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VPH-DARE@IT

Newsletter Issue II

SEPTMBER 2014

www.vph-dare.eu
Editorial

Welcome to the second issue to the VPH-DARE@IT newsletter! I hope everyone has had a great summer after a busy few months of reporting and preparing for our first periodic review. The periodic report and review took a lot of time and effort from all project partners, and we at the Project Management Office would like to thank all of our partners for their contributions and cooperation in preparing for these key project deliverables.

The review has definitely been a highlight of the last 6 months and in this issue of the newsletter, Dr Mark Pullinger gives an account of the review process and the feedback from reviewers. We also say goodbye to Mark who has moved on from the University of Sheffield and the project. Mark has worked hard during the past few months in preparing the periodic report and for the review and we would like to thank him for all of his work and support during his time managing the project.

While Mark moves on to new challenges and to spend more time with his family, we are delighted to welcome Dr Matthew Henry to the project. In this issue of the newsletter, Matthew tells us about himself, his background and how he is looking forward to working on the project. Welcome Matthew! We also hear about the other activities here in Sheffield, from Professor Iain Wilkinson and the role that he and his colleagues in the Faculty of Medicine Dentistry and Health play in VPH-DARE@IT. We also hear from partners Kinematix and VTT about their involvement in the project to date.

We are pleased to welcome our Scientific Advisory Board to the project and here we meet the 8 independent experts who sit on the VPH-DARE@IT Advisory Board. We also talk to Klas Pettersen at the University of Oslo and discuss his role in the project and the modelling electrodiffusion and water transport activities in workpackage 5.

As we continue to build on the links with other projects and initiatives established during period 1, we hear from David Mansett of Neugrid and the possibilities for collaboration with VPH-DARE@IT. Alex Teligadas also provides an overview of Alzheimer Europe and its activities in promoting dementia awareness across Europe.

In the spirit of collaboration, this month’s research highlights looks at how VPH-DARE@IT and VPH Share are working together and how the interaction between the two projects helps to progress VPH-DARE@IT project objectives.

It has been a busy few months and there are some more challenges and exciting times ahead! We hope you enjoy the newsletter and, as always we would love to hear your views, comments or suggestions for future articles or features. If you would like to make any comments or suggestions, please do not hesitate to contact us: contact@vph-dare.eu.

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The VPH-DARE@IT project met its first major milestone at the end of June 2014, the periodic review by the European Commission. The annual review is the main means that the European Commission uses to assess progress in the project.

A group of eighteen members of the project team travelled to Brussels for the review on June 26th and 27th. The team assembled at the Hotel Gresham Belson in Brussels on June 25th to finalise the account of the first year of the project to be presented to the European Commission. This preparation followed a number of project board teleconferences, so was mainly focused on polishing the narrative of the journey that the project had taken in its first year. The review team, consisting of the work package leadership team and most Year 1 deliverable authors, prepared two epic sets of slides, nearly 300 in all, charting the progress of the project, from its launch to the end of its first year, and outlining the plans for subsequent periods.

The review itself, which was held at the premises of DG Connect, allowed the project to present its progress before a panel consisting of our project officer, Dr. Amalina-Irina Vlad, and four external experts appointed by the European Commission. The external reviewers brought a range of expertise to the process: Dr. Rolf P. Würtz, Ruhr-University of Bochum; Dr. Manuel Gaviria, CEO of Workinbio, Montpellier; Dr. Aleksandra Suvalska of Poznan University of Medical Sciences; and Prof. Dr.-Ing. Galina Ivanova of Humboldt-Universität zu Berlin. They listened diligently to the presentations, having previously reviewed the periodic report and the project’s Year 1 deliverables, and asked a number of challenging questions.
questions. A great deal of discussion was devoted to the project’s activities to assess the relevance of lifestyle and environmental factors in Work Package 5.

After a day and a half of presentations and discussions, the VPH-DARE@IT Team was finally sent out of the room to allow the reviewers to reach their conclusions. After what seemed like an eternity, during which paranoia began to grip the more faint of heart, the team was called back in and received the welcome news that VPH-DARE@IT had been rated a good project, one that had achieved most of its objectives and technical goals for the period with relatively minor deviations. The project’s objectives were found to remain relevant and only minor recommendations for improvements were proposed.

The project board analysed the outcome of the review during its teleconference on July 24th and has decided, as a result, to make some changes to future reviews. First, there was a clear desire to see more partners’ representatives present, particularly from industry, so a larger team is likely to take part next year. In addition, the project board plans to have a greater focus on the scientific activities, in addition to the necessary presentations of management issues. This will be addressed through encouraging greater participation by early-career researchers and through the incorporation of a guided poster session during the review.

We would like to take this opportunity to thank all of our partners for their contributions and commitment in preparing for the review. We are very pleased with the outcome of the review and look forward to building on this and having an equally productive and successful year in year 2.

Example of different Quantitative Imaging Biomarkers (QIB): it is the aim of this WP to provide statistics on a number of QIBs as a function of ageing and other variables
Meet the Scientific Advisory Board

The Scientific Advisory Board (SAB) is formed by independent experts external to the project. The purpose of SAB is to seek advice from external experts that are not directly involved in the day to day running of the project.

**Dr. Daniel Marcus**
Dr. Marcus directs imaging informatics operations for a number of large scale research programs, including the Human Connectome Project, the Dominantly Inherited Alzheimer Network, and the Neuroimaging Informatics and Analysis Center. Dr. Marcus is also founder and president of Radiologics, Inc., which has developed a XNAT CR, a 21 CFR Part 11 compliant version of XNAT.

**Prof. Eszter Farkas**
Prof. Eszter Farkas is presently a Research Associate Professor at the University of Szeged, where she leads the Laboratory of Experimental Neuroimaging at the Department of Medical Physics and Informatics.

