

P-MEDICINE NEWSLETTER ISSUE NO 2



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EDITORIAL

by Norbert Graf, p-medicine coordinator

More than 400 years ago Michel de Montaigne in his essay 'Of the resemblance of children to fathers' wrote precisely what we need to pave the way to personalized medicine:

"Now if the doctor's error is dangerous... he needs too many details. considerations. and circumstances to adjust his plan correctly: he must know his patient's constitution, his temperament, his humours, his inclinations, his actions, his very wishes and fancies. ... He must know in the disease the causes. the symptoms, the effects, the critical days; in the drug the weight, the power, the country it comes from, the appearance, the age, the way of dispensing it; and he must know how to proportion all these factors and relate them to one another in order to create a perfect symmetry. ... God knows how difficult is the knowledge of all these details... The very promises of medicine are incredible...".¹

We do need all kinds of data, system biology models and treatment options to build models for clinical decision support so that patients can be treated on a more individualized basis. Nevertheless. two verv important points are missing in Michel de Montaigne's essay. First of all, doctors alone can never achieve the goal of establishing personalized medicine. They do need a team of stakeholders from different disciplines with whom they work hand in hand. And secondly, patients are of utmost importance in building up a sustainable infrastructure for personalized medicine.

In p-medicine we started to engineer



Towards a personalized medicine

the 'p-medicine train' knowing that only teamwork within a consortium of physicians, basic researchers, IT specialists, lawyers, ethicists and others can handle all the demands of personalized medicine, which is today regarded as P5 medicine: personalized, preventive, predictive, participatory and psycho-cognitive. By addressing participatory and psycho-cognitive medicine, p-medicine is fostering patient empowerment, which we believe needs to be a backbone of all projects in the area of personalized medicine.

After two years of the project we have achieved all of our ambitious goals so far. A few examples are highlighted here: the first prospective clinical trial will now start to collect data within p-medicine using ObTiMA and other tools developed so far, the legal and ethical framework is in place, allowing the upload of data into the data warehouse via the p-medicine portal very soon, the interactive patient empowerment service is under construction, a first version of the Ontology Annotator can be evaluated and the initial release of the Health Data Ontology Trunk (HDOT) is available. We will have our first Summer School in June this year, we have implemented a strong collaboration with VPH-Share and interfaced with many other European projects and Industry. We demonstrated the project on International conferences and developed a plan on how to maintain p-medicine beyond the funding period.

This success is mainly based on the hard work of all partners within the project, for which I am very grateful. This makes me proud. It also shows very clearly that our 'p-medicine train' is taking up speed.

Norbert Graf p-medicine coordinator

¹ Michel de Montaigne: Essays. book II, chapter 37: Of the resemblance of children to fathers. 1579–1580. Translation: Stanford University Press, Stanford California, Copyright 1943 by Donald M Frame. ISBN 0-8047-0485-6, 1958.

GETTING OBTIMA READY FOR USE IN A REAL CLINICAL TRIAL



Over the last couple of months, the ObTiMA team has been working hard on developing the system further to fulfill all functional and legal requirements towards clinical trial management systems used in realworld settings.

An initial production-ready version of ObTiMA was finalized at the beginning of this year in order to employ it within the new trial "Improving Population Outcomes for Renal Tumours of Childhood (IMPORT)." Before the roll-out of the system to the trial partners, an internal testing phase at the Saarland University Hospital has just started and includes the various end-user types, e.g. trial chairman, study nurse and data manager.

The main target goals for this initial version were the following:

CRF Creator

With the help of the CRF Creator, a trial chairman can design case report forms, i.e. questionnaires to collect patient data, in electronic form. Recent work on this module focused, among other things, on making the creation of complex questions and groups of such possible with special consideration of its ease of use.

CRF Repository

The CRF Repository is a centralized storage place – accessible directly from within the CRF Creator – where trial chairmen can

share their own CRFs or retrieve CRFs previously stored by themselves or other trial managers to, for example, allow reuse of existing CRFs instead of recreating them from scratch.

Master Protocol Creator

This creator provides trial chairmen with a template-based, straightforward interface guiding them through the preparation of the Master Protocol which has to encompass – besides the actual trial description – all additional legal and ethical information and documentation pertaining to the execution of the trial.

Biobank Connector

The Biobank Connector, developed by Fraunhofer IBMT, makes it possible to manage biomaterial specimen and related data directly within ObTiMA and link this to the clinical (treatment) data of the patients. It therefore becomes possible to access patient data stemming from different sources through one common access point.

Data Security

All patient data entered into ObTiMA is pseudonymized and encrypted onthe-fly using the industry-proven technology developed and integrated by our partner Custodix allowing for a data handling which conforms to all relevant legal regulations.

An in-depth presentation of the latest ObTiMA developments can be found in deliverable D8.4 "Provision of new modules for clinical trial management". This deliverable is intended to be a "living document" with periodic updates covering new modules: even though a first working production version exists and the stabilization of that one is the highest priority currently, new modules for, e.g., reporting adverse events or incorporating data directly from hospital information systems are already at their design stage.

