Bioinformatics in Québec :

A Cornerstone of Bioindustry Development

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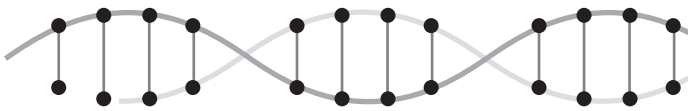
Advisory Report



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January 2001

Mr. Jean Rochon
Minister of Research, Science
and Technology
Government of Québec
Québec

Dear Sir:

In accordance with the provisions of Section 16 of the Act respecting the Ministère de la Recherche, de la Science et de la Technologie, I have the honor of forwarding the advisory report issued by the Conseil de la science et de la technologie entitled *Bioinformatics in Québec: A Cornerstone of Bioindustry Development.*

Yours sincerely,

Hélène P. Tremblay
President

Acknowledgements

This new Council report is the result of extensive cooperation from numerous contributors at all stages. These contributions deserve to be acknowledged.

I would like to begin by thanking the members of the Council for their participation in specifying the initial design, as well as the orientations and specific content of the document.

I would also like to thank the members of the steering committee: Mr. Martin Godbout, President of Hodran Inc. and Mr. Jean-Marc Proulx, Vice President, R&D for DMR Consulting Group Inc., both Council members; Mr. Paul Beaulieu, Executive Director of the Chair in Bioindustry Management at Université du Québec à Montréal; Thomas Hudson, Director of the Montréal Genome Centre; Jacques Hurtubise, Director of the Centre de recherches mathématiques at Université de Montréal; and Jean Morrissette, Senior Researcher at the Molecular Endocrinology and Oncology Research Center, Faculty of Medicine, Université Laval

Their recognized expertise and their availability for working sessions made it possible to provide the Council with a truly prospective overview of this fast-emerging sector.

I would also like to thank Council research officer Alain Bergeron for coordinating the project and writing the report. His mastery of the topic and his ability to synthesize key elements from disparate and changing information made his contribution extremely valuable.

Document layout was handled by Hélène Lafrance.

The President

Bioinformatics in Québec*:

A Cornerstone of Bioindustry Development

Foreword

Over the past several years, Québec has successfully established a strong and highly regarded biotechnology industry—notably in biopharmaceuticals—that ranks it first among Canadian provinces. It has also set up a new organization, Génome Québec, to support the development of its genomics and proteomics sector. These are significant advantages, yet they remain fragile given the intense competition between major international players to take scientific and economic leadership in these fields.

However, the development of bioindustries depends in large measure on the deployment of an upstream sector still very much in its infancy in Québec—bioinformatics.

Bioinformatics refers to the use of computer applications in biological sciences, a field of knowledge at the junction of the life sciences, computer science, and mathematics. Although it is not, for the time being, considered a specific industrial sector (the nomenclature of its components remains arbitrary), bioinformatics has already emerged as the platform on which repose research and development efforts in the various branches of the life sciences, including human health, agriculture, and environmental protection.

Bioinformatics is therefore a strategic key to the scientific and technological development of one of Québec's most promising new industries. But time is of the essence. Québec cannot aspire to a leadership role given its size, but if it acquires a critical mass of specialized resources, it will be able to support the growth of existing downstream industries, develop its own specialized expertise, and make well-informed decisions about the most appropriate societal choices that must be made.

The first priority for developing the bioinformatics sector is to quickly train sufficient numbers of university and industry researchers to satisfy demand for R&D purposes and the need for high-level trainers. Other priorities include the creation of major research facilities and networks, since discoveries in bioinformatics and related fields currently derive from basic research. Lastly, we believe it would be useful to assist corporate bioinformatics users in Québec for several years in their efforts to recruit bioinformatics specialists. International competition in the field is already fierce, and the playing field is not always level.

These are, in brief, the main conclusions reached by the Conseil de la science et de la technologie in this report entitled *Bioinformatics in Québec: A Cornerstone of Bioindustry Development.*

Readers will note that this report differs from its predecessors. The topic is highly specialized and the field still in its infancy. However, the issues discussed are such and the actions required so urgent that the Council, fully conscious of its prospective responsibilities, felt it advisable to share its concerns and suggest the avenues it considers most relevant in the short term.

The President

Summary

Purpose of Report

This report deals with bioinformatics, a multidisciplinary technology platform that plays a key strategic role in the development of genomics and proteomics. Its role is to efficiently organize, manage, and analyze the vast amounts of data generated by these cutting edge fields. Bioinformatics must be viewed as one of the cornerstones of current and future developments in biotechnology, pharmaceutical research, and bioindustries in general. However, the scarcity of qualified personnel in this emerging field remains the main stumbling block in the development of bioinformatics worldwide.

Structure of Report

The report is laid out in three chapters. The first provides an overview of the international scientific and industrial context in which the field of bioinformatics is currently evolving. The second chapter outlines the situation in Québec and the rest of Canada. It draws attention to the benefits and opportunities that developing bioinformatics in Québec will provide, as well as the main challenges ahead. The third chapter suggests an overall strategy for quickly organizing and structuring the nascent bioinformatics industry in Québec.

What's at Stake for Québec

The main challenges facing the development of bioinformatics in Québec are the following:

1) **Ensuring the growth of Québec's biotechnology industry**
   Since all indications are that expansion of the biotechnology industry will increasingly require mastery of bioinformatics tools and knowledge, the growth of Québec's biotechnology industry will depend to a large extent on local available of the resources the industry requires in this area.

2) **Maintaining the momentum of a leading edge pharmaceutical R&D sector in Québec**
   Pharmaceutical multinationals have set up mostly R&D facilities in Québec. We know that these companies need to reorient their research strategies in order to tap the potential of genomics and proteomics. It is therefore in Québec's best interest to develop expertise in bioinformatics to meet this need.

3) **Offering Québec's ICT companies attractive growth opportunities**
   One recent trend has been the massive move by key ICT players (IBM, Compaq, Hitachi, and others) into the field of bioinformatics. World demand is set to take off. If we can develop demand in the

Québec market, Québec ICT companies will enjoy very attractive growth opportunities.

4) **Speeding up the integration of genomics and proteomics into other Québec bioindustries**
   Despite the fact that the biopharmaceutical sector is driving world developments in bioinformatics, spin-off effects are already being felt in the biofood, silviculture, and environmental industries, among others. In the coming years, more and more bioindustries in Québec will have to integrate and take advantage of genomics and proteomics, and thus rapidly become users of bioinformatics..

Important Advantages for Québec

Although Québec, too, is faced with the problem of a shortage of human resources in bioinformatics, it has advantages it can exploit to develop expertise in the field.

1) **Scientific research of internationally recognized quality** in the biomedical sector, especially in fields dependent on bioinformatics such as pharmaceuticals

2) **A highly skilled scientific and technical workforce** in life sciences and biotechnology

3) **The presence in Québec of vibrant biopharmaceutical and biotechnology industries** that will increasingly have to depend on bioinformatics for growth

4) **A strategic location** providing quick access to major university and industry research centers and to the North American market

5) **A wide array of high tech development support measures** that could benefit the bioinformatics industry, notably very favorable tax treatment and the presence of venture capital corporations

6) **A very strong ICT industry**, as well as a number of high-performance computing centers

7) **The Genome Canada and Génome Québec programs** that in the coming years will be supporting projects heavily reliant on bioinformatics.

Presentation of the Strategy

The strategy chosen by the Council is to propose fast, targeted investment in a number of key areas that can spur bioinformatics development in Québec. This strategy will allow simultaneous action on three fronts—in human resources training, in making bioinformatics a key part of the Québec research network in genomics and proteomics and a field of research in its own right, and in supporting the development of industry know-how in bioinformatics.

Key Role of Génome Québec

For such a strategy to succeed, someone must be in charge of organizing and coordinating it. The Conseil de la science et de la technologie suggests that this mission be entrusted to Génome Québec. The Government of Québec set up Génome Québec to ensure the development of genomics and related fields in Québec. No other existing organization has a mandate so well adapted to meeting the requirements laid out here.

The Council therefore makes the following recommendations:

Training

Recommendation #1
As a number one priority, implement an intensive bioinformatics training and skills upgrading program in Québec by September 2001

Recommendation #2
Provide some ten fellowship candidates the opportunity to acquire advanced training in bioinformatics outside Québec, if possible beginning in winter 2002

Recommendation #3
Set up bioinformatics graduate study programs and activities in Québec as quickly as possible

Research and Networking

Recommendation #4
Develop the bioinformatics sector in Québec through a network of formative research projects in genomics, proteomics, and bioinformatics itself

Technology Transfer

Recommendation #5
Starting in 2002, provide Québec bioindustry companies with tax incentives specifically linked to the hiring of bioinformatics personnel

Industry Developments

Recommendation #6
Closely monitor the development of genomics, proteomics, and bioinformatics in Québec over the next three to four years, as much from a scientific point of view as from an industrial and social one.

Introduction

Purpose of Report

With the creation of Génome Québec, the government of Québec has clearly signaled its interest in genomics and proteomics, two fast-emerging scientific fields that will have major medium and long term economic impact.

This initiative is intended to help structure a network of expertise and foster an enhanced role for Québec in developing this vast domain of research and applications.

This Council report is a direct reflection of this perspective. It deals specifically with the development of bioinformatics, a field crucial to the development of the genomics and proteonomics sector in Québec. Bioinformatics expertise is essential both to research centers and to industry.

In fact, it is very clear that effective investments in genomics and proteomics in Québec must be based on a solid analytical capacity in bioinformatics. Putting this infrastructure in place requires precisely, carefully targeted measures in the very short term. It is essential that we act quickly and efficiently to establish training capacity in the field, that we link bioinformatics with the development of a genomics and proteomics research network, and that we facilitate the recruitment of bioinformatics specialists in bioindustries.[1] Time is of the essence. The next two or three years will be decisive.

