Co-operative and brain organization
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The concept of co-operativity, which is well known to the physical scientist, is now being applied to problems in neurobiology. To illustrate this the authors describe their recent work on the development of ordered nerve connections between eye and brain. Co-operativity may well find general applicability to the neurosciences.

In 1943 McCulloch and Pitts proved that any conceivable logical input-output function could be implemented by appropriately interconnecting simple model nerve cells (see Ref. 1). This result and the success of the new electronic computer inspired a great wave of enthusiasm, since it implied that the brain could ultimately be understood as a complex network of logical switching devices. Although this approach has been fruitful in inspiring and shaping whole lines of research, the computer analogy has to date not brought about any significant breakthrough in brain theory. One striking difference between computer and brain is that the computer must carry out its instructions in sequence whereas much of the analysis in the brain appears to be undertaken by multiple systems operating in parallel.

No efficient and universal self-programming scheme has yet been proposed for the conventional computer; it relies heavily on intimate communication between the machine and human programmer. The sequence of events in a computer is an extremely sensitive function of the structure both of the machine and of the programme; if one connection is cut or one part of the programme changed the effect is usually a complete breakdown of useful action. There is, therefore, no natural and universal strategy of continuous improvements which could lead to a functional computer or programme. Only with the help of the programmer is it possible to create functional structures; the computer is in no way a self-contained entity.

Conversely, the nervous system has evolved by stepwise improvement. Every intermediate structure has had to be functional. The nervous system is re-created for each individual by the ontogenetic process of self-organization; it is self-programming, since it can learn; and its action is robust against all kinds of disturbance. The nervous system most likely contains, even in its basic mode of action, the principles necessary to guarantee these features, which in the computer could at best be the result of very special and complicated programmes.

Fig. 1. The influence exerted on a synapse (black square) by the others (in a one-dimensional retina and tectum). The presence of other synapses within the shaded region increases its growth rate. Synapses within each horizontal band, made by one retinal fibre or a small retinal region, compete with each other; likewise synapses within each vertical band, which are those contacting a given tectal cell or region. Interactions are optimally concanetated if synapses are arranged in a diagonal, i.e. in a retinotopic arrangement. The two-dimensional case is analogous, but would need a four-dimensional display.

Fig. 2. The results of a computer simulation of the development of a projection between a one-dimensional retina and tectum, using the model outlined in Table 1A; (A) Retinal markers. Four molecule types, with inhomogeneous but continuous distribution, the result of synthesis in isolated source locations, diffusion and decay. (B) Early distribution of synapses. Each square represents the 'weight' of a synapse. The contacts made by each retinal fibre are represented by a row of the matrix. Orientation information is imposed by suppression of synapses between retinal extremes and the 'wrong' ends of the tectum. Smaller squares are synapses created by sprouting from larger, initial, synapses. Filled squares correspond to growing synapses. Note that growth starts at the ends of retina and tectum. (C) Intermediate configuration. (D) Final configuration. (E) Tectal distribution of markers in the final configuration. It is a distorted copy of the retinal markers. Details of the simulation are described in Ref. 13. Here, a ten times smaller diffusion constant was used for the tectal markers.

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The starting point for a new approach to brain theory is the observation that the non-biological world is full of complicated patterns which arise by self-organization. Basic examples, including crystal lattices and magnetic domains, have been intensively studied and are fairly well understood in physical terms. Central to the relevant theories is the notion of 'cooperativity'. Recently the analogy has been exploited in a number of papers which discuss neurobiological phenomena as cooperative⁵. We will try to illustrate this approach by the discussion of an example which has been well studied both theoretically and experimentally⁴.

The retinotopy problem

In the course of vertebrate ontogenesis, the ganglion cells of the retina send axons through the eye stalk to the brain, where they establish connections with cells of central structures, such as the optic tectum. In the adult animal the retina-tectum connections are arranged 'retinotopically', i.e. the fibres from neighbouring retinal cells project on to neighbouring points in the tectum. Experimental manipulations performed on animals of various species have shown that there is enormous plasticity in the system⁶. For instance, if the eye is rotated prior to the establishment of the projection, the course of fibres is altered so that they still project to the appropriate regions of the tectum. In other experiments where the retina or the tectum is reduced surgically, the regenerating fibre projection is expanded or compressed to form an ordered projection extending across the whole of the tectum.

