

THE RELATION OF TEMPERATURE TO THE  
PULSE RATE OF THE FROG.

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THE object of the present paper was, by a comparative study of the temperature coefficients of the hearts of certain cold- and warm-blooded animals, to gain further knowledge of the point at which the nervous system commences to dominate the response of pulse rate to temperature and, if possible, to ascertain the nature of the nervous control if such were found to exist. It deals with the effect of temperature on the pulse rate of the frog.

The general scheme has been to compare the effects of temperature on the excised heart with that on the pulse rate in the intact animal, to observe the difference if any, and to test whether this difference was due to nervous influences.

This problem has attracted the attention of workers from time to time. No complete solution having been arrived at, it has been reviewed with each relevant advance in knowledge or technique. Newell Martin's heart-lung preparation (1883) showed that, freed from both the vagus and the sympathetic, the heart rate increased on warming and decreased on cooling, whilst G. N. Stewart [1892] believed the vagus activity to be reduced at lower temperatures. Cyon [1874] reported that warming the brain slowed the heart.

Langendorff [1895] carried Newell Martin's work to fruition by his elimination of the lung from Martin's preparation and its replacement by an artificial system for the aeration of the blood, thus producing the "excised mammalian heart." Langendorff showed that in the excised heart the rate of increment of frequency rose when the organ was warmed above the normal body temperature, and decreased when cooled below that level. Knowlton and Starling [1912], in their mammalian heart-lung preparation, showed that within certain limits the heart rate was nearly a linear function of the temperature.

Since the work of van 't Hoff and of Arrhenius interest has centred largely in whether the frequency of the heart followed the equation

$$K_1 = K_0 e^{\frac{\mu}{2} \cdot \frac{T_1 - T_0}{T_1 T_0}},$$

in which equation  $T_1$  and  $T_0$  are two temperatures recorded on the Kelvin scale,  $K_0$  being the frequency of the heart at  $T_0$ ,  $K_1$  at  $T_1$  and  $\mu$  is a constant.

It has been shown by Krogh [1916] that, in the metabolism of the body, there is a falling-off of the value of the temperature coefficient ( $Q_{10}$ ) as the temperature rises, and Clark [1927] has given figures which show the same thing for the excised frog's heart. Crozier [1926] and his pupils have carried out very detailed researches on many animal tissues which lead them to the view that the alteration in  $Q_{10}$  is not a gradual affair, and that such a curve as that given by Clark is in reality made up of two or more straight lines, which either may be at different inclinations or may be parallel. Crozier's paper [1926] gives an account of this literature.

#### THE EXCISED HEART.

In making measurements of the temperature coefficient of the excised frog's heart, the difficulty at first presented itself that, if the temperature were lowered and then raised, the number of beats being noted the whole time, the curve relating the frequency to the temperature was not the same on the downward as on the upward grade. We, therefore, sought in the literature for some record of an experiment in which, at a constant temperature, the frequency remained constant over a considerable period of time; this on the heart we failed to find, though on the rate of respiration of the grasshopper, etc., such data exist as shown by Crozier and Stier [1924 a].

A preliminary research was undertaken in order to study the conditions necessary to maintain the beat of the sinus at a constant rate over a long time. The results of the research have been given by one of us in a previous paper. The methods and precautions described have been used in the present work to insure that, over the whole period of one experiment, the rate of beat would not vary by more than three or four beats as the result of chance occurrences.

We have carried out two sets of experiments, one in December and January, the other in July<sup>1</sup>. They gave different results. Future experi-

<sup>1</sup> These results have been confirmed by N. B. Taylor in June 1930, as shown in a subsequent paper [1931].

ment may show whether the difference is really seasonal, or whether it was in some way accidental. Crozier and Stier found seasonal variations in the temperature coefficient of the heart of *Limax* [1924 b]. We will first describe the experiments carried out in winter.

*The effect of alteration of temperature on the hearts of frogs investigated during the winter.*

*Apparatus and experimental errors.*

The types of apparatus used in the above and following experiments were those described in a previous paper for the observation of excised hearts in about 50 c.c. of saline solution [1930].