LINKS

<u>www.p-medicine.eu</u> <u>www.obtima.org</u>



The ObTiMA user interface.

LITERATURE BASED DISCOVERY FOR PERSONALIZED MEDICINE

Personalized Medicine (PM) is a rapidly growing field of healthcare, where the key goal is tailoring decisions and treatments such that they are patient specific. The underlying ideology is that treatment for a patient must be directly based on the individual patient's characteristics, such as age, gender, diet, environment, etc., as well as on their individual genomic profiling. A consequence of this goal is the need for both physicians and patients to be able to access and utilize heterogeneous data sources in order to arrive at a case-specific plan tailored to the patient's needs.

Over the last decades, breakthrough research in the genomics field has inevitably lead to an overflow of clinico-genomic information, which often remains unexploited. Moreover, advancements in high-throughput techniques making diverse measurements possible in large numbers, and computing platforms, allowing large-scale robust data of heterogeneous origin to be processed, have been the driving force behind the recent growth observed in the field. Despite all these advances, many challenges need to be addressed to make personalized medicine a reality. Due to the vast amount of knowledge cataloged in biomedical literature databases, such as PubMed, text mining techniques are critical to PM.

Unstructured data in biomedical databases captures relations between biological concepts such as genes, diseases, drugs etc. A key role of information extraction (IE) in the domain is to accurately identify these relations in large volumes of documents. This is because typical literature search operations can be reduced to finding correlated biological concepts. This class of searches can be efficiently processed if catalogs of relationships between concepts have been previously created.



Biovista's literature based predictive platform

The modern trend in processing unstructured data is to use semantic natural language processing (NLP) tools to discover relations between biological concepts or identify biomarkers/phenotypes relevant to a patient's condition. Of specific interest are relations that capture protein-protein interactions. protein-disease associations and relations involving genes or proteins including gene expression, binding, or regulation. It is easy to see how casespecific treatment can benefit from having access to such information.

Within the p-medicine framework Biovista has extended its literature based predictive platform, based partly on NLP technologies, to make use of heterogeneous data available in the project. The ability to utilize heterogeneous/multi-level data is one of the key aspects in PM because patient specific data naturally appears in different forms. Through the use of such heterogeneous data, together with documented knowledge, the platform is able to predict possible Adverse Events given patient specific information, assist in determining a suitable course of treatment based on the patient's history etc., in real time. Biovista intends to further

extend the platform, to leverage more sophisticated NLP techniques as well as incorporate other useful data sources into the heterogeneous mix during the projects lifetime. Experiments will be carried out using the platform for the three clinical trials that fall in the scope of the project.

The combination of knowledge extracted from literature mining using NLP techniques with the multilevel data available in the p-medicine project will allow show casing the extent to which such a combination of heterogeneous/multi-level data sources and documented knowledge can facilitate better clinical decision support. Application of such decision support systems for a patient subpopulation or ideally an individual patient will ultimately result in translating current practice into personalized medicine.



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HOKKAIDO UNIVERSITY AND THE TRIAL OUTLINE BUILDER (TOB)

At Hokkaido University we have developed a tool called the Trial Outline Builder (TOB) in the ACGT and p-medicine projects.

It supports the designing of the flow of a trial, data collection during trials, and explorative visualization of the data collected. We believe the TOB will be useful for gaining new insights when analyzing the huge amounts of data collected in cancer trials. treatment run, what data should be collected at what times, etc. The TOB has since evolved and now also helps with the collection of data when running trials, and with analyzing data from finished trials.

TOB runs as a plugin inside the ObTiMA system and was built using a pluggable software components technology developed at Hokkaido University called "Webbles". This

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Designing cancer trials. The left side has a repository of events that can be dropped onto the right hand side work flow window. Events can be dragged around, resized, have data input forms attached, etc.

The TOB started out as a tool for supporting the design of trials, to help the trial chairman decide what to do in the trial, e.g. what treatments should there be, how long should the is the latest version of the "Meme Media IntelligentPad" technology, which aims to make services and functionality as easy to reuse as copypasting texts or images is today.

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Running clinical trials. A flow chart for the whole trial on top, and the individual treatment plan of one specific patient below. Clicking on an event brings up the data input form(s) attached to this event.

This makes it easy to add new functionality and to reuse the components in other systems. We have, for example, used some of the visualization components in a system for showing traffic conditions during severe snow conditions in Sapporo. The Webble technology was useful since the TOB was developed together with clinicians and we were able to have discussions on what type of things they need and want in a system, and we did a lot of prototyping of different ideas that clinicians could then give us their opinions on.

The Webble technology is freely available to anyone, and the TOB will be made available as open source software.

In the p-medicine project we have mainly looked at the data visualization, exploration, and analysis parts of the TOB. We have added more components for different types of visualization, for instance a heat map component to show and interact with genomic data. Currently we are working with Professor Norbert Graf and using example Wilm's tumor data, and we plan to test the system with other clinical trial or patient genomic data in the future.

