factor(s) provided by the Schwann cell during the migratory phase is necessarily the same as that provided by the target. The critical point is that the development of target dependence of neurons is more a change in the behavior of Schwann cells than a change in the behavior of neurons or targets.

In summary, data obtained over the past few years indicate that Schwann cells can express NGF receptors and make NGF. It appears that axonal contact is the critical signal that suppresses their expression. Therefore, the simple two-cell model of NGF action shown in Fig. 1 may apply only to the 'mature' stable PNS. We suggest that during development and after neuronal injury, a third cell type, the Schwann cell, is an active participant in the trophic maintenance of NGF-responsive neurons, at least partly owing to its ability to express NGF receptors and to produce NGF. We presume that other trophic factors will be shown to function via the Schwann cell in similar ways.

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perspectives

The significance of neuroscience for philosophy

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The ground is shifting under the traditional approaches to problems in the philosophy of mind. Earlier doctrines concerning the independence of cognition from the brain now appear untenable. As neuroscience uncovers more about the organization and dynamics of the brain, it becomes increasingly evident that theories about our nature must be informed by neuroscientific data. Consistent with this progress, we may expect that philosophical problems about the mind will be productively addressed and perhaps radically transformed by a convergence of neuroscientific, psychological and computational research.

For most of its long history, philosophy encompassed a wide range of problems, including the nature of space, time and the heavens, and the principles governing motion, life, the origin of order, and the nature of matter. Additionally, philosophers addressed problems about specifically human phenomena: the nature of knowledge, learning, consciousness, free will, and the self. As specific problems succumbed to scientific methods, and as testable theories evolved to explain certain phenomena, special disciplines branched off to call themselves natural philosophy. Thus, one by one, astronomy, physics, chemistry, biology, and experimental psychology left the fold to become distinct scientific disciplines, and by the end of the nineteenth century, the name 'natural philosophy' was quietly dropped in favour of 'natural science'. Philosophy, as pursued in the twentieth century, has been dominated by issues in logic and mathematics, and by whatever problems had yet to become the focus of fruitful empirical research. In particular, questions about the mind endured as largely intractable to science.

Nevertheless, by the 1970s, some philosophers began to envisage a scientific future for the traditional problems in the philosophy of mind. The initiation of this shift in view was made possible mainly by W. V. Quine[1] and independently by Paul Feyerabend[2], who undermined the conventional wisdom that philosophy was an a priori discipline whose truths were accessible by non-empirical methods, and whose discoveries supposedly laid the a priori foundations for any science. In contrast with the contemporary consensus, Quine and Feyerabend saw philosophy as essentially continuous with science and, like science, open to revision as a result of empirical discoveries and theoretical progress.

They considered the philosophical enterprise to be different from the scientific only in panoramic scope, integrative ambitions, and in embracing problems that are still too ill-defined and too mysterious to be addressed by existing sciences. Philosophy, in their view, does not differ from science either in the status of its theories or in its ultimate dependence on empirical data. It is just the crucible in which we struggle to find some useful conceptual expression of the problems that will help launch them into the realm of systematic empirical research. This view is known as naturalism and it advocates that metaphysics and epistemology should no longer be isolated from the rest of science. Though naturalism is still a minority view, it has exerted a major influence on philosophy in North America.

Within this naturalistic framework, perhaps the most fundamental point for philosophers of mind was that modern science rendered mind–body dualism highly implausible. Dualism is the theory that mental phenomena, such as perceiving, thinking, deciding and feeling are not phenomena of the physical brain at all. Rather, they are processes of a unique, non-physical substance – the mind or the soul – that interacts with the brain. Descartes, and Plato before him, were unremitting dualists, and in the modern period, dualism has been defended by neuroscientists such as Eccles[3] and Dykes[4], and by philosophers such as Swinburne[5] and Jackson[6].

Cartesian dualism

The implausibility of dualism derives from four main sources: (1) it is inconsistent with evolutionary biology and modern physics and chemistry[7]; (2) mental phenomena are systematically dependent on neurobiological phenomena, such as chemical changes in the brain, lesions of pathways, and so on[8]; (3) computer science shows how it it possible to achieve very complex results by means of the appropriate organization of very simple units, which undermines the Cartesian idea that a non-physical intelligent homunculus is necessary[9]; and (4) there is a complete absence of any positive evidence for a non-physical substance, a lack of any genuine explanation of how the two substances (mind and brain) might interact, and there simply is no distinctly dualist methodology or testable theory. One possible source of positive evidence for dualism – parapsychology – has so far notoriously failed to produce any robust data that could lend support to the dualist hypothesis, though there are many amazing anecdotes, plentiful results displaying miniscule statistical deviations, and a distressing abundance of flawed methods and outright fraud[10]. Notwithstanding its many difficulties, predilection, if not argument, for dualism remains remarkably widespread.

