A NEURAL SIMULATION OF CLASSICAL CONDITIONING IN APLYSIA

Howard N. Henry
Information and Computer Science Department
University of California — Irvine

Psychological research into behavioral conditioning of animals is some of the most advanced work on learning available. Many biologists studying learning, on the other hand, have focused on the processes causing changes in the strength of the synaptic connections between neurons, and their research is most advanced in invertebrates such as *Aplysia.*

Relating the observable behavior and the cellular processes would help the overall understanding of learning. Recently, the cellular mechanisms for habituation, sensitization, and classical conditioning have been postulated for the defensive withdrawal reflex in *Aplysia* (Hawkins & Kandel, 1984).

It would be useful to test these mechanisms to establish the constraining limits on the learning they control. Simulating a model of neural mechanisms is ideally suited to the task, since it allows a wide range of controlled internal configurations to be tested under a wide range of controlled external conditions in a short time.

Already, a neural simulation of this reflex has identified a problem in producing "blocking", in which an established association between stimuli prevents formation of an association with a new stimulus (Gluck & Thompson, 1986). Another neural model has shown the implications of blocking and conditioned inhibition on animal processing of stimuli during classical conditioning experiments (Barto & Sutton, 1985).

This paper explores learning by a reflex in *Aplysia* in response to variations in *contingency* in classical conditioning presentations, using a neural simulation model. The main finding is that the learning is extremely sensitive to even very small changes in parameters such as the rate of decrement of synaptic strength with habituation.

THE DEFENSIVE WITHDRAWAL REFLEX IN APLYSIA

In mollusks such as *Aplysia,* a respiratory chamber *(mantle cavity)* contains the gill and is covered by a protective sheet *(mantle shelf)* that terminates in a fleshy spout *(siphon).* The gill, mantle shelf, and siphon all contract vigorously and withdraw into the mantle cavity when the siphon or mantle shelf is stimulated by touch.

Three forms of learning have been demonstrated in this reflex: habituation, sensitization, and classical conditioning (Hawkins & Kandel, 1984). Habituation involves a depression of neurotransmitter release at the synapses that the sensory neurons make on the motor neurons and interneurons. Sensitization is caused by an increase in neurotransmitter release at the same synapses, produced by a facilitator neuron that terminates on or near these synapses; stimulating the tail initiates this *presynaptic facilitation.*

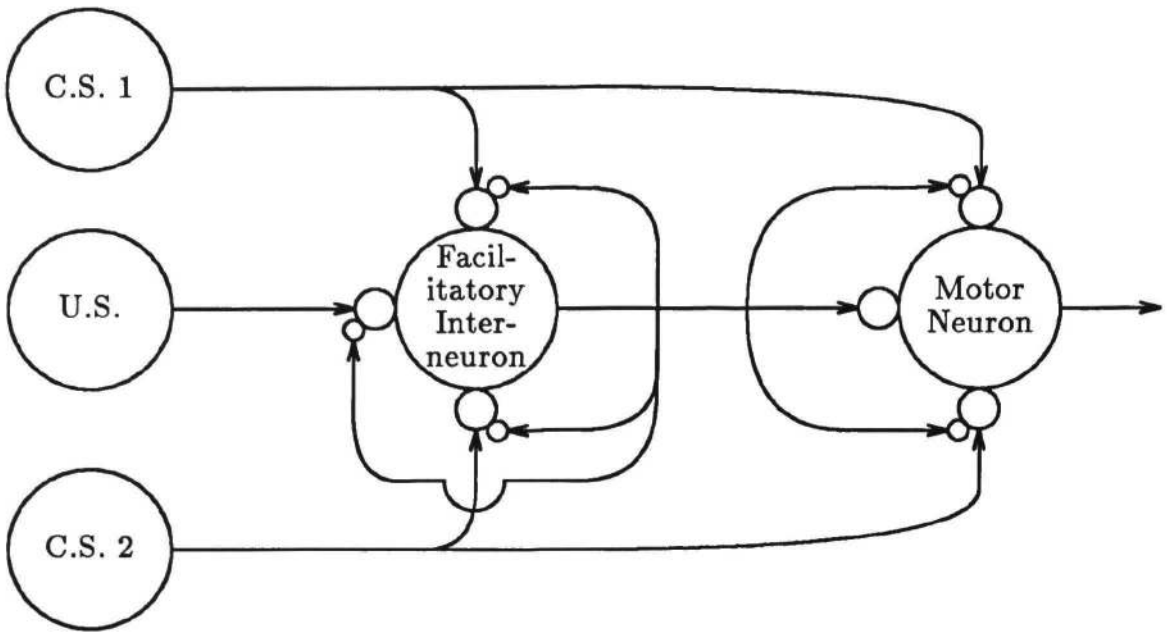

Figure 1. Simulated defensive withdrawal reflex circuit, after Hawkins & Kandel (1984).

