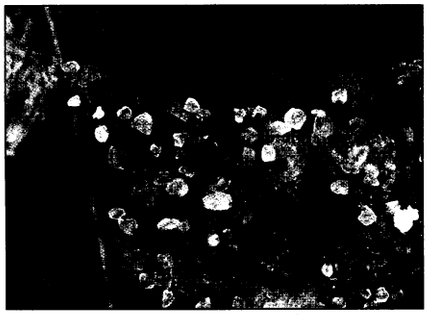
PHOTOS BY: U. G. MUELLER



Yeast garden of the ant *Cyphomyrmex*.

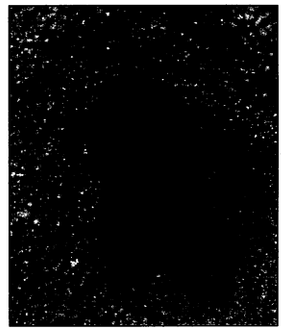
Although a given ant nest contains only one crop, different nests of the same ant species usually alternate between at least two, in one case up to eight, different crops. There is even more variation in the crops on which different farms of the same human society specialize, as can be appreciated from the dozens of different fruits and vegetables sold at a local Farmers' Market and all grown within 100 miles.

Mueller *et al.* identified seven cases in which the same crop is shared among different ant species of the same genus, and four more cases involving ant species belonging to different genera. Such sharing of domesticates among different human societies is the rule; for instance, even before the European overseas expansion that began in A.D. 1492, maize was widespread among Native American societies of both North America and South America, and wheat and horses were widespread among Old World societies.

Some of that crop sharing among ants results from lateral transfer of the same crop clone between ant species. For example, one ant species introduced into Florida in the 20th century has already acquired a crop cultivated by an indigenous Florida ant species. Such sharing develops when one ant species borrows a crop from another's nest, or when several nests become disturbed and mixed. Lateral transfer of crops is ubiquitous among modern humans. A typical McDonald's restaurant meal includes foods based on beef, chicken, potatoes, and kola nut (Coca Cola), originating from the Fertile Crescent, China, Andes, and tropical West Africa, respectively. Our lateral transfers were widespread even before 1492, extreme examples being the pre-Columbian transfers of Andean sweet potatoes to Polynesia and of Asian bananas and rice to East Africa.

Nevertheless, some ant sharing of crops apparently arose through multiple independent domestications of the same wild fungal clade. Among human farmers, multiple independent domestications were common in the Americas (such as squashes, tobaccos, cottons, and beans), where the continents' north-south major axis impeded lateral transfer, but uncommon in Eurasia because of rapid lateral transfer along an east-west axis (exceptions being the repeated independent domestications of pigs and cows) (*6*).

Mueller *et al.* identified two cases of ant fungal crops identical or nearly identical to wild-growing mushrooms. They interpret these cases as evidence for ongoing recent domestications of wild fungi, rather than escapes of cultivated fungi to the wild. In contrast, humans have largely ceased re-domesticating valuable crops from the wild, even though wild ancestral populations still exist for many of our crops. Most wild populations of our domestic animals, such as wild dogs and horses and cattle, represent feral escapees.



Entrance to the fungus farmers' nest.

Clearly Mueller *et al.* have opened rather than exhausted an interesting area. I cannot resist mentioning three tantalizing directions for future work. First, their methods could be applied, by straightforward lateral transfer, to studying the crops of the Old World's fungus-growing termites, which are evolutionary parallels to the New World's fungus-growing ants. Second, modifications of our own crops and livestock under artificial selection by farmers are so obvious that Darwin devoted the entire opening chapter of his *Origin of Species* to the subject. Corresponding modifications of the ant fungal crops are (surprisingly at least to me) not obvious, even though the ants themselves have evolved obvious modifications. As Mueller *et al.* note, chemical modifications of the fungi to match olfactory and gustatory capabilities of ants are a promising area to begin to look. Finally, since the rise of agriculture, human farmers have also "domesticated" the specialized human pathogens responsible for our crowd epidemic diseases and mostly derived from similar pathogens of the domestic animals with which farmers live closely (*6*). Human measles, tuberculosis, and flu evolved from pathogens of cattle, cattle, and pigs, respectively. What might sequencing of the smallpox virus and of syphilis treponema, and of their potential "wild ancestors" among domestic animal pathogens, reveal about the likely time and place of origin of these diseases that played so large a role in human history?

