

Nature's Subway: Do enzymes use tunnelling to take a shortcut?

Nina Carlo

Enzymes are complex, highly efficient natural catalysts – i.e. substances that are able to greatly accelerate the rate of a chemical reaction. Understanding how they have evolved the features they possess to do this has beneficial implications for a wide range of modern chemistry, such as pharmaceutical development, prediction of drug metabolism, or the design of new synthetic or biomimetic catalysts.

For the past 12 months, Professor **Dominik Marx**, together with his research team led by Dr. **Ian Grant** at the Chair of Theoretical Chemistry at the Ruhr-University Bochum, Germany have sought to understand the complex nature and role of so-called quantum tunnelling phenomena in the catalytic cycles of enzymatic processes. By doing so, the group hopes to show if there are special cases where this non-classical promotion effect increases the catalytic power of enzymes.

The research work of Professor Marx's team is focused on understanding the structure, dynamics and chemical reactions of complex molecular systems in a broad sense. Utilising advanced ab initio simulation methods and algorithms in conjunction with capability computing, the team seeks to understand these processes via computational means, capturing and understanding complex (bio)chemical processes by examining them at the nanoscopic level – i.e. in terms of the motion of individual atoms consisting of nuclei and electrons.

The progress in recent years of computing power and development of hybrid simulation methods such as QM/MM (quantum mechanics/molecular mechanics) techniques has enabled researchers to investigate very large, highly complex biological systems such as proteins, which were hitherto largely inaccessible due to their size and structural as well as dynamical complexity.

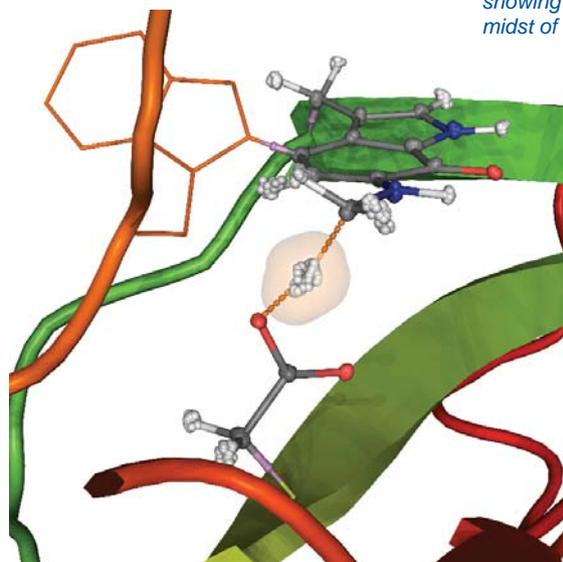
– In some ways, then, it was a natural progression for us to accept the challenge of investigating these esoteric quantum tunnelling ef-

fects in such overly complex biomolecular systems as enzymes, thus bridging the gap between physics, chemistry and biology, says Marx.

And, as Marx continues, this was only possible after significant method development and implementation into the so-called CPMD code in order to marry QM/MM methodology with the ab initio path integral technique done by Dr. **Gerald Mathias** and Dr. **Sergei Ivanov** in this research group.

Investigating the role of quantum nuclear motion

Quantum tunnelling refers to the general physical phenomenon where a particle tunnels through a barrier that it classically could not surmount, i.e. it takes a shortcut. Tunnelling plays an essential role in several physical, chemical and biological phenomena, such as radioactive decay or the manifestation of exceedingly large kinetic isotope effects in chemical of enzymatic reactions. It also has important applications to modern devices such as the semiconductor tunnel diode or the scanning tunnelling microscope (STM), which is an instrument for imaging surfaces at the atomic level.



Page 1–2

Nature's Subway: Do enzymes use tunneling to take a shortcut? PRACE aisbl – new staff members

Page 3

PRACE's Industrial award goes to Xcelerit

Page 4

News in brief
Featured PRACE events

Page 5

Featured project:
HP-SEE

Page 6

PRACE User Forum is on its Way

Below left: At the transition state in the proton transfer reaction in MADH, quantum delocalization of the proton is most profound.