In classical conditioning, the sensory neurons of the CS path fire just before the facilitator neuron of the US pathway becomes active. The facilitator neuron produces much more enhancement of a recently-active synapse, an effect termed an *activity-dependent amplification of presynaptic facilitation.* This enhancement is maximized when the CS precedes the onset of the US by 0.5 seconds.

The neurons, synapses, and presynapses involved in learning by this reflex are illustrated in the circuit of Figure 1 (Hawkins & Kandel, 1984). This circuit is a simplification of the actual neuroanatomy (Carew et al., 1984; Hawkins et al., 1981a), but is sufficient to demonstrate the learning in the neural simulation.

THE NEURAL SIMULATION MODEL

The input to the neural simulation model includes a description of the circuit to be simulated in terms of its neurons, synapses, and presynapses, followed by the timing of every external stimulation of a neuron for the course of the simulation. The system outputs the firing frequency of each neuron and the weight of each synapse at specified times.

Every quarter-second simulation cycle, the simulation checks for frequency changes in the input file. Then it computes the firing frequency for each neuron from the frequencies of its input neurons in the preceding cycle and the weights of the synapses between the input neurons and this neuron. Finally it updates the weight of each synapse for four possible impacts:

1. Habituation
2. Recovery from habituation
3. Sensitization and conditioning raise the weight of a synapse that has a presynapse from a rapidly-firing facilitator neuron.

4. Conditioning additionally requires recent firing of the neuron leading to the synapse. This recent activity is maintained between cycles in a *synaptic plasticity* value for each synapse.

LEARNING IN ANIMALS

A classical conditioning experiment may be described in terms of four distinct "contingency conditions" or "presentation conditions", each representing some combination of CS and US presentations (Granger & Schlimmer, 1986):

1. Perfect Pairings, containing CS - US pairs and *non-events* (having neither CS nor US);
2. Partial Reinforcement, combining CS - US pairs, spurious CS — events, and non-events;
3. Partial Warning, with CS - US pairs, spurious — US events, and non-events; and
4. Composite, having all four types of events.

All of these conditions also implicitly contain *context cues,* which are stimuli other than the CS and the US that remain constant throughout the trials.

From experiments covering various presentation conditions, Rescorla (1968) formulated a precise constraint describing those conditions that enable or prevent classical conditioning in mammals: for excitatory conditioning to occur, $P(US|CS) > P(US|\overline{CS})$. In terms of the presentation conditions, this constraint means that there should be no significant excitatory conditioning for the Composite condition, much learning for the Perfect Pairings case, and some positive conditioning for the Partial Reinforcement and Partial Warning contingencies (Granger & Schlimmer, 1986). In other words, the four presentations should be ordered as follows:

$$\textit{Perfect Pairings} > \textit{Partial Warning} \approx \textit{Partial Reinforcement} > 0 \approx \textit{Composite}.$$

Rescorla's contingency constraint is still widely held by researchers in the field of conditioning (e.g., Colwill & Rescorla, 1986).

SIMULATIONS

The simulations generally produce an increase in the strength of the synapse connecting the CS+ neuron to the motor neuron that causes the withdrawal action of the reflex. One measure of this change in strength is the *relative associative strength,* given by $(w-0.5)/0.5$, where w is the final synaptic strength and 0.5 is the initial synaptic strength.

The first simulation modeled a frequently-cited *differential conditioning* experiment in *Aplysia.* The withdrawal reflex in *Aplysia* can be differentially conditioned by pairing a tail shock reinforcing US with stimulation of either the siphon or mantle shelf, and leaving stimulation of the other unreinforced. Then stimulation of the site paired with the US (the CS+) produces greater response than the unpaired location (the CS-). In the experiment to be simulated (Carew et al., 1984; Hawkins et al., 1983; Hawkins & Kandel, 1984),

