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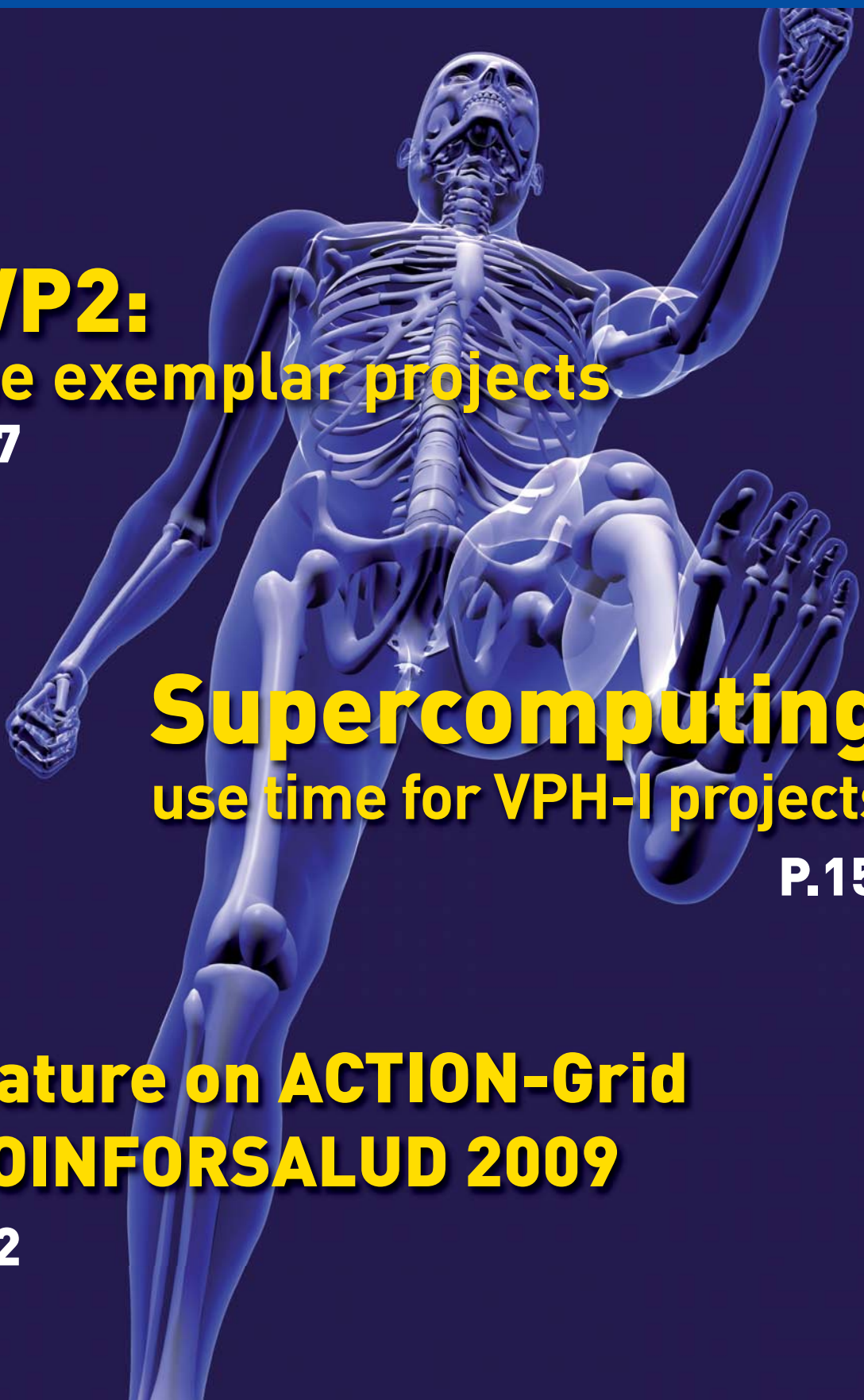
VPH NoE newsletter

