

methodological problems related to forecasting supply and demand for scientists and engineers and the use of such forecasts in policy making, as well to finalize the agenda for a workshop on these issues to be held early next year. According to the NAS, "Conflicting assessments that have emerged from recent analytical efforts have resulted in a considerable amount of confusion about the future state of labor market conditions for scientists and engineers." □

Brendan Horton is in Nature's Washington Office.

Choices and challenges

Potter Wickware

Computers have changed biology forever, even if most biologists don't yet realize it, says Michael Levitt, a structural biologist at Stanford University and the founder of Molecular Applications Group (MAG), in Palo Alto, California. Already, drug discovery is driven by the need to apply powerful computers to voluminous data sets, and the trend, he says, is certain to extend into all other disciplines in biology.

Chris Lee, Levitt's former graduate student and co-founder of MAG, agrees, noting that most biologists today use computers only in the most elementary way as a typewriter and graph-paper substitute. "Bioinformatics is really going to surge when biologists realize that there's a lot of value, and a lot of new insights, in being able to work across large amounts of data that they and all the other scientists in the world have produced," says Lee.

Levitt began using computers to solve problems in protein folding when working under John Kendrew, Max Perutz, Francis Crick and other eminent molecular biologists in the "golden age" of the 1960s at the Laboratory for Molecular Biology at Cambridge, United Kingdom. Today the 7lb laptop he carries in his backpack has more than a thousand times the computing power, at less than a thousandth of the cost, of the punch-card behemoths of 30 years ago.

Accompanying the relentless increase in computing power is a breathtaking expansion of biological data from the human and other organism genome-sequencing projects. Complementary information from the pharmaceutical chemistry, neuroscience, microbiology, immunology, clinical trials, toxicology, teratology, epidemiology and other disciplines waits to be integrated with the genetic and structural data. There is no way to obtain a global view of all this information, to establish links between disparate fields of knowledge, without the computer.

Myra Williams, MAG's new president, has a PhD in biophysics from Yale and was hired this summer from Glaxo Wellcome to

launch the company's GeneMine Pro suite of bioinformatics tools. She observes that rates of data acquisition, far from levelling off, are accelerating. Soon innovations like Affymetrix's high-density oligonucleotide array microchip will come online, generating terabytes ('terror-bytes') of new sequence information. How scientists navigate this ocean of biological information will be crucial.

"To be effective," Williams says, "bioinformatics tools must not merely automate data retrieval, but give researchers the information in usable form, through clustering, filtering, analysis and visualization, allowing them to perceive insights which might well have eluded them had they attempted to process the information manually."

The bioinformatics capabilities of MAG's GeneMine Pro program are built around its Discovery Engine, an automated Web browser which retrieves biological information in 22 categories from servers worldwide. After processing, the information is presented at the user interface, where it can be visualized in the context of sequence alignments and three-dimensional protein structures, or read as text. Large pharmaceutical companies, challenged by expiring patents and the high cost and slow pace of conventional drug development, are now the main source of sustenance for bioinformatics. The fact that genomics and bioinformatics are creatures of big industrial research environments inevitably leads to a blurring of distinctions between academic and industrial science.

Despite a strong and growing demand for bioinformaticists, there are few established training centres, perhaps 20 in the world, estimates Levitt. The field is still defining itself, and those who do have formal training are quickly snapped up by industry on hefty pay scales, leaving a deficit in the numbers of those available to train the next generation.

Nevertheless, Lee believes that the candidate who, on his or her own initiative, "can demonstrate the ability to cross over and generate results — not even necessarily original ones — is the one who will capture the recruiter's attention."

Levitt adds that the shortage of formal training slots coincides with exceptional opportunities for self-learning: with an Internet connection and inexpensive computer, one can download all the databases, programs and papers needed to undertake an original research project. "Spend two days looking at the results and thinking about what you don't understand. Use e-mail to contact someone who does, and ask, 'what should I be doing?'" he recommends. Prize-winning discoveries can be made in this way. "The problems are so difficult, and there is so much to be analysed, that the boom will not go away. It's a great time to be getting in. There's a wonderful lightness to the field." □

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Running to catch up in Europe

Helen Gavaghan

Across Europe, the story is the same. Demand for those skilled in bioinformatics exceeds supply. Like biochemistry and biophysics before it, bioinformatics is crushing the barriers between traditional academic fields, and demanding flexibility and a new way of thinking from its adherents.