**Prof. Giovanni B Frisoni**
Giovanni Frisoni is Professor of Clinical Neuroscience at the University of Geneva, Switzerland, and Head of the Memory Clinic of the Geneva University Hospital. Scientific Director at the National Alzheimer’s Centre in Brescia, Italy and Head of the local Laboratory of Neuroimaging and Translational Care Unit.

**Prof. Judith Campisi**
Judith Campisi a Professor at the Lawrence Berkeley National Laboratory. In 2002, she established a laboratory at the Buck Institute for Age Research, where she is a Professor. At both institutions, Campisi established a broad program to understand various aspects of aging, with an emphasis on the interface between cancer and aging.

**Prof. M.Hofmann-Apitius**
Martin Hofmann-Apitius is Professor for Applied Life Science Informatics at the Bonn-Aachen International Centre for Information Technology (B-IT) at the University of Bonn. In addition, he holds a position as Head of the Department of Bioinformatics at Fraunhofer Institute for Algorithms and Scientific Computing (SCAI) in St Augustin, Germany.

**Prof. Michael Weiner**
Prof. Michael Weiner is currently Director of the Center for Imaging of Neurodegenerative Disease, and is Professor of Radiology, Medicine, Psychiatry, and Neurology at the San Francisco VA Medical Center/UCSF. His grants include studies of Alzheimer’s disease, vascular dementia, frontotemporal dementia, gulf war illness, posttraumatic stress disorder, HIV and other neurodegenerative diseases. He is the Principal Investigator of the NIA funded $60 million Alzheimer’s Disease Neuroimaging Initiative.

**Prof. Nikolaos Scarmeas**
Prof. Scarmeas is Associate Professor of Neurology at the Cognitive Neuroscience Division Taub Institute at Columbia University. His current research includes: Lifestyle, nutrition and Dementia – Alzheimer’s disease, Cognitive Reserve, Predictors of progression in Dementia - Alzheimer’s disease, Epilepsy and Dementia.

**Prof. Ron Kikinis**
Dr. Kikinis is the founding Director of the Surgical Planning Laboratory, Department of Radiology, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, and a Professor of Radiology at Harvard Medical School. His activities include technological research (segmentation, registration, visualization, high performance computing), software system development, and biomedical research in a variety of biomedical specialties.
The CISTIB research group in the department of Mechanical Engineering at the University of Sheffield is the lead partner of the VPH-DARE@IT Project. In addition to the involvement from the Faculty of Engineering, the Faculty of Medicine, Dentistry and Health at the University of Sheffield also play a vital role in the project. Here, Professor Iain Wilkinson (Department of Academic Radiology) explains his involvement and that of his colleague, Professor Annalena Venneri (Department of Neuroscience) both from the Faculty of Medicine, Dentistry and Health and the role they play in VPH-DARE@IT.

We asked Professor Wilkinson how academics from the faculty of Medicine, Dentistry and Health came to be involved in the VPH-DARE@IT Project. Iain told us how the department of Academic Radiology, which forms a cross-departmental clinical research imaging hub with several groups across the University of Sheffield and with local NHS hospitals, has been involved in previous EU-funded multicentre research, including the neurIST project. The latter provided the initial link with the VPH-DARE@IT Coordinator, Professor Alejandro Frangi, which developed an interest in water-transport modelling and even further when Prof Frangi made Sheffield his new home! As well as Iain’s pursuit of answers to neuroscientific problems using MR, the appointment of Professor Annalena Venneri to the Department of Neuroscience with her experience, interests and focus in cognitive impairment and the Dementias made a perfect match for the project.

The faculty has 2 main contributions to the project: the provision of retrospectively and prospectively acquired data, especially (but certainly not exclusively!) MRI, and knowledge of clinical aspects of neuro-degenerative diseases. Incorporation of both of these are fundamental to the development, guidance of and outcome from mechanistic modelling in this context.

Prof Iain Wilkinson leads adult neuroimaging research within Academic Radiology, part of

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the Faculty of Medicine, Dentistry & Health. His background started in physics, spun into MRI and then he became attached to clinical neuroimaging problem-solving. One of his main academic interests is unravelling the pathological mechanisms of the CNS that lead to impairments associated with diabetes and other degenerative diseases. Iain is a registered UK Clinical Scientist, providing imaging support to local hospitals as well as performing usual academic duties. The Royal Hallamshire Hospital (where the Faculty of Medicine is based) is the region’s neuro-centre, providing a service to over 2 million people in the UK. In his role in the project, Iain helps to develop and implement the prospective MR data acquisition strategy (with our other MR partners in work package 2) and directs the acquisition of new MR data in Sheffield as part of Work Package 1.

Dr Deirdre McGrath (based in Prof Frangi’s CISTIB lab in the Faculty of Engineering) spends half of her time with Academic Radiology, working with Iain and bringing together modelling and data acquisition strategies, particularly in the areas of elastography and perfusion.

Prof Annalena Venneri leads the Translational Neuropsychology Group within the Department of Neuroscience, Faculty of Medicine, which investigates the early and differential diagnosis of the Dementias. During her 25 years of research experience, Annalena has performed many studies applying the most up-to-date functional imaging techniques. Particular interests have included studying the Default Mode functional connectivity Network in early AD, MCI and response to pharmacological and behavioural therapies. Annalena also provides a clinical neuropsychology service within the Royal Hallamshire Hospital. In addition, Prof Venneri is the ‘Scientific Director’ at the RCCS Fondazione Ospedale San Camillo and also leads the functional imaging laboratory at the same research hospital, the Lido, Venice, where she organised our 2nd General Assembly in March 2014.

In her role in VPH-DARE@IT, Annalena supports the clinical questioning within the project and applies her clinical neuropsychology expertise to both retrospective and prospective patient data deliverance (Work Package 1).

The work carried out to date by the team at the Faculty of Medicine, Dentistry and Health includes, initiating the sorting of retrospective data, helping to assemble the clinical questions and assimilating the ‘MRSUB1’ protocol.

