

of approach as is that of the mouse or rat. Finally, as Price *et al.* point out, recombinant viruses can be engineered to produce any gene and thus can be used to perturb CNS development (or function) by ectopic expression of certain gene products, or to cure diseases or disease models by delivering specific enzymes or drugs in regulated ways into the CNS.

Selected references

- 1 Wilson, E. B. (1898) in *Biological Letters from the Marine Biological Laboratory*, pp. 21–42
- 2 Sulston, J., Schierenberg, E., White, J. and Thompson, N. (1983) *Dev. Biol.* 100, 64–119
- 3 Garcia-Bellido, A. (1969) *J. Exp. Zool.* 170, 61–76
- 4 Rossant, J. *Curr. Top. Dev. Biol.* (in press)
- 5 Weisblat, D. A., Sawyer, R. T., Stent, G. S. and Yound, J. D. (1978) *Science* 202, 1295–1298
- 6 Jacobson, M. (1986) *Annu. Rev. Neurosci.* 8, 71–102
- 7 Kimmel, C. B. and Warga, R. M. (1986) *Science* 231, 365–368
- 8 Pedersen, R. A., Wu, K. and Balalkier, H. (1986) *Dev. Biol.* 117, 581–595
- 9 Sanes, J. R., Rubenstein, J. L. R. and Nicolas, J. F. (1986) *EMBO J.* 5, 3313–3342
- 10 Price, J., Turner, D. and Cepko, C. (1987) *Proc. Natl Acad. Sci. USA* 84, 156–160
- 11 Herrup, K. (1987) *Curr. Top. Dev. Biol.* 21, 67–98

Computational models and the development of topographic projections

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Topographic maps are found throughout the nervous system. In the mammalian visual system, for example, the ganglion cells in the retina project to orderly topographic maps in the superior colliculus and the lateral geniculate nucleus of the thalamus. Experimental manipulations have demonstrated the specificity of the mappings and have established some general constraints on the mechanisms by which they are generated^{1,2}. Based on these constraints, several computational models have been proposed showing how the global ordering of connections could be achieved from local interactions between growing nerve fibres and target cells^{3–7}. More recently, similar models have been proposed to account for the formation of structure within these maps, such as ocular dominance columns and orientation columns in visual cortex^{8–12}. Two criteria can be used to judge the suitability of a given model: first, whether the assumptions it requires can be biologically justified, and second, whether it can explain the complexity of the patterns that form during development. Evidence is accumulating, though not yet definitively, that the general account of mappings provided by this type of model is roughly correct. It is a good indication of convergence that old models are being rediscovered as new experimental results are uncovered¹³. A new demonstration by Durbin and Willshaw shows that some of these models have a much wider application than previously realized¹⁴.

One way to test the computational strength of an algorithm is to apply it to a problem whose diffi-

culty has been well established, such as the Traveling Salesman Problem. This is characteristic of a class of difficult combinatorial problems called *NP*-complete¹⁵; all these optimization problems are interconvertible, but the computing effort required to solve them increases faster than any power of the number of elements involved. In the simplest version of the Traveling Salesman Problem, a given number of cities, *N*, are randomly distributed within a unit square, and the problem is to connect all the cities with the shortest closed path that visits all the cities once. The number of possible paths is approximately proportional to N^N , so that exhaustive enumeration to find the shortest tour is prohibitively time-consuming. Reasonably good tours can be found with simple algorithms, such as the greedy algorithm, which starts from a random city and successively adds cities to the tour by choosing the closest city. A large number of more complex algorithms have been investigated for this problem¹⁶, most of which were developed with the hardware available in digital computers in mind.

