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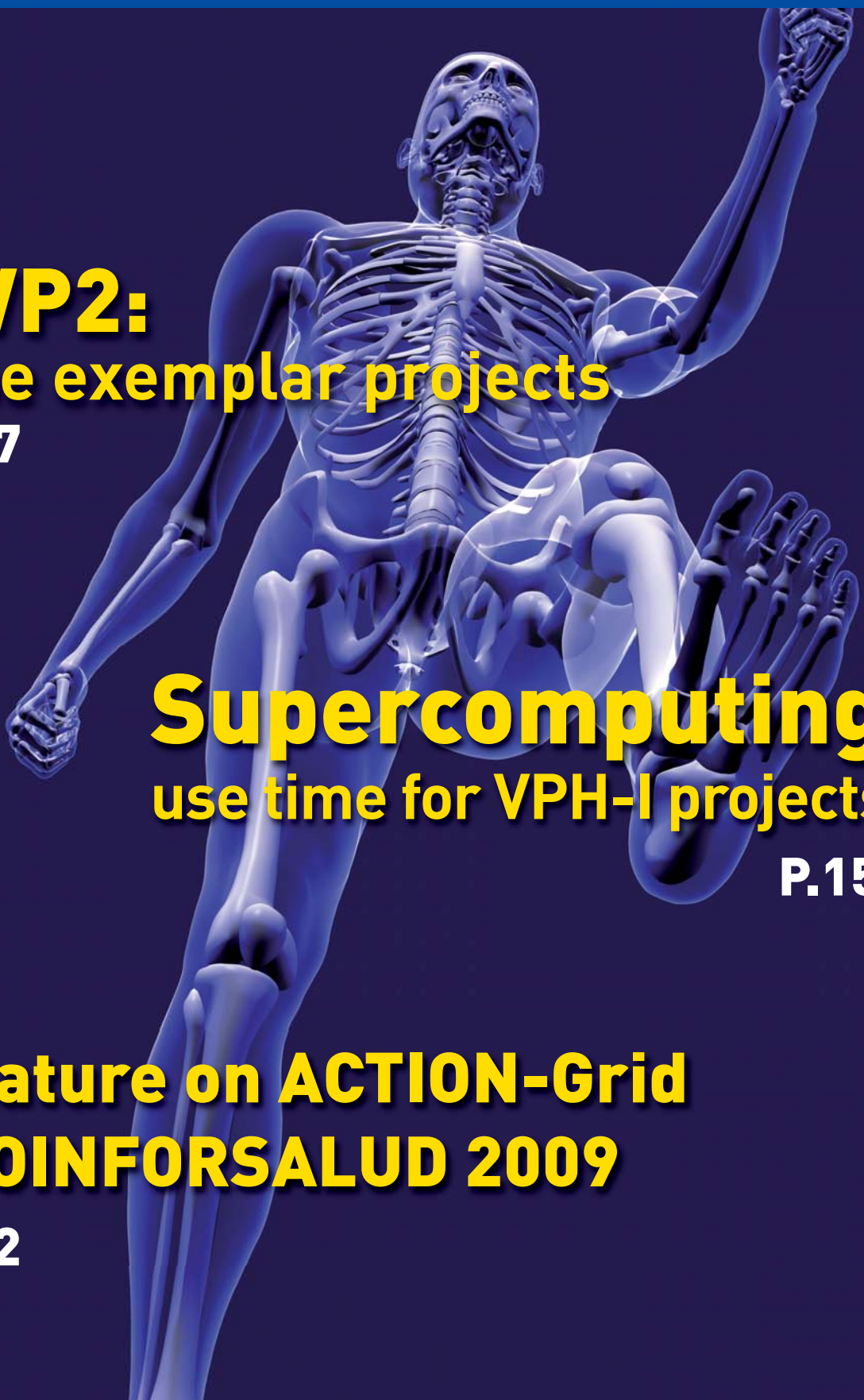
VPH NoE newsletter

VIRTUAL PHYSIOLOGICAL HUMAN NETWORK OF EXCELLENCE



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Virtual Physiological Human
network of excellence

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EDITORIAL

After the first year of building the Virtual Physiological Human Network of Excellence (VPH NoE) we are now preparing our first Interim Report for the European Commission. We take this opportunity to look back, assess our progress, as well as to identify strengths and weaknesses of the current VPH Network of Excellence efforts.

The primary objective of the Network of Excellence is to strengthen the Virtual Physiological Human community by addressing issues of common concern that affect VPH-I projects collectively, such as research tools, infrastructure, training and dissemination.

A detailed article about the VPH Toolkit that is going to provide the technical and methodological framework to support and enable VPH research was included in the previous newsletter. In the VPH-I section, Peter Coveney, Stefan Zasada and Steven Manos report on the establishment by the VPH NoE of a VPH Virtual Community which provides access for all VPH-I projects (and others) to the EU FP7 DEISA high performance computing infrastructure, as well as the Application Hosting Environment, a software tool designed to facilitate access to it.

The discussions at the ICT-Bio event in Brussels in October 2008 identified the need to set up VPH Standards and Data working groups. On page 5 Steven Manos discusses this group, which focuses on protocols, formats and systems used within the VPH technologies and the methodologies themselves.

We report on the considerable progress of VPH-I projects. There is a feature on ACTION–Grid by Diana de la Iglesia, the Project Coordinator, which details the white paper being written following their BIOINFORSALUD 2009 grid technology conference held this year. Kyriakos Hatzaras of RADICAL provides a report on the results of their survey on VPH user requirements in Security and Privacy and Luc Soler, project coordinator of PASSPORT, gives details of a new anatomical and medical imaging database which has been made available to the scientific community. We also interview Serge Van Sint Jan and Debora Testi about the recently completed FP6 LHDL project which was judged to be 'outstanding' by the European Commission.

Looking ahead, we will be holding our first Annual Meeting, September 10-11 2009 in Brussels, which will follow our annual review with the European Commission (September 8). This will be a chance to consolidate the work of the last 12 months by assessing our strategic direction in line with the developing needs of the growing VPH community. We also plan to hold a VPH-I day (September 9), to provide means for interaction with funded VPH projects and Associate and General Members of the NoE. The VPH-I working group was set up earlier this year and seeks to improve communication between the projects, exploit common dissemination opportunities and avoid scientific duplication across VPH-I projects. All members of the VPH Initiative (VPH-I) working group and VPH Coordinators will be invited to this day. We hope these events will be well attended and look forward to three days of constructive discussion and feedback, as the success of the NoE is reliant on input from the community it is trying to serve.

An additional initiative that we are currently exploring is the concept of running 'summer schools' to assist with user engagement through dissemination and training, with the aim being that we assist those new to the field who will then act as evangelists to their institutions. Whilst this is at the concept stage, we would welcome input and ideas from people who have had experience of running summer schools before or who have attended events such as the Grid Summer School, to help with determining the best approach. Watch this space!

Finally, we are pleased to report that in March of this year the NoE Project Office was joined by Miriam Mendes and Vanessa Díaz who will be responsible for project management and scientific coordination of the VPH NoE (respectively). Miriam will be the primary point of contact for all external inquiries to the Network (miriam.mendes@ucl.ac.uk +44 2081 334 594). Vanessa and Miriam will continue the excellent work of Cat Gale, who has accepted the post of science programs producer at the BBC. We are sure you will want to join us in thanking Cat Gale for her major contribution to the VPH NoE, first in securing funding from the Commission for this initiative, and then for keeping us all on the narrow path to success during the launch of this network.

Further congratulations are called for to Katherine Fletcher, who on March 25 gave birth to healthy twin boys, Tom and Sam. Both mother and sons are making excellent progress and, incredibly, all three have already attended recent strategy meetings of the project office team!

Finally, we would like to extend a cordial welcome to Alexandra Masindova. We have been fortunate to be able to recruit her to cover Katherine's maternity leave, to help keep the Oxford Project Management of preDiCT and NoE well-coordinated. Alex will benefit from advice from Sharon Lloyd, who coordinates the technical toolbox development at Oxford.

Peter Coveney and Peter Kohl
Joint Coordinators, VPH NoE

VPH NoE Section

NoE News

Waiheke Workshop Report

By Catherine Lloyd, Research Fellow, University of Auckland

The combined CellML SBGN SBO BioPAX MIASE Workshop was held at Waiheke Island, New Zealand from 5th-9th April 2009. 32 speakers presented their research and over 50 delegates attended the meeting, including visitors from the UK, Ireland, Singapore, Germany, America, Japan, and Australia. The presentations were divided into themed sessions and following each set of talks there were chair-led group discussions. We were not disappointed. True to form, some of these discussions were rather "lively", and all of them were considered to be productive.

One of the most positive outcomes from the CellML "et al." Workshop was a community consensus towards the interoperability and connectivity of biological standards, ontologies and domain specific languages. In the last few years several domain specific standards have been developed. For example, amongst the systems biology community, there are the Systems Biology Markup Language (SBML), CellML, BioPAX and many other standards specialising in the different aspects of computational modelling. Historically the development and maintenance of these initiatives have been relatively independent. However, we have come to recognise the value and importance of combining our efforts and resources. We acknowledge there will be never be one single standard to satisfy all requirements, but we are looking towards a more united future.

Taking this idea further, it was suggested there could be an umbrella organisation for systems biology standards. This organisation would focus on language interoperability, joint meetings, improved converters and generally raising community awareness of the different standards.

Some other key conclusions to come out of the meeting were as follows:

- The adoption of the same methods for describing simulation metadata (MIASE and SED-ML).

- CellML and SBML models will be visualised using SBGN.
- For model annotation MIRIAM URIs will be implemented.
- There is a plan to bring more physical terms into the Systems Biology Ontology (SBO) in order to mirror the Ontology of Physics for Biology (OPB). It was also highlighted that the ontologies used by the SBML community are insufficient for annotating the electrophysiological models in CellML. This may be resolved with collaboration with OBO.
- We need to coordinate our model curation efforts. It has been noted that there is a considerable overlap between the content of the BioModels Database and the CellML Model Repository. The curators are working together to define a single standard for model curation, and are also trying to curate different models and then exchange them. Such model exchange will be facilitated by improved language interconversion tools.

At the request of those who were unable to attend the workshop, all of the presentations are available in PDF format for download from the workshop website. The proceedings were filmed and the sound recorded, and once this footage has been processed and edited it will also be made available for download.

Thank you to everyone who attended, and contributed to, the workshop – especially those who travelled from Europe. Further, this meeting took place right after the SBML Hackathon and the BioModels Meeting in Hinxton, UK, and many of the delegates at the Waiheke Workshop attended all three meetings. It has to be agreed that this was an admirable effort, as was highlighted by one anonymous delegate:

"At this rate, the joint standardization efforts will turn into a month-long annual conference. It will become like a neutron star, so dense that its gravitational pull will attract surrounding meetings into itself."

Poetic… But I think that even this person will agree that this workshop was a great success, and it was well worth the effort of travelling to the other side of the world. We hope that this will be the first of many future combined meetings within this community. ■

For a complete workshop report visit the following website
http://www.cellml.org/workshop/workshop2009/

Can we talk? Standards in the VPH

By Steven Manos, Research Fellow, University College London, Vanessa Diaz, VPH NoE Coordinator, University College London and Keith McCormack, University of Sheffield

During the VPH NoE Concertation day which took place in Brussels, October 2008, three workshops were held to begin to identify and address the needs of the VPH community. With the focus on improving the uptake of VPH technology use in the real world, workshop 1 discussed three areas; the clinical involvement in and acceptance of the VPH approach, integrating validation and verification in computational clinical systems from the onset of projects and tightening VPH and industrial take-up and exploitation. The reasons for these were clear. Clinical systems require extensive validation, and with no examples of physiome-like systems in use in the real world, the development path is long and the involvement of clinicians for this entire period (5-10 years typically) may be difficult. Many tools will be developed as a result of VPH-I projects and there is an immediate need to work out how to better integrate these innovative tools. The effort of validation and verification is currently led by industry via their development pipelines, taking clinical solutions developed in academia and applying the necessary QA and standardisation to bring clinical products to market. This separation of academic and industrial responsibilities results in a much longer time-to-market for VPH technologies. Born out of these requirements was the VPH Standards Working Group, with the aim of developing common standards descriptions and actively disseminating standards information to VPH researchers in collaboration with competent standardisation bodies. The first meeting was held at UCL in January, and as a result of ongoing discussions with ETSI - the European Telecommunications Standards Institute, representatives of the VPH Standards Working Group took part in the 2nd ERCIM-ETSI Infinity Initiative meeting, April 2-3 at ETSI in Sophia Antipolis, France.

