

THE HEAT PRODUCTION OF CAT'S NERVE.

By L. BUGNARD¹ (*Toulouse*).

(*From the Department of Physiology, University College,
London.*)

(*Received July 25, 1935.*)

THE heat production of frog's nerve has been studied by A. V. Hill and his collaborators since 1926, and its physiological nature as a response to excitation has recently been confirmed [Hill, 1934*a*]. The heat production of the nerves of Crustacea was studied by Hill [1929] and later by Beresina and Feng [1933].

Improvements in the technique have permitted the extension of heat measurements to the case of mammalian nerve at temperatures of 30–34° C.

METHODS.

The thermostat described by Feng and Hill [1933], as modified by Bugnard [1934], was used. The air between the box containing the thermostat and the outer wall was maintained at a constant high temperature by automatic electrical regulation. During the intervals between separate experiments the heating was maintained as it was necessary to continue the regulation for 2 days in order to obtain a really stable temperature in the interior of the thermostat.

The thermopile was that described by Hill [1934*a*]. The junctions were of manganin-constantan; two separate pairs of stimulating electrodes were employed, and "heat-leak" from the stimulating electrodes to the thermopile was tested and found to be negligible. The current from the thermopile was passed to a Zernicke Zc galvanometer and either read on a scale or registered photographically on a drum taking strips of paper 13 cm. wide. The drum (or the scale) was 3 m. distant from the galvanometer. The stimuli were condenser discharges controlled by a revolving commutator as described by Hill [1934*b*]. Usually shocks alternating in direction were employed.

¹ Rockefeller Fellow.

The popliteal nerves of the cat were used. During the earlier experiments the decerebrated animal was kept under artificial respiration and the nerves were dissected with the circulation still intact. From each leg two separate portions of the popliteal nerve can be prepared, each long enough for use with the thermopile; two such nerves are sufficient to cover each face. It is easy to spread out a nerve so that its thickness is no greater than that of the frog's sciatic. As in the usual experiments with frog's nerve, the central portion of each is placed above the thermopile so that the impulses are descending.

In the later experiments it was realized that it is unnecessary to maintain the animal under artificial respiration during dissection. Nerves dissected immediately after the animal was killed behaved just as well as others. It has not been possible, however, to obtain good results with nerves so prepared and kept in Ringer's solution at 0° C. The following procedure, therefore, was adopted. The nerves were dissected in $\frac{3}{4}$ -1 hour and were then placed in mammalian Ringer's fluid, with oxygen bubbling, for 1 hour at a temperature of 34° C., then immediately mounted on the thermopile in fresh Ringer's solution. The thermopile was then placed in the thermostat and a further interval of 2 hours allowed in order to obtain thermal equilibrium in the instrument. The Ringer's fluid was then replaced by oxygen. In making heating control curves it was unnecessary to kill the nerves: a series of low-frequency condenser discharges along them was sufficient to give the necessary heat, with a physiological response too small to be measured. An attempt was made to use the cat's phrenic, but bad results were obtained as it was difficult to dissect the nerve without pulling on it; it is, moreover, of small diameter, so making it impossible to cover the thermopile with nerves from a single animal. A single experiment was made with the popliteal nerve of the dog, which gave good results.

The temperature varied from 30 to 34° C. from one experiment to another. The thermal response was good, showing no diminution of the maximum deflection and providing a good base line; it was possible to continue observations for 3 hours, that is to say until 5 hours after dissection.

OPTIMUM STIMULUS.

