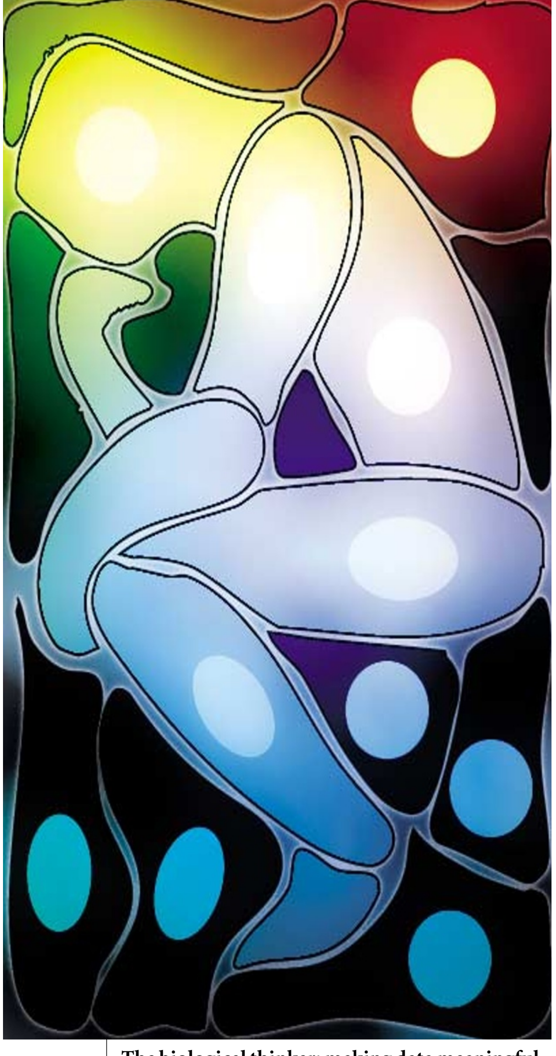
Reasoning for results

Theoretical biology

Theory needs to be embraced and to become part of the mainstream of biological research. The quality and accuracy of predictions will then inexorably rise.

Dennis Bray

Let's start on safe ground. We all agree, surely, that theory — the formulation of hypotheses — is important in biology. Techniques are essential, as is the careful collection of quantitative data. But without ideas to give them shape and meaning, those endless successions of base sequences, expression profiles, electrical recordings and confocal images are as featureless as a plate of tofu. All really big discoveries are the result of thought, in biology as in any other discipline. Allostery, genes, DNA structure, chemi-osmosis, immunological memory, ion channels were all once just a twinkle in someone's eye. And the work of most contemporary research laboratories still takes place within a framework of hypothesis, although practitioners may not always recognize this fact. As Charles Darwin once remarked: "How odd it is that anyone should not see that all observation should be for or against some view if it is to be of any service."



The biological thinker: making data meaningful.

But assuming that biological theory exists, does it therefore follow that theoretical biology is a distinct and legitimate subject? My guess is that there is less agreement on this proposal; there may even be virulent opposition to it. One of the most common arguments against it is that living systems are so prodigal, so unpredictable and, above all, so historical that any attempt at a grand theoretical framework is doomed to failure. The shape of a leaf in a forest is the product of so many chance events, not only during its growth but also in the aimless blundering of its evolution, that it is inconceivable that it could be predicted from first principles. An all-encompassing theory of biology is no more possible than a predictive theory of other large, inchoate systems, such as the weather, the stock market or London's Heathrow Airport.

Moreover, the argument goes, even in cases in which laws and patterns have been observed in living systems — as in zebra stripes, Hodgkin–Huxley equations and protein coiled-coils — these are not truly biological laws. They belong to mathematics, chemistry or physics, and reflect what living systems have in common with the non-living world, not their own unique biological characteristics.

One can argue with these views, but they are rational and worthy of debate. What is harder to understand is the irrational opposition to theory that often surfaces. Many experimentalists seem to regard theoreticians as carpetbaggers. "We spend months in the lab getting data," they say, "and then along comes some character who doesn't know how to hold a pipette and explains our results to us." Apparently, you're not licensed to theorize unless you put the time in and get the data. This is unfortunate because people are good at different things, and some really enjoy reading papers, juggling possibilities and formulating ideas, even if they can't work a pipette. It is true that certain 'biological theorists' in the past have indeed been carpetbaggers, rushing into print with ill-conceived and carelessly prepared ideas, and this gave the subject a bad name. But this is a sociological problem, not a scientific one. The cure is to embrace theoretical work and let it become part of the mainstream of biological research. The quality and accuracy of predictions will then inexorably rise.

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Returning to the chase, the term 'theoretical biology' seems to me just silly — a frozen joke, an oxymoron. Whoever coined the phrase (I'd love to know who it was) was probably being deliberately provocative by drawing parallels with theoretical physics. But although the name is misbegotten, the thing it has come to represent is healthy and growing like a weed. Surfacing briefly in a seminar the other day, I realized that I had no idea whether the traces on the screen were actual electrical recordings made in a physiological experiment or the output of a computer program. It was impossible to tell.

Computer models of action potentials, synaptic integration, heart contraction and even the movements of ions and molecules in cells are now so accurate that they can often be used as experimental objects in lieu of the thing they represent. Biologists can now design and test small genetic circuits in theory and then make them in actual living cells. It seems inescapable that, at least at the level of molecules and cells, biology is moving from an era of data-collection to one of hypothesis-driven research. Progress in this new field will be driven by informed and increasingly quantitative theories — whatever name we choose to give it. ■

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FURTHER READING

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