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Editorial

We would like to welcome you to this issue of *Philosophical Transactions of the Royal Society A*, which is the first of two back-to-back issues devoted to the Virtual Physiological Human (VPH).

The VPH is a specific European initiative that aims to develop a methodological and technological framework to enable investigations of the human body as an integrated (though hugely complex) system. The main objective is to develop a systemic approach that avoids the pitfalls of subdividing biological systems in any particular way—by dimensional scales (body, organ, tissue, cells, molecules), scientific discipline (biology, physiology, biophysics biochemistry, molecular biology, bioengineering) or anatomical sub-system (cardiovascular, musculoskeletal, gastrointestinal, etc.). For further details, see Fenner *et al.* (2008).

This framework should allow experts from a large variety of disciplines to work collaboratively, analyse and interrelate observations and measurements obtained from multiple sources and develop systemic hypotheses. It should also make it possible to combine predictive models, defined at various scales, with a range of methods operating at different levels of detail, in order to produce concrete hypotheses and allow their validity to be tested against existing results or output from targeted experimentation.

This range of activities is suitably illustrated in the papers contained in the present issue, which commences with a thorough discussion of the interplay between genes and causation, highlighting the need for a new approach towards linking genomic data to functionally relevant insight (Noble 2008). This sets the scene for consideration of the practicalities involved in relating molecular-level data to large-scale simulations (Hofmann-Apitius *et al.* 2008; Ortega *et al.* 2008). Suitable tools, modelling environments and computational strategies are discussed (Bajaj *et al.* 2008; Garny *et al.* 2008; Pitt-Francis *et al.* 2008; Thomas *et al.* 2008), and the importance of combining structural and functional insights is illustrated (Spaan *et al.* 2008). This ability crucially depends on improved non-invasive imaging techniques and automated analysis of the vast amount of data obtained (Young *et al.* 2008), to eventually move towards patient-specific modelling and simulation (Sadiq *et al.* 2008).

More generally, the framework of methods and technologies representing the VPH will have to possess three fundamental attributes, as subsequently described.

— Descriptive. The framework should allow observations made in laboratories, hospitals and the field, at a variety of locations situated anywhere in the world, to be collected, catalogued, organized, shared and combined in any possible way.
— Integrative. The framework should enable experts to analyse these observations collaboratively and develop systemic hypotheses that involve the knowledge of multiple scientific disciplines.

One contribution of 12 to a Theme Issue ‘The virtual physiological human: building a framework for computational biomedicine I’.

— Predictive. The framework should make it possible to interconnect predictive models defined at different scales, with multiple methods and varying levels of detail, into systemic networks that solidify those systemic hypotheses; it should also make it possible to verify their validity by comparison with other clinical or laboratory observations.

In its long-term objectives, the VPH is not unique. There are a number of current initiatives, at national and international levels, which target the human physiome, while other projects have focused specifically on individual organs or organ systems. The Physiome Project of the International Union of Physiological Sciences (http://www.physiome.org.nz/) is possibly the most prominent, but generally all existing projects and initiatives form a loosely connected set of activities.

What is significant about the VPH is that it is receiving substantial funding from the European Commission in order to generate coherent and coordinated scientific progress in the area. Given its stated priorities, the European Commission is also insistent that VPH-related projects demonstrate strong industrial participation and clearly indicate a route from basic science into clinical practice. In this way, the European Commission hopes to ensure that the VPH does not evolve simply as an ivory tower activity, but that it will be capable of making an impact in the real world.

In Framework 7, Call 2 of the Information and Communication Technologies Programme in October 2007 allocated €72 M to the VPH projects. The Commission was impressed by the quality and ambition of the proposals received, and there is a clear prospect of further such Calls in the later stages of Framework 7. This volume is appearing as these projects spring to life, so this is a particularly good time to look back on the early development of the VPH and, simultaneously, to look forward to its future.

In mid-2005, several developments came together at about the same time. The feeling that the available technology, particularly in terms of ICT infrastructure, was reaching a sufficient stage of advancement that it would be capable of supporting a challenge as ambitious as the VPH was beginning to become more widespread (a trend that found support in previous focused issues of *Philosophical Transactions A*; e.g. Hunter *et al.* 2001; Gavaghan *et al.* 2006).

A consortium, formed by scientists who had previously been working on the multiscale modelling of particular physiological systems (such as heart, kidney, musculoskeletal, gastrointestinal, epithelium, etc.), submitted a proposal to the European Commission to identify a Strategy for the EuroPhysiome (STEP). This request was granted as a coordination action to produce a roadmap to define how European research in this area should best be organized in the future. The Commission also coordinated a meeting within a conference in Barcelona to discuss this field as a possible future priority within the ICT for Health unit. Although STEP had not formally been approved at that time, representatives from STEP (G.C., M.V. and others) were invited to that meeting. The outcome, in the autumn of 2005, was a White Paper[1] outlining the immediate way forward. The term EuroPhysiome was coined to denote the increasingly coherent physiome-related work in Europe, and this has continued as an informal umbrella title.

[1] http://ec.europa.eu/information_society/activities/health/docs/events/barcelona2005/ec-vph-white-paper2005nov.pdf.

STEP formally commenced in January 2006 and concluded in March 2007. It ran two successful conferences in Brussels, which helped galvanize a broad range of interest and activity in the area. The roadmap that was produced, *Seeding the EuroPhysiome: a roadmap to the Virtual Physiological Human*, was circulated widely among scientists, industrial companies, professional bodies, political figures and personnel at the Commission and in health ministries throughout Europe. It can be downloaded from http://www.europhysiome.org/roadmap.

None of these European developments were 'inward facing'. From the outset, STEP insisted on inclusivity and invited many eminent figures from around the world to join its advisory board. In addition, STEP has played a leading part in developing worldwide links so that data and software can be shared freely across the international community. This is most evident in the World Integrative Research Initiative (WIRI) to which most of the major physiome-related projects are signatories. It is a fundamental precept of EuroPhysiome that its work should be as compatible and convergent as possible with similar work that is taking place in other parts of the world.

Since the conclusion of the STEP project in 2007, there has not been an easy means of continuing the coordination of EuroPhysiome work. However, from June 2008, this mantle has fallen on the newly established VPH Network of Excellence (NoE; see http://www.VPH-NoE.eu/). It is symbolic of this 'handover' that two of the editorial team for this issue were coordinators of the STEP project (G.C. & M.V.), while the other two (P.V.C. & P.K.) are involved in leading the coordination of the NoE.

The EuroPhysiome community wishes the NoE well and hopes that over its 4.5-year lifespan it will provide great support for all EuroPhysiome activities, whether formally funded via the VPH call or not, and that this period will bring many important advances for the Virtual Physiological Human, as we build a framework for computational biomedicine.

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