEmployeeGroup		
	GroupId:NUMBER	Identifier for inventor group.
	GroupName:VARCHAR2(50)	Name of inventor group.
	Comments:VARCHAR2(50)	Comments.
	GroupList:VARCHAR2(255)	Written out list of inventor names.
tblEmployeeGrpMap		
	EmployeeId:INTEGER	Reference to employee table for inventor/employees.
	GroupId:NUMBER	Reference to inventor group table.

It is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims. For example, tables may be deleted, contents of multiple tables may be consolidated, or contents of one or more tables may be distributed among more tables than described herein to improve query speeds and/or to aid system maintenance. Also, the database architecture and data models described herein are not limited to biological applications but may be used in any application. All publications, patents, and patent applications cited herein are hereby incorporated by reference.

WHAT IS CLAIMED IS:

1. A computer-readable storage medium having stored thereon:

an item table listing a plurality of item records identifying items; an item attribute table listing a plurality of item attribute records identifying attributes of said items; and

wherein there is a many-to-many relationship between item records and item attribute records.

2. The computer-readable storage medium of claim 1 wherein

an item attribute item map table implements said many-to-many relationship between item records and item attribute records, said item attribute item map table listing a plurality of map records identifying both a particular item attribute and a particular item.

3. The computer-readable storage medium of claim 1 having further stored thereon:

an item derivation table listing a plurality of item derivation records identifying transformations between ones of said items used in biological analysis.

4. The computer-readable storage medium of claim 3 having further stored thereon:

a protocol table listing a plurality of protocol records specifying parameters of said transformation.

5. The computer-readable storage medium wherein said items are used in a biological analysis.

6. The computer-readable storage medium of claim 1 wherein said biological analysis comprises a polymorphism analysis.

7. A computer-readable storage medium having stored thereon:

an atom result table listing a plurality of atom result records, specifying relative wild-type and mutant sequence concentrations in targets; and

a subject sequence position table listing a plurality of subject sequence position records, specifying combinations of subjects from whom said targets are derived and sequence positions, each said atom result record being associated with one or more atom result records.

8. The computer-readable storage medium of claim 7 wherein said atom result records further specify upper and lower bounds for said concentrations.

9. The computer-readable storage medium of claim 7 having further stored thereon:

a subject table listing subject records specifying said subjects.

10. A computer-readable storage medium having stored thereon:

a polymorphism table listing polymorphism sequence records specifying sequences known to contain polymorphisms; and

a patent application table listing patent application records specifying one or more polymorphisms specified by said polymorphism sequence records.

11. The computer-readable storage medium of claim 10 wherein said polymorphism sequence records specify for each one of said polymorphisms a polymorphism position, a reference allele, and a base allele.

12. The computer-readable storage medium of claim 11 wherein said polymorphism sequence records further specify for each one of said polymorphisms a measured heterozygocity.

13. A computer-implemented method comprising:

creating n item table listing a plurality of item records identifying items used in biological analysis; and

creating an item attribute table listing a plurality of item attribute records identifying attributes of said items; and

wherein there is a many-to-many relationship between item records and item attribute records.

14. The computer-implemented method of claim 13 further comprising the step of:

creating an item attribute item map table implements said many-to-many relationship between item records and item attribute records, said item attribute item map table listing a plurality of map records identifying both a particular item attribute and a particular item.

15. The computer-implemented method of claim 13 comprising:

an item derivation table listing a plurality of item derivation records identifying transformations between ones of said items used in biological analysis.

16. The computer-implemented method of claim 15 further comprising:

creating a protocol table listing a plurality of protocol records specifying parameters of said transformation.

17. The computer-implemented method of claim 13 wherein said biological analysis comprises a polymorphism analysis.

18. A computer-implemented method comprising:

creating an atom result table listing a plurality of atom result records, specifying relative wild-type and mutant sequence concentrations in targets; and

creating a subject sequence position table listing a plurality of subject sequence position records, specifying combinations of subjects from whom said targets are derived and sequence positions, each said atom result record being associated with one or more atom result records.

19. The computer-implemented method of claim 18 wherein said atom result records further specify upper and lower bounds for said concentrations.

20. The computer-implemented method of claim 18 further comprising:

creating a subject table listing subject records specifying said subjects.

21. A computer-implemented method comprising:

creating a polymorphism table listing polymorphism sequence records specifying sequences known to contain polymorphisms; and

creating a patent application table listing patent application records specifying one or more polymorphisms specified by said polymorphism sequence records.

22. The computer-implemented method of claim 21 wherein said polymorphism sequence records specify for each one of said polymorphisms a polymorphism position, a reference allele, and a base allele.

23. The computer-implemented method of claim 22 wherein said polymorphism sequence records further specify for at least one of said polymorphisms a measured heterozygocity.

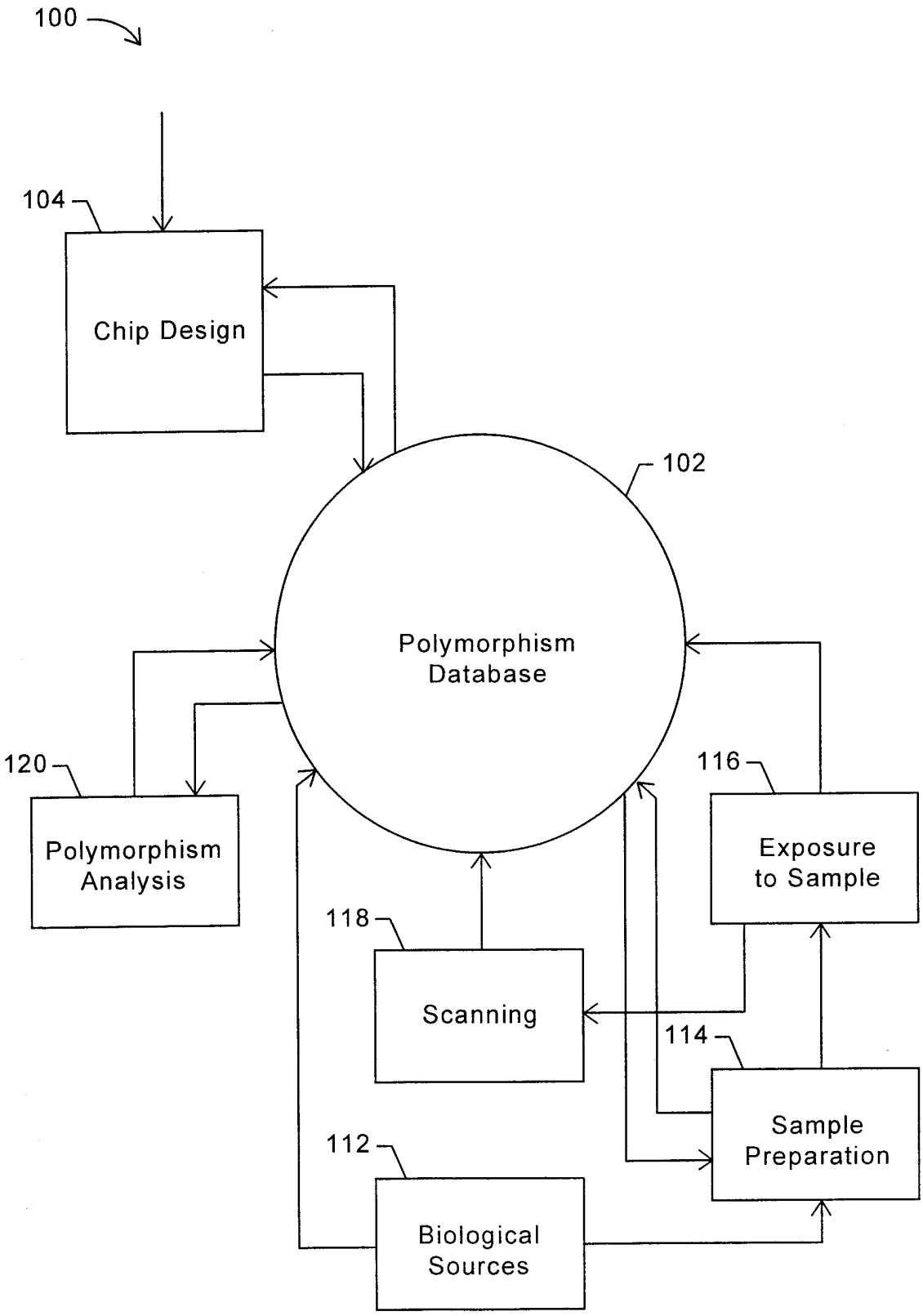

100
104
Chip Design
102
Polymorphism Database
120
Polymorphism Analysis
116
Exposure to Sample
118
Scanning
114
Sample Preparation
112
Biological Sources