For cancer trials, huge amounts of data are collected. It is difficult to model which data has which kind of impact on the outcome. We believe that interactive exploration and visualization of such data can be helpful in understanding the underlying system and to give insights into what factors are important. If the exploration can be done by domain experts (e.g. cancer specialists) instead of statisticians, data mining or machine learning experts, they can also make use of their expert knowledge or intuitions about the domain.

Thus, the TOB was made to be easy to use for experts on cancer, not

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only for data mining or computer experts, and it has an easy to use visual interface based on direct manipulation. To for example remove some subgroups of patients, just slide a little marker on a line to exclude for instance those patients that had metastatic cancer. The visualizations in all other components such as life tables, charts, or the heat map of genomic data, automatically react and immediately update the display to show the results for the newly selected subset of patients. The cancer specialists we have showed the system to have been excited about the possibilities this real time interactive exploration would give them.



Data visualization of trial results. The flow chart of the trial is used to select data to visualize. Various visualization components can be used to group data, remove subsets of patients, and visualize results or compare groups of patients.



A life table showing the percentage of relapse free patients, grouped by treatment received. A heat map shows the genomic data of the patients (one column is one patient). Patients with metastatic cancer have been deselected using a parallel coordinate, so they are not counted in the life table, not shown between the parallel coordinates, and blacked out in the heat map. More information on the Trial Outline Builder (TOB)

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Short CV Yuzuru Tanaka

Yuzuru Tanaka is a full professor of knowledge media architecture at the Department of Computer Science, Graduate School of Information Science and Technology, Hokkaido University, and the director of Meme Media Laboratory, Hokkaido University. He is also an adjunct professor of National Institute of Informatics.

His recent research areas cover meme media architectures, knowledge federation frameworks, proximity-based federation of smart objects, and their application to digital libraries, e-Science, clinical trials, and social cyber-physical systems for the optimization or improvement of social system services such as snow plowing and removing in Sapporo City and urban disaster management and response.



Meme Media Laboratory, Hokkaido University

Meme Media Laboratory Hokkaido University

<u>Meme Media Laboratory at Hokkaido</u> <u>University</u> has been focusing on R&D on meme media architectures, knowledge federation frameworks and their applications to largescale visual analytics for almost two decades. As one of its technology applications, it is involved in the FP7 p-medicine project to extend the graphical Trial Outline Builder (TOB) developed in the preceding FP6 ACGT project for ObTiMA, ACGT's ontologybased clinical-trial management tool.

Hokkaido University is one of the national universities of Japan. It is a member of the National Seven Universities, which were established as the best national higher education or research institute. It had its beginnings in Sapporo Agricultural College, founded in 1876 as the first college in Japan. In 1949 it was re-organized as a 'new system' university with seven faculties and one department of general education. It now consists of 12 faculties, 29 graduate schools and 21 research institutes and centers, with 2,053 academic staff, 11,400 undergraduate students, and 5,989 graduate students. The main campus of the University occupies a 170 hectare site close to the center of Sapporo. With the introduction of western customs and scientific technology, and lectures by foreign teachers, the Sapporo Agricultural College opened its mind to diverse directions from the beginning. From this time on, Hokkaido University strives to encourage its students and staff to acquire "Global Perspectives" and to contribute to the development of an international society. Since 2004 the university has been incorporated as a National University Corporation under a new law which applies to all national universities.

Meme Media Laboratory of Hokkaido University was established in 1995 for the advanced research on multimedia and knowledge media technologies that will form the infrastructure for the worldwide knowledge distribution and reorganization. Meme Media Laboratory was involved in EU FP6 Integrated Project ACGT and also in EU FP7 Best Practice Network Project on Digital Library ASSETS.

From an ICT point of view, what the p-medicine project requires is a special case of global research infrastructures which allow researchers distributed across countries, ensuring the protection of personal information, to publish and reuse a huge variety of large scale knowledge resources including data, information. multimedia contents. tools and services, and to collaborate in analyzing these data with related information and contents for decision making, checking hypotheses, and leading to new findings. The R&D of such global research infrastructures requires the following technological challenges; (1) а world-wide repository to publish and reuse a huge variety of large scale knowledge resources, (2) how to support people in their collaboration processes of analyzing these data with related information and contents, (3) how to support people's exploratory visual analytic processes which extensively utilize improvisational combinations of a huge variety of available tools and data sets, and (4) how to ensure the protection of personal information.

Since meme media our architecture and knowledae federation framework had been studied as potential solutions respectively to the first, the second, and the third challenges, Meme Media Laboratory at Hokkaido University was first invited to join the preceding FP6 project ACGT (Advancing in Clinico-Genomic Trials on Cancer) as the sole non-European team of the 25-partner ACGT consortium on the basis of Prof. Yuzuru Tanaka's long-term research collaboration and researcher exchanges with the project leader FORTH.

The intensive collaboration especially with Prof. Norbert Graf in the ACGT project led us to develop the graphical Trial Outline Builder (TOB) for ObTiMA, ACGT's ontology-based clinical-trial management tool. The details of the TOB system can be found in another article in this issue. The exploratory visual analysis of trial data enabled by TOB has provided doctors and data statisticians with more capabilities of making more than one analyzing and visualizing tool and/or service as well as varieties of data sets to interoperate with each other, which is not possible with conventional workflow-based interoperation definition systems.

