DISEASE MARKERS, VOL. 12, 11–21 (1994)

REVIEW ARTICLE

BIOINFORMATICS AND BIOTECHNOLOGY INFORMATION — SOME MOVES IN EUROPE.

JACK FRANKLIN
ASFRA BV, Voorhaven 33, 1135 BL Edam, The Netherlands.

While the term *biotechnology* is sometimes dismissed as being nothing more than a modern version of traditional biological research, there is little doubting its importance in today's world. Biotechnology has revolutionised many procedures and products but it has also spawned a new scientific discipline — bioinformatics — the application of computing and information technology to biotechnology related research. This discipline, and its techniques, has become an essential component in much bench R&D; especially in medically related research.

Bioinformatics started as a discipline in the early 1980s, probably with the decision of the European Molecular Biology Laboratory directors to build a nucleotide sequence database. Now, the collaboration between the National Center for Biotechnology Information in Bethesda (NCBI), the DNA Database Japan (DDBJ) and the successor to the EMBL team — the European Bioinformatics Centre in Cambridge, produces an integrated database of sequence records which form the basis for much research and many other databases (for instance, protein structures). A series of other databases on genetic maps, biological descriptors, probes, clones and the other necessary components of research are now available on a variety of media from a variety of hosts/producers and we will definitely see an increasing range of products and services being offered from all "bio" disciplines.

There is little doubt that these developments are of interest to many in the Disease Markers field and the following articles note two European initiatives currently taking place which are working on the foundations of an infrastructure that will probably be of great importance to all who carry out medical research.

These European initiatives differ in structure from the US scene in that Europe, unlike the US, relies greatly on its commercial information sector to produce the central literature and other database and publication products needed to support science. This policy offers competition and variety, but lacks the solid financial support the American National Institute of Health gives to, for instance, the National Library of Medicine and the National Center for Biotechnology Information. These two institutes can therefore produce excellent products for subsidised prices (e.g. MEDLINE) — a boon for most of the world but a threat to the European biomedical database industry - and they also provide a focal point for American research and service development in this area. Europe has reacted to the challenge from these centres by bundling together its individual strengths into "consortia". The "laboratory without walls" concept — using networks to interact and concentrate skills from many interested and expert groups that do the same basic tasks. The following pages detail two of these initiatives.

THE BIOTECHNOLOGY INFORMATION STRATEGIC FORUM (BTSF)

Eleven European organizations involved in biotechnology information formed a strategic forum in response to a report published in 1990 entitled 'Bioinformatics in Europe — Strategy for a European Biotechnology Information Infrastructure'. The report — co-financed by the Commission of the European Communities (CEC) and produced by the Federation of European Chemical Industries (CEFIC) and a consortium of 3 publishers: Elsevier, Derwent and Springer — concluded that *Europe lacked the focus and infrastructure to provide long term stability to both academic and commercial biotechnology information products.* This stimulated the concerted action by the publishers who were joined by C.A.B. International (UK), Excerpta Medica (NL), INIST: PASCAL (France), Derwent (UK), Pergamon Press (UK), Springer Verlag (Germany), The Royal Society of Chemistry (UK), Wolters-Kluwer Academic Publishers (NL), the EMBL Data Library (Germany), J. Wiley & Sons Ltd, (UK), and INSERM/CERDIC (France) establish the forum.

The BTSF agreed the following initial tasks, to:

- identify and characterise user needs through interactions with industry-platforms, advisory groups, market sectors and individual purchasers/users;
- measure these needs against commercial, technical and political limitations;
- develop potential solutions to such market-led questions;
- develop systems for the long-term support of non-commercial products (e.g. R&D databases, National Biotechnology Associations products, non-commercial registration databases);
- examine ways of inter-linking products to ease the use of both individual and combinations of files and products;
- examine ways of securing the future of independent database hosts for the European user;
- strengthen the European information industry's response to international market and political demands.

The first year has been spent interviewing users of biotechnology information. The result is the following Strategic Issues paper.