Fig. 1

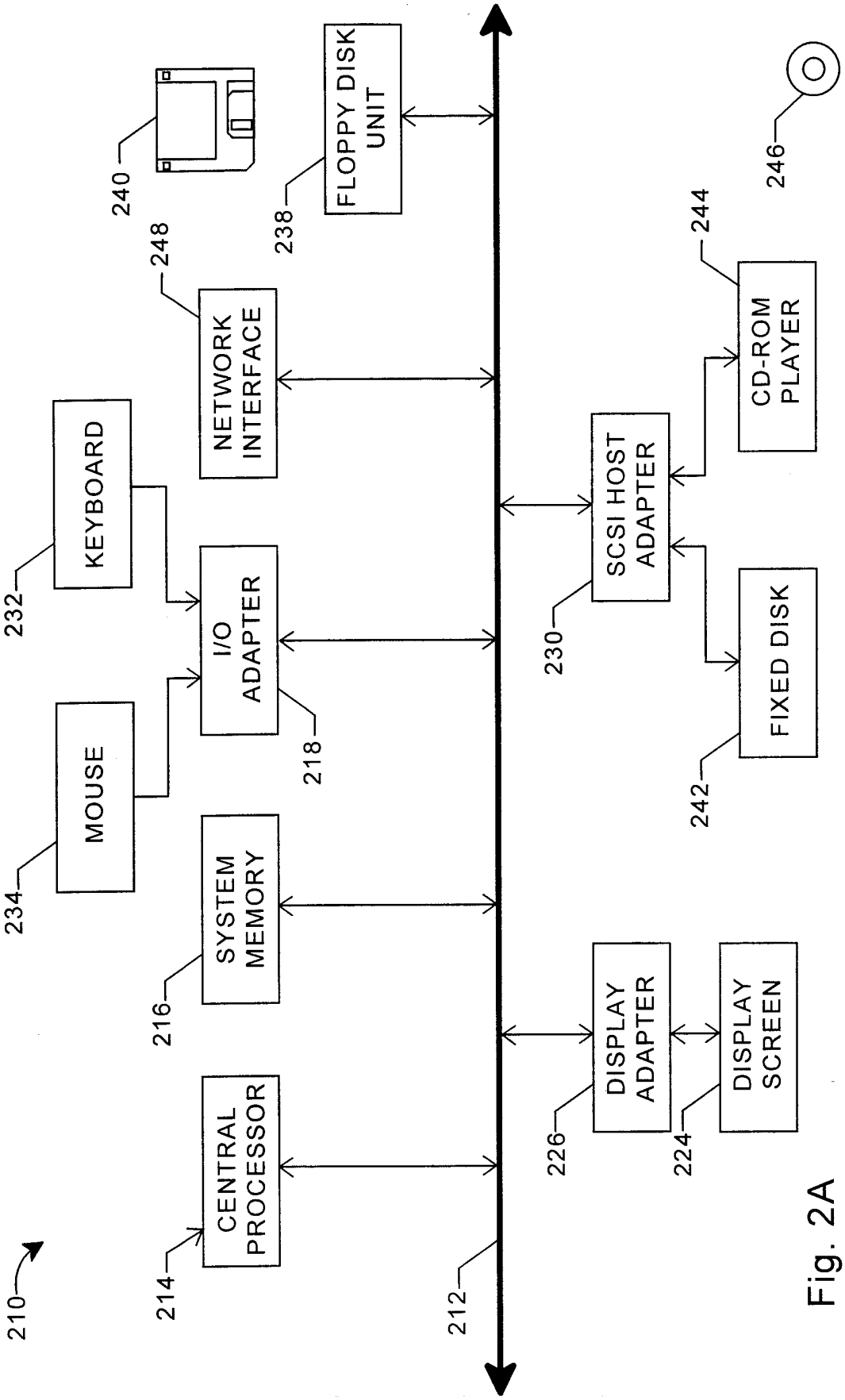

210
212
214
CENTRAL PROCESSOR
216
SYSTEM MEMORY
218
I/O ADAPTER
220
DISPLAY ADAPTER
222
DISPLAY SCREEN
224
226
SCSI HOST ADAPTER
228
230
FIXED DISK
232
KEYBOARD
234
MOUSE
236
FLOPPY DISK UNIT
238
240
NETWORK INTERFACE
242
244
CD-ROM PLAYER
246