When Prof. Norbert Graf initiated p-medicine, he invited our team to join the project. Our main role in p-medicine is to extend TOB to additionally integrate the access and analysis of patients'genomic data, DICOM image files and, furthermore, biomedical molecular data as well as various bio markers obtained by their processing in the same graphical environment. Our team is involved in the following work packages: WP3, WP7, WP8, WP11, WP12, and WP17.

Yuzuru Tanaka: Meme Media and Meme Market Architectures, Wiley-IEEE Press, 2003

... This book ... cannot be compared to any other book—It opens the gates to new territories and time will tell how readers apply this information about knowledge media. ... (E-Stream Vol.7, No.4)



Visit to Yokohama, Japan

On November 29, 2012 Norbert Graf, the coordinator of p-medicine, had the opportunity to take part in an information and exchange meeting between the Keihin Costal Area Life Innovation project of the City of Yokohama, Japan and the p-medicine project. The meeting, which took place at the Pacifico Yokohama Conference Center, was initiated by Professor Yuzuru Tanaka. The objective was to discuss views and opinions of both projects and to reinforce possible collaborations.

The participants of the meeting are shown in the following table:

Innovation" project collaborates with the Kanagawa prefecture and the city of Kawasaki und thus aims to form via life science and healthcare related industry an engine for economic growth in the Tokyo metropolitan district of 37 million people. The proximity of 35 universities with science engineering faculties and graduate schools and the close relationships with research institutes at the Yokohama City University Medical School and Hospital, the existence of a cluster of healthcare industries and the easy access to Haneda and Narita international airport fosters this

Toho University	Associate Professor	Teruyoshi Hishiki
DNA Chip Research Inc	Director Advisor Director	Kenichi Matsubara Masafumi Shimoda Takuro Tamura Yuko Hata
Hitachi Solutions, Ltd.	Department Manager Department Manager	Toshiaki Ito Tetsuji Yamada
City of Yokohama	Director Manager Manager Assistant Manager	Kazuyuki Kawana Hiroshi Hanauchi Yoshinobu Hayakawa Koichiro Nakano Arifumi Okuzumi
Hokkaido University	Professor Dr.	Yuzuru Tanaka
Saarland University	Professor Dr.	Norbert Graf

lifestyle diseases and public health and preventive healthcare. The target issue is the realization of individualized medical treatment and preventive healthcare. One of the individual projects is personalized medicine. Besides the collaboration within the network of domestic zones an international innovation network will be established with overseas research institutes.

The most interesting topics for further exchange between p-medicine and the "Keihin Coastal Area Life Innovation" project include the legal framework, the solutions regarding interoperability semantic and ObTiMA, including the Trial Outline Builder. Patient empowerment is a much needed research area, where p-medicine can contribute extensively.

The meeting ended with the commitment to establish further contacts and to define collaboration topics.

In December 2011, the Japanese government designated the City of Yokohama as a comprehensive and strategic special zone for international competitiveness development.

Comprehensive Special Zones are set up to realize new growth strategies through breakthroughs in policy and economic challenges. Seven zones have been established across Japan. Three of them – including Keihin Coastal area – set the theme of 'Life Innovation'. The benefits of special zones are: relaxation of regulation, financial support and a favorable tax regime (tax reduction).

The "Keihin Coastal Area Life

approach. Mr Kawana, Director of the City of Yokohama, expressed the desire for new medicines and medical devices launched from this area in collaboration with DNA Chip Research, Inc. and Hitachi Solutions. Ltd. and other industries like Takeda Pharmaceutical. Chugai Pharmaceutical, Fujitsu, NEC, Canon, Toshiba, Nikki and others that did not participate in this meeting. It is expected that the advantages of the Keihin Coastal Area, as well as the efforts of high-tech research will facilitate a growth strategy for individualized medical treatments and preventive healthcare. Three maior envisaged: pillars are regeneration medicine, cancer and



P-MEDICINE – OTHER RELATED PROJECTS AND INITIATIVES



EURECA – Enabling information re-use by linking clinical research and care

The goal of the <u>EURECA</u> project is to enable secure and scalable bidirectional linkage of healthcare information residing in clinical research and clinical care systems, supporting the two currently separated worlds of clinical research and clinical practice to connect and benefit from each other.

