STUDIES ON THE DEVELOPMENT AND ORGANISATION OF THE NERVOUS SYSTEM OF CAENORHABDITIS ELEGANS

by

Richard Michael Durbin

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SUMMARY

The nematode Caenorhabditis elegans is a small invertebrate whose nervous system, general anatomy, and normal development are all (comparatively) extremely simple and reproducible, and have all been well characterised. This dissertation describes work based on two different approaches to the study of the control of neural development in C. elegans.

In the first part the course of neural outgrowth in the region of the ventral nerve cord was followed from electron microscope reconstructions of a series of fixed embryos. Following this, neurons whose processes grew out early were removed by laser ablation of their parent cells and the effect on subsequent nerve outgrowth was assayed by electron microscope reconstruction. The first process to grow along the ventral cord is that of AVG, and its presence is required for the normal, highly asymmetrical structure of the cord. Two more examples of dependancy on particular nerve processes for correct guidance can be deduced from experiments in which cells at the back of the animal were removed. The observations of normal development and the ablation experiments can in some cases be related to defects seen in uncoordinated mutants with defective nerve process organisation.

The second approach was to establish and analyse a computer data base containing all the synaptic connectivity data obtained by White et al. (1986), who reconstructed at an electron microscope level the entire central nervous system regions of two C. elegans. specimens. Since the circuitry is highly reproducible, comparisons of connections between equivalent pairs of cells can be used to infer properties of synapse formation. Overall, the C. elegans circuitry is anatomically highly directional, and what little chemical synaptic feedback that is seen is mostly part of reciprocal synaptic connections. There is also evidence for physical organisation of the nerve processes in subbundles of the main process tract in the central nervous system.

PREFACE

The work described in this dissertation was carried out between January 1984 and March 1987 at the MRC Laboratory of Molecular Biology, Cambridge. As described in the summary, two different approaches were used in this work, and the main body of the dissertation is split into two parts, each with its own introduction. However the introduction to the first part provides much of the general background. There is a final conclusion which considers both parts in a broader setting.

It is customary to list a long series of acknowledgements somewhere in the preface to a dissertation. I have derived enormous personal and scientific benefit from my time spent at the Laboratory of Molecular Biology, both from the people who work here and the environment that they have created. I am only going to thank personally two people, my supervisor John White, to whom I owe so much that it would be pointless to try to encapsulate it, and Nichol Thomson, who does all the serial sectioning of C. elegans at the MRC with remarkable consistency, and ultimately without whom none of this work would have been possible. I would also like to thank the Medical Research Council for a Training Award, and King's College for a Research Fellowship.

With the exception of the technical serial sectioning for the first part, this dissertation is the result of my own work and includes nothing which is the outcome of work done in collaboration. No part of this dissertation has been or is being submitted to any other University.

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