BIOTECHNOLOGY INFORMATION IN EUROPE — SOME STRATEGIC ISSUES FOR PRODUCERS AND USERS

This increasing use of factual, as well as literature, databases, in all aspects of R&D, is causing scientific information professionals to review their needs, training, and future policies. Biotechnology is at the forefront of these changes, probably because it has become so information-dependent. More and more research is based upon accessing the correct information, and analysing and modifying it to the needs of the user.

The changes in the use and access of information and data, are deeper than just moving from literature to factual data. Firstly, a new breed of information user is evolving, one that uses data as part of the research process rather than as the end-point of a research story. Secondly, because the factual databases are almost all in the public domain, funding is different, and the chances for cooperation between the commercial marketing organisations and the product developers clouded. Thirdly, the almost exclusive use of the academic networks to access this data is establishing an "alternative infrastructure"

which could eventually "swamp" the present more established commercial dissemination systems used in Europe.

In the USA there is a relatively seamless join between the literature and data services, and a huge use of Internet, a communications protocol that has revolutionised the data communications networks in the US (and elsewhere). The NCBI's link to the NLM has strengthened this tendency in biotechnology, but the USDA, and many other activities such as the Genome Databank at Baltimore, have also been able to find good, secure, public funding to exploit the present infrastructure and computer-literate user groups.

The heavy funding these central organisations have received has caused strains on the national as well as international scene, and will continue to do so; unfortunately cooperation is not helped by one side saying ..."we're going to do it this way". R&D information is international and Europe and American information sources need each other if science is to succeed. Unfortunately, many feel that the European comments on the funding in-balance is meant to be destructive: that is not the case, most in the European industry would love to have a similar regime on this side of the Atlantic. The USA is committed to supporting this area and so American commercial competitors and similar European strategies will have to find a way of living with the present system if all to are enjoy a place in the market.

Whatever else happens, Europe cannot operate in isolation, the American services are available via Internet — the global electronic village has arrived — and other networks and the present network capacity allows European users to obtain vast quantities of information, for free, from the USA, whatever the European producers offer. The one-stop shopping approach is such that many European users prefer to log-into an American system, such as the NCBI, or the University of Stanford, rather than struggle around their own systems finding a European node with the same information.

America could curtail this free offer and strand many European users; although few feel it will. However, European biotechnology and informatics research requires good participation at R&D and project level, and so the European industry should try to address such difficulties and find ways of offering the markets what they require. Furthermore, European biotechnology R&D users do not always just want American services and service.

As Europe lacks a central facility, any response will have to come from an alliance: possibly from the database producers, the EMBL/EBI and the many individual centres of expertise such as the EMBnet nodes.

DISTRIBUTION ISSUES: NETWORKS AND HOSTS — EUROPE AND AMERICA

Biotechnology information is spread over a very wide range of products. Few users experience difficulty in obtaining paper publications; although many openly criticise the price of these (be it as journals or single articles). Many of those using electronic sources feel that the journal has outlasted its use and that the primary publishers have to take the matter in hand and provide new forms of information dissemination; others feel that the journal will be pushed into a different role — basically the end-product of a series of other "information products" and so will survive but perhaps as a collection of single articles. In this regard, many point to the need for Europe (or The World) to establish standards and a central log of scientific information.

Of more relevance to most users, is the increasing need and reliance upon electronic information resources. Virtually the whole biotechnology sector uses new technology information sources, ranging from traditional on-line through the bulletin boards (computer note boards where news and other items can be posted) and gopher-driven (systems which allow various databases at different sites to be searched for relevant material) services, the academic networks and their "offers," to the commercial networks and then stand-alone products such as diskettes and CD ROMS.

Librarians recognise that this is a new world, driven by a new breed of user. There is a gulf of awareness and a lack of good training and information sources. This has to be done on a national basis, supported by the industry as a whole. If not, then it will be led by the USA with their excellent, free/cheap, services which are as easily available from Padua as they are from Washington. At the same time the new breed of producers are often unaware of the traditional services, and uninterested. Many "re-invent" services to suit their needs (a CEFIC Study criticism that has not disappeared) and most design to limited, rather than market, needs (resulting in a loss of portability).