Fig. 2A

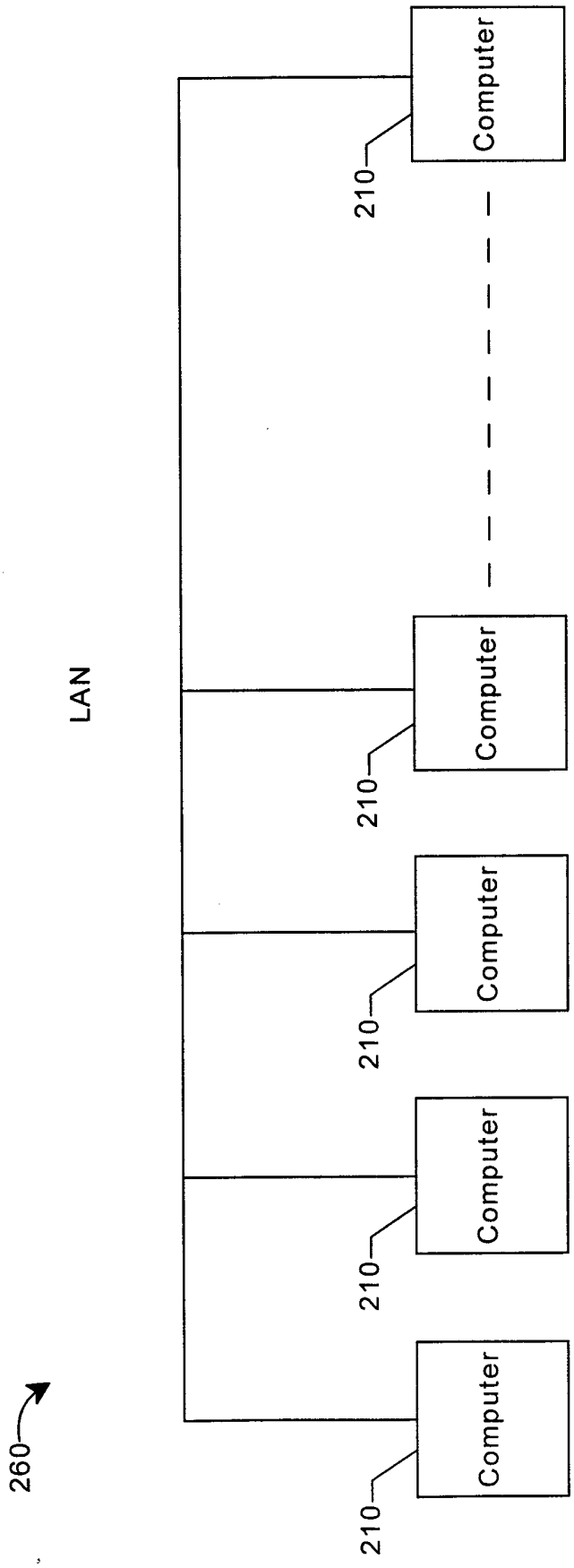

LAN
260
Computer
210
Computer
210
Computer
210
Computer
210
Computer
210

Fig. 2B

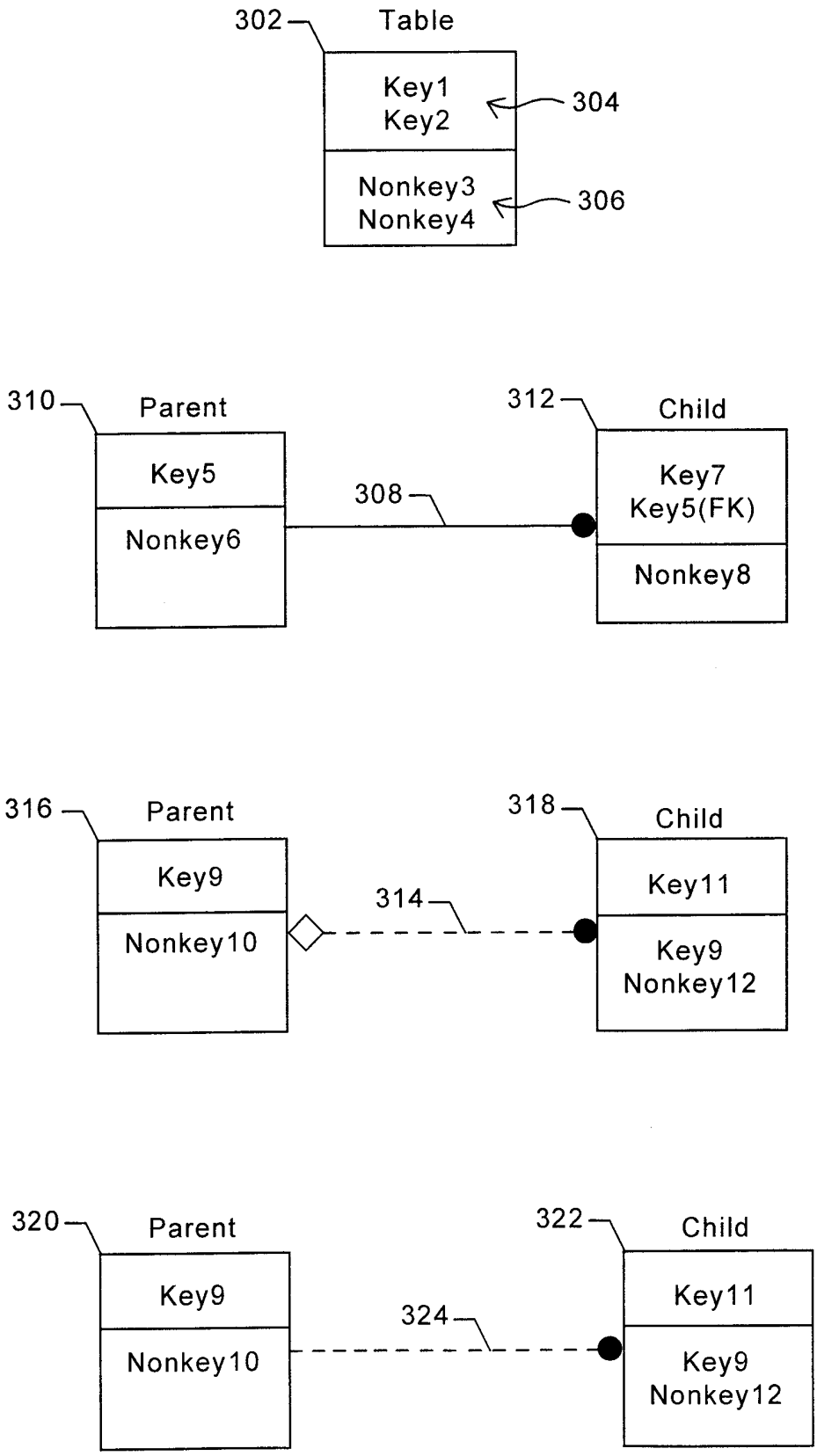

302
Table
Key1
Key2
304
Nonkey3
Nonkey4
306
310
Parent
Key5
Nonkey6
308
312
Child
Key7
Key5(FK)
Nonkey8
316
Parent
Key9
Nonkey10
314
318
Child
Key11
Key9
Nonkey12
320
Parent
Key9
Nonkey10
324
322
Child
Key11
Key9
Nonkey12