The theme of the 2-day symposium was Bio ICT-The Heart in the Computer, with a special focus on the modelling and simulation of organs. The event was run in cooperation with the European Commission and was supported by the VPH NoE. Speakers included Dr Vanessa Diaz (VPH NoE), Dr Steven Manos (VPH NoE), Dr Keith McCormack (VPH NoE), Prof. Norbert Graf (University of Saarland), Prof. Martin Hofmann-Apitius (Fraunhofer Institute) and Prof. Nicholas Ayache (INRIA), amongst others. This meeting confirmed the need to build relationships between VPH members, standards bodies and industry with the focus on standards. The working group now aims to hold meetings between VPH members and standards bodies on an annual basis, with the first one planned for late 2009. As part of the NoE's continuing activities towards the identification and formulation of standards for VPH data and model interchange, the NoE is providing representation to an existing ETSI initiative aimed at the introduction of standards for eHealth. It is anticipated that this participation will both inform the standardisation discussions within the NoE itself and broaden insights into the strategies, partnerships and timescales required for the consultative processes appropriate to the instigation of formal standards-setting activities in an emerging discipline. More broadly in the long run, the working group will maintain guidelines available to VPH researchers to better identify and implement protocol, procedure and format standards within their VPH research. ■

For further information on Standards in the VPH, contact
vph-noe-standards@ercim.org
For more information on the symposium visit the website:
http://www.etsi.org/WebSite/NewsandEvents/Past_Events/2009_BIOICT_INFINITYINITIATIVE.aspx

NoE News

to focus on clinical as well as ICT news and events

Membership of the VPH NoE

By Marco Cortopassi, European Project Manager, UCL

The VPH NoE has launched its ambitious membership scheme. As of January 2009, any organization with an interest in the work of the VPH NoE can apply to the VPH NoE membership. The scheme aims at ensuring a wider engagement with the research community by offering members the opportunity to get involved in the activities of the NoE and contribute to the wider VPH initiative.

We are four months into the membership and already 20 organizations have joined in. The current list includes research centers such as the Istituti Ortopedici Rizzoli in Italy (http://www.ior.it/Sito/frmDefault.aspx) and the Institute of Bioengineering of Catalonia in Spain (http://www.pcb.ub.es/homePCB/live/en/p369.asp), along with industrial players such as Fujitsu Laboratories Europe (http://www.fujitsu.com/emea/) - as well as other stakeholders such as the European Medical Association (http://www.emanet.org/), to name but a few.

By becoming a VPH NoE Member, researchers within the selected organizations become eligible and are encouraged to get involved in many areas of NoE. These include:

- **VPH website/VPH Initiative online networking activities**
- **VPH project meetings and International symposia**
- **VPH ToolKit development**
- **VPH exemplar projects**
- **Training Activities**
- **Contribution to dissemination materials**
- **Contribution to online discussions and debate.** ■

More information on the VPH NoE membership is available on the VPH NoE website: **http://www.vph-noe.eu/vph-noe-membership**

Upcoming VPH Survey

By Carlos Martin, Project Manager CISTIB, Universitat Pompeu Fabra

WP4 is undertaking a fact finding task that is hoping to provide reliable information on academic, industrial, and clinical sectors educational needs and to guide planning of educational activities for the VPH NoE. At the end of 2008, a first survey on the educational background and personal training requirements for a group of about 100 VPH researchers from 5 VPH Core Institutions was conducted. This initial survey provided valuable information on some specific issues that should be taken into account while developing VPH training strategies. The new survey will be rolled out across the entire membership of the VPH NoE, in order to widen its scope and reliability. In addition to the focus on current researchers within university and research centres, the VPH Survey will explore the needs of the two principal non-academic career paths for VPH practitioners: the Design/Manufacturing Industries and Healthcare. The goal of the data acquisition process is to obtain an accurate picture of employers' expectations in terms of the requirements for future trained personnel capable of operating in VPH related activities.

For the VPH NoE, the key information concerns the nature and extent of the education that is expected for new recruits and any associated assumptions concerning additional training that will be provided by host organisations. This data will provide a 'snapshot' of the situation at a particular point in time. The VPH represents a rapidly developing area of scientific expertise and any programme of training must be responsive to changing needs. Consequently, the survey will be designed to require minimal time to fill in, hoping that we will be able to reach all key sectors with the view of updating this information at regular intervals.

WP4 has been actively involved in looking at the different needs of VPH researchers. Aside from the initial survey on VPH research, a strategic document looking at the promotion of mobility schemes was produced in May, a large WP4 meeting was held in June which discussing various different strategies WP4 will take to promote VPH training and the first study group took place at the end of June. ■

If you would like to find out more or get involved with WP4 activities, (including the VPH survey) then please contact Carlos Martin **(carlos.martin@upf.edu)** or visit the VPH NoE Webpage: **http://www.vph-noe.eu/wp4**
Further details on the initial survey can be found on the following website: **http://www.vph-noe.eu/vph-repository/cat_view/12-vph-related-strategy-documents?start=5**

VPH NoE Focus

WP2 update: Exemplar Projects

By S.Randall Thomas, WP2 Leader, Centre National de la Recherche Scientifique

The NoE Exemplar Projects (EPs) were conceived as a direct attempt to address two principal challenges to development of the VPH ToolKit (the Featured subject of the last NoE Newsletter) namely: 1) to avoid production of theoretically sound tools that turn out not to be useful for real applications, and 2) to establish transversal, or horizontal, connections between the classic domains of investigation.

To these ends, EPs are existing physiome-related projects, already ongoing and financed outside the NoE, which accept both to **adapt** and generalize their own tools to the ToolKit context and to **adopt** appropriate VPH ToolKit resources as they become available. The NoE provides funds for a postdoc or engineer for 6-12 months with precisely the mission of establishing the links between the focused ongoing project and the general aims of the NoE. It is of course expected that the other projects (i.e., STREPs, IPs) funded under the VPH calls will also work in this direction, but the EPs, which are ongoing projects with independent funding, will receive a budget directly from the NoE specifically for this mission.

In order to provide EP support for ToolKit development right from the start of the project, five research areas exploiting existing expertise of VPH NoE core members were identified during development of the NoE. These were designated as the **"seed EPs"** and were each allocated 12 person-months in the first year of the NoE to enable early feedback for WP3. These initial seed EPs did not actually get underway until the end of 2008 due to the delay in hiring, so progress on their goals is now palpable but is not yet completed. A budget of 500k€ was also earmarked for a small number of new EPs in the 2nd, 3rd, and 4th years of the NoE, in response to a yearly call open to Core- and General-Members of the NoE consortium.

We give here brief descriptions of the seedEPs and also of the first of the new EPs, which was selected just this Spring and will begin in July 2009.

The Five seedEPs

seedEP1: A multi-organ Core Model of arterial pressure and body fluids homeostasis (CNRS). Long-term regulation of arterial blood pressure (BP), which necessarily involves several organ systems and regulatory feedback loops, is determined essentially by the balance between fluid and salt intake and their excretion, the latter being characterized by the relation between BP and urinary output, manifested in the renal function curve (RFC). This paradigm serves as the basis not only for understanding normal BP regulation but also for treatment of hypertension (necessarily involving modification of the RFC), and was developed by Arthur Guyton and colleagues based importantly on their quantitative control-theory based models, which were firmly grounded in experimental results (mainly from animal experiments) and several decades of clinical experience.

This seed EP will, first, inform the WP3 ToolKit development team of specific requirements for this type/level of model integration, and, subsequently, be explicitly adapted to the protocols of the VPH ToolKit (WP3) as they become available. In particular, this will involve: 1) integration or link-up of the SAPHIR quantitative parameter database (QKDB) with a more generic VPH DB (to be implemented under WP3), 2) contribution of the Multiformalism Multilevels Simulation Library® (M2SL, developed at LTSI INSERM, Rennes), to the VPH ToolKit collection of numerical solver packages, 3) specification of inter-module I/O connection protocols, 4) markup language versions of the various modules (in DAEML and also, in most cases, in CellML), and 5) cross-discipline ontology integration.

seedEP2: Integrated multi-level modeling of the musculoskeletal system (ULB). A number of problems met in daily clinical practice relating to the musculoskeletal system still call for the development of new integrative approaches.

Seed EP2 aims to carefully define the various needs arising in the musculoskeletal field based on the experience of previous projects. It is expected that the next step within this EP will be the development of an ontology to allow further integration of the musculoskeletal models with other sub-systems (e.g., the nervous system and both cardiac and vascular systems). This EP extends previous work using the Multimod Application Framework (MAF) that already integrates many routines required for MS modelling (data import, visualization, processing, storage and management). MAF will be a contribution of this seed EP to the ToolKit.

seedEP3: (DoW Task 2.3) The Vertical and Horizontal Atherome (WHAM) (KI) Our limited mechanistic understanding of Coronary artery disease (CAD), and especially of atherosclerosis, in terms of the identity of the disease-related genes, polymorphisms, proteins, and their interactions, within and between cells and organs, constitutes a severe bottleneck to preventing and developing efficient drugs which can regress the development of atherosclerosis.

The WHAM program requires both a vertical and horizontal integration. Available vertical data ranges from molecular information (gene-expression, protein-protein interactions data) to angiograms (imaging) reflecting the degree of disease from patients undergoing by-pass sur-

Focus

gery. Horizontal molecular information is obtained from tissue biopsies (liver, muscle, fat, affected and unaffected aorta). Similar data-types are available from the aorta from a mouse model prone for atherosclerosis. Molecular data from macrophages, a key cell-type involved in atherosclerosis, are also available. This seed EP will aim to harness the development of the VPH ToolKit and accelerate the success of WHAM, since such features have not been developed within the WHAM project itself, this being a clinical and experimental project that was launched and run without these considerations in mind. Therefore, VPH tools enabling "simple" things like storing different types of data (patient descriptions, experimental protocols, expression, SNPs etc) are urgently needed. At the other end of the spectrum, the issue of integrating the molecular information obtained across different model systems and imaging is most likely a central methodological problem for a VPH tool-box addressing clinical needs. This includes visualization but also how molecule X affects the tissue and 3D properties etc, interaction between flow (blood) and expression of various molecules.

seedEP4: Multi-scale simulation and prediction of the drug safety problems related with hERG (IMIM). An important field of application of the VPH concept is the drug development process, since multi-scale simulations can be extremely useful for the understanding of the physiological mechanisms related to the therapeutic efficacy of the drugs, as well as with their adverse effects (drug safety problems). This requires computational models sensitive to the differential molecular characteristics of the drugs, which have to be coupled with models simulating the target biological system or organ. The hERG-related cardiac adverse effects of drugs are a paradigmatic example of this approach. Most drugs associated with pathological prolongations of the QT segment of the electrocardiogram are known to interact with the hERG potassium channel. The differential interaction of a series of drugs under development with the hERG potassium channel can be simulated at the molecular scale by means of atomistic simulations coupled to drug discovery tools based on quantitative structure-activity relationships. In this way, one will be able to obtain quantitative predictions of the effects of each drug on the electrophysiological parameters of hERG that could be used in both mesoscopic simulations dealing with macromolecular behavior of the channels and, more importantly, in macroscopic electromechanical simulations of the heart with the aim of predicting the change in the QT segment generated by the drugs under study.
This seed EP aims to integrate existing software tools dealing with the several levels of complexity of the QT elongation. The expected outcome of the next step will be the standardization of formats for easy integration of simulation scales and the computational implementation of the different levels of detail.

seedEP5: Modeling and visualizing brain function and pathophysiology (ERCIM, Digital Patient Working Group). The ERCIM project models brain function based on clinical data in order to better understand the causality of brain diseases such as epilepsy, dementia, schizophrenia, and alcoholism. At the first functional level, linear and nonlinear synchronization methods are applied to study neuronal dynamics. The latter have been increasingly recognized to be an important mechanism by which specialized cortical and sub-cortical regions integrate their activity to form distributed neuronal assemblies that function in a cooperative manner. Synchronous oscillations of certain types of such assemblies in different frequency bands relate to different perceptual, motor or cognitive states and may be indicative of a wider range of cognitive functions or brain pathologies. At a second level, source estimation models and graph theoretic measures are applied to better describe and understand the functional characteristics of brain networks.
The project also investigates brain tumors (especially glioblastoma) and normal brain tissue behavior at the cellular and higher levels of biocomplexity. Such models will be individualized, therefore requiring pertinent image analysis, data processing and visualization techniques in order to extract the necessary information, which will be the input to the cancer simulator. In particular, image analysis tasks (such as image registration fusion, segmentation, etc) will be applied at different scales (e.g. tissue 3DMRI images, microarray data, etc).
This seed EP requires some "fine-tuning" of certain VPH ToolKit elements in order to meet the brain's specific needs. In particular: 1) web-accessible repositories for data, annotations, patient information etc.; 2) model solutions to the inverse or forward brain source localization problems; 3) patient-specific customization of models; 4) data fitting; and 5) GUIs specifically tailored to visualize causal and functional relations between different brain lobes. ■

For further information and the latest developments in work package 2, visit our website:
http://www.vph-noe.eu/wp2

The First of the New EPs: "Establishing ontology-based methods to improve interoperability between data and models for the VPH ToolKit: the Guyton case study."
Coordinated by B. de Bono (EBI)
Other partners: CNRS, Univ. of Auckland & Univ. of Washington

This Exemplar Project will investigate an interoperability framework for physiology models and gene expression data. In particular, this EP sets out to achieve the following goals:

- the design and implementation of representational classes for the annotation of anatomy and physics in physiology model parameters and gene expression data,
- the demonstration and verification of such an approach via the annotation of (a) the parameters of a classic model that represents blood pressure regulation (namely, the Guyton model), implemented in the SAPHIR project (from the VPH NoE seedEP1) and marked up in the CellML repository, as well as (b) related human gene expression datasets in ArrayExpress that correspond to the anatomical locations these parameters address; and finally,
- the contribution of the outcomes of this work to the VPH toolkit effort, as a reference example of the role of a communal anatomical and physics framework for resource interoperability.

