INTRODUCTION

The virtual physiological human: computer simulation for integrative biomedicine I

Contemporary biomedical research and clinical practice face a major challenge: the classic reductionist approach, which we successfully used for decades to dissect at more and more detail the components and mechanisms underlying the physiology and pathology of organism, is now showing its limits. Most of the grand challenges in biomedical research and practice involve mechanisms that emerge from complex systemic interactions of different parts, defined at radically different spatio-temporal scales, belonging to different organ systems, and requiring different methodological approaches that are spread over many different academic disciplines and domains of knowledge. We need to complement the recent reductionist approach by ‘returning back to basics’—an integrated view of biomedicine, as has been typical for traditional research areas, such as physiology, over centuries. Of course, we can return to this more holistic approach from a different position, now that we have at our command the tools and insights from modern biology—but how do we do that, without drowning in the flood of reductionist data generated?

To make integrative biomedical research and practice possible, we need a new framework of methods and technologies which makes it possible to investigate living organisms as a whole. This is at the heart of the virtual physiological human (VPH) initiative (Fenner et al. 2008). The VPH is ‘a methodological and technological framework that, once established, will enable collaborative investigation of the human body as a single complex system’ (STEP consortium 2007). VPH research targets biomedical study, application development and clinical practice. For research and development, the collective framework will make it possible to share resources and observations between institutions and organizations, creating disparate, but integrated, computer models of the mechanical, physical and biochemical functions of a living human body. For clinical practice, VPH technologies will make possible a new form of medicine that is personalized (based on all available data on the patient), predictive (supporting longitudinal ‘what if?’ analyses) and integrative (synergistically combining all available information and expertise).

We are delighted that the Philosophical Transactions of the Royal Society A has given a home and focal point to these developments, by making special issues on the VPH a regular feature. A double issue on ‘Biological modelling’ (Gavaghan et al. 2006), compiled by D. Gavaghan, A. Garny, P. Maini and

One contribution of 13 to a Theme Issue ‘The virtual physiological human: computer simulation for integrative biomedicine I’.
P. Kohl, coincided with the European ‘STEP’ process (Strategy Towards a European Physiome, led by M. Viceconti and G. Clapworthy (STEP Consortium 2007)) that led to the establishment of the VPH initiative.

After the launch of the VPH, this was followed in 2008 by focused issues on ‘The virtual physiological human: building a framework for computational biomedicine I & II’ (Clapworthy et al. 2008), edited by M. Viceconti, G. Clapworthy, P. V. Coveney and P. Kohl, and on ‘Biomedical applications of systems biology and biological physics’ (Mosekilde & Tass 2008), compiled by E. Mosekilde and P. A. Tass. The dynamic development of the VPH found reflection in 2009 by ‘The virtual physiological human: tools and applications I & II’ (Gavaghan et al. 2009), edited by D. Gavaghan, P. V. Coveney and P. Kohl; by ‘Crossing boundaries: computational science, e-Science and global e-Infrastructure I & II’ (Coveney & Atkinson 2009), compiled by P. V. Coveney and M. P. Atkinson; and by ‘From biological and clinical experiments to mathematical models’ (Demongeot et al. 2009), compiled J. Demongeot, J.-P. Françoise and D. Nerini. The present issue contains a selection of papers presented at the IVth International Congress on Computational Bioengineering, including the 1st European Symposium on Biomedical Integrative Research, held in Bertinoro (Italy), 16–18 September 2009. Of the hundreds of abstracts submitted to that conference, 35 were invited to submit a full-length paper, out of which 26 completed the editorial process and were included in this two-volume issue on ‘The virtual physiological human: computer simulation for integrative biomedicine’.

This first Theme Issue is opened by an editorial entitled ‘A vision and strategy for the virtual physiological human in 2010 and beyond’ (Hunter et al. 2010). This has been compiled as a result of discussions within the VPH Network of Excellence, and represents an update on the 2007 VPH Research roadmap (STEP Consortium 2007).

The remaining 11 papers offer an excellent overview of current biomedical integrative research, and on the VPH technology that makes it possible. In this Theme Issue, we collected papers that tackle relevant problems, mostly related to connective tissues. Each paper focuses on a preferential range of dimensional scales. ‘Developments of coarse-graining DNA models for single-nucleotide resolution analysis’ (Doi et al. 2010) centres its attention at the molecular level; ‘Cytoskeleton reorganization of spreading cells on micro-patterned islands: a functional model’ (Loosli et al. 2010) at the cellular level; ‘Multi-scale modelling and nonlinear finite-element analysis as clinical tools for the assessment of fracture risk’ (Christen et al. 2010) at the tissue level, and so on.

Probably because the conference was hosted by the Rizzoli Orthopaedic Institute, this Theme Issue contains several papers that focus on the musculoskeletal system, an organ system that received relatively little attention in previous instalments. Levels of investigation range from the tissue level, as in ‘Trabecular bone remodelling simulation considering osteocytic response to fluid-induced shear stress’ (Adachi et al. 2010) and ‘In silico design of treatment strategies in wound healing and bone fracture healing’ (Geris et al. 2010), to the whole organ, as in ‘Predicting the yield of the proximal femur using high-order finite-element analysis with inhomogeneous orthotropic material properties’ (Yosibash et al. 2010) and ‘Mechanical testing of bones: the positive synergy of finite-element models and in vitro experiments’ (Cristofolini et al. 2010) or even the entire organ system, as in ‘Influence of fatigue on the simulated

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relation between the amplitude of the surface electromyogram and muscle force’ (Dideriksen et al. 2010) and ‘Effect of fatigue on force fluctuations in knee extensors in young adults’ (Singh et al. 2010). All papers share the integrative approach that is characteristic of VPH research.

We also included a paper that deals with one of the most complicated (and most ‘integrative’) physiological systems: the immune system. In ‘ImmunoGrid: towards agent-based simulations of the human immune system at a natural scale’ (Halling-Brown et al. 2010), the authors report relevant achievements of a European research project recently completed.

To close this first Theme Issue we chose ‘An overview of recent applications of computational modelling in neonatology’ (Wrobel et al. 2010), which highlights the utility of the VPH approach in exploring the functioning of complex medical devices for neonatology in a more integrative manner.

This Theme Issue would not have been possible without the incredible work of our Editorial Assistant, Martina Contin, whom we would like to thank for her commitment.

We hope you will have as much fun in reading these papers as we had in editing this Theme Issue. Working with the authors and the peer reviewers, who ensured the high quality of accepted papers, was a pleasant and on some occasions a truly enlightening experience.

Enjoy the reading.

We thank all regional, national and international funding bodies that recognize the value of biomedical integrative research and support it. Special recognition is due to the European Commission in general, and the ‘ICT for Health’ unit of the DG-INFSO in particular, which have made VPH research and development a core target of the present 7th Framework Programme.

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