A new approach to optimization problems based on network models was proposed by Hopfield and Tank¹⁷, who demonstrated that a network could be designed to find short paths for Traveling Salesman Problems. Their algorithm was analogue (rather than digital, in which the variables used occupy discrete states) and could be made to run very efficiently on special purpose analogue hardware. In essence, the network allows many possible tours to be simultaneously considered and compared. How-

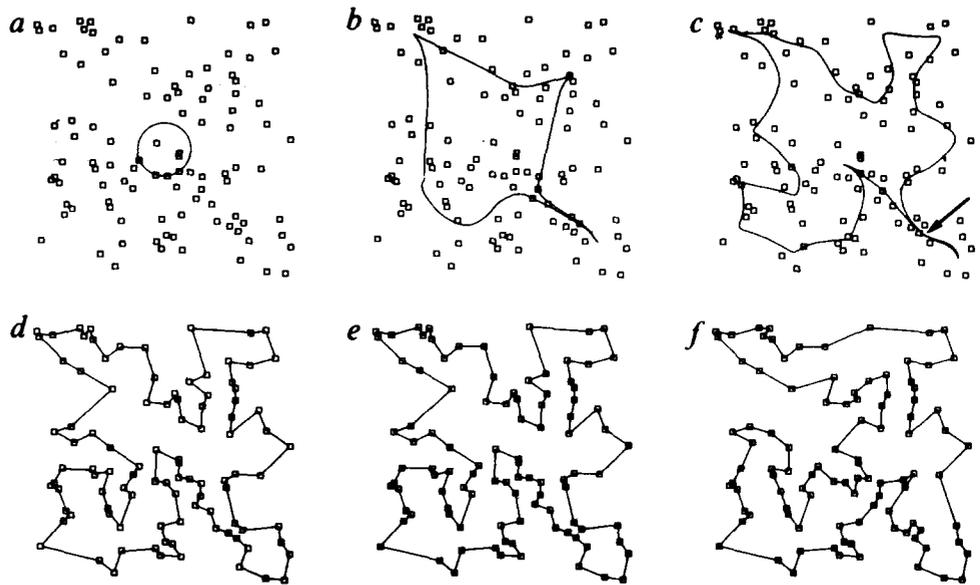
ever, the amount of hardware needed grows rapidly with the size of the problem, and the quality of the solution is not comparable to existing algorithms. The technique suggested by Durbin and Willshaw for the Traveling Salesman Problem is also analogue, but is based on the 'Tea-Trade' Model that was previously proposed to account for the formation of mappings between neural populations^{3–7}.

In the Tea-Trade Model there is local cooperation between outgrowing fibers that originate in nearby regions of the source map, and competition between these fibers for limited postsynaptic sites in the target map. The maximum cooperation will take place when the topography of the target and source maps are the same, so that neighboring neurons in the source map make synaptic contacts with neighboring neurons in the target map. A fanciful analogy helps to explain the process that takes place during the innervation of the target map by the source map. Imagine that the neurons in the source map are tea traders and that neurons in the target map are tea tasters. Tea varieties vary throughout the source map. The goal is for the tea traders to sell locally grown tea, blended from nearby plantations, to the tea tasters, who prefer tea from a trader if it is similar to tea that they are already buying. The tea traders 'discover' by trial and error that they can sell more tea to the customers who are already buying tea from traders who are their neighbors at home. During the process of trying to maximize their sales, the tea traders eventually spread out over the target map while trying as best as possible to preserve their local neighborhoods. Computer simulations show that these local mechanisms alone typically produce fragmented maps that consist of locally ordered patches.

A globally ordered map can be produced if there is an additional global mechanism that provides an overall orientation for the entire map. The local and global mechanisms that have been suggested include correlations in the firing of action potentials and gradients in the density of molecules on the surfaces of cells.

In the visual system, the source and target are both two-dimensional, but the method is quite general and applies to maps between spaces with arbitrary dimensions. In the case of the Traveling Salesman Problem, the source space is a one-dimensional loop, and the target space is the two dimensional map of cities. Points on the loop move under the influence of two forces: attraction toward the cities and attraction toward neighboring points on the loop. The progress of the model is shown in Fig. 1. The loop starts out as a small circle that elastically deforms because of attraction to the cities. As it expands it eventually passes through all the cities, as required for a legal tour. The analogy with an elastic net is made more precise by the existence of an energy function that guides the dynamics of the loop. The energy function is a global measure of how well the loop satisfies the problem, and it is reduced at each step during the progress of the loop toward the final state. This algorithm provides better solutions than the Hopfield-Tank network on a 30 city problem, and quite respectable solutions are reported for problems with 50 and 100 cities.