The future will therefore require a "coming together" of the various information services, technologies and infrastructures. This will require more than one sector taking an initiative; and it will therefore require a strong guiding hand. The BTSF is seen as one possible candidate.

Networks

The essential need for a new form of information infrastructure is good networks. The molecular biology community in Europe is not happy with European connectivity. Many biologists feel ignored by the physicist and engineers who design or manage the telecommunication networks and there is also a continuing annoyance at the cost of crossing boundaries.

Calls for political pressure to be increased upon individual PTTs so as to improve Europe's infrastructure for better on-line exploitation have been made by several scientists. Biological data is increasingly being sent along broad band lines, and Europe will need to constantly improve these to remain competitive with the USA. The UK scientific community claim they needed to "lobby" at Governmental level to get SUPERJANET, and suggest that the CEC, starting with the technical rather than the biological, people is a good starting point.

In this regard President Clinton's "Technology for America's Economic Growth" (February 1993) makes a clear statement of the US administration's determination to establish a modern telecommunications infrastructure upon which America technology-based industries can grow. Europe's response in the Rubbia Report — "High Performance Computing and Network" gives a similar call and also clearly shows that biotechnology must be considered as a user of such new infrastructures.

Hosts

Networks lead to hosts and the USA has a series of biotechnology-relevant hosts in the public sector which guarantee unfettered and cheap access to biotechnology-relevant files such as Medline, the Supplementary File on Biotechnology, AGRIS, and the many other bases such as Toxline etc. In addition the USA houses the dominant commercial database host in the scientific area — Dialog — which has just acquired its main competitor in Europe, DataStar. This could be a serious loss for Europe which, in general, does not have subsidised hosts (DIMDI is supported by the German Ministry of Health)

but, until recently, boasted a number of hosts competing with Dialog and DataStar that offered sufficient competition to the producer and the user for most if not all relevant files to be mounted and made accessible.

DataStar was the most successful of the biotechnological hosts; and the first to offer a biotechnology register of files. The decision by the parent body Motor Columbus to sell DataStar to Dialog is seen by many as a serious blow to Europe. While "free market forces" are politically acceptable in both the EEC and the USA, Europe does not have the safety-net the US scientific databases have of using their own subsidised networks and hosts, and so is increasingly dependent upon decision makers that need not have European R&D industries, nor European producers, in mind.

This sale of DataStar has raised questions of concern from both the producers, "where can we get our files mounted, will an American company continue to listen to European data requests", and from users, "will such a concentration of services in one company lead to higher prices and less choice"? Calls for the strengthening of the remaining database hosts have been made by librarian groups in the UK and France. However, at the same time, alternative calls are being made for Europe to stop "mindless competition and duplication", so that a healthy infrastructure of hosts can be established which each concentrate upon specific areas and files. The users would like this but one could question whether they, in their free market place, would appreciate being told to stop one particular product so that Europe had a stronger player. Nevertheless, this indicates that many see information and data as a central resource upon which they can build their products rather than a product in itself.

These changes are adding to Europe's vulnerability. The US enjoys a securely funded public sector information service which can and does offer excellent products to the world at low prices. At the same time they have been allowed to purchase, or in some cases, absorb, key databases which were developed with the help of European expertise or investment. The result is that the US is able to market strongly in Europe; and although not all of their products are actually significantly better than the European competitor, they are often preferred due to their lower cost. Many European users fondly believe that they will turn back to the European products if the US ever stops access; but this might not be possible — by that time the European products may no longer be available.