Staff changes,
awards and publications

We would like to welcome...

Vanessa Diaz,
Scientific Coordinator
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Vanessa obtained her degree in Mechanical Engineering from University Simon Bolivar (Venezuela), and a PhD in Automatic Control and Industrial Informatics from Ecole Centrale de Lille (France) in 2003. She was a Marie Curie Fellow at the University of Sheffield between 2005-2007. Vanessa joined the Department of Mechanical Engineering at UCL as a Lecturer in 2007. She is in negotiation for an EU FP7 Marie Curie ITN (PhD Training Network, called MeDDiCA), focusing on the use and development of VPH technology for Cardiovascular Engineering and Medical Devices. In joining the VPH NoE, Vanessa will maintain her own research, devoting the rest of her time to guiding the VPH NoE into the next phase of growth and interaction with the broader VPH research community.

Miriam Mendes,
Project Coordinator
miriam.mendes@ucl.ac.uk

Miriam holds a BSc and MPhil degrees in Molecular Genetics from the University of Sao Paulo, Brazil, and an MA in Philosophy & Government focused in scientific international cooperation from the University of Essex, UK. She worked in scientific research at the University of Cambridge and the Sanger Centre, before moving into industry at Stratagene, Affymetrix and Eppendorf. She was later a research fellow on evolution of knowledge networks at Warwick Business School. Miriam joined the University of Oxford in 2005 to coordinate DC-THERA, a Network of Excellence which translates genomic, proteomic and bioinformatics information, molecular cell biology and pre-clinical models into therapies for cancer. Miriam also manages CHAIN, a new FP7 Integrated Project on HIV/AIDS (€10M) led by UCL.

Philippe Rohou,
WP5 leader
philippe.rohou@ercim.org

Philippe obtained his MSc in Mathematics and Statistics at Paris university. After spending 6 years in Northern Ireland as a systems analyst with Dupont de Nemours, he joined Digital Equipment Corporation in the South of France where he spent 14 years managing projects, programmes, consulting groups and the company's European customer briefing centre. Completing his corporate experience with a 5 year spell as general manager of a small events company, Philippe then created his own enterprise in 2004 offering corporate events and golf circuits on the French Riviera, before joining ERCIM as a European project coordinator in 2006. Philippe has coordinated several FP6 and FP7 European projects, including large Networks of Excellence (DELOS, CoreGRID). In May 2008, Philippe was promoted manager of the ERCIM project group, while maintaining his European projects activities.

Frederic Cervenansky,
Research Engineer
frederic.cervenansky@creatis.insa-lyon.fr

Frederic holds a PhD in Signal Treatment and Image Processing focused on brain's autoregulation from the University of Clermont-Ferrand, France. He developed in collaboration with France Telecom a system to create hospital protocols and manage a patients-practitioners database. Over the last five years, Frederic has been working on different commercial softwares in medical image processing: for Philips Medical System on their new nuclear platform JETSPHERE focused on renal and pulmonary protocols, for Segami on their new client-server application (OASIS), and for Medasys on epilepsy problems. Frederic has recently worked as project manager for a biomedical company (Fresnenius-Kabi). Now, Frederic has joined CNRS, CREATIS to integrate WP3 Imaging Tools subgroup, focused on DICOM layer problems and GUIDE.

Alexandra Masindova,
Project Manager VpH NoE and preDiCT
alexandra.masindova@dpag.ox.ac.uk

Alexandra holds a Master Degree in International Trade from the Vienna University of Economics and Business, Austria and a Master of International Management from the Community of European Management Schools (CEMS), for which she also studied at the University Luigi Bocconi in Milan, Italy. She is a veteran of the Wolseley PLC leadership development graduate programme, involving project management work across Europe. Prior to this she played a key role in the Quintiles business development team for Central and Eastern Europe and Middle East.

Raul Alcantara,
Research Technician
realcant@gmail.com

Raul holds a MA in Biophysics from Washington University in St. Louis, USA and a MS in Physics from New Mexico Tech in Socorro, USA. He has worked as research assistant in the area of biomolecular modeling in the Barcelona Super Computing Center. Raul is now employed as a research technician in the laboratory of Jordi Villà at the Parc de Reserca Biomedica de Barcelona, IMIM, where he is responsible for developing the Adun molecular simulator.

Staff changes,
awards and publications

World Class New Zealander working for the VPH NoE!

Professor Peter Hunter recently received a World Class New Zealander award in Auckland on 1st April 2009.

Professor Hunter is director of the Auckland Bioengineering Institute, a large scale research institute at The University of Auckland. Seven awards were presented by Kea New Zealand and New Zealand Trade and Enterprise to the country's greatest "tall poppies", for giving their time, knowledge and skills to help New Zealand companies and industries succeed internationally. The KEA award is actually named after a cheeky parrot that lives in the mountains in the South Island of New Zealand (it can undo the straps on your pack to extract food or strip the rubber out of a car windscreen to remove the glass!). Professor Hunter won the award for the category of "Research, Science, Technology and Academia". Professor Hunter is best-known for his pioneering mathematical modelling of the human heart. He also heads the Institute's flagship Human Physiome Project, an international network of researchers developing mathematical models of all aspects of human physiology. He is also a fellow of London's prestigious Royal Society.

For more information on VPH NoE news please visit our website:
http://www.vph-noe.eu/news

Professor Peter Coveney nominated one of the top 25 most influential figures in engineering and technology

Professor Peter Coveney, Director of the Centre for Computational Science, University College London and co-coordinator of the VPH NoE, has been nominated one of the top 25 most influential figures in the world of engineering and technology today, by Engineering & Technology magazine. "I am honoured and delighted to have been included in this prestigious Top 25 list. It provides recognition for our work at the Centre for Computational Science, draws attention to the immense strategic significance of the Virtual Physiological Human Initiative, and is a testament to the exceptionally fertile interdisciplinary atmosphere so strongly fostered at UCL." Peter named alongside luminaries such a Vint Cerf, Tim Berners-Lee and Richard Stallman, was cited for his leadership in the field of patient-specific medical simulation, and application of high performance computing to the Virtual Physiological Human Initiative.
Peter is continually giving presentations on behalf of the VPH NoE and has recently been invited or has been keynote speaker in the following conferences: DEISA-PRACE Symposium (Amsterdam) 11-13 May, HealthGrid 2009 (Berlin) 28 June – 01 July, ICCS 2009 (Louisiana, USA) 25-27 May and TeraGrid 09' (Virginia, USA) 22-25 June.

For more information on up and coming events please visit our website:
http://www.vph-noe.eu/vph-events

Recent VPH NoE member publications

Virtual Physiological Human tools and applications I and II

We are pleased to announce the availability online of the June 2009 issue of Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences. This is the second of two issues dedicated to the VPH : 'The virtual physiological human: tools and applications II' and was compiled by David Gavaghan, Peter Coveney and Peter Kohl.
Articles within this issue include research on several computational models of the kidney and the heart, Purkinje fibre cells, multiscale simulation of electrophysiology, gas magnetic resonance imaging in chronic obstructive pulmonary disease, simulation of the human intracranial arterial tree, connectivity of overt speech production. Articles within the previous May issue, 'The virtual physiological human: tools and applications I ' include research on CellML and FieldML, robust modelling on human and animal metabolic systems and different approaches to bone tissue engineering amongst other VPH related research.

Crossing boundaries: computational science, e-Science and global e-Infrastructure I and II.

We are further pleased to announce the availability online of the June 2009 issue of Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences (Vol. 367, No. 1897). The theme of the issue is 'Selected

To make a note of...

A new Commission initiative on a European Large Scale Action (ELSA) may take the form of a very large scale project in a few years from now and could add further support to the VPH initiative in addition to research funded under FP7 and FP8. The European Large Scale initiatives are described in the Communication COM2916.

For more information go to: **http://ec.europa.eu/information_society/tl/research/documents/ict-rdi-strategy.pdf**

papers from the UK e-Science All Hands Meeting 2008' and was compiled by Peter Coveney and Malcolm Atkinson, Director of the e-Science Institute, University of Edinburgh, UK. Articles within this issue include building a scientific data grid with DIGS, standards based network monitoring for the grid, and improved performance control on the grid. Volume II is also available online in the July issue (Vol. 367, No. 1898) and includes articles on in-silico experiments, information security and adaptation and development of software simulation methodologies for cardiovascular engineering by Vanessa Diaz, VPH NoE Scientific Coordinator.

GPU-accelerated molecular dynamics in the press

VPH members can now cross the scale gap between the molecular and biological time-scales leveraging the high arithmetic performance of graphical processing units (GPUs), a breakthrough technology which can offer an edge in molecular dynamics simulations. The GPUGRID team, part of VPH NoE WP2, discussed the exciting implications in a new paper on ACEMD, a bio-molecular dynamics (MD) simulation program designed specifically for GPUs, to appear in the Journal of Chemical Theory and Computation. ACEMD is able to compute 40 nanoseconds/day for all-atom protein systems with over 23,000 atoms. The ability to gather such a large amount of computing power from cost-effective hardware will open the way for VPH researchers to routinely reach the microsecond time-scales, with important implications in terms of scientific applications.

For more information please see the ACEMD website: **www.multiscalelab.org/acemd** or see the article (Harvey et al. 2009) listed in publications.

Recent publications by VPH NoE members

Gavaghan D, Coveney PV, and Kohl P. 2009. The virtual physiological human: tools and applications I. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 367:1817-1821.

Clapworthy G, Viceconti M, Coveney PV, and Kohl P. 2008. The Virtual Physiological Human: building a framework for computational biomedicine I. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 366:2975-2978.

Coveney P, and Atkinson MP. 2009. Crossing boundaries: computational science, e-Science and global e-Infrastructure I. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 367:2425-2427.

Coveney P, and Atkinson MP. 2009. Crossing boundaries: computational science, e-Science and global e-Infrastructure II. Selected papers from the UK e-Science All Hands Meeting 2008 . Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 367.

Zasada SJ, and Coveney P. (In Press). Virtualising Access to Scientific Applications with the Application Hosting Environment. Computer Physics Communications. doi: 10.1016/j.cpc.2009.06.008

Díaz-Zuccarini V, Narracott A J, Burriesci G, Zervides C, Rafiroiu D, Jones D, Hose DR, Lawford PV. 2009. Adaptation and development of software simulation methodologies for cardiovascular engineering: present and future challenges from an end-user perspective. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 367: 2655-2666

Harvey M, Giupponi G, and De Fabritiis G. 2009. ACEMD: Accelerated molecular dynamics simulations in the microseconds timescale. Journal of Chemical Theory and Computation. http://pubs.acs.org/doi/abs/10.1021/ct9000685

Kohl P, Coveney P, and Gavaghan D. 2009. The virtual physiological human: tools and applications II. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 367:2121-2123.

Kohl P, and Noble D. (In Press). Systems biology and the Virtual Physiological Human. Molecular Systems Biology.

Kohl P, Coveney P, Clapworthy G, and Viceconti M. 2008. The Virtual Physiological Human: building a framework for computational biomedicine II. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 366:3223-3224.

Sadiq SK, Mazzeo MD, Zasada SJ, Manos S, Stoica I, Gale CV, Watson SJ, Kellam P, Brew S, and Coveney PV. 2008. Patient-specific simulation as a basis for clinical decision-making. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 366:3199-3219.