The Council considers that Québec has what it takes to become a major international player in bioinformatics and to foster the development of its bioindustries so long as it acts quickly and effectively. The strategy it sets out in Chapter 3 to this effect is unavoidable. All stakeholders must familiarize themselves with it and work closely together to reach the objective.

Importance of Bioinformatics

Bioinformatics is a multidisciplinary technology platform that brings together computer scientists, software and hardware developers, mathematicians, statisticians, and biologists. Its primary role is to efficiently manage and analyze data generated by the life sciences. It encompasses a range of integrated knowledge and techniques requiring specialized training in all the disciplines it draws upon.

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[1] The term bioindustries is a general term used to describe all companies active in the vast and varied biotechnology sector. For example, the member businesses of BIOQuébec, formerly the *Association québécoises des bio-industries*, include companies in fields such as human health (including biopharmaceuticals), animal health, agriculture, biofood, forestry, and the environment.

Economic and Social Impact

The economic impact of bioinformatics is primarily indirect. It is too early to predict the creation of a genuine bioinformatics industry. In contrast, however, the huge bioindustries sector will increasingly require bioinformatics resources to design and develop product. The pharmaceutical industry, for example, is undergoing a sea change in how it organizes R&D activities. Identification of therapeutic targets and drug development is increasingly dependent on information resources, i.e., massive use of gigantic computerized databases.

On a global scale, the development of genomics and proteomics holds out immense promise for the well-being of the world's population. In the health field, for example, major breakthroughs in the prevention and treatment of genetic illnesses, cancer, and degenerative nerve disease are expected in the years ahead. This is particularly significant for Québec, which is on the cutting edge in a number biomedical research sectors. Here, again, the development of bioinformatics will prove a crucial tool.

We cannot overlook the controversy surrounding the genetic manipulation of certain living organisms. Not all scientific and technological breakthroughs are socially desirable or acceptable. Although these ethical preoccupations do concern bioinformatics directly, the Council is fully aware of the issue. It also believes that the existence of concern and potential risk is a very good reason for Québec to be actively involved in developing the genomics and proteomics sector. It is by developing independent expertise in these cutting edge sectors that Québec society can effectively stay abreast of international developments in the field and make the most well-informed decisions possible. Génome Québec has a major responsibility in this regard since it must keep the public informed and assess the social impact and ethical dimensions of genomics and proteomics research.

In a similar vein, the Minister of Research, Science and Technology held a vast consultation on his draft science and technology policy in the summer of 2000. In the draft document, he announced plans to set up a science and technology ethics committee under the auspices of the Conseil de la science et de la technologie. Although a final version of the policy had not yet been released at the time of writing, the Council will clearly take a close interest in the ethical dimensions of its report topics in the years ahead.

Report Structure

The report is laid out in three chapters. The first provides an overview of the international scientific and industrial context in which the field of bioinformatics is currently evolving. The second chapter outlines the situation in Québec and the rest of Canada. It draws attention to the benefits and opportunities of developing bioinformatics in Québec, as well as the main challenges ahead. The third chapter suggests an overall strategy for quickly organizing and structuring the nascent bioinformatics industry in Québec.

Chapter 1

International Perspectives for Bioinformatics

1.1 What is bioinformatics?

A Multi-Disciplinary Science

The term bioinformatics (or computational biology) originated in the mid 1980s and refers to the use of computer technology in the biological sciences. Bioinformatics is an interdisciplinary science derived from the convergence of the life sciences and information technology. It involves the organization, storage, processing, analysis, and dissemination of biological information by computer and has applications in fields as diverse as genetics, molecular biology, neurophysiology, ecology, and artificial life (simulations of natural living systems).

Bioinformatics is employed worldwide by research groups at universities, corporations, and national and international consortiums. It is considered one of the cornerstones for present and future developments in biotechnology.

Bioinformatics and Genomics

The contribution of bioinformatics to the development of genomics over the past several years has focused particular attention on its importance. During the course of the past decade, molecular biology has progressed rapidly on two main fronts: the increased automation of sequencing processes, and the development of the information technology required to compile and analyze the results. The phenomenal quantity and complexity of the information gathered and analyzed as part of the Human Genome Project has generated strong demand for the use of a high capacity computer platform. At the same time, the genomes of several other organisms (including the fruit fly and the mouse) were being systematically mapped in American, European, and Japanese labs, leading to the creation of ever-larger comparative databases.

From Genomics to Proteomics

Although the focus of intense media attention, the major scientific breakthrough announced by the president of the United States on June 26, 2000, was more a starting point than any kind of true conclusion. The mapping of the human genome, now almost complete, has been a vast international effort in scientific cooperation (and competition), which will very soon yield a complete and remarkably precise description of our genetic identity. However, to make this information fully usable, we must still determine the function of each gene (and the circumstances in which each gene expresses itself) as well as the possible relationships between gene mutations and known physiological disorders. An improved understanding of gene function will lead to another, even more challenging and complex phase of research—analyzing the structure and functions of the proteins expressed by genes.

High-Powered Equipment and Networks

The quantity of data generated by such operations is one of the reasons why bioinformatics has become such a crucial technology platform for supporting genomics and proteomics research. It also explains why access to high-powered data processing capability is key to bioinformatics operations. In 1998, for example, biomolecular applications accounted for the largest proportion of machine time on U.S. National Science Foundation computers. We also know that the success of Celera Genomics, the company famous for its work mapping the human genome, is largely due to a powerful network of computers interfaced with sequencing devices. However, since this type of equipment is extremely expensive, most laboratories must seek out alternative solutions, such as networks of microcomputers or workstations. In addition, more and more people are turning to the Internet to access and exchange data and software, and to farm out high volume data processing operations and calculations.

Large Public Databases Accessible Via Internet

Genomics and bioinformatics are among the fields of scientific endeavor that have benefited the most from the Internet, not only in terms of collaboration and information-sharing between labs and research centers, but also because a number of major databases can be consulted via the Web: the GDB (Genome Data Base) at Johns Hopkins University, the Genbank at the National Center for Biotechnology Information, the EMBL at the European Molecular Biology Laboratory, SWISS-PROT at the University of Geneva, the European Institute of Bioinformatics, etc.

Since its establishment some twenty years ago, Genbank, for example, has seen the number of database entries increase exponentially since the debut of the Human Genome Project in the early 1990s. It now includes over six million DNA sequences and seven billion nucleotide sequences, and reportedly doubles in size every seven months. The Protein Data Bank (PDB) run by the Research Collaboratory for Structural Bioinformatics (RCSB) consortium is also expected to triple in size over the next five years.[2]

A Tidal Wave of Data

The fundamental role of bioinformatics is to effectively organize, manage, and analyze vast quantities of information. Celera Genomics, which announced the completion of the first "draft" map of the human genome in April 2000, claimed to have 50 terabytes of information—the equivalent of 80,000 compact discs—at its disposition. Company vice president Gene Myers has described it as a "tsunami of information."[3]

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[2] Helen Berman et al., "The Protein Data Bank and the Challenge of Structural Genomics," *Nature: Structural Biology*, Volume 7, Supplement, November 2000, p. 957.

[3] Quoted in Ken Howard, "The Bioinformatics Gold Rush," *Scientific American*, July 2000, p. 58.

Data Mining

However, it is not enough to simply store information correctly in a database. Researchers must be able to explore the raw data obtained through sequencing and transform it into usable knowledge. To do so, programs must be designed and used to search, compare, and analyze data in an intelligent manner. *Data mining*, a modern-day version of data analysis that draws upon statistical techniques, artificial intelligence, and neuronal networks, makes it possible to go through huge quantities of information stocked in data warehouses and extract the most relevant relational schemes, schemes undetectable by any other means. The development of this fast-growing technique, which is also used in other sectors dependent on fast, effective analysis of information (finance, marketing, transportation, etc.), is directly linked to increases in computing power.

Data Integration

Another important challenge in bioinformatics is the integration of data from different sources. Every sequence indexed in a genomics or proteomics database must be "annotated" to include information on the state of knowledge on each. Information attached to each sequence includes the source organism, a relatively brief description of sequence functions, and bibliographic references. However, annotation structure and quality vary from one database to another. Systemizing the annotation process means cross checking data and information from a wide variety of sources that is structured in different ways. As a result, one of the basic operations in bioinformatics is to search for similarities and homologies between new and existing DNA sequences. Among other things, this type of integration makes it possible to determine which type of proteins new sequences are likely to code and opens up additional avenues for research.

Standardization

Another major bioinformatics challenge is ensuring database interoperability, i.e., the ability to jointly use different databases to meet user needs. This is no mean feat and efforts are currently underway, notably by international organizations, to standardize basic genomics and proteomics database formats. One example, the BioStandards project of the European Bioinformatics Institute (EBI), an initiative jointly financed by the European Commission and a large number of participating pharmaceutical companies, aims to standardize the practice of bioinformatics in the industry with measures aimed at database structure, software, and training.

Despite what is sometimes said in the media, genomics is not about to disappear just because the mapping of the human genome is virtually complete. The genomes of other species remain to be mapped, notably for applications in agriculture, silviculture, and livestock breeding, for example. More importantly, in order to use data on the human genome effectively, we must be able to compare it with genomic data from other species.

