

WISDOM'S NEW FIGHT AGAINST MALARIA

The WISDOM initiative went into top gear with its latest drug discovery challenge, which finished 31 January with an average of 80,000 compounds analysed each hour on the EGEE Grid infrastructure. In total, the challenge processed over 140 million possible docking arrangements between drug compounds and target proteins of the malaria parasite.

This virtual screening challenge of the international WISDOM (World-wide *In Silico* Docking On Malaria) initiative between 1 October and 31 January targeted compounds that are of interest for drug discovery against neglected diseases. WISDOM uses *in silico* docking techniques, where researchers use computing systems to compute the probability that potential drugs will dock with a target protein. This lets researchers rule out the vast majority of potential drugs, so that they can concentrate on the most promising compounds in laboratory tests. This speeds up the screening process and reduces the cost of new drug development to treat diseases such as malaria.

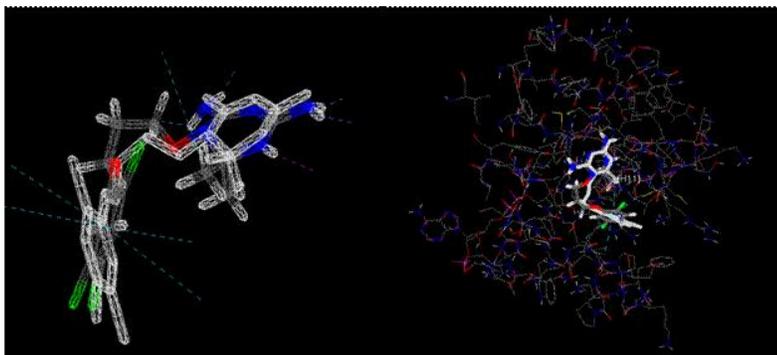
"The impact of WISDOM goes much beyond malaria," declared Doman Kim, Director of the Bioindustry and Technology Institute at Jeonnam National University in Korea. "The method developed can be extended to all diseases and this opens exciting industrial perspectives. Until now, the search for new drugs in the academic sector was done at a relatively small scale, whereas the WISDOM approach allows a systematic inquiry of all the potentially interesting molecules."

This challenge was the consequence of the first, very successful large scale *in silico* docking, which ran on the EGEE Grid in summer 2005, when WISDOM docked over 41 million compounds in just six weeks, the equivalent of 80 years work for a single PC. The WISDOM team identified some 5000 interesting compounds, from which they found three interesting families of molecules that could be effective against the malaria parasite. Laboratories at the University of Modena, CNRS in France and CNR-ITB in Italy are now carrying out more advanced studies of the molecules using molecular dynamics. Following those studies, the enzymology laboratory of the Jeonnam National University in Korea will test them *in vitro*.

A second computing challenge targeting Avian Flu in April and May 2006 has significantly raised the interest of the biomedical research community. Laboratories in France, Italy, Venezuela and South Africa proposed targets for the second challenge against neglected diseases.

The WISDOM endeavour would be impossible without the support from BioSolveIT, a German firm who provided more than 6000 free floating licenses for their commercial docking program FlexX. "The WISDOM programme is very interesting and BioSolveIT is happy to sponsor this work," says Dr Christian Lemmen, CEO of BioSolveIT. "The initiative takes full advantage of the speed and accuracy of FlexX – demonstrating the potential of the virtual screening technique in the search for drugs against

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Docking of the WR9-molecule into the structure of a target protein of the Malaria parasite (quadruple-mutant DHFR of *Plasmodium Falciparum*).

The docking solution on the left is represented in colour while the binding mode of WR9 before docking is shown in white. The same docking solution inside the active site of the target protein is shown on the right. This figure was generated using the FlexV software from BioSolveIT.

neglected diseases.” Due to the initial success of the data challenge, the company even decided to extend the FlexX license for several weeks which allowed studying a new target.

In addition to the computing power that the EGEE Grid provided, AuverGrid, EELA, EUChinaGRID, EUMedGRID and South East Asia Grid all provided additional resources. The Embrace and BioinfoGRID projects are contributing to the development of a virtual, *in silico* screening pipeline that will allow researchers to select, for any given target protein, the most active molecules out of the millions of compounds commercially available.

Over the 10 weeks of the challenge, the project used the equivalent of 420 years of computing power of a single PC. Up to 5000 computers were used simultaneously in 27 countries, generating a total of 2000GB of useful data.

Note to Editors:

1. For more information about the Drug Discovery application, visit: <http://wisdom.healthgrid.org/> or contact Nicolas Jacq, email: jacq@clermont.in2p3.fr

2. The Enabling Grids for E-science (EGEE) project is co-funded by the European Commission. It operates the largest multi-science Grid infrastructure in the world with some 200 sites connected around the globe, providing researchers in both academia and industry with access to major computing resources, independent of their geographic location. For more information see <http://www.eu-egee.org/> or contact Hannelore Hämmerle, email hannelore.hammerle@cern.ch or telephone +41 22 767 4176.

3. WISDOM Partners:

- LPC Clermont-Ferrand, CNRS-IN2P3 Université Blaise Pascal, France, <http://clrpcsv.in2p3.fr>
- SCAI, Fraunhofer Institute, Germany, www.scai.fraunhofer.de
- HealthGrid <http://www.healthgrid.org>
- CNR-Institute of Biomedical Technology, Italy, <http://www.itb.cnr.it>
- University of Modena, Italy, www.unimo.it
- Academia Sinica, Taiwan, <http://twgrid.org>
- Jeonnam University, South Korea, <http://www.chonnam.ac.kr/en/>

4. Grid projects involved in this data challenge

- EGEE www.eu-egee.org
- AuverGrid www.auverGrid.fr
- TWGrid www.twGrid.org
- EELA www.eu-eela.org
- EUMedGRID www.eumedGrid.org
- EUChinaGRID www.euchinaGrid.org
- BioinfoGRID www.bioinfoGrid.eu
- Embrace www.embraceGrid.info

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