Below right: Cartoon illustration of methylamine dehydrogenase (MADH) suspended in water, showing the active site of the enzyme in the midst of the protein as spheres.



– Quantum tunnelling occurs most easily when light atoms such as hydrogen are involved; hydrogen transfer reactions and the manipulation of carbon–hydrogen bonds feature prominently in a wide range of biomolecular systems, in particular in enzymatic hydrogen transfer reactions, explains Dr. Ian Grant.

According to Grant, there are still many fundamental questions regarding the feature of hydrogen tunnelling that the scientific community would like to probe, such as: what is the catalytic effect – if any – of tunnelling?

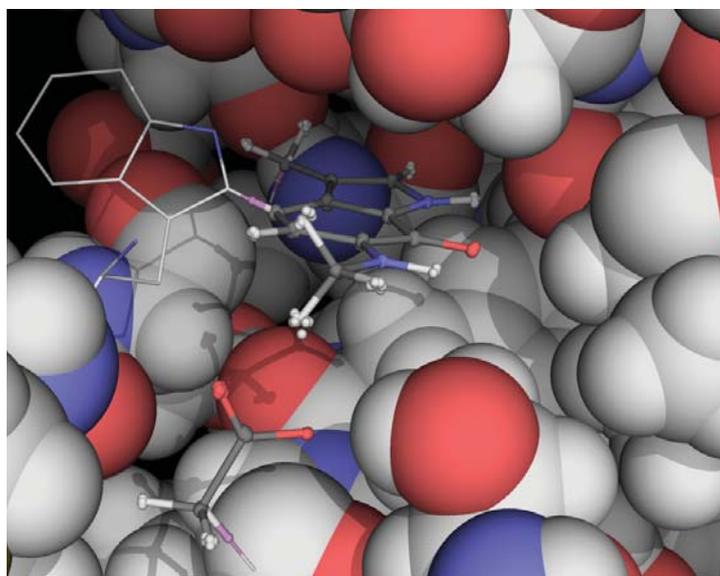
– This is a core issue that is currently addressed by **Theo Zelleke**, MSc, in his PhD thesis, he says.

The results of the study will eventually help to understand the mechanism of tunnelling in enzymes and, based on these insights, to find out if certain enzymes incorporated such subtle nuclear quantum effects into their catalytic cycle.

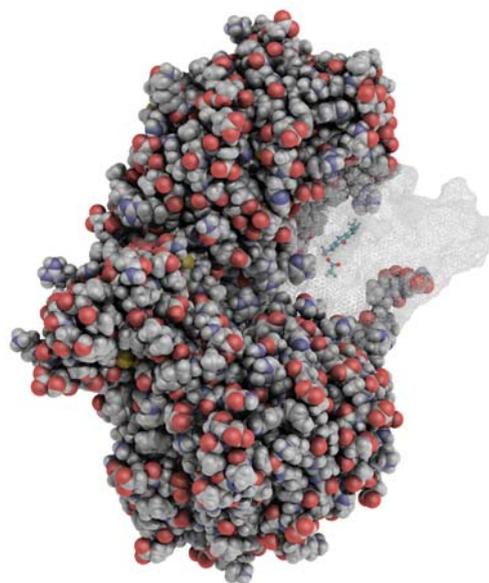
– The sum of knowledge regarding our comprehension of fundamental processes in biology is great, but far from complete, despite it having, in principle, wider implications in a range of applications, including pharmaceutical drug development, drug metabolism in predictive medicine, as well as in artificial protein synthesis and biomimicry – i.e. a new discipline that focuses on “innovation inspired by nature.”

– Clearly, many biological processes involve proton transfer where, in principle, quantum tunnelling could be important. This phenomenon, however, is very subtle in the senses that small changes make big effects. It remains to be seen if nature exploited tunnelling in evolution and, if so, if similar mechanisms could be used in pharmaceutical drug development. But our research is really about increasing our basic knowledge of how enzymes work. Consideration of nuclear quantum effects can play a part in this, complementing the classic barrier model we’re used to working with, Grant says.

www.cpmnd.org



In the active site, the path integral method shows how individual atoms are modelled by clusters of beads, indicating that light atoms like hydrogen have larger quantum spreads



The active site lies in one sub-unit of MADH, buried towards the centre of the whole enzyme.