Fig. 3

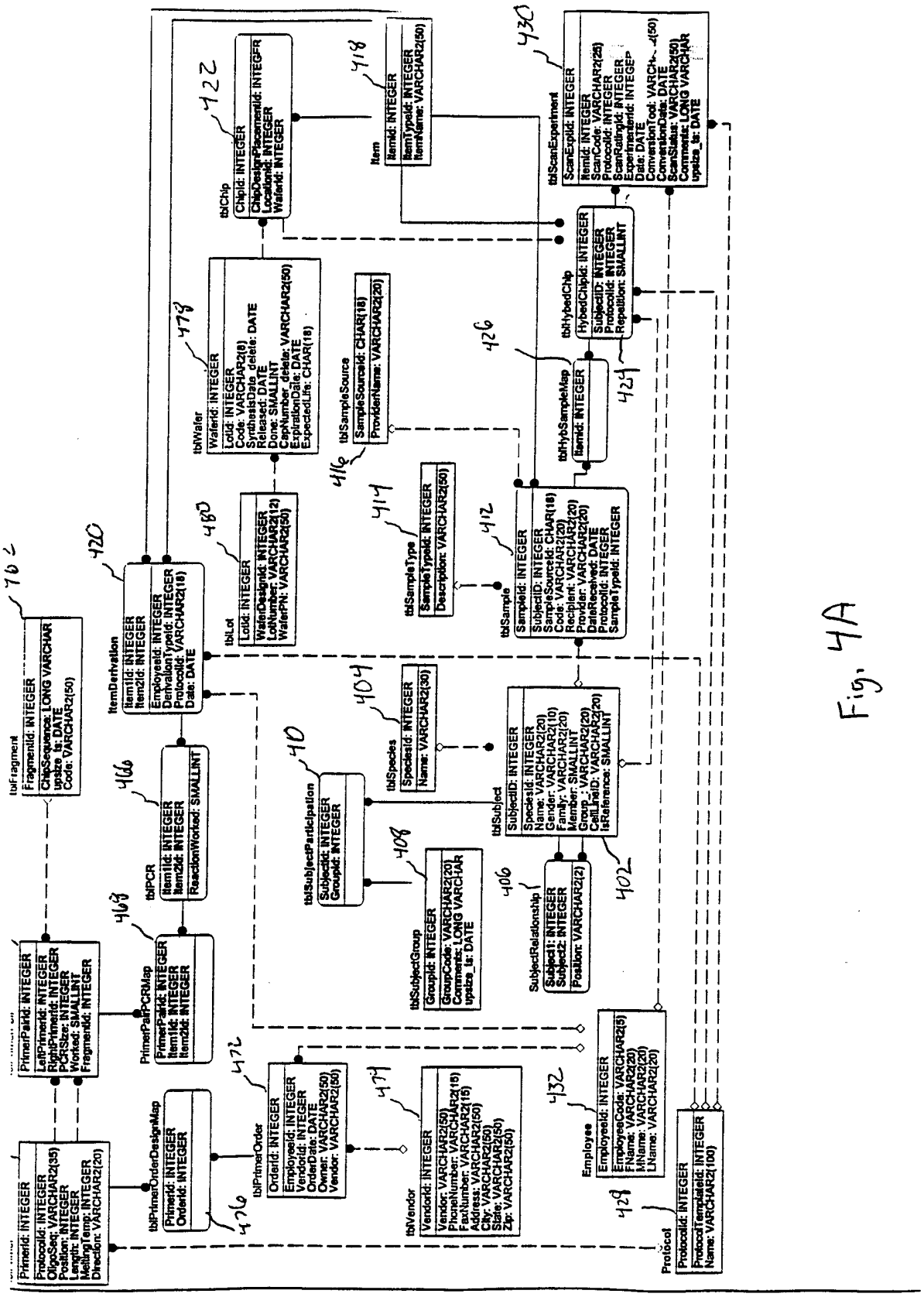

tblFragment
FragmentId: INTEGER
ChipSequence: LONG VARCHAR
upsize_ts: DATE
Code: VARCHAR2(50)
PrimerPairId: INTEGER
LeftPrimerId: INTEGER
RightPrimerId: INTEGER
PCRSize: INTEGER
Worked: SMALLINT
FragmentId: INTEGER
PrimerId: INTEGER
ProtocolId: INTEGER
OligoSeq: VARCHAR2(35)
Position: INTEGER
Length: INTEGER
MeltingTemp: INTEGER
Direction: VARCHAR2(20)
tblPrimerOrderDesignMap
PrimerId: INTEGER
OrderId: INTEGER
PrimerPairPCRMap
PrimerPairId: INTEGER
Item1Id: INTEGER
Item2Id: INTEGER
tblPCR
Item1Id: INTEGER
Item2Id: INTEGER
ReactionWorked: SMALLINT
ItemDerivation
Item1Id: INTEGER
Item2Id: INTEGER
EmployeeId: INTEGER
DerivationTypeId: INTEGER
ProtocolId: VARCHAR2(18)
Date: DATE
tblPrimerOrder
OrderId: INTEGER
EmployeeId: INTEGER
VendorId: INTEGER
OrderDate: DATE
OrderDate: DATE
Owner: VARCHAR2(50)
Vendor: VARCHAR2(50)
tblVendor
VendorId: INTEGER
Vendor: VARCHAR2(50)
PhoneNumber: VARCHAR2(15)
FaxNumber: VARCHAR2(15)
Address: VARCHAR2(50)
City: VARCHAR2(50)
State: VARCHAR2(50)
Zip: VARCHAR2(50)
tblSubjectParticipation
SubjectId: INTEGER
GroupId: INTEGER
tblSubjectGroup
GroupId: INTEGER
GroupCode: VARCHAR2(20)
Comments: LONG VARCHAR
upsize_ts: DATE
tblSpecies
SpeciesId: INTEGER
Name: VARCHAR2(30)
tblSubject
SubjectID: INTEGER
SpeciesId: INTEGER
Name: VARCHAR2(20)
Gender: VARCHAR2(10)
Family: VARCHAR2(20)
Member: SMALLINT
Group_: VARCHAR2(20)
CellLineID: VARCHAR2(20)
IsReference: SMALLINT
SubjectRelationship
Subject1: INTEGER
Subject2: INTEGER
Position: VARCHAR2(2)
Employee
EmployeeCode: VARCHAR2(5)
FName: VARCHAR2(20)
MName: VARCHAR2(20)
LName: VARCHAR2(20)
Protocol
ProtocolId: INTEGER
ProtocolTemplateId: INTEGER
Name: VARCHAR2(100)
tblLot
LotId: INTEGER
WaferDesignId: INTEGER
LotNumber: VARCHAR2(12)
WaferPN: VARCHAR2(50)
tblWafer
WaferId: INTEGER
LotId: INTEGER
Code: VARCHAR2(8)
SynthesisDate_delete: DATE
Released: DATE
Done: SMALLINT
CapNumber_delete: VARCHAR2(50)
ExpirationDate: DATE
ExpectedLife: CHAR(18)
tblChip
ChipId: INTEGER
ChipDesignPlacementId: INTEGER
LocationId: INTEGER
WaferId: INTEGER
Item
ItemId: INTEGER
ItemTypeId: INTEGER
ItemName: VARCHAR2(50)
tblSampleSource
SampleSourceId: CHAR(18)
ProviderName: VARCHAR2(20)
tblSampleType
SampleTypeId: INTEGER
Description: VARCHAR2(50)
tblSample
SampleId: INTEGER
SubjectID: INTEGER
SampleSourceId: CHAR(18)
Code: VARCHAR2(20)
Recipient: VARCHAR2(20)
Provider: VARCHAR2(20)
DateReceived: DATE
ProtocolId: INTEGER
SampleTypeId: INTEGER
tblHybSampleMap
ItemId: INTEGER
tblHybedChip
HybedChipId: INTEGER
SubjectID: INTEGER
ProtocolId: INTEGER
Repetition: SMALLINT
tblScanExperiment
ScanExpId: INTEGER
ItemId: INTEGER
ScanCode: VARCHAR2(25)
ProtocolId: INTEGER
ScanRatingId: INTEGER
ExperimenterId: INTEGER
Date: DATE
ConversionTool: VARCHAR2(50)
ConversionDate: DATE
ScanStatus: VARCHAR2(50)
Comments: LONG VARCHAR
upsize_ts: DATE
402
404
406
408
410
412
414
416
418
420
422
424
426
428
430
432
460
462
466
468
472
474
476
478
480

Fig. 4A

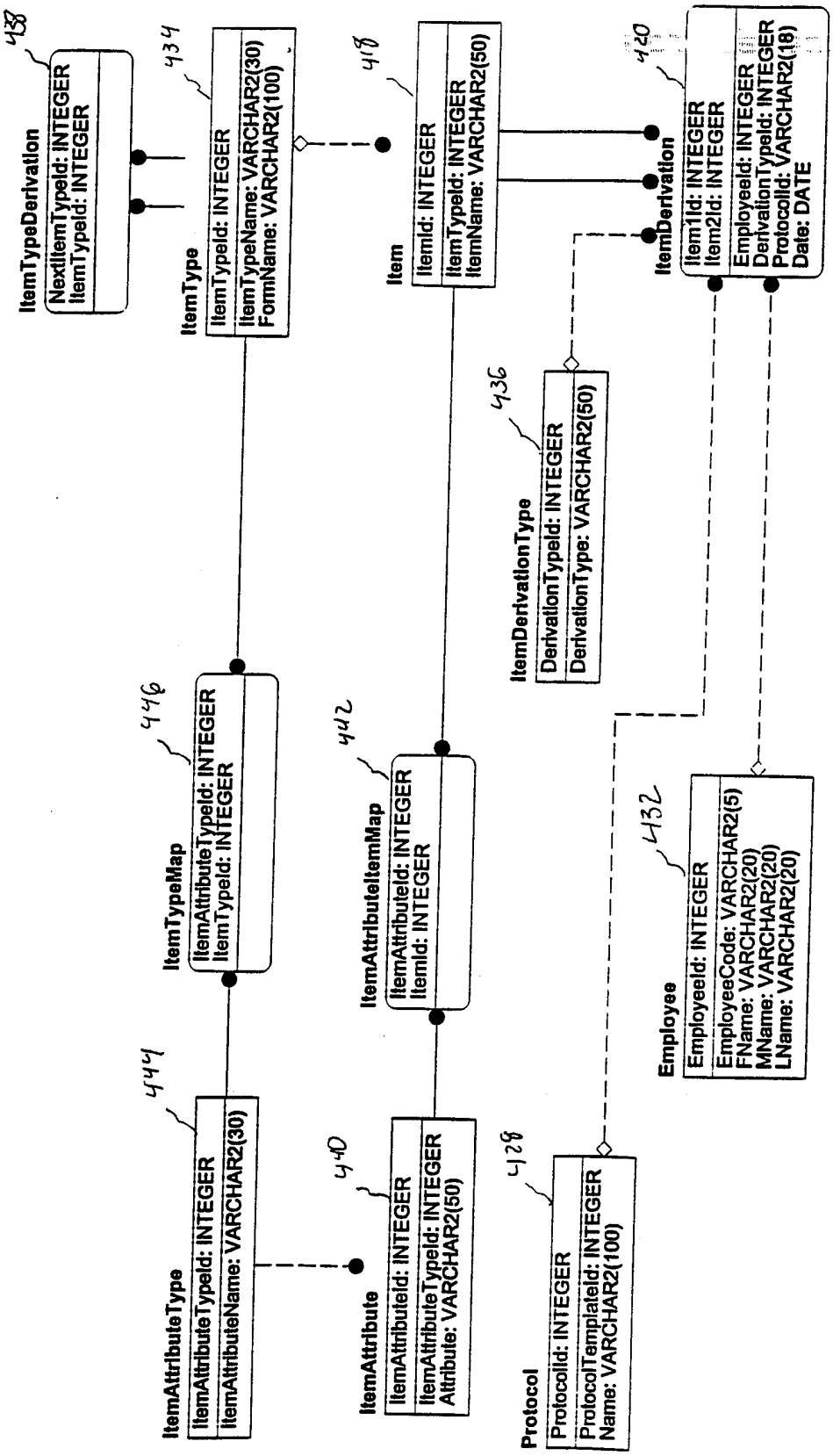

438
ItemTypeDerivation
NextItemTypeId: INTEGER
ItemTypeId: INTEGER
434
ItemType
ItemTypeId: INTEGER
ItemTypeName: VARCHAR2(30)
FormName: VARCHAR2(100)
418
Item
ItemId: INTEGER
ItemTypeId: INTEGER
ItemName: VARCHAR2(50)
420
ItemDerivation
Item1Id: INTEGER
Item2Id: INTEGER
EmployeeId: INTEGER
DerivationTypeId: INTEGER
ProtocolId: VARCHAR2(18)
Date: DATE
436
ItemDerivationType
DerivationTypeId: INTEGER
DerivationType: VARCHAR2(50)
446
ItemTypeMap
ItemAttributeTypeId: INTEGER
ItemTypeId: INTEGER
442
ItemAttributeItemMap
ItemAttributeId: INTEGER
ItemId: INTEGER
444
ItemAttributeType
ItemAttributeTypeId: INTEGER
ItemAttributeName: VARCHAR2(30)
440
ItemAttribute
ItemAttributeId: INTEGER
ItemAttributeTypeId: INTEGER
Attribute: VARCHAR2(50)
428
Protocol
ProtocolId: INTEGER
ProtocolTemplateId: INTEGER
Name: VARCHAR2(100)
432
Employee
EmployeeId: INTEGER
EmployeeCode: VARCHAR2(5)
FName: VARCHAR2(20)
MName: VARCHAR2(20)
LName: VARCHAR2(20)