From these experiments two simple rules can be abstracted to describe the final outcome of the process of fibre growth from retina to tectum: (i) match the perimeter of the retinal piece of tissue on to that of the tectal piece of tissue in a predetermined orientation (which in normal cases is genetically programmed); (ii) fill the interior of this frame with a continuous projection (that is, neighbouring retinal cells project to neighbouring tectal cells).

The situation is complicated by the facts that new boundaries can be created in retina or tectum and that one piece of tissue may take part in more than one projection. These facts are exploited in the 'compound-eye' experiments⁷, in which pieces of different eyes are joined in one eye socket, and in 'graft manipulation' experiments⁸, in which either a square graft is cut out of the tectum and rotated in its plane or two grafts are interchanged.
Although there is little direct information available on the nature of the cellular mechanisms involved in the formation of projections, the information we have concerning retino-tectal projections, accumulated through experiments such as those outlined above, severely restricts the number of possibilities.

A method for the establishment of ordered connections

We now describe a general mechanism for the formation of topographic projections. Some of the finer details will have to be determined by future experiments and these may also depend on the particular species or even on the special situation at hand.

The model proposed operates at two levels: a local one and a global one. The local mechanism is of more general interest and will be described first. It deals with the ability of fibres to form a continuous projection (or pieces of a continuous projection), independently of position, scale and orientation of that projection.

A. Local mechanism. Suppose fibres from the retina have already grown to the tectum and have established synapses there (in a haphazard fashion). The development of the retino-tectal projection is then determined by the following rules which govern the development of the individual synapses, each of which has a 'weight' (which may stand for size, or functional effectiveness):

1. A retinal fibre can form new synapses in the tectum in the neighborhood of its existing synapses. Synapses are broken if they have fallen below a lower threshold weight or are unsuccessful according to some other criterion.

2. A synapse is allowed to grow in proportion to the total weight of the synapses nearby which are from fibres of similar retinal origin to its own fibre. The ability of fibres to recognize each other's retinal origin requires an appropriate code on the retinal fibres, for which two possibilities are described in Table I.

3. The total growth of the synapses made by one retinal cell (or small retinal region) is limited. Consequently the growth of some synapses must be compensated by the decrease in weight of less successful ones. A similar growth limitation operates on those synapses which contact the same tectal cell (or small tectal region).

The effects of these synaptic interactions can be shown most easily in a simple model with a one-dimensional chain of cells for both retina and tectum (Fig. 1). The synapses are displayed as a matrix whose rows correspond to retinal cells or fibres and the columns correspond to tectal cells.

Fibres from different small retinal regions will co-operate maximally with each other if all their synapses are concentrated in one of the two diagonals of the matrix, i.e. in a retinotopic projection. The system therefore, has the tendency to develop from most initial states into a series of retinotopic part-projections. Lining up the part-projections in a consistent fashion is one of the functions of the global mechanism. (In the case of a two-dimensional retina and tectum, there are, of course, more than two possible orientations.)

B. Global mechanism. The general boundary conditions are: (1) that retinal fibres must be guided to the tectal surface in the first place and must be restrained to within the correct boundaries; and (2) that the orientation of the projection within those boundaries must be specified. This can be done by a positioning mechanism which acts on each fibre separately. Many orientation mechanisms can be imagined. It is possible that different mechanisms act in different species, or under different conditions (development or regeneration) in the same species. The orientation mechanism might act only initially. Only extremely weak influences are needed to guide the local interactions to form a projection in the desired orientation. Even if the orientation mechanism were very precise, it could never supplant the local mechanism of fibre–fibre interactions as it is too rigid.