The optimum stimulus was determined by the procedure described by Hill [1934*a*], using the thermal response of the nerve as index. For a series of potentials between 2 and 25 volts, the maximum deflection was determined for a stimulus of given duration, for a series of different

capacities. For each voltage a curve was constructed, deflections (representing heat production) against \log (capacity). (The resistance of the discharge circuit was constant throughout the experiments, being chiefly determined by a shunt of 400 ohms across the stimulating electrodes.) On these curves it is easy to read off the capacity corresponding to a given voltage and given heat production. One can then construct a "strength-duration" curve, with ordinates $\log V$ and abscissæ $\log RC$. If the scales of ordinate and abscissa are the same, the tangent of slope $-\frac{1}{2}$ gives the value of RC corresponding to a stimulus of

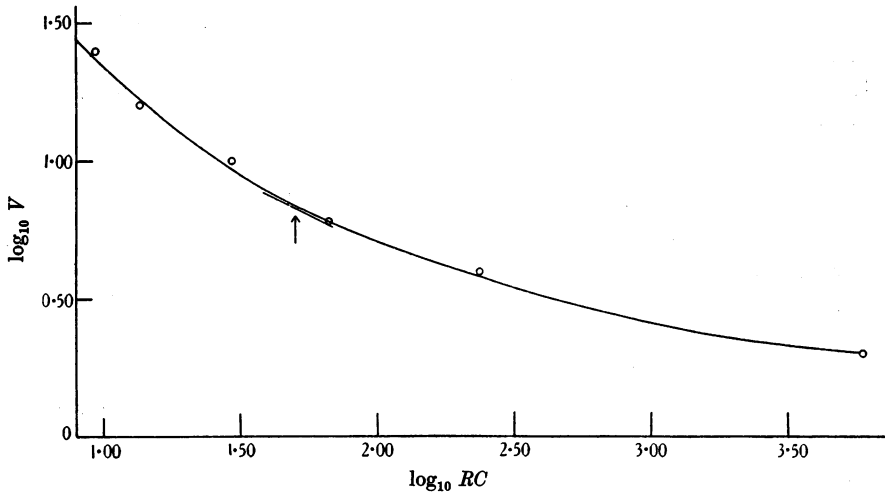


Fig. 1. Voltage-capacity (strength-duration) curve of popliteal nerve of cat at 33°C ., heat production being used as index of excitation. For description see text. The optimum stimulus (point of minimum energy) occurs where the tangent to the curve has a slope of $-\frac{1}{2}$. At this point $\log RC = 1.70$.

minimum energy (see Fig. 1). Expressing R in ohms and C in microfarads, in three experiments, made respectively at temperatures of 29.5 , 33 and 33°C ., the optimum stimulus was found for a $\log RC$ in the neighbourhood of 1.7 , corresponding to a time constant of 50 microseconds. This value is in the neighbourhood of that found by Hill [1934*a*] by a similar method for frog's nerve at a temperature of 25°C . The frequency of the two-way shocks used in the present experiments was about 500 per sec.

In one experiment the optimum stimulus was determined by the second method described by Hill [1934*a*]. Curves for heat production against $\log RC$ were constructed for different shocks corresponding to the

same energy value in the stimulus. The form of the curves was exactly similar to those given by Hill [1934*a*, p. 209]. The results, however, are less precise than by the preceding method. This is probably due to the greater time taken by this procedure, and to the deterioration of the nerve, which did not allow a "reverse" series to be made. The optimum stimulus, however, was still in the neighbourhood of $\log RC = 1.75$.

According to Rosenberg [1935, Fig. 2, p. 58] the point of minimum energy for the stimulus of a cat's sciatic and ulnar at 21° C. is about 170 microseconds; with a temperature coefficient of 2 per 10° C. this would give 85 microseconds at 31° C. for comparison with the present experiments. The 50 microseconds found for the latter agrees fairly well; Rosenberg's experiments were for a single semi-maximal electric response, the present were for a thermal response to high-frequency stimulation. Exact agreement could not be expected.

THE EFFECT OF FREQUENCY.