Main barriers of secondary use of EHR data for research and of enabling a consistent feedback loop to care are the lack of common technology standards and concept terminologies. While solving the interoperability issue in healthcare at a generic level is not a realistic approach, EURECA aims at semantic interoperability on domains of concepts (i.e. describing specific clinical areas). The approach taken in EURECA is to rely, whenever possible, on existing initiatives and previous efforts in terminology development and standardization. We start from disease- and treatmentrelated sets of concepts in the oncology domain and demonstrate our solution in concrete clinical scenarios. EURECA joins top European clinical and research centres (clinical, ICT, bioinformatics, legal & ethics) and focuses on topics that are in our view key in oncology. We support more effective and efficient execution of clinical research by:

- allowing faster eligible patient identification and enrolment in clinical trials,
- providing secure access to the large amounts of patient data collected in the EHR systems to be re-used in clinical research;
- enabling long term follow up of patients, beyond the end of a clinical trial;
- Avoid the current need for multiple data entry in the various clinical care and research systems;
- Allow data mining of longitudinal EHR data for early detection of patient safety issues;

 Enable healthcare professionals to extract relevant patient's data and treatment information.

The project develops a range of ICT tools and models to support the clinical scenarios described above in several domains of oncology. In this context, EURECA shares the core goals of p-medicine to achieve personalization of treatments. The two projects will closely collaborate, share results and compare approaches.

EURECA can bring to p-medicine the link to ICT systems deployed in the context of care, such as Electronic Health Record systems. Our semantic approach is based on widely used ICT standards such as HL7 RIM and standard terminologies (e.g. SNOMED-CT, LOINC) and attempts at achieving interoperability in several specific domains. The synergy the two projects will enable of the evaluation of their respective semantic approaches in the different domains and in the context of the various applications developed in the projects.

MyHealthAvatar

MyHealthAvatar is an attempt at a proof of concept for the digital representation of patient health status. It is designed as a lifetime companion for individual citizens that will facilitate the collection of, and access to, long-term health-status information. This will be extremely valuable for clinical decisions and offer a promising approach to acquire population data to support clinical research, leading to strengthened multidisciplinary research excellence in supporting innovative medical care.

A significant feature of VPH is its evolutionary approach of collecting and integrating predictive models

and heterogeneous data through a large number of VPH related projects and activities (including p-medicine), which have laid down the foundation for new knowledge discovery. However, access to these resources for clinically meaningful use is still a largely unresolved problem. Also, the highly fragmented healthcare systems developed during the long history in Europe make it extremely difficult to access a consistent record of individual patients. Within this context, the consortium perceives the concept of a "Digital Patient" as an innovative representation and potential solution to the abovementioned problem by acting as an interface to collect, store and manage individual patient information; an interface for data

sharing and information exchange with other people; an interface to access external resources and information; an interface to access a toolbox that offers a range of clinically proven tools to support the display of clinical information and to assist in clinical analysis and decision making; a means to contribute data to biomedical and clinical research for new knowledge discovery.

MyHealthAvatar will be built on the latest ICT technology with a special emphasis on engaging public interest to achieve its targeted outcomes. It is expected to exert a major influence on the reshaping of future healthcare in the handling of increased life expectancy and the ageing population in Europe.



ContraCancrum – Clinically Oriented Translational Cancer Multilevel Modelling

<u>ContraCancrum</u> aimed at developing a composite multilevel platform for simulating malignant tumour development and tumour response to therapeutic modalities and treatment schedules. The project's primary impact was on

(a) the better understanding of the natural phenomenon of cancer at different levels of biocomplexity and,
(b) the disease treatment optimization procedure in the patient's individualized context by simulating the response to various therapeutic regimens.

The ContraCancrum project developed an advanced multiscale simulation platform of tumour growth and response to treatment, driven by real clinical needs, and initiating the clinical translation process of the simulation system within the context



CHIC – Computational Horizons in Cancer: Developing Meta- and Hyper-Multiscale Models and Repositories for In Silico Oncology

The about-to-start transatlantic integrated project CHIC focuses on robustness, reproducibility and the interoperability of collaboratively developed hyper-models of diseases and normal physiology. It therefore proposes the development of a suite of tools, services and secure infrastructure that will support accessibility and reusability of Virtual Physiological Human (VPH) multiscale mathematical and computational hypermodels. These will include a hypermodelling

of clinical trials/tests. Both molecular level and tissue level models were developed. integrating patient specific tissue-biomechanics and medical image analysis components. A dedicated repository has been developed allowing the remote access of a large number of multimodal and temporal datasets of glioma and lung cancer patient data. Integration work has been the central focus for the third year resulting in two demonstrators one in glioma and one in lung cancer. To enhance the dissemination of the project, a summer school in computational oncology was organised during this period.

p-medicine will exploit specific components and tools developed during the implementation of the ContraCancrum project as well as the important experience gained in its context in relation to the integration of various Virtual Physiological Human (VPH) modelling modules into complex multiscale oncosimulators.