Since on balance physicalism appears to be more probable than dualism, in the sense that mental phenomena are probably phenomena of the physical brain, the traditional mind–body problem has been replaced by a different set of problems posed within the physicalist framework. The contemporary problems in the philosophy of mind concern, among other things, the relations between experimental psychology and neuroscience, and the best research strategies for understanding the nature of perception, cognition, reasoning, consciousness, and language-use. A central question, therefore, is whether psychology will reduce to neuroscience. More exactly, the question is whether it will be possible to find neural mechanisms for psychological phenomena and thus whether we should expect neurobiological explanations of psychological processes. The answers to these questions will affect quite profoundly the design and motivation of wider research programs.

Opinion on these questions is very diverse. The most salient disagreement is between those who regard psychology as autonomous with respect to neuroscience[11,12], and those who envisage the co-evolution of high and low level theories, with the eventual unification of psychology and neuroscience into something like 'cognitive neuroscience'[13].

The autonomy of psychology

Despite adherence to physicalism, proponents of the autonomy thesis argue that neuroscience is, by and large, irrelevant to determining the nature of cognition. The fundamental idea supporting this conception is that cognitive psychology and neuroscience address completely different levels, and that facts about such matters as connectivity patterns of cells are at the wrong level to inform cognitive hypotheses. The cognitive level is characterized by analogy with the higher levels of function in a digital computer. Thus Fodor[11] and Pylyshyn[12] see cognition as analogous to the operations of a computer program, while they take the brain to correspond to the implementation – the computer hardware. Just as it is fruitless to attempt to understand features of a word processing program by examining the wiring of one's IBM, so, they argue, it is fruitless to attempt to understand cognition by looking at the brain. David Marr[14], also drawing on the computer metaphor, characterized a three-part division of levels – the level of task analysis, the level of the algorithm, and the level of implementation. He then argued that analysis of the higher levels was largely independent of the lower levels.

From this conceptual foundation, Fodor and Pylyshyn made the further claim that representations at the cognitive level have an irreducibly semantic dimension and are related by virtue of logical properties. By contrast, events at the neurobiological level lack semantics and are only causally related. In their view, the higher levels must be understood in their own terms, and cannot be explained in terms of neurobiological processes – hence the irreducibility of the higher level to the lower.

The semantic dimension is exemplified in psychological states such as beliefs, which are always complex representations that are meaningful and refer to objects. Thus, consider Ronald Reagan's belief that 'the Contras are worthy of support'. The sentence specifying what Reagan believes has a certain structure and composition; its parts ('the Contras', 'are worthy of support') are meaningful and can occur in other contexts such as 'the Contras do not want to negotiate with the Sandinistas'. Reagan's representations, therefore, have meaning, composition, and logical relations[15]. In brief, the autonomy of cognitive psychology is alleged to be unavoidable because cognition is mainly a matter of manipulation of meaningful representations at the program level.

Although many philosophers and psychologists do not accept the Fodor–Pylyshyn package in its entirety, selected themes in their approach are widely espoused and defended, and the prevailing sentiment is rather firmly against reductionism[16,17] in the limited sense that entails explainability. There is still substantial sympathy with the underlying conviction that very little can be learned about cognitive processes by studying the brain.

Convinced that to ignore the brain is an unrewarding strategy, some philosophers of science have explored the reductive possibilities from a different and overtly biological perspective[13,18–22]. This has entailed reviewing the meaning–logic model as the paradigm for representations and computations[22], devising an adequate account of what reduction actually is[19–21], and critically examining the propriety of the computer metaphor and the doctrine of levels[23]. Because of its pervasive influence in both philosophy and psychology, the doctrine of levels will be the main focus of the following discussion.

Co-evolution of psychology and neuroscience

Thinking of the brain as the implementation of cognitive programs is right in a limited sense, inasmuch as it is the brain that processes and stores information, perceives, plans, etc. However, there is a deeper sense in which it is misleading. When we measure Marr's three 'levels of analysis' against levels of organization in the nervous system, the fit is poor and confusing at best. In nervous systems, there are different scales of organization and structure: molecules, membranes, synapses, neurons, circuits, nuclei, and systems. At each of these structurally specified levels, we can raise the computational question: what does that organization of elements do? The multiplicity of levels of structural organization implies that there are also many levels of implementation, each with its own task description and 'algorithm'[23].

Moreover, the same level can be viewed computationally (in terms of its functional role) or implementationally (in terms of the substrate in which the function is implemented), depending on what questions you ask, and from which perspective you ask them. For example, from the point of view of communication between distant areas, the details of how an action potential is propagated might be considered implementation, since it is an all-or-none event and only its timing carries information. A different membrane chemistry might serve just as well. However, from a lower structural level – looking at ionic distributions – the action potential is a computational construct, since its regenerative and repetitive nature is a consequence of the global non-linear interactions between several different types of channels distributed over the spatial extent of a long neuronal process. Neither implementation nor computational defines a single, monolithic level, and hence Marr's simple three-way division of levels of analysis needs revision[24].