The new elastic net optimization method can be applied to other biological mapping problems in which variables other than position have to be organized in a map, such as the orientation and disparity preference of cells in visual cortex. It will be interesting to compare these results with other approaches to this problem, such as Linsker's model for the development of orientation columns based on the Hebb rule for synaptic plasticity¹⁰⁻¹² (see also Ref. 18). Linsker's model as well as that of Hopfield and Tank also depend on the optimization of 'energy' functions. It remains to be seen whether computational problems during development and neural network processing depend on such hidden energy functions; if so, the consequences are significant.



The realization that some biological problems have close relationships with optimization problems in computer science may influence research in both fields. In computer science, analogue methods have been out of favor for the last 25 years, in part because digital computers are so effective. VLSI technology, however, has now made it possible to design circuits that perform many analogue operations in parallel, so that tasks that require an enormous amount of digital computation can be solved with special-purpose analogue devices. For example, Mead has designed an analogue VLSI chip that performs some of the operations carried out in the retina¹⁹. The equivalent digital processing would require a Cray-class supercomputer to duplicate the processing in real time, and it has been estimated that many thousands of Crays would be required to duplicate the processing in other parts of the visual system²⁰. In addition, analogue network models can be made fault tolerant and self-healing, desirable properties as chips get larger and the yield of perfect chips gets smaller. Our view of computation may change as chips begin to emulate neural circuits.

Even with complete knowledge of the properties of single neurons it is difficult if not impossible to predict emergent properties that depend on the non-linear interactions between neurons, whether during development or as a result of dynamical activity. The ability to simulate large neural networks on conventional digital computers and

to design VLSI implementations of them will open new avenues for investigation into the organization of the nervous system.

Selected references

- 1 Sperry, R. W. (1944) *J. Neurophysiol.* 7, 57-69
- 2 Gaze, R. M. (1970) *The Formation of Nerve Connections*, Academic Press
- 3 Willshaw, D. and von der Malsburg, C. (1976) *Proc. R. Soc. London Ser. B.* 194, 431-445
- 4 von der Malsburg, C. and Willshaw, D. (1977) *Proc. Natl Acad. Sci. USA* 74, 5176-5178
- 5 Willshaw, D. and von der Malsburg, C. (1979) *Philos. Trans. R. Soc. London Ser. B.* 287, 203-243
- 6 Whitelaw, V. A. and Cowan, J. D. (1981) *J. Neurosci.* 1, 1369-1387
- 7 Fraser, S. E. (1980) *Dev. Biol.* 79, 453-464
- 8 Swindale, N. V. (1980) *Proc. R. Soc. London Ser. B.* 208, 243-264
- 9 von der Malsburg, C. (1979) *Biol. Cybern.* 32, 49-62
- 10 Linsker, R. (1986) *Proc. Natl Acad. Sci. USA* 83, 7508-7512
- 11 Linsker, R. (1986) *Proc. Natl Acad. Sci. USA* 83, 8390-8394
- 12 Linsker, R. (1986) *Proc. Natl Acad. Sci. USA* 83, 8779-8783
- 13 Gouze, J.-L., Lasry, J.-M. and Changeux, J.-P. (1983) *Biol. Cybern.* 46, 207-215
- 14 Durbin, R. and Willshaw, D. (1987) *Nature* 326, 689-691
- 15 Garey, M. R. and Johnson, D. S. (1979) *Computers and Intractability*, W. H. Freeman
- 16 Lawler, E. L., Lenstra, J. K., Rinnooy Khan, A. H. G. and Smoys, D. B. (1985) *The Traveling Salesman Problem*, John Wiley & Sons
- 17 Hopfield, J. J. and Tank, D. W. (1985) *Biol. Cybern.* 5, 141-152
- 18 von der Malsburg, C. (1973) *Kybernetik* 14, 85-100
- 19 Mead, C. (1987) *Analog VLSI and Neural Systems*, Addison-Wesley
- 20 Sejnowski, T. J. *J. Math. Psychol.* (in press)

Fig. 1. Example of the progress of the elastic net method for the Traveling Salesman Problem with 100 cities randomly distributed in the unit square. (A) Initial path. (B)-(D) Paths generated at three stages in development of the tour. (E) Final tour with length = 7.78. (F) Shortest tour found by alternative methods with length = 7.70. (Taken from Ref. 14.)