

et al. model¹ is an idea of considerable power. Using it successfully against a long-standing computational problem is further evidence of its generality; this is a significant consolidation. The success of this model in this instance will no doubt drive others to test this architecture against their favorite problems, and many more complex problems await.

The model also makes a number of specific predictions about the circuitry between cortical areas. In particular, it proposes particular afferent architecture to bestow either simple (component) or more complex (pattern) responses on MT cells. These predictions are, unfortunately, rather difficult to test at present, as the tests will require paired recordings between MT neurons and their afferents. Such experiments, though possible with current technology, are arduous, difficult and slow. Some of the simplifying predictions will no doubt prove wrong, as the authors freely admit. MT receives afferents from many sources other than V1, and indeed these are likely to convey different kinds of information. Another simple prediction of the model is almost certainly wrong on the basis of current evidence; we are pretty sure that divisive inhibition operates not only in V1, but also in MT itself⁴. So, bringing a circuit reality to the nonlinearities at the MT level is a target for the next generation of experiments.

The lesson from physics is that models turning out to be wrong is all part of the game and should be viewed with approval. We get to better understanding by climbing a ladder built of the bones of dead models. If there is a core truth, some useful generality achieved by any

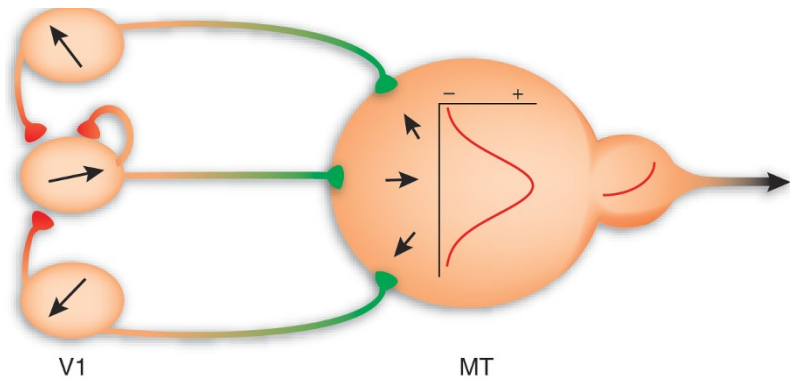


Figure 2 Structure of the Rust *et al.* model. Each black arrow indicates the preferred direction of a V1 neuron in a (hypothetical) population of afferent neurons. Each cell's response is reduced by both tuned (recurrent) and untuned (lateral) inhibition from V1 neurons. Additionally, the tuning bandwidth of each V1 neuron is a free parameter. The MT cell integrates responses from V1 population inputs by calculating a weighted sum; inputs can be either excitatory or inhibitory. The weighted sum then passes through a nonlinear function to be transformed to firing rate.

generation of model, this is major progress. There has long been a desire to find general mechanisms of information processing that will apply across cortical areas¹⁵, and this paper marks a notable step in that direction. It is starting to look as if the LN family of models might be such a unifying framework.

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New clues for axonal repair in ALS

In amyotrophic lateral sclerosis (ALS, also called Lou Gehrig's disease), corticospinal neurons progressively degenerate, causing the loss of motor function and eventual paralysis seen in these individuals. Damage to these neurons also contributes to the loss of motor function in spinal cord injury. However, little is known about the mechanisms that regulate the survival and differentiation of corticospinal neurons. A paper on page 1371 by Hande Özdinler and Jeffrey Macklis describes new techniques to purify and culture these motor neurons, allowing the authors to dissect the mechanisms by which the morphology of these neurons is regulated.

The authors retrogradely labeled corticospinal neurons with fluorescent microspheres and used fluorescence-activated cell sorting to obtain homogeneous populations. These cultured neurons maintained the morphological and molecular phenotypes of developing corticospinal neurons *in vivo*. Insulin-like growth factor (IGF-1) specifically enhanced axonal outgrowth in these neurons, an effect mediated by the IGF-1 receptor and the PI3K and MAPK signaling pathways. Brain-derived neurotrophic factor, in contrast, induced dendritic branching and outgrowth, but did not affect axonal outgrowth. *In vivo* blockade of the IGF-1 receptor caused axonal outgrowth defects in the corticospinal tract. Critically, this effect of IGF-1 was independent of its effect on survival of these neurons, as corticospinal neurons isolated from mice lacking the apoptosis protein *Bax* behaved similarly to wild-type neurons in response to locally applied IGF-1. By demonstrating that IGF-1 is a potent enhancer of axonal outgrowth in corticospinal neurons, these results may help guide future efforts to use IGF-1 to enhance the outgrowth and functional connectivity of damaged neurons in diseases such as ALS and primary lateral sclerosis.

Kalyani Narasimhan