infrastructure consisting primarily of a hypermodelling editor and hypermodelling а execution environment, an infrastructure for semantic metadata management. repository, hypermodel а а hypermodel-driven clinical data repository, a distributed metadata repository and an in silico trial repository for the storage of executed simulation scenarios. Multiscale models and data will be semantically annotated using the ontological and annotating tools to be developed. An image processing and visualization toolkit. and cloud and virtualization services will also be developed. The CHIC tools, services, infrastructure and repositories will provide the community with a collaborative interface for exchanging knowledge and sharing work in an effective and standardized way. A number of open source features and tools will enhance usability and accessibility. In order to ensure clinical relevance and foster clinical acceptance of hypermodelling in the future, the whole endeavour Three oncosimulators are under development within the framework of p-medicine: one for the case of nephroblastoma treated with chemotherapy, one for the case of acute lymphoblastic leukaemia treated with chemotherapy and a third one for the case of breast cancer treated with targeted antiangiogenic therapy. All three versions will serve as platforms for conducting experiments in silico, i.e. on the computer, by exploiting the multiscale data of the individual patient. The goal of such a process is to select the optimal treatment scheme and/or schedule for a given patient before starting the administration of the actual treatment. Obviously, clinical adaptation and validation of the complex oncosimulator models are sine qua non prerequisites for the eventual clinical translation of the latter. To this end multiscale data sets provided by the p-medicine clinical partners are currently under exploitation.

will be driven by the clinical partners of the consortium. Cancer hypermodels to be collaboratively developed by the consortium cancer modellers will provide the framework and the testbed for the development of the CHIC technologies. Clinical adaptation and partial clinical validation of hypermodels and hypermodel oncosimulators will be undertaken. Experimentation in silico is expected to serve as both a patient individualized treatment optimizer by exploiting the patient's own multiscale data and a fundamental science based suggestion generator in designing the branches of new prospective clinical trials.

CHIC will utilize a number of both elementary and complex models developed within the framework of the p-medicine project as component models and building blocks for the development of advanced hypermodels. Those constituent models will be annotated by pertinent metadata in accordance with the CHIC strategies.

P-MEDICINE AND VPH-SHARE COLLABORATION

Sankt Augustin in August 2012

Introduction

collaboration The between p-medicine and VPH-Share was most evident at the joint meeting held in the 19th Century Schloss Birlinghoven, in Sankt Augustin, at the end of August, where p-medicine kindly extended their hospitality and invited key members of VPH-Share as an extension of their Consortium meeting. Beneath the magnificent neo-Baroque ceiling of the Gallery Hall, overlooked by tier upon tier of 16th to 18th century oil-paints, pairs of presenters representing both projects described how their respective groups had been working together towards understanding different aspects of the two projects and their plans for further collaboration.

Coordination

The project coordinators Norbert Graf and Rod Hose set the scene, outlining the differences and similarities of each project. They used the analogy of coarse and fine fishing nets with respect to the scale and focus of the two projects, with VPH-Share providing a widely spanning, but generic framework for projects from many domains and p-medicine providing more specific functionality and tools for projects in the domain of oncology. The analogy of the development funnel was also used to illustrate the different stages of model development and transfer through clinical trials and testing to clinical practice, with VPH-Share providing support for early development and collaboration formation of a VPH (Virtual Physiological Human) projects and p-medicine representing an instance of a more streamlined and refined project positioned for clinical trial, representing a model for projects from other domains. So despite both being infrastructure projects for VPH research, they support very different scales and positions in the VPH project development landscape. The coordinators also reprised the discussions, collaborations and agreements that had led to the successful Joint Review, in Brussels in November 2011, which formed the foundation of the work presented during the rest of the day.

Clouds

Cyfronet. Marian Bubak, AGH. Juliusz Pukacki, and Poznan Supercomputing and Networking Center (PSNC), both from Poland, described the cloud platforms that had been developed by both projects, identifying synergies and areas of cooperation, including routes to the sharing of data and computational resource access and security solutions. Five possible scenarios for sharing resources between p-medicine and VPH Share were outlined, the most promising appearing to be the deployment of p-medicine applications as VPH-Share atomic services.

The first p-medicine application identified to be deployed through VPH-Share was the ONCO Simulator, which is a model that simulates the response clinical tumours to several treatment schemes in a patient individualised context.

Data Integration and Management

Benjamin Jefferys, University College London, and Steven Wood, Sheffield Teaching Hospitals, both from the UK, described the two projects' different approaches to the storage of structured data. p-medicine stores all of its data in a curated Data Warehouse, whereas VPH-Share allows data providers to publish individual datasets through the Data Publication Suite, annotated with semantic data to allow discovery and interpretation of the dataset.

The Data Publication Suite was demonstrated to the p-medicine



consortium after the formal meeting to provide a model for the integration of the data anonymisation and pseudonymistation, sematic annotation and publishing tools. There was interest from p-medicine in the further evaluation of this Suite.

EUDat

Juliusz Pukacki described this recent Framework Programme 7 project, which supports the storage and access of large datasets for several scientific research areas including VPH. It was clear that the other domains which EUDat supports do not have the same legal and ethical considerations that patient derived clinical data imposes on VPH research. However, the storage and access to large datasets is an issue common to both projects and the implications of the EUDat project will be collaboratively explored.

Workflow Engines

Stelios Sfakianakis, The Foundation for Research and Technology – Hellas (FORTH), Greece, described how

p medicine's approach has moved from the creation of a new workflow engine to that of supporting existing workflow engines, such as Taverna and Galaxy. This is similar to VPH– Share's approach of supporting an existing workflow engine, again Taverna. The groups from the two projects working on the workflow engines will continue to share experience and expertise in this area.