PRACE aisbl - new staff members



*Tanja Bergrath
Assistant to the Board of Directors*



*Marjolein Oorsprong
Communications officer*



*Estelle Emeriau
Peer Review Officer*



*Iñigo Yenes
Financial and Legal Officer*



*Dr. Renelle Guichard
Peer Review Officer*



*Tatiana Gonzalez-Ovin
Office Administrator*

PRACE Award for the Most Innovative Industrial High-Performance Computing in Europe goes to Xcelerit



Marcin Ostasz, BSC Prospect Administrator and Business Analyst

Mr Hicham Lahlou, Xcelerit CEO and co-Founder receives the Award from Richard Kenway, PRACE Scientific Steering Committee.

Xcelerit, a Dublin-based software company specialising in cross-platform acceleration tools, was awarded the First Prize in the competition for the Most Innovative Industrial HPC Solution in Europe. The award was presented at the 4th PRACE Industrial Seminar, the annual PRACE event aimed at developing relationships with industry.

This year's seminar, held in Bologna on 16th and 17th of April, attracted 96 attendees from 15 countries, including 67 companies and research organisations not affiliated with PRACE, of which 42% were Small and Medium-Sized Enterprises. The event lasted two half-days and it included 20 talks, 4 workshops and a networking event, putting 30 speakers on the podium.

The main purpose of the event was to announce the PRACE Open R&D Access Model which has been developed in order to allow companies to conduct open research using the organisation's resources. PRACE is a pan-European research infrastructure that includes the top level of the European High-Performance Computing eco-system. For more information on this programme, visit www.prace-ri.eu.

The objective of the competition, held this year for the first time in parallel with the

seminar, was to recognise the boldest industrial HPC application and illustrate how far this technology can be taken to change the present best practice of European industry.

The competition is open to organisations from all fields of HPC.

The conditions were as follows:

- The solution must pertain to industry, i.e. it must be possible to apply it in an industrial context with clear benefits – there must be a market potential for that kind of solution

- The solution must represent some level of implementation maturity – we are not looking just for ideas but rather for working solutions, although we will also accept those in early implementation stages

The applicants were required to demonstrate why HPC had been chosen as the technological vehicle and how has it been implemented and to show the benefits for the industrial user in terms of competitive advantage. The award criteria were:

- Novelty and originality
- Clear benefit for industry
- Maturity and market perspectives

The selection of the overall winner was carried out by a jury consisting of members of the

PRACE Scientific Committee and its Industrial Relations Work Package. At the Seminar, the award was presented by PRACE Managing Director Dr Maria Ramalho, and Prof. Richard Kenway representing PRACE's Scientific Steering Committee According to PRACE, Xcelerit's solution addresses the key obstacles to adopting HPC by businesses as identified in a number of studies, including PRACE's own report 'The Requirements of Industrial Users'. Among these obstacles are: a lack of knowledge about HPC, the cost of adopting and maintaining new technologies and lack of easy-to-use application tools.

The learning curve for developing HPC applications is steep and companies that recognise the potential of using HPC usually face the challenge of having to pay expensive software licences, the fees of engineering or consultancy companies, or having to hire specialised, hard-to-find staff in order to develop on-site products. The Xcelerit software development kit addresses this problem by providing a framework that enables engineers with no knowledge of parallel computing to produce results taking advantage of HPC machines. The solution presented by Xcelerit will thus help to broaden the use of HPC within European industry.

NEWS IN BRIEF

PRACE Award for Most Innovative Industrial HPC in Europe goes to Xcelerit Tuesday 22 May 2012

BOLOGNA, 16th April 2012.- Xcelerit, a Dublin-based software company specialising in cross-platform acceleration tools, was awarded First Prize in the competition for the Most Innovative Industrial HPC Solution in Europe. The award was presented at the 4th PRACE Industrial Seminar, the annual PRACE event aimed at developing relationships with industry.