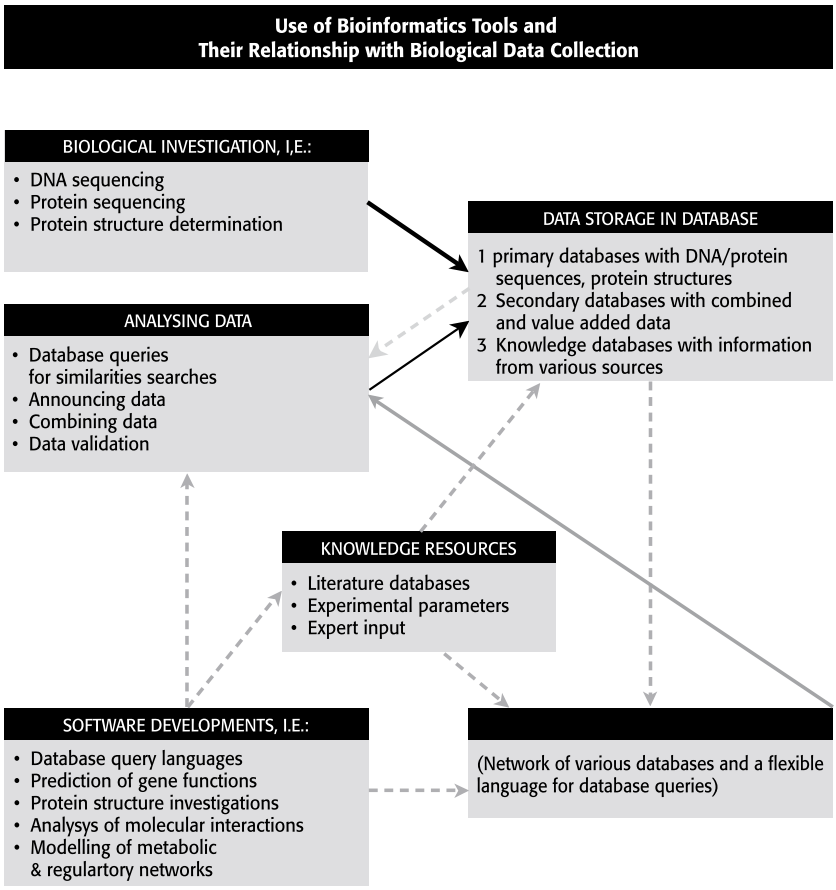
An Area of Growing Importance

There is, however, no denying that the center of attention has shifted away from genomics *per se* in recent months to what is called post-genomics or proteomics. This "second phase," which focuses on how genes express

themselves in the form of proteins and enzymes, as well as on the functional and structural analysis of the proteins themselves, will further enhance the importance of bioinformatics and fuel even greater demand for specialists in the field. Industry and research centers alike will be required to build and operate more complex databases, develop new analytical software, and mobilize even greater computing power than that available in the past.

The linear analysis of DNA sequence composition and the identification and localization of genes on chromosomes are huge tasks (and as yet incomplete). Identifying how and under what circumstances genes express themselves in the form of proteins, either individually or in groups, is even more complex. And analyzing protein composition (tabulation of amino acids) and especially protein architecture (their shape and the way they deploy in space) represents an even higher degree of complexity.

However, it is only when we reach this ultimate step—correctly describing the structure of proteins and deducing their functions—that the real benefits of proteomics and bioinformatics will truly be felt.



Based on: Petra Düx and François Moille, *Bioinformatics: An Inventory and Analysis of Recent Developments in Bioinformatics and Related Areas of Research and Development,* Institute for Prospective Technological Studies, Seville, September 1999, p. 12.

In silico

Bioinformatics is constantly evolving. Some observers unhesitatingly affirm that it will play a crucial role in all major developments in biology in the 21st century, a role comparable to that of math in physics. Others talk of a new paradigm. More and more people are using the term *in silico* (as opposed to *in vivo* and *in vitro*) to describe this new way of analyzing information on biological processes through intensive use of computers.

Bioinformatics will also become a focus for high tech convergence. For example, photonics technology plays a role in the reading of biochips and microarrays, biochemical probe matrixes that allow for rapid genetic analysis. In the long term, we can envisage a linkage with nanotechnology and, eventually, the creation of biomolecular or DNA-based computers.

1.2 Bioinformatics and industry

A Fast-Emerging Field

It is very difficult to assess the growth of bioinformatics in economic terms. The lack of reliable statistical data should come as no surprise given that bioinformatics is a fast-emerging field for which industrial standards have yet to be established. For example, much of the technology in use (much of it software) has been developed and circulated free of charge, particularly via the Internet, and therefore escapes the usual market analyses. By late 1999, however, bioinformatics companies (or companies with extensive bioinformatics operations) were springing up in increasing numbers, even though most were not yet listed on the stock exchange. In 1999, the performance of so-called bioinformatics firms considerably exceeded that of the biotechnology sector as a whole.[4]

Like all multidisciplinary technologies with considerable potential for enabling applications, the exact future of bioinformatics is impossible to predict. Although observers agree that it will play a crucial role in the new post-genomics era, growth projections vary by up to 100%. In early 1999, Strategic Management Consulting Inc. predicted that the international bioinformatics market would quadruple in five years, from $290 million in 1998 to $1.2 billion in 2005.[5] Another firm, SRI Consulting, believes the market will hit the billion

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[4] Lulu Pickering, "BioInformatics Public Firm Stocks," *Genetic Engineering Ne*ws, Vol. 19 No. 20, November 15, 1999, p. 17.

[5] Cited in *Genetic Engineering News*, Vol. 19, No. 4, February 15, 1999, p. 1.

dollar mark somewhere around 2004.[6] Other analysts, such as Oscar Gruss & Son, predict sales of up to two billion dollars by 2005.[7]

A study conducted by the Chair in bioindustries management at UQAM suggests dividing the bioindustry into five main segments:

1) **Technology providers** who supply bioinformatics operating systems and other technology platforms (biochips, sequencing)

2) **Providers of analytical instruments** who design software, data mining and visualization systems, etc.

3) **Providers of databases** in the form of annotated sequences

4) **Knowledge providers** who transform raw data into client-usable knowledge

5) **Integrated genomics enterprises** simultaneously involved in gene identification, functional genomics, proteomics, and the development of therapeutic agents

The fourth segment is viewed as particularly promising. Knowledge providers supply custom-tailored structured information to their clients by way of subscription systems, partnership agreements, or Internet portals.[8]

A Bioinformatics Industry?

It is undoubtedly too early to talk about the establishment of a veritable bioinformatics industry. A number of companies have developed and commercialized data analysis software, but these are highly specialized products that do not necessarily have broad market applications. Bioinformatics solutions continue to be developed in large measure to meet specific needs, with little hope of standardization in the short term. Analysts have noted that companies set up to provide bioinformatics services still have difficulties staying for the long haul.[9] The reasons for this can be multiple. One of them is that much of the software developed for bioinformatics applications has been made available

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[6] Andrew Broderick, *Bioinformatics: An Emerging Role in Life-Sciences Research*, SRI Consulting, 2000, p. 1.

[7] Quoted in Ken Howard, *op.cit*., p. 58.

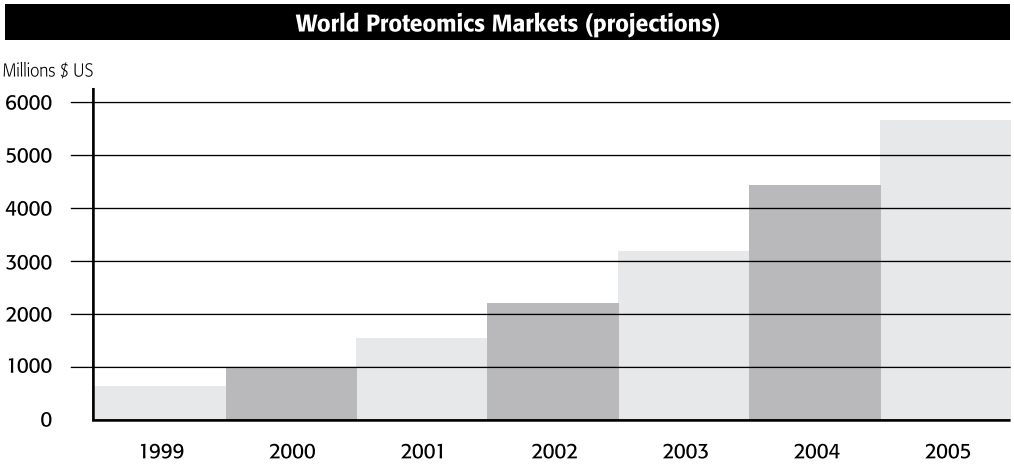
[8] *Développement de la bio-inormatique au Québec: Opportunités et priorités*, Chaire en gestion des bio-industries, École des sciences de la gestion, Université du Québec à Montréal, forthcoming.

[9] Petra Düx and François Moille, *op.cit.*, p. 29-31.

free over the Internet. The European Bioinformatics Institute has listed over 500 of these tools.[10]

Even though the future of bioinformatics as a distinct industry remains rather uncertain for the moment, the field is clearly crucial to the development of a number of genomics and proteomics-based industrial sectors. "The ability to gather, store, classify, analyze, and distribute biological information derived from mapping and functional analysis projects is so fundamental to modern biotechnology that companies and funding bodies alike are banding together in unprecedented ways to help each other and scientists at large to perform the task." [11]

It is in this fundamental supporting role that bioinformatics will have its greatest economic impact. In the years ahead, the growth of the platform will be closely linked to that of its industrial customers, who will seek to take advantage of this strategic resource. Proteomics, in particular, with its shorter term potential for commercial applications, should experience phenomenal growth. The field is so huge, and the niches so plentiful, that untold numbers of small proteomics-based firms are springing up worldwide. Large companies are also jumping in: on the heels of its success in mapping the human genome, Celera Genomics has created a new subsidiary, PE Corp., which is expected to develop a protein sequencing capacity of 30,000 samples an hour.



Source: Frost & Sullivan, *World Proteomics Markets*, Report # 5822-55, October 2000; reproduced in Stefan H. Unger and Justin Saeks, "Proteomics Research and Development Takes Off," *Genetic Engineering News*, Vol. 20, No. 16, September 15, 2000, p. 17.