Security

Elias Neri, Custodix, Belgium and Dario Ruis, Atos, Spain described their analysis of the security approaches of the projects and identified areas of existing and potential interoperability. The largest barrier to interoperability is the handling of attributes and a number of possible approaches have been explored. However, they sought guidance from a policy level on the level of security interoperability that would be necessary and desirable. This was addressed under legal and ethical issues.

Semantics

Holgar Stenzhorn, University of Saarland, Germany, described the contrasting approaches to semantics: p-medicine manages and curated a set of ontologies suitable for data in the oncology domain, whereas VPH– Share supports a more eclectic group of ontologies, representing the wider



number of domains and, in addition, annotates its tools and services as well as its data. Both projects use a linked data approach. VPH-Share will index p-medicine's collection of ontologies, so that they will be available to VPH-Share users and p-medicine data can be annotated and searched using VPH-Share tools or annotated with a wider base of ontologies, if desired.

Ethical & Legal Issues

Nikolaus Forgó, Hannover University, Germany, described how p-medicine has created a secure space. where the data would be de facto anonymous. The data will be double pseudo-anonymised by a trusted third-party and contractual and technical measures will be in place to prevent users from re-identifying the data. Anyone wishing to access p-medicine's data will be required to sign p-medicine contracts and access it through p-medicine's Data Warehouse. Consequently, it is not desirable for the access to be given to p-medicine data through the VPH-Share, even though many of the technical cloud and security issues could be addressed. A preferred approach would be for the meta-data. which describes the nature of the data stored and not the individual records. associated with p-medicine's data could be shared through VPH-Share, allowing users to be able to discover that the data exists. Anyone wishing to access p medicine's data would then be directed to p-medicine and their contractual agreements. There would be a continued exploration of the ethical and legal issues between the two projects.

Technological Evaluation

Karl Stroetmann, Empirica, Germany, described the approaches employed to evaluate VPH Share in the context of its four flagship workflows and offered to treat p-medicine as a 'fifth' workflow, extending the evaluation evidence available to p-medicine.

Typology of Models represented by the Projects

Georgios Stamatakos. Institute of Communication and Computer Systems, Greece, presented the metadata collected from seven models represented by the two projects, seven from p-medicine and six from VPH Share, describing the following properties of the models: the systems or diseases modelled; the principals or laws used; their multiscale policy; their mathematical approach: and computational resources. Georgios's analysis of this data was that between the two projects there was a wide spread of models spanning all the categories of the properties described, as such the projects provide a good representation of the VPH community.

Discussion triggered bv this highlighted the multiplicity of model simulations required to cover the variation and uncertainty in parameters for both the individual patient and across populations of patients. VPH-Share offered the tools being developed from our tasks: Parameter Estimation, which looks at methods to identify missing or uncertain values, Physiological Envelope for Simulation and Model provides Interpretation, which sensitivity analysis, and VPH Mark-Up Languages, which is focusing the representation of parameter uncertainty.

The Collaboration Continues ...

There was general agreement to share project deliverables and discuss them at future joint meetings, and to that purpose VPH-Share looks forward to inviting representatives from p-medicine to Atos Spain SA, Madrid in early March.

LINKS

<u>www.p-medicine.eu</u> <u>www.vph-share.eu</u> www.biomedtown.org

ANNOUNCEMENT OF UPCOMING EVENTS



EFMI STC Prague

April 17–19, 2013 Prague, Czech Republic

The special topic conference (STC) "Data and Knowledge for Medical Decision Support" is hosted by the Czech Society of Biomedical Engineering and Medical Informatics and the European Federation of Medical Informatics (EFMI). The conference aims to bring together both scientist and industry interested in the various key aspects of medical decision support such as sharing knowledge and tools in biomedicine or perspectives for health information management in Europe.

More information

Second Workshop on Interoperability in Scientific Computing (WISC '13)

June 5–7, 2013 Barcelona, Spain



The goal of this workshop is to bring together researchers from across scientific disciplines whose computational models require interoperability. The outcomes of this workshop will be to better understand the nature of multidisciplinary computational modelling and data handling. Moreover, the workshop aims at identifying common abstractions and cross-cutting themes in future interoperability research applied to the broader domain of scientific computing.

More information

The WISC'13 will be held in conjunction with the 13th annual International Conference on Computational Science (ICCS).

For more details on the main conference, please visit the *conference website*.

eHealth Week 2013: Delivering Innovative Healthcare & Well Being

May 13-15, 2013 Dublin, Ireland



eHealth Week 2013 is one of the essential Pan-European conferences for the healthcare industry. Apart from offering a space for professional networking, eHealth Week 2013 will bring together two large events: the High level eHealth conference organized by the European Commission and the current Irish Presidency of the Council of the European Union, and the World of Health IT Conference and Exhibition (WoHIT). Amongst others, the programme includes themes like patient empowerment, cross-border eHealth Solutions and interoperability as well as eHealth as a Business Driver. Registration is now open!