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PERSPECTIVES: NEUROSCIENCE

The Saturation Debate

T. V. P. Bliss

Here's a question often debated in the examination halls and coffee rooms of neuroscience and psychology departments during the last two decades: Does long-term potentiation (LTP)—the enduring enhancement of synaptic efficacy triggered by bursts of high-frequency stimulation—provide the cellular basis for hippocampal-dependent behavioral learning? Or, to be more succinct, does LTP = learning? The question is easily posed, but—as might be expected of an issue lying at the boundary of the physiological and the cognitive—an unequivocal answer is proving remarkably elusive. On page 2038 of this issue, Moser and colleagues (*1*) revisit the problem by using an approach first attempted around 10 years ago in the laboratory of McNaughton and Barnes (*2*, *3*).

If learning is the result of changes in synaptic weight, then blocking such changes should impair hippocampal-dependent learning. One way to achieve this would be to drive all synapses to their maximum efficacy—in other words, to use LTP itself to block the potential for further change. McNaughton *et al.* implanted recording electrodes bilaterally in the dentate gyrus of the hippocampal formation in rats, and using single bilateral stimulating electrodes delivered multiple episodes of tetanic stimulation to axons of the perforant path (the fiber tract that is the principal input to the dentate gyrus) until LTP was saturated. When they trained

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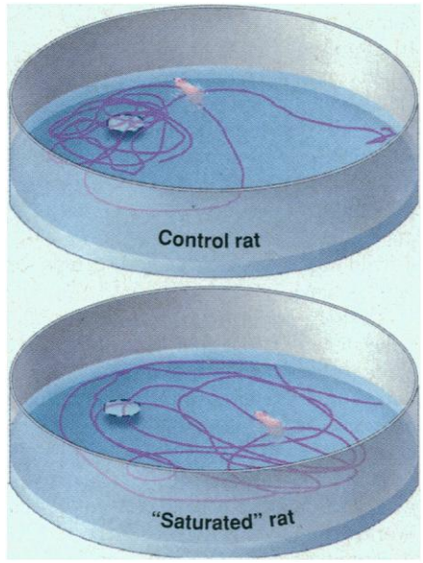
rats in spatial tasks known to require the hippocampus, they found deficits in the tetanized animals relative to untetanized controls. Despite the unimpeachable logic of the approach, the result was in some ways surprising, because it was difficult to see how in practice a single stimulating electrode could activate a sufficient number of perforant path fibers to saturate LTP across the dentate gyrus. Attempts in several laboratories to replicate the experiments met with little success (*4*). The new results of Moser *et al.* suggest that the original conclusion was correct after all: Saturation does impair learning. Their results will be seen as materially strengthening the case for the LTP = learning hypothesis.

Moser *et al.* have added a number of ingenious new twists to strengthen the original experimental design. First, they reduced the volume of functional hippocampal tissue by destroying the hippocampus unilaterally with neurotoxic lesions—rats can learn spatial tasks such as the water maze (see the figure) provided that at least the dorsal part of the hippocampus is intact on one side. Second, they increased the likelihood of saturating a substantial proportion of the perforant path synapses in the dorsal hippocampus on the remaining side by implanting two bipolar stimulating electrodes so as to straddle the fiber tract carrying the perforant path fibers. Multiple episodes of tetanic stimulation were then given in a "cross-bundle" design in which each pole of each pair of electrodes was used in turn as the active cathode, with the objective of stimulating the maximum possible number of axons and thereby inducing LTP in the maximum possible number of synapses. Finally, a third stimulating electrode was implanted between the other two electrodes. The purpose of this was to monitor the progress of potentiation produced by the cross-bundle electrodes, and, in a tetanus delivered through the third electrode itself, to provide an estimate of the degree of saturation. If cross-bundle tetanization had achieved its intended purpose of saturating LTP, tetanization through the third electrode should produce no further potentiation.