We asked Iain what he found most interesting about VPH-DARE@IT. Iain said that

“helping to model a very complex, interactive set of pathologies that form what we term the dementias is, well, fascinating and very much needed”.

Iain went on to say that being part of the interaction between so many expert centres that have different specialities and skills in such a large collaborative project is very rewarding.
Kinematix is a pioneer in the design and development of intelligent medical devices that extract knowledge from movement and posture. “Body dynamics” may be the richest unexplored frontier in healthcare. Each body part is a source of vital information about a person’s health. Using sophisticated sensing capability, Kinematix products offer cutting edge technology, smart design, and sophisticated software analytics for real-time reporting of critical clinical information.

Kinematix was established in 2007, and at that time it was a start-up from the University of Porto and INESC Technology and Science and was called Tomorrow Options. In 2013, entering the US market they announced the new company name Kinematix, to better reflect the dedication to monitoring body dynamics during real-life activities.

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Kinematix Products

Kinematix’ products incorporate the latest in micro-electronic sensing, with connected health features designed for customization, efficiency and enhanced communications. To help turn subjective observation into objective evidence, Kinematix “smart” products don’t just monitor and measure, they make information meaningful and actionable for patients and care-givers. Kinematix, innovative technologies keep patients engaged and clinicians informed to ensure more effective, more efficient care and better outcomes.

By targeting intractable problems brought about by chronic conditions caused by diabetes, osteo-arthritis, stroke, musculoskeletal disorders and orthopaedic injury, Kinematix provides patients, providers and payers with the knowledge they need to ensure that care given is better, faster, more convenient and less expensive.

New WALKiNSENSE® applied to a shoe

WALKiNSENSE® is a portable, easy-to-use tool for orthopedic specialists, physical therapists, podiatrists, orthotists as well as athletic trainers and other professionals treating conditions that require corrective footwear and bracing. Using sophisticated sensors to introduce a quantitative, evidence-based approach to the diagnosis and treatment of diabetic foot ulcers, stroke rehabilitation and other posture and mobility disorders, WALKiNSENSE® eliminates the guesswork that characterises a multi-stage fitting process that relies mostly on trial and error to achieve desired fit, functional and cosmetic results.

MOViNSENSE® basic features

MOViNSENSE® is a portable, wearable “smart” device targeted to hospitals, nursing homes and skilled nursing facilities that travels with the inpatient to measure, track and automatically record patient movement and safer transitions across the care continuum, post-discharge and in the home in real-time. MOViNSENSE® assists clinicians, nurses and caregivers in the early detection and prevention of those mobility- and position-associated risks including hospital-acquired pneumonia, pressure ulcers, falls, and out of bed wandering alert care givers to adverse events.

The role of Kinematix in VPH-DARE@IT

Kinematix has previously engaged with the University of Sheffield in several other initiatives, and due to its knowledge and expertise in pervasive sensing of body dynamics, Kinematix were invited
by the University of Sheffield to join the VPH-DARE@IT project, where monitoring and modelling of environmental and lifestyle factors are researched in order to shorten the delay for early detection and diagnosis of cognitive impairments and dementia.

Kinematix contributes to the VPH-DARE@IT project with its accumulated knowledge and R&D in pervasive and quantitative sensing of human movement, gait analysis and physical performance in everyday living activities. For its known links with dementia, the project patient cohorts will be monitored against physical performance, gait and posture. Kinematix will develop and improve its WALKiNSENSE® devices to achieve these goals.

From evidence in recent studies, there is a general belief that personal lifestyle factors that result in sustained altered physiological regimes will chronically affect brain fluid balances, transport and metabolic mechanisms that will precede structural and functional deterioration of brain function. Testing and validating this hypothesis will allow the project to develop subject-specific models of normal subjects and subjects with different levels of cognitive impairment.

Kinematix is committed to conceive and develop the necessary equipment, software algorithms and data provision for incorporating and quantifying circadian and lifestyle variations, and potential effects on brain and dementia.

Key people involved

Paulo Ferreira Santos, co-founder and Chief Executive Officer at Kinematix, is a serial entrepreneur that has already created 6 companies in different areas, from IT to real estate - and is the person that initially pushed to startup Kinematix. He holds a Master in Technological Entrepreneurship from the University of Porto, and a long term experience in SME management. Paulo plans and manages the Kinematix research team and resources committed to the project.

Miguel Velhote Correia, co-founder of Kinematix and inventor of WALKiNSENSE®, holds a PhD in Electrical and Computer Engineering from the University of Porto, has a tenure position since 2002 as Assistant Professor at U.Porto, Faculty of Engineering and research position at INESC Technology and Science. His main research interests are in Electronics and Biomedical Instrumentation, Computational Vision and Image and Signal Processing, with focus in sensing methods, technologies and data fusion for the measurement and analysis of human movement, perception, action and performance. Miguel coordinates the research and development activities assigned to Kinematix in the project.

Pedro Silva, is the Chief Technical Officer at Kinematix. He has a Master in Electrical and Computer Engineering from the University of Porto, and
began his career at Kinematix in 2008 as a product developer in the R&D department. He is responsible for all hardware and firmware development.

Jorge Pinto has a Master in Computer Sciences from the University of Porto, and has been working for Kinematix since 2008, started as a software developer and is now the Chief Development Officer. He is responsible for all software development, platform adoption and downstream product support.

**Key Interests in the Project**

It is interesting how such a large project involving a considerable number of universities, research institutions as well as large and small companies, all with different organisations, working methods and agendas, come together to embrace a common mission and goal. The leadership of Professor Alejandro Frangi and the management team at the University of Sheffield are paramount to this accomplishment. Additionally, the project is clearly in the forefront of research in an extremely important subject that so severely affects the life of a large and increasing part of the world population. Dementia is a multifactorial health problem that can only be tackled properly from many different fields and perspectives, which is the whole purpose of VPH-DARE@IT.