Fig. 4B

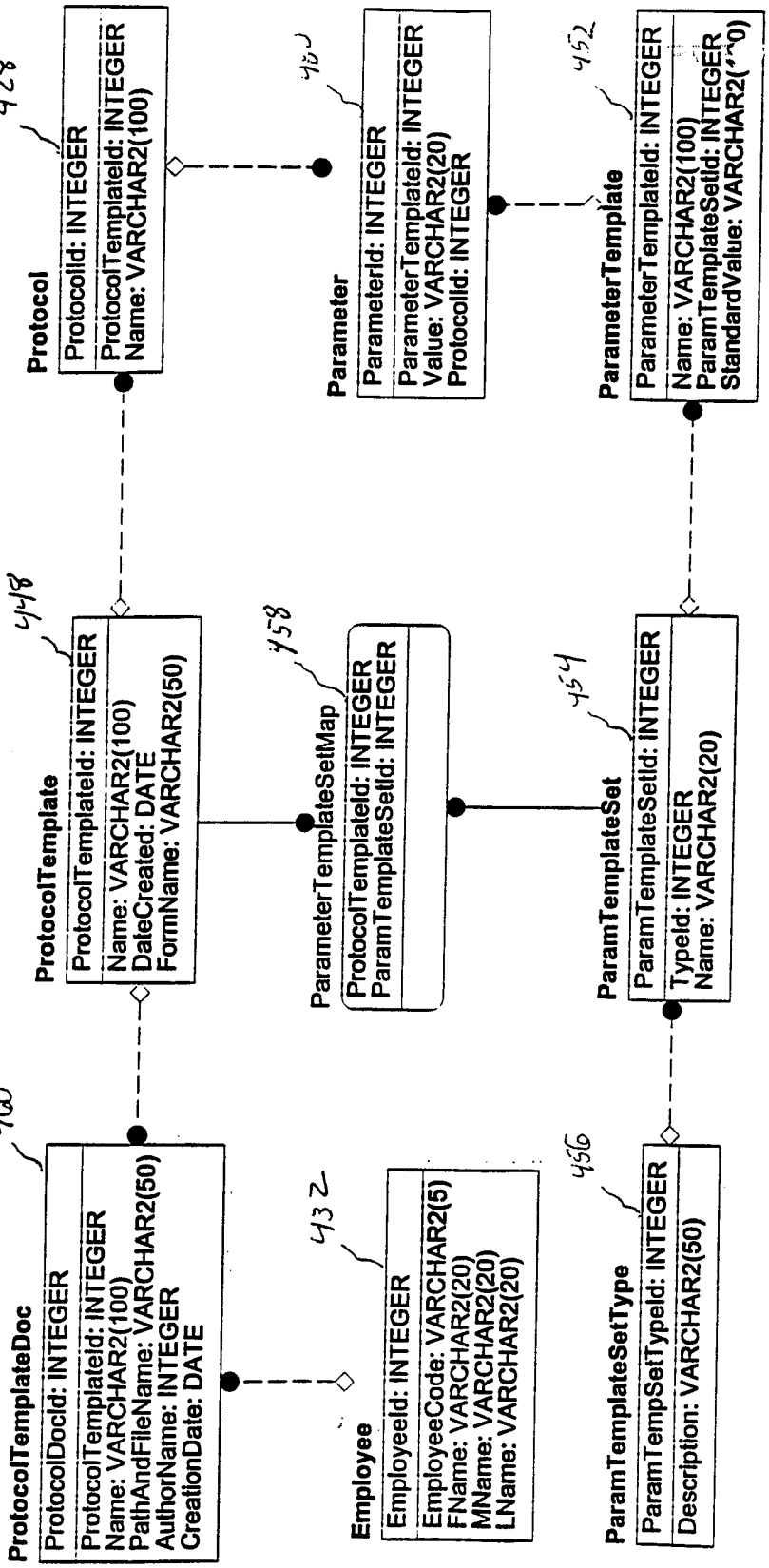

428
Protocol
ProtocolId: INTEGER
ProtocolTemplateId: INTEGER
Name: VARCHAR2(100)
Parameter
ParameterId: INTEGER
ParameterTemplateId: INTEGER
Value: VARCHAR2(20)
ProtocolId: INTEGER
ParameterTemplate
ParameterTemplateId: INTEGER
Name: VARCHAR2(100)
ParamTemplateSetId: INTEGER
StandardValue: VARCHAR2(
ProtocolTemplate
ProtocolTemplateId: INTEGER
Name: VARCHAR2(100)
DateCreated: DATE
FormName: VARCHAR2(50)
ParameterTemplateSetMap
ProtocolTemplateId: INTEGER
ParamTemplateSetId: INTEGER
ParamTemplateSet
ParamTemplateSetId: INTEGER
TypeId: INTEGER
Name: VARCHAR2(20)
ProtocolTemplateDoc
ProtocolDocId: INTEGER
ProtocolTemplateId: INTEGER
Name: VARCHAR2(100)
PathAndFileName: VARCHAR2(50)
AuthorName: INTEGER
CreationDate: DATE
Employee
EmployeeId: INTEGER
EmployeeCode: VARCHAR2(5)
FName: VARCHAR2(20)
MName: VARCHAR2(20)
LName: VARCHAR2(20)
ParamTemplateSetType
ParamTempSetTypeId: INTEGER
Description: VARCHAR2(50)