Computational biology has meant different things to different people. Not too long ago, says Hans Prydz of the University of Oslo's Biotechnology Centre, it meant handling NMR data or analysing Doppler echograms. Now renamed bioinformatics, it means looking for patterns in DNA and RNA, predicting protein structure, modelling proteins and mining massive databases that continue to grow. When the DNA database run by the European Bioinformatics Institute (EBI) was first set up, it contained 700,000 nucleotides: now there are more than a billion.

Driven by the scientific and commercial importance of bioinformatics in genomics and drug discovery and development, governments, universities and industry are responding with varying degrees of vigour and success to the skills shortage and are seeking ways to cross the boundaries between disciplines as diverse as engineering, physics, mathematics, computer science, statistics, protein chemistry, genetics and molecular biology.

At European level, the EBI, based near Cambridge (United Kingdom), is funded to the sum of about DM 9 million (\$5 million) by members of the European Union and Israel via their contributions to the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. Contributions from the pharmaceutical and agricultural industries roughly double the institute's income. The EBI, an offshoot of EMBL, develops tools for bioinformatics, seeks innovative ways to apply the tools, and runs training courses for academics and industrialists. Initiatives with industry include the Industry Affiliates Initiative, which helps small and medium-sized companies to identify and apply new techniques; the BioTitan Project, running nodes to enable faster access to databases; and the Biostandards project, funded jointly by industry and the European Union for promoting and developing standards.

National initiatives also exist, particularly in the United Kingdom and Germany. Says Andrew Lyall, responsible for bioinformatics at Glaxo Wellcome, "I think the UK is in pretty good shape." There are two government-financed initiatives in the United

Kingdom, both of which received a second lease of life earlier this month.

One of these schemes, supported by the Biotechnology and Biological Sciences Research Council (BBSRC), coordinates the UK bioinformatics community. Since 1994, the scheme has concentrated on developing software that would enable biologists without information technology (IT) skills to use some of the many tools important to their trade that are found on the World Wide Web. At a meeting earlier this month, the steering committee of the scheme decided to change the focus to training. Andy Brass, who runs a masters' degree course in bioinformatics at the University of Manchester and is a member of the committee, says, "We have a massive skills shortage. We need training at every level." The main aim will be to "train the trainers", says Brass, adding, "There are very few academics with the knowledge to teach bioinformatics because they have all been nicked by the companies." The view is echoed by others, and could account for Lyall's optimism.

The United Kingdom's second public scheme to promote bioinformatics is jointly funded by the BBSRC and by the Engineering and Physical Sciences Research Council. It too was started in 1994 (spending £1 million per year and making 25 awards in three years). This scheme was also renewed for a further three years earlier this month. Chris Miles, who heads the initiative for the BBSRC, explains that research proposals must have both a strong biological and computational component. During the next phase, researchers will address priorities such as finding methods for condensing and representing data visually and seeking informatics techniques allowing the prediction of protein structure from sequence data.

In Germany (see below) the country's main grant-giving body has launched a six-year bioinformatics programme, while in France, CNRS has allocated FF_r 15 million (\$2.6 million) for bioinformatics research this next year. Not all French scientists are convinced that they will see the money. Jean Thierry-Mieg from the CNRS in Montpellier

says that during the past five years spending in bioinformatics has been announced more than once, but because of political disagreements no money was forthcoming. The tide does seem to be turning, though. France is setting up a new sequencing laboratory in Paris and the University of Versailles is teaching a dedicated course on bioinformatics.

The picture elsewhere is less focused. Cecilia Saccone, a professor in the department of biochemistry and molecular biology at the University of Bari and one of Italy's leading bioinformaticists, is working with colleagues to design a bioinformatics doctoral programme for the country. Saccone has already started a project in bioinformatics, but Italy's national research council (CNR), although admitting that the subject is important, says that there is no money to support it.

Spain's leading light in bioinformatics, Alfonso Valencia from the Centro Nacional de Biotecnología in Madrid, is coordinating a group of researchers to promote training. Uniquely for a scientist, Valencia says: "We probably have enough money for bioinfor-

Germany on the trail of the Americans

Germany will not quickly end North America's lead in bioinformatics. But in the current biotechnology boom, the prospects seem bright.

Determined to make up for its lag in biotechnology research, a consequence of vociferous public opposition to genetic engineering, the German ministry of research (BMBF) has in the past few years launched several campaigns. Bioinformatics is a vital part of this initiative. Between 1993 and 1996, for example, the BMBF allocated DM37 million (US\$20 million) in research grants and pumped a further DM30 million into research institutes with a strong interest in bioinformatics. The BMBF plans to increase this support.

