phase known to permit ready access to enzymes. Following completion of the synthesis, incubation with a lipase allowed enzyme-induced fragmentation that released the library compounds. The quinone methide intermediate (**6**) was conveniently left attached to the resin beads where it could be trapped by water or another nucleophile.

This method has been used for the cleavage under very mild conditions of tetrahydro-β-carbolines, prepared via the Pictet-Spengler reaction, and protected thymidine derivatives.

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Emerging therapeutic targets

Molecular targets for weight control

Smoking cessation is well known to be associated with weight gain, which may be relieved by nicotine patches or gum during the withdrawal period. Activation of nicotinic acetylcholine receptors (nAChR) may modulate several neurotransmitter signalling pathways implicated in the control of body weight, including leptin, neuropeptide Y and biogenic amines. For example, a recent study demonstrated that serum leptin concentrations in smokers were significantly lower than in non-smokers – an association which was independent of diabetes status [Hodge, A.M. *et al. Int. J. Obes. Relat. Metab. Disord.* (1997) 21, 50–53]. This suggests that nicotinic signalling may modify the sensitivity of hypothalamic leptin receptors and consequently modulate leptin synthesis, thereby reducing body weight.

Selective neuropeptide Y antagonists and β_3-adrenergic agonists are being developed as weight control drugs [reviewed recently by Strader, C.D. *et al. Drug Discovery Today* (1998) 3, 250–256]. Chronic nicotine administration has been shown to reduce neuropeptide Y protein levels in the rat hypothalamus [Frankish, H.M. *et al. Brain Res.* (1995) 694, 139–146] and to increase norepinephrine turnover, a measure for sympathetic activity, in brown adipose tissue of obese mice [Yoshida, T. *et al. J. Nutr. Sci. Vitaminol.* (1990) 36, 123–130]. All these nicotinic effects have been correlated with weight loss, without affecting food intake. The nicotine-stimulated sympathetic activity on adipose tissue is also illustrated by its capacity to elevate plasma free fatty acids levels [Batt, R.A. and Topping D.L. (1979) *Int. J. Obes.* 3, 7–13].

It thus appears that with respect to weight control, nicotine might deliver the same effects as both neuropeptide Y antagonists and β_3-adrenergic agonists. However, nicotine possesses certain undesired side effects, such as induction of T cell anergy [Sopori, M.L. and Kozak, W. *J. Neuroimmunol.* (1998) 83, 148–156]. More studies are therefore required to elucidate which specific nAChR subtype(s) are involved in nicotinic body weight control, so that subtype-selective nicotinic agonists might be developed for fighting obesity, possibly alongside neuropeptide Y antagonists and β_3-adrenergic agonists.

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Bioinformatics

Learning bioinformatics

Bioinformatics is a science that essentially uses a combination of computer technology, information science and biological knowledge to collect, store, retrieve, analyse, relate and model biological data. Virtually any fact, concept or principle concerned with the biomedical sciences (this includes health, medical and biological sciences) can be included as 'biological data'. Of course, DNA, RNA and protein sequence data has considerably increased this pool of data. It is this sequence data, and its subsequent analysis by bioinformatics, that attracts most attention because it promises a considerable reduction in both time and cost for drug discovery. Consequently, trained research and scientific staff are needed to extract meaning from this complex and growing mountain of biomedical and sequence data.

Aims of training

The aims of training in bioinformatics are to enable the scientist to understand what bioinformatics can achieve and to use (or develop) bioinformatics tools effectively. These aims enhance communication and promote effective problem solving skills. Communication is particularly important between a computer scientist (who designs the computer applications) and a biological scientist (who needs to extract biologically relevant information). Consequently, much of industry bioinformatics training is really cross training of existing professionals – training computer scientists in biology and biologists in computer science.

Courses available

Mainstream bioinformatics courses are offered mainly for undergraduates and postgraduates at university. Most undergraduate courses in disciplines such as chemistry, molecular biology, biochemistry and computer science now offer units in bioinformatics, but very few (as yet) offer a full degree. Some academic and industry practitioners think it's 'too early' for institutions to develop a full degree course in bioinformatics, because the science is advancing so rapidly that it would be difficult for a degree course to keep up to date.

Presently, it seems that the preferred option for training is through either a professional (non-degree) course, a graduate course (i.e. as a 'unit' contributing to a higher degree), or a postgraduate degree such as an MSc or PhD in bioinformatics. Staff can be trained by

Table 1. Professional and on-line courses in bioinformatics[a]

