RS Ph-45-3

AN OVERVIEW OF SEVERAL STANDARDIZATION EFFORTS FOR SYSTEMS BIOLOGY

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A computational model represents a modeler's understanding of the structure and function of parts of a biological system. As the overall number of quantitative models continues to grow, and they become ever more sophisticated, they collectively represent a significant accumulation of knowledge about the structural and functional organization of biological systems. Enabling effective sharing of such quantitative models is the driving vision behind SBML and several related efforts that I will describe in this presentation.

•SBML (the Systems Biology Markup Language) is a machine-readable exchange format for computational models in systems biology.

•MIRIAM (Minimum Information Requested in the Annotation of Models) is a set of guidelines for model annotation

•SBO (Systems Biology Ontology) is an ontology of mathematical concepts used in computational models

•MIASE (Minimum Information About a Simulation Experiment) is a set of guidelines for making simulation results reproducible.

•SBGN (Systems Biology Graphical Notation) is a standard for graphical drawings of biological networks.

All of these efforts are, at their core, a means of improving our ability to communicate our discoveries and understanding.

RS Ph-45-4

VPH TOOLS

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Within the European Virtual Physiological Human (VPH) Network of Excellence (NoE), a key deliverable is the “VPH ToolKit”, defined as "a technical and methodological framework that will support and enable VPH Research through the creation, accumulation, and curation of VPH research-related 'capacities'." In particular, the VPH ToolKit consists of markup languages for models and for data, software for signal and image analysis, infrastructure for grid access, and various other elements grouped under the heading "VPH Tools". I will present progress within the VPH toolkit development team on adaptation of a number of such tools for the VPH framework, in particular, tools for collaborative development of multi-scale models, robust multi-formalism numerical solvers, visualization of simulation results, interactive model repositories, and others.

RS Ph-45-5

MULTISCALE, MULTI-PARADIGM MODELLING OF EPITHELIAL TISSUE

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The understanding of development, homeostasis and wound healing in epithelial tissues (the skin and lining of body cavities) has to be centred around the behaviour of individual cells. An individual-based modelling approach is used, with each cell represented by a finite-state machine (a communicating stream x-machine, originally formulated by Eilenberg as a Turing-complete computational machine). State transitions are controlled by a set of functions, modulated by information from the state machine's memory and the input data stream. At the end of each time step, information is written to the output data stream. The functions describe both the biochemical and the physical behaviour of each cell [Walker 2004, Sun 2007]. Three aspects will be discussed - the cell-level model; incorporating signalling models (sub-cellular); and embedding the cell in a physical environment in which it can grow, divide and exert forces on other cells (tissue-level) - with examples drawn from work on wound healing.

Walker D C, Hill G, Wood S M, Smallwood R H, Southgate J (2004) IEEE Trans Nanobioscience 3:153-163

Sun T, McMinn P, Coakley S, Holcombe ,M Smallwood R, MacNeil S (2007) J Roy Soc Interface 4:1077-1092

RS Et-46-1

ANIMALS IN MEDICAL RESEARCH: MAGIC OR TRAGIC?

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There is an abiding tension between the desire of reasonable people to avoid deliberate harm and their wish to benefit from advances that accrue from the use of animals in research.

Many opponents of animal research argue that ‘alternative’ approaches make the use of animals unnecessary. Moreover, some claim that animal research is unreliable as a guide to understanding human function and developing and testing new treatments. Politicians and the public face powerful arguments that animal research is unethical, unnecessary and even dangerous.

What should be done in response? A strong regulatory framework; strict requirements for welfare and husbandry; certification of researchers and projects; good record-keeping. These all help to maintain public confidence. But clear, informative communication, both proactive and reactive, is also essential. Recent experience in Europe, and especially Britain, shows how important it is that the scientific community should take the lead in promoting not only impeccable standards of practice in animal research but also openness, honesty and rational debate. The willingness of researchers to speak openly about their work has done a great deal to secure the increased trust of the media and the public in Britain.

RS Et-46-2

GUIDELINES FOR PROPER TREATMENT OF ANIMALS IN RESEARCH

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The International Council for Laboratory Animal Science (ICLAS), as an international umbrella organization, published harmonization guidance in *Science* in 2006 focusing on the principles for humane endpoints & animal euthanasia. The second guidance addressed animal user training programs & experimental protocol review. The latest manuscript under discussion is regarding the care & use of genetically engineered animals.

Based on an inquiry from the related ministries, the Science Council of Japan (SCJ), as the ICLAS National Member, established the SCJ Guidelines for Proper Conduct of Animal Experiments in 2006. These Guidelines were elaborated by collaboration of representatives from all scientific fields related to animal experiments including the biological, pharmaceutical, agricultural, veterinary & medical sciences. The SCJ considers that animal experimentation ethics should agree with scientific rationale & motivates scientists to conduct animal experiments with creativeness and flexibility.

To implement the Guidelines, Hokkaido University School of Veterinary Medicine will develop a 3R-based high-level educational program. The program includes quantitative measurement of pain using isolated neonatal rat spinal cords & functional MRI technology on anesthetized rats.

RS Et-46-3

STANDARDS FOR GOOD RESEARCH PRACTICE: SCIENTIFIC INTEGRITY AND DEALING WITH MISCONDUCT

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While some countries, notably the USA, have been aware of the problem of scientific misconduct for some time, and have indeed established bodies to deal with allegations of misconduct professionally, most countries have only recently realized their vulnerability and lack of preparedness in this regard. Some well publicized scandals during the last years initiated a number of national and international activities with the aim to deal with scientific misconduct and to foster scientific integrity. The Global Science Forum of the OECD has looked at the need of international cooperation and standards for best practice in dealing with scientific misconduct. The first World Conference on Research Integrity was held in Lisbon 16-19 September 2007. One has come to realize that the hard-core of scientific misconduct, so called FFP (fraud, fabrication, plagiarism), needs to be understood within the wider framework of so called QRPs (questionable research practices, such as e.g. honorary authorship etc). Episodes of FFP are in general rare, though they are disturbing for the progress of research and undermining the trust in science in general. Episodes of QRP are more wide-spread and can serve as indicators of a lack of awareness about normative constraints for good research practices.