

## Keeping the Wires Short: A Singularly Difficult Problem

It is commonly thought that cortical maps are a solution to an optimization problem in which the length of axons required to make the necessary connections between cells is kept to a minimum (Cowey, 1979; Durbin and Mitchison, 1990). The conditions under which this might be true can be illustrated by the following thought experiment: take a cortical map and interchange the positions of all the cells at random, keeping the connections between them and their extra-cortical inputs unchanged. Since the cells remain identically connected, the physiological behavior of the tissue will remain the same. But the map will be destroyed and, given that the connections were initially mostly local and between cells with similar physiological properties, the axonal lengths of connections between cells will be greatly increased. Communication between cells will be slower, and the volume of the brain will increase substantially (the bulk of the brain consists of axonal wiring as it is). These are both presumably highly undesirable events from the standpoint of evolution. Bigger brains may mean more maternal deaths, for humans at any rate; for animals with proportionally smaller brains, perhaps speed of communication is more significant. One can therefore argue that the only real—and somewhat uninteresting—function of cortical maps is to minimize connection lengths.

One can of course find holes in the argument: if cells communicate by means other than synapses (e.g., by local diffusion of messengers), then the physiology of the scrambled map will not be the same, and it is also possible that timing cues might be disrupted because of the extra or more variable distances action potentials have to travel to reach their target neurons. In spite of these caveats, it seems plausible that an important function of maps in the brain is to minimize wire length. Can one go further and show that real cortical maps are actually optimal solutions to wiring problems? A considerable amount is now known about the structure of maps in many cortical areas, particularly in visual cortex, where the organization of the retinotopic map, the representation of orientation preference, and ocular dominance have been studied in detail. Evaluating how well these maps optimize wire length is difficult, however. Before connection length can be determined, it is necessary to know the physiological rules that determine which cells are connected to which, and how axons branch before reaching their multiple targets (Mitchison, 1991). Even if these rules were completely known, discovering the optimal map layout would be an extremely difficult computational problem even for a small region of cortex because the number of possible map configurations that need to be examined in order to determine the single optimal arrangement is astronomically large.

Because of these difficulties, very few studies have examined wire length constraints directly: those that have, have necessarily adopted highly simplified approaches. For example, Durbin and Mitchison (1990) applied the following framework to maps of orientation and receptive field position: (a) assume a finite number

of discrete orientations and receptive field positions; (b) only take into account connections between pairs of cortical points representing neighboring receptive field values; (c) assume that wire length scales with the distance in the cortex between the points to which these neighboring stimulus values are mapped. They were able to show that a particular model for visual cortex map formation (the elastic net algorithm) produced mappings of preferred orientation and receptive field position that closely resembled real visual cortex maps, and at the same time they demonstrated that the model was likely to be minimizing their measure of wire length.

A more direct, although still highly simplified, approach has now been taken in the paper by Koulakov and Chklovskii published in the current issue of *Neuron*. Here, the authors consider only an orientation map (retinotopic position can be considered to exist but does not play a role in determining connections). Within the map, each neuron must make a fixed total number of connections with other neurons. The distribution of these wiring connections is chosen to be the sum of a Gaussian riding on a constant plateau. The greatest number of connections is between points with zero orientation difference; the width, height, and plateau are varied systematically in the different simulations. Thus, for a narrow Gaussian with no plateau, connections are made only between map points with similar preferred orientation. At the other extreme, if the connection function is flat, connections are uniformly distributed over all orientations. The maps that minimize wire length are calculated for a given connection function.

For any given layout of orientation preference, and a particular connection function, it is not difficult to find the pattern of connections that minimizes the total connection length. For each point in the map, take the surrounding points in order of proximity and make a connection providing the total number of connections allowed by the connection function has not been exceeded. Once this is done, a total wire length can be calculated for the entire map. The problem is then to search among all maps of orientation preference and find the one that minimizes the connection length for a given connection function. Although easy to state, this problem is difficult to solve, and it requires over a week of computing time to find the (probable) optimal layout for even a small ( $50 \times 50$  pixel) map. Having persevered heroically with these computations, Koulakov and Chklovskii show how the structure of the optimal orientation map varies with the type of connection function. For a flat function, the optimal layout is a “Salt&Pepper” arrangement, in which orientation preferences are intermixed and scattered uniformly across the map. For a relatively broad connection function, the optimal arrangement is an “Iceland” layout, where orientations vary smoothly and iso-orientation domains are parallel stripes of uniform width. When the connection function is narrow, i.e., highly orientation specific, the optimal arrangement is similar to that found in most biological orientation maps and contains periodically spaced singularities (also known as pinwheels)—that is, points where a single complete set of orientation domains meet.