In addition, the Deutsche Forschungsgemeinschaft (DFG), Germany's main grant-giving body, is about to launch a six-year bioinformatics programme that will distribute about DM5 million in project grants in its first two years. The BMBF also has a scheme called Bioregio, a regional competition for a prize of DM150 million. Regions have

to present a collaborative programme involving industry and academic research institutes.

One company to benefit from the local contacts this programme promotes is Heidelberg-based LION Bioscience. Founded in spring this year, LION offers commercial services in bioinformatics and has ambitious plans to become Europe's leader. As a result of close collaboration with the European Molecular Biology Laboratory (EMBL), located on the same campus, it has been able to adapt EMBL's developments – efficient software and the fastest sequencer in the world – to its own needs.

LION is a sign of the good times that are almost certain to come for bioinformatics in Germany. The company started with 10 employees, will recruit a further 20 before the end of the year, and plans further expansion. "The technology was there, the human resources were there and we were just the first ones who had the idea to use it commercially. We filled a vacuum," says Peter Wiesner, senior manager of

business development.

The traditional large German pharmaceutical companies also have a growing need for specialists in bioinformatics, and find there are simply too few around. "Job opportunities in the field are so good that, at the moment, potential employers are finding the cupboard bare," says Hugo Kubinyi, head of drug design at BASF.

Academic institutes have even more ground for concern. "The battle between industry and academic research for competent bioinformaticists is, understandably, almost always won by industry," says Sandor Suhai, head of the department of molecular biophysics at the Deutsches Krebsforschungszentrum (DKFZ, the German national cancer research institute) in Heidelberg. In his group of 30 scientists (mainly graduate students) only two plan a career in academic research, says Suhai: industry can offer long-term employment, high salaries and sometimes more exciting jobs. He complains about the high turnover in his group and

says that he gets too few responses to advertisements.

The first university course for scientific informatics was established in response to this need in 1989 at Bielefeld. "We teach the basics of informatics but then focus on methods relevant to biology. The biology we teach is similarly restricted to that relevant to bioinformatics," says Robert Giegerich, dean of the technical faculty. Despite sceptics who believe the graduates are neither informaticists nor biologists, he has no doubt that his students will succeed on the job market. He believes bioinformatics will become a 'proper' science just as informatics separated from mathematics.

First employers' reactions to graduates from Bielefeld are enthusiastic. "In contrast to trained bioinformaticists, we have to teach an informaticist not only biology but also the basics of bioinformatics. This can take up to one year," says Martin Vingron, head of theoretical bioinformatics at the DKFZ.

Matthias Strobl

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matics." But he adds: "We need more courses at all levels." The only course dedicated to bioinformatics in Spain is postdoctoral. Valencia is seeking formal relationships with the EBI as he believes that bioinformatics is not really promoted as a separate discipline in Spain. As in Italy, the money goes to molecular biology or protein chemistry groups that include a person with bioinformatics skills.

Away from academic institutions, the picture is equally vibrant and varied. Europe's pharmaceutical giants latched on to the significance of bioinformatic skills early on, and have indulged in aggressive poaching from the lower-paid public sector. The pharmaceutical industry's competition when recruiting high-quality staff, says Chris Rawlings, UK director for bioinformatics at SmithKline Beecham, is not from academic institutions, but from smaller genomics companies that can offer stock options and a prominent, leadership role in a small group.

Rawlings is less concerned by the competition for new recruits from the small bioinformatics companies that have recently begun the search for capital. The big pharmaceutical companies are building up a strong body of in-house expertise. "We go and talk to these people [in bioinformatics companies] and find out who they are. We are looking for niche technologies," he says. For the brave, the well informed and, above all, those with business acumen, there is nevertheless a whiff of money to be made from a start-up bioinformatics company.

"A lot of people see bioinformatics as the current technology frontier and believe, as they did eight years ago about the Internet, that there are a lot of opportunities out there," says Joseph Bergen of the venture-capital company 3i. But, says Bergen, it's all about timing, and bioinformatics has not broken cover yet. So far, he has seen interesting technology, but not the commercial sense that would convert an idea into hard cash. When the small companies do break cover, the SKBs and Glaxo Wellcomes of the world will be waiting. So far, says Lyall of Glaxo Wellcome, it is all smoke and mirrors.