More information



A unique forum for research funders and performers in Personalised Medicine

EuroBioForum 2013

May 27–28, 2013 Munich, Germany

The focus of EuroBioForum 2013 will lie on policy development and deployment in the field of personalized medicine. It will be a forum for exchanging ideas on how to face current and future challenges with respect to policies, implementation strategies and required investments. Of special interest will be the exploration of potential areas for transnational and transregional collaboration, also in the context of Horizon 2020. The EuroBioForum Annual Meeting is free of charge.

More information



6th Mildred Scheel Cancer Conference (6th MSCC)

June 5–7, 2013 Königswinter, Germany

For more than four decades, the Dr. Mildred Scheel Foundation for Cancer Research has been sponsoring conferences on current topics in cancer research. The 6th Mildred Scheel Conference fosters the exchange with internationally leading experts in cancer research and the exploration of new perspectives in this field. This year's programme includes, amongst others, sessions on chemistry/small molecules, biomarkers, targeted therapy and resistance as well as extended poster sessions. <u>More information</u>

Biomedica 2013

June 18-19, 2013 Aachen, Germany

The Biomedica summit is a large networking event where the world of science and the world of business meet. Designed for the purpose of initiating collaborations between scientists and industry and fostering new products and application, this year's key topics include medical devices and care as well as business development and product innovations. Participants will also have the opportunity to promote their career and/or their business at the job fair and the one-onone matchmaking sessions with experts in various scientific and business disciplines. For more information, please visit.

More information is available on the *conference website*



EMBC2013

July 3–7, 2013 Osaka, Japan

The 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC'13) will take place at the Osaka International Convention Center, in Osaka, Japan.

The conference will cover diverse topics such as biomedical engineering, healthcare technologies, and medical and clinical applications. The conference programme will consist of invited plenary lectures, symposia, workshops, invited sessions and oral and poster sessions of unsolicited contributions. All papers will be peer reviewed; accepted papers of up to four pages will appear in the Conference Proceedings and be indexed by IEEE Xplore and Medline/ PubMed



5th International Conference on Computational Bioengineering (ICCB2013)

September 11-13, 2013 Leuven, Belgium

The conference will have a strong focus on "integrative" Computational Bioengineering in a broad spectrum of research areas and ranging from the molecule to the body. Included are topics such as integrative and multilevel modeling, integration of technologies for model development in personalized medicine, e.g. imaging, and sensing, and ICT topics such as cloud computing.

More information

ICIMTH 2013

International Conference on Informatics, Management, and Technology in Healthcare (ICIMTH2013)

July 5-7, 2013 Glyfada, Greece

The major focus of this conference will be on the application of biomedical informatics from the decision support systems, ontologies and imaging to public health informatics and ICT applications in the healthcare domain. To broaden the technical perspective, papers, workshops, panels and/or tutorials on organizational and management issues are also welcome. Registration will be open until March 24, 2013.

More information

Since the section of the website on upcoming events is regularly updated we invite you to visit our website for most recent changes.

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2ND SUMMER SCHOOL IN COMPUTATIONAL ONCOLOGY



p-medicine Summer School

June 23–28, 2013 Wadern, Germany

The first summer school in Computational Oncology took place in Heraklion, Crete on June 13th–18th 2011. It was organised by our partners from FORTH. This year, the renowned "Schloss Dagstuhl – Leibniz Center for Informatics", will host us. At our summer school, we will provide basic training on the new research dimension of computational oncology based on the experience and expertise acquired in various European collaborative projects (p-medicine, EURECA, VPH–Share and CHIC).

Together with the participants, international experts in the field of computational oncology will cover a broad range of multidisciplinary aspects including both clinical and engineering/basic science viewpoints. Moreover, we will introduce the participants to the legal and ethical issues at stake in the field of personalized medicine.

We give students, PHD candidates, young researchers, legal scholars and engineers from diverse backgrounds and disciplines the opportunity to gain the necessary knowledge and skills required to understand the basics of multiscale cancer modeling, its legal and ethical implementations and the biomedical informatics framework. Insight into all these areas is crucial if we want to bring this new technology closer to the clinical setting and decision making process. The latter is crucial for achieving our ultimate goal: to place patients into the centre of interest of medicine and offer tailor-made therapies for as many people as possible. The summer school is one step into this direction.

The lectures and workshops will cover the following themes:

- Impact of IT towards personalized medicine
- Molecular Biology and Bioinformatics
- · Law and Ethics in IT frameworks for personalized medicine
- Usability
- Interoperability and sustainability

Schloss Dagstuhl is the home of the renowned Leibniz Center for Informatics which promotes scientific research, academic education and networks between researchers and engineers. Schloss Dagstuhl offers a space well-equipped for our needs, with conference rooms, accommodation for the night and full catering.

More information is available on the *conference website*

There are still places available, if you are interested, please register here!



The Venue: Schloss Dagstuhl, home of the renowed Leibniz-Center for informatics

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The p-medicine newsletter is published once a year by the p-medicine consortium and is distributed free of charge.

All issues of the newsletter are available on our website.

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