Health & Pharmaceuticals

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The marriage of IT and medicine

Vast computing power is being harnessed to help researchers better understand the mechanisms of disease and develop highly focused drug treatments tailored to patients' genetic makeup

BY KEVIN MARRON

Visitors to Toronto's Hospital for Sick Children might easily make the mistake of assuming that the air-conditioned chamber on the 10th floor contains nothing but a set of refrigerators with their doors to the wall.

But these unassuming objects are, in fact, the brains of a supercomputer with the power of about 4,000 desktop machines.

It is the largest publicly accessible computer in the world that is dedicated to the new science of Bioinformatics – the marriage of information technology with life sciences.

And the supercomputer is at the hub of a burgeoning new industry, as Canadian biotechnology companies search the vast database it contains to get a more precise understanding of the human body than possible before, and use this to develop highly focused drug treatments tailored to each patient's genetic makeup.

"It's creating a wonderful opportunity for Canada in this field," says Jamie Cuticchia, director of the Ontario Centre for Genomic Computing, which runs the computer, making it available to biotechnology companies as well as academic researchers, working in the new field of genomics and the even newer field of proteomics (which analyzes the proteins that genes instruct the body to produce).

It may come as a surprise to many people that some of the world's most powerful computers are located in medical-research labs, rather than in space-exploration or nuclear-physics facilities. But, according to Mr. Cuticchia and other experts, figuring out the workings of the human body is where today's greatest computational challenges lie.

"We have massive amounts of data to sort through and mine. Each year, we are generating more biological data than has ever been generated before," Mr. Cuticchia says. Vast computing power and sophisticated software can be harnessed to bring all this data into a format that will help researchers understand the mechanisms of disease, says Sean McNicholas, president and chief executive officer of Mississauga-based biotechnology company **Synx Pharma Inc**.

"You can determine the disease pathways and at which point in the pathways you can apply pharmaceutical products to help ameliorate the side-effects or the outcomes of the disease," Mr. McNicholas says. "Then you can test your logic in the computer, as opposed to spending time, money and a lot of sleepless nights trying to do it all in the lab."

It is even possible to carry out biochemical tests and experiments directly on computers, using products such as Mountain View, Calif.-based **Caliper Technologies Corp**.'s Lab-on-a-Chip, which allows samples of fluids to be prepared an analyzed within the confines of a microchip.

"The convergence of [medical] science and technology …is what makes the whole field of proteomics and Bioinformatics so wonderful at the moment," Mr. McNicholas says.

The human-genome sequencing project, which uncovered humanity's basic genetic code, was only the beginning, according to Steven Pelech, a professor of medicine at the University of British Columbia who is also president and CEO of Vancouver-based **Kinexus Bioinformatics Corp**. "We have the blueprints for the parts, but we don't have the schematics for how the parts fit together and we don't know what the parts do," he says. "It's almost like we have discovered an alien technology and now we're trying to figure out how it works. The problem is that this thing is 10,000 times smaller than anything we can make and it's about a billion years old."

Decoding all this information – a take that would be impossible without advance computing power – can lead to a radical change in the way drugs are developed and prescribed, according to Prof. Pelech.

Computer-aided drug design on way

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This could lead to a more personalized form of medicine, he says.

Understanding the human genome can help doctors and drug companies understand which people are most susceptible to what diseases, so they can figure out who the best candidates for clinical trials are and which patients would benefit most from certain drugs, Prof. Pelech says.

Genetic profiling also can contribute to preventing disease by making patients aware of the risks they are facing. For example, many smokers now play Russian roulette with their health, choosing to live with the risk that they have a one-in-seven chance of dying from lung cancer. But

genetic profiles could identify smokers who have a predisposition to lung cancer, thus warning them that "the bullet is lined up with the barrel of the gun,' Prof. Pelech says.

But even more exciting than that, he says, is the prospect of figuring out what proteins in the body are responsible for triggering certain diseases – for example, what the malfunction is that causes cells to multiply unnecessarily to create a cancerous tumour. Once such a trigger is identified it may be possible to use computing power to design a drug that can fix the faulty mechanism, Prof. Pelech says.

This would involve a process akin to reverse engineering, he adds. "It would be like discovering a door lock and the computer would have to generate all the millions of possible key shapes that could fit, then run through them all to discover the one that is the right shape."

Prof. Pelech says his company's research focus is on the cell-communication system proteins that act like biosensors, telling cells what is going on and what to do. Comparing the body to a biological computer, he describes the communication system as "kind of like the human operating system."

Sometimes, this human computer gets short-circuited, he says. "And we can assist the cell in its own repair, taking advantage of the pretty heavy computing power that exists inside each and every one of the cells of our bodies."

He says this is a fundamentally different approach to that of many drug therapies today. For example, chemotherapy treatment is often prescribed on the basis of a statistic al probability – that a certain drug is successful for 60 per cent of patients with a particular kind of cancer.

'With Bioinformatics … we should be able to tell right away that a particular drug doesn't work for you and that this is the drug you should be taking.'

