ON THE ROLE OF MATHEMATICS IN BIOLOGY

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It has been widely acknowledged that a key ingredient in the flourishing of Physics in the XX Century was the use of sophisticated mathematical techniques. In consequence, the term "Mathematical Physics" has enjoyed an unrivalled prestige for most of that period, and monographs like Courant and Hilbert´s "Methods of Mathematical Physics" have been acclaimed as milestones by mathematicians and physicists alike.

It is worth noting that, at about the same time, an attempt was made to establish Mathematical Biology as a discipline. However it did not succeed (1). This initiative was not without precedents. For example, the flow of blood in veins was uppermost in Euler´s mind when he performed his seminal work on fluid mechanics (2). Slightly earlier, theoretical models to describe the spread of diseases had been discussed by Bernouilli (3), but they did not resurface until the XX Century (4). In spite of these successes, biologists (and, more generally, life scientists) have remained sceptical about Mathematics. The excessive complexity of living organisms and the related issue of variability in biological systems have presented formidable obstacles to mathematical modelling. In order to make progress, the mathematician is usually forced to make a large number of simplifying assumptions. Although this reductionist strategy has proved to be successful in Physics, it has met with serious reservations from biomedical practitioners.

In spite of this, there is some evidence to suggest that Mathematics is starting to make significant inroads in Biology and Medicine. A possible reason for this is that the concept of modularity is pervading these disciplines. Using a modular approach, a complex biological system can be viewed as an aggregate of relatively simple (but inter-related) modules, each of which can be studied in isolation using mathematical models. At the same time the system derives part of its identity through the coupling of the constituent modules (5). Thus Mathematics is gradually being incorporated into the Biomedical sciences as an efficient auxiliary tool, much as has happened with Crystallography with respect to Physics and Chemistry - or Biology for that matter. For instance, the simulation of differential equations has proven instrumental in uncovering key regulatory loops in Developmental Biology (6, 7). Our current computing power makes it relatively easy to handle the corresponding simulation packages, a fact that would certainly have shocked Turing, who, in his celebrated 1952 paper, complained that even simple nonlinear systems remained beyond the reach of the analytical and computing knowledge of his time (8).

However, in pursuing its relationship with Biology, Mathematics (or rather the mathematician) faces some challenges. To begin with, it may well be that the word ¨Mathematics¨ will be lost when naming the **new** discipline which eventually incorporates it, be it Systems Biology, Synthetic Biology, or some other denomination that arises. As a matter of fact, any of these terms has received a better reception from biologists than Mathematical Biology or Biomathematics ever obtained. Of course, we could see this issue through Juliet´s eyes, and say:

What is in a name?
That which we call a rose
By any other name would smell as sweet.

In this case, however, an important question is at stake: is it possible to combine Mathematics and Biology in a common discipline that will be accepted and respected by both communities? For many centuries, a distinctive aspect of Mathematics has been the insistence that rigorous proofs are the essence of mathematical arguments. However, proofs are notably absent in most published articles on Mathematical Biology. This is often seen as related to the fact that most of the mathematics used in these works (as for instance the numerical simulation of systems of ordinary differential equations already mentioned) are considered standard fare by many distinguished mathematicians, including a good deal of the leading figures in their fields.. Actually, to many mathematicians, the quality of a work is measured by the simplicity in the formulation of the problem, the difficulty of the analysis, and the rigour displayed in its solution. This is how Fermat´s problem (already solved) and Riemann´s conjecture (yet to be proven) achieved celebrity. However some of these criteria (simplicity in the problems, mathematical rigour in the proofs) are not so easily accepted by biologists. According to this view, Mathematical Biology might contain too much Mathematics for biologists, and too little for mainstream mathematicians.

A sharp contrast thus arises with the situation concerning Physics in the last century, where new developments often required (or gave raise to) significant mathematical progress, so that both sciences felt invigorated by their mutual interaction: think, for instance, of the cross-fertilization between Functional Analysis and Quantum Mechanics. This may, perhaps, help to explain why Mathematical Physics is highly-regarded by the two communities involved, whereas Mathematical Biology is far from eliciting a similar consensus.

It may seem that we have reached a crossroads. Mathematics can probably continue to help Biology (even at an increasing pace) by focusing, above all, on modelling, computing power and statistical validation. In this way, outstanding scientific results can be obtained, that would eventually contribute to Biology achievements. This is what happened with what is usually considered as the most significant biological achievement of the XX Century, identifying the structure of DNA. This work was essentially done by Physicists, Chemists and Crystallographers, using the techniques with which they were familiar. But a different situation might also take place. Namely, in the future Biology and Medicine may provide Mathematics with challenges analogous to Fermat´s problem. While at present this is mere speculation, there has already been evidence of effective feedback from Biology into Mathematics. For instance, the modelling of epidemics and the study of signal propagation in nerves have been driving forces behind the robust growth of differential equations and studies of dynamical systems in the XX Century. Also, many developments in Statistics that took place during the same period were stimulated by biological research, with stochastic analysis in particular being boosted by (and providing insight into) the Life Sciences in general. Thus the stage now seems to be set for exciting events to happen: only time will tell if and when they come.

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