



The Virtual Physiological Human Industry Meeting (Feb'09)
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Peter Hunter (University of Auckland), Marco Viceconti (Rizzoli Institute)
24th February 2009

This two-day event was tailored to foster **closer engagement of biomedical scientists with the VPH concept**, with particular focus on the clinical and industrial communities. The meeting was attended by a number of VPH Network of Excellence and allied VPH Initiative project members, as well as medical geneticists, biological ontologists, mouse disease modelers, pharmaceutical scientists, bioinformaticians, bioengineers, pharmaceutical regulatory physicians, and UK National Health Service clinicians.

The event was funded by the **European Bioinformatics Institute's Industry Programme**, thanks to support from Janet Thornton (Director, EBI) and Dominic Clark (Industry Programme co-ordinator). The scientific committee of the meeting included Bernard de Bono, Alex Frangi and Peter Hunter. Crucial support in industrial outreach was also provided by Peter Coveney (Co-ordinator, VPH Network of Excellence) and Marco Viceconti (Co-ordinator, VPHOP Integrated Project).

The first day consisted of an open meeting to tackle the issue of **interoperability**. The key outcome of this discussion was to highlight the need for the biomedical community to establish a common standard for **multiscale anatomy** for VPH data and models to address. The second day took the form of an invitation-only event where **the role of modeling in industry and the clinic** was discussed. Closer engagement with **modeling infrastructure initiatives** was identified as a key requisite for industry to reap the benefits that modeling technologies have to offer.

The first section of this document provides a brief outline of the key categories of (i) **Clinical Data Access Points** and (ii) **VPH Modeling Environments** that were discussed in the context of a communal framework for multiscale anatomy on Day 1. The points raised during the **modeling infrastructure** session on the second day are summarized in the last section of this report. This is followed by a full listing of the meeting agenda.

Day 1: Multiscale anatomy connecting CDAPs with VPHSEs

Clinical Data Access Points (CDAPs)

Connectivity to healthcare data on a large scale is essential to ensure, for example, that model parameters accurately reflect disease characteristics. This may be achieved by ensuring interoperability of VPH resources to the following categories of Access Points to healthcare data, namely:

- 1) **Clinical Terminologies:** A number of terminology standards are already in place to organize and classify clinical information. **SNOMED-CT**, for instance, is the required standard for the annotation of hospital records both in the US and the UK (as well as a number of other European countries). The FDA also requires that official clinical indications for drugs are mapped to SNOMED-CT terms. In both the EU and Japan, the **MedDRA** terminology is a requisite for the reporting of adverse drug reactions. The Genotype-to-Phenotype community is also actively working to index its resources using a phenotype terminology standard – the **Human Phenotype Ontology (HPO)**, which is itself the result of an effort to organize OMIM data) is becoming increasingly well established in this respect.
- 2) **Radiology Models:** Recent developments in image processing techniques have made it possible to quantify anatomical interindividual variation based on 3D radiology data. Although the use of **Statistical Radiology Models (SRMs)** is still in its infancy, the formal representation of those characteristics of radiological anatomy associated with a particular disease will create a quantitative approach to clinical diagnosis based on image analysis. SRMs also provide a crucial opportunity to create patient-specific mathematical models of physiology. Furthermore, the community-based annotation of SRMs will also bridge a wide variety of biomedical data onto the same volumetric framework of anatomical structures.

VPH Simulation Environments (VPHSEs)

Two key biomedical modeling areas that would benefit from a common standard for model interoperability are:

- 1) **Models of drug distribution and response:** Pharmacokinetic (PK) methods that predict the bio-availability of a drug by modeling its Absorption, Distribution, Metabolism and Excretion (**ADME**) are crucial in estimating a compound's availability and potential toxicity (ADMETox). Such techniques are at the core of pharmaceutical drug development pipelines, and are based on modular representations of (a) molecular pathways that are active across key body tissues, and (b) the way such tissues interconnect (*e.g.* via the bloodstream). This aspect of pharma modeling uses techniques that are based on VPH concepts.
- 2) **Physiology models:** Physiology models range from cellular biochemistry to the multi-scale simulation of cardiac electro-mechanical coupling, blood pressure control and the regulation of bone density. A key objective of the VPH Network of Excellence is to attain improved interoperability between these different types of model. The SBML and CellML communities, in particular, are seeking ways to further support such a goal.

