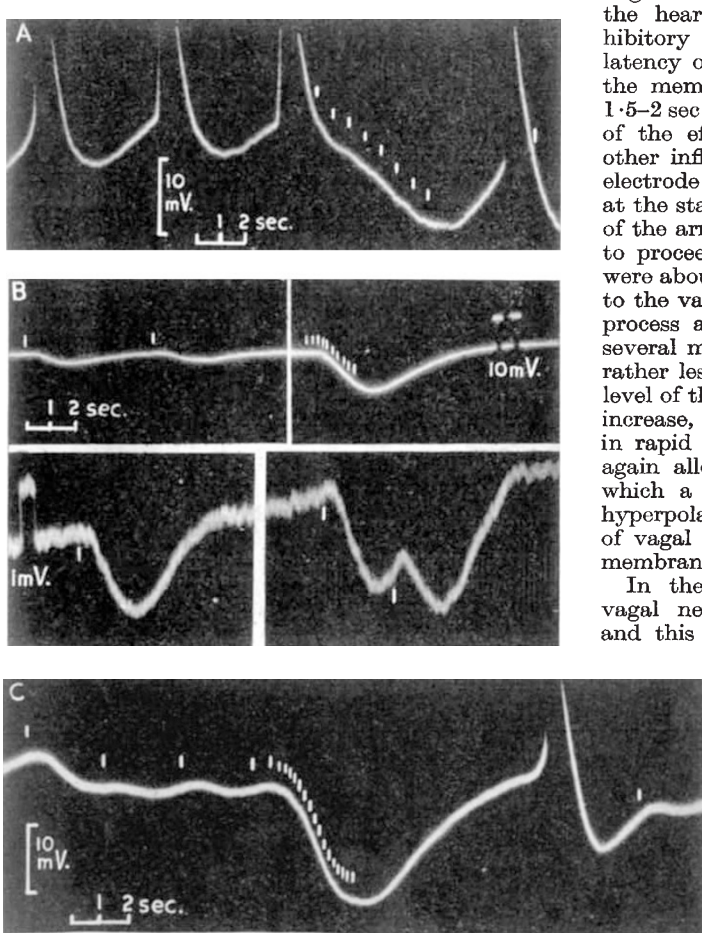
Production of Membrane Potential Changes in the Frog's Heart by Inhibitory Nerve Impulses

THE observations reported here were made in the course of preliminary experiments concerned with the electrical changes which vagal and sympathetic nerve impulses produce in the pace-maker region of the heart. The preparation was the sinus venosus of the frog together with its nerve supply (one or both vagi; more recently, the intra-cranial roots and sympathetic components of the vagus were prepared for separate stimulation). A micro-electrode was used for intracellular recording of the membrane potential, the electrode being introduced into the sinus through the exposed sino-auricular ostium or through the cut inferior vena cava. Although the nervous control of the heart is not restricted to its pace-maker region, we were especially interested in the mechanism by which nerve impulses regulate the beat frequency, and an attempt was therefore made to place the recording electrode as close as possible to the point of origin of the rhythmic activity. This place can be recognized by the appearance of a slow depolarization preceding each action potential[1,2], and the accompanying records were obtained from such regions.



Intracellular recording from the sinus venosus of the frog's heart. Single stimuli to the vagus are indicated by white dashes. Depolarization is signalled by upward deflexion of trace. Note: slow spontaneous depolarization precedes the spike potential; vagal impulses are followed by transient hyperpolarization

In (*A*), the recording electrode had been inserted into an active part of the sinus, beating at a rate of about 12 per min. The highest level of the membrane potential, in the interval between the action potentials, was about 50 mV. After the third beat, a series of stimuli (indicated by dashes) were applied to the vagus, causing an increase of the membrane potential (downward displacement of the trace) accompanied by a stoppage of the beat. After the end of the vagal stimuli, the membrane potential fell and another impulse arose.

In (*B*) and (*C*), the effects of single and repetitive vagal shocks are shown during a state of arrest of the heart produced by a preceding burst of inhibitory impulses. Each shock is followed, after a latency of about 0·5 sec., by a transient increase of the membrane potential reaching a peak in about 1·5–2 sec. and lasting 5–7 sec. (16° C.). The amplitude of the effect varied greatly; it depended, among other influences, upon the position of the recording electrode and the timing of the stimulus. For example, at the start of record *C*, the slow local depolarization of the arrested pace-maker region had been allowed to proceed towards a level at which renewed beats were about to occur. A single shock was then applied to the vagus (first dash), stopping the depolarization process and increasing the membrane potential by several millivolts. The next few shocks contributed rather less and only served to maintain the average level of the potential; to obtain a further substantial increase, it was necessary to fire a series of impulses in rapid succession. After this, depolarization was again allowed to develop, this time to a point at which a new action potential arose. The largest hyperpolarization so far obtained during a burst of vagal impulses amounted to 33 mV. (raising the membrane potential from 50 to 83 mV.).

In the experiment illustrated here, the mixed vagal nerve ('vago-sympathicus') was stimulated, and this may have resulted in some complication. Thus, the obvious enhancement of the 'post-vagal' spike and its lowered firing threshold (in *A* and *C*) may have been due, in part, to a delayed action of sympathetic impulses (as was found to occur in other experiments in which the component nerves were stimulated separately). However, the hyperpolarization which accompanies the immediate inhibitory effect was confirmed when the intracranial vagal roots were excited alone. These observations agree well with the classical, but sometimes disputed, findings made by Gaskell[3] on the quiescent auricle of the tortoise, namely, the occurrence of a positive variation of the injury potential during excitation of the inhibitory nerve fibres of the heart.

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[1] Weidmann, S., *J. Physiol.*, 115, 227 (1951).
[2] Trautwein, W., and Zink, K., *Pflüg. Arch. ges. Physiol.*, 256, 68 (1952).
[3] Gaskell, W. H., *J. Physiol.*, 8, 404 (1887).