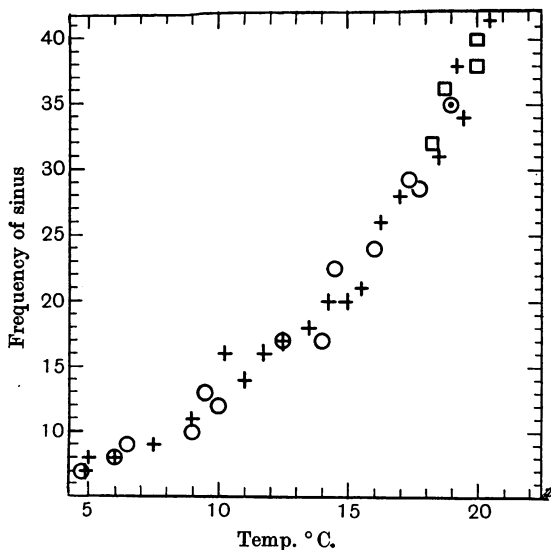


Fig. 1. Isolated frog's heart, 26 (winter series). The relation of the beats to temperature, as in the others, was investigated only when the steady state had been established. Circles, coming down; crosses, going up; squares, coming down a second time.

A typical curve of the effect of temperature on the beat of the frog's heart, so far as reproductibility of heart rate at any given temperature is concerned, is shown in Fig. 1. The first observation was made at 19°. The circles show the measurements going down the curve at gradually decreasing temperatures until 4° C. was reached. The crosses show the points on the gradual subsequent ascent, and the squares on a second descent. The whole time taken for the portion of the experiment shown was 3 hours and 39 minutes, the time between the circle at 19.0° and the cross at 18.5° C. was 3 hours; between that cross and the square at

18.3° was 39 minutes. Thus the combined effect of the reversals of temperature over a range from 19° to 4° C. and of the causes incidental to a lapse of time of more than 3½ hours did not produce an alteration of more than four beats in the measurement at any one temperature, thirty-three measurements in all being made during the experiment.