Furthermore, he says, the drugs often attach fast-growing cancer cells by killing all fast-growing cells, so healthy cells are also destroyed, thus affecting the immune system and resulting in side-effects such as hair loss. Prof. Pelech likens this treatment to trying to hit the cancer cells with a sledgehammer.

"With Bioinformatics, on the other hand, we should be able to tell right away that a particular drug doesn't work for you and that this is the drug you should be taking."

Mr. McNicholas says Bioinformatics and proteomics can also lead to early detection of diseases that are currently hard to spot. Alzheimer's disease, for example, is not usually diagnosed until a patient is already showing signs of dementia; even then, the diagnosis is exclusionary, meaning that patients are treated for Alzheimer's, if it is found that they are exhibiting symptoms and there is no other explanation for their symptoms.

The new science and technology, on the other hand, soon may be able to identify specific proteins that show up in the blood of Alzheimer's patients so that it will be possible to detect the disease even before symptoms appear. This will make a huge difference, he says, because drugs already exist that can slow the loss of cognitive abilities, providing the patient can be diagnosed early.

Once the proteins causing Alzheimer's have been identified, Mr. McNicholas says, it ultimately may be possible to develop medication that can stop them from developing, and thus prevent the disease or slow its progress.

But finding the proteins that may cause Alzheimer's or any other disease and developing the right medications would be almost inconceivable without supercomputers and Bioinformatics, Prof. Pelech says.

He notes that there are at least 50,000 human genes and 50,000 proteins, about 10 per cent of which look attractive as drug targets. Given that it costs a pharmaceutical company about $500-million to find a drug for a target and to get approval to use it, there is no way that it would be possible for the industry to investigate 5,000 drug targets thoroughly, he says.

"The industry is looking to Bioinformatics to hasten the process by which it can sift through all the potential targets and home in on those proteins that will be the most attractive drug targets. Then it can use molecular modeling and advanced computing to develop drugs in a virtual lab," Prof. Pelech says.

Special to The Globe and Mail

Silicon Bridge

The thin wafer of silicon that Patrick Zimanyi displays represents a bridge between biology and electronics.

Mr. Zimanyi, head of life sciences for Missisauga-based Agilent Technologies Canada Inc., says the five-centimetre chip, developed by Agilent's partner, **Caliper Technologies Corp**. of Mountain View, Calif., can replace a set of laboratory instruments that would normally occupy a workbench 1.5 metres long.

The chip contains tiny holes into which samples of fluid can be inserted. The chip can then be put in a machine call the Agilent 2100 bio-analyzer. This analyzes the sample with electrodes, sending its results directly into a computer.

Not only is the process far less messy and labour intensive, but it also reduces the possibility of error quite dramatically, Mr. Zimanyi says.

"The technology used today is almost archaic in comparison," he says, noting that the lab on a chip can produce results that are accurate to within 5 or 10 per cent, where as normal lab equipment may have a margin of error that is as high as 40 per cent.

Steven Pelech, a professor of medicine at the University of British Columbia who is also president and chief executive officer of Vancouver-based **Kinexus Bioinformatics Corp**., says chips such as these are used mainly for experimental purposes but probably will be used in screening labs within a few years.

He says it eventually will become routine for patients to give small blood samples that can quickly be analyzed in a computer to determine whether they have a genetic predisposition to certain illnesses.

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Molecular Ownership

Most people probably would be surprised to learn that some of the molecules flowing through their bloodstream are actually owned by Mississauga-based **Synx Pharma Inc**.

But, in the strange new world of Bioinformatics, the building blocks of life are intellectual property for the biotechnology companies that discover them.

"Every protein we identify, we then own through the next 20 years. We can develop them and sell them." Says Sean McNicholas, president and chief executive officer of Synx, which has filed patents for about 70 discoveries.

Developing information about human genes and proteins is a crucial first step to creating drugs and identifying patients who may benefit from the drugs, so intellectual capital is a crucial asset for biotechnology companies working in this field, Mr. McNicholas explains.

Synx builds this intellectual capital by doing research in collaboration with pharmaceutical companies, then patenting the output of the discoveries that it makes, building a powerful private database of proteins associated with certain diseases it has chosen to focus on, Mr. McNicholas says.

Steven Pelech, a professor of medicine at the University of British Columbia and president and chief executive officer of Vancouver-based **Kinexus Bioinformatics Corp**., says his company also is building a private database of protein research, though its business model is slightly different.

Kinexus conducts highly specialized proteomic analysis of samples sent to its laboratory by research scientists from all over the world. The data from its analysis on a fee-for-service basis, but it also keeps the data in its own files, thus amassing a huge amount of specialized information that it can piece together for drug-development research, Prof. Pelech says.

The specialized data in private databases, such as those of Synx and Kinexus, can then be married with publicly available data, such as that collected at the Ontario Centre for Genomic Computing, where one of the world's most frequently accessed databases stores the research finding of scientists from around the globe.

"Drug-discovery companies need to be able to take information from any private database they purchase or create themselves and link that to all the available public databases," says Jamie Cuticchia, director of the center, noting that in Bioinformatics, as in many other areas of information technology, one of the greatest challenges is "to get different databases and different analytical tools to talk to one another."

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