For those contemplating a slightly less risky life in the commercial world, the big companies are still seeking people who will be effective from day one. "Bioinformatics is strategically important to us," says Rawlings. "The company's philosophy is that all new drug targets are expected to be discovered by genomics." SKB has two main informatics groups: in Philadelphia and Harlow (United Kingdom), whereas Glaxo Wellcome has three main centres for bioinformatics: Stevenage (United Kingdom), employing about 30 specialists; North Carolina, 25-30 specialists; and Geneva, between 5 and 10. There is also a small group in Madrid that collaborates with Valencia. Both Wellcome and SKB are not too far from Hinxton, where the EBI, the Sanger Centre (sequencing about a third

Useful Web sites for bioinformatics in Europe

The most useful site for those curious about bioinformatics in Europe is that of the EBI (<http://www.ebi.ac.uk>). The site is extensive, with a newsletter, job vacancies and a lot of educational material as well as further links, including one to its parent organization EMBL (<http://www.embl-heidelberg.de/>). It may just be my software, but I cannot always get through to this site.

A good starting point for a tour of European national centres is the

page of the European Science Foundation, which provides links to members. For example, (<http://www.esf-strasbourg.fr/members/map.htm>) will take you to French members, including the CNRS (<http://www.cnrs.fr/>). There is an English version of this site. One can also reach UK sites, including that for the BBSRC (<http://www.bbsrc.ac.uk/>). Finding information about bioinformatics on these sites requires some searching.

Also at European level is a page from the science directorate (<http://europa.eu.int/en/comm/dg12/biotech/biot-n.htm>). This provides links to biotechnology sites, including the European Federation of Biotechnology.

In the United Kingdom, the Wellcome centre provides a list of job vacancies at (<http://wisdom.wellcome.ac.uk/>). The page gives the option of searching for jobs in a given area, but I got no results. **Helen Gavaghan**

of the human genome) and the Medical Research Council's human genome mapping programme resource centre are sited.

SKB divides its bioinformatics activities into three areas: research; bioinformatics tool development and databases; and user support and services. This split accurately reflects the kind of jobs available to people interested in bioinformatics. The dream *curriculum vitae* for someone wanting to go into research in SKB or Glaxo Wellcome would show a bachelors' degree in a biological science, a masters' in computational science and a doctorate focusing on a problem in computational biology. Rawlings adds that he would like to see a stint or two as a post-doc. With this background, you are practically guaranteed to have Glaxo Wellcome and SmithKline Beecham fighting for your services. Says Brass: "You would probably earn in the mid to high thirties [£30,000+ a year], which compares with a salary in the mid thirties for a full professor in the UK."

The people working in bioinformatics tool development and user support and services will need a strong computing background. Of the support group, Rawlings says, "These people are not sitting on a help desk. They are performing sophisticated bioinformatics analyses for scientists without a Unix workstation." The pay scale, roughly — and both companies are a little coy about this — is low-to-mid £20,000 range for a person with a masters' degree, and high £20,000 to low £30,000 range for one with a masters' and a doctorate. "There is definitely a premium for having a masters' in bioinformatics compared with molecular biology," says Brass.

Given the boundaries that someone in bioinformatics must cross, perhaps the premium is justified. "It is not a field of science like genetics," says Michael Ashburner,

director of research at the EBI and a professor of genetics at the University of Cambridge, "it is a field in which nearly everyone comes from somewhere else." Slowly those people, in the United Kingdom at least, are being channelled through specialized masters' programmes. The universities of York, Manchester, Aberdeen and Birkbeck College (part of the University of London) offer masters' degrees in bioinformatics. There are more masters' courses in the pipeline, says Lyall, Edinburgh being one example.

Ashburner says: "We need to put more resources into training at the masters' level." The recent introduction of graduate schools into the United Kingdom on the US model (rather than having students attached to individuals in departments) makes the introduction of masters' degrees in interdisciplinary subjects like bioinformatics easier than it is in Europe, says Brass. The Manchester course takes up to 20 people each year; most come from a biology background, but Brass would like more from computer science, physics or mathematics.

The Manchester course concentrates on problem solving, being project- rather than lecture-based. The field is moving so fast that it would be difficult to construct a course otherwise. For example, when the EBI ran a workshop on 'common object request broker architecture' (CORBA — a way of transferring blocks of code between applications) earlier this year, it anticipated 40-50 attendees. In the event, 200 registered and a further 50 unregistered scientists turned up. Yet it is only this coming year that Manchester will teach CORBA. Even as they start their first job fresh from university, last year's graduates will find themselves running to catch up with the technology. □

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