This environment has therefore opened the following strategic questions:

- What problems could exist if the remaining European database hosts are taken over, or removed? All now choose their materials and so act as a filter to the user and offer variety to the producer. How can database hosts be encouraged to develop market-niche skills so that quality and not quantity are promoted? A monopoly could be disastrous for the user and the producer alike, but too much competition in a small market will force the user to use the secure product and could force the rest to the wall.
- What steps should producers take to ensure they have a way to reach their market? How can this market be best served? What guarantees are required, and might be obtained, to ensure that the present situation remains open and free? To whom should such a policy/request be addressed?
- While connectivity is usually "acceptable" within national boundaries, Europe still suffers from poor links between countries. This is recognised as a political problem but it forms a real barrier for the successful development of an on-line market. What steps can information producers take to improve the situation?
- "Could biotechnology database producers make better use of the academic infrastruc-

ture"? Several users have indicated their preference for the Internet based information infrastructure and have suggested that the commercial database producers look towards mounting their files on these services. At the same time, many commercial users are anxious to gain better access to the networks. Concerns about hacking and computer security prevent many companies from doing so, but increased security from the host side could solve this worry in many cases. What policies need to be considered to use these facilities?

- What will be the role of the smaller database in the future? How will they be mounted,and can they be linked to other services/products to enhance the total value of the data/information? As data collections become larger and larger the need to select the specific database before the detailed search will increase. What strategies can be effected to protect the smaller collection? How can the SF help organise the different players (from the academic and commercial, and the producer and the host worlds) into a coherent group for the common good. Is the CCDB the ideal solution?
- What steps should European providers and database hosts take to ensure that they remain an equal players in the provision of biotechnology information. Such discussions should take note of the fact that the secondary and related services are of utmost importance to the continued success of the primary products — the control of the abstracting/alerting service can determine the usage of the primary research article; especially in the coming environment of document delivery.

COSTING, OWNING, AND LINKING, INFORMATION

There is an increasing awareness that many senior information professionals are (still) unaware of the *alternative* forms of information available on the bioinformatics scene. Two distinct cultures are appearing — literature, or factual, based, and few librarians are able to handle both scenarios. There is a general acceptance that the factual databases need to be used by actual end-users, an intermediary is unable to use a sequence database package as biological training is required but, at the same time, the growth in form and number of databases and services mean that the librarian needs to become a "guide". The biologist increasingly only looks towards the librarian for the delivery of a single article and this is too narrow.

An added difficulty is the fact that few attempts to link factual and literature data have been made (ENTREZ from the NCBI being a commonly named exception). The European producers are being pressed to come up with suitable competitors, or better, with new and novel groupings of information which serve a market need better. Opportunities clearly exist, from better grouping of data, software tools for improved use of information and data and even possibly the use of AI systems for better linking and identifying of information.

The user market, strongly pushed by the primary publishers, also appears to be moving increasingly towards single article information. This opens up a potential conflict as to which part of the publishing chain is best suited to serving the market: the primary publishers who own the journals and the single articles, the secondary database producers who identify and locate the material, or, for instance, the agents who serve the major customers. Thus we have:

– Image management technology, of great potential in the production of secondary databases, offers the secondary database producers the option of also sending, via

telecommunications, the image of the article that is being captured for secondary processing. This allows a closer link between primary and secondary product. But, what repercussions might this have for copyright and use of primary products in secondary systems?

In the same light, what repercussions might be expected from the entry of intermediaries such as the British Lending Library Division, often using the academic networks ?

Furthermore, most critics agree that these developments will increase the chance that users can select individual articles and products and pay-on-demand. Strategically, this will reduce the pre-paid subscription income of the primary producers, but one solution might be to price according to the medium (e.g. fax, electronic file, floppy disc) so that the fee includes a percentage for the information?

- (Much/most) Factual data is currently *free* and there are deep reservations among the scientific community against having to pay for data that has been entered into the databases for free. Unfortunately, some form of "sales income" might be required in the future. Base lines defining "free" are required. What should these be and should they not be linked to "freedom of access" i.e. such data can be accessed by everyone.
- Biotechnology information is international. What possibilities might exist for the main international databases to be integrated to a degree that the world's literature and related data is linked into one global product (or series of integrated products)? What difficulties exist and are these media (e.g. CD ROM) related? This last point was stressed many times: why do we need more than one database? The fear of becoming dependent upon "American" sources varies greatly. Many companies find it irrelevant, others find it too dangerous for words. Most users accept that Europe should pay its way and that the best way to do this is to ensure that European data source, be they literature or factual, are available for international use.

