crease in action potential velocity down very long nerves is required. Rapid nerve conduction is critical for escape maneuvers as well as for effective predation. In cephalopods, the conduction problem has been solved by vastly increasing the diameter of those axons for which fast conduction is essential. Certain of these single axons can be as thick as a few millimeters in diameter. In contrast, vertebrates have developed a much more efficient system that creates a thin, compact membrane sheath around their axons—myelin—allowing them to conduct action potentials with speeds of 50 to 100 meters per second along an axon with a diameter of only 1 to 40 micrometers (see the figure). The myelin sheath is synthesized by oligodendrocytes in the central nervous system and by neural crest–derived Schwann cells in the peripheral nervous system.

With respect to Gans and Northcutt's theory, it is interesting that protovertebrates (lancelets, hagfishes, and lampreys) are not myelinated. The presence of the myelin sheath exactly parallels the development of the jaw. The oldest contemporary vertebrates that are myelinated are the jawed cartilaginous fishes (sharks and rays), consistent with the concept that a large-bodied, fast-reacting predator requires myelin-mediated, highly rapid conduction of the action potential. One might retrodict that the jawless ostracoderms and conodonts were not myelinated, and so would not have been successful competitors with other fish (for example, placoderms) that had developed neural crest–derived myelin, and jaws.

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Dynamic and Permanent

Donald A. Windsor's letter titled "A question of permanence" (3 Mar., p. 1592) points out that the immutability of an academic paper is essential to the network of citations that is so important to scientific communication. He expresses worries about citing "ephemeral" online articles now that even prestigious journals such as the *British Medical Journal* are allowing authors to make changes to their papers online.

At the *Stanford Encyclopedia of Philosophy* (SEP), we have found a solution to this problem. The SEP is a dynamic encyclopedia by which the philosophy profession collaboratively maintains an up-to-date reference work. It deals with many scientific and technical topics, and the authors are not just permitted but are required to revise their entries and submit them for editorial review on a 3-year rotation in order to ensure their currency and accuracy. To preserve the authenticity of citations to SEP, it is our policy to publicly archive the entire contents of the SEP every 3 months. All proper citations to encyclopedia articles must be specific to a dated archived version. (This citation policy is described in detail at http://plato.stanford.edu/cite.html)

A great strength of the Internet is its dynamic nature. By providing a means to cite the public archives of the SEP, we believe we are able to reconcile the view of younger generations, who are likely to see the Internet as the preeminent source of scientific information, with those of self-described old-timers such as Windsor who

regard documents on the Internet as too impermanent to play the essential role of being the fixed public record of science.

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Antiscrapie Drug Action

In their report "Porphyrin and phthalocyanine antiscrapie compounds" (25 Feb., p. 1503), Priola *et al.* present data showing that pthalocyanine tetrasulfonate (PcTS) and related compounds prolong scrapie incubation. They suggest that these compounds interact with host prion protein (PrP), or with the infectious agent, to directly reduce the accumulation of pathologic PrP and thereby slow the onset of disease. Although this is one possibility, their data could be explained by a drug effect on recipient cells that normally take up the infectious agent in brain homogenates.

First, there is an unusually large range of incubation times in the drug-treated group but not in the control groups (for example, a scatter of points between ~85 and 380 days as compared with ~75 to 95 days, respectively). The incubation time was measured as the time from scrapie infection until death, and in these experiments drug treatment began on the same day as infection. Additionally, if a drug interacts directly with the infectious agent, as it should have in the subsequent direct-mixing experiment in figure 3 of Priola *et al.*, more uniform incubation times would be expected than were found. In contrast, drug effects on heterogeneous peritoneal cells could have more variable outcomes.

Second, the colored PcTS was taken up by many peritoneal cells (detected visually by Priola *et al.*), and its effects were more profound as drug accumulation approached saturating levels (judged by the intense color of the peritoneal tissues). These findings also indicate cellular effects not necessarily confined to either agent or PrP interactions.

Third, the drugs were effective when given 14 or 28 days before infection. This again suggests an inhibitory effect on pretreated cells rather than a specific interaction with PrP or the infectious agent. Although it is tempting to study drug candidates for scrapie and Creutzfeldt-Jakob disease in terms of PrP conversion, many different drugs that affect macrophage function but have no obvious PrP interaction can significantly alter incubation times (*1,*