$> f_1$. In some cases it might even be sufficient to have a single cell system with a high enough resting frequency to cope with negative as well as positive values of $(f_1 - bf_2)$.

In any case, it is important to note that, as in all "servo" comparators, the linearity or the exact form of the response-function ϕ (Eq. 8) is of little consequence for the overall performance, provided that the sensitivity of O is high enough: that is, in technical jargon, "loop gain" large compared with unity. Moreover, it is totally unnecessary for ϕ to be "exponentiating" in form. It could quite well be linear, as in analog operational amplifiers (*7*). Only if the interaction of f_1 and f_2 were not linearly subtractive would serious departures from a power law be likely on our present model.

By the same token, there is no reason why the process we have called "comparison" should not take place in more than one stage or even in a continuously distributed interaction between efferents from O and afferents reaching O from R. Although the functional distinction between C and O is useful in Fig. 1, the neurological correlate might well be reduced in principle to something like Fig. 3, where the subtractive process is shown as occurring on the way in to the active system that organizes response. In this case, however, the requirement of high loop gain demands that O generates a high (aggregate) frequency f_2 in response to a low-frequency mismatch signal.

Histological and physiological evidence of this kind of self-inhibitory action abounds in the central nervous system (*8*). The problem of greatest interest, if the model of Fig. 3 were at all correct, would be to identify the "activity" that gives rise to the matching frequency in this case. Since we postulate a logarithmic relation between activity ψ and firing rate f_2, there is little attraction in the idea that the activity is itself linearly represented by some other neural firing rate. More plausible would seem the identification of this activity (and so, in turn, of perceived intensity) with the intensity of some metabolic or other physical disturbance known to be logarithmically related to firing frequency, in the kind of way that stimulus intensity is related to receptor firing frequency (*9*). I am aware this comes close to suggesting a heretical doubt that all conscious experience is tied directly to patterns of nerve impulses; but the task of intelligibly linking conscious perception with brain action seems neither more nor less perplexing if we fasten it upon the physicochemical "effort" of the cell or its environment, rather than upon the impulses it emits. If anything, the first would seem a little easier to square with the unity and continuity of perceived experience.

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7. See, for example, D. M. MacKay and M. E. Fisher, *Analogue Computing at Ultra-High Speed* (Chapman and Hall, London, 1962), pp. 38–40.
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9. A brief note may be in order regarding the "naturalness" of the logarithmic transformation (or something near to it) as a basic operation in a neurophysiological model. One might well ask: why logarithmic, rather than linear or power-law? There are in fact two reasons, one functional, the other structural. First, receptor organs, especially of mobile organisms, have to function over wide ranges of intensity. Moreover, the significant information conveyed by most sense organs depends on spatial and/or temporal patterns (for example, of surface brightness) which are specified by the *ratios* between various received intensities, regardless of overall level. Thus, for example, if the ambient daylight on an object waxes or wanes, it is obviously desirable that the contrast between signals representing different parts of its optical image should be preserved from significant change. A logarithmic transfer function would ensure this in the simplest possible way, since it would leave the differences between firing-frequencies unaffected by changes in intensity of illumination. Second, logarithmic laws arise naturally in the kinetics of self-equilibrant chemical reactions, and can therefore be postulated with the minimum of *ad hoc* assumptions in the context of neural activity. They imply simply that the "gain" or incremental sensitivity of the transducer in question is automatically reduced in proportion to the intensity of input.

2 January 1963

Reversible Section of the Brain by a Wall of Cold

Abstract. *A fork made up of hollow tubing may be chronically implanted in the cat's brain. When cooling fluid is pumped through this fork a reversible plane lesion is formed. This technique permits analysis of functional parts of the nervous system in unanesthetized animals.*

Cooling may be used to block conduction reversibly in nerves. This phenomenon has been used in the study of the peripheral nervous system (*1*) and in the study and treatment of diseases of the central nervous system (*2*).

Local extravascular cooling is one subdivision of a recently published classification of hypothermia (*3*). We feel that it is useful to further classify cooling techniques by purpose, method, and geometrical dimensions of the source and cooled area. The cooled area must, of course, be three-dimensional, regardless of the nominal dimension of the source. The region of complete conduction block, however, may be adjusted to be a good approximation of zero, one, two, or three dimensions by varying the temperature of the thermodes.