How can, and/or should, the current services be organised so that *joint* databases are produced which give a form of *meta* analysis?

- Most database builders adhere to their own formats and standards which leads to confusion and inefficiency. Should not producers adhere to basic guide-lines (rather than intricate details of technology) such as "unique identifiers", and establish links to other database builders and nomenclature groups.

These discussion points were debated at a workshop in the summer of 1994 – the report of which can be obtained from the author.

THE EUROPEAN MOLECULAR BIOLOGY NETWORK — EMBNET — LINKING MANY RESOURCES TOGETHER

The days when a "database search" meant going to the library to ask for an overview of the literature, based on a series of key words designed to locate articles of relevance, have passed; increasingly, and especially in biomedical research, the searching of databases and databanks have become part of the research process itself.

Databases now contain huge arrays of information. Some describe molecules, others list nucleotide sequences, microbial cultures are detailed, as are cancer resources and plant taxonomics. Some services offer software to model the data graphic terminals and others allow the user to order the targetted products.

The boom in databases — often grouped under the new term bioinformatics — the use of computers and in biotechnology started in the early 1980s with the decision at the European Molecular Biology Laboratory in Heidelberg (EMBL) to begin to build their Nucleotide Sequence Database. This soon became an international effort and today three centres, in Japan, America and Europe, combine their input to form a coordinated core database.

This nucleotide sequence database became the basis for many other similar sequence and structure databases and we are now able to carry out sophisticated molecular modelling, structure prediction and related activities based on the genome sequence and the resulting amino acid chain. But the science that has grown out of the use of computers and networks is growing rapidly and will continue to develop into an essential component of biological R&D.

The files dealing with 3D structures and genome maps as well as others detailing the literature, characteristics of the cell lines, germ plasms and specialised molecules needed in research have to be delivered to the client. Furthermore, they have to be handled with sophisticated hardware and software, and the users have to be trained. In 1988 a group of European national biocomputing centres met to see if they could work closely with the EMBL Data Library to distribute this data better. Since then, EMBnet — the European Molecular Biology Network, has grown to 24 nodes spread across Europe from Norway to Israel and Austria to the UK. There are additional "specialist nodes", such as the Human Genome Resource Centre in the UK or the Swiss-Prot centre at the University of Geneva, and more are expected, especially from Eastern Europe — Poland and Hungary are already members.

These nodes primarily handle data from one or more of the collating nodes, such as the EMBL Data Library, to offer it to their (national) users. The nodes support their services with training and user-friendly software, as well as national language HELP services; the nodes usually take a special interest in one or more scientific or informatics problem.

EMBnet is a perfect example of subsidiarity. Each node is funded by its national authority but the group as a coordinated whole has been supported by the European Commission under their BRIDGE Programme and, in many ways, mirrors the popular "institute without walls" concept promoted by the Commission. Thus the sum of the individual expertises comes to more than that which could be found in any one site and EMBnet certainly seems to be fulfilling its planners hopes in terms of putting together excellent training and service systems; furthermore, because the nodes are "user-driven" they are able to react to user needs rapidly and efficiently in terms of devising new software or other technical solutions to perceived problems.

The databases carried on EMBnet are of essential use to bench scientists in industrial or academic research. Many industrial companies currently access sequence and protein structure data from CD ROM databases so as to ensure security. Hopefully, improvements in network security will mean that an increasing number of industrial clients also start to use the national services on offer. The EMBnet training team are certainly willing to mediate if needed.