Diary dates for 2009

20th – 24th July – The Cardiac Physiome Cambridge, UK
20th – 24th July – IUPS 2009 Kyoto, Japan
10th – 11th September - Internal VPH NoE Annual General Conference Brussels, Belgium
16th - 18th September – ICCB 2009 Bertinoro, Italy London,UK
20th - 24th September - MICCAI 2009 London,UK

For more information on up and coming events please visit our website: **http://www.vph-noe.eu/vph-events**

Events

Building a Virtual Physiological Human

IUPS Satellite Symposium, Kyoto, 26 July 2008

By Alexandra Masindova, Project Manager VPH NoE and PreDiCT, University of Oxford

A one-day satellite, dedicated to Building the Virtual Physiological Human will be held on 26th July at Ritsumeikan University, just prior to the launch of the XXXVI International Congress of Physiological Sciences in Kyoto. This will bring together about 60 scientists, researchers and developers from around the world to discuss the current state of play and important further directions for the world-wide Physiome Initiative, launched at the 1997 IUPS Congress in St. Petersburg (http://www.physiome.org.nz/).

Organised jointly by the Virtual Physiological Human Network of Excellence and Professor Akinori Noma's team at Ritsumeikan University, the Satellite will build upon the 2007 World Integrative Research Initiative Agreement and the 2007 Osaka Accord, to further foster international collaboration, contributing to the development of Integrative Research in Biomedicine. Topics for discussion include international integration of efforts, standards and ontologies, community building, outreach and visibility.

A number of keynote lectures will address aspects ranging from 'lessons from the Genome Project' to information exchange mechanisms, first-order standardisation, funding, public visibility and benefits to society. ■

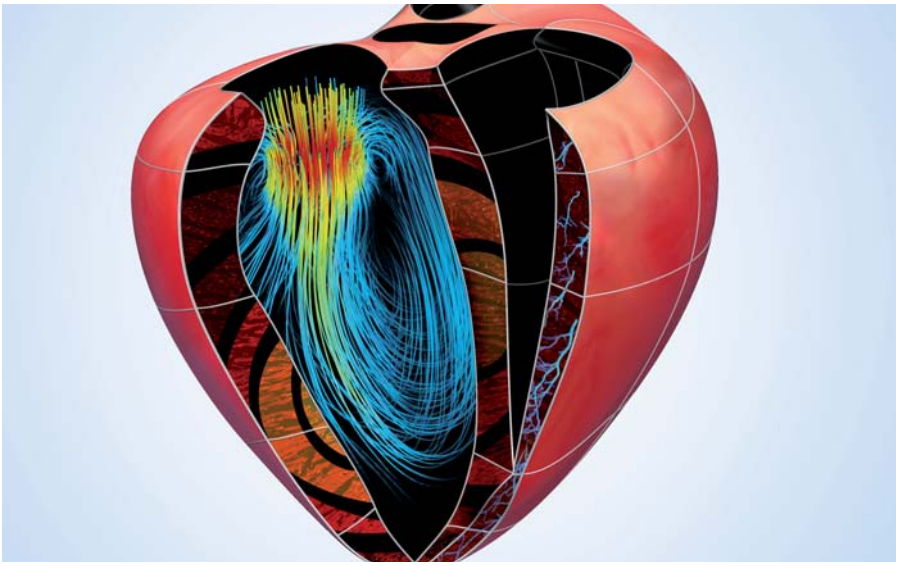
If you have any questions, would like to make a suggestion, or would be interested in attending, please contact Alexandra Masindova at the University of Oxford (**alexandra.masindova@dpag.ox.ac.uk**), or visit the website **http://www.vph-noe.eu/?option=com _content&id=114**

More information on the Research Initiative Agreement and the 2007 Osaka Accord can be found in Biomedtown: **http://www.biomedtown.org/biomed_town/VPH/wiri**

The Cardiac Physiome:

Multi-scale and Multi-physics Mathematical Modelling Applied to the Heart

By Nicolas Smith, Project Coordinator, euHeart, University of Oxford



The ability to predict physiological behaviour from genomic data is a compelling, yet unfulfilled, goal of post-genomic biology. It is the central aim of The VPH and Physiome Projects, and represents an, undeniably, ambitious objective.

The complexity of the problem extends from the fact that there exists, presently, a rich and varied collection of experimental data for which we have not yet devised an adequate means of integration. It is therefore an essential step, on the path to predictive ability, to develop

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.

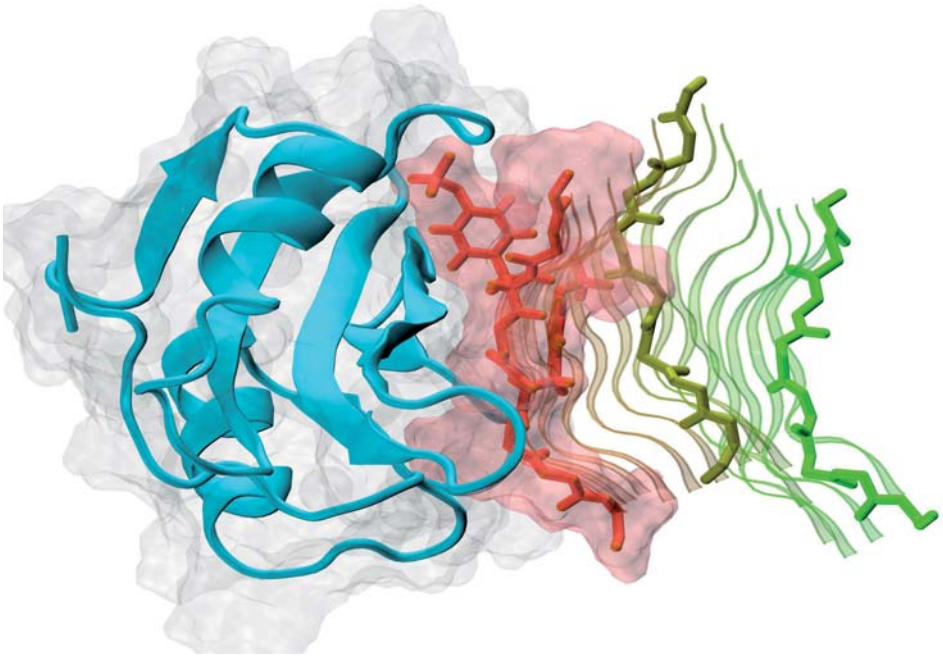
How can an interval *of four* orders of magnitude in computer time be filled? We asked for the support of the public. With the help of thousands of people, we built GPUGRID.net, one of the largest distributed computing projects worldwide. A *distributed computing* system allows scientists to gather the 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).

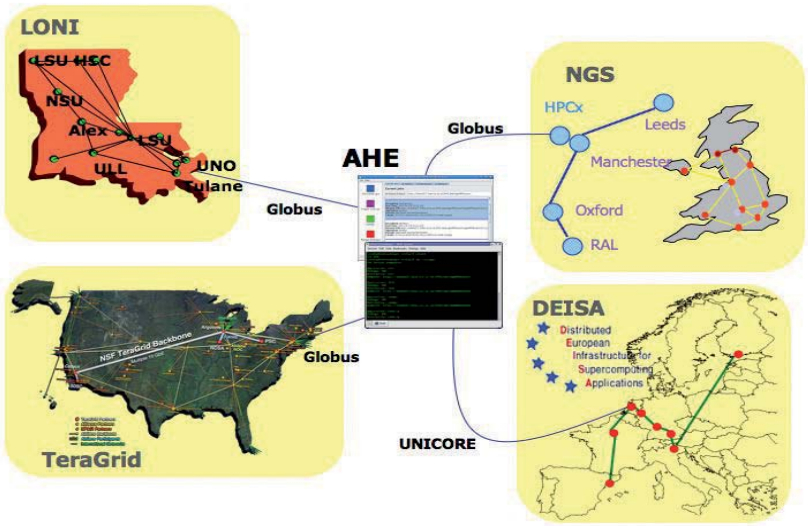
This event lies at the beginning of a complex series of reactions which affect the cell. In practice, the cell "responds" to external changes by "feeling" them when a SH2 becomes associated to a tyrosine. Studying the strength and dynamics of this binding is therefore extremely important.

VPH-I SECTION

VPH-I news roundup

Allocation of supercomputing time for use by VPH-I projects

By Peter Coveney, VPH NoE Project Coordinator, Steven Manos, Research Fellow and Stefan Zasada, Research Fellow, University College London



We are pleased to announce that the VPH NoE has secured an allocation of time on the DEISA infrastructure for use by VPH-I projects. Following on from an initial requirements gathering exercise conducted by NoE WP3 staff toward the end of 2008, an application to the DEISA (Distributed European Infrastructure for Supercomputing Applications) Virtual Communities Programme was made in February. The VPH Initiative has now been awarded an allocation of 2 million CPU hours in 2009, available to any VPH-I project, to support research that requires access to high performance compute faculties. Continuing allocations should ensue for the lifetime of the VPH-I. Contra Cancrum (an EU FP7 VPH-I STREP) is already making use of these allocations, as well as the EU FP6 ViroLab project.

DEISA (www.deisa.eu) operates a heterogeneous high performance computing (HPC) infrastructure currently formed by eleven European national supercomputing centres that are interconnected by a dedicated high performance network. The DEISA supercomputing resources incorporates several different platforms and operating systems: IBM AIX on Power5-6, IBM Linux on PowerPC, IBM BlueGene/P, SGI Linux on Itanium, Cray XT, and NEC vector systems.

Since the inception of VPH NoE, partners at UCL have been petitioning DEISA to establish a Virtual Communities Programme to underpin HPC requirements of long term (i.e. 3-5 year) EU funded projects, as previously DEISA project access and allocations had been decided

on a national basis, with no reference to EU funded initiatives.
The DEISA VPH Virtual Community is being administered by VPH NoE WP3 staff. The Application Hosting Environment, (see 'Simplifying grid computing for research and medical purposes' article), is a key component of the upcoming VPH NoE Toolkit release, and is the recommended way for VPH projects to access DEISA resources.
VPH NoE is continuing to work with DEISA to provide support for emergency medical computing requirements, by providing the ability to reserve in advance time on computational resources, so that it can be scheduled in to clinical workflows, as well as the ability to submit urgent ("emergency") jobs that pre-empt the current workload of the machine. VPH scenarios are also key to an NSF-funded project to enhance interoperability between DEISA and the US TeraGrid infrastructure (see box),
The Partnership for Advanced Computing in Europe (PRACE) is laying the groundwork for the creation of a persistent pan-European HPC service, which we expect will provide VPH researchers with access to capability computers that will form the top level of the European HPC ecosystem. ■

Peter Coveney was an invited speaker at this year's DEISA-PRACE Annual Symposium in Amsterdam 11-13 May, where he spoke under the heading "DEISA, PRACE & the Virtual Physiological Human". See link for further information:
http://www.deisa.eu/news_press/symposium/Amsterdam2009/deisa-symposium-amsterdam-may-11-13-2009
VPH-I projects wishing to make use of the allocation should contact our dedicated email allocations **vph-allocations@ercim.org**

LONI-TeraGrid-DEISA Interoperability Project

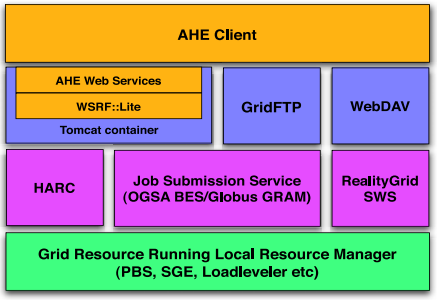
A year long Science-Driven Project Using Advanced Cyber Infrastructure funded by NSF via a HPCOPS award to LONI (one of the TeraGrid Resource Providers), aims to establish TeraGrid-DEISA Interoperabilty on a firm but extensible footing and began on 1 June 2009.
The high-level aim of this project is to enable scientific applications to utilise the federated capabilities of the TeraGrid, DEISA and LONI systems, to enhance the understanding of HIV-1 enzymes and epidermal growth factor receptors (EGFR) implicated in lung cancer. Specifically, the aim of this project is to use several Replica-based and Replica-Exchange simulations for HIV-1 & EGFR research on multiple TeraGrid, LONI and DEISA resources. The project will also work closely with researchers from the VPH-I project ContraCancrum. In addition to scientific advances, this project will provide working implementations and tools that can be utilised by a broad range of applications to utilize resources and effectively scale-out on the TeraGrid, DEISA and LONI.
This project is being co-led by Dr Shantenu Jha (Louisiana State University) and Prof. Peter Coveney (UCL). ■

Contact and further details can be found at:
http://www.teragridforum.org/mediawiki/index.php?title=LONI-TeraGrid-DEISA_Interoperabilty_Project#Kickoff_Meeting
Further details on the project can be found at:
http://www.teragridforum.org/mediawiki/index.php?title=LONI-TeraGrid-DEISA_Interoperabilty_Project

