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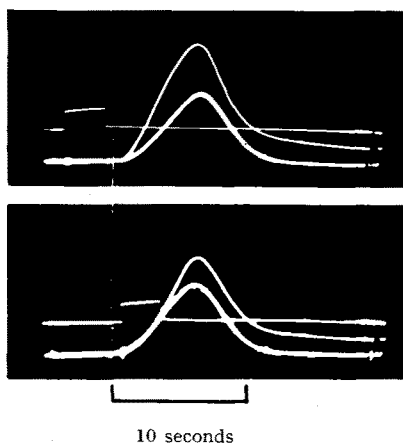
### Summary

A new synthesis of flavopereirine is described, starting from the quaternary salts of gramine and N-phenacyl-3-ethyl-pyridinium bromide.

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## Effect of Increasing the Calcium Concentration During a Single Heart-Beat<sup>1</sup>

Ca ions serve as a link between electrical and mechanical activity<sup>2-4</sup>; their concentration is an important factor determining the contractile strength. The question arises whether it is the Ca level at the onset of electrical activity which sets the degree of shortening (trigger effect), or whether Ca ions are essential throughout the phase of electrical activity in order to link shortening to membrane depolarization. The plan of the experiment was to raise the Ca concentration rapidly, after the beginning of an action potential, and to see whether this would still result in a stronger contraction.



Effect of admixing Ca ions to the perfusate of a turtle ventricle. In each of the two records, the film was exposed during three successive contractions, of which the first two coincide. Calcium was admixed, as indicated by the 2.5 sec square pulse, preceding the third beat (top record) and during the third beat (bottom record). The retouched vertical line marks the moment of stimulation.

Turtle ventricles were immersed in a bath of cooled Ringer's solution (8°C) and driven electrically at a rate of 1 beat/min. A cannula was inserted into the single coronary artery and the vascular bed was perfused with

Ringer's solution of a low Ca concentration (0.7 mM). A calcium-rich solution (100 mM CaCl<sub>2</sub> in Ringer's) was kept ready in a thin tube ending inside the tip of the arterial cannula. Relatively small volumes of this solution could be admixed for periods of 2.5 sec. Contractions were recorded by means of a mechano-electrical transducer (RCA 5734). The method has been described in more detail in connexion with a different type of experiment<sup>5</sup>.

The Figure shows the effect of momentarily raising the Ca concentration before and during systole. The lower record makes it clear that an increment of contractile strength could still be obtained if the Ca concentration in the perfusate started to rise at the beginning of systole, i.e. after the onset of membrane depolarization.

Membrane potentials were recorded on several occasions by means of LING-GERARD<sup>6</sup> electrodes. A 'pulse' of calcium ions had the effect of slightly shortening the action potential. This would not, *per se*, be expected to result in a stronger contraction. It seems permissible, then, to conclude that Ca ions mediate between electrical and mechanical activity throughout the period of membrane depolarization.

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### Zusammenfassung

An Schildkrötenherzen verstärkt eine Zugabe von Ca-Ionen, die nach Beginn des Aktionspotentials erfolgt, die bereits begonnene Kontraktion. Es wird daraus geschlossen, dass Ca-Ionen während der ganzen Erregungsphase (und nicht nur zu deren Beginn) zwischen der elektrischen und der mechanischen Aktivität vermitteln.

<sup>5</sup> S. WEIDMANN, J. Physiol. 132, 157 (1956).

<sup>6</sup> G. LING and R. W. GERARD, J. cell. comp. Physiol. 34, 383 (1949).

## Calcium and the Activation of Contraction

It has recently been proposed<sup>1</sup> that the contraction of heart muscle is initiated by a negatively charged Ca-compound (an 'activator') which is moved during depolarization of the cell membrane from the surface into some deeper cellular compartment. This hypothesis is based for the most part on an analysis of two experimental observations on the frog's heart: (1) that tension developed in twitches and contractures depends on the ratio  $[Ca]/[Na]^2$  (these being the Ca and Na concentrations in the outside fluid)<sup>2,3</sup>. This observation suggested in turn that Na and Ca ions compete for a site or molecule 'R' which becomes active only when it combines with Ca. (2) Contracture tension obtained at a given ratio  $[Ca]/[Na]^2$ , i.e. at a given concentration of the proposed 'activator CaR', is larger the greater the degree of membrane depolarization (which was varied experimentally by altering the external K-concentration)<sup>1</sup>. This effect suggests that the normal mem-

<sup>1</sup> H. C. LÜTTGAU and R. NIEDERGERKE, J. Physiol. 143, 486 (1958).

<sup>2</sup> W. WILBRANDT and H. KOLLER, Helv. physiol. Acta 6, 208 (1948).

<sup>3</sup> R. NIEDERGERKE and H. C. LÜTTGAU, Nature, Lond. 179, 1066 (1957).

<sup>1</sup> Aided by the Swiss National Science Foundation, Grant No. 1138.

<sup>2</sup> I. DE B. DALY and A. J. CLARK, J. Physiol. 54, 367 (1921).

<sup>3</sup> H.-C. LÜTTGAU and R. NIEDERGERKE, J. Physiol. 143, 486 (1958).

<sup>4</sup> R. NIEDERGERKE, Exper. 15, 128 (1959).