

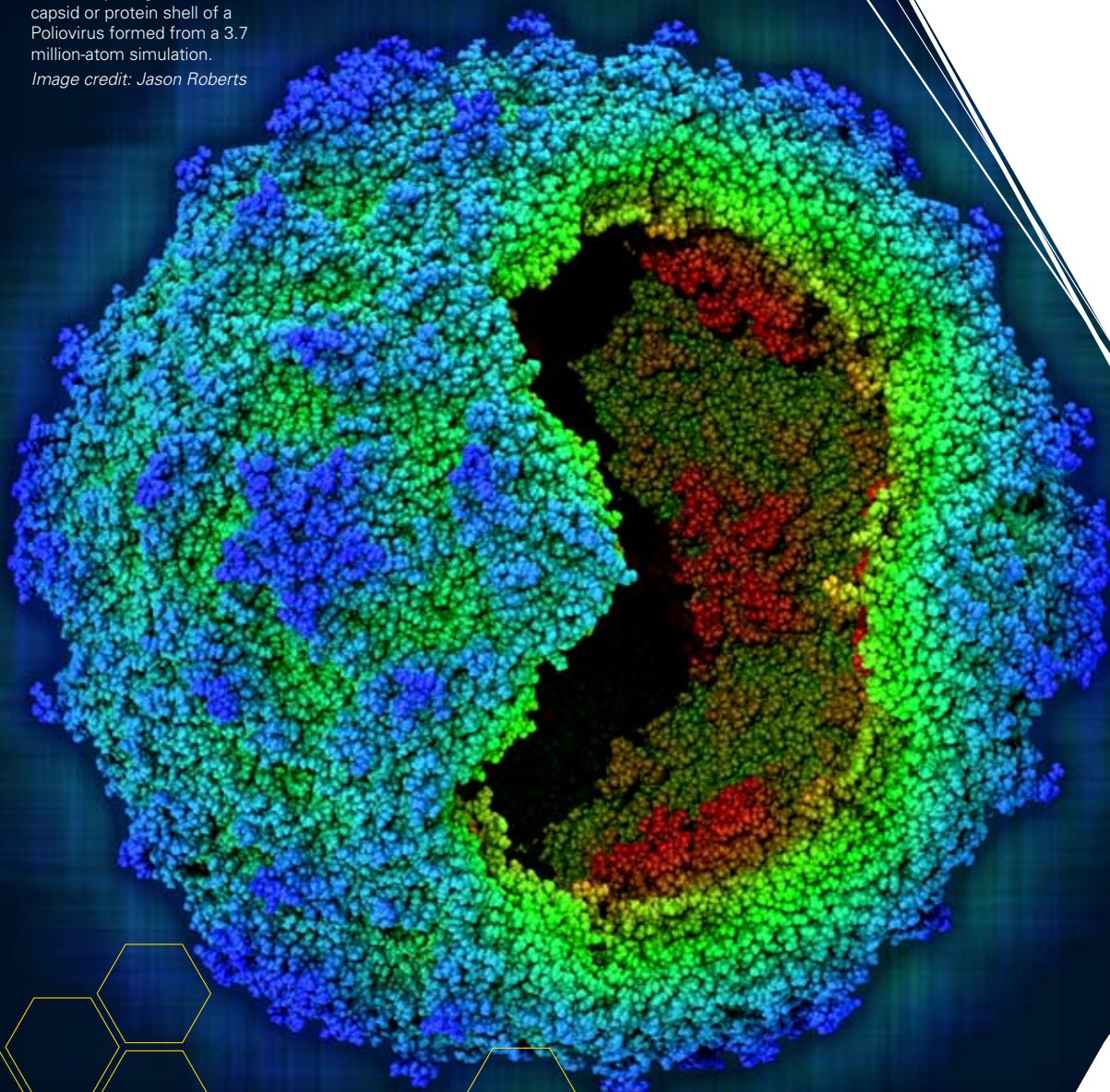
CONSTRUCTING THE POLIO VIRUS – ONE ATOM AT A TIME

Jason Roberts has built a moving, three-dimensional simulation of the polio virus from the ground up. He fed data on the structure of the 240 proteins and 60 lipids from which the virus is constructed into a supercomputer. And it put together the virus in a simulated water environment – a jigsaw of more than 3.6 million atoms of which the virus comprised only 900,000.