Fig. 4C

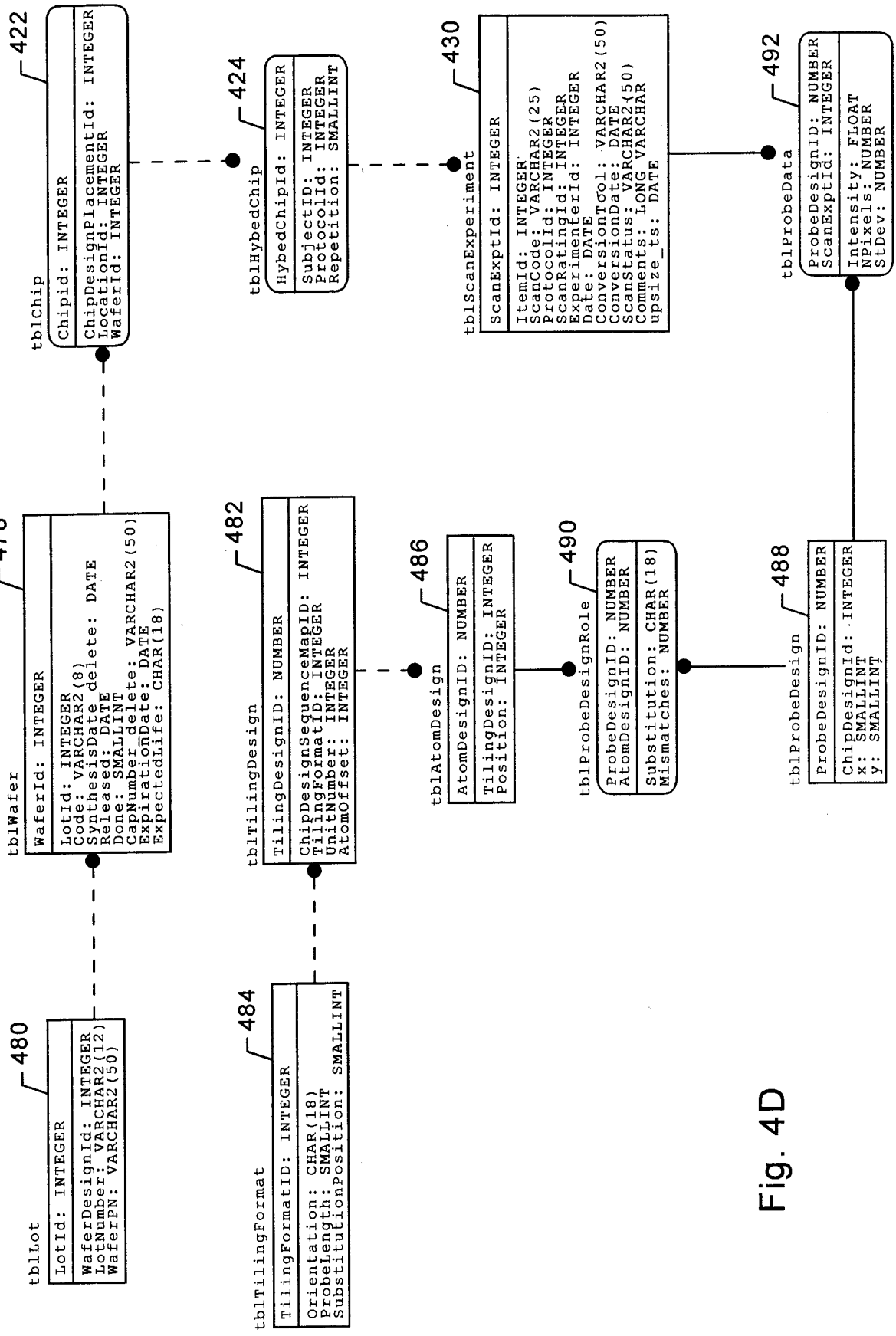

422
tblChip
ChipId: INTEGER
ChipDesignPlacementId: INTEGER
LocationId: INTEGER
WaferId: INTEGER
424
tblHybedChip
HybedChipId: INTEGER
SubjectID: INTEGER
ProtocolId: INTEGER
Repetition: SMALLINT
430
tblScanExperiment
ScanExptId: INTEGER
ItemId: INTEGER
ScanCode: VARCHAR2(25)
ProtocolId: INTEGER
ScanRatingId: INTEGER
ExperimenterId: INTEGER
Date: DATE
ConversionTcol: VARCHAR2(50)
ConversionDate: DATE
ScanStatus: VARCHAR2(50)
Comments: LONG VARCHAR
upsize_ts: DATE
492
tblProbeData
ProbeDesignID: NUMBER
ScanExptId: INTEGER
Intensity: FLOAT
NPixels: NUMBER
StDev: NUMBER
478
tblWafer
WaferId: INTEGER
LotId: INTEGER
Code: VARCHAR2(8)
SynthesisDate_delete: DATE
Released: DATE
Done: SMALLINT
CapNumber_delete: VARCHAR2(50)
ExpirationDate: DATE
ExpectedLife: CHAR(18)
482
tblTilingDesign
TilingDesignID: NUMBER
ChipDesignSequenceMapID: INTEGER
TilingFormatID: INTEGER
UnitNumber: INTEGER
AtomOffset: INTEGER
486
tblAtomDesign
AtomDesignID: NUMBER
TilingDesignID: INTEGER
Position: INTEGER
490
tblProbeDesignRole
ProbeDesignID: NUMBER
AtomDesignID: NUMBER
Substitution: CHAR(18)
Mismatches: NUMBER
488
tblProbeDesign
ProbeDesignID: NUMBER
ChipDesignId: INTEGER
x: SMALLINT
y: SMALLINT
480
tblLot
LotId: INTEGER
WaferDesignId: INTEGER
LotNumber: VARCHAR2(12)
WaferPN: VARCHAR2(50)
484
tblTilingFormat
TilingFormatID: INTEGER
Orientation: CHAR(18)
ProbeLength: SMALLINT
SubstitutionPosition: SMALLINT

Fig. 4D

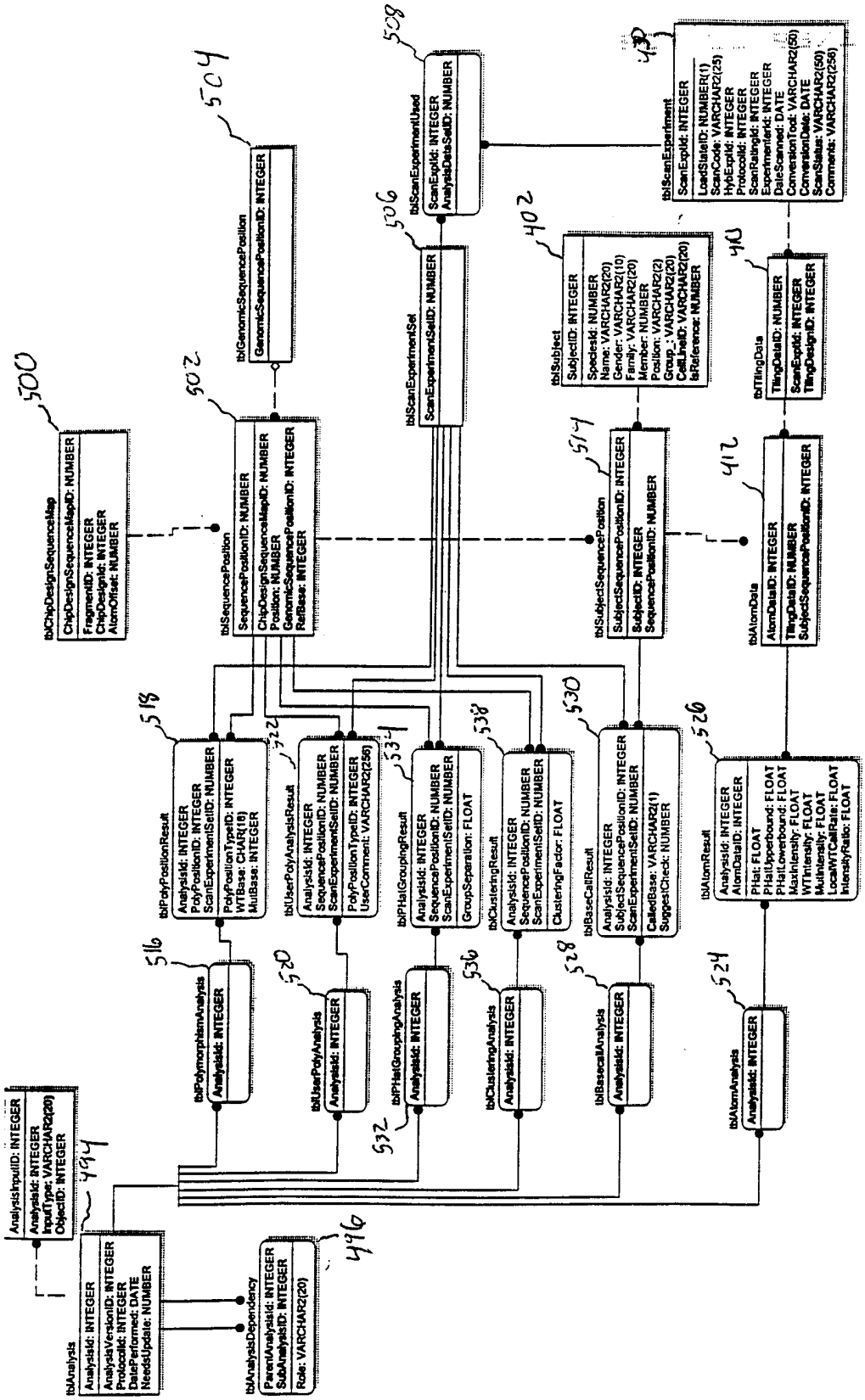

tblChipDesignSequenceMap
ChipDesignSequenceMapID: NUMBER
FragmentID: INTEGER
ChipDesignId: INTEGER
AtomOffset: NUMBER
tblSequencePosition
SequencePositionID: NUMBER
ChipDesignSequenceMapID: NUMBER
Position: NUMBER
GenomicSequencePositionID: INTEGER
RefBase: INTEGER
tblGenomicSequencePosition
GenomicSequencePositionID: INTEGER
tblScanExperimentSet
ScanExperimentSetID: NUMBER
tblScanExperimentUsed
ScanExpId: INTEGER
AnalysisDataSetID: NUMBER
tblScanExperiment
ScanExpId: INTEGER
LoadStateID: NUMBER(1)
ScanCode: VARCHAR2(25)
HybExpId: INTEGER
ProtocolId: INTEGER
ScanRatingId: INTEGER
ExperimenterId: INTEGER
DateScanned: DATE
ConversionTool: VARCHAR2(50)
ConversionDate: DATE
ScanStatus: VARCHAR2(50)
Comments: VARCHAR2(256)
tblSubject
SubjectID: INTEGER
SpeciesId: NUMBER
Name: VARCHAR2(20)
Gender: VARCHAR2(10)
Family: VARCHAR2(20)
Member: NUMBER
Position: VARCHAR2(2)
Group_: VARCHAR2(20)
CellLineID: VARCHAR2(20)
IsReference: NUMBER
tblTilingData
TilingDataID: NUMBER
ScanExpId: INTEGER
TilingDesignID: INTEGER
tblSubjectSequencePosition
SubjectSequencePositionID: INTEGER
SubjectID: INTEGER
SequencePositionID: NUMBER
tblAtomData
AtomDataID: INTEGER
TilingDataID: NUMBER
SubjectSequencePositionID: INTEGER
tblPolyPositionResult
AnalysisId: INTEGER
PolyPositionID: INTEGER
ScanExperimentSetID: NUMBER
PolyPositionTypeID: INTEGER
WTBase: CHAR(16)
MutBase: INTEGER
tblUserPolyAnalysisResult
AnalysisId: INTEGER
SequencePositionID: NUMBER
ScanExperimentSetID: NUMBER
PolyPositionTypeID: INTEGER
UserComment: VARCHAR2(256)
tblPHatGroupingResult
AnalysisId: INTEGER
SequencePositionID: NUMBER
ScanExperimentSetID: NUMBER
GroupSeparation: FLOAT
tblClusteringResult
AnalysisId: INTEGER
SequencePositionID: NUMBER
ScanExperimentSetID: NUMBER
ClusteringFactor: FLOAT
tblBaseCallResult
AnalysisId: INTEGER
SubjectSequencePositionID: INTEGER
ScanExperimentSetID: NUMBER
CalledBase: VARCHAR2(1)
SuggestCheck: NUMBER
tblAtomResult
AnalysisId: INTEGER
AtomDataID: INTEGER
PHat: FLOAT
PHatUpperbound: FLOAT
PHatLowerbound: FLOAT
MaxIntensity: FLOAT
WTIntensity: FLOAT
MutIntensity: FLOAT
LocalWTCallRate: FLOAT
IntensityRatio: FLOAT
tblPolymorphismAnalysis
AnalysisId: INTEGER
tblUserPolyAnalysis
AnalysisId: INTEGER
tblPHatGroupingAnalysis
AnalysisId: INTEGER
tblClusteringAnalysis
AnalysisId: INTEGER
tblBasecallAnalysis
AnalysisId: INTEGER
tblAtomAnalysis
AnalysisId: INTEGER
AnalysisInputID: INTEGER
AnalysisId: INTEGER
InputType: VARCHAR2(20)
ObjectID: INTEGER
tblAnalysis
AnalysisId: INTEGER
AnalysisVersionID: INTEGER
ProtocolId: INTEGER
DatePerformed: DATE
NeedsUpdate: NUMBER
tblAnalysisDependency
ParentAnalysisId: INTEGER
SubAnalysisID: INTEGER
Role: VARCHAR2(20)
500
502
504
506
508
402
410
412
514
516
518
520
522
524
526
528
530
532
534
536
538
430
494
496

