

The Bioinformatics Institute

## Genetics and Viral Research

### New Zealand Supercomputing Centre accelerates biotech research

The Bioinformatics Institute in Auckland, New Zealand has been a significant contributor to worldwide genomic and genetics research and projects, partnering with institutions worldwide, including Oxford, the University of Washington and the University of California at San Diego.

The Bioinformatics Institute is co-funded by AgResearch Ltd and The University of Auckland. Within the University it is affiliated with several departments including Biology, Computer Science, Mathematics, Statistics, and the Medical and Health Sciences Department. The Bioinformatics Institute's core goal is to ensure New Zealand biologists are trained in bioinformatics and New Zealand remains at the forefront of excellence in computational-based research.

#### Bioinformatics and HIV Research

Among the Bioinformatics Institute's current projects is a study into the evolutionary dynamics of HIV within and between infected individuals. The Bioinformatics Institute is looking into how the virus evolves in humans and how viral evolution influences an individual's rate of progression to AIDS. Much of the new research project requires heavy computational power to analyse large amounts of data.

Allen Rodrigo, Director and Professor of Computational Biology and Bioinformatics, explains the depth of the project and how the NZSC is progressing the research.

"The NZSC allows us to take our data and refine our analysis, to get better estimates and make better predictions about the evolutionary behaviour of HIV. The methods may at one point look like a massive number crunching game but the results are biologically pertinent and address real biological problems. The NZSC enables us to address those problems and find potential solutions quickly and more accurately.

"By examining how HIV evolves in humans, we can assess why and how soon the disease may progress to AIDS," said Rodrigo. "Research in our laboratory has the potential to highlight how the virus and host interact, and how this interaction leads to the rapid or delayed onset of AIDS. One of the key aims of our research is to uncover why some people live for years with HIV and others progress to AIDS within months or weeks.

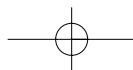
"The results may allow other researchers and medical experts to design better, more effective therapies."

Rodrigo also cites the on-call benefits of the NZSC.

"Having the processing power of the NZSC on standby means we have a massive new computing resource to handle these problems when we need it. It also means we don't need a massive budget to build and manage our own infrastructure."

#### Conservation Genetics

The Bioinformatics Institute runs a number of projects concurrently and is using more and more of the NZSC to help with its research.



With collaborators in Associate Professor Scott Baker's laboratory, the Bioinformatics Institute have developed a web-based phylogenetic identification tool for unknown samples of cetacean tissue, using mitochondrial sequence information. Other work in conservation genetics includes a recent Marsden funded grant to study the integration of population dynamics and population genetics to estimate historical population size trajectories of conservationally relevant species.

Rodrigo notes, "In all these cases, the computational overheads are massive. Dealing with potentially hundreds of genetic sequences, each hundreds of nucleotides long, and attempting to uncover the detailed history of mutations that have occurred requires sophisticated mathematical analyses that can only be solved by computers. Some analyses run for several months on a desktop PC."

To emphasise the enormity of the computational task, Rodrigo uses the following analogy:

"Imagine that you and a friend are given the combination of a rather unusual safe. The safe has 500 dials, and each dial has four numbers. However, to open the safe, you have to know the exact sequence of numbers for the 500 dials. But the person who gives you the combinations throws a curve ball – approximately 10 per cent of the numbers in the combinations you have been given are incorrect, and you don't know which are correct and which are not. How do you work out the correct combination?"

This problem is directly equivalent to the types of problems that evolutionary biologists deal with on a daily basis, except that evolutionary biologists have many 'safes' and many mutated 'combinations'. Needless to say, there are sophisticated mathematical and computational solutions to the problem, but all solutions require us to consider a very, very large space of possible combinations. In mathematical parlance, these problems fall in the domain of combinatorics, and many are known to be exceptionally difficult to solve".

The NZSC's computing power allows bioinformaticists to break up these computational tasks into manageable chunks.

"We can compartmentalise our methods so that each computer only considers a restricted number of combinations".

#### Partnering in High Powered Computing

Working alongside the NZSC, The Bioinformatics Institute is developing new programs for the cluster that will allow biologists to better analyse genetic data.

"We are looking to set up a program that will solve some of the challenges involved with essential computational analysis. As it stands, many users need to choose the variables and parameters to determine the course of their analysis. In many instances, it's a guess from the user. The problem arises when an inexperienced user of computational techniques chooses the wrong values," said Rodrigo.

The Bioinformatics Institute is working to automate the process of deciding the best value for the data. In the end, the computer would automatically choose the best parameters for the analysis.

"To be able to set up an automated process, we need to use the NZSC. The computer search for the best parameters for a given set of data requires a huge amount processing power," said Rodrigo. "The final application though would, in most cases, free the user from having to make arbitrary decisions about parameter values; he or she could simply plug it in data and get best results".

The Bioinformatics Institute and the NZSC aren't alone in their quest to automate bioinformatics analysis.

"We've entered a global race. It's being worked on in many different research institutions and we should start seeing the results of that race within the next 12 to 18 months. We, as well as others, are looking to build complete automated pipelines for sequence analysis. These pipelines would take data in one end, translate it into information, which we can then turn it into knowledge."

#### Working with the NZSC

The Bioinformatics Institute currently logs on via a fast Internet connection. Along with other partners in the NZSC though, they are working to develop an online interface for the NZSC, which can be used readily by anyone with an equivalent connection.

"The interface will be accessible through a secure Internet connection and will allow scheduling and access from almost anywhere in the world."

#### About The Bioinformatics Institute

The Bioinformatics Institute is jointly funded by AgResearch Ltd and The University of Auckland. It is New Zealand's only centre of research excellence dedicated to computational biology and bioinformatics. The Bioinformatics Institute is located at The University of Auckland's City Campus within the Faculty of Science, and offers a suite of training and research opportunities to students, scientists, and commercial clients. For more information about the Bioinformatics Institute, please visit <http://www.bioinformaticsinstitute.org>.

#### About Gen-i and the NZSC

Located in New Zealand's capital, Wellington, the NZSC is managed by Telecom New Zealand subsidiary, Gen-i. The NZSC is available to universities or research and development organisations - or indeed any institution across any sector that requires on-demand power and performance to analyse large amounts of data but lack the computing infrastructure.

Telecom New Zealand provides dedicated national connectivity between all main centres up to one Gigabit per second, as well as dedicated international connectivity to a number of global sites.

Gen-i provides business solutions from the design and development of leading edge technology through to implementation and support. Gen-i's rapid uptake of proven technology, speed to market, flexibility and responsiveness gives its clients the competitive edge that is key to business success. Gen-i was purchased by Telecom New Zealand in July 2004. Now as a company of almost 1300 people with a breadth of IT services unparalleled in a local company Gen-i is uniquely placed to provide value and support for clients in achieving their strategic business objectives.