nature neuroscience

From CaM kinase to cognition

That neuroscience is interdisciplinary is a truism. The brain is studied at levels of analysis ranging from biochemistry to cognitive science, and considerable lip service has been given to the importance of integrative research, in these pages and elsewhere. In practice, though, good interdisciplinary work is rare, and only between certain fields do such partnerships often seem to produce significant insights. Communication between experts in different specialties is clearly part of the formula for success, but saying so only serves to push the problem back a step. What are the obstacles to productive research across traditional discipline boundaries?

At their best, interdisciplinary studies forge solid, causal links between findings from different levels of analysis. Each specialty has its own questions, techniques and explanations, and understanding how the brain works will obviously require determining the relationships among them. This is a considerable challenge, and merely studying the same problem at different levels is not sufficient to provide an integrated view. For example, consider schizophrenia, which has been intensively studied by such diverse approaches as genetics, pharmacology, neuroanatomy, functional imaging and psychology. Yet the accumulation of information in each of these domains has not led to an overall understanding of how the phenomena are related. We know, for instance, that antipsychotic drugs act on dopamine receptors to alleviate behavioral symptoms, but without a detailed understanding of the intervening steps—how a drug affects cellular physiology, which in turn affects circuit function, leading to the change in behavior—the number of plausible interpretations of this finding is so large that it yields only limited theoretical insight, despite its obvious practical value. This is a general problem in trying to link molecular and behavioral findings; unless these connections can be filled in, such work produces little more than a catalog of phenomenological relationships.

Perhaps it will be most productive, at least initially, to build bridges between adjacent levels of analysis. This approach provides another, more subtle advantage as well. Related fields often share an important understanding that people working in very different areas lack: a common view of what constitutes an 'answer' to a scientific question. Understanding what sorts of explanations are satisfying to experts in another field can be a more challenging task than learning specialized terminology or new technical approaches. Differing views of science can interfere not only with communication between collaborators, but also with publication, because getting interdisciplinary work through peer review typically requires convincing referees in several different fields that the work makes a substantial contribution. It has been argued that journal editors should simply be more lenient about the degree of progress in any one area when the paper covers a broad territory, but if referees find the paper unsatisfying, it will probably be no more compelling to readers.

Not all barriers to interdisciplinary research can be attributed to philosophical disagreements. Even if scientists appreciated one another's viewpoints with telepathic precision, studies that cross discipline boundaries would remain vulnerable to problems that are less frequent within traditional fields. One issue is that the techniques of one field may be ill-suited to solving problems at another level. Interdisciplinary success often requires acquiring new technical expertise, directly or through collaboration, yet the path of least resistance is to make do with the tools that are already available. A more serious problem is that many interdisciplinary studies lack focus or depth. It is rarely sufficient to combine isolated observations from several different fields with a plausible story of how they might be related. Even if a study contains a large number of diverse experiments, that matters little if the results leave open a substantial possibility that the conclusions are incorrect. Many such studies are oversold because the authors have not come to grips with the fundamental issues, and are instead trying to market their work under the trendy banner of an 'interdisciplinary approach'.

To take a concrete example, there is a whole genre of papers that describe studies of hippocampal long-term potentiation (LTP) and water maze performance in a knockout mouse. Is such work intended to explore the molecular mechanisms of synaptic plasticity or the link between LTP and learning? In many cases, the findings give only superficial insight into either problem. Removing a gene and showing an LTP phenotype does not by itself clarify whether the corresponding protein is directly or indirectly involved in synaptic plasticity. Similarly, the precise relationship between synaptic plasticity in hippocampal slices and memory remains unclear, perhaps because the role of the hippocampus varies depending on which neural circuits are activated by different behavioral tasks and conditions. Increasing molecular sophistication in targeting genetic manipulations to particular brain regions and developmental time points may help to address some of these concerns, but at least so far, knockout studies have not provided any shortcuts to a well-developed theory of the role of hippocampal synaptic plasticity in memory.

What practical steps can be taken to promote better interdisciplinary work? A partial solution might be to improve the infrastructure for communication, for instance by setting up meetings, journals or institutes focused on interdisciplinary dialogue. Another possibility is for funding agencies to support sabbaticals and collaborations across fields to facilitate the exchange of technical expertise and scientific viewpoints. In any event, it seems clear that building links between fields that can be related at a mechanistic level will be more rewarding in the long run than simply accumulating lists of interdisciplinary phenomenology.