[10] Cited in "Bioinformatics," *Nature Biotechnology*, Vol.18, Supplement 2000, p. IT31.

[11] *Ibid*.

The Pharmaceutical Industry: A Prime User

The pharmaceutical industry is one of the sectors that should benefit most directly from discoveries in genomics and bioinformatics. This industry has experienced growing pains in recent years, especially due to ever-increasing drug development costs. The world's twenty most powerful pharmaceutical companies have virtually doubled their R&D spending over the past seven years. A Price Waterhouse Coopers study found that to maintain reasonable growth in sales (approximately 7% per year for the industry as a whole), the big pharmaceutical companies will have to entirely rethink their approach to R&D and significantly cut costs.[12]

A Paradigm Shift

The advent of genomics and proteomics will allow for more effective rationalization of the drug development process through the use of highly precise therapeutic targets. Many observers have spoken of a "paradigm shift." Better understanding of molecular interaction will allow for more "intelligent" R&D design as the classical trial-and-error approach yields to a predictive approach that is more effective, more economical, and safer, too.[13] Through what is now called pharmacogenomics—the study of interindividual genetic variations and their influence on response to drugs—pharmaceutical companies will be able to develop highly specific new drugs that are adapted to individual patient profiles and have fewer side effects.

The SNP Consortium

For the pharmaceutical industry, the stakes are high. Rather than duplicate their efforts, over ten of the world's biggest drug companies recently teamed up with five major public genomics labs to form the international SNP Consortium, whose goal is to identify 300,000 SNPs within two years. SNPs (single nucleotide polymorphisms or "snips") are sites in the human genome marking genetic variations between individuals. SNPs are of considerable strategic importance for accelerating the localization of genes associated with different diseases and developing drugs adapted to patient profiles. The Consortium, which is also financed by Wellcome Trust, will make its database public.

In-House Bioinformatics Development

To acquire expertise in bioinformatics, companies in the pharmaceutical sector sometimes call upon other firms, but are more inclined to develop in-house capacity rather than outsource it, as they do for other information technology services. The same can be said for the big biotech firms, especially those active in genomics.[14] This preference for in-house expertise in bioinformatics has attracted the attention of the Institute for Prospective Technology Studies, which attributes the trend to the difficulty in establishing a productive dialogue between specialists in the life sciences and computer scientists. The dialogue is

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[12] *Pharma 2005*, *An Industrial Revolution in R&D*, Price Waterhouse Coopers, 1999.

[13] See Broderick, *op. cit.*, p. 9.

[14] "Bioinformatics", p. IT33.

more likely to yield results when all parties work for the same company. Yet even when companies do develop in-house bioinformatics expertise, it is not always easy for the experts to understand user needs and develop the appropriate data processing tools.[15]

Other Applications

In the medium term, industrial applications for bioinformatics will multiply outside the pharmaceutical sector. The environmental protection field is a good example. In agriculture, the increasingly important role of biotechnology in new product development and in the fight against pathogens and parasites will increasingly depend on developments in genomics and proteomics. As in the biopharmaceuticals sector, the mapping of plant genes will lead to the creation of huge databases that businesses will be able to use on a systematic basis. Here, the boundaries between industrial sectors are anything but closed. The pooling of information on plant and animal genes and proteins could help the pharmaceutical industry as much as the agrifood sector. Companies like Incyte Pharmaceuticals are developing plant genomics activities, whereas giants like Monsanto and Millennium Pharmaceuticals have teamed up to create a new agricultural biotechnology company, Cereon Genomics.[16]

Major Investments by ITC Firms

Lastly, bioinformatics has started to attract the attention of software and electronics manufacturers. In Japan, Hitachi recently announced a $56 million R&D investment in bioinformatics. Compaq Computers, a partner of Celera Genomics and the supplier of much of the computer equipment used to map the human genome, has created a center of expertise in bioinformatics in Marlboro, Massachusetts. In December 1999, IBM announced the construction of Blue Gene, a computer a thousand times faster than its celebrated Deep Blue and whose first task will be to the analyze the three-dimensional folds of an extremely complex protein made up of 324 amino acids. IBM estimates that the international market for information technology applications in the life sciences will climb from $3.5 billion to $9 billion by 2003.[17]

1.3 National and International Initiatives

Numerous International Initiatives

Development of bioinformatics is the focus of initiatives in research, training, and dissemination of information in many countries. There are a number of international organizations in the field, such as the International Society for

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[15] Düx and Moille, *op.cit.*, p. 27-28.

[16] *Ibid*., p. 13.

[17] Anita Flanagan, "Racing to Conquer Biodata With Computers," *Genetic Engineering News*, Vol. 20, No. 17, October 1, 2000, p. 8.

Computational Biology, APBioNet (for the Asia-Pacific nations, including Canada), and the European Bioinformatics Institute. An Internet search turns up bioinformatics organizations and agencies in several European countries—especially Germany and France—as well as in Japan, Australia, and especially the United States. There are also bioinformatics centers in countries like India, Korea, Malaysia, Singapore, and Israel.

In the United States

In the United States, the main players are private corporations. However, the big American universities also have bioinformatics centers linked to research groups working on the mapping of the human genome. Some of these groups only use existing tools whereas others develop software, methods, and services of their own.

U.S. government agencies are also active in the field. Both the Energy Department and the Defense Department finance projects in bioinformatics. However, the biggest player is the network of National Institutes of Health (NIH), the sponsor of the Human Genome Project. Since 1988, one particular network institution—the National Center for Biotechnology Information (NCBI), which is affiliated with the National Library of Medicine—has emerged as a key reference center in the field. NCBI develops and manages public databases, designs tools for data interrogation and analysis, conducts research, and disseminates information

NIH recently launched the Protein Structure Initiative, under which $125 million is to be invested over five years. One NIH member institution, the National Institute of General Medical Sciences, has set a target of identifying the structure and deployment of 10,000 proteins within 10 years, and recently invested $30 million in a first round of research.[18] There is also a significant portion of bioinformatics funding that comes from private foundations, such as the Howard Hughes Medical Institute.

In Europe

In Europe, the leading bioinformatics facility is the European Bioinformatics Institute, a component of the European Molecular Biology Laboratory (EMBL), which groups together organizations from 15 countries. The Institute, which is located at the Wellcome Trust Genome Campus in Hinxton, England, is one of the world's major centers for research in genomics, proteomics, and macromolecular structures. Its chief mission is to make findings in genomics and proteomics available to research groups and industry. Forty percent of funding comes from the European Community, 30% from EMBL, and 30% from industry.

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[18]John C. Norvell and Alisa Zapp Malachek, "Structural Genomics Programs at the U.S. National Institute of General Medical Sciences," *Nature Structural Biology*, Volume 7, Supplement, November 2000, p. 931.

A number of bioinformatics centers are part of the European Molecular Biology Network (EMBnet). From its initial European core, the network has expanded to include centers in countries like Argentina, Canada, Russia, China, India, and Israel. Funding is shared by the European Community and the various member countries.[19]

In France

Certain countries have launched major genomics and post-genomics initiatives. In 1999 in France, for example, the Ministère de l'Éducation Nationale, de la Recherche et de la Technologie set up a national bioinformatics resource center—INFOBIOGEN—to replace the consortium of the same name in existence since 1995. The center's mission is to accelerate cooperative genomics research by providing computer tools and developing new services available to the scientific community as a whole.

INFOBIOGEN

The mission of the INFOBIOGEN Resource Center is to—

1. Develop and operate general bioinformatics services for the following purposes:
   - Provide the French scientific community with access to databases, notably by providing user connections to national and international networks and facilitating access to up-to-date biological information (access to EMBL daily sequences and other major international databases)
   - Establish data analysis and interrogation facilities to make use of available databases
2. Provide training and assistance to Center users
3. Coordinate the national computer network for Genomics research and services and take part in national and international discussions and coordination initiatives in bioinformatics
4. Promote French-made software and databases
5. Develop and operate on a national level the calculation codes and databases used in genomic research
6. Conduct research and development in applied computing in the genomics field, notably with regard to software for intensive genome analysis, modes of interconnection and dissemination for large databases, and environments fostering cooperative research through communication networks

Source: http://www.infobiogen.fr/presentation/infobiogen.html (Our translation)

[19] Düx and Moille, *op.cit*. p.21. See also Helen Gavaghan, "Europe Seeks Solution to Bioinformatics Shortfall," *Nature*, 404, April 6, 2000, p. 688.

1.4 A Worldwide Shortage of Human Resources

Demand for Specialists Far Outstrips Supply

The bioinformatics field is still relatively new and global demand for specialists is growing fast. As genomics and proteomics databases develop and grow and potential for industrial data applications expands, demand will only increase further. In fact, there is already a shortage. In Europe, despite the presence of respected bioinformatics centers and numerous client industries, the shortage is the main problem identified in a study commissioned by Seville's Institute for Prospective Technology Studies. The authors of the study affirm that the problem is serious enough to compromise Europe's ability to compete with the United States in the bioinformatics field.[20]

Yet the United States also faces recruitment problems in bioinformatics. especially in the university community. Industry demand for graduates is so strong that it is extremely difficult to ensure an influx of new blood for training and basic research. The situation has been deemed sufficiently critical to justify targeted intervention by the NIH and private foundations like the Howard Hughes Medical Institute. The NIH network is about to provide funding for 20 national bioinformatics training centers. Another organization, the Alfred P. Sloan Foundation, recently called for tenders for the creation of a two-year Master's program in bioinformatics, the idea being to meet industry demand more effectively while keeping more Ph.D.s in university.