120 million core hours on CRAY XE6 Hermit allocated to three research groups in the PRACE 4th Call for Proposals Tuesday 22 May 2012

PRACE awarded 120 million core hours on the brand new CRAY XE6 Hermit supercomputer at HLRS@GCS in Germany to three successful projects submitted to the 4th PRACE Call for Proposals. Two awardees will be using their allocated core hours for research in the field of Engineering & Energy; the third one comes from the field of Chemistry and Materials.



PRACE Scientific Conference 2012 Monday 7 May 2012

The PRACE Scientific Conference 2012, hosted by the Partnership for Advanced Computing in Europe (PRACE) will be held on Sunday 17th June 2012 at the Radisson Blu Hotel in Hamburg, Germany. The keynote speakers include:

Richard Kenway, Chair of PRACE Scientific Steering Committee & Conference Chairman, **Maria Ramalho**, Chairman of the Board of Directors, PRACE aisbl, **Yves Ineichen**, Paul Scherrer Institut, PRACE Award Winner, **Paolo Carloni**, German Research School for Simulation Sciences GmbH, **Bing Liu**, Max-Planck-Institut für Eisenforschung, **Jeremie Bec**, Observatoire de la Côte d'Azur, **Ricardo Fonseca**, Instituto Superior Técnico, Lisbon, and **Frank Jenko**, Max Planck Institute for Plasma Physics. www.prace-ri.eu/PRACE-Day-2012

PRACE Summer School on Code Optimisation for Multi-Core and Intel® MIC Architecture Wednesday 2 May 2012

The Partnership for Advanced Computing in Europe (PRACE) is pleased to announce the Summer School on Code Optimisation for Multi-Core and Intel® Many Integrated Core (MIC) architecture, which will be held from 21st to 23rd June 2012 at the Swiss National Supercomputing Centre in Lugano, Switzerland.

PRACE 4th Call for Proposals accepted 43 applications and granted 1.134 million core hours on Tier-0 systems: a record! Monday 30 April 2012

For the PRACE Project Access 4th Call for Proposals on Tier-0 systems, 1136 million core hours on 5 Tier-0 machines were made available by PRACE hosting members – the largest number of supercomputers for any PRACE call so far. PRACE received 78 applications requesting 1.927 million core hours. The peer review process for the project applications allocated 1134 million core hours to 43 proposals. Researchers awarded access to the infrastructure will start using their allocated core hours from 1st May 2012 until 30th April 2013.

PRACE celebrates 2nd anniversary and launches 5th Call for Proposals Monday 23 April 2012

PRACE, the Partnership for Advanced Computing in Europe, celebrates its second anniversary on 23rd April 2012. Since its birth on 23rd April 2010, PRACE has seen a continuous growth and now has 24 member organisations from EU Member States and associated countries. Negotiations with interested parties from further countries are under way.

Featured PRACE events

2012 European-U.S. Summer School on HPC Challenges in Computational Sciences in June 24-28, 2012 in Dublin, Ireland

The Partnership for Advanced Computing in Europe (PRACE) and the Extreme Science and Engineering Discovery Environment (XSEDE) have collaborated to offer the third European-U.S. Summer School on HPC Challenges in Computational Sciences. Goals of the summer school are for attending graduate students and postdoctoral students to gain greater knowledge about high performance computing (HPC) and its applications in multiple fields of science and engineering and to foster new collegial friendships and partnerships among the international presenters and attendees.

PRACE at ISC'12 in Hamburg

Welcome to PRACE at ISC'12! PRACE's highlights at ISC'12 are: PRACE Tier-0 infrastructure of Petascale systems. Presentation by the PRACE Award winner on Sunday, June 17, during the PRACE Scientific Conference 2012 PRACE Award ceremony during the ISC'12 Opening Session Most Innovative Industrial HPC Application in Europe at the booth during the Press tour on Monday, June 18, between 15.00 - 16.00. PRACE Prototype Evaluation Results BoF on Tuesday 9:00-9:45.