When asked about Kinematix interests in the project Dr. Miguel Velhote Correia indicated “It is very stimulating to participate in such a pluricultural and multi-disciplinary project embracing a very wide set of different scientific research topics, from molecular level biology research, brain imaging and modelling to behavior, lifestyle and environmental factors”.

**The Challenge for Kinematix**

Keeping up with the contributions from other partners can be challenging as these have possible implications for Kinematix contribution to the research outcomes. To turn the research outcomes into products and solutions for real life health problems and everyday clinical practice is a challenge for which we believe Kinematix is very well positioned.

This project is an excellent opportunity to become more knowledgeable and increase the company’s visibility, both in the scientific community and in the application and clinical fields related to cognitive impairments and dementia.

Kinematix expects to be able to develop and contribute with novel devices and solutions for the increasing elderly population, in particular with dementia conditions, that may help to deploy screening methods at the onset of early symptoms and reduce delays in the detection and diagnosis of dementia. In line with the company’s strategy of targeting difficult problems brought about by chronic health conditions, it will help to provide solutions to decrease the burdens of dementia related impairments and improve the quality of life of the elderly population.
VTT Technical Research Centre of Finland is the largest multidisciplinary research organisation in Northern Europe, with a turnover of 245 million euros and staff of 2700 experts. VTT provides high-end technology solutions and innovation services in wide-ranging customer sections, including smart industry, low carbon energy and health and wellbeing. VTT is a not-for-profit government agency of the Finnish innovation system under the domain of the Ministry of Employment and the Economy. 69% of VTT's funding is external (private), 31% from the government and 18% international.

In general, VTT's main tasks are technology research and development, and the transfer of technologies into business opportunities which will benefit its clients and partners. VTT steers and develops its activities in cooperation with industry, research institutes, universities and the authorities in charge of technology policies and research funding.

VTT has a strong tradition in research on ICT for wellness and healthcare. The research group working in project VPH-DARE@IT is called ‘Systems medicine’. Our core competences include biosignal and image processing, electronic health records, eHealth/mHealth technologies, systems biology and bioinformatics.

The role of VTT in VPH-DARE@IT

Between 2008 and 2011, the VTT, Systems medicine research group was working on a 7th EU Framework (FP7 – 224328) research project called PredictAD (http://predictad.eu). PredictAD aimed
to provide standardised and objective solutions for enabling earlier diagnoses of AD, improved monitoring of treatment efficacy, easier patient selection for drug trials and improved cost-effectiveness of diagnostic protocols. During the project over thirty journal papers were produced and after the excellent results it was clear that our group would continue research in the area of dementia. As VTT and UPF were planning to prepare a new project and J. Lötjönen (VTT) and A. Frangi (UPF) knew each other previously, they decided to join forces.

VTT is working on several work packages in VPH-DARE@IT. VTT is developing new MRI image processing methods for quantification of changes vascular dementia, as well as doing connectivity modelling, studying the correlations between biological, medical and environmental data and their relation to dementia. In addition, the team is also active on modelling metabolomics in neurodegenerative diseases.

Finally, VTT is responsible for developing the clinical platform in VPH-DARE@IT. It is a clinical decision support system (CDSS) that allows earlier, more objective and more accurate differential diagnostics of dementia by combining heterogeneous patient data, including the data produced in the other work packages mentioned above.

**VTT people involved in VPH-DARE@IT**

Dr Jyrki Lötjönen, PhD, is a principal scientist in ICT for Health team at VTT and adjunct professor at Aalto University. His research interests are in medical image segmentation, statistical modelling and data mining. Jussi Mattila, PhD, is a software developer with machine-learning expertise. He led the development effort on a CDSS tool developed in project PredictAD and recently received his PhD on the same topic. Other key researchers involved in VPH-DARE@IT are Juha Koikkalainen, PhD, and Antti Tolonen, who are working on image processing and data analysis tasks within the project, respectively, and Artturi Koivuniemi who is working on metabolomics modelling.

Jyrki Lötjönen is leading Action Line 1 and is also the leader for Work Package 8. He is actively supervising the work done in VPH-DARE@IT at VTT in all the work packages they have a stake in. Jussi Mattila is leading the development of the clinical platform and developing new methods for clinical decision support in differential diagnostics of dementia. Juha Koikkalainen has started working on novel algorithms for quantifying vascular dementia in MRI images. Antti Tolonen will be validating the image processing and decision support methods as they are being finalised.

When asked what he finds most interesting about the project, Jyrki said the project provides a great opportunity to work with the top experts on producing better tools for diagnostics of several dementing diseases. “It is a very exciting opportunity that can have a huge impact on the medical field. VPH-DARE@IT approaches the challenge from many different angles starting from individual modelling and image processing methods, to tools that accelerate research efforts, and finally to clinically viable solutions that help doctors in their daily work.”

Working with such a diverse group of organisations, there are naturally challenges in aligning the different parties to a common cause. Jyrki went on to suggest “when people are able to do what they do best in an environment where the goal is shared, the buzz and synergy that it generates is definitely worth the effort. It is also a privilege to be able to access people in several different countries and organisations, allowing for example fine-tuning the clinical platform to fit as many workflows as possible.”

“Even though the work to be done has been specified in the description of work, there are still many interesting avenues for research that fall within scope of the project. Choosing the ones to pursue in depth is quite challenging. There is never enough time to do everything that one finds interesting or promising.”
The main activities at VTT to date

Work on the clinical platform has started in earnest, with new image processing and machine-learning algorithms being developed and integrated into the clinical platform CDSS for performing differential diagnostics of dementia. This work has been described in the first software deliverable that was delivered to European Commission in July. Work on connecting biological, medical and environmental data has also started now, as new people have joined the Systems medicine group. The modelling of metabolomics is also actively ongoing.

