An essay published in 2004 has the perceptive heading: “Mathematics Is Biology’s Next Microscope, Only Better; Biology Is Mathematics’ Next Physics, Only Better” [1]. This title neatly summarises the developmental path taken by biology over the past 30 years or so. It emphasises both the exciting role that mathematics and statistics are adopting in the identification and quantification of wholly unimagined and entirely new realms within biology as well as the repercussions biology is precipitating in the prompting of new developments in mathematics and statistics. The title also underlines the intensifying interlinking of numerous disciplines: the complexity of biological and clinical phenomena requires increasingly sophisticated, specialised and discipline-transcending expertise to complete a technical workflow comprising experimental design, generation and analysis of data, interpretation of results and subsequent transparent reporting (Fig. 1).

Natural systems are highly complex and challenging to model, as variables are frequently random, volatile and even contradictory. Hence the drive to constrain parameters by developing simplified model systems such as organotypic or tissue cultures that are less complex but more defined and so can be more easily controlled. Such systems are of course still highly intricate, and so invite further reductionism in the shape of engineered systems that include a few components in a test tube and eventually result in mathematical modelling, which provides ultimate control but may no longer reflect the complexity under initial investigation.

For many years, biological data were descriptive and even the introduction of cell and molecular biology techniques did not have an impact on the publication of data that were small-scale, descriptive and univariate. Results were often referred to as “semi-quantitative” and whilst having the appearance of being quantitative, they usually were based on highly variable, subjective interpretations of data images. The analysis of RNA by northern blotting, of proteins by western blotting or the comparison of mRNA levels by reverse transcription-PCR and subsequent gel analysis readily come to mind. However, the development of increasingly sensitive, specific and high throughput techniques such as real-time quantitative PCR (qPCR), microarrays, digital PCR (dPCR), next generation sequencing (NGS) and mass spectrometry has led to their use in a wide variety of applications in a broad range of biological and clinical subjects. This continuous expansion of molecular technologies has swiftly resulted in a demand for more rigorous quantification of nucleic acids, proteins and small molecules in, for example, molecular diagnostics [2]. However, compared with a qualitative yes/no result, reliable, reproducible and biologically relevant quantification poses significant problems in terms of sample preparation and quality control, assay design, optimisation and validation, collection of data, their analysis and, importantly, prudent and transparent reporting [3].

Quantitative experiments investigating physiology frequently involve the investigation of individual cellular processes either by

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**Fig. 1.** Interpretation and publication of quantitative results requires interaction between a wide range of scientific disciplines. The diagram does not imply a linear relationship between the disciplines and every stage of the experimental process is benefiting from cross-discipline interaction.

[http://dx.doi.org/10.1016/j.bdq.2014.09.001](http://dx.doi.org/10.1016/j.bdq.2014.09.001)

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studying the dynamic interplay of distinct cell types in various tissues or analysing a small number of single cells. In either case, error may be introduced, and this must be both captured and, where possible, reduced using appropriate experimental design and normalisation strategies. Ultimately, the generation of quantitative multivariate measurements enables the application of statistical tests and correlation analyses that allow scientists to report detailed information about their own experiments in a more prescribed and systematised manner.

Systems biology generates prodigious amounts of complex, integrated data from the fields of functional genomics, proteomics and metabolomics and has started to emerge as a driving force at the interface of biology, biochemistry, mathematics, computing engineering, and physics [4]. It has become accepted, albeit also widely ignored, that the complexity of a biological organism cannot be described by a static listing of even the most well-characterised components such as DNA sequence, genetic and epigenetic modifications, levels of coding and noncoding RNAs, proteins and their many isoforms or the range of metabolites being synthesised or entering individual cells. Instead, it is the temporal, special and dynamic arrays of interactions of each one of these constituents that determines cell responses and, ultimately, an organism’s behaviour. Consequently, an understanding of complex biological systems requires the extensive support of computational tools [5] together with agreed standards to enhance information exchange, results compatibility and mutual understanding [6–8].

There are numerous issues relating to the entire quantification workflow that are difficult to standardise and automate. These include variables such as the wide variety of sample types that can be tested, the complex steps involved in sample preparation and, not least, a frequent switch to novel technological platforms leading to inconsistent results as well as complex post-testing analysis methods [9]. Sample preparation affects the reliability of PCR [10], the sensitivity and robustness of mass spectrometric analysis [11] and the accuracy of protein–DNA interaction maps used for chromatim immunoprecipitation followed by high-throughput sequencing (ChIP-seq) [12]. Similarly, ELISA measurements can be compromised by technical issues [13], interfering endogenous and exogenous effects [14] or measurement methodology [15], with significant consequences for diagnosis and or clinical decision-making. One consequence of these challenges is many omics assays are insufficiently sensitive or specific to meet clinical needs [16]. Worse, most biomedical research cannot be independently replicated [17], a finding consistent with an estimate that around 85% of research funding is wasted [18].

The need for more rigour has been recognised for a long time, with detailed discussions published regarding the reliability of results obtained from qPCR [19,20], dPCR [21–23] or microarray analyses [24,25]. These have resulted in a range of proposed solutions aimed at improving the quantitative nature of such technologies, for example recommendations such as the MIAME [26], MIQE [27–28] and dPCR MIQE [29] guidelines. Unfortunately there is a wide disregard for these recommendations, an attitude characterised by one “scientist”s comment that compliance with PCR guidelines was being “too dogmatic”. It has also become apparent that unless proper guidance is accorded to NGS [30–33], this powerful technique will join all the others and also go powerfully wrong when not appropriately used or reported.

Discussion of the many methods in use today, as well as their advantages and disadvantages needs to be coupled to improvements and innovations that can only arise from the interplay between different expertise, ideas and communication. These must thrive in a milieu that adapts the scientific rigour of mathematics, statistics, chemistry and physics whilst retaining the versatile and dynamic characteristics of biological scientists. 

**Bioluminescence Detection and Quantification (BDQ)** is an open access, peer-reviewed international journal dedicated to championing excellence in molecular study design, measurement, data analysis and reporting. Its focus is on the application of qualitative and quantitative molecular methodologies to all areas of clinical and life sciences. The journal has two main aims:

- to provide a forum for discussion and recommendation of guidelines designed to improve the accuracy of molecular measurement, its data analysis and the transparency of its subsequent reporting;
- to publish molecular biology based studies that adhere to best practice guidelines, both current and future.

The deliberately broad scope of the journal covers clinical areas such as cancer, epigenetics, metagenomics, and infectious diseases as well non clinical subjects including environmental, microbiology and food science. BDQ revolves around the common theme of promoting excellence in molecular measurement and its data analysis. It will serve as a repository for sharing key findings across what may otherwise be disparate specialties.

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Available online 10 September 2014