Simplifying grid computing for research and medical purposes

By Stefan Zasada, Research Fellow, University College London

We are pleased to announce the release of AHE 2.0, a lightweight middleware tool designed to facilitate scientific investigations using grid resources. AHE provides scientists with application specific services to utilize grid resources in a quick, transparent manner with the scientific objective as the main driver of the activity.
Today's scientists and clinicians face a growing number of challenges that affect their ability to fully exploit computational resources available to them. Unprecedented amounts of available computational power, compounded by the growth in hybrid computational architectures, present new challenges to scientific disciplines and researchers that rely on computer based modelling and simulation.
In order to meet this challenge researchers at UCL, as part of the EPSRC funded RealityGrid project, have developed the Application Hosting Environment (AHE), a tool that allows scientists to run computational applications on high-performance grid computing (HPC) resources in a quick, transparent manner.
Grid computing - the application of several computers to a single computational problem at the same time – is meant to ensure that scientists have access to resources that are more than just a sum of their individual parts. Version 2.0 of the AHE is intended to bring us a step closer to this goal, ensuring that HPC grids are fully transparent to the



scientist user, with the focus constantly on simplifying grid and HPC use.
The key aspect of AHE V2.0, say UCL researchers, is the adoption of a novel approach to simplifying the use of grid computing: grid application virtualisation. The motivation behind this approach is to simplify grid use: a layer of user friendly Web services have been placed between the user and the computer grid resources, which hides much of its complexity and provides a virtual interface for any given scientific application in deployment.
The AHE will also manage computer simulations started by a scientist, taking care of the many data files that need to be moved around the computational grid. By removing the need for the scientist user to remember the complex series of commands associated with manual simulation, the AHE allows the scientist to concentrate on doing actual science. Use of the AHE also applies to clinical practice, where biomedical modelling and simulation is set to increasingly augment the clinical decision making process. The AHE has been used in such a situation within GENIUS (Sadiq et al, 2008), an EPSRC funded project concerned with the use of real-time patient-specific blood flow modelling and simulation in the diagnosis and treatment of cerebral aneurysms. The AHE will also form a part of the VPH ToolKit, and be made freely available to the VPH community.
AHE V2.0 is a necessary step towards opening up grid infrastructure, and therefore making the use of HPC a reality for both researchers and clinicians. A development roadmap has been drafted, covering the future technological, security and privacy challenges which must be overcome if grid computing – be it as part of basic research practice, or in patient-specific medical modelling and simulation-related applications - is to become a reality.
The development of the AHE is funded by the VPH NoE Toolkit initiative, as was previously funded by EPSRC "Rapid Prototyping of Usable Grid Middleware" Project, GR/T27488/01, and by OMII under the Managed Programme RAHWL project. ■

Find out more and download the latest release at **http://www.realitygrid.org/AHE** See (Zasada and Coveney, 2009) in publications or visit the following website: **http://ccs.chem.ucl.ac.uk/projects/AHE2_0_full.pdf**

Cardiac modelling from stochastic ion channel fluctuations to pump function: relevance for drug and device applications

By Blanca Rodriguez, Medical Research Council Career Development Fellow and Nic Smith, euHeart Project Coordinator, University of Oxford

Within the VPH community, significant efforts are currently being focused on developing and applying integrated cardiac models to significantly change and improve the prevention and treatment of heart disease across Europe. The main targets of this work are ICT-based tools for modelling and simulation of cardiac physiology in health and disease to support a move towards personalisation of treatment plans based on individual physiology. Within this overarching goal, the aims of two FP7 VPH projects, euHeart and preDiCT, are focused on two complementary and fundamentally important arenas within cardiac care: clinical intervention (euHeart), and drug discovery and safety (preDiCT).
The main aim of preDiCT is to build an advanced computational framework for the in silico assessment of drug safety. Cardiac toxicity (in particular, whether a new drug will have undesirable side effects by causing dangerous changes in heart rhythm – 'arrhythmias') is a principal factor leading to abandonment of otherwise promising drug candidates. Through close collaboration between academic and industrial partners,1 the preDiCT consortium is developing the validated computational models, numerical methods and tools required for the simulation of drug action on cardiac electrophysiology from the ion channel to the ECG level (see Figure 1). The computational framework is applied to the investigation of inter-species differences and mechanisms of drug-induced cardiac arrhythmia, and to propose potential new sensitive and specific biomarkers for the assessment of the pro-arrhythmic potential of drug compounds.
Across the academic (scientific coordinator Oxford) and industrial (project coordinator Philips) partners within the euHeart consortium2 similar multiscale electrophysiology computational frameworks to those applied in PreDICT are being augmented with mathematical models of coronary haemodynamics (Figure 2(a)), blood flow, and myocardial mechanics (Figure 2(b)). Central to this project is overcoming the current challenge of parameterising and personalising these frameworks for humans using state-

1. http://www.vph-predict.eu/; preDiCT partners include University of Oxford, Aureus Pharma, Center for Advanced Studies, Research & Development in Sardinia, Fujitsu Laboratories of Europe, GlaxoSmithKline, Novartis, F. Hoffmann-La Roche, University of Szeged, and Universidad Politécnica de Valencia.

2. http://www.vph-euheart.eu/; euHeart Partners include INRIA, INSERM, University of Karlsruhe, UPF, University of Sheffield, University of Oxford, Amsterdam Medical Center, Kings College London, DKFZ, Heidelberg, Berlin Heart, Berlin, HemoLab, Philips Medical Systems, Philips Research, PolyDimension, Volcano.

VPH news roundup

of-the-art, but only minimally-invasive, clinical measurements. To address this issue robust ICT tools are being developed to parameterise and then customise models to simulate the key functionality required to understand and tailor treatments for a particular heart patient. Examples clinical applications within which these tools are now being tested include customising cardiac resynchronisation, coronary revascularisation and atrial ablation therapies and device implantation including LVAD implantation (figure 2(c)) and valve replacement.

Our hope and expectation, perhaps echoed across the VPH community, is that through these projects we will be able collectively to make a significant positive impact on the treatment and prevention of heart disease and on drug discovery, through engagement with the Network of Excellence and other VPH projects. ■

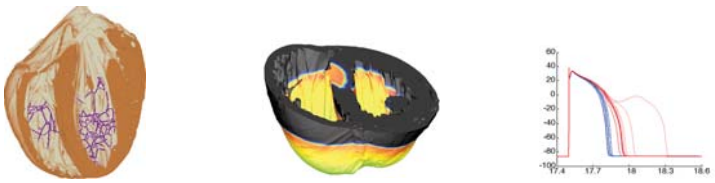


Figure 1. (a) Anatomically-based model of the ventricles with representation of Purkinje network (Work from Rafel Bordas). (b) Electrical propagation through the ventricles simulated using the Chaste software package (Work from Miguel Bernabeu and Martin Bishop). (c) Simulated effects of ion channel block on cellular electrophysiology (Work from Esther Pueyo and Alberto Corrias).

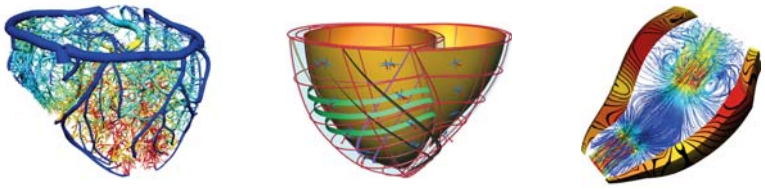


Figure 2. (a) Simulation of coronary blood flow coupled to myocardial contraction. (b) Model highlighting fibres (in green) showing principle stresses at end inflation (work from Steven Niederer). (c) Ventricular stream lines and myocardial deformation calculated during inflation for LVAD simulation (work from Mathew McCormick and David Nordsletten).

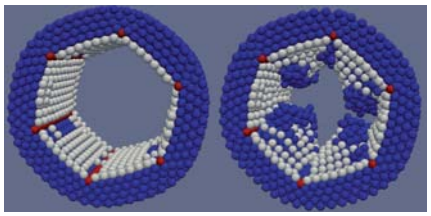
Predictive Modelling of Cardiovascular Disease: the Case of In-Stent Restenosis

By David Evans, Post-Doctoral Research Associate, University of Sheffield

Coronary artery disease (CAD) refers to the accumulation of atherosclerotic plaque within the vessel wall of coronary arteries. A major adverse reaction to current treatment strategies for CAD, is the development of in-stent restenosis; that is a re-narrowing of the vessel due to the proliferative response of vascular smooth muscle cells to injury induced by the stent deployment. The ability to prevent in-stent restenosis whilst avoiding undesirable side-effects (such as late stent thrombosis) remains elusive to researchers and clinicians alike. Whilst significant insight has been gained into individual pathways of disease progression, including mechanical, biological and device related effects, redundancy of these pathways in vivo, and a failure to consider restenosis as a multi-science pathology has resulted in the lack of success reported for many therapeutic approaches. A global trend towards increased use of stenting and recent evidence linking the use of drug eluting stents with late-stent thrombosis clearly highlights the need for further refinement of stent design and technology.

COAST (Complex Automata Simulation Technique) is a European Union FP6 funded project which has developed a computational framework (MUSCLE: Multiscale Simulation Coupling Library and Environment) for the simulation of multi-scale systems. COAST has studied in-stent restenosis, identifying and constructing individual single scale models of the biological and physical sub-processes critical to the development of this complex pathology. When developing a model of a complex system it is informative to consider the sub-processes involved in terms of their time and length scales. Restenosis as a system is defined here in such a way by implementation of a scale separation map. This tool plots sub-processes and interactions according to their distinct temporal and spatial scales.

Extensive tuning and validation of the sub-models using an in vivo dataset and subsequent coupling using MUSCLE has produced a prototype application which can now be used to test hypotheses relevant to the prevention of restenosis, thus informing future experimental design. A key question which the project aims to address is: "What causes cessation of vascular smooth muscle cell prolifera-



Output from a 3D simulation of smooth muscle cell behavior A) Immediately after stent deployment B) 3 weeks after stent deployment (Red=Strut, Blue= Smooth Muscle Cell, White=Endothelial Cell)

tion in some individuals, and not in others?" Indeed, the use of such in silico models allows an iterative process of rational experimental design and subsequent model development to proceed, such that the research and development process is streamlined. Our application takes into account the multi-scale, multi-science environment in which they have to operate. ■

For further information email:
coast@complex-automata.org
or visit the website:
www.complex-automata.org
EU-FP6-IST-FET Contract 033664

The Future - MUSCLE

The framework and methodologies developed in the course of this project are transferable to many other VPH (virtual physiological human) related applications. The framework can be downloaded for use at
http://developer.berlios.de/projects/muscle/

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Analysis of VPH User Requirements in Security and Privacy

By Kyriakos S Hatzaras, Research Assistant, Imperial College Business School

The integration and availability of medical and genetic data are essential for research and technological development (RTD) within the Virtual Physiological Human (VPH) framework. However, the extensive use of personal health data requires an evaluation of systems seeking to safeguard data and system security, and personal privacy.
RADICAL aims to scientifically reveal the beyond the state-of-the-art research and policy roadmap for S&P enhancement in the VPH. To this end, a key deliverable has been the investigation and analysis of security and privacy (S&P) requirements of the VPH user community. RADICAL conducted an examination of actors participating in the development of VPH technology, and defined four 'user' or stakeholder categories. These are (a) the VPH research community; (b) industrial market actors; (c) governance organisations; (d) professional (e.g. hospital personnel) associations. VPH users are construed as stakeholders taking benefit from the development and deployment of VPH technology, as individuals who are 'embedded' in their professional and organisational context and interact with VPH systems.
Data collection methods used have included semi-structured face-to-face and telephone interviews, questionnaires and secondary research. Questionnaires included a conception of S&P in the form of System and Data Availability, System and Data Integrity, and Data Privacy (Gollmann 2003:5-9). Our respondent in category (a) included research teams of three VPH precursor projects: eDiaMoND, @neurIST, ImmunoGrid; three VPH-I research teams: ARTreat, ContraCancrum, VPHOP; and three NoE Exemplar Project teams: EP1, EP2, EP4. In category (b) we interviewed executives of PHILIPS, PointOne, and of two representative organisations: EDMA, EFPIA. In the realm of governance and public institutions, we spoke with the European Commission DGs Freedom, Security and Justice, and Public Health and Consumers, the Health Committee of the UK House of Commons, EUMETSAT, the UK Census and MetOffice. Finally, our research examined the views of three professional organisations: EAMBES, EFMI, EMA.
Our data analysis revealed a number of S&P-related requirements in each category:

(a) In the VPH research community, requirements centre on the promotion of best S&P practice and holistic S&P policies developed through collaboration between researchers, clinicians and IT experts. Technology needs relate to data use and consent monitoring, secure single sign-on user authentication, rigorous quality and acceptance (Q&A) procedures for data and model validation, and interoperability. The harmonisation of consent frameworks in the EU and introduction of a user

VPH news roundup

forum facilitating exchange on S&P are also favoured.