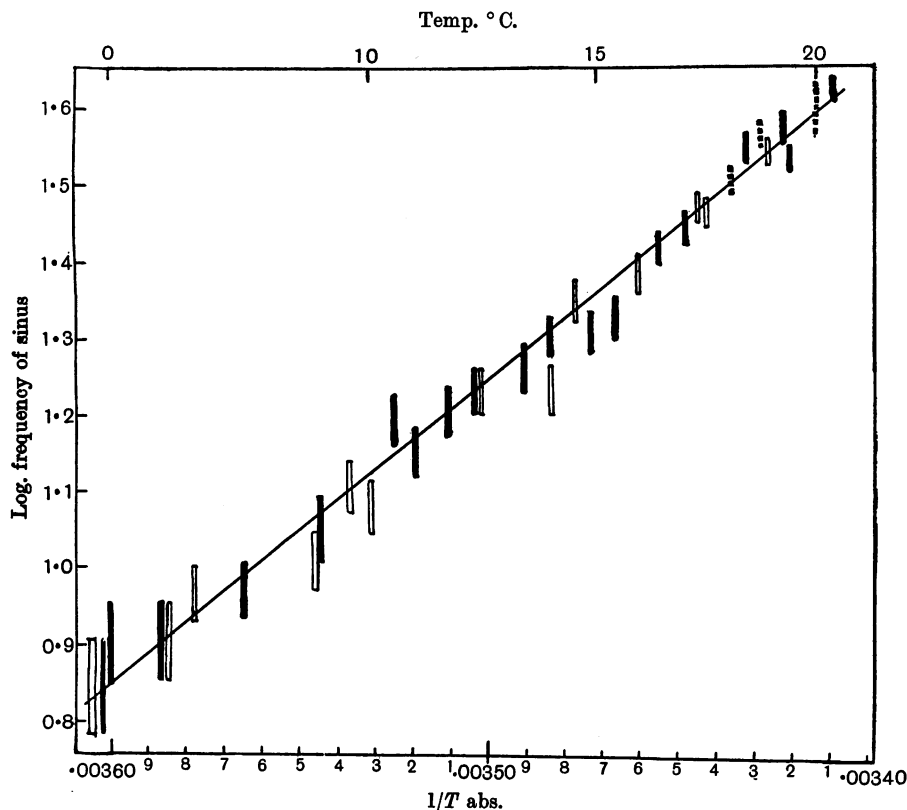


Fig. 2. The data in Fig. 1 with the frequency plotted logarithmically. The areas represent the known experimental error. Open areas, cooling; black areas, subsequent heating; chequered areas, cooling the second time.

The experimental error when the points are plotted logarithmically is shown in Fig. 2. The experiment is the same as that shown in Fig. 1.

### Results.

1. The first series of experiments to which we shall allude refers to temperatures between 5° and 20° C. When plotted with the logarithm of the frequency against the reciprocal of the absolute temperature the

points of each experiment fall approximately on a straight line, but it is clear that the slope of the line is different in different cases.

Frog	Temperature coefficient between 5° and 15° C.
24	2.09
25	2.90
26	2.95
27	2.63
28	2.40
55	2.14
56	2.08

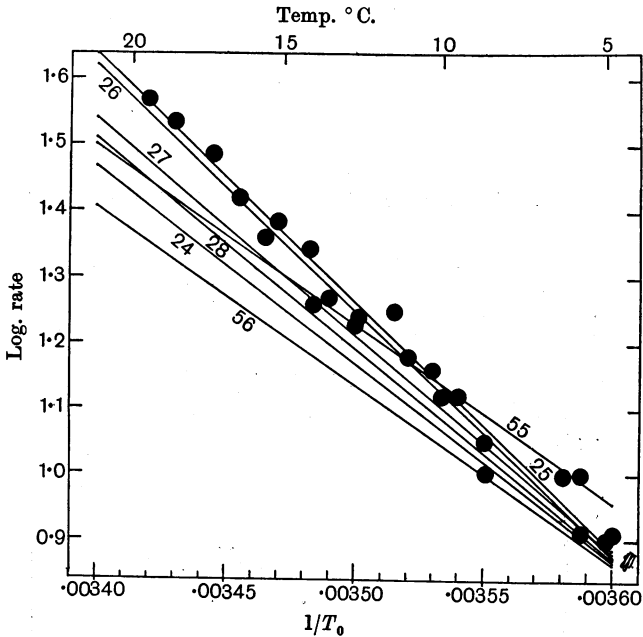


Fig. 3. The logarithms of heart rates in isolated heart 25 are plotted against reciprocals of temperature. For comparison the results in hearts 24, 26, 27, 28, 55 and 56 are represented by lines. (All from winter series.)

The increased accuracy which we believe we have obtained has not introduced uniformity into the results. The experiments conform to those of former workers [Crozier, 1926], who found that the value of the coefficient varies between 2 and 3.

Fig. 3 shows the results of a single experiment, No. 25, and on it also have been placed the lines corresponding to other observations, the number and standard of accuracy of the individual observations being of the same character as those plotted.

2. The following frogs' hearts have been observed at various periods

between the second and thirty-fifth hour after excision. The temperature coefficient of the pulse rate is seen to vary considerably.

Frog	$Q_{10}$ ( $5^{\circ}$ - $15^{\circ}$ C.).			
	2-3 hr.	11 hr.	24 hr.	35 hr.
A	2.6	3.2	2.6	2.1
B	2.7	2.7	3.0	—
C	2.8	3.5	3.2	—
D	3.4	2.5	2.7	2.3
E	3.2	2.8	2.2	3.0
F	2.5	2.2	2.1	2.8
G	2.6	2.4	2.9	3.0
H	2.7	2.5	2.6	—

Over higher ranges of temperature the coefficient either becomes less, as has been found by others, or remains sensibly unchanged.