VIRTUAL PHYSIOLOGICAL HUMAN NETWORK OF EXCELLENCE



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quantitative methods capable of synthesizing and examining diverse data, so that we may extract the full value from experimental information that is currently available.
Multi-scale mathematical modelling has emerged as a promising candidate for tackling this difficult problem. These quantitative models are uniquely capable of integrating disparate physiological data, into a consistent framework, whose functioning can be both controlled and studied. These developments offer significant promise for the prediction of physiological behaviour and enabling the untangling of the complex cause and effect relationships embedded within physiological systems.
In order for such models to produce optimally informative data, however, it is essential that the mathematical techniques on which they are based exhibit a sufficiently high level of complexity and robustness. The creation of a physiologically valid model is contingent on the ability to balance these two properties, and the development of metrics and techniques to define and support a model's fitness, remains a challenge to the Physiome's scientific community.
On the 20th to 24th of July we will hold the 3rd Cardiac Physiome workshop. Using the heart as an advanced example of integrated organ system model we will discuss these issues, present progress in model advances and define priorities for ongoing development. The scientific programme of this conference will focus on the combination of experimental and modelling research required for developing integrated multi-scale and multi-physics cardiac models with Keynote speakers oral and poster presentations dedicated to specific spatial scales, modelling and experimental tools and translational outcomes. ■

For further information on the conference please visit the Events section on our project website **http://www.newton.ac.uk/programmes/CPP/cppw01.html**
The graphic was created by Jack Lee (PhD student) and David Nordsletten (PhD student), UOXF.

Technical focus

GPUGRID - Technical report

By T. Giorgino, I. Buch, K. Sadiq, M. Harvey and G. De Fabritiis - Computational Biochemistry and Biophysics Lab (GRIB-IMIM) and Universitat Pompeu Fabra, Barcelona Biomedical Research Park

Atomistic simulations have proven an extremely useful tool for the investigation of molecules of biological importance, such as proteins. We can use them to study not only the dynamics of these building blocks of life, but also their interactions, which are at the basis of the rich existence of organelles and cells: their division, functioning, and death are regulated by how proteins interact with each other and with other substances. In fact, computational techniques offer us unprecedented "peeks" in those interactions, at levels of detail that were never reached before.
Computational modelling is however no simple task. The main reason for the difficulty of *in silico* techniques is well captured in the words of the physicist R. P. Feynman at the 59th annual meeting of the American Physical Society: "There's plenty of room at the bottom". The meaning of this motto is that, in terms of spatial and temporal scales, there is a daunting distance between the macro-world accessible to our senses and single molecules (such as DNA and proteins). This gap affects our ability to treat those systems computationally. The power of PCs has been advancing steadily since decades, but even the most recent central processing units (CPUs) are far from being able to follow the dynamics of an average protein, with atomic detail, for milli- or even microseconds of simulated time: this is the "scale gap" between the

Comments from a forum contributor

"People want to identify with the activity they undertake; if they don't, they are liable to move on."
"My daughter has schizophrenia, a classic case that surfaced in late teens, and formally diagnosed when she was 22. It's now ten years later, and I am always interested in hearing and seeing long term trends on the topic. She will not be "cured", all that can be done is symptom treatment, at present and for the foreseeable future, a cure is an unrealistic expectation. However it may happen for future generations given resource and research, who knows, and if we can play a small part in helping that happen, that can only be a good thing. I would - quite literally - not wish schizophrenia on my worst enemy, its an horrific debilitating condition."

Zydor, (volunteer)

molecular and the biological macroscales. The mission of GPUGRID at IMIM, part of the VPH NoE Toolkit, is to provide members of the VPH with the tools to bridge this gap.

