activity as defined by the population vector. When monkeys make circular arm movements (whose direction changes continuously), the direction of the hand was found to lag behind that of the population vector, with a time interval that varied with the degree of curvature[5]. For tight circles, the lag was about 100 ms, but for large circles the lag was only 30 ms. These results were interpreted as evidence that the motor cortex is involved in controlling movements with high curvature, but not movements that are more straight. Todorov's model, however, predicts the exact same time differences between the population vector and hand movement, even while assuming a fixed time lag between the firing of the cortical neurons and the activation of the muscles. This is because the interplay between the mechanical properties of the musculoskeletal system related to length, velocity and acceleration create a systematic temporal shift between population vector direction and hand motion. In other words, the mechanical complexity of the limb leads to complexity of the population vector.

Todorov's article also illustrates some of the pitfalls that can occur when statistical approaches are used to correlate neural activity with different movement parameters. Various investigators have used multiple regression techniques to look for parameters of hand movement that show correlations with neural activity. A common finding has been that many parameters show some correlation, but that the correlations are greatest for movement direction and smallest for acceleration[6]. Because acceleration is tightly linked to force (according to Newtonian mechanics), this finding has been interpreted as suggesting that force is not among the major parameters coded by M1. Todorov shows, however, that a muscle-based model predicts virtually the same results: high correlations with movement direction and low correlations with acceleration. The model also predicts that, because of the force-velocity relationship of muscle, neural activity should also correlate with hand velocity; this too has been observed experimentally[7]. Finally, Todorov illustrates how the methods used to analyze neural data can have considerable consequences for the observed correlations. Specifically, squaring the discharge rate of neurons in order to stabilize the variance (as is commonly done; see for instance ref. 6), causes a dramatic increase in the percentage of neurons that appear to represent movement direction (from 17% to 43% in Todorov's model). This implies that previous studies may have overestimated the representation of movement direction in M1; indeed, Todorov suggests that many of the previously described correlations may be epiphenomenal, given that similar correlations arise in his model even though movement direction is never specified directly.

The new model is not meant to capture all the nuances of motor cortical activity during movement, and it does not prove that motor cortical activity is devoid of all higher-level features of movement related to the hand. It does, however, demonstrate two important points. First, even the simplest model of motor cortical function, treating it as a generator of muscle activity patterns, can lead to unanticipated and complex correlates of hand motion due to the mechanical properties of the limb and its musculature. Second, given these complexities, the relationship between neural activity and limb movement is not easily determined. Therefore, before concluding that brain activity reflects complex representations of movement, the data must be scrutinized to ensure that the observed correlations are not merely a reflection of properties of the peripheral motor apparatus. Engineers have to understand the plant before they can figure out how to control it. Why should it be any different when examining biological control?

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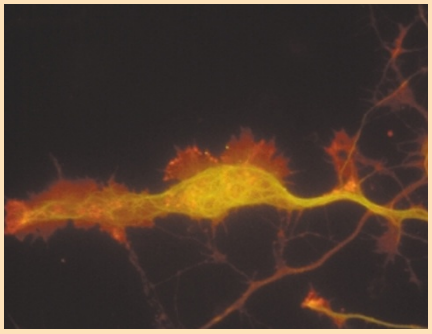
A signal for synapse formation



When growth cones reach their synaptic targets, they must both send and receive signals in order to promote formation of mature synapses. We know little about the identity of such signals, but a recent paper (Hall, A.C., Lucas, F.R. & Salinas, P.C. *Cell* **100**, 525–535, 2000) offers provocative evidence that WNT-7a may be one such molecule. The WNT factors are a family of secreted signaling proteins, and are known to be involved in early developmental patterning. Several are also expressed in the brain, and the presence of WNT-7a in cerebellar granule cells during the period of synaptogenesis prompted the authors to examine a possible role in this process.

Hall *et al.* studied the formation of synapses between mossy fibers, originating in the pons, and granule cells. Cultured granule cells secrete factors that induce remodeling of pontine axons *in vitro*; the effects include a spreading of the growth cones, changes in their cytoskeletal structure and an increase in filopodial length. These effects were blocked by an antagonist of WNT signaling, and were mimicked by conditioned medium containing WNT-7a (the figure shows a treated growth cone, stained for GAP-43, red, and tubulin, green). Remodeling could also be induced by low concentrations of lithium, which mimics WNT signaling by inhibiting a downstream kinase called GSK-3β. Finally, mice lacking WNT-7a show a delay in the formation of mossy fiber-granule cell synapses *in vivo*. The synapses do form eventually, suggesting that other members of the WNT family might be able to substitute for WNT-7a, but the phenotype nevertheless indicates that WNT-7a is involved in this process. It will be interesting to determine whether WNT factors play similar roles at other synapses, and whether they are also involved in adult plasticity. It will also be interesting to know whether any of the clinical effects of lithium (used to treat manic depression) can be attributed to its effects on WNT signaling.

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