# AN EXAMPLE OF INFORMATION RETENTION IN RABBIT VENTRICULAR MUSCLE FIBRES

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ABSTRACT The preparation was stimulated externally and transmembrane action potentials were recorded with intracellular microelectrodes. The relationship between the area of the first action potential after a pause in stimulation and the duration of the pause was examined. It was found that the area retained its dependence on the pattern of stimulation prior to the pause. These experiments confirm one of the predictions of a mathematical model (Gibbs *et al.*, 1963) which describes the relationship between the area of action potentials and the pattern of stimulation.

## INTRODUCTION

We have formulated in a previous paper (Gibbs *et al.*, 1963) a mathematical model which describes quantitatively the relationship between the area of rabbit ventricular action potentials and the pattern of stimulation. An interesting consequence of the model is that each muscle fibre should possess a degree of memory, erasable by stimulation, but which persists when the muscle is left unstimulated. The model predicts, as one would expect, that the area of an action potential initiated after a period of rest depends both on the duration of the rest period and on the stimulation pattern applied to the muscle prior to the rest period. However, when the period of rest is sufficiently long (about 2 minutes, depending on the fibre and the previous rate of stimulation), the area of the first action potential initiated after it should (*a*) become independent of the duration of the rest period and (*b*) retain its dependence on the pattern of stimulation prior to the rest period. This paper contains experimental evidence which confirms the second of these predictions.

## METHODS

The apparatus was the same as described in our previous paper (Gibbs *et al.*, 1963).

## RESULTS

Two experiments were performed with each fibre. These were designed to determine the relationship between the area of an action potential initiated after a pause in stimulation and the duration of the pause for two different sets of initial conditions. In the first experiment the muscle was stimulated at 0.3 sec.$^{-1}$ until the action potential area became constant. Stimulation was then stopped for a known length of time and the area of the first action potential after the pause was recorded. This was repeated for different durations of the pause. In the second experiment the same procedure was followed, except that an extra stimulus was added about 200 msec. after the last stimulus at the constant rate so that each pause was preceded by two closely spaced action potentials. The area of the first action potential after each pause was again recorded and plotted against the duration of the pause. The results of the two experiments are shown in Fig. 1 where the area of the first action potential after a pause is plotted against the duration of the pause.

The results can be described as follows: As the duration of the pause in stimulation is increased, the area of the first action potential after the pause decreases rapidly to a minimum value and then slowly rises. The difference in the results of the two experiments is that in the second experiment the area always declines to a lower minimum value and thereafter remains lower during the slow rise.

We were unable to examine the complete duration and magnitude of the slow rise for two reasons: (*a*) All preparations had a tendency to beat spontaneously when they were left unstimulated for long times. (*b*) The force of contraction associated with the first action potential increased as the duration of the pause was increased and the microelectrode was often dislodged from the fibre after a long pause. The maximum useful rest period was found to be 2 to 3 minutes. The complete results as described above were obtained in thirteen fibres in six hearts. Incomplete results were obtained in more than twenty other fibres.

## DISCUSSION

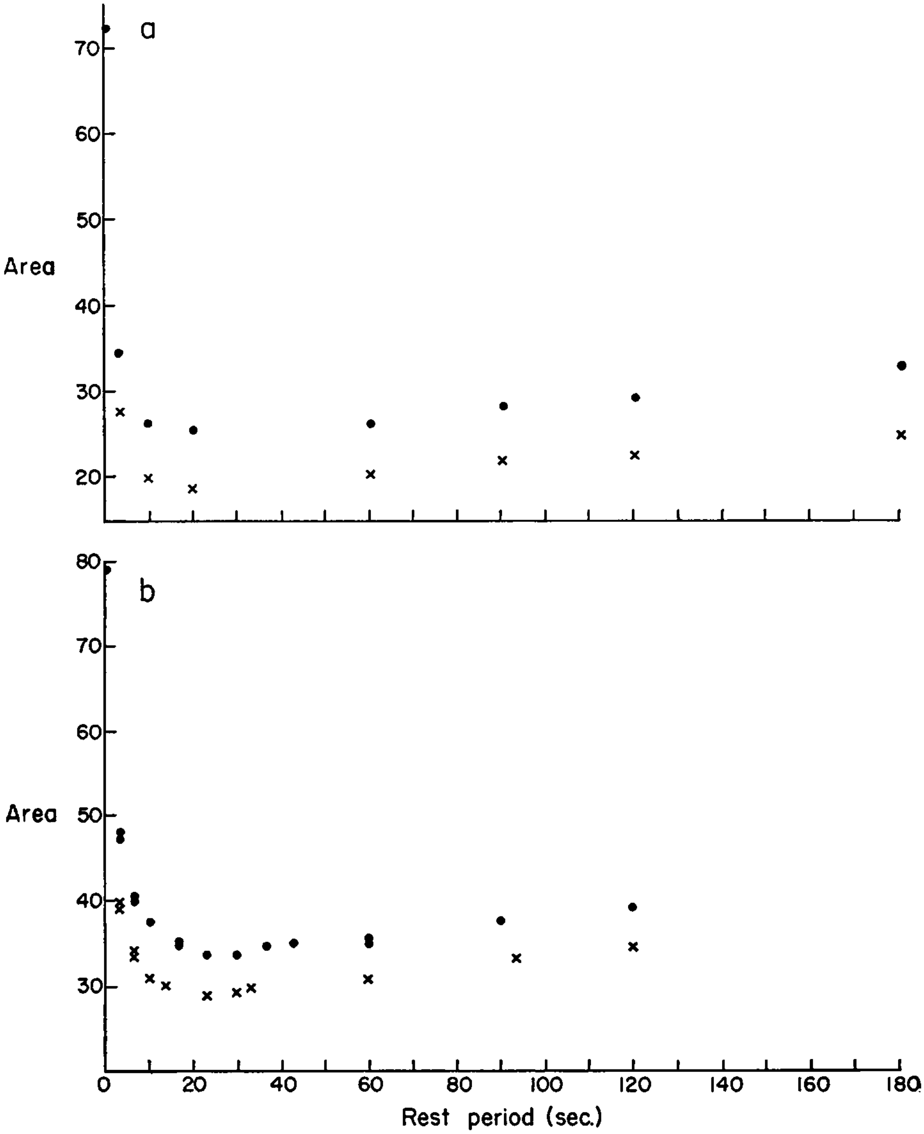
According to the model described by Gibbs *et al.* (1963) the area of an action potential is a linear function of the product of two independent variables, $M$ and $N$. Thus