One of the criticisms of European bioinformatics in recent years has been the lack of a focal point. This is in stark contrast to the USA where Congress approved the establishment and financing of a National Center for Biotechnology Information in the last years of the 1980s and the Bethesda based NCBI has rapidly grown into a well

respected central source of guidance and investment in this field. Happily, however,Europe will soon have their own European Bioinformatics Institute, being built at this moment at Hinxton in Cambridge. The EBI will house the present EMBL Data Library team, plus a small R&D group. It is based next to the Sanger Centre and so will be close to advanced research on genome mapping and sequencing.

EMBnet was formed in association with the EMBL Data Library and its prime role is still to distribute that centre's data; this will continue from Cambridge and EMBnet hopes to continue to be an efficient distribution system for the EBI's products. Overall, EMBnet sees itself as a complement to the EBI — by providing a series of local specialist centres which can feed back intelligence and need as well as provide a customer core.

Scientists active in the field of Disease Marker research will almost certainly be interested in bioinformatics. Those in America will be able to get further information on the bioinformatics world from the NCBI; Europeans might like to contact their local EMBnet node:

- BioBase, Ole Worms alle, Building 170, Aarhus Universitet, DK-8000 Aarhus C, Denmark. Contact: Hans-Ullitz Moller, hum@biobase.aau.dk, Tel.: +45-86-202711, after new tone 2776, Fax: +45-86-131160.
- EMBL, European Molecular Biology Laboratory, Meyerhofstrasse 1, Postfach 10 22 09, 69012 Heidelberg, Germany. Contact: Peter Stoehr, datalib@EMBL-Heidelberg.de, Tel.: +49-6221-387258, Fax: +49-6221-387519.
- CSC, Centre for Scientific Computing, P.O. Box 405, FIN 02101 Espoo, Finland. Contact: Rob Harper, harper@convex.csc.fi, Tel.: +358-0-4572076, Fax: +358-0-4572302.
- Service de Bioinformatique CNRS-INSERM, 7 rue Guy Moquet –BP 8, 94801 VILLEJUIF Cedex, France. Contact: Phillipe Dessen, dessen@genome.vjf.inserm.fr, Tel.: +33-1-45 59 52 41, Fax: +33-1-45 59 52 50.
- GENETHON, 1 rue de l'Internationale, BP60, 91002 Evry Cedex, France. Contact: Claude Scarpelli, claude@genethon.fr, Tel.: +33-1-44162725, Fax: +33-1-45885220.
- German EMBnet node – GENIUSnet, Department of Molecular Biophysics, German Cancer Research Centre (DKFZ), Im Neuenheimer Feld 280, D-6900 Heidelberg, Federal Republic of Germany. Contact: Weiyun Chen, dok419@genius.embnet.dkfz-heidelberg.de, Tel.:+ 49-6221-422349, Fax: +49-6221-422333.
- Greek EMBnet Node, Institute of Molecular Biology and Biotechnology (IMBB), Foundation for Research and Technology Hellas, PO Box 1527, Heraklion 711 10, Greece. Contact: Babis Savakis, savakis@myia.imbb.forth.gr, Tel.: +30-81-212-890, Fax: +30-81-231-308.
- The HGMP Resource Centre, Clinical Research Centre, Watford Road, Harrow, Middlesex, HA1 3UJ, United Kingdom. Contact: Francis R.Rysavy, f.rysavy@crc.ac.uk, (BITNET: f.rysavy%CRC@UKACRL), Tel.: +44-81-869 3291, Fax: +44-81-423 1275.
- ICGEB, International Centre for Genetic Engineering and Biotechnology, Padriciano 99, I-34012 Trieste, Italy. Contact : Sándor Pongor, pongor@genes.icgeb.trieste.it, Tel.: +39-40-3757300, Fax: +39-40-226-555.
- Weizmann Institute of Science, Biological Services, Biological Computing Division,

Rehovot 76100, Israel. Contact: Leon Esterman, Isestern@weizmann.bitnet, Tel.: +972-8-349470, Fax: +972-8-344113.