After a barrage of five episodes of cross-bundle tetanization, given over several hours on 1 day, had produced a plateau level of LTP (as reported by test stimuli to the third electrode), animals were trained on the water maze (see the figure). The tetanized animals showed an unexpectedly large range of ability. Some learned as well as nontetanized controls; others were severely impaired. Immediately after training, the animals were again returned to the recording chamber, and the degree of saturation in each animal was tested by delivering a tetanus to the previously untetanized third electrode. About half the animals showed normal LTP (>10%), demonstrating that LTP had not been saturated. Others showed less than 10% potentiation and were accordingly classified as saturated. It now became clear why some animals had done well, and others badly in the water maze; the saturated animals were the poor learners, and the unsaturated animals were the good learners, as predicted by the LTP = learning hypothesis.



Swim paths of rats in a water maze. Well-trained control rats swim mostly over the region of the pool where the submerged platform (square at left) was located during training. "Saturated" rats, in which LTP in the dentate gyrus is saturated before training, swim randomly, showing no memory of the platform's location. Rats in which the saturation procedure failed behave like control rats.

Striking though the results of Moser *et al.* are, skeptics may remain unconvinced. Almost half the tetanized animals demonstrated residual LTP; in fact, the average residual potentiation in this group was no different from that seen in previously untetanized control animals. Moser and his colleagues have exploited this failure to provide a useful tetanized-but-not-saturated control group, but the saturation strategy clearly does not work all the time. It is worth thinking about what saturation means in this context. When repeated tetani at a constant intensity are given to a population of fibers, steplike increases in LTP are often seen, until eventually saturation is reached. At individual synapses, as Petersen *et al.* (*5*) have recently shown in vitro, the induction of LTP is all-or-none, and if this is the case in vivo, any further potentiation by subsequent tetani must be due to the recruitment of LTP at previously unpotentiated synapses, rather than to a graded increase in already potentiated synapses. If, after multiple cross-bundle tetanization, the third electrode fails to produce further potentiation, then we can conclude that all the synapses it activates must already have been potentiated by the cross-bundle electrodes. This would amount to a convincing indication that all synapses are potentiated—in other words, the system is saturated with respect to LTP—if the test electrode activates a random selection of axons. But two considerations suggest this may not be the case: (i) the central position of the test electrode is likely to preclude access to outlying axons accessible to the two cross-bundle electrodes, and (ii) no LTP was reported by the test electrode after the first episode of cross-bundle tetanization. Despite these caveats—and the authors themselves concede that complete saturation is probably unattainable—the new data clearly demonstrates that even partial saturation of synaptic weights in a distributed neural network will degrade its function.

The division of tetanized animals into two subgroups, saturated (<10% residual LTP) and nonsaturated (>10% residual LTP), presumably masks a range of effects from no saturation to near-complete saturation. It would be interesting to know whether the degree of residual LTP correlates with performance in individual animals. Furthermore, LTP is not permanent in the dentate gyrus, and another prediction, not tested in this report, but confirmed in an earlier study of Castro *et al.* (*3*), is that after a few days the impaired animals in the saturated group would regain their navigational skills. Finally, the technical advantages of the hippocampal pyramidal CA1 and CA3 cell fields for this kind of experiment should not be overlooked (*6*); the strong commissural connections between the two sides of the hippocampus should in principle allow the entire extent of CA1 and CA3 to be saturated with a single-stimulating electrode placed in the hippocampal commissure.

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