Local cooling has been used for study of temperature-sensitive receptors (*4*), for reversible block of conduction (*5*), and for permanent surgical lesions. The heat-sink requirements of thermodes for each of these purposes are quite different and so have lent themselves to different techniques of refrigeration. As one would expect, lower temperatures require more involved systems.

The geometric dimensions of the heat sink (thermodes) may be defined as follows: 0: point, or zero-dimensional thermodes for cooling small masses of tissue on the surface of or in the depths of the brain; 1: line, or one-dimensional thermodes for cooling cylinders of tissue (the area of interest may be only at the tip of the thermode and thus be zero-dimensional); 2: plane, or two-dimensional thermodes for cooling the surface of the brain; 2-D: planar cooling thermodes which are not full planes but provide a planar thermal field in the depths of the brain; 3: solid, or three-dimensional thermodes which may be either special configurations of one-dimensional heat sinks or multiple one-dimensional heat sinks arranged to form an even thermal field in a large mass of tissue. The configuration of only the heat-sink portion of the thermode is of importance because this defines the area which will be cooled.

Zero-, one-, and three-dimensional cooling are now being used in surgery and physiology. This report describes a technique for two-dimensional cooling

based on a rearrangement of multiple one-dimensional sources to provide planar cooling in the depths of the brain. The wall of cold thus provided is analogous to reversible surgical section, point-cooling to localized electrical or chemical lesion, and solid-cooling to surgical ablation of brain mass.

The potential applications of this technique extend to all areas of study of the nervous system where isolated functional areas of the brain are of interest. The reversibility of the section makes it a more powerful research instrument than the knife of the surgeon.

The principle of the method is straightforward. If a needle is cooled along its length, a cylinder of lowered temperature is formed in the tissue around it. When cooled needles, or thermodes, are placed in a picket fence or fork arrangement (Fig. 1), the cylinders of low temperature interlock and a wall of cold which blocks conduction is formed.

In order to investigate the feasibility of this principle we prepared a cooling fork of suitable dimensions to pass a plane of cold across the brainstem of cats. Each tine of the fork is made up of a hairpin loop of 27-gauge stainless-steel tubing soldered into a single needle with pure tin solder. The tines are connected in parallel to input and output manifolds. Cooling fluid (heptane) (*6*) is pumped by a specially constructed motor-driven syringe pump through a 5-μ Millipore filter, a helical stainless-steel heat exchanger immersed in a dry ice alcohol mixture, and thence through Teflon tubing to the intake manifold of the fork. The heptane returns from the output manifold through connecting tubing to a reservoir and then is recirculated. Teflon steel connections are made with a spring connector (*7*).

The fork shown in Fig. 1 has been implanted in six cats. Over 40 reversible decerebrations have been done in these animals, and there seems to be no residual neurological effect of either the implantation of the fork or the cooling. The fork has been kept in an animal as long as 2 months. The cooled animal provides an example of both a reversible decerebrate and a reversible *cerveau isole* preparation.

In a typical experiment, we anesthetized the cat and positioned it in a stereotaxic instrument. The fork was inserted at the midcollicular level, passing through the cortex into the medulla, and fixed to the skull with

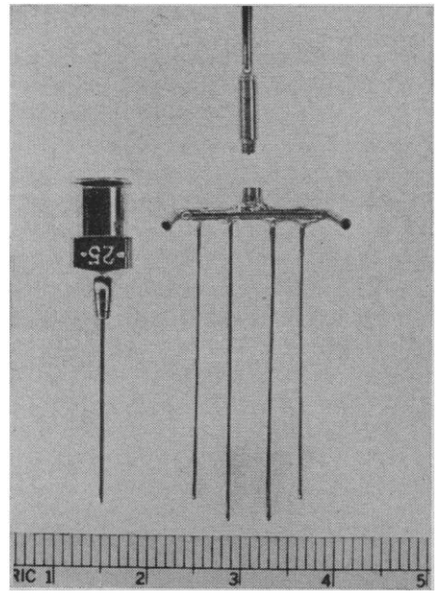

Fig. 1. Cooling fork of stainless-steel tubing compared to 25-gauge hypodermic needle. Input and output manifolds project from the top of the fork. A guide for stereotaxic placement is above the fork. The rule is a centimeter rule.

dental cement. Then the animal was allowed to recover for a few days to a week. We attached the input and output lines to the unanesthetized animal and measured temperatures with thermistor probes placed either at the input-output lines or on the top surface of the fork. The heat-exchanger bath temperature was kept between −20° and −30°C. This gave us a temperature of −3° to −5°C at the top surface of the fork (*8*).

