

## Systems: What's In a Name?

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## Systems: What's In a Name?

### *The Paradox*

I begin this Editorial with a paradox. Since becoming IUPS President at the Kyoto Congress in 2009, I have lectured and spoken with physiological scientists around the world. Almost everywhere, I have encountered anxiety about the role of physiology and how it is under-valued in modern biological and medical courses in universities. Many departments of physiology have disappeared, at least in name, or been assimilated into larger groupings. The consequence is that the subject contributes a smaller proportion of the teaching of students, particularly those studying medicine. In many countries, practical classes have all but disappeared.

So, is physiology in decline? Measured in terms of anxiety and closures and mergers of departments, the answer would seem to be yes.

The paradox is that, during the period (around 20 years) that these administrative changes have taken place, the large numbers of people attending IUPS Congresses (3,000 to 5,000 depending on the location) have held up extraordinarily well. There is no discernable decline. I recall the excitement in 1993 when the huge lecture hall at the Glasgow Congress was completely full for Sir Bernard Katz's lecture as part of the opening ceremony. That excitement was repeated at the Kyoto 2009 Congress when the equally large hall at the Convention Center was filled to capacity for the opening ceremony and some of the plenary lectures, one of them given by Nobel Prize-winner Erwin Neher. Even in a period of world recession, we can achieve phenomenally well attended meetings. I am confident that we will experience the same rush of adrenaline and excitement at the 2013 Congress in the UK, at the 2017 Congress in Brazil, and well beyond. Preparations for IUPS2013 in Birmingham are well advanced (look at the website <http://www.iups2013.org/>).

More importantly, the science presented at the Congresses has been impressive, cutting-edge work, as physiologists succeed in connecting genotypes to phenotypes

through respecting the complexity of the control networks that mediate those connections (see Ref. 11, Fig. 1). Physiology is essential to that enterprise. The old paradigm of genes “determining” the phenotype has collapsed. The genome is better viewed as a necessary database used by the organism. We need to understand how it is used, which is a functional, *physiological* question. That, in a nutshell, is why sequencing the human genome, although impressive and essential as a fundamental scientific achievement, has generally not delivered on the promises made for health care (8). The systems approach, whether you call it by its new name of “systems biology” or by its old name of “(systems) physiology,” has come into its own precisely because we now know that reductionism is necessary but not sufficient.

### *Does the Name Matter?*

What's in a name? Of course, systems biology and physiology are not exactly equivalent, partly because the word *systems* already has a different, long-established meaning in physiology: the circulatory, respiratory, nervous, digestive, reproductive, endocrine, hormonal, etc. *systems*. The meaning is different simply because the terms refer to systems primarily at levels higher than cells, whereas most of what is called *systems biology* today focuses on subcellular networks of proteins, genes, and metabolites. For that reason, much of it is biochemistry or molecular biology by another name. Nevertheless, systems biology and the systems approach to physiology share an important idea, which is that integrative control is essential to understanding the system. Regulation is not in the genome (7).

Some biologists have even gone so far as to criticize systems biology as being no more than “a new name for physiology” (3) or as “disappointing” in its results compared with what is often promised (5)—both of whom have been quoted and discussed in a recent article by Cornish-Bowden (6). That article appeared in a series on systems biology and synthetic biology in *The Biochemist*. The systems biology bandwagon is also rolling in the

various journals of physiology, the latest being a focused set of reviews in *The Journal of Physiology* under the title “Systems Biology in a Physiological World” (10), to which I also contributed an article highlighting the limitations of gene-centered views of evolution in a physiological context (14).

I agree with Cornish-Bowden that there is some limited truth in both the Brenner and Colquhoun criticisms. Sydney Brenner is correct in the sense that there are clear precedents for the systems idea within physiology. Specifically, I would refer to Jean Fernel (1497–1558), the first to define the science of physiology (he used the Latin *physiologia*), in the 16th century (16), William Harvey (1578–1657) and Benedict de Spinoza (1632–1677) in the 17th century (1, 13), Claude Bernard (1813–1878) in the 19th century (12), followed by Walter B Cannon (1871–1945) (4), August Krogh (1874–1949), and Arthur Guyton (1919–2003) (9) in the 20th century. All of these used systems approaches to define and understand physiology. The resurrection of the systems approach is, for physiology, a return to our long-established roots. It is not that new. What is new is that our understanding of the molecular elements—the genes, proteins and metabolites—has changed.