Frog	$Q_{10}$ ( $5^{\circ}$ - $15^{\circ}$ C.)	$Q_{10}$ ( $17^{\circ}$ - $27^{\circ}$ C.)
29	2.30	1.55
56	2.20	2.20
55	2.19	1.83
54	2.70	1.82

In the above observations the curve is reversible within limits shown in tracings in this paper.

In the above table the pace-maker of one heart (No. 56) over a range of about 20 degrees follows the equation of Arrhenius, but in the others there is the falling off of  $Q_{10}$  noticed by later workers.

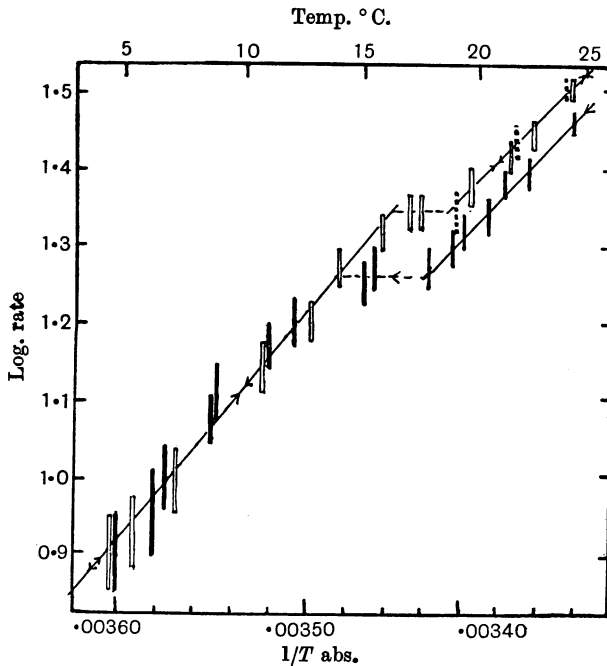


Fig. 4. Isolated heart, winter series, plotted as in Fig. 2.

Of our cases that which gives the most unequivocal support to Crozier is that shown in Fig. 4. The points appear to lie on two parallel lines with a break at about  $15^{\circ}\text{C}$ . Looking back at Fig. 2, there is the suggestion of a waver at  $15^{\circ}\text{C}$ . also.

Other experiments, which conform to other types described by Crozier, are shown in Fig. 5 A, B. In the latter case a smooth curve might alternatively be drawn through the points, but Fig. 5 A shows what Crozier would regard as the characteristic alteration at  $15^{\circ}\text{C}$ . in

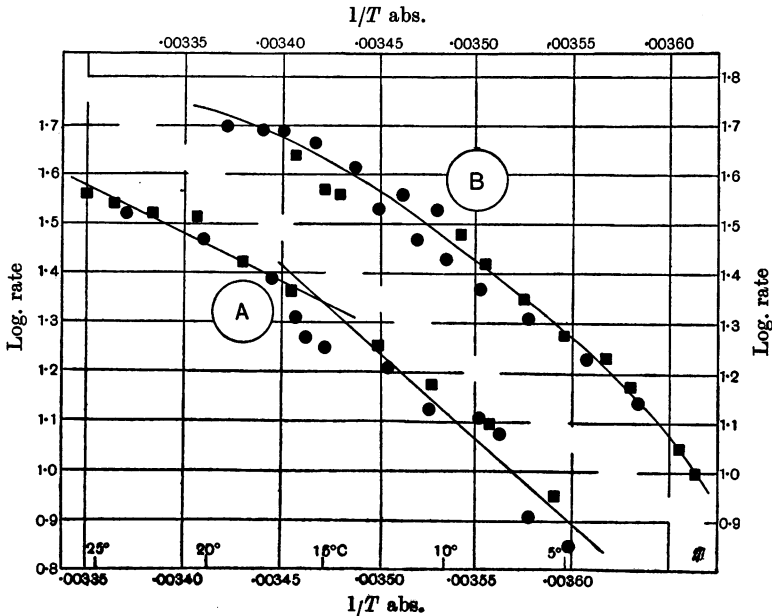


Fig. 5. Showing results obtained in A (isolated heart 54), and B (isolated heart 29). (Winter series.)

the inclination of the line. The point which seems to us remarkable is that in frogs we can get curves of all these types.