Reconceiving levels in this way invites reconsideration of the idea of 'the cognitive level'. From a neuroscientific perspective, some cognitive effects may be the outcome of interactions at the local circuit level (e.g. aspects of early vision, such as binocular depth processing), others may reflect processing at the systems level (e.g. holding information in short-term memory) or the level of nuclei (perhaps aspects of sensorimotor control). Talking of *the* cognitive level, in the singular, thus looks empirically unsound. In order to understand the way the functional effects are produced and how integration of various levels is achieved, it will be necessary to consider both psychological and neuroscientific data.

Two very different issues are typically combined in the doctrine of independence of levels. There is a purely formal issue concerning independence of algorithm from implementation. The point is that an algorithm specifies a formal procedure, but does not stipulate the physical properties (transistors, vacuum tubes, sodium channels or whatever) of the machine on which the procedure may run. Consequently, a given algorithm could be implemented in very diverse physical systems. However, this observation concerning formal independence has sometimes been taken as implying something much stronger, namely that discovering the computational principles used by nervous systems will be independent of understanding the micro-organization[13]. This interpretation has appeal, since if true, it would free us from the travails of investigating nervous systems.

Evidently the inference is fallacious, for the purely formal point cannot address the methodological question of how best to discover what computational strategies the nervous system acutally uses. On the contrary, current research suggests that considerations of architecture play a vital role in the kinds of algorithms that are devised, and the kind of computational insights available to the scientist[25]. Knowledge of the micro-organization of the brain is a rich source of insight into how it performs high-level functions. Because computational space is so vast, neuroscientific constraints on theory construction are essential.

The independence doctrine is also undermined by the observation that algorithms are not computationally indifferent to the architecture. Some algorithms that fall gracefully onto a parallel, analog architecture are handled only slowly and clumsily by a computer with a serial, digital architecture[26]. Different implementations display enormous differences in speed, efficiency, and elegance, and such considerations will have played a role in the evolution of nervous systems. Knowledge of brain organization, far from being irrelevant to the cognitive project, is indispensable for devising likely and powerful algorithms.

How representations about things in the abstract can be meaningful is certainly very puzzling, but here too a biological perspective should be fruitful. Representational capacities must have evolved in the context of natural selection and pressure for improved sensorimotor control. One research strategy may be to defer theorizing about linguistic representation until our knowledge of more basic kinds of representation has improved. A related strategy is to explore representation in simpler neural networks, and thus to discover how basic problems concerning planning, imaging, choosing, and using internal states rather than current stimuli to guide behavior were solved during evolution[27]. From a biological point of view, the fundamental semantic problem is how nervous systems interact with the world to produce adaptive, intelligent behavior[28]. Once we determine the basic principles for network representation we can begin to address the more complex problem of representation by language.

Given a co-evolutionary strategy, theories at all levels can inform and correct theories at other levels[13]. Neuroscientists need careful accounts of the behavioural parameters of capacities yielded by psychological research, and psychologists need neuroscientific data to constrain and inform their theories of information processing. Computational models showing how networks can achieve complex effects serve to connect behavioural and neural levels[29,30]. No single model can be expected to span all levels, and if a comprehensive theory of the brain does emerge, it will involve establishing a successive chain of explanations, from the lowest levels to the highest[23].

Correction and modification of higher level hypotheses occasioned by neuroscientific discoveries may have revolutionary consequences for our basic philosophical ideas of what we are and how we work. More generally, we may find that our commonly accepted ideas about knowledge, reasoning, free will, the self, consciousness, and perception, have no more integrity than prescientific ideas about substance, fire, motion, life, space and time. Making sense of ourselves is our enduring philosophical quest. What is exciting about this period in the history of science is that we may finally have the resources to succeed.

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letter to the editor

Means to immortalize neural cells

SIR:
In the January issue of TINS, various means of immortalizing neural cells were discussed[1]. A major goal of this work is to obtain immortal cell lines having properties of differentiated neurons; a major stumbling block in this effort arises because differentiated neurons are post-mitotic, hence may not incorporate exogenous DNA or might not re-achieve a mitotic state even after transduction with oncogenes. However, Cone and co-workers have reported that fully differentiated neurons from chick spinal cords *can* be induced to synthesize DNA, re-enter mitosis and divide, if they are depolarized with ouabain[2–5]. This work was reported in a series of publications in the 1970s; to my knowledge it has not been refuted, nor tried as a means of aiding the establishment of neural cell lines from differentiated neurons. Since this potentially important line of work appears to have been widely overlooked, I am bringing it to the attention of your readers.

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