The Training Issue

Bioinformatics calls for a relatively rare combined skills set for which the major disciplines of molecular biology and computer science traditionally provided no training. Even in the United States, where demand has increased exponentially, universities have been slow to set up suitable training and specialty programs.[21] Only since 1997 have universities in the United States and elsewhere begun to include bioinformatics courses in their programs. This means that many of the developments in bioinformatics have been the fruit of individuals with "ad hoc" training— life sciences researchers who have sought out additional courses in computer and information technology, or computer specialists who have adapted their skills to meet the needs of biotech, genomics, and molecular biology labs.

At present, countries like the United States and England have integrated bioinformatics into university curriculums, offering joint programs in biology and computer science that enable students to master both worlds. Yet according to the study by the Institute of Prospective Technology Studies in Seville on the

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[20] *Ibid*. p. 6.

[21] See Paula E. Stephan and Grant Black, "Bioinformatics: Does the U.S. System Lead to Missed Opportunities in Emerging Fields? A Case Study," *Science and Public Policy*, December 1999, p. 382-393.

state of bioinformatics in Europe, traditional compartmentalization continues to dominate in the training of specialists in life sciences and information technology. The authors of the study attribute this lag to the extensive shortage of professional bioinformatics resources in European industry.[22]

The general trend is to seek out solutions to this problem. An increasing number of universities worldwide are offering bioinformatics courses and degree programs. The International Society for Computational Biology lists them on its Website. An increasing number of training and skills development options are also available online via the Internet.

The situation in the bioinformatics industry can be summarized as follows: high demand for specialists that can be expected to increase in spectacular fashion worldwide, coupled with still insufficient training opportunities that must be organized and funded as quickly as possible.

[22] Düx and Moille*, op.cit.*, p. 22.

Chapter 2

Outlook for Bioinformatics in Canada and Québec

2.1 The Situation Across Canada

Canada Is Not A Leading Player in the Field

Existing Internet lists of international research organizations, centers, and groups contain only very few Canadian references under bioinformatics or even genomics. However, even without being leaders in the ongoing revolution in genetic research, Canada and Québec have strengths that, with the right resources and strategies, can enable them to reap economic benefits from this field. For one thing, massive worldwide demand for bioinformatics will increasingly affect Canada's and Québec's biopharmaceutical and biotechnology sectors. At the same time, the potential applications of genomics and proteomics research are so numerous and diverse that secondary players or late entrants into the race like Canada and Québec still have the opportunity to establish a strong position.

In both Canada and Québec, it is difficult to separate the evolution of bioinformatics from the field of genomics, as the two have been very closely linked. Thus, a reference study conducted for Genome Canada by the OST (Observatoire des sciences et des technologies) reveals that from 1995 to 1997, Québec (40%) and Ontario (39%) led the way in genomics or genomics-related research in Canada. However, only 0.7% of Canadian articles in this area were clearly devoted to the specific field of bioinformatics.

The NRC Technology Network, the BRI

The National Research Council of Canada (NRC) technology network includes a number of centers of excellence in bioinformatics. For example, the Informatics Group at the Institute for Biodiagnostics in Winnipeg specializes in the computer analysis of biological data, while the Institute for Marine Biosciences in Halifax is charged with operating and managing the Canadian Bioinformatics Resource (CBR), a national facility providing access to biotechnology-related databases and bioinformatic software tools. The CBR also provides services to biotechnology firms and university research teams.

In Québec, the genetics department of the NRC's Biotechnology Research Institute (BRI) does work on genomics and bioinformatics. The BRI is particularly interested in the development of microarrays. With a 500 strong research team and an annual operating budget of about $20 million, the BRI is considered one of the biggest biotechnology research centers in North America. To a very large extent, the BRI's research activities are carried out jointly with or for industry.

Networks of Centers of Excellence (NCEs)

The biggest Canadian network of centers of excellence (NCE) involved in bioinformatics is the Canadian Genetic Diseases Network (CGDN), which conducts leading edge research in human health. In collaboration with the Biotechnology Human Resources Council, a not-for-profit organization that promotes the quality of human resources in biotechnology, the CGDN puts on bioinformatics training workshops in all regions of the country. The objective set back in 1998 is to train at least 300 bioinformatics experts and 1,500 advanced users over the next few years.

Another important NCE is the Protein Engineering Network of Centers of Excellence (PENCE). PENCE's lead center is based at the University of Alberta, but it includes 12 university researchers in Québec, 12 in Ontario, and 13 in British Columbia. It should also be noted that, in early 2000, the federal government issued a call for proposals to establish a new NCE in the area of "genomics technologies and society."

Other Canadian Centers of Excellence in the Field of Bioinformatics

Other major Canadian centers of excellence in the field of bioinformatics include the following:

1) The Bioinformatics Supercomputing Centre (BiSC) at Toronto's Hospital for Sick Children, which manages and is partly developing the Genome Database at John Hopkins University in Baltimore, which serves as the repository for data from the Human Genome Project

2) The Samuel Lunenfeld Research Institute (SCRI) of the Mount Sinai Hospital in Toronto, a prestigious research center founded in 1985 that has pioneered research in genomics, proteomics, and bioinformatics in Canada

3) The Vancouver-based Centre for Molecular Medicine and Therapeutics (CMMT), which is affiliated with the University of British Columbia and is doing bioinformatics work related to research in genetic diseases

4) The Vancouver-based Centre for Integrated Genomics (CIG), a network of centers created in 1999 by the University of British Columbia and the BC Cancer Agency that is conducting bioinformatics research on applications for genomics in medical oncology

Genome Canada

Until the recent creation of Genome Canada, a not-for-profit corporation, Canada was one of the few developed countries to have no national genomics program. With a $160 million startup federal government grant spread over five years, Genome Canada plans to raise $800 million to enable it to significantly expand genomics research both, at the university and industry levels. The organization plans to create a network of five Canadian genomics centers in the

various regions of the country. These centers would in turn be responsible for bringing together and coordinating local resources.[23]

Canadian Institutes of Health Research (CIHR)

The restructuring of federal government funding programs for health research presents another opportunity for the development of bioinformatics in Canada. The new federal agency for health research—the Canadian Institutes of Health Research (CIHR), more or less fashioned after the U.S. National Institutes of Health—plans to establish 13 specialized institutes across Canada, including one focusing on the application of genetics and genomics research to health care. CIHR has a total budget (including research grants) of $340 million.

Few Firms, Often Small in Size

A survey of Canadian biotechnology firms conducted by the Chair in Management of Bioindustries at UQAM (Université du Québec à Montréal) reveals that the sector is still very much in its infancy. Indeed, there are only 14 dedicated biotechnology firms (DBFs) in Canada, most of which are just starting out. Ten are based in Ontario and a good number of them would appear to be spinoffs from university centers or research networks. These firms mostly fall into the category of "suppliers of analytical instruments" (see glossary in section 1.2). Although Québec still has few DBFs, it is home to 40% of Canadian companies involved in functional genomics—major consumers of bioinformatics. However, the total internal Canadian market is extremely small and mostly constitutes a late and still modest extension of the expanding genomic-proteomic-bioinformatics industrial cluster in North America. It is clear that for the vast majority of Canadian firms, the competition is abroad.[24]

Competitive Advantages

Nevertheless, a number of competitive advantages are taking shape for Canadian companies. To begin with, the growth potential of the general field of applied genomics and proteomics is so great and possible applications so diverse that, for several years to come, there will still be ample room for new and specialized firms able to position themselves to satisfy emerging needs. Secondly, these Canadian companies have a significant leg up given their university origins and their proximity to high caliber centers of excellence, seeing that they operate in an industry in which the main engine of growth is leading edge scientific research. Lastly, one of the strong trends in the world bioinformatics market is the increasing expansion of the knowledge provider segment, notably specialized knowledge providers who process and analyze raw data for the specific needs of clients (identification of gene targets in drug research, for example). This is an area where Canadian expertise can make its mark.

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[23] Genome Canada, *Business Plan*, November 29, 1999.

[24] *Développement de la bio-informatique au Québec: Opportunités et priorités.*

Major Challenges for Canadian Bioindustries

At the same time, one of the major challenges facing the bioindustry sector in Canada, like elsewhere, remains the issue of human resources. BIOTECanada, the non-governmental organization dedicated to the advancement of biotechnology in Canada, recently submitted a brief on the development of the bioinformatics sector to Industry Canada.[25] In its analysis of the Canadian situation, BIOTECanada identifies as our main strength the world-renowned excellence of a few researchers and teams of scientists already involved in the field of bioinformatics, be it in universities and hospitals, industry, or government sponsored research centers. The main weakness, on the other hand, remains the glaring lack of training programs in bioinformatics, resulting in a shortage of qualified human resources for the industry.

This diagnosis is similar to what other countries have discovered, but the stakes for Canada are likely still higher than elsewhere. This is because if no training programs are quickly forthcoming to meet the demand for qualified personnel, Canadian bioindustries—a high proportion of which are concentrated in Québec—will have to look outside the country for the human resources they need. The bioinformatics industry is a strategic resource and existing companies, as well as those to come, could be tempted to relocate to where human resources are available. A brain drain is also possible—in the absence of the right infrastructure in Canada and Québec, the best specialists will migrate to places where bioinformatic centers exist and are growing. In the mid-term, this may compromise the growth of firms dependent on genomics and proteomics research as well as weaken all bioindustries in Canada and Québec.

2.2 The Situation in Québec

A Thriving but Still Fragile Québec Biotech Industry

Over the past 20 years, a thriving biotechnology sector has developed in Québec. According to a study for BIOTECanada in 1998, 42% of biotechnology firms in Canada were based in Québec, compared to 24% in Ontario, and 18% in British Columbia. Ontario was, however, found to be ahead of Québec in terms of volume of R&D activity and proportion of companies listed on the stock exchange.[26] These findings differ slightly from data published by Statistics Canada based on a 1997 survey.