(b) Industrial market actors see the practice of holistic S&P policies, which include all users/stakeholders to the use of a system in research or treatment, as a key requirement. S&P- enhanced systems are favoured and viewed as enablers of business development. A coordinated approach to regulation and the exchange of best practice through e.g. a VPH S&P user forum are supported.

(c) Key requirements of governance organisations are the protection of personal data and fundamental rights. Secure flow of information and interoperability are seen as crucial to the realisation of public welfare. This includes improved illness prediction and treatment, and efficiency gains.

(d) Professional associations also see the conduct of holistic S&P approaches as important. Other requirements include the launch of a S&P user forum facilitating best practice dissemination and localisation, further RTD in data use and consent monitoring, anonymisation/ pseudonymisation, data and model validation techniques.

Radical will organize a panel workshop in the HealthGrid2009 conference in Berlin, on Monday 29th of June. The theme of this public workshop will be "security and privacy challenges in personalised healthcare in the 21st Century'', where our research will be presented and invited speakers will discuss best practice. ■

For further information contact the Project Coordinator:
Dr. Ing. Zaharya Menevidis **zaharya.menevidis@ipk.fraunhofer.de**
or visit the website: **http://www.radicalhealth.eu/**

"Wiki" science and GPUGRID featured in EMBO reports

By Toni Giorgino, Research Fellow, and the GPUGRID team, Barcelona Biomedical Research Park

New generations of Internet-based collaborative tools are revolutionizing the way in which we create and exchange information: the digital network creates opportunities for both specialists and the general public to join their efforts, and knowledge can be created and shared with very low "barriers of entry". Not everyone, however, knows that the "wiki spirit" is spreading even in the academic circles. For example, right now a few pioneering projects are gathering the computer time, otherwise unused, donated by volunteers worldwide, and using it to solve problems of unprecedented magnitudes. Other groups are even collecting... idle grey matter, by asking people to competitively solve puzzle games that contribute to solve protein-folding problems.

Andrea Rinaldi, in a column for the "Science & Society" section in EMBO reports (published by the Nature Publishing Group for the European Molecular Biology Organization) has reviewed several exciting trends that are shaping the public involvement with research through the Internet. A range of key considerations arises: firstly, before volunteers donate computer power, it is likely that they will be eager to learn about the project objectives, rationale, and ethics – and this communication needs to take place in the layman's language, not that of specialist journals. Other than this, sophisticated technical measures are necessary to "disassemble" the huge computations required by scientists into small bits which can be assigned to an innumerable number of computers dispersed across the world, and each of them must not hold the overall project from progressing, should they at any time disappear with their "paperwork". Among the projects, the paper features an interview with Prof. Gianni De Fabritiis, who is harnessing the processing power of Graphical Processing Units (GPUs) as one of VPH NoE's technologies. De Fabritiis explained how simulating proteins at the rate of microseconds per day is already a reality, thanks to the efforts of thousands of volunteers that "tune in" their GPUs to contribute to the knowledge of bio-molecules and their inner workings.

VPH NoE is involved in this process through GPUGRID.net, an high-end distributed computing project that enables volunteers to contribute their GPUs to molecular simulations. GPUGRID allows members of the VPH to run simulations of unprecedented scales, by leveraging a network of thousands of computers (and users!) that provide microseconds of simulation time per day. ■

For more information please see Andrea Rinaldi. Science wikinomics.
Mass networking through the web creates new forms of scientific collaboration.
EMBO reports 10, 5, 439–443 (2009) doi:10.1038/embor.2009.79 or visit the nature article
http://www.nature.com/embor/journal/v10/n5/full/embor200979.html

3D Image Reconstruction for Comparison of Algorithm Database: A patient-specific anatomical and medical image database

By Luc Soler, Alexandre Hostettler, Vincent Agnus, Arnaud Charnoz, Jean-Baptiste Fasquel Johan Moreau, Anne-Blandine Osswald, Mourad Bouhadjar, Jacques Marescaux IRCAD

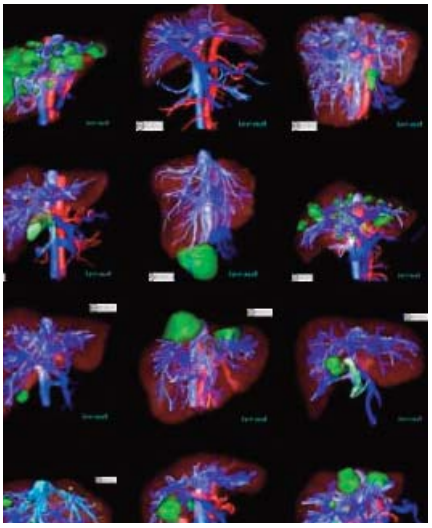
The medical world has known at the end of the last century a real revolution translated by several Nobel Prizes in physics or medicine: 3D medical imaging. By extracting the medical information contained in images into a set of 3D models, it is today possible to obtain a pre-operative 3D model of the patient, a kind of digital clone of the real patient. The visible human project initially limited to cadaveric models can thus be replaced by a visible patient with medical images of living patients. Such data can be used preoperatively to plan surgery, intraoperatively to guide the surgeon or postoperatively within the framework of anatomical education or medical simulation. It can also be used to compare various segmentations, mesh generations or simulation algorithms. In this aim, we have developed an open database called 3D-IRCADb (3D Image Reconstruction for Comparison of Algorithm Database) that includes several sets of anonymized medical images of patients and the manual segmentation of the various structures of interest performed by clinical experts. The 3D medical images and masks of segmented structures of interest are available as DICOM files. The representation of segmented zones is also provided as surface meshes in VTK format. Each model can be visualized using known freeware such as Osirix or 3D Slicer, or our freeware VR-Render combining a DICOM image 2D slice viewer, direct volume rendering and 3D mesh surface rendering visualisation techniques. Each 3D segmentation and modelling has been performed using the VR-Anat software developed on the same software framework used in VR-Render.

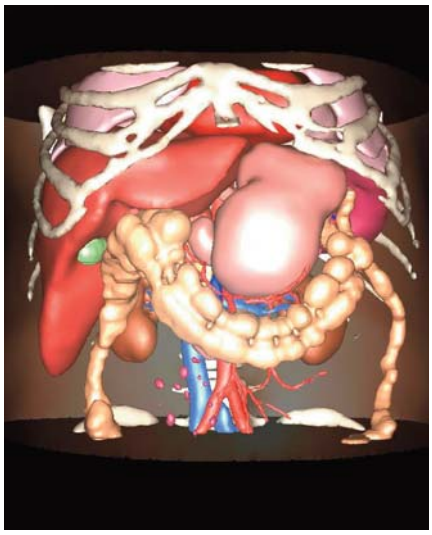
The first two databases have been created within the framework of the European project PASSPORT. The 3D-IRCADb-01 database is composed of the enhanced 3D CT-scans of 10 women and 10 men with hepatic tumours in 75% of cases. The 3D-IRCADb-02 database is composed of two anonymized thoraco-abdominal enhanced 3D CT-scans. The first one has been realized during the arterial phase in inhaled position, whereas the second one has been realized during the portal phase in exhaled position. The patient has a hepatic focal nodular hyperplasia in segment VII according to Couinaud's description.

The first benefit of this work was to validate a new anatomical segmentation of the liver modifying the current anatomical segmentation of Couinaud by removing its topological mistake. In the future, this database will be completed by many other cases including databases dedicated to adrenal tumours, parathyroid tumours and paediatric cases. We also plan to increase the current first two databases with new clinical cases. ■

This database is at the disposal of the scientific community for free on our IRCAD's website **http://www.ircad.fr/virtual_reality/3Dircadb/3Dircadb.php?lng=en**
For further information on the database contact: **luc.soler@ircad.fr**

The first two 3D IRCADb offer 3D models of 20 livers and 2 abdominal breathing positions.





VPH-I project focus

Feature on ACTION-Grid BIOINFORSALUD 2009

By Victor Maojo, Professor, Stefano Chiesa and Diana de la Iglesia, Universidad Politecnica de Madrid

On Monday March 16, 2009, the event "BIOINFORSALUD 2009: International Symposium on Research in Grid/Nano/Bio/Medical Informatics" took place at the "Palacio de Congresos", in Madrid. The conference, organized by members of the ACTION-Grid project and funded by the European Commission, sought to provide an overview of current initiatives on Grid computing, Nanomedicine, Biomedical Informatics and Nanoinformatics in different geographical areas. Experts from Europe, Western Balkans, North Africa, Latin and North America presented current work and developing lines of research in their groups.

The conference was divided into four different sessions:

1. ACTION-Grid: First European Initiative on Grid/Nano/Bio/Medical Informatics: The first session, chaired by the UPM professor Victor Maojo, introduced the ACTION-Grid project.

The latter is a Specific International Cooperation Project on healthcare information systems based on Grid capabilities and Biomedical Informatics (BMI) and nanoinformatics among Latin America, the Western Balkans and the European Union (EU). Members of the project consortium described their activities, defining the scientific context of the conference.

2. Nanomedicine and Personalized Medicine: Convergence of Technologies: The second session, chaired by SAIC-Frederick senior principal scientist Martin Fritts, introduced two aspects of the most recent trends in medicine: nanomedicine and personalized medicine. Recent research in medical therapeutics and diagnostics investigates how nanoparticles and nanodevices—i.e. particles and devices with size between 1 and 100 nanometer (1 millionth of a meter)—can be used to enhance medical treatment and how they can be adopted for individualized medical treatments.

3. Challenges for translational research informatics: The third session, chaired by the Instituto de Salud Carlos III area head Fernando Martin Sanchez, outlined the goals and requirements of translational informatics, particularly the application of methods and results obtained in laboratory research into clinical trials and studies in humans.

4. European Projects Towards the Virtual Physiological Human: Modeling and Simulation: The last session, chaired by professor Alejandro Pazos, provided an overview of the Virtual Physiological Human (VPH), funded by the European Commission. Speakers for this session have been working within the framework of the VPH. Their presentations addressed aspects of novel approaches like lab-on-chip devices, pharmainformatics and Grid technologies.

During the project meeting several round table discussions were celebrated, thoughts and experiences were exchanged that could be beneficial for both the project and the invited attendees. Furthermore, a first draft of the White Paper is now being written with all the information gathered during the congress.

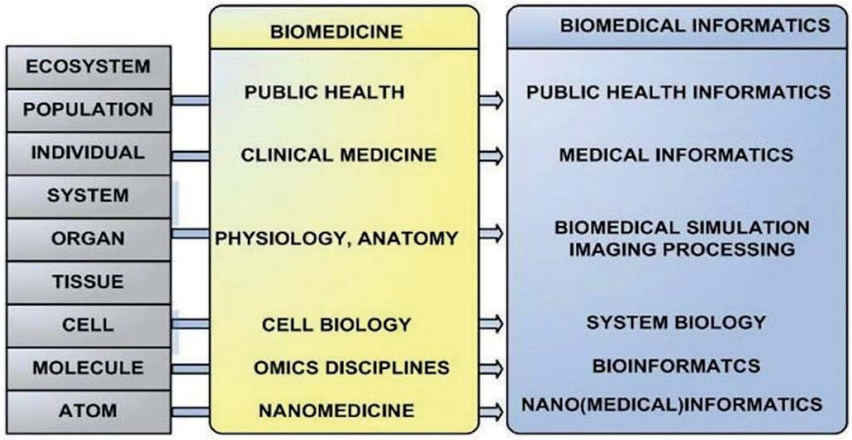
The first step of this task was focused on the design and implementation of a questionnaire with clear and concise questions that will help to harmonize contents and concepts. The second part included the analysis and posterior presentation of the results of the questionnaire, filled in by the Panel of Experts and the Consortium, in order to prioritize research lines that are more relevant. The Panel of experts provided feedback on specific questions and suggested different actions during the closed session of the congress. ■

More detailed information about speakers and their presentations can be found in the website **http://www.vph-action-grid.eu/BIOINFORSALUD2009**
For further information on ACTION-Grid contact the Project coordinator Diana de la Iglesia mail: **diglesia@infomed.dia.fi.upm.es**
or visit the website: **http://www.action-grid.eu/**

Interviews with members of the panel of experts

By Stefano Chiesa, Universidad Politecnica de Madrid

The Consortium of ACTION-Grid is assisted by experts in the different areas: Bioinformatics, Medical Informatics, Informatics applied to Nanomedicine and Grid Computing. The Panel of Experts will participate in the elaboration of a White Paper. This document will be delivered to the EC to establish a future agenda covering the Grid/Nano/Bio/Medical Informatics areas and will develop new plans in Latin America, the Western Balkans and North Africa. The Panel of Experts constitutes an Advisory Board that will provide feedback on specific questions and will suggest different actions, if needed. Its responsibilities include providing technical advice to the different work packages and exchanging ideas between partners. The BIOINFORSALUD meeting had an open session/conference where the ACTION-Grid Panel of Experts and the members of the Consortium had in depth discussions on the challenges and possible solutions to address these challenges behind the proposed topics of each session.



