A clash of two cultures

Physicists come from a tradition of looking for all-encompassing laws, but is this the best approach to use when probing complex biological systems?

Evelyn Fox Keller

Biologists often pay little attention to debates in the philosophy of science. But one question that has concerned philosophers is rapidly coming to have direct relevance to researchers in the life sciences: are there laws of biology? That is, does biology have laws of its own that are universally applicable? Or are the physical sciences the exclusive domain of such laws?

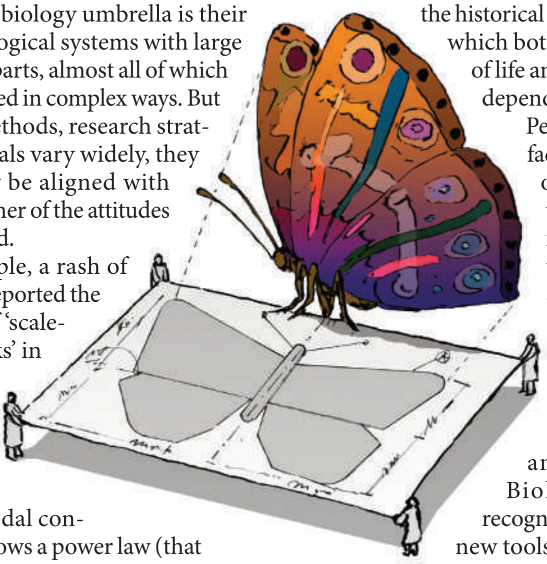
Today, biologists are faced with an avalanche of data, made available by the successes of genomics and by the development of instruments that track biological processes in unprecedented detail. To unpack how proteins, genes and metabolites operate as components of complex networks, modelling and other quantitative tools that are well established in the physical sciences — as well as the involvement of physical scientists — are fast becoming an essential part of biological practice. Accordingly, questions about just how much specificity needs to be included in these models, about where simplifying assumptions is appropriate, and about when (if ever) the search for laws of biology is useful, have acquired pragmatic importance — even some urgency.

In the past, biologists have been little concerned about whether their findings might achieve the status of a law. And even when findings seem to be so general as to warrant thinking of them as a law, the discovery of limits to their generality has not been seen as a problem. Think, for example, of Mendel's laws, the central dogma or even the 'law' of natural selection. Exceptions to these presumed laws are no cause for alarm; nor do they send biologists back to the drawing board in search of better, exception-free laws. They are simply reminders of how complex biology is in reality.

Physical scientists, however, come from a different tradition — one in which the search for universal laws has taken high priority. Indeed, the success of physics has led many to conclude that such laws are the *sine qua non* of a proper science, and provide the meaning of what a 'fundamental explanation' is.

Physicists' and biologists' different attitudes towards the general and the particular have coexisted for at least a century in the time-honoured fashion of species dividing their turf. But today, with the eager recruitment of physicists, mathematicians, computer scientists and engineers to the life sciences, and the plethora of institutes, departments and centres that have recently sprung up under the name of 'systems biology', such tensions have come to the fore.

Perhaps the only common denominator joining the efforts currently included under the systems-biology umbrella is their subject: biological systems with large numbers of parts, almost all of which are interrelated in complex ways. But although methods, research strategies and goals vary widely, they can roughly be aligned with one or the other of the attitudes I've described.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For example, a rash of studies has reported the generality of 'scale-free networks' in biological systems. In such networks, the distribution of nodal connections follows a power law (that is, the frequency of nodes with connectivity k falls off as $k^{-\alpha}$, where α is a constant); furthermore, the network architecture is assumed to be generated by 'growth and preferential attachment' (as new connections form, they attach to a node with a probability proportional to the existing number of connections). The scale-free model has been claimed to apply to complex systems of all sorts, including metabolic and protein-interaction networks. Indeed, some authors have suggested that scale-free networks are a 'universal architecture' and 'one of the very few universal mathematical laws of life'.

But such claims are problematic on two counts: first, power laws, although common, are not as ubiquitous as was thought; second, and far more importantly, the presence of such distributions tells us nothing about the mechanisms that give rise to them. 'Growth and preferential attachment' is only one of many ways of generating such distributions, and seems to be characterized by a performance so poor as to make it a very unlikely product of evolution.

How appropriate is it to look for all-encompassing laws to describe the properties of biological systems? By its very nature, life is both contingent and particular, each organism the product of eons of tinkering, of building on what had accumulated over the course of a particular evolutionary trajectory. Of course, the laws of physics and chemistry are crucial. But, beyond such laws, biological generalizations (with the possible exception of natural selection) may need to be provisional because of evolution, and because of the historical contingencies on which both the emergence of life and its elaboration depended.

Perhaps it is time to face the issues head on, and ask just when it is useful to simplify, to generalize, to search for unifying principles, and when it is not. There is also a question of appropriate analytical tools. Biologists clearly recognize their need for new tools; ought physical scientists entering systems biology consider that they too might need different methods of analysis — tools better suited to the importance of specificity in biological processes? Finally, to what extent will physicists' focus on biology demand a shift in epistemological goals, even the abandonment of their traditional holy grail of universal 'laws'? These are hard questions, but they may be crucial to the forging of productive research strategies in systems biology. Even though we cannot expect to find any laws governing the search for generalities in biology, some rough, pragmatic guidelines could be very useful indeed. ■

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