More surprisingly, perhaps, I also partly agree with David Colquhoun. Faced with the immense complexity of the relationships between genotypes and phenotypes, the initial results are bound to be disappointing. But I take a rather different set of messages from this fact. The first is that we should not make the mistake of the extravagant promises made on behalf of the human genome project. Delivering cures for major multifactorial diseases within a period of 10 years was wildly overoptimistic (8). As Paul Nurse (15) says, “our past successes have led us to underestimate the complexity of living organisms.” Proponents of the systems approach should not make the same public-relations mistake. I prefer to shock people in the opposite way by saying that it might even take centuries to achieve the aims! The second is that, although the task may appear to be “mission impossible,” it is also “mission imperative” in the sense that we cannot make complexity disappear merely by saying that the task

is impossible. The history of science is littered with incorrect claims to impossibility. Faced with complexity, there is no choice but to try to unravel it. A combination of reduction and integration will be required to do that (11).

### ***The Return to Whole Organism and Human Physiology***

So, far from being a discipline in decline, our science is at the front of what is now required to interpret all the “omics” data being accumulated. To quote again from Paul Nurse (15), “This is the return to whole-organism and human physiology that many have argued is long overdue, but with a renewed emphasis on the logic of life and the management of information.” His remark echoes an earlier one of James Black who referred in *The Logic of Life* (2) to the “progressive triumph of physiology over molecular biology.” Those remarks are sufficient in themselves to explain why the Congresses, and the national society meetings, still vibrate with excitement.

Why then should we be concerned about the decline of the use of the word *physiology* and the closure or merger of departments in universities? Does it matter?

The sciences have renamed and recategorized disciplines and areas time and time again. That process is even accelerating as work at the interfaces becomes more important. New journals on interdisciplinary, interface science are appearing with almost alarming speed, while the existing journals are making sure that they get in on the action. In such a climate of opinion, it has been hard to resist administrative change within universities, particularly when they are instigated by people who grew up with a negatively biased view of the importance of physiology. Nor have we been helped by the soaring costs of doing work above the cellular level. In some countries, whole animal work has effectively been squeezed out of existence by regulations and costs.

So, how to explain the paradox? The explanation is really rather simple. University administrators, particularly those who were once scientists themselves, grew up in a period when the dominant paradigm was reductive molecular biol-

ogy. They simply have not yet noticed that, as evidenced by the flourishing of IUPS and many of its national member organizations, the subject has not died out and is even more necessary now than it was before the onslaught on its departments.

### ***What Are IUPS and Its Member Societies Doing About It?***

All of this leads me up to the conclusions of this editorial. If IUPS and its constituent national societies have been responsible for keeping the flame alight, that is all the more reason for supporting them in what they are doing for our subject. As I emphasized in my speech to the closing ceremony in Kyoto (the text and video are on the IUPS website), the fightback starts here. We have a responsibility to defend physiology and to attract the young into our work. We are clearly succeeding in doing that. But we could do even better. We all need to work together in that aim.

That is one of the reasons why the Executive and Council of IUPS have been issuing a series of outreach documents. Those outreach proposals are designed to ensure that we pursue our aims in a way in which everyone can feel involved. The first outreach document in which we outlined proposals for each member society to nominate IUPS representatives was well received around the world, and two societies in particular engaged with us in critical and constructive dialogue on how to develop the idea. We have listened to those criticisms and, in response, have developed the idea into more concrete proposals for the future governance of IUPS.

The main development is that the voting Representatives should form a Board of the General Assembly, a body that would continue to function on behalf of the General Assembly between Congresses. The Board would be vested with important powers, including determining half the membership of the Nominating Committee that makes proposals for future Officers and Council members and the authority to bring proposals to the Executive Committee and Council. The full details are outlined in the new version of the outreach proposals now available on the website and already have been circulated to members. IUPS Council

feels sure that these changes will introduce a greater feeling of democracy within IUPS and produce a more active and comprehensive search for future officers and council members.

In addition to the main outreach document, we have produced a new paper on the benefits of IUPS membership. This was initially produced by the Membership Committee and developed by Executive and Council. We hope this will help the Membership Committee in seeking to extend IUPS membership around the world.

We have produced a document on the utility of IUPS, concerned with its aims and objectives and how it seeks to achieve these. Some of that document was based on the Report of the Long-Range Planning Committee.

Finally, the website is worth visiting for two other items. Marjan Rupnik (council member responsible for the website) has added two items.

First, under the section *All IUPS Congresses*, there is a link to the short history of international meetings between 1889 and 1968. The pdfs were scanned from the History of the International Congresses of Physiological Sciences 1889–1968 by W. O. Fenn. There is an update through to 1989, written by David Whitteridge, which we may also scan for the website. We hope this may stimulate members with a longer corporate history to dig into the reports from more recent meetings to complete the history project up to Kyoto 2009.

Second, under the section IUPS projects, Rupnik has made the teaching workshops more accessible. This material is from the book *Documenting Thirty Years of Physiology Education Workshops* by A. J. Sefton and P. Hansen.

As you can see, your Council and its Executive Committee are very busy. It is a pleasure to serve the international physiological community in this way. ■

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