

## Editorial

### Editor-in-Chief's introduction

*The Journal of Experimental Biology* caters for the work of scientists that are curious about the way animals 'make a living' and hence successfully occupy specific ecological niches. Our interest ranges from ant navigation, through the scaling of metabolism, to the fine-level molecular adaptations that allow animals to function in diverse environments. Our broad focus encompasses all disciplines of physiology and species from all animal phyla. The focus of the journal, therefore, is on research that explores and explains the mechanisms by which any physiological feat observed in the animal kingdom is accomplished.

The rise of molecular biology, and more recently of genomic science and systems biology, has posed a serious challenge to classical 'comparative physiology'. This is not only because funding has become increasingly difficult to obtain for the study of 'strange' species living in 'esoteric' environments but also because these new conceptual areas require completely different technological approaches and a range of new informatic and analytical skills capable of dealing with very large datasets. Initially, it looked as if comparative physiology would not lend itself easily to molecular or 'omics' scrutiny, a notion that was based on the specificity of gene sequences, which were expected to vary importantly among species. We have since learned that much of the coding part of the genome is highly conserved and, hence, most types of molecular tools and probes can be adapted for use across species. This development has not gone unnoticed by comparative physiologists. Many started to be attracted by the enormous power of the genomics approach to unravel the subcellular mechanisms that enable cells, tissues and organisms to perform specific functional tasks in animals facing difficult environmental situations. On the other hand, molecular biologists are beginning to realize that the cellular phenomena of signalling, transcription and translation, which they could dissect so elegantly, are not an end in themselves but are used by animals in the concerted effort for survival under a wide variety of environmental conditions.

This special issue of *The Journal of Experimental Biology* should make the point that the time has come for comparative physiology to embrace molecular biology, genomics and

systems biology, and *vice versa*. We have asked eminent scientists from both a genomics and a comparative background to review their perspective of 'comparative molecular physiology'. We have collected their reviews in this issue, asking them to abstain from using field-specific jargon, so as to achieve the interdisciplinary 'cross-talk' we seek. To this end, we have also provided a Glossary of terms used in the articles (pp. 1492–1496). We have included reviews on the use of statistics and modelling procedures, as most of the high-throughput technologies produce enormous data sets that cannot be approached with *t*-tests, ANOVAs and simple regression techniques.

We believe that the Journal must publish significant research using genomically enabled approaches. In particular, we are interested in work that uses genomic tools in a system-wide context, explaining animal function down to the level of its integrated functional elements, the genes and proteins. To this end, we are proud to announce that Julian Dow has joined *The Journal of Experimental Biology* as an Editor specializing in manuscripts with 'omics' content.

Julian Dow comes from a chemistry background but changed disciplines to do his PhD on ion transport in locusts with Simon Maddrell at the University of Cambridge (1977–1981). He was then awarded the prestigious Harkness Fellowship with William Harvey, another current Editor of JEB, at the Temple University, Philadelphia. As a lecturer at the University of Glasgow, Julian turned his attention to neurosciences and became acquainted with molecular biology and *Drosophila* genetics. He realized that integrative biology was just as important as reductionism and has since focussed on combining classical physiology with genetics, molecular biology and functional genomics. Julian currently works as a Professor at the University of Glasgow, Division of Molecular Genetics. We are very happy to welcome Julian, as a JEB 'old-timer', to the team of Editors of the journal, and hope that his particular focus and strength will encourage submissions using molecular techniques for investigating physiological phenomena of interest.

**Hans Hoppeler**

doi:10.1242/jeb.006387

## Guest editors' introduction

Bioscience in this new century is experiencing some particularly dramatic technological and conceptual advances, many of which hold outstanding promise for biologists working in comparative, integrative and evolutionary physiology. These advances have their early origins in the development of molecular genetics during the 1970s and 1980s, when the basic techniques for generating recombinant DNA and for sequencing DNA were established. But it was the industrialisation of DNA sequencing in the 1990s that had the greatest impact, culminating in the production of the human genome sequence. For the first time, these projects established the number and diversity of protein-coding sequences in a growing range of representative species. In turn, this empowered a range of so-called 'post-genomic technologies' to generate a genome-wide determination of transcript and protein abundances and the adoption of discovery-led, open screening approaches to understand function.

Thus, biologists of the 21st Century are now faced with the dual problems of dealing with enormous lists of partially described genes and of the rapid emergence of highly complex and extensive datasets describing the changes in gene and protein expression during responses of all kinds, including disease and stress from a suite of environmental factors. Fortunately, the solutions to these problems can be found in the disciplines of advanced statistical analysis, and pattern searching or clustering techniques, which have been used to good effect by physicists and engineers.

But a far greater conceptual problem comes in seeking to understand how these complex systems of thousands of genes and proteins work together to generate the phenotype that physiologists seek to understand and explain. The idea of complex adaptive systems (or complexity science) offers a theoretical framework for understanding the structure and function of systems ranging from the World Wide Web and the stock market to aspects of human social behaviour. Recent work shows that biological systems, including metabolic pathways and gene regulatory interactions, behave in the same manner as man-made systems, with an emergent orderliness and an in-built robustness that are products of their system-wide structure. These similarities between living and non-living systems suggest that general laws of complex systems operate to generate a stable form of complexity and that progress in dealing with biological complexity will undoubtedly draw on the more general fields of complexity science and systems theory.

Another important contribution to understanding is emerging from the development of mathematical descriptions that can be embedded in multi-scale and/or multi-physics computational models of physiological systems. These frameworks provide the capacity to integrate processes spanning the many spatial

scales present in biological systems into complex emergent properties. 'The Physiome Project' is an international and open collaboration that seeks to develop comprehensive predictive and mechanistic models of whole-organ behaviour, rather than solely an empirical link between knowledge of the underpinning genes and proteins and phenotypic function.

Despite the evident difficulties in implementation, these new approaches may add great power to the more traditional style of experimental analysis in physiology. Indeed, the reverse is also true, that pitching a research problem within an appropriate comparative and integrative context can make the new style approaches far more penetrating and relevant to a host of contemporary research problems. The papers presented in this special issue of *The Journal of Experimental Biology* are designed to offer a window into the new world of post-genomic science and systems-based biology, indicating not only its conceptual underpinnings but also some methodological implications. The papers also show how these same techniques and approaches can be adapted to address more conventional questions in comparative and integrative physiology, either from developing genomic resources for species of interest or by leveraging the opportunities offered by working on the so-called 'genomic' model species.

The papers also point to newer developments of revolutionary potential arising out of the current post-genomics and systems approaches that will again transform biology. Thus, the recent discovery of very large numbers of RNA products that are unrelated to protein-coding transcripts and that arise from so-called 'junk' DNA may provide the basis for generating the incredible levels of biological complexity that we take for granted. The discovery of this phenomenon and its functional implications are expertly considered in these papers. Another new development is the rapid deployment of a new range of ultra-high-throughput sequencing technologies that bring industrial scale operations within the reach of a university campus, or even a single research group.

The unavoidable implications in adopting these new opportunities are that, firstly, the training of future research biologists will need to be reorganised to adopt a wider range of skills, many of which come from other disciplines, such as computer sciences and theoretical physics. Secondly, further developments in dealing with large-scale systems and complexity will require a much more collaborative spirit between biologists and these non-biological disciplines. As these new opportunities are realised, we predict the occurrence of a 'golden era' of major breakthroughs in comparative, integrative and evolutionary physiology.

**Andrew Cossins**

**George Somero**

doi:10.1242/jeb.006346