$$\text{Area} = A + BNM \tag{1}$$

in which $A$ and $B$ are constants. $N$ is a fast changing quantity which is increased by an amount $\Delta N$ during the upstroke of each action potential and thereafter decays according to the equation

$$N(t) = N_0 \exp\left[-\frac{a_n}{b_n}\nu_0(1 - e^{-b_n t})\right] \tag{2}$$

in which $a_n$ and $b_n$ are contants, $N_0$ and $\nu_0$ are quantities depending on the previous pattern of stimulation, and $t$ is the time after the upstroke of the last action potential. The half-time of the decline of $N$ is of the order of 1 second or less. The variable $M$



FIGURES 1*a* and 1*b* The relationship between the area of an action potential initiated after a period of rest and the duration of the period of rest. The two figures show results obtained in two different fibres. In both cases the rate of stimulation prior to the period of rest was 0.3 sec.$^{-1}$ In each figure the full circles (●) are the results of the experiment in which the rest period was preceded by the last action potential initiated at the constant rate and the crosses (×) are points obtained in the same fibre when the period of rest was preceded by two closely spaced action potentials.

changes slowly; it is decreased by a small amount during every action potential and is regenerated at all times according to the equations

$$\frac{dM}{dt} = a_m \mu (1 - M) \tag{3}$$

$$\frac{d\mu}{dt} = c_m M (1 - \mu) \tag{4}$$

in which $a_m$ and $c_m$ are constants and $\mu$ is a variable which behaves similarly to $M$. The values of both $M$ and $\mu$ lie at all times between 0 and 1. The half-times of the changes in $M$ are of the order of 1 minute.

During a rest period the area will be a linear function of the product of $N$ as given in equation (2) and $M$ given by the solution of equations (3 and 4) which, in the absence of stimulation, is a function increasing asymptotically towards 1. The model thus predicts an initial rapid decline in area to a minimum value followed by a slow rise to a steady value. This steady value is given by

$$\text{Area} = A + BN_0 \exp\left[-\frac{a_n}{b_n}\nu_0\right] \tag{5}$$

in which the quantities $N_0$ and $\nu_0$ depend on the pattern of stimulation prior to the rest period.

The two experiments described in the Results were designed to begin the pauses with two different sets of values of $N_0$ and $\nu_0$ which, according to equation (5), should in general result in two different steady areas. We have found previously (Gibbs *et al.,* 1963) that when an extra action potential is initiated shortly after an action potential at a low constant rate, $\nu$ is increased significanly to a new value $\nu_0$ while $N$ is increased only slightly or may even decrease. Since the area given by equation (5) is more strongly dependent on $\nu_0$ than on $N_0$ (the ratio $a_n/b_n$ was found to be of the order of two), the extra action potential preceding the rest period should have the effect of lowering both the minimum and the steady-state values of the area.

The experimental results are in agreement with this prediction. In all fibres the addition of the extra action potential caused the area to decline to a lower minimum and thereafter the displacement in area of the two relationships was maintained. The experimental difficulties inherent in long rest periods prevented us from following the relationship long enough to attain a steady-state. However, even after rest periods of 3 minutes the curves appear to maintain their spacing. It is reasonable, therefore, to assume that the "memory" persists for considerably longer times.

The experimental results are not in agreement with the other prediction which follows from the model; *i.e.,* that the area should attain a steady value in about 2 minutes. In most fibres the slow rise in area was both too great and too prolonged to be accounted for by the increase in $M$. Our interpretation of the complete results is that the two variables $M$ and $N$ behave during a long pause as predicted by the model, but that some other effect which increases the action potential area may become important during long periods of rest. This effect could be described by an additional variable. The half-time of the changes in the new variable would have to be at least 3 minutes and these changes would not be detected except after a long pause.

This work was done during the tenure by J. Tille of a Fellowship of Merck, Sharp and Dohme (Australia) Pty. Ltd. The authors wish to thank the Life Insurance and Medical Research Fund of Australia and New Zealand for a grant in aid of this work.

*Received for publication, September 30, 1963.*

## REFERENCE

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