Name or contents of course	Location	Web address (URL) (Course notes on Web site?[b])
Professional courses		
The ANGIS Bioinformatics Course	University of Sydney, Australia	http://www.angis.su.oz.au/Education/ (Yes)
Bioinformatics with various topics (also interactive on line by subscription)	CAOS/CAMM Centre, University of Nijmegen, The Netherlands	http://www.caos.kun.nl/courses/teaching.html (Yes)
The Biocomputing Course	Norwegian EMBnet, University of Oslo, Norway	http://biomaster.uio.no/courses/index.html (No)
Bioinformatics Course	CyberGene AB, Huddinge, Sweden	http://www.cybergene.se/kursinfo.html (No)
Various bioinformatics courses	UK HGMP Resource Centre, Hinxton, UK	http://www.hgmp.mrc.ac.uk/About/Courses/ (No)
Various bioinformatics courses (also a graduate course)	Graduate School in Computational Biology, Bioinformatics, and Biometry (COMBI) University of Helsinki, Finland	http://www.cs.helsinki.fi/combi/program_spring_1998.html (Yes)
Course in informatics	Pasteur Institute, Paris, France	http://www.pasteur.fr/formation/infobio-uk.html (No)
Bioinformatics: Computer Methods in Molecular Biology	International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy	http://www.icgeb.trieste.it/crs98bio.htm (No)
Using Computers for Molecular Biology	New York University School of Medicine, USA	http://mcrcr0.med.nyu.edu/rcr/molbio/syllabus-98.html (Yes)
Bioinformatics	Oxford University, UK	http://www.conted.ox.ac.uk./Courses/biosciences.html (No)
Bioinformatics	Karolinska Institute, Huddinge, Sweden	http://kisac.cmb.ki.se/kisac/education/index.html (Yes)
On-line (Web-based)		
Bioinformatics Tools (professional course)	Virtual School of Molecular Sciences (VSMS) at the University of Nottingham, UK	http://ala.vsms.nottingham.ac.uk/vsms/catalog.html (Yes)
Molecular Biology Quiz (tutorial)	Göteborg University, Sweden	http://www.medkem.gu.se/edu/ (Yes)
Virtual School of Natural Sciences BioComputing Division (*VSNS-BCD*) (interactive course)	University of Bielefeld, Germany	http://www.techfak.uni-bielefeld.de/bcd/ (Yes)
Protein Sequence Alignment and Database Scanning (hypertextbook)	EBI, Hinxton, UK	http://barton.ebi.ac.uk/papers/rev93_1/rev93_1.html (Yes)
Sequence Analysis (tutorial)	Harvard University, Cambridge, MA, USA	http://twod.med.harvard.edu/seqanal/ (Yes)
Representations and Algorithms for Computational Molecular Biology (graduate course)	Stanford University, CA, USA	http://smi-web.stanford.edu/projects/helix/mis214/ (Yes)
Practical Biocomputing for the Bench Scientist (hypertext notes)	University of California, Irvine, USA	http://hornet.mmg.uci.edu/~hjm/projects/biocomp/biocomp.html (Yes)
A Taste of Bioinformatics (tutorial and part of a certificate course at UCL)	University College London, UK	http://www.biochem.ucl.ac.uk/bsm/dbbrowser/c32/ (Yes)

[a]This list and a list of undergraduate, graduate, and postgraduate courses can be found at http://www.curtin.edu.au/curtin/dept/biomed/teach/biochem/resources/resources.html

[b]Course notes vary from being brief to very comprehensive. A list of recent courses, workshops and meetings on bioinformatics can be found at http://www.informatik.uni-rostock.de/HUM-MOLGEN/hmg.html

Table 2. *Continuing Professional Development Course in Bioinformatics* at the University of Oxford[a]

Day	Theory	Practical
1	Computing, bioinformatics and discovery Databases and resources	Unix, GCG and database interrogations
2	Analysis methods and algorithms Sequence comparison methods	Analysis of sequences and databases
3	Multiple sequence analysis Evolutionary analysis Protein domains Analysing multiple sequences	Multiple sequences
4	Codon usage Finding genes Secondary structure prediction Finding patterns	Prediction from sequence

[a]Further details can be found at http://www.conted.ox.ac.uk./Courses/biosciences.html

allowing them to take a graduate or postgraduate course part time, but this is a relatively long-term option and may not develop the necessary knowledge or skills quickly enough. This aspect, and the industry's need for cross training, has led to training courses in bioinformatics at the professional level. These professional development courses are increasingly popular with industry.

In-house training

Of course, staff can also be trained in-house by using existing experienced and qualified staff, computer-based learning [Moss, S.H., Redfern, P.H. and Brown, K.N. *Pharm. Sci. Tech. Today* (1998) 1, 54–61], or a combination of both approaches. Unfortunately, the bioinformatic staff needed to conduct these in-house training courses are also in high demand for existing company projects and may not have the time to develop or deliver appropriate training courses. Moreover, it is questionable whether this would be an appropriate use of their skills given the highly competitive nature of the industry and the rapid progress of bioinformatics.

Taking a computer-based learning approach could overcome this problem, although at present, there is no specific computer software dealing with the teaching of bioinformatics. Another computer-based learning approach is to use an on-line (Web-based) course and there are more of these being developed (Table 1). Unfortunately, on-line training is a lonely activity and may not produce the necessary skills quick enough. Also, companies may not have the necessary resources to allow staff constant access to the Internet.

Professional courses

The professional courses seem to fulfil the requirements for quick, intensive and comprehensive training by skilled instructors. For example, the bioinformatics course at the University of Oxford is organized by the Department for Continuing Education and is one of several professional development courses offered in the biomedical sciences. The course content is comprehensive with the emphasis on understanding the basics and using bioinformatics as a tool to solve biological questions (Table 2). It does not deal with the mathematics or programming aspects of bioinformatics and is designed to be understood by both biologists and computer scientists alike. Although there seem to be only a few of these courses offered at present, judging from the popularity of the one which was run recently at the University of Oxford there will probably be more in the future.

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