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[25] BIOTECanada, *From Information to Knowledge: Canada's Capacity in Bioinformatics*, March 31, 2000.

[26] BIOTECanada, *op cit.,* p. 8.

Distribution of Biotechnology Firms in Canada by Province (1997)

	Number of Firms	%
Québec	86	30
Ontario	71	25
British Columbia	56	20
Alberta	19	7
Saskatchewan	21	7
Nova Scotia	9	3
Manitoba	8	3
PEI, NWT, NB	11	4
Total	**282**	

Source: Statistics Canada, Biotechnology Firm Survey—1997

The biotechnology sector is still far from maturity, to the extent that very few of the existing companies have reached the stage of bringing products to market. A recent study by Jorge Niosi highlights the great difficulty these companies have in getting access to venture capital (two-thirds reportedly don't hold patents on their inventions).[27]

[27] Jorge Niosi, *Explaining Rapid Growth in Canadian Biotechnology Firms,* Research Paper No. 8, Statistics Canada, February 2000.

Some Québec-based Firms Involved in Bioinformatics [28]		
Chemical Computing Group (CCG)	Montréal (1994).	Develops and markets high-end scientific software and services for high throughput screening and computer aided molecular design applied to life and materials sciences
DNA Landmarks Inc.	Saint-Jean-sur-Richelieu (1995).	Firm affiliated with Sweden-based Svalöf Weibull and specializing in the development of detailed genetic mapping tools using DNA markers for the agricultural industry
Ecopia BioSciences Inc.	Montréal (1998).	Identification of microbial genes potentially useful in drug discovery and development as well as genome analysis using high throughput DNA sequencing and bioinformatics
Galileo Genomics Inc.	Montréal (1999).	Identification of gene targets for the pharmaceutical industry using the founder population concept (with the Québec population as the founder population)
Geneka Biotechnology Inc.	Montréal (1995).	Specializing in transcription factors (TFs) and their role in gene regulation, Geneka manages public and commercial databases in this area and has introduced a new cell-based high throughput screening assay to test and validate the effect of screened compounds capable of affecting the regulation of TF expression
GenomicsOne Corporation	Laval (1995).	Develops technology platforms for the manipulation and identification of genes, as well as the development of therapeutic or diagnostic products, and provides genome database development services
PROCREA BioSciences Inc.	Montréal (1990).	A research center, clinic, and genetic diagnosis laboratory rolled into one, PROCREA is notable for using a technology developed at the Université de Montréal that provides a whole new approach to the quick identification of gene targets for therapeutic purposes
SignalGene Inc.	Montréal (1991).	Applied genomics and pharmacogenomics firm specializing in the development of genetic screening tools involving high throughput genotyping as well as statistical and bioinformatics analysis

[28] This list is not exhaustive. Notably, it does not include big pharmaceutical companies.

The Association québécoise des bio-industries currently has 150 members, yet it is difficult to find anyone in either the research community or in industry involved in core bioinformatics. It is certain, though, that the future of the biotechnology industry in Québec, like everywhere else, depends to a great extent on the mining of genomics and proteomics data and, by extension, on a solid bioinformatics infrastructure. Recently, the director general of the Québec Biotechnology Innovation Center (QBIC), the first Québec business incubator specializing in biotechnology, expressed the need for the development of companies specializing in bioinformatics.[29]

The Pharmaceutical Industry Will Increasingly Need Bioinformatics

The biopharmaceutical industry represents one of the most important high tech industries in Québec. The industry benefits from a high quality research community, the presence of major players like BioChem Pharma and the NRC's Biotechnology Research Institute, as well as distinctly favorable tax treatment of R&D activities. It is mainly concentrated in the Montréal area and represents almost half the entire Canadian pharmaceutical industry, with 163 companies, $2.3 billion in shipments and $610 million in R&D activities (1997 figures). A number of the big multinational drug companies have R&D facilities in Québec.

World growth trends in pharmaceuticals, also apply to Québec. The need for a paradigm shift in R&D is an imperative that directly concerns the Québec pharmaceutical industry. As the switch to a product development approach based on the mining of genomic and proteomic databases proceeds, Québec pharmaceutical companies and subsidiaries of multinationals will have to increasingly rely on bioinformatics resources.

A Growing ICT Industry

It should be noted, in addition, that one of the growth sectors of the Québec economy is the information and communication technologies (ICT) industry. An industry profile published by the MICST in June 1998 listed 3,500 companies, with over 80% involved in computer software and services, 10% in telecommunication services, and 10% in hardware and electronic components. In 1997, the industry as a whole posted an estimated $20 billion in sales and employed an estimated 80,000 people. R&D expenditure totaled $600 million in 1995.

To date, these companies do not seem to have paid much attention to the information technology needs of biotech companies, but they could become more active in the field as demand becomes manifest. The Centre de recherche en informatique de Montréal (CRIM), which has no previous project in the field, has just participated in funding a study on bioinformatics opportunities and priorities in Québec. The study was conducted by the UQAM Chair in Management of Bioindustries.

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[29] *Les Affaires*, November 11, 2000, p. A9.

University Centers

Biomedical research has long been the most flourishing field of research in Québec universities, with 38% of funding (compared to 25% for pure sciences and 17% for applied sciences). It is especially within the university research community that Québec's expertise in genomics, proteomics, and bioinformatics has developed, although spread among a number of university research centers such as the Centre de recherche sur la fonction, la structure et l'ingénierie des protéines (Laval) and the Groupe de recherche en modélisation biomédicale (Montréal).

The Montréal Genome Centre, based at the McGill University Health Centre's Research Institute, brings together several research teams working notably on functional genomics. The Centre pays particular attention to the use of computer technology to explore gene regulation processes. It is playing a key leadership role in the development of robotic systems and microarrays.

Over the past 30 years, Québec has developed a strong expertise in population genetics, beginning with the work of the Network of Applied Genetic Medicine and now involving a network of numerous researchers grouped within the Institut interuniversitaire de recherches sur les populations (IREP). This expertise plays an extremely important strategic role in genomics and proteomics research, since population gene databases can be mined to identify at-risk genetic profiles as well as gene targets for new therapeutic products. Indeed, countries like Island and Estonia have capitalized on the relative homogeneity of their populations to develop a pharmacogenomic industry.

High Performance Computing

Québec has also invested in the area of computer modeling and high-performance computing. An example of this is the Centre de recherche en calcul appliqué (CERCA), a scientific computing technology liaison and transfer center providing services to industries such as the pharmaceutical industry. Not only is CERCA the bridgehead for the Réseau québécois de calcul de haute performance (RQCHP), it has also joined other research centers in creating the Network for Computing and Mathematical Modeling (NCM^2) which is part of RQCHP. Lastly, we should note that about 40 Québec researchers from eight universities and 16 firms are part of a federally funded Network of Centers of Excellence involved in mathematical modeling—the Mathematics of Information Technology and Complex Systems (MITACS) network.

For its part, Université de Laval's Centre de calcul scientifique et de bioinformatique is supporting about a hundred subsidized projects by providing the required computing and data processing power and technical assistance. This center's expertise, however, goes way beyond bioinformatics to include such areas as the chemistry of materials and geomatics.

Génome Québec

In its 2000-2001 budget, the Québec government announced $10 million in seed funding for a Québec genome center project. Génome Québec is a not-for-profit corporation mandated to promote and support structuring and developmental activities in advanced genomics research programs and cognate disciplines. The ultimate goal is help to improve Québec's economic competitiveness and growth. Although created just recently, Génome Québec has already issued a call for proposals for projects in two broad categories:

1) **Major Projects and Technological Platforms**—a limited number of major genomics and proteomics research projects and state-of-the-art infrastructure proposals. The projects must have the potential to enhance Québec's impact in these disciplines nationally and internationally, as well as support the development of Québec's biotechnology industry.

2) **Centers of Expertise**—a limited number of centers of expertise providing high volume (service cluster) or more targeted (dedicated provider) services. Centers of expertise must sponsor one or more major project/infrastructure proposal defined in category 1.

The FRSQ has been mandated to evaluate, on behalf of and in collaboration with the other two Québec subsidy funds (FCAR and CQRS), genomics and/or proteomics structuring project proposals submitted to Génome Québec. Proposals are not only restricted to the biomedical field and can involve other areas of application such as agrifood and the environment. Génome Québec is also interested in the ethical, legal, and social aspects of genomics.

2.3 Québec's Challenges and Strengths in Bioinformatics

Challenges and Opportunities

The main challenges facing the development of bioinformatics in Québec are the following:

1) **Ensuring the growth of Québec's biotechnology industry**. Since all indications are that expansion of the biotechnology industry will increasingly require mastery of bioinformatics tools and knowledge, the growth of Québec's biotechnology industry will depend to a large extent on local availability of the resources the industry requires in this area.

2) **Maintaining the momentum of a leading edge pharmaceutical R&D sector in Québec**. Pharmaceutical multinationals have set up mostly R&D facilities in Québec. We know that these companies need to reorient their research strategies in order to tap the potential

of genomics and proteomics. It is therefore in Québec's best interest to develop expertise in bioinformatics to meet this need.

3) **Offering Québec ICT firms attractive growth opportunities**. One recent trend has been the massive move by key ICT players (IBM, Compaq, Hitachi, and others) into the field of bioinformatics. World demand is set to take off. If we can create demand in the Québec market, Québec ICT companies will enjoy very attractive growth opportunities.

4) **Speeding up the integration of genomics and proteomics into other Québec bioindustries**. Despite the fact that the biopharmaceutical sector is driving world developments in bioinformatics, spin-off effects are already being felt in the agrifood industry, environmental management, and silviculture, among others. In the coming years, more and more bioindustries in Québec will have to integrate and take advantage of genomics and proteomics, and thus rapidly become users of bioinformatics.