See you at booth 134 on the exhibition floor for a welcome cocktail on Monday at 6 pm.



www.prace-ri.eu



Featured project: HP-SEE – HPC infrastructure for South East Europe’s research communities

Danica Stojiljkovic,
Research assistant, Institute of Physics,
Belgrade

HP-SEE (SEE = South East Europe) works across several strategic lines of action to link the existing and upcoming HPC facilities in the region into an integrated South-East European HPC Infrastructure, implement solutions for it, and open it to the wide range of research communities with specific needs for massively parallel execution on powerful computing resources.

It brings together research communities and HPC operators from 14 countries in the SEE region, enabling them to share of HPC facilities, software, tools, data and results of their work, thus fostering collaboration and strengthening the regional and national human network.

HP-SEE puts the emphasis on supporting strategic groups in **Computational Physics, Computational Chemistry and Life Sciences**, encouraging the research communities in close collaboration and offering specific end-user services such as application porting on the regional HPC infrastructure, ensuring the ease of access to and the efficient use of available resources. HP-SEE boosts the knowledge of existing HPC users and helps the growth of the HPC community by organizing a series of national and regional trainings.

The HP-SEE initiative builds on the lasting cooperation in the SEE region, embodied in a number of infrastructure initiatives, co-funded by the EC, aiming at equal participation of less-resourced countries of the region in European trends. The SEEREN initiative established a regional network and the SEE-GRID initiative the regional Grid, while BSI project has established GÉANT link to Caucasus. The SEE-LIGHT project is working towards establishing a dark-fibre backbone that will interconnect most National Research and Education Networks in the Balkan region.

“The long-term strategy of regional electronic infrastructure collaboration is further strength-

ened through this current endeavor in High-Performance Computing, allowing the researchers to access Tier-1 HPC centres not only as an intermediate layer in the pan-European HPC hierarchy which includes PRACE, but also as a coherent regional facility”, said Dr. Ognjen Prnjat, HP-SEE project coordinator.

Among the HP-SEE main objectives is policy development and stimulating regional inclusion in pan-European HPC trends. The project will ensure that all participating countries in the region have access to the latest HPC facilities in the region and if necessary in Europe, through suitable and sustainable organizational and operational models. HP-SEE aspires to act as a catalyst for the establishment and the development of national HPC initiatives, and as a SEE bridge for PRACE.

Complementary action of the HP-SEE project has been the interconnection of the National Research and Education Networks (NRENs) in Armenia (NAS RA) and Azerbaijan (AzRENA) to the pan European data network dedicated to the research and education community – GÉANT. The network became operational in September

2011 and now provides two 45 Mbps links to South Caucasus and HP-SEE Network Operations Center (NOC) will operate these links for 24 Months.

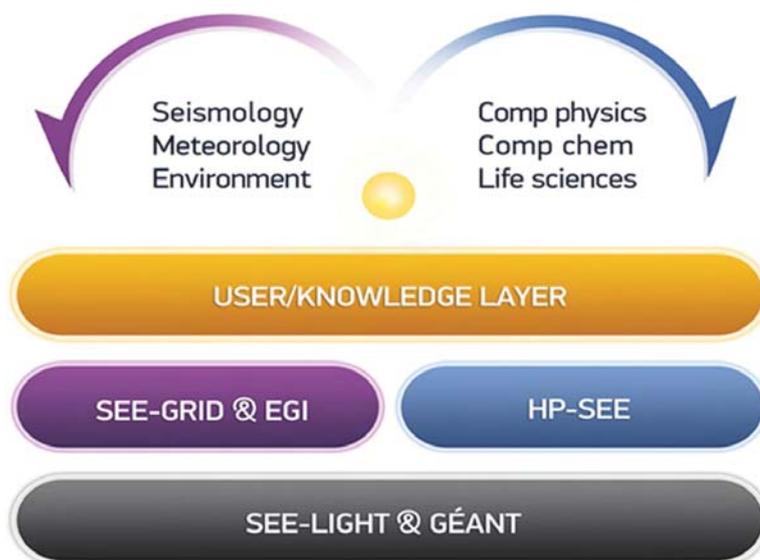
HP-SEE receives EC co-funding through FP7 under the «Research Infrastructures» action.