VTT has identified several commercialisation opportunities for the innovations being developed in VPH-DARE@IT. In fact, the methods and tools being developed further in this project have already generated a lot of interest amongst our partners. There have also been discussions regarding licensing or setting up a spin-off company that would take some of these technologies to the market. In short, VPH-DARE@IT, at least from VTT’s point of view, has a great chance of making life better for Europeans!
# Software Tools & Skills for Translating Research into Pre-Clinical Prototypes

**Hands-on Course, University of Sheffield, Sheffield, UK**

**Monday 20th to Friday 24th October 2014**

Bridging the gap between world-class research and professional software development to deliver the next generation of computational imaging software prototypes for clinical translation.

### Key Benefits

- Get advice on how to bring your image-based modelling and model-based imaging project to life from top Researchers and Software Professionals with extended experience in the area.
- Experience the whole Software Development Life cycle from conception to validation, guided through real use cases, illustrative examples or develop your own project.
- Learn basic Software Development Techniques and Skills that will increase the quality of your prototype.

### VPH Workflow

A real use case will drive the workshop to experience the delivery of pre-clinical prototypes using the GIMIAS platform, going through:

- **Segmentation**: Creating patient specific 3D models from medical imaging.
- **Personalization**: Personalization of FEM mesh with patient specific information.
- **Post Processing**: Execution of simulation using FEM as an input, and processing of the output.
- **Validation**: Make prototype available and validation process.

### Participant Space

Daily Specific slot for participants where:

- General questions will be addressed by Kitware and CISTIB.
- Obtain technical assistance from Kitware and CISTIB teams to progress on their personal projects.
- Progress in the proposed VPH workflow implementation.
- A retrospective will be conducted to improve any aspect of the workshop.

### Software Engineering Training

The participant will be introduced to:

- Best software engineering practice using CMake.
- Image processing tools provided by ITK.
- The image segmentation algorithms provided by ITK.
- The VTK rendering and processing pipelines.
- Use VTK for highlighting specific data aspect.
- Integrate ITK and VTK as a Command Line Plugin in GIMIAS.

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**Registration**

**Special Rate - £380**


For further information, please visit: [cistib-training@lists.shef.ac.uk](mailto:cistib-training@lists.shef.ac.uk)

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**Jérôme Velut** is an R&D Engineer at Kitware. He completed a PhD fellowship in Medical Imaging at the University of Rennes after his PhD in Information Processing from the INSA in Lyon.
Klas Pettersen
UIO / University of Oslo

Background and research

I come from an industrial town called Sarpsborg in Norway. I am the first member of my family to ever set foot inside a university building, and so I decided to do it properly. I was fascinated by physics as a way of understanding and explaining everything from daily life phenomena to more exotic observations at the atomic scale or at the much larger scale of solar systems. This led me to study physics at the Norwegian University of Science and Technology. My diploma thesis was about the Casimir effect, a quantum mechanical effect which causes the energy of vacuum to change as a function of its boundaries, and therefore gives rise to a purely quantum mechanical force acting between objects in close proximity to each other.

After I finished my diploma thesis I travelled around the world for six months and I brought a book with me, “Shadows of the mind”, written by the physicist Roger Penrose. At that time I had already decided to work for the consulting firm Accenture, but Penrose’s book was utterly inspiring and lightened my interest for neuroscience, although, or maybe because, the main hypothesis of the book is controversial.

As planned I returned back to Norway and started working as a consultant, but less than a year later I was lucky to be able to pursue my dream - an academic career within neuroscience. At that time Professor Gaute Einevoll at the Norwegian University of Life Sciences was looking for a PhD student within the field of computational neuroscience, and I was hired first as a lecturer at the university, then as PhD student in Professor Einevoll’s group. My doctoral thesis was titled “Electric potentials in the brain and the underlying neural activity”.

In the thesis, and also during my post doc period within the same group, we developed several methods for estimating the neural activity based on intracortical recordings of electric potentials. We studied extracellular features of neuronal spikes, and we developed methods and tools to compute extracellular potential around simulated multi-compartmental neurons and populations of neurons.

After my post doc period, which was prolonged with more than a year due to multiple paternity leaves (we are now expecting our fourth child), I continued to work at the same university but now in the group of Professor Stig Omholt. During this period I did mostly modelling on the cardiovascular system, studying how hypertension may arise with age as a consequence of stiffened arteries, and especially the role of the strain-sensitive receptors in the aortic wall, the baroreceptors.

From January 2014 I started working as a research scientist on the VPH-DARE@IT project with Stig Omholt, Ole Petter Ottersen and Erlend Nagelhus in the group of Erlend Nagelhus at the University of Oslo, Norway. I am now developing microscale models of water transport with focus on the astrocytes and their dedicated water channels, the aquaporins.

What is your specific role in VPH-DARE@IT?

My project title is “Microscale water transport within the brain”, which is part of Work Package 5. I am modelling electrodiffusion and water transport within and outside astrocytes. The effect of astrocytes on the macroscopic flow is particularly interesting as the astrocytes con-
tain dedicated water channels, and the density of these water channels is extremely high towards the perivascular surface and pia mater. The microscale astrocyte model I am building should be physiologically realistic, meaning that it should not only contain the water channels, but also other fundamental membrane proteins such as ion pumps and channels, as these may produce large osmotic forces and therefore influence the water flow. The goal is to connect the microscopic astrocyte model to the macroscopic poroelastic circulation model. State dependent variables of the microscopic astrocyte model may then be used as parameters in the macroscopic model and a link will be established between the membrane proteins of astrocytes (with a possible link to genes) and the macroscopic water flow.

What do you find most interesting about the VPH-DARE@IT project?