Table 1

% of Trials Spurious:	0 %	20 %	40 %	60 %	80 %	Avg. Rank	Constraint
Perfect Pairings	+0.44	—	—	—	—	1	1
Partial Warning	—	+0.22	+0.22	+0.16	+0.16	2-3 tied	2-3 tied
Partial Reinforcement	—	+0.32	+0.22	+0.14	+0.04	2-3 tied	2-3 tied
Composite	—	+0.28	+0.16	+0.04	0.00	4	4

one group of 20 *Aplysia* were given five trials of normal differential conditioning with a five-minute intertrial interval, while a second group of 20 were given the same training but with five additional US's inserted between the paired trials. The first group showed significant learning when tested, while the second group did not. Unlike the experiment but like the predictions of Rescorla's contingency constraint, the simulated second group did learn the association between CS+ and the US, though not as well as the first group without spurious US's; the relative associative strength of the first (Perfect Pairings) group was +0.44, while that of the second (20 percent Partial Warning) group was +0.22. (The presentation condition percentage refers to the proportion of spurious, unpaired trials; both figures assume a Habituation Rate equivalent to 50 percent per trial, a rate that will be tested later.)

The second set of simulations attempted to determine whether the learning by the circuit in this experimental situation conformed to Rescorla's contingency constraint. To test this required simulations over a range (0, 20, 40, 60, and 80 percent spurious trials, totaling 13 cases) of the four presentation conditions to identify the relative amount of learning under the contingencies. If learning adhered to the constraint, then performance under the four conditions would follow the prescribed relationship given earlier:

$$\textit{Perfect Pairings} > \textit{Partial Warning} \approx \textit{Partial Reinforcement} > 0 \approx \textit{Composite}.$$

The relative associative strengths for the 13 cases (at the assumed 50 percent Habituation Rate) are roughly consistent with this ordering, as shown in Table 1. Ranks of the results of the four sets of presentation conditions (1 = Highest) are also compared to the ordering of Rescorla's contingency constraint in Table 1.

The third set of simulations systematically explored the effect of variations in the Habituation Rate on the results. An analysis of the differential conditioning experiment assumed habituation at a rate equivalent to a 50 percent decrease with each US presentation (Hawkins & Kandel, 1984, p. 387). But neurophysiological measurements of habituation in this circuit's synapses average 3.9 percent per 0.1 Hz. neuron firing (Hawkins et al., 1981b), equivalent to a 25 percent decrease with each US presentation for this experiment. So in addition to the results reported at the 50 percent Habituation Rate, Figure 2 gives