HP-SEE Long Term Vision

- Being on a technological par with the rest of Europe
- Enabling local scientists to use their potential
- Integrating the region into the pan-European HPC landscape
- Role-model for regional developments
- Leading the way in wider contexts

For more information please visit www.hp-see.eu.

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Editor-in -chief:
Tiina Leiponen, CSC

The PRACE User Forum is on its way

Giovanni Erbacci PRACE Work package 4 leader and Laetitia Baudin, Communications manager at GENCI

The PRACE User Forum is a voluntary and independent organization open to all European scientific and industrial user communities using the PRACE HPC resources for the development of their research activity. The PRACE User Forum aims to establish an official communication channel between HPC users and the PRACE aisbl, by exchanging information, discuss needs and expectations regarding the HPC resources made available by PRACE, and more generally promote HPC usage and impact.

This body has been created step by step during the year 2011 by PRACE 1IP-WP4 "HPC Ecosystem Relations". Once the terms of reference of the PRACE User Forum were defined, a first PRACE User Forum was organized during the DEISA-PRACE symposium in Helsinki in April 2011, in order to lay the foundations of a persistent entity.

The 1st User Forum was a major step in the direction of the creation of a channel of communication between HPC users and PRACE aisbl. After the event, WP4 continued to work to fully structure and consolidate a sustainable User Forum.

The PRACE User Forum is organized with a Programme Committee which is responsible for its development: calling and organising the meetings, distilling recommendations from the discussions during the meetings and for communicating them to the PRACE aisbl. The Programme Committee includes a maximum of 15 representatives from the main scientific fields, already involved in using the PRACE HPC resources. The mandate of the members of the Programme Committee is two years with the possibility of renewal for one year.

The first Programme Committee was established on December 1st, 2011 in a meeting in Brussels organised by the PRACE 1IP- WP4, who invited the PRACE Scientific Steering Committee and all the PIs of the projects (from regular calls) supported by PRACE. The objective of the meeting was the election of the members of the Programme Committee, the Chairman and the vice Chairman. Then the body was endorsed by the PRACE Council in January 2012.

The Programme Committee organized the 2nd User Forum in Dublin on March 14, 2012 during the Scientific Case Update Workshop. More than 60 scientists and representatives of the SSC and PRACE aisbl attended the event.

The interaction between users from scientific

and industrial communities and PRACE aisbl during the 2nd User Forum proved the importance of the User Forum to give feedback to PRACE aisbl regarding its services and the perception of users about future developments of PRACE.

In addition to the annual general meeting, the Programme Committee can organise satellite meetings and workshops arranged either during main conferences dedicated to specific scientific fields or around a thematic issue of interest for a group of users, heavily dependent on the HPC resources made available by PRACE aisbl, or even during national meetings dedicated to HPC users.

The next appointment with the User Forum is at the PRACE Scientific Conference 2012, which will be held on June 17th, 2012 during the ISC event in Hamburg, Germany. In this occasion PRACE users will have a further opportunity to discuss their experiences of applying for, and using, PRACE resources.

Now that the PRACE User Forum is really on its way, it is very important that the users concretely perceive it as a strong opportunity for them, and cooperate to the grow and consolidation of this body, as a real and direct channel between all the PRACE users and the PRACE aisbl.

Members of the Programme Committee

Chair:

- Turlough Downes, Dublin City University (Ireland)

Vice-Chair:

- Gustavo Yepes, Universidad Autonoma de Madrid (Spain)

Members (in alphabetical order):

- Jeremie Bec Observatoire de la Côte d'Azur (France)
- Stefano Fabris CNR and SISSA (Italy)
- Ricardo Fonseca Instituto Superior Tecnico (Portugal)
- Derek Groen, University College of London (UK)
- Koen Hillewaert CENAERO (Belgium)
- Karl Jansen DESY (Germany)
- Aake Nordlund University of Copenhagen (Denmark)
- Elisabetta Pallante University Groningen (The Netherlands)
- Philip Schlatter Royal Institute of Technology (Sweden)
- Gabriel Staffelbach CERFACS (France)
- Federico Toschi Eindhoven University of Technology (The Netherlands)
- Pier Luigi Vidale University of Reading (UK)