If the process of organization starts out in one restricted region on the tectum, then the orientation decided upon in the first piece of projection imposes itself on the rest of the developing map. In analogy to crystallization starting from a seed, this sequence of events may be called nuclea-
tion. Graft manipulation experiments suggest that at the time of regeneration tectal cells accept contacts from only certain retinal cells. This could be the result of a 'memory' of the previous projection, or could be an expression of precise orientation information. The results of computer simulations of one of the models described in Table 1 are shown in Fig. 2.

Further examples of co-operative organization

The aim of this discussion on the problem of retinotopy was to provide a concrete neurobiological example of a co-operative system. There have been other applications of the co-operative idea to the nervous system, both to problems of ontology and of function. Julesz has proposed a co-operative model which accounts for the stereoscopic interpretation of binocular images in the visual system, i.e. the way in which particular visual features seen by one eye are identified with their counterpart in the other eye. The model was expressed by Julesz in terms of a physical analogy involving springs and magnets. A related problem is that of visual flow where points in a visual image seen at consecutive moments in time must be related to one another.

A common feature of these applications is the problem of establishing point-to-point connections between two (two-dimensional) patterned structures (retina and tectum, left-eye and right-eye image, two consecutive images, etc.). What makes these examples prototypes of co-operative systems is that in each case local interactions give rise to overall spatial continuity even though each element can choose among a number of states.

However, spatial continuity is not the central concept for co-operative systems. For instance, in animals with binocular vision there are projections from the two eyes which overlap in one central structure. In the mammalian cortex, for example, fibres from the two eyes segregate in layer IV to produce domains in the form of patches or stripes. Yet although the striking feature of ocellarity domains is geometrical discontinuity, a co-operative theory for their ontogenesis can still be formulated. Another example is the representation of orientation in the visual cortex. Here general retinotopic continuity is upset at the level of neighbouring cells in order to accommodate a continuous representation of orientation. A co-operative theory for the ontogeny of this structure has again been presented, showing that simple geometric continuity can be transcended.

Co-operative organization

Applications of co-operative effects which completely leave the context of geometry are known in the field of artificial intelligence under the name of 'relaxation method'. The gist of this idea is that there is a large set of physical entities, 'elements' (analogous to neurons or synapses). These elements have inner variables (e.g. excitory states of neurons), which vary continuously in time. The constellation of 'states' (the values assigned to each of the variables possessed by an element), can be interpreted as the representation of some situation, e.g. a perceived scene. The elements interact by exchanging signals. Each element has a 'neighbourhood' which consists of that set of other elements with which it can communicate. (Here, neighbourhood has to do with connectivity, not necessarily with physical proximity.) The state of an element makes sense only in the context of a certain constellation of states in its neighbourhood. This mismatch between the element's state and those in its neighbourhood leads to changes in its state so as to reduce the mismatch. These in turn entail changes of state in the neighbourhood. The system eventually comes to rest, but only when a globally ordered state has been installed in which the inner state of each element and the constellation of states in its neighbourhood are consistent with each other in terms of their interactions. There can be a rich multiplicity of globally ordered states satisfying this local consistency condition. In the retinotopy problem these are the ordered projections with different position, scale and orientation.

Co-operativity in this context is therefore the ability of a system of elements to form such globally ordered states.

In computer terminology, the programme resides in the structure of the local interactions; the result of the computation being the globally ordered state, which is arrived at by a parallel computation, and which is resistant to small alterations.

The programming of a co-operative system can be carried out in two ways. One corresponds to genetic programming: the a priori build-in of the local interactions. The other acts in the reverse direction: if, by some external means, a global state is projected onto the system, local interactions can adapt so as to be consistent with that global state.

We started out with a criticism of the computer as a model for the brain. The features that it lacks were found to be parallel action of a multiplicity of elements, inherent stability of action, and self-programmability. These are the basic features of co-operative systems. However, the great asset of the computer, its universality, is not inherent to co-operative systems. It remains to be determined how much of this desirable property can be obtained with the help of properly designed co-operative systems.

Reading list


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