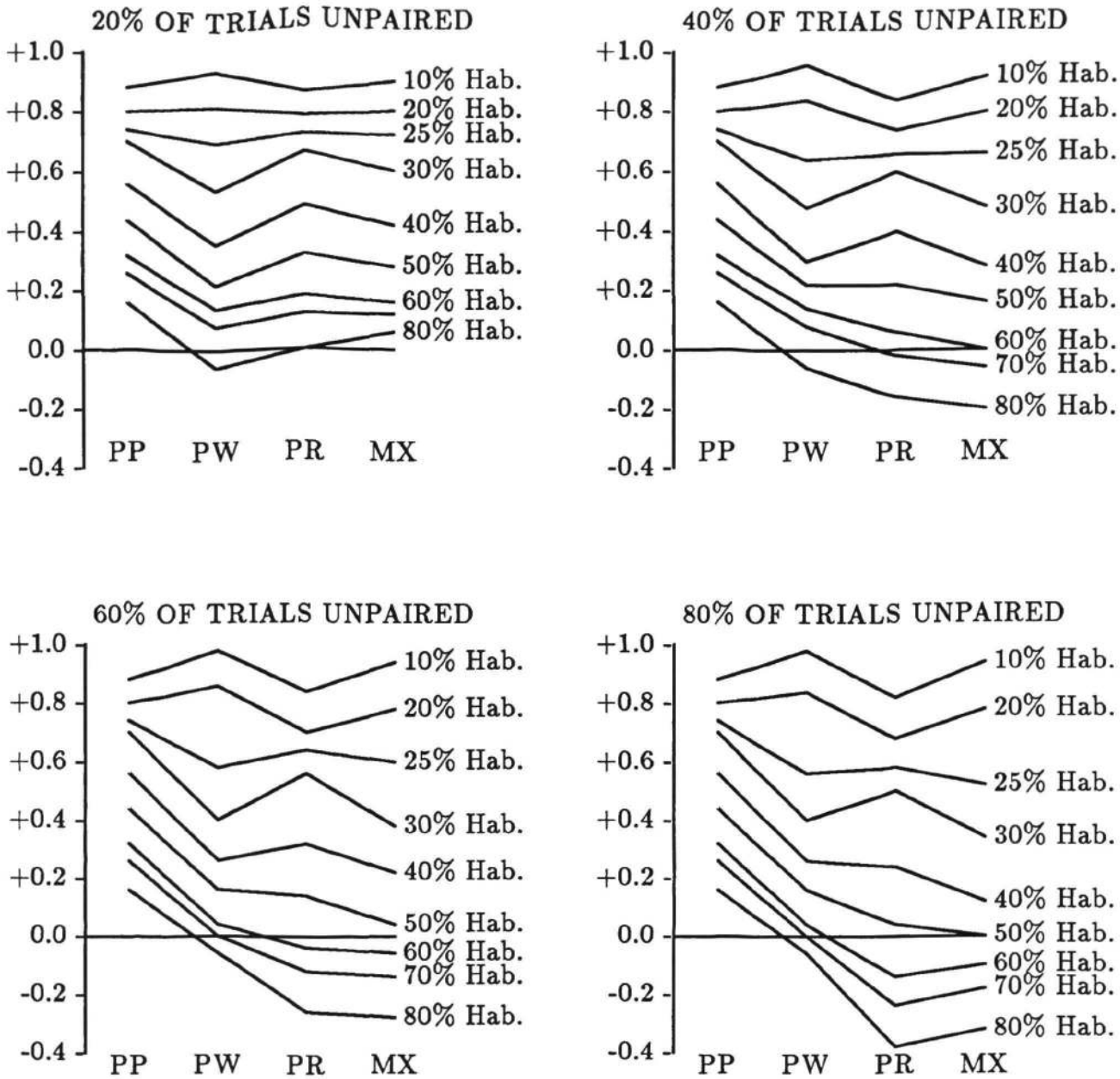

Figure 2. Each graph gives the relative associative strengths for one of the four percentages of spurious trials. Each graph contains nine curves of four points each, one curve per Habituation Rate. The four values on each curve relate to the four presentation conditions, which are situated beside each other across a graph, and are of equal levels of intensity (percentage of spurious trials). The Perfect Pairings (PP) condition is at the left, the Composite (MX) condition is at the right, and the Partial Warning (PW) and Partial Reinforcement (PR) conditions are in between. This ordering across the graph is the same as that required for Rescorla's contingency constraint, so adherence to the constraint is indicated by a curve's downward slope. (The slope of the curve between the two middle points need not fall, since these two presentation conditions should be approximately equivalent.) Conformity with the constraint also requires that the Composite value be near or below zero, and that the Partial Warning and Partial Reinforcement points be slightly positive.

Table 2

Habituation Rate	Perfect Pairings	Partial Warning	Partial Reinforcement	Composite
10	3	1	4	2
20	2	1	4	3
25	1	3-4 tied	2	3-4 tied
30	1	3-4 tied	2	3-4 tied
40	1	3	2	4
50	1	2-3 tied	2-3 tied	4
60	1	2	3-4 tied	3-4 tied
70	1	2	3-4 tied	3-4 tied
80	1	2	4	3
Constraint Prediction	1	2-3 tied	2-3 tied	4

results for the 25 percent rate and several intermediate and nearby rates so that the sensitivity of this parameter setting can be gauged. These results are summarized by Table 2's rankings of the four presentation conditions for each of the nine Habituation Rates.

DISCUSSION

These results indicate that the simulated performance of the circuit is highly sensitive to the Habituation Rate. Learning is too easy under too many conditions at low Habituation Rates, and too hard under too many conditions at high Habituation Rates. Conditioning conforms to Rescorla's contingency constraint only at a Habituation Rate approximating a 50 percent decrease per US presentation. But as indicated earlier, habituation recorded in cells of the reflex in *Aplysia* averages the equivalent of a 25 percent rate. There are four possible explanations for this discrepancy:

1. It is possible that the combination of parameter settings for the simulation is not appropriate for the experimental condition being simulated. There is likely to be an interaction among the learning rates and the timing and intensities (firing frequencies) of the stimuli in the experimental situation. While all these settings have been obtained from experimental measurements and expert assumptions discussed earlier, the various values were cast in several distinct contexts, instead of a single unified experiment. Thus each individual value may be valid for its situation, but together they may be incompatible for the experiment being simulated. Neurophysiological measurements under unifying experimental conditions would help test this possibility, as would neural simulations that systematically vary the values of each parameter to test interaction effects.

2. It is possible that the neural simulator incorporates assumptions that do not accurately reflect the processing of the neurons in the circuit.

