Patenting bioinformatic inventions: Emerging trends in Europe

A look at the European Patent Office's past stance on bioinformatics patents informs recent proposals for reform.

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In the field of molecular biology, the importance of protecting intellectual property is widely known and acknowledged. Increasingly, patents are also being awarded for research tools or technologies used in the development and discovery of genes and proteins. Initially researchers developed these tools to use in their work, for example, in sequencing the genome or screening potential drug candidates. More recently, researchers and their employers have been realizing that these tools may also be potentially valuable intellectual property assets in their own right. The current dispute between Affymetrix and its competitors over patents relating to microarrays is just one example of the value placed on such tools[1,2].

One research tool that has until recently not been the subject of many patents is the computer program. A recent study[3] carried out by the London-based consulting firm Silico Research reported that there have been very few patent applications filed in bioinformatics. The reasons cited for the scarcity of patents included the fact that many current bioinformatics products merely combine existing data sources into a single product, and the difficulty of proving infringement of software patents. A further reason noted was that the industry is so new that many patent applications may still be pending. In many countries, there is also a popular misconception that software is "not patentable" because it is apparently excluded from patent protection[4].

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The European Patent Convention states that patents cannot be granted for computer pro-

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grams[4]. The European Patent Office (Munich, Germany) realized fairly soon after its foundation in 1978 that this exclusion was illogical and, in its famous VICOM decision[5], pointed out that the wording of the European Patent Convention excluded only the patenting of computer programs as such[6]. A general-purpose computer programmed for a special purpose is, however, not excluded from patentability as long as it produces a technical effect.

The VICOM decision and other decisions that followed it in Europe opened the way for the patenting of inventions implemented by means of computers. The reasoning behind these decisions has often been adopted by courts in other countries, and much of the case law developed by courts in Europe on computer-implemented inventions is highly relevant to bioinformatics developments.

Recently the European Union has issued a proposal for a reform of the patent laws relating to computer-implemented inventions. These proposals will codify the court decisions of the past few years into the national laws of the European Union.

Protection of databases

Much early interest in bioinformatics was focused on the construction of databases to record data generated by gene sequencing experiments. The original data in such early databases were stored as a flat-file structure. Later, more sophisticated relational database structures were developed to allow more efficient and significant analysis of the data stored therein. Some relational databases have been put into the public domain by developers who have renounced their rights to them; such databases thus can be used without charge by researchers in academia and at companies. Other database developers have reserved their rights and may, for example, provide free access only to academic institutions. In this case, companies wishing to exploit the database and its constituent information would have to negotiate a contract with the database developers.

As an aside to the subsequent discussion concerning patenting of database structures, it should be noted that the information contained within a database can be protected

either by copyright protection or by so-called database rights, and that the extent to which database information can be protected by copyright varies widely depending on the country involved. In many countries, copyright protection is not available for information contained in databases. Other countries, such as Australia[7], consider that the arrangement and collection of the information may be so significant that copyright can be granted on the database. In contrast, the US Supreme Court in 1991 rejected the so-called "sweat of the brow" theory that previously had accorded copyright protection to informational compilations[8].

In order to harmonize protection within its member states, in 1996 the European Union adopted the European Database Rights Directive, which protects "a collection of independent works, data or other materials arranged in a systematic or methodical way and individually accessible by electronic or other means"[9]. Thus, a developer of a database can prevent the extraction and/or re-use of the whole or a substantial part of the contents of the database[10]. This means that a party who creates, for example, a database comprising genome sequence data or protein structure data can stop others from using this data without permission. Unfortunately, protection under the European Database Rights Directive is limited only to persons or legal entities residing in the European Economic Area (the European Union, Norway, Iceland, and Liechtenstein) or in countries having similar protection schemes. Proposals to introduce a similar protection right in the United States have not been successful, despite several bills in the US Congress.

In contrast to the informational content of the database, protection of the structure of the database can be obtained through patents. The European Patent Office's Boards of Appeal have considered the issue of patentability of a data structure[11] in a patent application for a picture retrieval system having data stored on or in a record carrier of a particular structure. The board pointed out that there was a difference between the functional data, which controlled the technical working of the system, and the cognitive

information, which represented the picture that could be retrieved and displayed[12].

The reasoning behind the European Board's decision can be applied not only to video or television systems, but also to data structures as bioinformatic inventions. Consider, for example, genomic screening carried out using microarrays in which target cDNA sequences or oligonucleotides are placed at a number of sites on a chip and the material to be analyzed is washed over the chip. At some sites, some of the genetic material becomes bound to the cDNA or oligonucleotides. The position of the sites is detected by fluorescence or another means. The sheer number of sites on a chip (Affymetrix, for example, has a chip with 400,000 sites) means that it is impossible for a human being to detect the sites at which the genetic material is bound to the target. Instead the detection is carried out automatically and the results are fed into a computer. The computer contains software that processes the data and produces them in a form that can be understood and interpreted by a human.

Applying the European Board's decision to the data generated in the use of microarrays would suggest that a data structure is patentable if the data relate to the control of a microarray experiment or to the display of information obtained from a microarray experiment. Furthermore, as data relating to the DNA sequences or protein structure are not merely "cognitive information," it is possible to argue successfully that data structures containing this information are patentable.