*The effects of temperature on the excised heart studied in the summer.*

Out of twenty-eight experiments which we have carried out on the hearts of eight frogs we have obtained only three curves of the type usually obtained with the winter frog. In the overwhelming majority of cases the pulse rate plotted against the temperature has been almost exactly a straight line. It is not suggested that the straightness of the line has an evident physical interpretation.

A good example is in Fig. 6, which shows four records of a heart taken

at different times after excision. The lines clearly do not coincide, but each is nearly straight. They cover a range of temperature between 4° and 22.4° C.

#### THE HEART IN THE INTACT FROG IN WINTER.

Although we carried out a number of experiments in winter time on the heart of the frog in the intact animal by the method described in a previous paper by one of us [Izquierdo, 1930], we were not able to obtain curves which were consistent with one another. In many cases the lines were quite irregular.

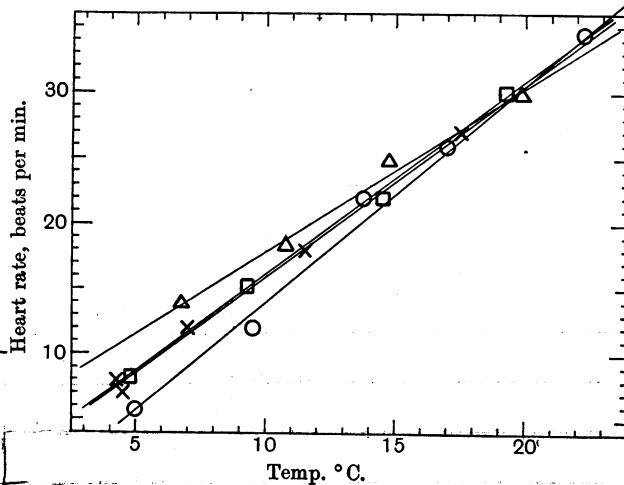


Fig. 6. Successive temperature lines obtained by cooling the isolated heart A (summer series) at different periods after isolation: after 3 hours (crosses); after 11 hours (circles); after 23 hours (squares), and 35 hours (triangles).

#### THE INTACT FROG IN SUMMER EXPERIMENTS.

Observations made on the intact frog in summer gave very consistent results.

Fig. 7 shows a typical record of such an experiment in a summer frog—(June 5) the line corresponds to the mean position of those in Fig. 6—over more than 20° C. Six experiments were carried out, all of which showed much the same characteristics. Like the excised heart at the same period the relation of pulse rate to temperature is nearly linear.

Frog	2° C.	22° C.	Difference	Difference per ° C.
A	5	35	30	1.5
D	8	34	26	1.3
F	8	35	27	1.35
G	9	39	30	1.5



The above, roughly, were the limits observed on healthy frogs which had recently been brought into the laboratory. The records in Figs. 6 and 7 are strikingly alike, which tends to confirm the opinion that the heart of the intact quiescent frog is free from vagus inhibition.

We carried out several experiments further to test the point, all of which gave the same result and confirmed the view that the vagus does not at any temperature at which we worked maintain an inhibitory action on the heart of the frog at rest. After testing the relation of pulse rate to temperature in the normal frog, atropine was administered under the skin of the thigh in doses which in different experiments varied from 0.5–3 mg., our intention being to give the minimal dose which paralysed

