UK Grid helps fight avian flu

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During April, computers in the UK have been working overtime in the fight against avian flu. As part of an international collaboration, computers at eleven UK universities and research labs have put in one hundred thousand hours of time searching for possible drug components against the avian flu virus H5N1. The analysis used a computing Grid, a new network that brings together worldwide computer resources to solve scientific problems.

The computing Grid used in the UK was originally built to help particle physicists examine the huge amounts of data from their experiments. But it is now part of a wider project called EGEE (Enabling Grids for E-sciencE), that lets other scientists share its resources. As Professor Tony Doyle, Project Leader for the UK particle physics Grid, explains, “The Grid is useful for any kind of research that needs lots of computing power. In this case it’s greatly speeded up a step in the search for drugs against avian flu, and we’ve been pleased to use the UK particle physics Grid to help.“

A collaboration of Asian and European laboratories used an international Grid to analyse 300,000 possible drug components against the virus. 2000 computers were used during 4 weeks in April – the equivalent of 100 years on a single computer. More than 60 000 output files with a data volume of 600 Gigabytes were created. Potential drug compounds against avian flu are now being identified and ranked according to the binding energies of the docked models.

The computers used in the UK came from the Universities of Brunel,

Birmingham, Durham, Edinburgh, Imperial College London, Lancaster, Manchester, Oxford, Royal Holloway University of London, University College London, and CCLRC Rutherford Appleton Laboratory. They are all part of the GridPP project, which runs the UK particle physics Grid.

Professor Keith Mason, CEO of the Particle Physics and Astronomy Research Council (PPARC), which funds GridPP says, “This project is a clear example of how developments in basic research can support wider applications. GridPP has been developed to help answer questions about the conditions in the Universe just after the Big Bang, but the same resources and techniques can be exploited by other sciences with a more direct benefit to society.”

“With these results, the Grid demonstrates that it is a powerful and reliable resource for scientists, opening up new research possibilities and improving existing methods,” said Viviane Reding, European Commissioner responsible for Information Society and Media. “I am very grateful to see that the European flagship Grid infrastructure is contributing to solving current and socially important problems such as avian flu.”

The goal was to find potential compounds that can inhibit the activities of an enzyme on the surface of the influenza virus, the so-called neuraminidase, subtype N1. One of the targets of existing drugs today on the market is viral neuraminidase, an enzyme that helps the virus to proliferate and infect more cells. As this protein is known to evolve into variants if it comes under drug stress, drug resistance becomes a potential concern in case of an influenza pandemic.

The challenge of the drug discovery application is to identify those molecules which can dock on the active sites of the virus in order to inhibit its action. To study the impact of small scale mutations on drug

resistance, a large set of compounds was screened against the same neuraminidase target but with various, slightly different structures. With the results from the computer screening, researchers can predict which compounds and chemical fragments are most effective for blocking the active neuraminidases in case of mutations.

“With the help of the high-speed computing and huge data managing capabilities of the Grid, possible drug components can be screened and studied very rapidly by the available computer modelling applications,” says Ying-Ta Wu, biologist at the Genomics Research Center of the Academia Sinica in Taipei. “This will free up medicinal chemists’ time to better respond to instant, large-scale threats. Moreover, we can concentrate our biological assays in the laboratory on the most promising components, the ones we expect to have the greatest impact.”

Taking advantage of the experience acquired in a previous WISDOM data challenge on malaria, the Grid-enabled process was implemented in less than a month on three different Grid infrastructures: AuverGrid, EGEE, and TWGrid, paving the way for a virtual drug screening service at a large scale. The next WISDOM data challenge against several targets of neglected diseases will take place in autumn 2006.

This drug discovery application against the avian flu virus was jointly deployed by the Genomics Research Center, Academia Sinica, Taiwan; Academia Sinica Grid Computing Team, Taiwan; Corpuscular Physics Laboratory of Clermont-Ferrand, CNRS/IN2P3, France; Institute for Biomedical Technologies, CNR, Italy, in collaboration with the EGEE project, the AuverGrid regional grid in Auvergne, and the TWGrid. This work took place in collaboration with the EMBRACE network of excellence and the BioInfoGrid project. The majority of computing is conducted on the WISDOM platform; in addition, a light-weight application framework called DIANE was also adopted in this challenge and used to perform a sizeable fraction of the total activity to enable

efficient computing resource integration and usage. The UK particle physics Grid is part of the EGEE project.

Source: Particle Physics and Astronomy Research Council