Québec's Strengths

Québec has over the years established itself as a very competitive location for R&D activities, especially in high technology. In the survey conducted by the UQUAM Chair in Management of Bioindustries, the factor most often cited by respondents (37%) to explain Québec's competitive advantages was the financial support of governments, particularly tax measures.

In addition to attractive tax treatment for high tech firms, Québec enjoys a great reputation for the quality of its brainpower. With the exception of the dearth of specialists in the specific area of bioinformatics, many biotechnology industry leaders cite the availability of a high caliber scientific workforce as the reason for their locating in Québec (Montréal). The expertise of the academic community and its scientific excellence were Québec's second most cited competitive advantage (30%) in the study.[30]

By analyzing these strengths, one can identify a number of key factors that give Québec a leg up in developing expertise in bioinformatics:

1) **Scientific research of internationally recognized quality** in the biomedical sector, especially in fields dependent on bioinformatics such as pharmaceuticals

2) **A highly skilled scientific and technical workforce** in life sciences and biotechnology

[30] *Développement de la bio-informatique au Québec: Opportunités et priorités.*

3) **The presence in Québec of vibrant biopharmaceutical and biotechnology firms** that will increasingly have to depend on bioinformatics for growth

4) **A strategic location** providing quick access to major university and industry research centers and to the North American market

5) **A wide array of high tech development support measures** that could benefit the bioinformatics industry, notably very favorable tax treatment and the presence of venture capital corporations

6) **A very strong ICT industry**, as well as a number of high-performance computing centers

7) **The Genome Canada and Génome Québec programs** that in the coming years will be supporting projects heavily reliant on bioinformatics

The Main Obstacles

The main obstacle to the development of a bioinformatics industry in Québec is the same as for the rest of Canada and elsewhere—the shortage of specialists in the field. As indicated earlier, Québec has a highly skilled scientific and technical workforce in life sciences. But life sciences graduates who also have information technology skills, especially in database management, are extremely rare. What is more, given the general shortage of computer specialists in all fields, it becomes clear that the first step towards the development of a bioinformatics industry in Québec will involve human resource training. The demand is already there—it is supply that needs to be urgently stimulated. By all accounts, the demand for bioinformatics specialists in the biotechnology and pharmaceutical industries, not to mention university research centers, is considerable and will only increase in the years ahead.

In 1998, the Canadian Network of Genetic Diseases estimated that 300 bioinformatics specialists with postgraduate education would be required across Canada within five years. Today, the demand is almost certainly double, or even triple, that figure. We also know that most of the job openings (two-thirds) in bioinformatics are not filled.

The shortage of specialists in certain fields, difficulties recruiting bioinformatics specialists, and insufficient venture capital (at least in this specific sector) were the three obstacles identified in the survey by UQAM's Chair in Bioindustry Management.[31]

[31] *Ibid*.

Chapter 3

A Bioinformatics Startup Strategy for Québec

Act Quickly and Effectively

The development strategy presented in this chapter is a proposal for fast and effective investment in several key areas that could accelerate the development of bioinformatics in Québec. The proposed strategy is essentially proactive and relies on Québec's principal assets to make up for the lag and the fact that bioinformatics has been virtually ignored by research institutes and funding agencies. The strategy sets out three target areas for simultaneous action:

1) Training of bioinformatics specialists

2) Organization of bioinformatics as a constituent component of Québec's genomics and proteomics sector, as well as a distinct field of research

3) Support for the development of expertise in industrial bioinformatics

These are startup measures, given that the field is still very much in its infancy. It would be premature to suggest a comprehensive industrial development strategy. The approach is to identify fast and effective measures for developing scientific and technological expertise in a sector offering very strong value-added potential for Québec. For the time being, the Council considers that training and research are the main priorities. However, it is also crucial to maximize industrial spinoffs from bioinformatics. This is the reason the Council insists on associating industry with the first two components of the proposed strategy.

Discoveries in genomics and developments in proteomics in the years (and even decades) ahead will be so far-reaching that the countries who invest seriously will inevitably benefit from the economic spinoffs. In practice, those who put the most resources into these areas will have the best chances of developing profitable niches. But speed and efficiency are of the essence. All observers agree that time is crucial in the field. Last April, for example, the Ontario Research and Development Challenge Fund (ORDCF) announced a $74 million investment in genomics. One of the projects to be funded is a Bioinformatics Supercomputing Centre at Toronto's Hospital for Sick Children.

Québec possesses a number of advantages that can spur the development of the sector, but only if it adopts an approach stressing organization and coordination.

Entrust Supervision to Genome Québec

To be successful, a strategy of this kind requires a leader to take charge of organizing and coordinating the development of genomics in Québec. The Conseil de la science et de la technologie recommends putting Génome Québec in charge. The organization was set up by the Québec government to ensure the development of genomics and related fields in Québec following the creation of Genome Canada. Its scope for action is wide, touching on sectors ranging from pharmaceuticals and agrifood to fisheries, forestry, and the environment. In addition, its general orientations and the objectives of its two-pronged funding program make it an agency well attuned to the research community and well suited to spurring development of industrial applications. No other existing organization has a mandate so well adapted to the requirements set out here. Furthermore, Génome Québec's corporate status allows it to act quickly and flexibly—two criteria of capital importance.

However, Génome Québec is a new organization still in the startup phase, having only just debuted its operations. In order to successfully lay the foundations of bioinformatics in Québec, it needs help from key partners such as university administrators, research centers like IRB, funding agencies, venture capital corporations, etc.

TRAINING

1- An intensive bioinformatics training and skills upgrading program

Top Priority: Training Specialists in Bioinformatics

The shortage of human resources in bioinformatics is a worldwide problem requiring rapid corrective measures and a strong commitment to action. In the medium term, graduate programs at the university level need to be established, but in the short term, fast track formulas will be required.

Given the generalized labor shortage in the information technology sector, bioinformatics training initiatives will have to turn to candidates other than those in the general computer science training stream, since computer science graduates are already aggressively courted by companies in communications, multimedia, and other sectors. It may be easier to train bioinformatics specialists by providing extra training to people with a specialty in the life sciences rather than trying to convince computer science students to specialize in the field. In the longer term, however, growing bioindustry demand for bioinformatics specialists and the rising salaries that result will draw increasing numbers of computer scientists *per se*.

Involving Business

Starting immediately, industry must be associated with these initiatives, especially companies already active in bioinformatics that could serve as locations for trainee internships.

Recommendation 1
As a number one priority, implement an intensive bioinformatics training and skills upgrading program in Québec by September 2001

Objective: Rapidly train (within six to ten months) ten to twenty individuals capable of sufficiently mastering the main aspects of bioinformatics in order to meet the most urgent needs of research and industry teams in Québec

Clientele: Graduates and/or professionals, academics, and industrial entrepreneurs with training in genetics, biochemistry, molecular biology, pharmacology or any other relevant discipline

Means: Recruit Canadian and foreign specialists to design and offer a training program starting in fall 2001

Negotiate with universities to provide the necessary facilities for the training program and with companies that use bioinformatics to offer internships for program trainees

Aggressively publicize the intensive training program and actively recruit candidates

Examine the possibility of providing financial assistance

Cost: In the order of $600,000

Agency in Charge:

Génome Québec (supervisory body), with the cooperation of partner academics and industrial entrepreneurs

2. Fellowships for advanced training outside Québec

Training Outside of Québec

Parallel to the establishment of a training and skills upgrading program—and for similar reasons—the second component of the training strategy should be providing fellowships to bioinformatics specialists for training outside Québec. Of course, this proposal involves an element of risk, i.e., the possibility that the most promising specialists end up being recruited by companies or universities outside Québec. However, until Québec develops a solid Ph.D. program in bioinformatics, graduate and postgraduate fellowships remain an excellent means of training scientists in the field. The best way to ensure that they come

back to stay is to stimulate strong demand for their services in Québec's university and industrial communities. Even after the creation of graduate programs in bioinformatics, it will still be in Québec's interests to send students abroad to train or upgrade their skills.

Recommendation 2
Provide some ten fellowship candidates the opportunity to acquire advanced training in bioinformatics, if possible beginning in winter 2002

Objective: Train the core group of experts we will need in the years ahead to develop bioinformatics research and training in Québec

Clientele: Ph.D. and postdoctoral candidates in the life sciences or computer science

Means: Establish a special fellowship program that could be jointly administered by Fonds FCAR (life sciences and computer science) and FRSQ (health sciences)

Publicize the program and recruit applicants

Hold a first competition in 2001

Cost: Between $500,000 and $600,000 annually (10 to 20 fellows) for three years

Agency in Charge:

Génome Québec (supervisory body) with the cooperation of Fonds FCAR and FRSQ

3- University graduate programs in bioinformatics

Graduate Programs

While taking steps to rapidly provide bioinformatics training, Québec must also look to establishing specialized university graduate programs in the field.

Major initiatives in bioinformatics training obviously require the recruitment of top-flight professors. Given the shortage of qualified personnel in the specialty, current university funding mechanisms are inadequate. Not only must we compete with American universities, but with the industry as well. The

industrial chair formula could be a solution. Another potential option is a competition along the lines of the FCAR strategic program for research professors. Strong institutional support from universities is vital for success.

However, the essential thing is to establish training programs capable of meeting the demand. To achieve this, industry involvement in assessing demand, determining program content, and organizing workplace internships is absolutely necessary.

Once again, time is of the essence. Little progress will be made if we have to wait three years or more for a university bioinformatics program to make it through the standard approval procedure. On the contrary, we need to be daring, to be prepared to innovate and experiment. Between the intensive training option put forward in the first recommendation and a conventional graduate program, there must be room for a range of intermediary options that could meet demand for bioinformatics specialists more quickly. Possibilities include a specialized graduate diploma in bioinformatics, the incorporation of a large bioinformatics component into existing life sciences programs, and the conclusion of interuniversity agreements for the rapid development of joint programs.