Fig. 4E

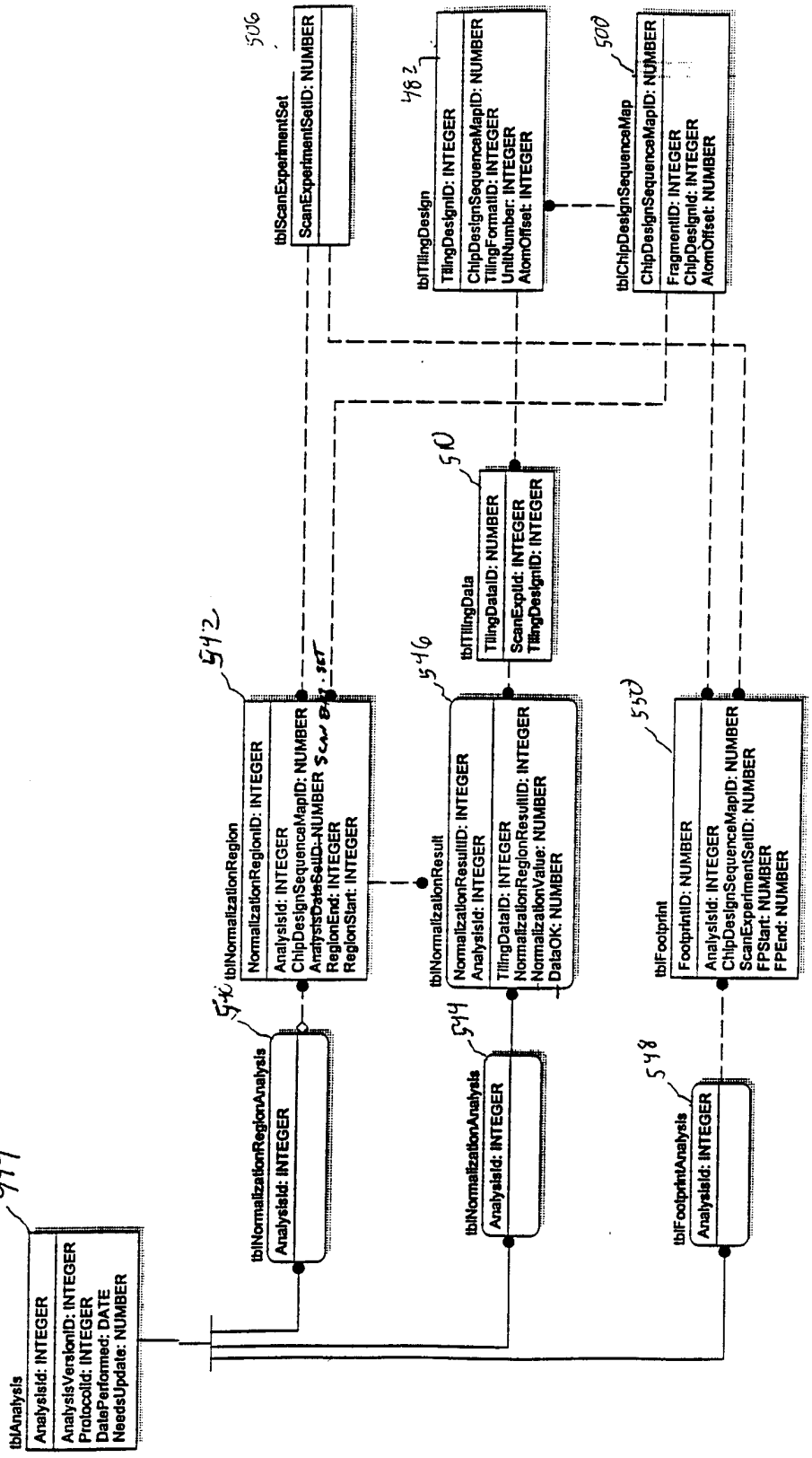

tblScanExperimentSet
ScanExperimentSetID: NUMBER
tblTilingDesign
TilingDesignID: INTEGER
ChipDesignSequenceMapID: NUMBER
TilingFormatID: INTEGER
UnitNumber: INTEGER
AtomOffset: INTEGER
tblChipDesignSequenceMap
ChipDesignSequenceMapID: NUMBER
FragmentID: INTEGER
ChipDesignId: INTEGER
AtomOffset: NUMBER
tblTilingData
TilingDataID: NUMBER
ScanExpId: INTEGER
TilingDesignID: INTEGER
tblNormalizationRegion
NormalizationRegionID: INTEGER
AnalysisId: INTEGER
ChipDesignSequenceMapID: NUMBER
AnalysisDateSetID: NUMBER
RegionEnd: INTEGER
RegionStart: INTEGER
tblNormalizationResult
NormalizationResultID: INTEGER
AnalysisId: INTEGER
TilingDataID: INTEGER
NormalizationRegionResultID: INTEGER
NormalizationValue: NUMBER
DataOK: NUMBER
tblFootprint
FootprintID: NUMBER
AnalysisId: INTEGER
ChipDesignSequenceMapID: NUMBER
ScanExperimentSetID: NUMBER
FPStart: NUMBER
FPEnd: NUMBER
tblNormalizationRegionAnalysis
AnalysisId: INTEGER
tblNormalizationAnalysis
AnalysisId: INTEGER
tblFootprintAnalysis
AnalysisId: INTEGER
tblAnalysis
AnalysisId: INTEGER
AnalysisVersionID: INTEGER
ProtocolId: INTEGER
DatePerformed: DATE
NeedsUpdate: NUMBER
506
482
500
510
512
516
520
514
518
494

