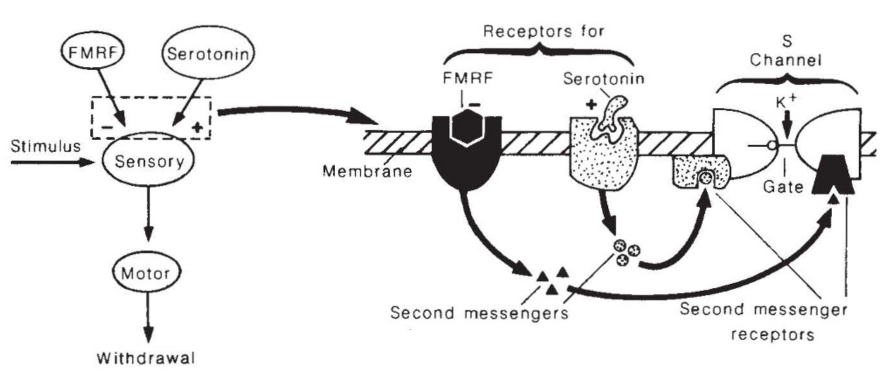

Redrawn from unpublished work of E. Kandel.

FOR many years, Eric Kandel and his colleagues at Columbia University have been unravelling the changes in neural activity that accompany the acquisition of learned behaviours in the sea slug *Aplysia*. On page 153 of this issue, F. Belardetti, E.R. Kandel and S. Siegelbaum report the latest step in their analysis of the modification of transmission between the sensory and motor neurons that mediate the gill-withdrawal reflex in response to a noxious stimulus to the animal's tail. Repeated stimulation of the tail sensitizes the reflex so that the gill is withdrawn more rapidly, a simple form of learning. This is accompanied by a broadening of the action potential in the sensory neuron, leading to increased release of transmitter at its synapses with the motor neuron, a process termed presynaptic facilitation. Siegelbaum *et al.* (*Nature* 299, 413; 1982) showed that the increased duration of the action potential results from the closure of a particular class of potassium channels, the S channels, which are regulated by the transmitter serotonin released by a modulatory neuron (see figure). Further work has shown that at least two neuromodulatory peptides have the same effect. All three facilitators activate a cyclic AMP-dependent second-messenger system, leading to phosphorylation of the S channel or an associated regulatory protein (see figure).

Recently, it has been shown at the Columbia laboratories that the small neuromodulatory peptide, FMRFamide, has the opposite effect. It produces presynaptic inhibition by hyperpolarizing the sensory neuron, decreasing the duration of its action potential and so reducing the amount of transmitter released. Now Belardetti *et al.* report that FMRFamide modulates the same channels as the facilitatory modulators, but in the opposite direction: FMRFamide keeps the channels open or reopens them if they have been shut by serotonin. The authors also provide evidence that the action of FMRFamide involves a different second-messenger system that does not depend on cyclic AMP. So far they have not revealed the identity of the second messenger but promise a surprise. It is not known which neurons produce FMRFamide and the conditions that activate either the complete facilitatory or the inhibitory pathways remain to be determined. The neuronal and molecular modulation of even such a simple piece of behaviour is proving remarkably complex. Jennifer Altman

based on a simple chain of inter-item associations, where the response to one item in the sequence becomes the stimulus for its immediate successor? Although sequential associations are involved in human learning, item position (associations between each item and the representation of its serial position in the list) and other factors are also implicated[2,3].

One way to evaluate a simple chaining account of serial learning is to conduct transfer tests which delete intermediaries that linked items in training. In the case of the alphabet, for example, a subject might be asked which comes first, P or M? For the bird, the tests involve a subset of the original sequence, for example, ABCDE is reduced to B versus D, and so on. For groups with supportive chunking arrangements, transfer is high, suggesting that more is learnt than simple sequential associations alone. The fact that birds without such support and who have learnt the sequence fail on several of the critical 'gap-filling' tests suggests, however, that positional information is restricted to the ends of the sequence unless there are boundary or marker cues that provide additional anchors[4,5].

Terrace argues strongly against chaining theories of animal learning and suggests that "sequences may be represented spatially by birds (thanks to their hard-

Fig. 2 Four-year-old girl performing a conditional rule version of a seriation task. In a given row a colour specifies the size relation of the object to be chosen.

wired sense of space) and that the processes they use to compute their position in the sequence define true precursors to human list learning" (personal communiction). Certainly, human subjects frequently report the use of a spatial image device when attempting to order 'in the mind's eye' items conveyed symbolically, for example, "Eve is bigger than Sally; Sally is bigger than Jane; Jane is bigger than Henry"[6]. In these tasks, subjects report mapping items onto a spatial vector, usually the vertical one — a device that is plausibly implicated in the frequent finding that inference or 'skipped intermediary' tests are solved faster than the time that is taken to recall the original training information[7] (see Fig. 1).

Series representations such as the inference ones illustrated, however, are not of sequences. They do not commit the subject to a specific order of action nor do they necessarily require a particular sequence of input; so "Edith is fairer than Susanne, Edith is darker than Lilly" results in a placement that does not reflect the strict order of mention. Equally, the control of lexical items in a sentence frame is determined as much by the meaning of the constituent lexical items and the overall sense that the speaker wishes to convey, as it is by certain order conventions. Of such a performance, Lashley[8] pointed out "the individual items do not in themselves have a temporal 'valence' . . . the order is imposed by some other agent".

Such an analysis demands at least two representations from the subject — modular and cooperative. Not interchangeable, they participate in a system that is essentially hierarchical. As Lashley puts it, "these space characters of the memory trace can be scanned by some other level of the coordinating system and so transformed into succession". In contrast, there is no requirement for such executive devices in serial learning tasks. Whether spatial or temporal, serial codes are essentially directional, designed to resist other patterns of succession (try whistling a tune backwards). Here, then, is a possible divide between serial learning mechanisms and thought processes.

But animals can represent a series, as shown by recent studies by my own group[9,10] on inference and seriation. The inference task is based on a five-term series problem used in research on child development. Essentially it requires the subject to learn four connected pairs of relations (as in A>B, B>C, C>D and D>E) presented in random order. The subject's ability to construct a series is then assayed in skipped intermediary tests