The most interesting part for me is to build a fundamentally new framework for simulations of astrocyte activity and to use this to inform the macroscopic poroelastic model. There is no established framework for simulation of the combined electro-diffusion and advective water flow within astrocytic cables. Of course, the neuronal cable equation can be used, but this does not take into account diffusion or advection. The validity of the cable equation is therefore limited if the time window is on the level of seconds or above, and a new formalism for simulation of astrocyte activity on longer time scales will be built. The state-dependent variables of this microscopic model, such as the swelled astrocyte volume, will then be used to inform the macroscopic poroelastic model about its state-dependent parameters, such as the porosity.

The macroscopic model may give feedback to the microscopic model about the hydrostatic pressure gradients. To combine these microscopic and macroscopic models, and to study how age-dependent changes such as stiffening of arteries and age-dependent anatomical changes affects this system will be truly interesting and valuable.

What do you find most challenging about working in VPH-DARE@IT?

As often is the case, the most challenging parts are identical to the most interesting parts of a project. To build a new framework for microscopic astrocyte function and to combine this with a macroscopic poroelastic model is a true challenge, both how to do this conceptually, and also how to handle this technically.

How do you find working as a part of a large collaborative project?

The collaboration has increased my awareness on how to build a model that can be used within a larger framework and possibly within a new context.

Have you attended any of the VPH-DARE@IT project meetings and if so, what benefits did you get from attending these events?

I attended the VPH-DARE@IT General Assembly meeting in Venice in March. This was my first VPH-DARE@IT meeting and it gave me a broader overview of the project. I was fortunate to be introduced to many of the scientists that I now collaborate more closely with, and in June many of them came to Oslo for a two-day visit to further plan our joint modelling efforts. And, of course, for one who is interested in water channels Venice was the perfect host city!

How has working on VPH-DARE helped to develop your career?

By now the project has made me able to further develop my skills within modelling, and especially given my valuable insight into poroelastic models and dementia. It has also been of great value for me as a modeller to work close with experimentalists.
We are very pleased to welcome our new project manager, Dr Matthew Henry to VPH-DARE@IT. Matthew takes over from Dr Mark Pullinger who has moved on to a new role to be closer to his home and family. Matthew took over from Mark at the end of July 2014 following the review of period 1 and his looking forward to working on the project over the coming months and years. We caught up with Matthew to find out a bit more about him, his background and his plans for managing the VPH-DARE@IT project.

Background

My background is in Immunology: I first studied at University College London, and then did a PhD in Applied Immunology at Newcastle University. From there I moved to the Edward Jenner Institute for Vaccine Research (now part of Oxford University) where I worked on fundamental research underpinning vaccine development for malaria, TB and HIV. My research mainly revolved around primary and secondary cell culture and flow cytometry. I then spent a short while at the Wellcome Trust in London, where I used my science background to help assess funding applications and provide advice to potential applicants.

In 2005 I joined the commercial team at the Health & Safety Laboratory to help grow their technical services in the Chemical and Pharmaceutical sectors. Then in 2007 the opportunity arose to move into project management. Starting on relatively small projects I rapidly progressed to managing more complex technical projects for a range of clients including the Health & Safety Executive, Office for Nuclear Regulation, Defra, National Institute for Health Research and various commercial clients.

The majority of my projects have focused on using advanced statistical modelling and analysis to solve important industrial health and safety issues. The teams have been very diverse with input from an exotic mix of statisticians, engineers, ergonomists, psychologists, health professionals, software developers and even graphic designers. Examples of projects I’ve managed include mapping noise pollution and the associated health risks, modelling heat flows in nuclear power stations, and determining the causes and mapping falls by patients with dementia in different ward environments.

The highlight of my career so far has been the opportunity to have a personal guided tour round an operating nuclear power station and walk across the top of the reactor core (thankfully there were several metres of concrete and steel in-between myself and the fuel!).

Outside of work I enjoy hill walking, mountain
biking, being involved in church activities, landscape photography and immersing myself in a good second-hand bookshop.

**How do you see the role of VPH-DARE@IT Project Manager?**

I see the role of the VPH-DARE@IT Project Manager to help coordinate all the aspects of the different work-packages so that they seamlessly work together and everyone is clear what the ultimate goal is. Everything from ensuring the technical work of each work package fits together, the right people are available to work on each task at the right time, and managing risks and issues which inevitably arise, and reporting progress to the EU.

**What are you looking forward to most in this role?**

I am really looking forward to working with an interesting mix of clinicians, modellers and software engineers from different organisations and to work on a project which is breath-taking in its ambition.

**What do you find most interesting about the VPH-DARE@IT?**

The fact that the project combines such a diverse mix of disciplines and partnering organisations and that it is tackling, until recently, a sadly neglected area of medical research is what makes this project really interesting.

**What for you are the challenges of managing such a large-scale project?**

The biggest single challenge in managing large scale projects is ensuring that the whole project team remain focussed on the project goals. My experience managing similar multi-discipline projects at the Health & Safety Laboratory will help to manage the VPH-DARE@IT project.

**How do you envisage working on VPH-DARE will help to develop your career?**

The project will broaden my experience to include EU projects, working with and managing a team comprising academic, clinical and commercial organisations.
VPH-DARE@IT and VPH-Share Working together

Strong collaborative links between VPH-DARE@IT and VPH-Share were established from the outset of the VPH-DARE@IT project. One of the aims of VPH-DARE@IT is to demonstrate how effective collaboration between European projects can help to reduce overall costs and time spent on common tasks, maximising the investment and results in areas where projects will add value and make a real difference to the community.

The collaboration between VPH-DARE@IT and VPH-Share is evidence of this working effectively and in VPH-DARE@IT we are fortunate to have partners in our team who have developed strong collaborative links and interactions with the VPH-Share project.

The interaction between the two projects helps to progress VPH-DARE@IT project goals by identifying potential gaps and the way to overcome them.

An example of this is that the VPH-Dare@IT Research Platform requires a number of underlying services to provide users with access to data, tools and workflows in a secure way. Most of these services are already available in VPH-Share, which will facilitate the development of the VPH-Dare@IT Research Platform.