In the end, close cooperation by all partners (universities, the Québec government, and industry) will be crucial if we are to develop university graduate programs within two years or less. Intense lobbying by Génome Québec will be necessary in order to succeed.

Recommendation 3

Set up bioinformatics graduate study programs and activities in Québec as quickly as possible

Objective: Respond in flexible fashion to specialized training needs in bioinformatics

Clientele: Students with an undergraduate degree in computer sciences or the life sciences

Means: Meet with and convince university officials of the importance and urgency of developing graduate programs in bioinformatics

Obtain the backing of the Minister of Education for this purpose

Undertake steps as quickly as possible to recruit Canadian and foreign research professors. Set aside funds to this effect for positions of potential interest to fellowship recipients completing their training abroad (Recommendation #2)

Negotiate, as required, interuniversity agreements on program development

Involve industry throughout the entire process

Include workplace internships as a compulsory program requirement

Cost: Substantial investments will be required to design and establish programs as quickly as possible with all the required resources.

Agency in Charge:

Génome Québec for initiative coordination; Québec universities willing to collaborate on program development; companies that use bioinformatics technology as partners throughout the process; the Minister of Research, Science and Technology to back Génome Québec efforts, especially with the Minister of Education

Perspectives

In the longer term, life sciences training programs can be expected to increasingly integrate an *in silico* perspective, a major trend in the future evolution of life science disciplines. However, we cannot wait for this process to occur naturally if we want bioinformatics to develop rapidly in Québec. Without formulating a recommendation as such, the Council believes that we must prepare for the future now and ensure that life sciences programs from the college level upward place greater emphasis on the mastery of computer tools.

RESEARCH AND NETWORKING

The second component of the proposed strategy concerns network-based development of bioinformatics activities. The establishment of such a network is absolutely essential. We know that developments in bioinformatics generally occur in conjunction with genomics and proteomics projects drawing upon bioinformatics applications. As a result, Génome Québec's formative initiatives in genomics and proteonomics should help consolidate Québec expertise in project-related bioinformatics. Génome Québec is also charged with supporting R&D projects in bioinformatics as such, a task that must be given top priority

Network or Focal Point?

To rapidly build a base for bioinformatics research in Québec, two types of solution were examined:

1) Develop bioinformatics resources within a network of major projects, such as that of Génome Québec

2) Concentrate resources at a special center or institute and strive to provide it with the necessary critical mass as quickly as possible

Although these two options are based on completely different organizational strategies, they are not entirely incompatible. The Council believes that, in light of the state of bioinformatics in Québec and the urgent need for action, the first option offers the best perspectives for short term results. In contrast, the second option should not be ruled out in the longer term. There is more than one way for a research network to develop. In some cases, it may even be possible to gradually strengthen a network focal point and move toward a more concentrated option. Among the structural options to be considered are a liaison and transfer center (like CRIM or CERCA), a peri-industrial center like INO, or a multiuniversity research and training center.

Benefits Sought

In the immediate term, it is crucial to structure a genomics/proteomics research network that allows for the optimal development of bioinformatics. The sought-after spinoff effects are significant and many:

- Offer an environment that will attract and retain the bioinformatics specialists we wish to train
- Support graduate training in bioinformatics through advanced research
- Establish a foundation for active university-industry cooperation in bioinformatics
- Provide a skills incubator for industry
- Serve as a business incubator by creating spinoffs
- Put Québec on the international map for its bioinformatics capabilities
- Attract several large companies with specific need for such capabilities
- Establish the basic core of a future genomics-proteomics-bioinformatics industrial cluster

Recommendation 4

Develop the bioinformatics sector in Québec through a network of formative research projects in genomics, proteomics, and bioinformatics itself

Objective: Develop a high level capability in bioinformatics in Québec and maximize the impact through networking

Clientele: University and industrial research teams in genomics, proteomics, and bioinformatics with high potential for excellence and economic spinoffs

Means: Ensure that genomics and proteomics projects supported by Génome Québec include a significant bioinformatics component with suitable financial backing

Provide priority support to one or two formative research initiatives in bioinformatics *per se*

Take steps to associate industrial partners with each of the projects

Potentially design a special component Génome Québec program component to support bioinformatics research projects once the number and caliber of research teams so warrants.

Cost: We must await the outcome of the first Génome Québec competition before putting a dollar figure on specific projects in bioinformatics

Agency in Charge:

Génome Québec, with the cooperation of Fonds FCAR and FRSQ.

TECHNOLOGY TRANSFER

As mentioned at the beginning of this chapter, it would be premature to suggest an industrial development strategy for bioinformatics given that the field is still in its infancy. The measures proposed above to create the preconditions for developing Québec's expertise in bioinformatics should have a major impact on industry, either as companies integrate this expertise for business development purposes or as new firms spring up to exploit it directly.

In which of Québec's bioindustry niches will bioinformatics develop? It is still too early to tell. The next three years will be crucial in this regard. If intensive research and training efforts are initiated, as the Council suggests, we can expect to see a spinoff effect in industry. In fact, this is why the Council has insisted on industry involvement in determining the orientation and design of the strategy's training and research components (Recommendations #1 to #4)

The Issue of Venture Capital

A number of problems could arise in the years ahead, although it is too early to analyze them or find solutions. For example, a number of Canadian and international observers have pointed out the difficulties of securing venture capital for startup firms in this field. It is still to soon to tell whether this problem will also occur in Québec, or whether existing venture capital firms will be ready to invest when necessary. However, if Génome Québec and its partners are able to rapidly build a Québec research network of high quality resources in genomics, proteomics, and bioinformatics, this expertise should attract investors. Without minimizing the importance of this issue, the Council has decided not to issue a specific recommendation regarding venture capital, but strongly suggests (see Recommendation #6) that the government monitor the situation very closely over the next three years.

The fifth recommendation specifically aims to facilitate the integration of bioinformatics into Québec industrial practice. Tax measures are undoubtedly the most appropriate instrument for achieving this goal, as they were in other areas (multimedia, for example). The temporary five-year tax measures suggested are designed to encourage companies to recruit bioinformatics specialists. Their impact should be evaluated after four years.

Why Measures to Stimulate Demand?

Why recommend measures to stimulate industrial demand in bioinformatics when demand is already high and predicted to increase significantly in the years ahead? Let us be very clear on this point: bioinformatics expertise is rare and expensive. Throughout the world, trainees in the field receive so many job offers that they have difficulty completing their studies. Of course, salaries are proportional to the demand. We must take into account that fact that Québec companies seeking to recruit bioinformatics specialists have to compete with numerous outside firms looking for the same type of personnel—many of them with a much greater capacity to pay. For this reason, the Council considers that specific bioinformatics tax incentives could give Québec bioindustries the edge they need.

Recommendation 5
Starting in 2002, provide Québec bioindustry companies with tax incentives specifically linked to the hiring of bioinformatics personnel

Objective: Accelerate recruitment of bioinformatics specialists by Québec bioindustries

Clientele: Québec bioindustry companies, including subsidiaries of foreign firms, that need to rapidly recruit bioinformatics specialists to maintain or increase their competitiveness

Means: Support recruitment efforts in parallel with measures to increase availability of human resources, notably by reducing the cost to companies of hiring bioinformatics personnel. This measure should be evaluated after four or five years

Cost: To be confirmed

Agency in Charge:

MRST and its partners, i.e., the Ministère des Finances and the Ministère de l'Industrie et du Commerce

INDUSTRY DEVELOPMENTS

The Importance of Monitoring

The startup measures proposed in this report are necessary. But they alone are not enough to ensure optimal development of bioinformatics in Québec. Given the importance of the issues identified at the end of Chapter 2, we also recommend extremely attentive monitoring of developments in the field over the next three to four years, as much from a scientific point of view as an industrial or even social one.

A Shared Role

The Council plans to monitor the action taken in response to its recommendations, but it is not the Council's role to regularly monitor Québec's bioinformatics sector. This responsibility lies with other bodies: Génome Québec, of course, because it is the main architect, but also, and perhaps most of all, the MRST, in light of the fact that this cutting edge scientific and technological field holds out remarkable promise for Québec's socioeconomic development. Other departments also have a role to play in their respective sectors: the Ministère de l'Industrie et du Commerce, the Ministère de

l'Éducation, the Ministère de la Santé et des Services sociaux, the Ministère de l'Environnement, the Ministère de l'Agriculture, des Pêcheries et l'Alimentation, etc.

Numerous Aspects to Cover

These monitoring and technology watch initiatives must not focus exclusively on bioinformatics. The entire field of genomics and proteomics and their related applications deserve careful monitoring in order to understand how bioinformatics is developing in Québec, assess progress, and identify difficulties. Areas requiring special attention include the rapid development of bioinformatics training programs, venture capital reactions to business startups, infrastructure and equipment needs, and the intervention of other players such as grant agencies, federal agencies, Valorisation-Recherche Québec and its four university research development corporations, etc. Through all of this, it is also important to keep the public informed and allow people to express themselves regarding the social and ethical concerns related to the evolution of the field. The new Commission de l'éthique de la science et de la technologie, if it is established, should make a valuable contribution in this regard.

Recommendation 6
Closely monitor the development of genomics, proteomics, and bioinformatics in Québec, as much from a scientific point of view as from an industrial and social one.

Objective: Verify results achieved, make adjustments as required, and prepare the next generation of support measures

Clientele: All those involved in launching the bioinformatics sector in Québec

Means: Review developments in the field at least once a year with all stakeholders

Put monitoring indicators in place for all of the most important dimensions

Stay closely attuned to potential difficulties by maintaining regular dialogue with scientific and industrial research teams

Organize public and media forums to discuss issues

Agency in Charge:

MRST and its partners: Génome Québec and other departments concerned

Appendix 1

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