- CNR Area di Ricerca di Bari, Via Amendola 166/5, I-70125 Bari, Italy. Contact: Marcella Attimonelli, attimonelli@mvx36.csata.it, Tel.: +39-80-483745, Fax: +39-80-484467.
- Max-Planck-Institut für Biochemie, MIPS , Am Klopferspitz, 81243 Martinsried, Germany. Contact: Dr. H.W. Mewes, mewes@ehpmic.mips.biochem.mpg.de, Tel.: +49 89 8578 2656, Fax: +49 89 8578 2655.
- CAOS/CAMM Center, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands. Contact: Jan H. Noordik, noordik@caos.kun.nl, Tel.: +31-80-653 386 (or 391); Fax: +31-80-652977.
- Norwegian EMBnet Node, Biotechnology Center of Oslo, Gaustadalleen 21, N-0371 Oslo, Norway. Contact: Rodrigo Lopez, rodrigol@biomed.uio.no, Tel.: +47-22958756, Fax: +47-22694130
- Hoffmann-La Roche, CH 4002 Basel, Switzerland. Contact: Dan Doran, doran@embl-heidelberg.de, Tel.: +41-61-6888270, Fax: +41-61-6881745
- Centro Nacional de Biotecnología, CSIC, Universidad Autónoma de Madrid, 28049 Madrid, Spain , Contact: Luis Pezzi and Jose-Maria Carazo, Lpezzi@ cnbvx3.cnb.uam.es and Carazo@cnbvx3.cnb.uam.es , Tel.: +34-1-585-4505 and +341-585-4543, Fax: +34-1-585-4506.
- Computing Department, Biomedical Centre, Box 570, S-751 23 Uppsala, Sweden. Contact: Peter Gad, gad@perrier.embnet.se, Tel.: 46-18-174016, Fax: 46-18-551759.
- Biocomputing, Biozentrum der Universität Basel, Klingelbergstrasse 70, CH-4056 Basel, Switzerland. Contact: Reinhard Doelz, embnet@comp.bioz.unibas.ch, Tel.:+ 41-61-2672247, Fax: +41-61-2672078.
- SEQNET, SERC Daresbury Laboratory, Daresbury, Warrington WA4 4AD, United Kingdom. Contact: Alan Bleasby, bleasby@dl.ac.uk. Tel. +44-925-603351, Fax: +44-925-603100.
- Bio Computing Center, University of Vienna, Dr.Bohr-Gasse 9, A-1030 Vienna, Austria. Contact: Martin Grabner, grabner@embdec.bcc.univie.ac.at, Tel.: +43-1-79515 6108, Fax: +43-1-7986224.
- Belgian EMBnet Node (BEN), ULB/VUB Computing Center, C.P. 300, 50 Av. Franklin Roosevelt, 1050 Brussels, Belgium. Contact: Dr. Robert Herzog, rherzog@ulb.ac.be, Tel.: +32-2-6509762, Fax: +32-2-6509767.
- Instituto Gulbenkian de Ciência, Apartado 14, 2781 Oeiras Codex, Portugal. Contact: Pedro Fernandes, Tel.: +351-1-4431408, Fax: +351-1-4435625.
- Agricultural Biotechnology Center, Szent-Györgyi u. 4 , 2100 Gödöllö , Hungary. Contact: József Reményi, remenyi@abc.hu, pongor@abc.hu, Tel: +36-28-330-600, Fax: +36-28-330-338.
- SWISS-PROT, Departement de Biochimie Medicale, Centre Medical Universitaire, 1211 Geneva 4, Switzerland. Contact: Amos Bairoch, Bairoch@cmu.unige.ch. Tel: +41-22-618492.

or

- The European Bioinformatics Institute, Hinxton Hall, Hinxton, Cambridge CB10 1RQ, UK.. Contact: Graham Cameron, Cameron@EMBL-heidelberg.de, Tel: +44-223-494967, Fax: +44-223-494968.

In the USA:

- The NCBI, National Institutes of Health, Building 38a, Bethesda Md 20894, USA. Contact: David Lipman, Tel: +1-301-496 2475, Fax: +1-301-480-9241.