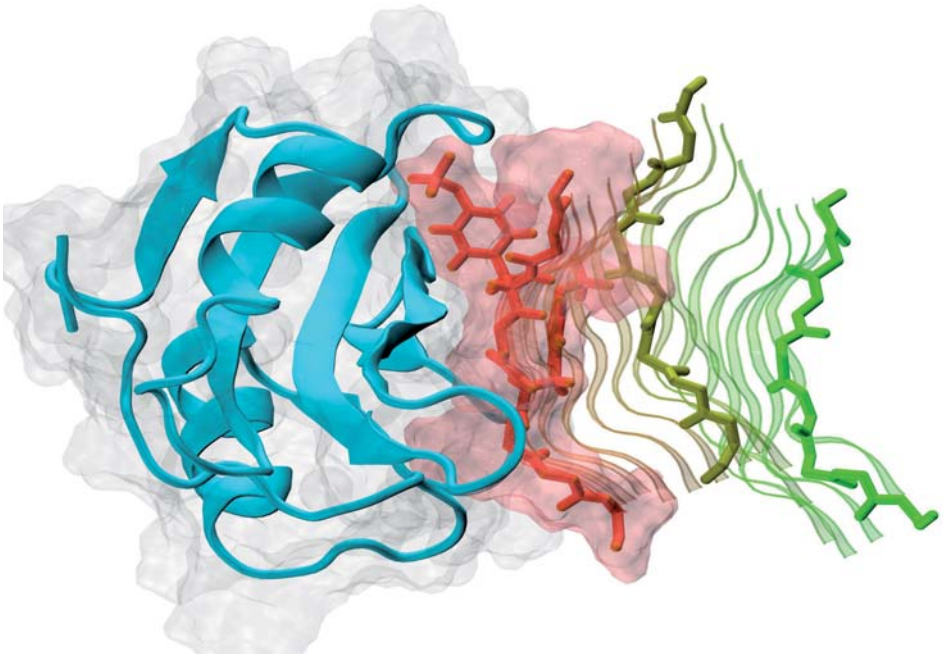
How can an interval *of four* orders of magnitude in computer time be filled? We asked for the support of the public. With the help of thousands of people, we built GPUGRID.net, one of the largest distributed computing projects worldwide. A *distributed computing* system allows scientists to gather the processing power donated by volunteers, dispersed worldwide, and connected through the Internet. Researchers prepare their computational experiments and arrange them in several "units of work". When volunteers read about a project and decide to join it, they install a small "client" software, and leave it running on their PC as long as they wish. The rest proceeds transparently for them: the client downloads the work units, processes them, and uploads the results back to the server. Computations typically last half a day, and are executed with a negligible impact on the normal use of the PC. Our server coordinates the task distribution: it keeps track of hosts and work packages, keeps into account the varying computational capabilities of each, and even their reliability. The progress of the whole experiment, in fact, will not be affected by the vicissitudes of individual computers, which are of course under the control of their owners, who could decide to disconnect at any time.

The *relationship* between volunteers and the project is an essential aspect in distributed computing efforts: real people, not just machines, are investing part of their attention and time. Many of them may have chosen to join the project because they share its scientific objectives, and therefore they will be interested in its progress; results will have to be communicated in terms that they can understand (see quotes). Volunteers use online forums to communicate, discuss, and stay informed about the meaning of computations and the scientific progress. Right now, approximately two thousand volunteers are connected and computing for GPUGRID.net. Their contribution is allowing us and other VPH groups to simulate 5 microseconds of molecular trajectories per day, modelled with the well-known CHARMM or AMBER force-fields.

At its core, GPUGRID leverages the emerging technology of *accelerated processors*. Graphical processing units (GPUs) are commodity components that are ordinarily employed by videogamers to play in virtual worlds of ever-increasing visual realism. In recent years, these devices evolved at a breathtaking pace, so much so that they acquired general-purpose capabilities far beyond the handling of two- and three-dimensional images, their initial scope. The demand from the consumer market was in fact so pronounced that card makers have, on average, doubled the computational power of their products every 12 months, compared to 18-24 months for traditional processors. The compute capability of GPUs have now surpassed those of CPUs by almost a factor of ten, and the gap is widening still further. We are exploiting this power through ACEMD (Harvey et al, 2009) the computer code which maps bio-molecular computations onto the complex multi-core architecture of recent GPUs.

The combination of dedicated volunteers and leading-edge technology has made GPUGRID *the fifth* distributed computing project worldwide, in terms of floating points operations computed per day. What's more, it is growing steadily, thanks to dedication, attention to the users' reports, and the adoption of latest advancements in GPUs and distribution technologies. With ACEMD and GPUGRID, the VPH can be considered at the forefront of computational biophysics and biochemistry. We hope that our efforts will push the scale of the problems that VPH members can tackle substantially beyond the state of the art, changing the very idea that we have about the reach of experiments performed in silico. ■

For further information please see Harvey et al (2009) in publications or visit the project website: **www.gpugrid.net** and ACEMD website: **www.multiscalelab.org/acemd**



A small peptide (in red) containing two phosphorilated tyrosines has been "captured" at the surface of a "Src Homology 2 domain", or SH2 (in grey). The picture shows a snapshot in the course of an experiment conducted with the help of GPUGRID.net volunteers: an ensemble of computations, called steered molecular dynamics (SMD), forced the tyrosine to be detached from the SH2 in a controlled sequence (in color scale).

This event lies at the beginning of a complex series of reactions which affect the cell. In practice, the cell "responds" to external changes by "feeling" them when a SH2 becomes associated to a tyrosine. Studying the strength and dynamics of this binding is therefore extremely important.