Patenting of algorithms

Much of the original analysis of DNA sequence data was carried out by manual processing of the data. In many early gene-matching experiments, experienced operators compared newly discovered DNA sequences to detect similar known sequences. As the amount of data in academic and commercial databases grew, it became necessary to automate such techniques and develop algorithms, such as the Smith-Waterman algorithm.

The European Patent Office, like the US Patent and Trademark Office (Washington, DC) and the US courts[13], will not allow patenting of an algorithm *per se* without any reference to its practical application[14]. Consistent with this, when a practical application is involved, patent protection can be secured. For example, the European Patent Office points out in its Guidelines for Examination[15] that an electrical filter designed using a mathematical method would not be excluded from patentability. In a decision relating to the interactive rotation of displayed graphic objects on a screen[16], the

European Patent Office Board of Appeal stated that the invention did not relate to a mathematical method as such, but that the "calculating steps mentioned are only means, or tools, used within the overall method claimed, for entering a rotation angle value into a draw graphic system"[17].

This certainly suggests that an algorithm used in the analysis of DNA sequence or protein data should be patentable as long as it is not couched in purely mathematical terms but is applied to achievement of a useful, concrete, and tangible result. Thus, for example, an algorithm to identify homologies among genes should be patentable because it offers a useful, concrete, and tangible result, and is only a means of obtaining information about the homologies. An algorithm to mine existing data for potentially useful properties is also protectable: an example would be an algorithm that matches similarities in pro-

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tein structures with identical annotations of properties in order to determine which protein structures might also have the same properties.

Interfaces

Because bioinformatics programs must interact with human users or with other programs, the interfaces to the program have to be documented. The European Patent Office considered the patentability of a user interface in a 1988 decision (ref. 18). In that case, a method was claimed for displaying one of a set of predetermined messages indicating a specific event that may occur in an input/output device of a word-processing system. The European Patent Office Board of Appeal stated that giving visual indications automatically about conditions prevailing in an apparatus or system is basically a technical problem[19] and thus is not excluded from patentability. Thus, it is probable that the European Patent Office would have a generally favorable view of the patentability of an interface through which information is exchanged about conditions prevailing in an apparatus or system.

In the microarray example described earlier, the information exchanged between the computer program that analyzed the microarray data and the microarray itself relates to conditions prevailing in the apparatus. Therefore, the interface should be patentable. Similarly, displays of DNA or protein sequence data on an output device give information about conditions prevailing in a microarray experiment, and a method for displaying this information should, consistent with the board's reasoning, also be patentable.

Publication issues

Finally, when considering a strategy to protect developments in bioinformatics for later exploitation, it is important to ensure that the value of the intellectual property is not accidentally destroyed. In Europe (in contrast to the United States[20]), at the time a patent application is filed, the invention must not have been published. If the invention has been disclosed at a conference, in a PhD thesis, or in a journal by its discoverer, then it can no longer be patented in Europe[21].

1. Bouchie, A. *Nat. Biotechnol.* **19**, 399 (2001).
2. Bouchie, A. *Nat. Biotechnol.* **19**, 193 (2001).
3. Toner, B. Bioinformatics patents remain a rarity in IP-heavy biopharmaceutical industry. *GenomeWeb*, 4 July 2001 (http://www.genomeweb.com).
4. Art. 52(2) of the European Patent Convention states, for example, that the following in particular shall not be regarded as inventions: "(c) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers; (d) presentations of information."
5. T 0208/84 of 15 July 1986 "Computer-related Invention/VICOM." *Official J. Eur. Pat. Off.* 14–23 (1987).
6. See point 6 of T 0208/84 (ref. 5).
7. *Telstra Corporation Limited v. Desktop Marketing Systems Pty Ltd*, [2001] FXA 612 (15 May 2001).
8. *Feist Publications v. Rural Telephone Service Corp.*, 499 US 340 (1991).
9. Directive 96/9/EC of the European Parliament and of the Council adopted on 11 March 1996 on the legal protection of databases. *O.J. Eur. Union* No. L77, 27 March 1996, 20 (the "Database Directive"), Art. 1, §2.
10. Art. 7, §1 of the Database Directive.
11. Decision T 1194/97–3.5.2 of 15 March 2001. "Data Structure Product/PHILIPS."
12. See point 3.3. of decision T 1194/97 (ref. 11).
13. The US Court of Appeals for the Federal Circuit, for example, has emphasized that in order to include an algorithm as part of a patent claim, it is necessary that the algorithm be applied to produce a "useful, concrete and tangible result." *State Street Bank & Trust Co. v. Signature Fin. Group, Inc.*, 149 F.3d 1368, 47 USPQ2d 1596 (Fed. Cir. 1998).
14. Note, however, that the lines of code that implement the algorithm are protectable by copyright.
15. Part C, Chapter IV, 2.3.
16. T 0059/93–3.5.1. of 20 April 1994.
17. See point 3.2 of T 0059/93 (ref. 16).
18. T0115/85 of 5 September 1988 "Computer-related Invention/IBM." *Official J .Eur. Pat. Off.* 30–34 (1990).
19. See point 7 of T0115/85 (ref. 18).
20. In the US, the inventor can still file a patent application during a period of one year after disclosure. However, no valid patent rights can be obtained outside of the US.
21. Garabedian, T.E. *Nat. Biotechnol.* **20**, 401–402 (2002).