Collaborative Framework for Multiscale Anatomy

The setting up of a community-wide standard to support the integration of different types of **biomedical data** by VPHSEs was actively discussed. The key step towards the three-way interoperability between data silos, VPHSEs and CDAPs may be achieved by establishing a communal Multiscale Anatomy Framework by the VPH, as described in **Figure 1**.

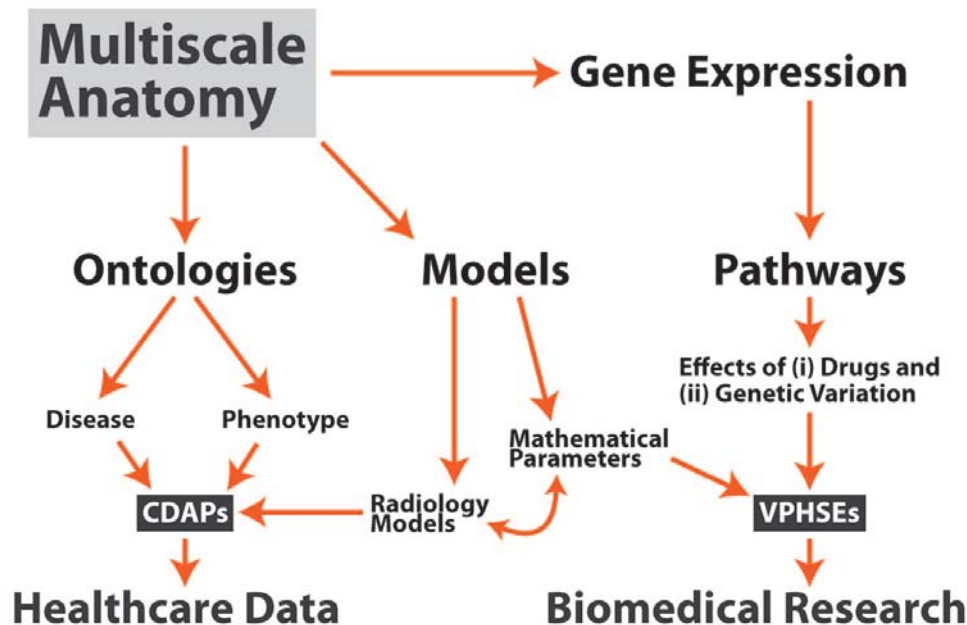


Figure 1. Bridging biomedical research to the clinic via a shared anatomical framework. A common multiscale anatomy standard would connect disease ontologies that annotate clinical records to (a) models of radiology, (b) the mark-up of physiological parameters, as well as (c) molecular and genomic data.

Day 2: Modeling and Infrastructures

A more detailed view of VPH modelling projects (**ViroLab**, **preDiCT**, **@neurIST**), and infrastructure development initiatives (**HealthGrid**, **VPH Toolkit**) was presented to EBI Industry programme representatives on Day 2. The purpose was to engage directly with Industry researchers, and identify how best they may engage with this growing research field.

A key point was raised regarding research in industry concerned with **drug safety testing**. A major hurdle in the current screening of potential new bioactive compounds is the use of animal models in determining dose-response. If computational models could be put to better use in reducing target attrition at this stage, this could have a huge impact on the Pharma industry. The preDiCT project is good example of such an effort, and the talk on this particular project provoked significant discussion.

The computational infrastructure that has, and continues to be, developed to support VPH research is largely aimed at meeting the requirements of the academic research community. **Grid access**, for example, remains relatively peripheral to the industry domain. It is understood, however, that this will not necessarily remain the case and increased effort will have to be invested in linking up infrastructure development to the requirements of industrial and clinical end users. The **VPH Toolkit** presentation generated considerable interest from industry representatives, who were keen to understand how they might be able to expose research-level software (models, tools), in development, to the VPH research community. Several opportunities for doing so will be pursued by the VPH NoE.