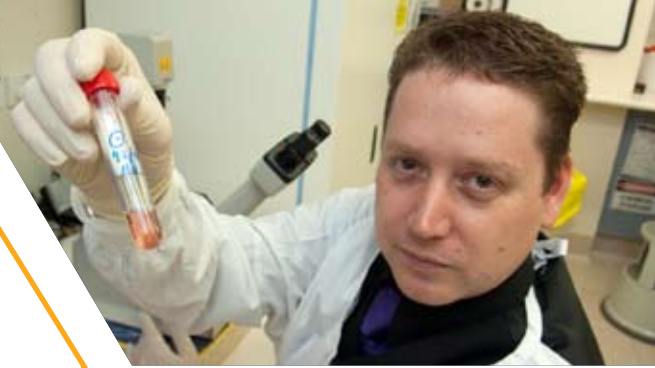
Tim Thwaites, Science Writer

A cutaway image of the capsid or protein shell of a Poliovirus formed from a 3.7 million-atom simulation.

Image credit: Jason Roberts



“I can't believe how quick that was...”



Jason Roberts. Image credit: David Paul

Jason can now use his model to study how the virus interacts with water, how its shape changes with temperature, what happens when a mutation affects the structure of one of the proteins, where drugs dock and the impact they have. And he can compare wild polio virus with the attenuated varieties used in vaccines – all inside the computer.

His expertise and access to the activity of the virus at the atomic level have already inspired collaborations with virus research teams in Japan, Taiwan and the US.

Of course, given the level of complexity involved, he was not using just any computer. Jason, who works in the Poliovirus Reference Laboratory at the Victorian Infectious Diseases Reference Laboratory, is one of the early users of the IBM Blue Gene supercomputer at the Victorian Life Sciences Computation Initiative (VLSCI) in Parkville. But this machine is only about one twentieth the size and power of what is planned to be installed by the end of 2012 – a machine which will rank with the most powerful devoted to life sciences anywhere.

Less than a month after Blue Gene was switched on in August 2010, Jason had run a simulation of the polio virus. The computer took about 10 minutes to put it together, a job that would have taken weeks on any other system in Victoria. Jason was speechless.

“Oh my God!” he wrote to the VLSCI staff. “I can't believe how quick that was! Speechless. Well gentlemen, you have made my day. Very exciting.”

Apart from genuine astonishment, the reason for Jason's outburst was that he recognised that his goal of constructing a working model of the polio virus inside a computer had gone from being “ambitious” to “doable”. And now that he has done it, his work has taken on

a whole new significance. “It put me about three months ahead in one day.”

The work is important because, even though polio has been eradicated from Australia and most of the rest of the world, there are still significant issues, says Dr Bruce Thorley, the head of the Polio Reference Laboratory. For instance, while the Sabin oral vaccine has made mass vaccination possible on a global scale, the disabled poliovirus at the heart of it can revert to an active, infectious state in areas where vaccination levels are low. Research to counter that problem will be boosted by the new simulation.

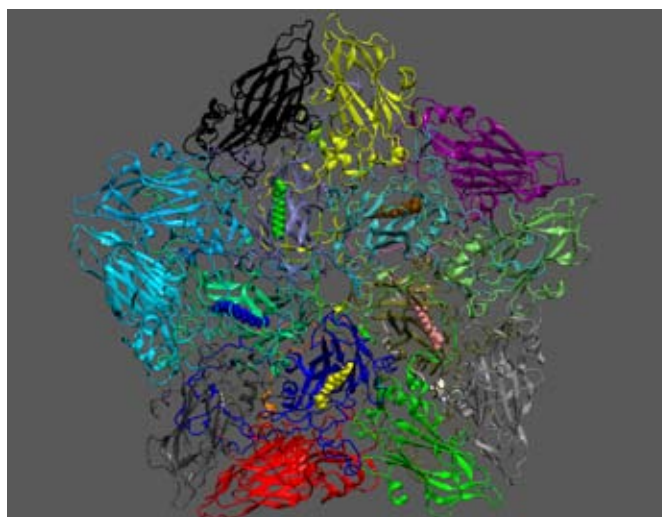
What's more, Thorley says, many closely related viruses, in the group known as the enteroviruses, cause other important infectious diseases, such as viral meningitis and diarrhoea. And, after 60 years of research, polio is the most studied of all animal viruses – it has become the model virus that provides a generic picture of what viruses are like.

The new simulation can be used to validate or check previous knowledge and generate new insights and hypotheses which can be tested in the laboratory. It is already providing a more realistic picture of what a virus looks and acts like.

The standard method of determining protein structures – x-ray crystallography – depends on crystallisation, and therefore removes the protein from its natural environment, water. Jason's atomic simulation lets him model and investigate the virus's interaction with water, salts and drugs, as well as the effects of temperature. Thus, the supercomputer provides us with a better approximation to the natural world.

For further information about this research contact Jason Roberts at Jason.Roberts@mh.org.au

To contact VLSCI, go to www.vlsci.org.au



A simulation of a Poliovirus pentamer, one of the subunits from which the capsid or protein shell is put together. This image shows the different protein chains (coloured ribbons) and the fats or lipids (bead clusters). Image credit: Jason Roberts