Fig. 4F

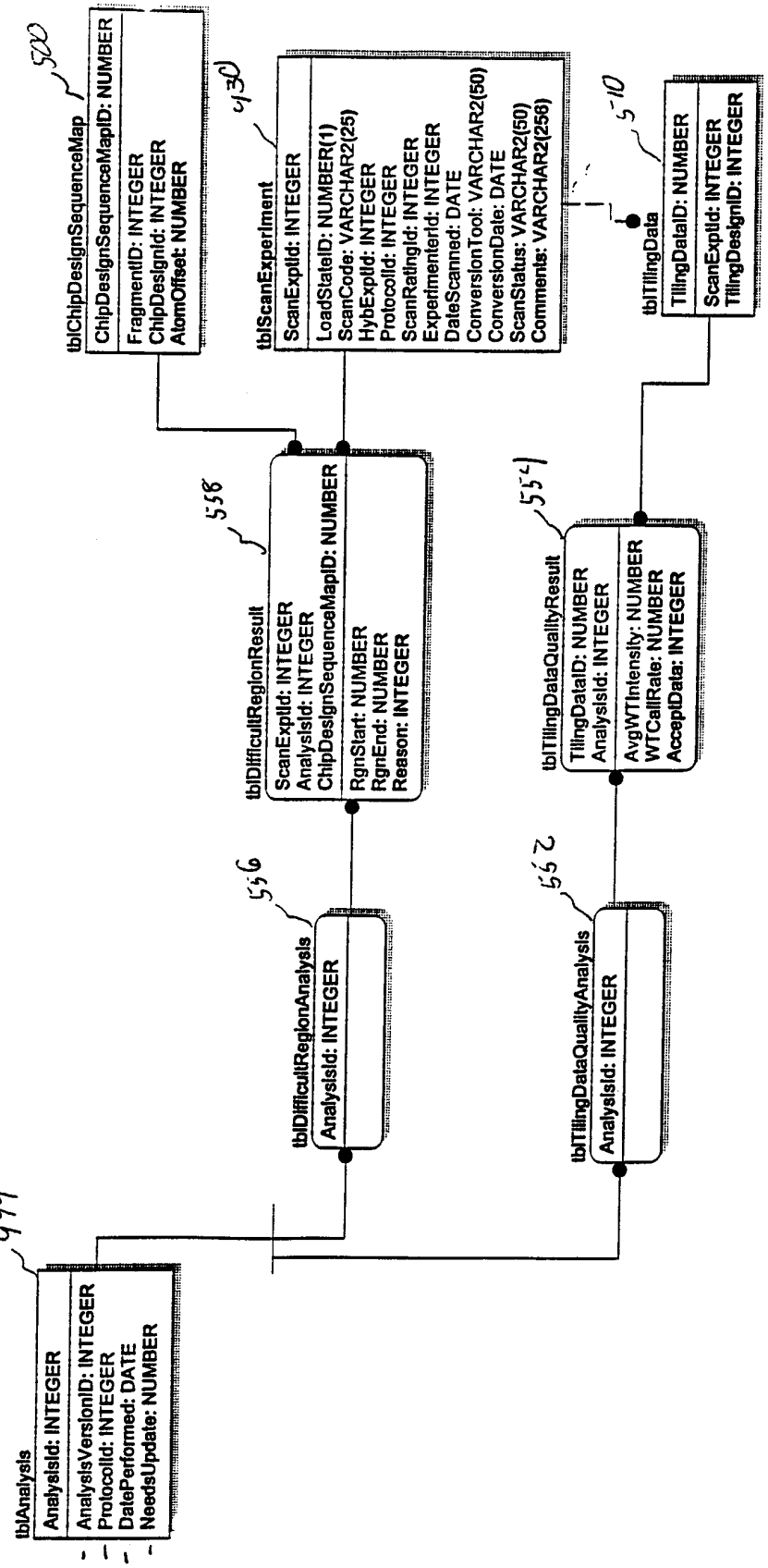

tblChipDesignSequenceMap
ChipDesignSequenceMapID: NUMBER
FragmentID: INTEGER
ChipDesignId: INTEGER
AtomOffset: NUMBER
520
tblScanExperiment
ScanExptId: INTEGER
LoadStateID: NUMBER(1)
ScanCode: VARCHAR2(25)
HybExptId: INTEGER
ProtocolId: INTEGER
ScanRatingId: INTEGER
ExperimenterId: INTEGER
DateScanned: DATE
ConversionTool: VARCHAR2(50)
ConversionDate: DATE
ScanStatus: VARCHAR2(50)
Comments: VARCHAR2(256)
530
tblTilingData
TilingDataID: NUMBER
ScanExptId: INTEGER
TilingDesignID: INTEGER
510
tblDifficultRegionResult
ScanExptId: INTEGER
AnalysisId: INTEGER
ChipDesignSequenceMapID: NUMBER
RgnStart: NUMBER
RgnEnd: NUMBER
Reason: INTEGER
558
tblTilingDataQualityResult
TilingDataID: NUMBER
AnalysisId: INTEGER
AvgWTIntensity: NUMBER
WTCallRate: NUMBER
AcceptData: INTEGER
554
tblDifficultRegionAnalysis
AnalysisId: INTEGER
556
tblTilingDataQualityAnalysis
AnalysisId: INTEGER
552
tblAnalysis
AnalysisId: INTEGER
AnalysisVersionID: INTEGER
ProtocolId: INTEGER
DatePerformed: DATE
NeedsUpdate: NUMBER
494

Fig. 4G

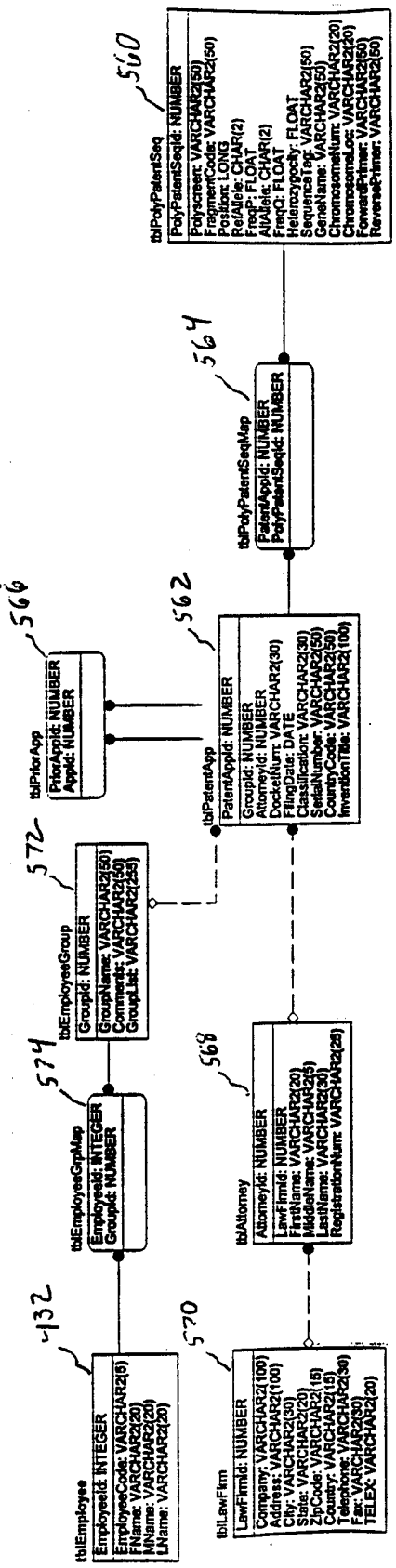

560
tblPolyPatentSeq
PolyPatentSeqId: NUMBER
Polyscreen: VARCHAR2(50)
FragmentCode: VARCHAR2(50)
Position: LONG
RefAllele: CHAR(2)
FreqP: FLOAT
AltAllele: CHAR(2)
FreqQ: FLOAT
Heterozygocity: FLOAT
SequenceTag: VARCHAR2(50)
GeneName: VARCHAR2(50)
ChromosomeNum: VARCHAR2(20)
ChromosomeLoc: VARCHAR2(20)
ForwardPrimer: VARCHAR2(50)
ReversePrimer: VARCHAR2(50)
564
tblPolyPatentSeqMap
PatentApplId: NUMBER
PolyPatentSeqId: NUMBER
562
tblPatentApp
PatentApplId: NUMBER
GroupId: NUMBER
AttorneyId: NUMBER
DocketNum: VARCHAR2(30)
FilingDate: DATE
Classification: VARCHAR2(30)
SerialNumber: VARCHAR2(50)
CountryCode: VARCHAR2(50)
InventionTitle: VARCHAR2(100)
566
tblPriorApp
PriorApplId: NUMBER
ApplId: NUMBER
572
tblEmployeeGroup
GroupId: NUMBER
GroupName: VARCHAR2(50)
Comments: VARCHAR2(50)
GroupList: VARCHAR2(255)
574
tblEmployeeGrpMap
EmployeeId: INTEGER
GroupId: NUMBER
568
tblAttorney
AttorneyId: NUMBER
LawFirmId: NUMBER
FirstName: VARCHAR2(20)
MiddleName: VARCHAR2(5)
LastName: VARCHAR2(30)
RegistrationNum: VARCHAR2(25)
532
tblEmployee
EmployeeId: INTEGER
EmployeeCode: VARCHAR2(6)
FName: VARCHAR2(20)
MName: VARCHAR2(20)
LName: VARCHAR2(20)
570
tblLawFirm
LawFirmId: NUMBER
Company: VARCHAR2(100)
Address: VARCHAR2(100)
City: VARCHAR2(30)
State: VARCHAR2(20)
ZipCode: VARCHAR2(15)
Country: VARCHAR2(15)
Telephone: VARCHAR2(30)
Fax: VARCHAR2(30)
TELEX: VARCHAR2(20)

Fig. 4H

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/15458

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C12Q 1/68; G06F 17/30 // 159:00
US CL : 435/6; 707/104

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6; 707/104

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96/23078 A1 (INCITE PHARMACEUTICALS, INC) 01 AUGUST 1996, PAGE 1 LINE 26-PAGE 2, LINE 34 AND PAGE 5, LINE 17-PAGE 15, LINE 11.	1-23
A	US 5,206,137 A (IP ET AL) 27 APRIL 1993, COL. 5, LINE 25-COL. 6, LINE 9.	1-23
A	US 5,593,839 A (HUBBELL ET AL) 14 JANUARY 1997, COL. 2, LINE 11-COL. 3, LINE 10.	1-23
AP	US 5,707,806 A (SHUBER) 13 JANUARY 1998, COL. 2, LINES 37-68	1-23

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
01 OCTOBER 1998	29 OCT 1998

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	JACK M. CHOULES
Facsimile No. (703) 305-3230	Telephone No. (703) 305-9840

Form PCT/ISA/210 (second sheet)(July 1992)★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/15458

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

APS, DIALOG, MAYA, NPL
search terms DNA, cDNA, RNA, mRNA, gene, genome, genetic, data, database, relational, entity, relationship, many to many, polymorphism, database, microbiology, allele, mutant, sequence, analize, heterozygocity.