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13. ABSTRACT (Maximum 200 words)


**Our primary objective is to carry out a cellular and computational analysis of operant conditioning of the head waving response in *Aplysia*. During the last twelve month period, progress has been made in five areas: We have carried out a detailed kinematic analysis of the operant response; (2) We have identified the biomechanical principles underlying the operant response; (3) We have identified the precise pattern and timing of muscles and motor neurons during head waving. Advances in areas 1-3 above have allowed us (4) to construct a quantitative computational model of head waving using biological parameters. In addition (5) We have identified a novel form of reinforcement for conditioning of head waving that significantly advances the cellular and computational analysis.**


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**ANNUAL TECHNICAL REPORT**
Thomas J. Carew
AFOSR-89-0362

## A. OBJECTIVES

The overall research project has three primary objectives:

1. **The first objective is to carry out a detailed circuit analysis of the neural networks underlying operant conditioning in Aplysia.**

To perform a complete circuit analysis of operant conditioning we are specifying: a) the operant response circuitry; b) feedback circuitry; and c) reinforcement circuitry involved in the learning.

2. **The second objective is to analyse the expression of operant conditioning in identified neural circuits.**

Three experimental strategies are being used: a) We are examining neural correlates of the conditioning in previously trained animals; b) we are producing the operant conditioning *in vitro* while recording from relevant circuit elements; and c) we are examining neural analogues of the conditioning by direct activation of relevant circuitry.

3. **The third objective is to generate a quantitative computational model of operant conditioning.**

An essential feature of the computational model we plan to generate is that it will use empirically derived biophysical parameters, synaptic weights and circuit properties in its construction. The modelling analysis will be carried out at three levels: a) individual circuit elements; b) restricted neural networks; and c) simulations of adaptive changes within elements and networks.

## B. STATUS OF THE RESEARCH EFFORT

In the third year of this award we have made significant progress towards achieving all of the research objectives described above. During this year, important progress has been made in a quantitative understanding of the operant response on kinematic, biomechanical, muscular and cellular levels, which in turn has premitted formulation of a computational model of the head waving response and its modification through learning. I will discuss these advances in the paragraphs that follow.

**1. We have carried out a detailed kinematic analysis of the operant response (head waving).**

These studies allowed us to specify the major components of the headwaving response in quantitative terms. These data were essential for building the computational model of the head waving response (see #4 below).

**2. We have identified the biomechanical principles underlying the head waving response.**

We have described, for the first time, that head waving in *Aplysia* cannot be explained in terms of a "muscular hydrostat" (a prevailing model in the field). Rather, head waving requires coordinated antagonism between identified longitudinal muscle groups.

**3. We have identified the timing and pattern of muscle and motor neuron activity underlying head waving.**

These studies used chronic EMG recording in intact animals to determine the precise pattern and timing of muscular and neural activity during head waving. These studies also provided critical data for the computational model (See #4 below).

**4. We have developed a quantitative computational model of head waving using empirically identified biological parameters.**

These studies now allow us to examine operant conditioning of head waving in quantitative terms, combining both neurocomputational and theoretical levels of analysis.

**5. We have identified a new form of reinforcement in conditioning of head waving that allows a simultaneous cellular analysis.**

We have found that, in addition to light as an aversive reinforcer (Cook and Carew 1986, 1989a,b; 1991) mild electric shock to the anterior tentacle produces also rapid conditioning. In addition we have identified the sensory neurons carrying this reinforcing input and shown that, even at this very early neural stage in information processing, learning-specific changes can be identified in the sensory neurons. These studies now permit a detailed cellular (and ultimately computational) analysis of the reinforcement pathway for operant conditioning.

## C. Publications

1. Kuenzi, F.M. and Carew, T.J. (1992). A quantitative analysis of the head waving response in *Aplysia californica*: I. Kinematic identification of primary components of head waving. *J. Neuroscience* (in preparation).

2. Kuenzi, F.M. and Carew, T.J. (1992). A quantitative analysis of the head waving response in *Aplysia californica:* II. A biomechanical model of antagonistic motor control. *J. Neuroscience* (in preparation).

3. Kuenzi, F.M. and Carew, T.J. (1992) A quantitative analysis of the head waving response in *Aplysia californica:* III. Pattern and timing of muscle and motor neuronal activity. *J. Neuroscience* (in preparation).

4. Kuenzi, F.M. and Carew, T.J. (1992). A quantitative analysis of the head waving response in *Aplysia californica:* IV. Interganglionic coordination. *J. Neuroscience* (in preparation).

5. Mercer, A.R., Emptage, N.J. and Carew, T.J. (1991). Pharmacological dissociation of modulatory effects of serotonin in *Aplysia* sensory neurons. *Science* **254:** 1811-1813.

6. Fischer, T.M. and Carew, T.J. (1992). Activity dependent potentiation of recurrent inhibition: A mechanism for dynamic gain control. *J. Neuroscience* (submitted).

7. Blazis, D.E.J., Fischer, T.M. and Carew, T.J. (1992). A neural network model of inhibitory information processing in *Aplysia*. *Neural Computation* (in press).

8. Fitzgerald, K. and Carew, T.J. (1992). Learned modification of head waving behavior in *Aplysia* with aversive reinforcement. *Soc. Neurosci. Abs.* (in press).

9. Bunin, L., Fitzgerald, K., Kuenzi, F.M. and Carew, T.J. (1992). A quantitative model of the head waving response in *Aplysia* and its modification through learning. *Neural Computation* (in preparation).

D. PERSONNEL

1. Frederick Kuenzi, graduate student (Ph.D., 1992).

2. Kent Fitzgerald, graduate student (fourth year)

3. Diana Blazis, Ph.D., post doctoral fellow.

4. Thomas Fischer, Ph.D., post doctoral fellow.

**E. INTERACTIONS**

*Papers at scientific meetings*

1. Carew, T.J. (1991) Inhibitory information processing in the siphon withdrawal reflex in *Aplysia*. *Neur. Info. Proc. Soc., Denver, CO.*

2. Fischer, T. and Carew, T.J. (1991) Activation of the facilitatory interneuron L29 produces inhibition of reflex input to siphon motor neurons in *Aplysia*. *Soc. Neurosci.*, **17**, 1302.

3. Blazis, D.E.J., Berkowicz, D.A., Kairiss, E.W. and Carew, T.J. (1991) A network model of inhibitory information processing in the siphon withdrawal reflex of *Aplysia*. *Soc. Neurosci.*, **17**, 1302.

4. Mercer, A.R. and Carew, T.J. (1991) Cyproheptadine blocks 5-HT-induced spike broadening but not 5-HT-induced anti-accomodation: Evidence for multiple 5-HT receptors in *Aplysia* sensory neurons. Soc. Neurosci., **17**, 1591.

Invited colloquia and plenary presentations

1. Brown University (Winter 1992)

2. Cornell Medical School (Spring 1992)

3. Columbia University (Spring 1992)

4. Dahlem Conference, Berlin (Spring 1993)

5. Invited lecture series, Free University, Berlin (Spring 1993)

**F. DISCOVERIES, INVENTIONS, PATENTS**

not applicable