Although the pinwheel arrangement occurs in the majority of species that have been examined so far, the

authors point out that “*Salt&Pepper*” occurs in the rat, where there is no evidence for an ordered map of orientation (Girman et al., 1999) and that large areas free of singularities can be found in some regions of cat visual cortex (Shmuel and Grinvald, 2000). They hypothesize that these different patterns occur because the connection function is different in the different cortical areas concerned: it is predicted to be broadest in the rat, less so in those areas of cat cortex that lack singularities, and narrowest in primates and other species where a relatively high density of singularities is always found (Obermayer and Blasdel, 1997).

These findings are interesting because they show, for the first time, that singularities may be adaptive features whose role is to minimize wire length. (The authors do not say by how much, although presumably it would not be difficult to calculate.) There are some additional interesting implications. It can be shown that previous models of orientation map development tend to favor the *IcCube* layout of orientation as a final stable state. This can be proved analytically, as Koulakov and Chklovskii do for one particular model, or it can be observed in simulations that singularities tend to disappear slowly over time (Wolf and Geisel, 1998). Technically, this means that the cost functions for these other models are minimized by arrangements in which singularities are absent. From the point of view of these previous models (and perhaps the modelers as well), singularities are developmental artifacts and represent nonoptimal configurations of the map. That singularities are present in most model maps is because the models either contain features that prevent the optimum configuration from being reached or because it simply takes too long to compute the optimum solution. In reality, this may not be a problem because development, like the models, may also only incompletely minimize the cost function. For example, the factors that bring the critical period to an end may “freeze” the map in what is, from a computational perspective, an intermediate state. This would result in a map that fortuitously produces a shorter wire length than if the process were to proceed to completion. However, Koulakov and Chklovskii suggest that it might be better to abandon these models in favor of others that do explicitly minimize wire length. They propose experiments that may help to decide whether evolution has selected developmental mechanisms of map formation primarily on the basis of their ability to minimize wire length, or whether it has selected mechanisms that do a reasonably good job of minimizing wire length, but whose main role is something else. Since the “something else” has not yet been identified, perhaps it is time, despite the difficulties, to start looking more carefully at the ability of wire length constraints to explain what we know about cortical maps.

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#### Selected Reading

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## Turning the Dial on Object Perception

One of the more challenging aspects of neuroimaging studies of higher cortical function is the isolation of a mental operation of interest. An experimental condition that evokes the cognitive process of working memory, semantic retrieval, or spatial representation, for example, can be expected to evoke a number of other processes as well (e.g., stimulus perception, eye movements, response preparation, etc.). The “cognitive subtraction” method tackles this problem by comparing the neural activity evoked by matched experimental and control conditions that putatively differ only in the cognitive process of interest. The assumptions, however, that cognitive subtraction requires are themselves problematic (Friston et al., 1996; Zarahn et al., 1997) and stem in part from the need to evoke the mental operation under study in an all-or-nothing fashion. Parametric manipulations of cognitive processes (in which the level of the operation, as opposed to its presence or absence, is varied) have less stringent assumptions and therefore provide for stronger inference.

In this issue of *Neuron*, Bar and colleagues present an fMRI study of object recognition that is parametric in a clever way (Bar et al., 2001). Subjects were asked to identify simple objects briefly flashed on a screen and to rate the confidence of their recognition on a scale of 1 to 4. The speed of presentation and a poststimulus mask made the task rather difficult, with the result that sometimes stimuli were clearly identified by the subject, but sometimes the subject was uncertain, or worse. The authors reasoned that if a region of the brain contributes in a computationally meaningful way to object recognition, then there should be a systematic relationship between the magnitude of neural activity at that location and the subject’s report of recognition confidence. Consider the two regions with the patterns of neural activity illustrated by the solid and dashed lines in the figure. The solid line represents the pattern of neural activity found by the authors in retinotopic, “early” visual areas, while the dashed line represents the pattern found in the anterior fusiform gyrus (interestingly, other patterns of response, such as a “U” function, were found in other areas).