VPH-Dare@IT is also helping VPH-Share to adapt the current service range to the concrete needs of a VPH project; the result of this collaboration will facilitate the adoption of VPH-Share by other projects and foster additional collaboration between projects as the one already started with NeuGrid.

VPH-Share Environment

Building VPH workflows can be cumbersome and time consuming. Without the right infrastructure their implementation can cost an institution time, money and resources. VPH Share has built the environment to make workflow development quick and easy for VPH DARE@IT users.

The web based services produced by VPH-Share allows clinicians, researchers and developers in VPH-DARE@IT to build new workflows with the help of different composition engine (Taverna Workbench, OnlineHPC.com), which, by automating over half the tasks usually associated with workflow construction, enables VPH-DARE@IT users to concentrate on the design process.

These services also overcome the restrictions often imposed by individual institutions in different ways, e.g.: allowing complete control of data, tool and service sharing and enabling local platform deployment when data or tools cannot be used outside of the institution boundaries.

Once a single tool, service or dataset is deployed onto the VPH-Dare@IT research platform and shared, it will be made available to the rest of the project’s users who can then select the tool, service or dataset required to be used in their workflows, saving time and effort and making data accessible to all VPH-DARE@IT users.
VPH-Share Data

VPH-Share includes an online store of personalised biomedical data. Different data providers can publish their data collections into VPH-Share at any moment; these data collections can also be imported into the VPH-DARE@IT Research platform once an agreement has been obtained.

With an expansive volume of data that can be stored within VPH-Share’s cloud infrastructure, VPH-Share simplifies the process of locating biomedical data, by offering a single comprehensive repository. VPH-DARE@IT users retain complete control by setting permissions to define access as well as managing the requests from those looking to use it.

VPH-Share has developed a sophisticated search facility to allow users to save time and retrieve highly relevant results.

Through free text, semantic or guided search tools, VPH DARE@IT can specify terms to be located within the associated metadata and semantic labels.

The guided system eases the search process by suggesting relevant semantic terms. VPH-Share’s security settings ensure that only registered users that are given permission to use data by the Data Controller are granted access, guaranteeing the safety of data, while allowing its research potential to be fully realised. Understandably, there will always be a requirement to agree on the ontology and terms to be used when publishing data, tools and services.

How VPH-Dare@IT will use VPH-Share

VPH-Share provides VPH-DARE@IT with the foundation services required by its research platform. It will fully leverage several datasets related to dementia; at the moment only partially leveraged because not easily pooled together. VPH-DARE@IT aims at gathering all of these datasets into a uniform collection by using VPH-Share data publication capabilities and semantic services.

As the VPH-DARE@IT project progresses, we will use more of the VPH-Share facilities; a possible scenario is the processing of retrospective and prospective cases: it is expected to be streamlined by performing the computations within the VPH-Share, where the infostructure orchestrates search results, workflow management and automated instantiation of web-servicing Virtual Machines (VMs).

Dr. Tim Chico and Dr Paul Morris working on the VPH-Share Platform
For more information about VPH-Share please visit: www.vph-share.eu
Alzheimer Europe (AE) is an NGO aiming to raise awareness of all forms of dementia. Formed in 1996, AE is based in Luxembourg and operates a common European platform through cooperation among its 33 members, which are all active Alzheimer organisations in Europe.

AE is primarily a lobbying organisation that promotes dementia awareness, care and research within the EU institutions. This effort includes the European Alzheimer’s Alliance, a group of 82 MEPs that aims to make dementia a health priority.

In addition, AE is a source of information on all aspects of dementia, including annual research publications that focus on specific topics. AE’s newest research report addresses the ethical issues linked to the perceptions and portrayal of dementia and people with dementia. AE also publishes the “Dementia in Europe” magazine and issues a monthly newsletter to more than 4,200 subscribers.

AE’s popular annual conferences attract people with varied backgrounds in dementia. This includes people with dementia, their carers, representatives of national Alzheimer associations, healthcare professionals, academics and researchers, as well as policy makers. This year, the 24th Alzheimer Europe Conference will take place in Glasgow on 20-22 October 2014 under the theme “Dignity and autonomy in dementia”.

Finally, Alzheimer Europe is an active partner in numerous research projects - including all of the current IMI projects on dementia research: AETIONOMY, EMIF, PACE and PharmaCog. AE is also on the Steering Committee of the NILVAD clinical trial and an applicant in numerous Horizon 2020 projects that are currently in development.

www.alzheimer-europe.org
@AlzheimerEurope on Twitter
Our members are helping people with dementia and their carers in 31 countries
neuGRID is an e-Infrastructure which aims to help neuroscientists do high-throughput imaging research, and provide clinical neurologists automated diagnostic imaging markers of neurodegenerative diseases for individual patient diagnosis. NeuGRID’s user-friendly environment is customized to a range of users from students to senior neuroscientists working in the fields of Alzheimer’s, psychiatric, and white matter diseases. Here, Dr. David Manset tells us about NeuGRID, how it came about and how neuGRID is building links with VPH-DARE@IT.

About neuGRID

New imaging technologies significantly affect diagnostic and prognostic accuracy. They can facilitate progress towards the cure of brain diseases, in particular Alzheimer’s Disease. However, the impact of these new technologies largely depends on the speed and reliability with which the imaging data can be visualized, analyzed, and interpreted. Thanks to distributed services and Grid, HPC and Cloud computational resources, analyses in neuGRID are incomparably faster than traditional-style lab-based ones. The combination of medical imaging with Distributed Computing Infrastructures (DCI) has demonstrated the potential to make a significant impact in the translation of medical research from the lab into the clinical practice.