Here also results have been obtained analogous to those with frog's nerve. As the frequency increases the heat production in a short stimulus increases also, then attains a maximum in the neighbourhood of 1000 two-way shocks per sec. The only difference is that for cat's nerve the response is relatively better at the higher frequencies than for frog's nerve. Thus, in one experiment at 29.5° C. a frequency of 3800 per sec. (two-ways) gave only a slight diminution in the response, as compared with the deflections obtained at frequencies of 1600 and 2200 per sec. The difference may be due to the fact that the experiments were made at a much higher temperature than those previously reported on frog's nerve.

At a low frequency of excitation it is possible to reach a steady state of heat production which can be maintained for a long time, followed by a good return to the original zero after the stimulus ends.

ANALYSIS OF THE HEAT PRODUCTION.

The procedure has been as usual. To study the general form of the curves of heat production a certain number of analyses were made in units of 4 sec. and continued up to 112 or 120 sec. Control heating of 4 sec. was employed. The curves for analysis and the controls were measured every 4 sec., and the means for at least four curves were taken.

The curves of heat production are analogous to those obtained with other nerves already studied (see Fig. 2). There is an initial heat and a recovery heat. For the durations of stimulus employed (16-24 sec.) the

initial heat is nearly the same if one determines it by the sudden rise at the beginning of excitation, or by the sudden fall at the end of excitation. The latter, as usual in frog's nerve, is slightly less.

In order to obtain more precisely in absolute units the value of the initial heat, a certain number of analyses have been made in 2 sec. units. The curves shown in Fig. 3 were obtained as follows: first an analysis was

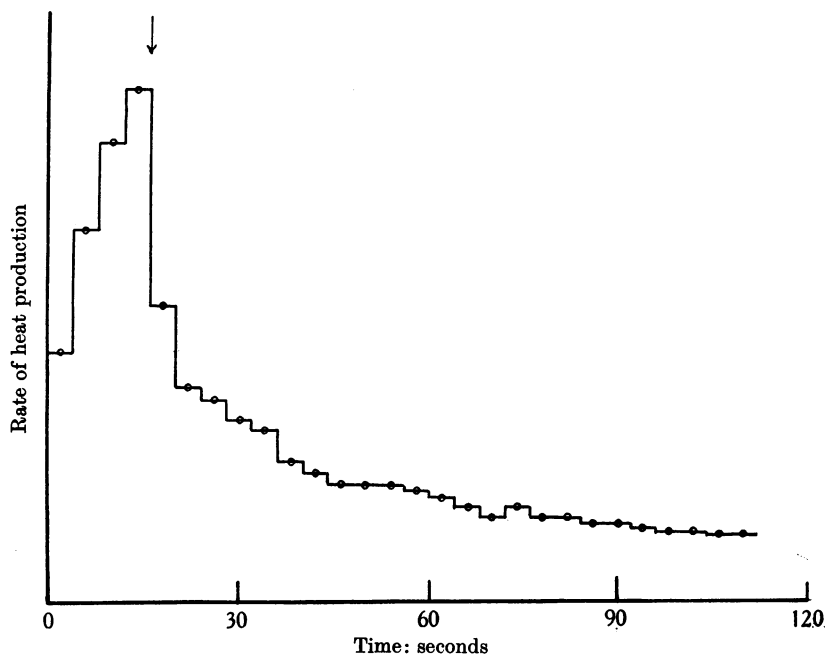


Fig. 2. Analysis in 4 sec. units of heat production of popliteal nerve of cat at 33° C. Stimulus 8 volts, 0.2 μ F, 400 ohms shunt, frequency 480 per sec., 10,000 ohms in series with nerve. Stimulus 16 sec. duration. The arrow indicates the end of the stimulus.

carried out in units of 4 sec.; through the results of this analysis a smooth curve was drawn for the production of heat; breaking this up into 2 sec. blocks and "synthesizing", a result was obtained which was approximately the same as that to be analysed; the differences were analysed in 2 sec. time units.