Conclusion

This meeting provided an excellent forum for the showcasing of VPH concept, as well as the discussion about the challenges and opportunities such novel modeling technologies present to industry researchers. The further advancement of the VPH field will require both **Industry** and the **Clinic** as key stakeholders in use of biomedical modelling and simulation, and as part of new and increasingly 'virtualised' drug and medical device development pipelines. The two key follow up actions that focus on the setting up of communal multiscale anatomy and grid access frameworks are now being actively pursued by the VPH community.

AGENDA: Feb 2nd 2009

Open Meeting: The [Virtual Physiological Human](#) - the Anatomical Basis of Disease
 Francis Crick Auditorium, Wellcome Trust Genome Campus, Hinxton CB10 1SD

Time	Item	Presenter
08.30	Registration	
09:00	Welcome and Introductions	Dominic Clark (EBI) Janet Thornton (EBI) Peter Coveney (UCL) Bernard de Bono (EBI)

SESSION 1: Concepts of Anatomy and Disease.**Chair: Lynn Schriml (University of Maryland).**

09:30	The Foundational Model of Anatomy	Onard Mejino (University of Washington School of Medicine)
10:00	Connecting to clinical data - mapping SNOMED to anatomy	Kent Spackman (IHTSDO)
10:30	Integrating data and models using the Disease Ontology	Warren Kibbe (NorthWestern University)
11:00	Tea	

SESSION 2: Organizing anatomical models.**Chair: Bernard de Bono (EMBL-EBI).**

11:30	Statistical models of radiological anatomy	Alex Frangi (University Pompeu Fabra)
12:00	Volumetric annotation of mouse anatomy	Duncan Davidson (MRC, Edinburgh)
12:30	FieldML - a standard for anatomically based physiological modelling	Peter Hunter (University of Auckland)
13:00	Lunch	

SESSION 3: Modeling anatomical physiology.**Chair: Dan Cook (University of Washington School of Medicine).**

14:00	Multi-scale modelling in musculoskeletal mechanics	Marco Viceconti (Rizzoli Institute)
14:30	Multi-scale modelling of kidney function in the context of blood pressure regulation and fluid homeostasis	Randy Thomas (CNRS)
15:00	Virtual organisms in the prediction of pharmacokinetics – principles and applications	Simon Thomas (Cyprotex Ltd)
15:30	Tea	

SESSION 4: Bridging across anatomical scales.**Chair: Jesper Tenger (Karolinska Institute).**

16:00	Interoperability across resources via anatomy	Jonathan Bard (Weatherall Institute, Oxford)
16:30	Towards global pharmacodynamics - predicting the compartmental location of proteins	Thomas Skot-Jensen (Denmark Technical University)
17:00	Achieving multi-scale interoperability of VPH data and models	Bernard de Bono (EMBL-EBI)
17:30	Closing remarks	

AGENDA: Feb 3rd 2009

The [Virtual Physiological Human](#) – Modeling for the Pharma & Biotech Industry
 European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton CB10 1SD

Time	Item	Presenter
08.45	Welcome and Introductions	Dominic Clark (EBI) Peter Coveney (UCL) Bernard de Bono (EBI)

SESSION 1: Modeling at molecular scale.

Chair: Peter Hunter (University of Auckland).

09:00	Molecular modeling and computing infrastructures	Peter Coveney (UCL)
09:30	VPH strategies in predicting cardiotoxicity	Blanca Rodriguez (University of Oxford)
10:00	Computational fluid dynamics simulation for the clinic	Rod Hose (University of Sheffield)
10:30	Tea	

SESSION 2: Large scale interoperability.

Chair: Catherine Gale (UCL).

11:00	The HealthGrid Project	Yannick Legre (HealthGrid)
11:30	The VPH toolkit - challenges, standards and protocols for VPH interoperability	Sharon Lloyd (University of Oxford)
12:00	Interactive Discussion	Jonathan Cooper (University of Oxford)
13:00	Lunch	
14:00	Industry meeting closes	