Biomedicine and Biomedical Informatics levels: from ecosystem to atom. Extracted from: López-Alonso V, Hermosilla-Gimeno I, Lopez-Campos G, Maojo V, Martin-Sanchez FJ. Action GRID: assessing the impact of Nanotechnology on Biomedical Informatics. AMIA Annu Symp Proc. 2008 Nov 6:1046.

Martin Fritts: Senior Principal Scientist, Nanotechnology Characterization Laboratory, National Cancer Institute (NCI-NIH). USA)

Which are the main objectives of your current research?

The main objective of the Nanotechnology Characterization Laboratory is not research, but rather to accelerate the translation of nanotechnology concepts for cancer diagnosis and treatment from the research stage into the clinic. However, because the NCL characterizes a large number of different nanoparticles, there is ongoing research to establish the relationships between the structure and type of the nanoparticles and their activity.

How do you see nanomedicine for providing new methods for diagnosing and treating cancer?

There are already dozens of clinical trials involving nanomedicine, primarily using liposome and emulsion formulations of therapeutics. The Cancer Nanotechnology Plan seeks to foster bringing these and other new concepts to the market through a collaboration among the NCI, the FDA and NIST. This alliance can accelerate the drug development process as the ability to intelligently design and produce these particles improves. The work of the NCL to better understand the structure/activity relationships of these nanoparticle formulations is a central element of that process. In addition to the improved therapies, nanomaterials are being developed for better imaging, diagnosis and early detection of cancer.

How do you see the use of informatics for cancer research in the forthcoming years?

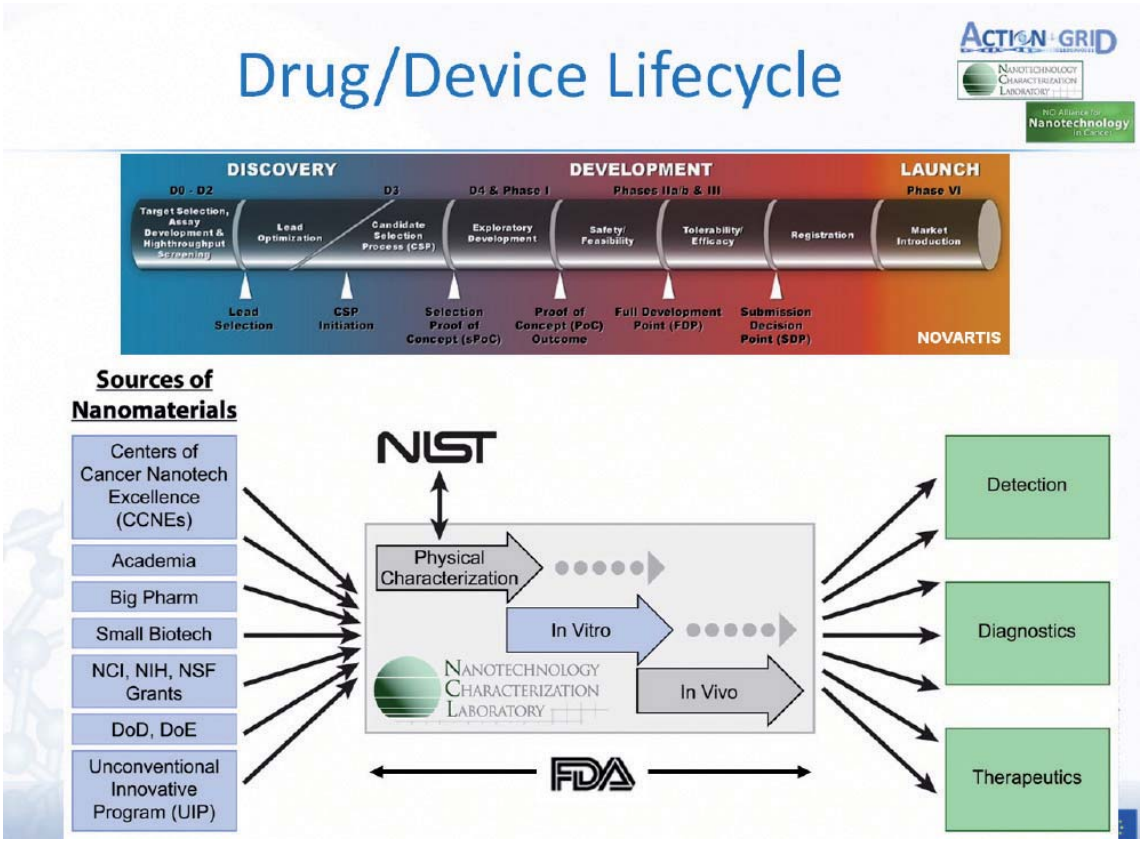
Right now the translation of cancer nanotechnology research to the clinic is limited by the amount of reliable characterization data available for these formulations. Providing a consistent and accurate body of physical/chemical, in vitro and in vivo data is one of the aims of the NCL. To achieve that goal we must have well documented assays and protocols so that measurements can be replicated from one lab to another, enabling us to reliably compare and aggregate the data coming from different laboratories and research institutions. We have just begun to see the first appearance of standard protocols for characterization of nanoparticles and the first completed interlaboratory studies using those standard protocols. As the data from these studies grows we will accumulate a large body of reliable data on a range of nanoparticles which we can mine to develop structure activity relationships. So informatics will be a key mechanism both for research and for translating that research to the clinic.

What do you think about the links between biomedical Informatics and nanomedicine?

Developing successful nanomedicine therapies and diagnostics will depend on how well we understand, at the molecular scale, the interactions between nanoparticles and the environments they encounter at the system, organ, tissue, cell, or subcellular levels. Accumulating the data describing those interactions, organizing it, annotating it, and using it to guide research and development is an immense informatics undertaking. It will require access to other existing and emerging genomic, proteomic, metabolomic and systems biology databases. But that informatics infrastructure will be an essential part of the foundation on which nanomedicine will be built. That informatics infrastructure will also be a core enabling technology for personalized medicine since it requires data of the same scope and at the same level of detail.

For more information on the work of the Nanotechnology Characterization Laboratory contact Martin Fritts **frittsmj@mail.nih.gov**
Or visit the website: **http://us.mc657.mail.yahoo.com/mc/compose?to=frittsmj@mail.nih.gov**

VPH-I project focus



About the NCL-NIH research in Nanotechnology and Nanoinformatics, presented at the congress by Martin Fritts.

Peter Ghazal
(Chair of Molecular Genetics and Biomedicine's department in University of Edinburgh)

Which are the main goals of your research?

Our central goal is to integrate post-genomic science with medicine in order to provide a better mechanism-based understanding of disease processes. This will provide the basis for the development of new medical innovations for the diagnosis and treatment of human diseases.

What it the idea about the genomic nanoprocessor?

What we aim to achieve in the future is the concept of personalised medicine. For example, one of the areas on which we currently focus is the integration of biological sensors with electronics. We hope to use these sensors, or biochips, as tools for the diagnosis and treatment of disease at the point of care.

Which application do you envision in medicine?

We are particularly interested in infectious diseases and treatment responses. In the future, sensors could be used to detect infection in your system and produce data which would be used to prescribe personalised treatment. Imagine you woke up feeling unwell and wanted to know if you had an infection or a hangover. Sensors would detect an infection and aid prescription of a treatment that would be right for you. Also, we have a strong interest in treatment responses in patients. In general, not all patients respond to medications and the issue is to identify those patients as early as possible so that they can be treated with a different medication.

For more information on this research contact: **pathwaymedicine@ed.ac.uk** or visit the website: **http://www.pathwaymedicine.ed.ac.uk/ghazal.html**

VPH-I researcher focus

Interview with Debora Testi, R&D Manager, Istituto Ortopedico Rizzoli, Bologna, Italy

Dr Debora Testi has an Electronic Engineering Degree from the University of Bologna (1997) and a PhD in Bioengineering from the University of Bologna (2002). She has published about 20 papers in international peer-reviewed journals. Most of her publications are related to computer-aided software for the pre-operative planning of total hip replacement, and for the prediction of femoral neck fractures in osteoporosis patients. From FP5 she has been involved in many European Projects. She has worked for many years as a researcher at Istituto Ortopedico Rizzoli (Bologna, Italy) and from 2005, she has been the R&D manager of BioComputing Competence Centre division (B3C), within SCS (start-up established by CINECA to exploit its research results). She has recently finished working for the completed LHDL project.

LHDL was an FP6 eHealth project funded by the European Commission. The Project ran from February 2006 and was completed in February 2009. For further information visit the website **http://www.livinghuman.org**

Tell me about LHDL: The Living Human Digital Library in a few short sentences.

LHDL developed and deployed the resource-sharing infrastructure required by the Living Human project (www.livinghuman.org) community and by many other groups involved with biomedical research and practice. Thanks to LHDL results, it is now possible to share biomedical data in an easy, controlled, safe, and financially viable way.

What was your specific role for LHDL?

I am working for a spin-off of partner CINECA, B3C, which is in charge of the exploitation of LHDL results. In this context, I have always been involved by CINECA in all ICT aspects of the project, from the architectural choices to the implementation issues.

What do you feel was your biggest contribution to the project?

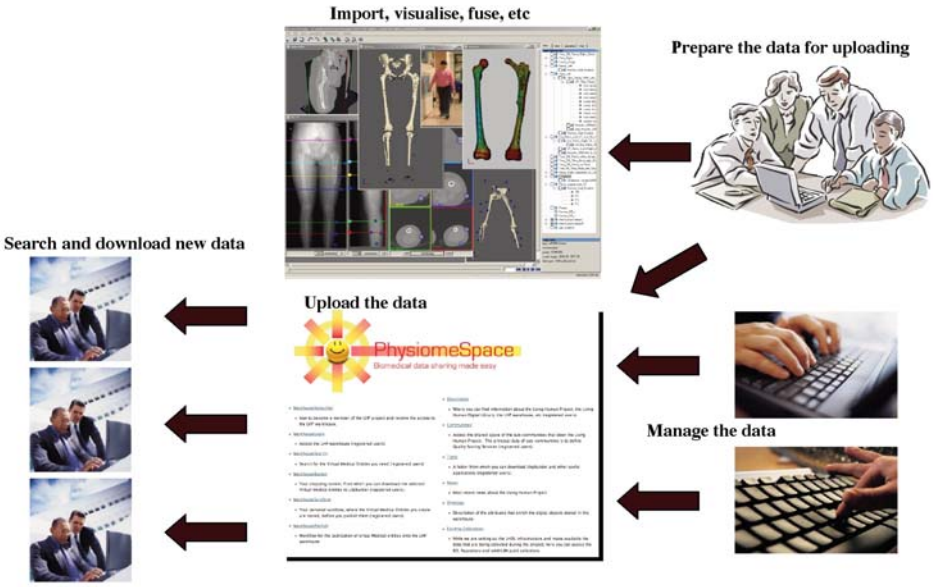
My biggest contribution to the project was to keep the ICT infrastructure and results monitored and make sure that the results would have been sustainable and made available as much as possible to the research community after the end of the project. I made frequent revision of the developed tools suggesting improvements and worked with all project partners to the definition of the exploitation plans. In particular, for the digital library services (PhysiomeSpace) and the modelling software (LhpBuilder) which B3C will exploit also commercially in the future.

How close are we to completing an in silico model of the human neuromusculoskeletal system?
Why is it important to have this model?
What else is needed to complete this model?

LHDL project provided a step forward into the in-silico model of the neuromusculoskeletal system. It has made available a complete set of tools that let you import your data collection and share it with other researchers. Some work is still needed with respect to the ability of visualise and interact with data and very different temporal and spatial scales. LHDL provided very interesting proofs of concepts on how both temporal and spatial multiscale data may be managed but further research is necessary to achieve a complete and easy to use interaction interface.

What tools came out of the LHDL project?

LHDL project provided many useful results to the research community but from my perspective the most important are the software tools for an easy sharing of data among different researchers and institutions. In particular, PhysiomeSpace (www.physiomespace.com) the first professional data management and sharing service dedicated to biomedical data, and PSLoader, an application that runs on your PC and lets you import virtually any biomedical dataset, organise your collection of data in space and time, and then upload it to the data manage-



VPH-I researcher focus

ment service. The set of implemented tools is completed by an application called LhpBuilder, a software tool with a long list of specialised functions for processing and modelling neuro-musculoskeletal system data.

