sheathed sodium cables for the transport of electricity has failed and the factory has had to be closed.

From our Materials Science Correspondent

Synaptic Ghosts

THE arresting phrase "ghosts of childhood" was used by Merrill and Wall (*J. Physiol.*, **226**, 825; 1972) when they were discussing the presence of ineffective synaptic connexions in the spinal cord of adult cats. It had previously been widely assumed that the existence of a morphological synapse between two neurones indicated a functional connexion, either excitatory or inhibitory, between these two cells. Merrill and Wall, however, described synapses that were effective only if activated artificially, by electrical stimulation, and were not driven by natural stimuli. They suggested that these synapses may have been naturally active early in development, only subsequently losing their effectiveness.

Mark and his colleagues (*Brain Res.*, **19**, 41, 53; 1971; and **46**, 131, 149; 1972) had earlier described a related phenomenon after regeneration of the oculomotor and trochlear nerves in fish. The normal nerve supplying an eye muscle was cut and that muscle forced to receive innervation from a foreign nerve. Functional synapses were established between the foreign nerve and muscle. When the normal nerve regenerated into the muscle, not only did it establish functional synapses, but its arrival also repressed the activity in the previously functional synapses formed by the foreign nerve. This repression occurred very rapidly and in the absence of observable morphological changes in the repressed synapses.

On page 201 of this issue of *Nature*, Cass, Sutton and Mark report on the finding once again of ineffective synapses, in this case in the salamander limb. Electrical stimulation of a segmental nerve supplying the limb yielded muscle contraction and functional potentials within a well defined muscular territory. Section of that segmental nerve, however, produced degenerating synapses which extended beyond the functionally defined territory of that nerve. Conversely, within the territory were found undegenerated synapses deriving, presumably, from other segmental nerves, although electrical stimulation of these latter nerves did not produce synaptic activity within the territory. This non-functional innervation occupied a band about 0.5 mm wide on either side of the territorial boundary. These ineffective synapses in the salamander differ from those described in the cat in that they are unresponsive even to electrical stimulation.

The presence of such synapses raises two questions. What do they represent, and what is responsible for the repression of their activity? Cass *et al.* suggest that chemospecific developmental forces direct nerve fibres to approximately their natural muscle territories but this process is refined by a competition between terminals for the control of muscles. The authors are a little vague as to the nature of this competition implying, in one instance, that it may be based on selective chemospecific recognition between nerve and muscle cells and, in another, suggesting that relative amounts of impulse traffic in competing terminals may be the critical factor. The end result of the competitive process is not the destruction of the defeated synapses, but their functional repression, leaving

a fringe of functionless synapses bracketing the territorial boundaries. The mechanism of the repression is not known, but the experimental situation indicates that it occurs at the neuromuscular synapse. The repression is not, however, an irreversible change occurring once and for all during development, but rather seems to be a dynamic on-going process. Function can reappear at these repressed synaptic sites.

The spinal nerve supplying a muscle territory was cut and the muscle was paralysed. Within 2 to 3 days, however, stimulation of adjacent nerve roots led to activity in the boundary fringe region. Cass *et al.* suggest that this early appearance of activity reflects the emergence of function in pre-existing but functionless nerve terminals. One to two weeks later, activity appeared in the remainder of the denervated muscle and this was attributed to collateral sprouting from fibres of adjacent nerve roots. Later, the original sectioned nerve regenerated back into the muscle, re-established functional synapses and suppressed all the foreign innervation. The suppressed synapses do not apparently disappear because cutting the normal nerve a second time resulted in the rapid derepression of foreign innervation; in this case activity appeared within 2 to 3 days throughout the denervated muscle instead of just at the boundary fringe. This conclusion is plausible but should be confirmed by the demonstration that after regeneration of the normal nerve, section of an adjacent root produces degenerating synapses throughout the muscular territory of the normal nerve.

The concept that during development synaptic relationships are established more widely than is apparent from the adult pattern is not new—it was one of the principal thrusts of Cajal's speculation on neurogenesis. What is new is the notion that these excess synapses, or a proportion of them, survive in a morphologically normal, albeit functionally ineffective, form. The substantiation of this view would mean that one could no longer accept that the anatomical demonstration of a synaptic connexion is necessarily equivalent to the demonstration of a functionally effective pathway. The suggestion by both Merrill and Wall and Cass *et al.* that functional activity in competing pathways may determine the pattern of effective synapses seen in the adult animal deserves further investigation.

From a Correspondent

Foetal Antigens and Cancer

ENTHUSIASM for the notion that the growth of malignant cells is regulated by an immunological mechanism has, as Prehn has pointed out, waxed and waned over the years. Thomas initially put forward the idea that there might exist an immunological surveillance mechanism operative against potentially malignant cell populations and Burnet has popularized this theory. Experimental validation for it has been strangely slow to accumulate although, in recent years, the relatively high incidence of malignancies in certain groups of chronically immunosuppressed patients has been cited as evidence for the hypothesis. In spite of these uncertainties many attempts are presently being made to apply immunotherapeutic techniques in the treatment of various kinds of cancer, and the concept that malignant cell populations are antigenically different from the normal cells