The results obtained for the initial heat vary considerably from one experiment to another. For example, in one experiment with nerves weighing 255 mg., at 33° C. and a frequency of 500 per sec. of two-way stimuli, the initial heat was 2×10^{-6} cal. per g. per sec. In another experiment at 31° C., with a frequency of 2090 per sec., the initial heat was

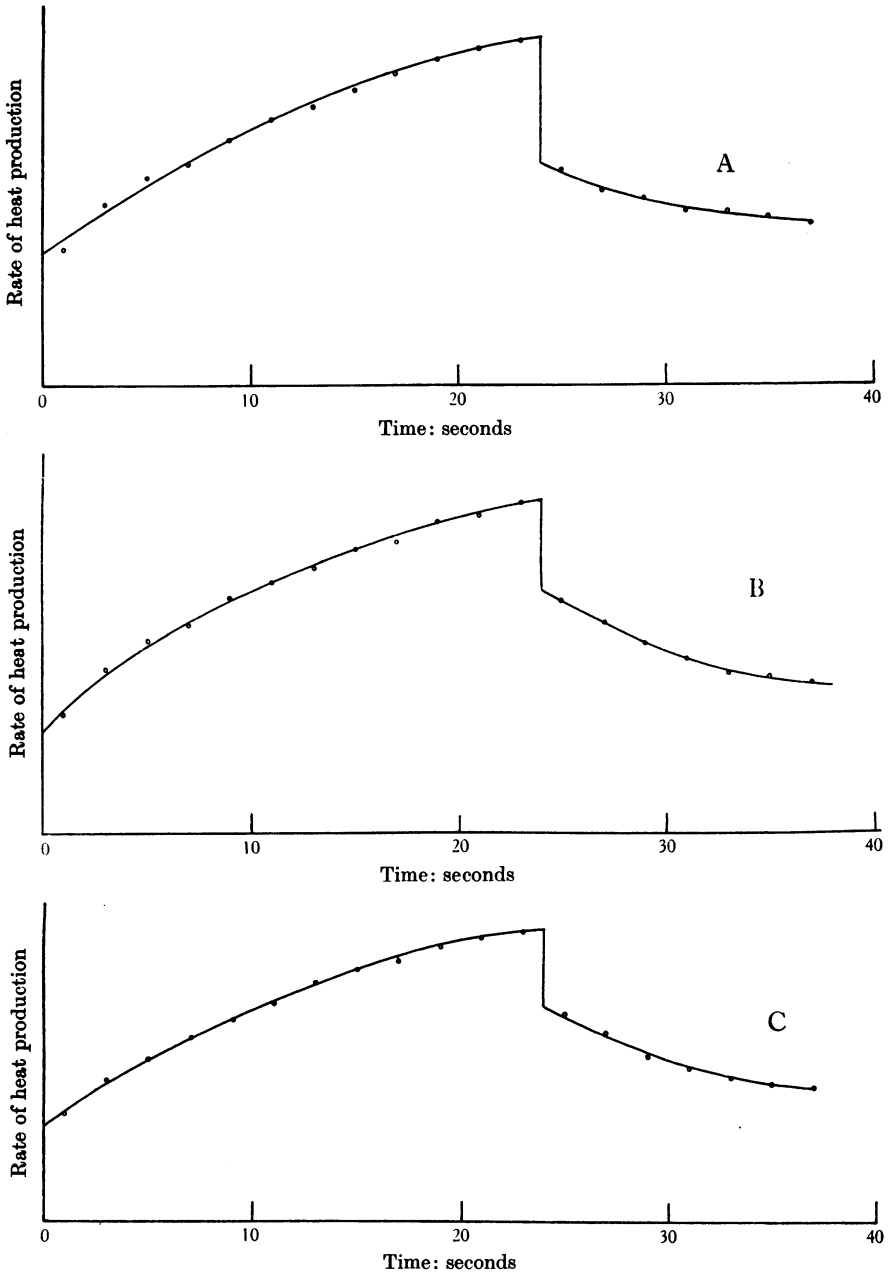


Fig. 3. Analysis in 2-sec. units of heat production of popliteal nerve of cat at 31° C. 24 sec. stimulus. Otherwise as in Fig. 2. Curve *A*, frequency 2090 per sec. (two-ways); curve *B*, frequency 1031 per sec.; curve *C*, frequency 406 per sec. The circles mark the values given by the analyses, each at the centre of its interval. A smooth curve has been drawn through them.