3. It is possible that the small circuit isolated for the simulation is not sufficient for reproducing the quantitative contingency results of classical conditioning, though it is enough for demonstrating some of the more qualitative effects (e.g., Gluck & Thompson, 1986). In that case, one of the more elaborate circuits identified for the defensive withdrawal reflex in *Aplysia* (Hawkins et al., 1981a; Carew et al., 1984) may be adequate.
4. The Rescorla contingency constraint is based upon mammalian conditioning results. It is possible that learning in *Aplysia* does not adhere to the same constraints.

Further work is needed to determine which of these four possibilities best explains the discrepancy between those Habituation Rates producing learning under Rescorla's conditions and those rates that have been measured in *Aplysia*.

CONCLUSIONS

These simulations have attempted to establish whether this circuit is capable of mammalian conditioning, by testing its adherence to Rescorla's contingency constraint. The simulations have shown the sensitivity of learning to neurophysiological measures, particularly the Habituation Rate. It might be that synaptic weight change rates and neural firing frequencies will need to be completely specified before the performance of a circuit can be fully determined.

It appears that neural simulations would benefit from more extensive and detailed neurophysiological measurements for setting the values of the synaptic strength learning rates, and the *in vivo* firing frequencies resulting from stimulation by CS, US, and context stimuli. Making these various measurements under unified experimental conditions would increase the confidence in predictions made from simulating their interactions.

In addition, it would be useful to use neural simulation to systematically explore the space of joint parameter values. This would permit identification of those combinations that replicated physical experiments and those that produced results consistent with the mammalian contingency constraint. Finding the parameters most sensitive in determining performance would help prioritize the neurophysiological measurements needed.

ACKNOWLEDGMENTS

This research was supported in part by the Office of Naval Research under grants N00014-84-K-0391 and N00014-85-K-0854, by the Army Research Institute under contract MDA903-85-C-0324, and by the National Science Foundation under grants IST-81-20685 and IST-85-12419.

REFERENCES

Barto, A.G. & Sutton, R.S. (1985) Neural problem solving. In *Synaptic Modification, Neuron Selectivity, and Nervous System Organization.* Levy, W.B., Anderson, J.A., & Lehmkuhle, S. (Eds.), Lawrence Erlbaum Associates, Hillsdale, N.J.

Carew, T.J., Abrams, T.W., Hawkins, R.D., & Kandel, E.R. (1984) The use of simple invertebrate systems to explore psychological issues related to associative learning. In

Primary Neural Substrates of Learning and Behavioral Change. Alkon, D.L. & Farley, J. (Eds.), Cambridge University Press, Cambridge.

Colwill, R.M. & Rescorla, R.A. (1986) Associative structures in instrumental learning. *The Psychology of Learning and Motivation,* **20**, in press.

Gluck, M.A. & Thompson, R.F. (1986) Modeling the neural substrates of associative learning and memory: A computational approach. *Psychological Review,* in press.

Granger, R.H. & Schlimmer, J.C. (1986) The computation of contingency in classical conditioning. *The Psychology of Learning and Motivation,* **20**, in press.

Hawkins, R.D., Carew, T.J., & Kandel, E.R. (1983) Effects of interstimulus interval and contingency on classical conditioning in *Aplysia. Society for Neuroscience Abstracts,* **9**, 168.

Hawkins, R.D., Castellucci, V.F., & Kandel, E.R. (1981a) Interneurons involved in mediation and modulation of gill-withdrawal reflex in *Aplysia.* I. Identification and characterization. *Journal of Neurophysiology,* **45**, 304-314.

Hawkins, R.D., Castellucci, V.F., & Kandel, E.R. (1981b) Interneurons involved in mediation and modulation of gill-withdrawal reflex in *Aplysia.* II. Identified neurons produce heterosynaptic facilitation contributing to behavioral sensitization. *Journal of Neurophysiology,* **45**, 315-326.

Hawkins, R.D. & Kandel, E.R. (1984) Is there a cell-biological alphabet for simple forms of learning? *Psychological Review,* **91**, 375-391.

Kupfermann, I. (1985) Learning. In *Principles of Neural Science: Second Edition.* Kandel, E.R. & Schwartz, J.H. (Eds.), Elsevier, New York.

Rescorla, R. (1968) Probability of shock in the presence and absence of CS in fear conditioning. *Journal of Comparative and Physiological Psychology.* **66**, 1-5.

Shepherd, G.M. (1983) *Neurobiology.* Oxford University Press, New York, 545-561.