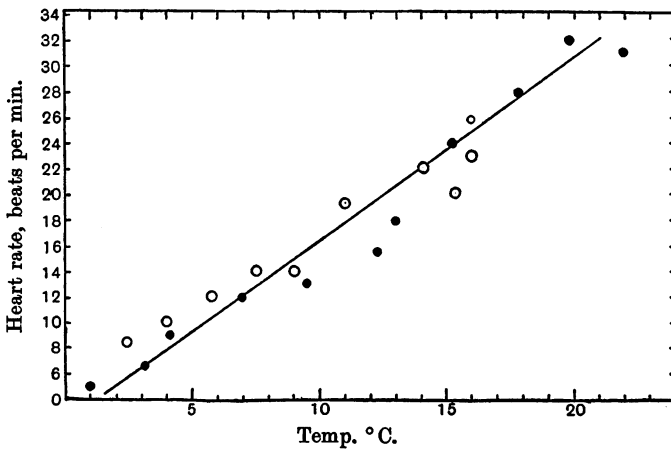


Fig. 7. Heart of intact frog (summer series): ○, going down; ●, going up. Line corresponds to mean position of lines in Fig. 6.

the vagal endings. It was found that, by direct stimulation of the sinus after the experiment was complete, the doses in question had done so. In the three experiments out of seven stimulation gave acceleration.

We purposely avoided large doses of atropine which we, in common with previous workers<sup>1</sup>, found to introduce complications.

In no case did we find the relation of temperature to heart beat in the atropinised frog to differ from that previously found for the un-atropinised frog. A typical record is given in Fig. 8.

<sup>1</sup> Though evident alterations of the frog's heart are only observed in 30–40 g. animals when 20 mg. are injected—a dose very near to the lethal one (25 mg.) [Dixon, 1920]—full doses are well known to slow the rhythm [Meuriot]. A dose of 3 mg. (recommended by Dixon) according to our experience is excessive for the purpose of paralysing the vagi. As no acceleration follows, the only safe method of testing its effectiveness is as described in the text.

## SUMMARY AND CONCLUSIONS.

1. The excised frog's heart studied in winter time usually gave a linear relationship between the logarithm of the frequency of the sinus beat and the reciprocal of the absolute temperature between 5° and 20° C.

2. The value of  $Q_{10}$  varied in the minority of cases, as the temperature rose the frequency decreased as compared with the above relationship. Most of these cases could be claimed by Crozier as examples of one or other of his patterns, but they did not all conform to the same pattern.

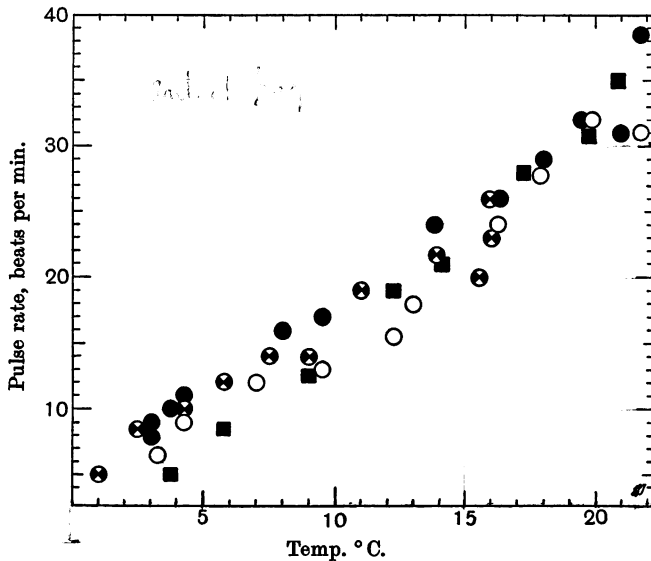


Fig. 8. Results obtained in Frog *N* (summer series), when intact (⊙, going down; ○, going up), and after injection of 1 mg. atropine sulphate (●, going down; ■, going up).

3. In the intact frog in winter the results were irregular.
4. The excised heart of the frog in summer showed a different property. The frequency bore a nearly linear relation to the temperature.
5. This was true also of the heart of the intact frog.
6. The relation of the frequency to the temperature was little, if at all, influenced by doses of atropine of the strength which just sufficed to block the vagus. Our results confirm those of observers who regard vagus tone as practically absent in the heart of the resting frog.

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