11.7×10^{-6} cal. per g. per sec.; for a frequency of 1031 per sec., 9.6×10^{-6} cal. per g. per sec.; for a frequency of 406 per sec., 9.6×10^{-6} cal. per g. per sec. In another experiment, the mean of results obtained at different frequencies (2218, 1084, 632, 267, and 109 per sec.) for the initial heat was 3×10^{-6} cal. per g. per sec. In another experiment at the same frequencies, the initial heat was 4.5×10^{-6} cal. per g. per sec.

The mean of four experiments gave 4.9×10^{-6} cal. per g. per sec.; this result is lower than that found by Hill [1932] for frog's nerve at 20° C. The variations observed, however, in the present experiments show that too much importance must not be attached to the absolute values, which are certainly low. Doubtless a certain number of fibres are destroyed by dissection, and at the high temperature, and respond no more to excitation. The form of the heat production is not altered by their disappearance, but the absolute value must be too low. It would probably be fair to conclude that maximal stimulation of a cat's medullated nerve in good condition gives an initial heat production of about 10 microcalories per g. per sec.

It might be suggested that the variations observed in the absolute value of the initial heat of a cat's popliteal, and its difference from that of the frog's sciatic, are due to differences in the amount of inertia material. In the present experiments, however, the cat's popliteal nerves were carefully dissected in order to remove the thick connective sheath and to allow the various branches of which the nerve is composed to spread out on the thermopile. Some of the branches used for the experiments were sectioned and compared with sections of the frog's sciatic. Both were anatomically comparable, consisting of about the same fraction of actual fibres.

The recovery heat production has not been followed for more than the first 2 min. It is the same in character, up to that time, as in frog's nerve.

SUMMARY.

1. The heat production has been measured in cat's medullated nerve maintained in oxygen and stimulated electrically at temperatures of $30-34^{\circ}$ C.

2. An optimum stimulus exists for the heat production of cat's nerve, which in the neighbourhood of 33° C. is such that $RC = 50$ microseconds, R being resistance in the stimulating circuit, and C the capacity of the condenser used for stimulation.

3. The effect of frequency is analogous to that obtained with frog's nerve. The effect of high frequency (a decreased response) occurs only at frequencies considerably higher than in the frog. This may be due to the higher temperature of the present experiments.

4. The analysis of the records shows the existence of an initial heat and of a delayed heat. The maximum value of the initial heat during maximal stimulation is probably of the order of 10 microcalories per g. per sec.

5. The general results of these experiments is that cat's medullated nerve behaves, in respect of its thermal response to electric stimulation, in the same manner as does frog's medullated nerve.

My sincere thanks are due to Prof. A. V. Hill who has provided the means and the encouragement necessary for this work. I am indebted to Mr J. L. Parkinson for much help and to Dr Stella who was kind enough to assist in the artificial respiration of the experimental animals.

REFERENCES.

- Beresina, M. and Feng, T. P. (1933). *J. Physiol.* **77**, 111.
Bugnard, L. (1934). *Ibid.* **80**, 441.
Feng, T. P. and Hill, A. V. (1933). *Proc. Roy. Soc. B*, **113**, 356, 369.
Hill, A. V. (1929). *Ibid.* **B**, **105**, 153.
Hill, A. V. (1932). *Ibid.* **B**, **111**, 106.
Hill, A. V. (1934*a*). *Ibid.* **B**, **115**, 200.
Hill, A. V. (1934*b*). *J. Physiol.* **82**, 423.
Rosenberg, H. (1935). *Ibid.* **84**, 50