Can other projects and individuals use these tools?
Many LHDL results have been made available to the research community after the end of the project. The PhysiomeSpace service is now running in beta phase and is accessible for free to any biomedical researcher; when registered to PhysiomeSpace, also PSLoader can be also downloaded for free, while LhpBuilder will be soon commercially distributed by B3C. PhysiomeSpace is expected to start as a commercial service near the end of 2009. Everyone will be entitled to open a PhysiomeSpace account for free and to store and share up to 1 GB of data. Additional storage and bandwidth can be bought at convenient rates, under a pay per use model. We plan to sign block agreement with research projects and large consortia, ensuring mostly favourable conditions.
Apart from the ICT tools other information and results have also been made publicly available such as the ontologies, developed by the project partners, to annotate the data resources and the white paper data collection protocol. All these are accessible through the LHDL building on the BiomedTown community portal (www.biomedtown.org/biomed_town/LHDL).

What was the greatest success of the LHDL project? (I.e. how was the project received by the European Commission?)
The results of the LHDL project were considered very well by the European commission reviewers; the project was judged outstanding and also covered by the "monthly focus" of the ICT unit (http://ec.europa.eu/information_society/activities/health/docs/monthly_focus/200905lhdl.pdf).

How do you feel the achievements made by LHDL can be sustained? Are there any other projects in the pipeline?
As already said, some LHDL results will be further exploited commercially, while from a research point of view the experience of LHDL will be used as starting point in other EC-funded projects and in particular for the VPHOP project (http://www.vphop.eu), IP project funded in the first VPH call. Among other LDHL partners, B3C is directly involved in the project being the leader of the ICT infrastructure activities. Within VPHOP activities we plan to extend the digital library services and its integration with execution web-services to remotely preprocess the data, and also to extend LhpBuilder to be able to cope with data from the body to the cell level with a complete integration with the hypermodel technology that will allow to predict the risk of fracture in osteoporotic patients.

Email: d.testi@scsolutions.it

Interview with Serge Van Sint Jan,
Professor, Université Libre de Bruxelles, Brussels, Belgium

Serge Van Sint Jan has been Professor of Anatomy at Universitié Libre de Bruxelles since 2001. Serge has a background in both Physiotherapy and computer modelling and obtained his PhD in Physiotherapy and Rehabilitation, which was based on modelling systems for 3D reconstruction, kinematics analysis and joint motion simulation from medical imaging. He has produced over 65 articles from peer reviewed International journals and has worked on many European Commission funded projects, including JPD, LHDL, BIONET, MULTIMOD, Vakhum (as Project Coordinator) and most recently DhErgo and the VPH NoE as a member of WP2, WP3 and WP5.

Tell me about LHDL: The Living Human Digital Library in a few short sentences.
The Living Human Digital Library Project (LHDL) is a grass-roots initiative aimed at developing an in silico model of the human neuromusculoskeletal system that can predict how mechanical forces are exchanged internally and externally, from the whole body down to the protein level, consistently with scope of the European Virtual Physiological Human initiative.

What was your specific role for LHDL?
I was in charge of coordinating all data collections within the project (also at the location of other partners). I was also Application Expert for the development of all LhpBuilder aspect relative to modelling (musculo-skeletal modelling, data representation, ontology, motion, etc).

What do you feel was your biggest contribution to the project?
Coordinating the data collection was not an obvious task as there were several partners involved. Partners based

at several locations were supposed to work on the same specimen and for small samples like a muscle biopsy, this was easy. However the ethics involved in sending bones or a full corpse to different locations was not so obvious. We had to check the legalities of sending a donated specimen from ULB abroad. We discovered that whilst there are National legislations for this kind of transportation, there is no European legislation and therefore if there is no law, it is allowed. We contacted DHL to request the transportation of large boxes of human remains and anticipated we would have problems. The problems turned out to be not related to human remains but to the transportation of dry ice, which is listed as a dangerous product. Once we had obtained special authorisation to ship dry ice we were then able to send the human remains, with an extra cost.
I was also application expert for the development of LhpBuilder (integrative software platform developed from MAF2) http://www.openmaf.org. This involved advising and making strategic choices with other people about priorities on development. ULB was also responsible for the development of the code, although the software was developed by many different LHDL partners.
ULB as a whole further contributed to the project by undertaking, for the first time, a large dissection on one specimen and collecting a lot of data on that specimen, preparing and using validated protocols. The functional anatomy ontology was also developed here at ULB. Finally, some of the modelling activities were performed here – mainly joint kinematics and motion analysis and integration of in-vivo data into the in-vitro model.

How close are we to completing an in silico model of the human musculoskeletal system?
Why is it important to have this model?
What else is needed to complete this model?

Despite recent progresses, we are far from obtaining the ultimate model. To me, as a professor of Anatomy, I think this is one of the more complicated anatomical systems. It is not only the physiological level which is complicated, (i.e. the mechanism of muscle fibre contraction and its control at cellular level) but even to understand how one muscle functions is a challenge. There is also the fact that one muscle is never acting on its own but is acting simultaneously with many other muscles, introducing an amazing mechanical redundancy. As the cherry on the cake there are not only muscles in the musculoskeletal system, you also have bones and joints which are built from extremely heterogeneous elements (bone, cartilage, ligaments, synovial fluid). To complete the complexity of the endeavour, all these elements are interacting with the external physical world as they are all involved in motion and they are directly interacting with gravity. Therefore physical laws, like Newton's should also be directly integrated in the whole modelling process.
We are still in the bone and joint decade, promoted by UNESCO, and statistics have shown that disorders related to the musculoskeletal system like joint pain and arthritis are a disorder which has a large impact on society, i.e. because of work absences. It is rarely fatal but there is a large financial cost to society and that's just one reason why we need to work on that problem. Governments don't pay enough attention to research related to the musculoskeletal system (certainly in Belgium).

What tools came out of the LHDL project?
PhysiomeSpace, MAF2 and LhpBuilder. Tools that came from LHDL were already in preparation from other European funded projects, like Multimod and VAKHUM (at the data level), so these tools are the fruits of a long term thought process and not just a three year project.

Can other projects and individuals use these tools?
During the project, we realised we needed a tool to allow researchers to exchange data, to process data to make new models and then to share these models with their research communities. PhysiomeSpace is a great asset for researchers as it allows for this type of data exchange. It is also the same thing for MAF. MAF2 is an open source development platform. As mentioned above, it has been developed for many years and because of that most problems encountered early on have disappeared. The library for MAF2 is ready to be used by other researchers. As an example of application LhpBuilder was developed from MAF2 . The third tool is BiomedTown which is the first web community of its kind trying to give a common place for researchers from different horizons to virtually meet, exchange ideas and create a sense of community.

What was the greatest success of the LHDL project? (i.e. how was the project received by the European Commission?)
The European Commission gave the project the highest distinction, of 'outstanding' in their final review report. I think they liked it because not only did the project develop a very strong ICT platform (PhysiomeSpace, MAF2, LhpBuilder, and BiomedTown) but it developed these tools keeping in mind the requirements from the field, i.e., data visualisation, data storage, data definitions.

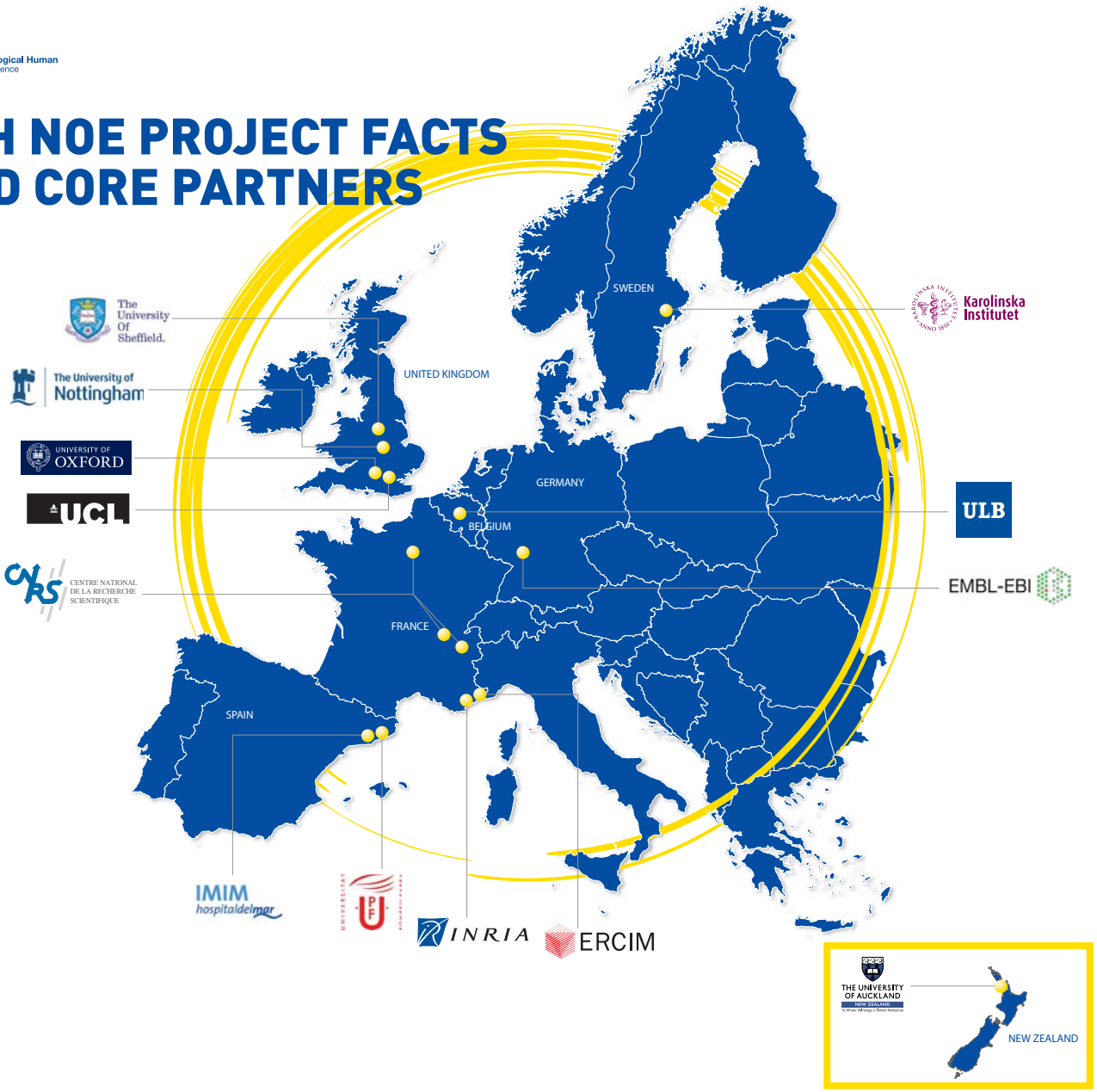
How do you feel the achievements made by LHDL can be sustained? Are there any other projects in the pipeline?
The project coordinator created a spin off (B3C) to continue this effort and ensure it is used. LhpBuilder is used every day in ULB for research with medical and physiotherapy students. We have the intention to continue developing and using LhpBuilder as we are convinced by the usefulness of this kind of platform. We are also using MAF2 in other European projects (DHERGO) at ULB.

What impact do you think LHDL will have on future clinical healthcare?
Once we solve all problems (mentioned above) it will have a huge impact. However whilst it does depend on the pathology and what you want to achieve, we are not at that point yet. From an ICT point of view the system could be very useful in clinical healthcare. The problem is (as above mentioned) that there is a still huge work to do in term of integrative research and better understanding of the links between all the levels involved. This could be seen as future work for many other European projects.

For more information on results please go to the following article: **http://www.ehealthnews.eu/content/view/1608/27/**

Virtual Physiological Human
network of excellence

VPH NOE PROJECT FACTS AND CORE PARTNERS



VPH NoE project facts and core partners
VPH NoE is a network of excellence funded by the European Commission's Seventh Framework Programme. It contributes to the Virtual Physiological Human initiative.

EC Project No: **FP7-2007-IST-223920**
Instrument: **Network of Excellence**
Start Date: **June 1st, 2008**
Duration: **4.5 years**
Project Management : **UCL/UOXF**
Workpackage Leaders : **UCL, CNRS, UOXF, UPF, ERCIM**
Core Project Members: **EMBL, KI, IMIM, ULB, UNOTT, UOA, USFD, INRIA**
Total Project Cost: **9.65 million euros**
EC Funding: **8 million euros**
Further Information : **www.vph-noe.eu**

Core Partners:

The VPH NoE is comprised of 13 Core Project Partners and an extended Associate (for industrial bodies and organisations) and General (for academic institutions) Membership.

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For additional information and to take and active part in the VPH NoE activities, please visit:
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