NeuGRID was born in 2008. Its first proof-of-concept was carried out in 2009 when an Alzheimer’s disease biomarker (i.e., cortical thickness measure with Freesurfer and CIVET applications) was extracted from 6,500 MR scans in 2 no more than weeks time, versus 5 years that it would have taken in a traditional setting.
Key People

The key people involved in NeuGRID are Dr. David Manset, Prof Richard McClatchey, Prof Giovanni B. Frisoni, Prof Frederik Barkhof, and Prof Lars-Olof Wahlund.

Dr David Manset, Founder and CEO of a French innovative company specialising in Big Data and Cloud computing, leads the Services Activities at NeuGRID. David has worked in the field of computer sciences for over 10 years. David leads the Services Activities, from the system architecture to its delivery to end-users and accompanying support, and along with Prof Richard McClatchey, leads the technical team (Joint Research Activities).

Richard McClatchey is Professor at the University of the West of England and has considerable experience in large European projects and several years’ consultancy experience with UK industry. His main research interests are biomedical Grid applications, large-scale data and process management.

The scientific team at NeuGRID is led by Prof Giovanni B. Frisoni, coordinator of the project, along with Prof Frederik Barkhof, and Prof Lars-Olof Wahlund.

Giovanni B. Frisoni is a Neurologist, Scientific Director of the National Alzheimer’s Disease Centre in Brescia, Italy, and Full Professor at the University of Geneva. His main interest is neuroimaging of cognitive impairment. He is the coordinator of NeuGRID and the reference expert for neuroimaging in Alzheimer’s disease and psychiatric diseases.

Frederik Barkhof is Medical Doctor and Full Professor of Neuroradiology at the University of Amsterdam. He is Principal Investigator for the Amsterdam University in NeuGRID and the reference expert for neuroimaging in white matter diseases and dementia.

Lars-Olof Wahlund is Medical Doctor and Full Professor at Karolinska Institute in Sweden. He has a long experience in clinical neuroimaging of dementia. He is Principal Investigator for Karolinska Institute and the reference expert for neuroimaging in dementia.

We asked Dr. Manset about NeuGRID’s current projects. David told us that NeuGRID are in the process of setting up a dedicated company to provide advanced support to their users. The latter will become operational later this year and will be part of NeuGRID’s sustainability plans.

Working together

We asked how NeuGRID first became involved with VPH-DARE@IT. David told us how he was the principal system architect of former VPH FP6 Health-e-Child project (www.health-e-child.org). As a supporter of the VPH concept, David has been following the community developments over the years and this how he discovered VPH-DARE@IT. David told us that he finds the way in which VPH-DARE@IT is turning know-how and methods into an innovative, integrative and objective clinical decision support platform really interesting. “I believe the way VPH-DARE@IT is turning know-how and methods into an innovative, integrative and objective clinical decision support platform for the early and differential diagnosis of memory disorders is key to speeding up migration of meaningful biomedical research findings into clinical practice”.

David went on to say that he likes the interoperability challenge behind the objective of integrating heterogeneous multi-modal data together with different modelling techniques towards the creation of innovative new markers and thus potential decision support tools. He also said that he appreciates the difficulty related to possible future clinical validation of such tools.

We asked what interaction there has been between the two projects. David told us how he met VPH-DARE@IT Project Coordinator, Prof Alejandro Frangi a few times where they discussed sharing information on respective ongoing initiatives and came to the conclusion that there were very interesting possible intersections between VPH-DARE@IT and NeuGRID. These interactions led to further discussions and NeuGRID was invited to give a presentation at VPH-DARE@IT’s General Assembly meeting in Venice in March 2014.

David told us of the opportunities he sees for VPH-DARE@IT and NeuGRID working together. “Over the last 8 years of activities, NeuGRID carefully developed a scientific market place, integrating data, applications and computational resources as requested by its users. As a result, NeuGRID comes preloaded with interesting contents which could serve VPH-DARE@IT’s objectives. NeuGRID’s market place is open and can be extended to others willing to use it. VPH-DARE@IT will be welcome to use and extend it, while NeuGRID also looks forward to using VPH-DARE@IT decision support tools in the future.

For more information about NeuGRID visit: https://neugrid4you.eu/
Publication Highlights


Deliverables and Milestones completed

**D 3.1 UCL** Detailed workflow specification and component roadmap for high-througput image analysis of large-scale studies

**D 4.1 ASD** Design specifications and requirements for a dementia-specific metabolic network model

**D 6.1 EMC** Normal ageing brain models – Initial phenomenological model and links to mechanistic modelling framework

**D 7.1 USFD** Architectural framework design and interoperability

**D 9.1 EMP** VPH-DARE@IT Health Technology Assessment conceptual framework

**D 10.3 USFD** First periodic progress report, including public summary of each work for publication

**MS102 USFD** Appointments to Scientific Advisory Board Completed
Upcoming events

- 6th European Conference of the International Federation for Medical and Biological Engineering (MBEC 2014) - Dubrovnik, Croatia, 7 - 11 September 2014
- International Conference on Computational and Experimental Science and Engineering (ICCESEN 2014) - Antalya - TURKEY, 25-29 October 2014
- 2014 IEEE Conference on Biomedical Engineering and Sciences (IECBES) - Sarawak, MALAYSIA, 8 - 10 December 2014
- Grand challenge on computer-aided diagnosis of dementia: http://caddementia.grand-challenge.org
- A workshop is organised at the MICCAI conference, where the results will be presented: http://caddementia.grand-challenge.org/workshop/

In the next issue...

- Action Line 2 Focus
- Partner Profiles: ESI and Empirica

To ensure that we capture all the important issues from across the research arena, we invite you to send us your ideas, comments and suggestions for future editions to contact@vph-dare.eu. Non-VPH-DARE@IT participants interested in receiving this newsletter can subscribe via the VPH-DARE@IT website at www.vph-dare.eu
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VPH-DARE@IT
Virtual Physiological Human: DementiA Research Enabled by IT
Project coordinator: Alejandro Frangi - The University of Sheffield
Timetable: April 2013 to March 2017

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