The onset of symptoms was rapid. The cat first lost its postural and righting reflexes, then its response to pain, and finally showed classic decerebrate rigidity and typical reflexes. This took about 2 minutes. We have cooled for periods as long as 45 minutes in the unanesthetized cat. Recovery (initiated either by turning off the pump or immersing the heat-exchanger coil in warm water) took about 4 minutes. Between decerebrations the animals appeared to be neurologically and behaviorally normal (*9*).

We measured brain temperatures in two acute experiments and plotted isothermal lines within the brain during cooling. The cats were anesthetized with pentobarbital and placed in the stereotaxic instrument. A 26-gauge stainless-steel needle with a thermistor mounted in epoxy at the tip was driven into the brain at an angle of 45° to the plane of the fork. Temperature measurements on insertion and withdrawal were made at 1-mm intervals. A plot of interpolated isothermal lines with the heat-exchanger bath temperature at −20°C is shown in Fig. 2. These data demonstrate that in truth a wall of cold is formed by the interlocking cylinders of lowered temperatures around the fork tines.

Since the tines of the fork are identical in construction and are arranged in parallel, the heat-sink capacity of each is equal. The isothermal lines are shown for only two tines, since the sagittal sinus and the cleavage between the cerebral hemispheres prevent meaningful or simple measurements between the center tines.

Calorimetric studies of the fork-and-pump system under identical conditions

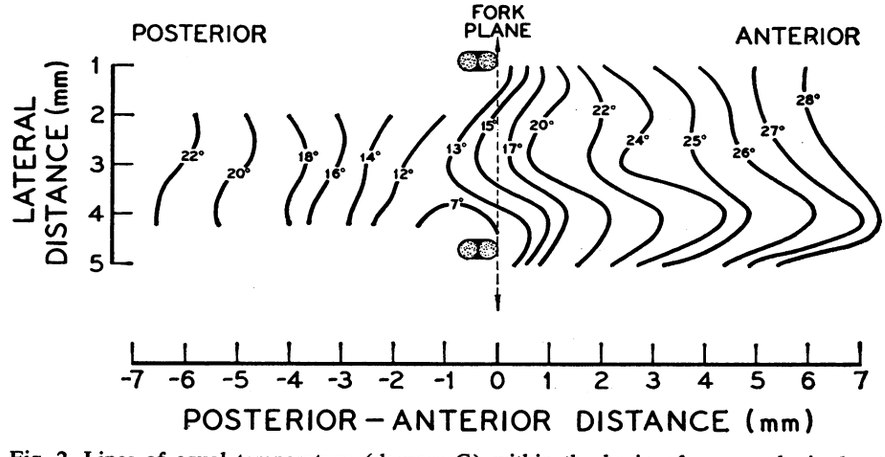

Fig. 2. Lines of equal temperature (degrees C) within the brain of an anesthetized cat with cooling fork in place. The figure is a horizontal projection of a plane which intersects the fork at an angle of 45 degrees. Lower "posterior" temperatures are due to the thermal conductivity of the steel thermistor probe, which is cooled as it passes between the tines.

of heat-exchanger bath temperature and flow rate showed a heat-sink capacity of the four-pronged fork averaging 0.2 cal/sec. The average temperature difference between the input and output lines measured from the surface of the fork was 3°C. Unfortunately, this value is subject to the errors produced by the thermal gradient across the top surface of the fork. Because of the high pressures (intermittent pressures of over 100 lb/in.^{2} at flow rates of 70 cc/min occur) and the small diameter of the flow lines, thermistors could not be placed in the liquid system. The heat-source capacity of any area of brain varies with the blood flow, and the blood flow is quite temperature-dependent. The feedback aspects of this dynamic system and the requirements of relatively steady states for accurate calorimetry necessitate separate measurements of the heat-sink capabilities of the fork and the thermal gradients produced in brain. Therefore, the value given above (0.2 cal/sec) may not be a true representation of the heat-source properties of the brain.

The relationship between low temperature and nervous activity has been extensively investigated. Temperatures below 20°C abolish electroencephalographic activity in mammalian brains (*10*), reduce cerebral metabolic rate to less than one-fourth of normal (*11*), and decrease acetylcholine production by choline acetylase to one eighth of normal (*12*). The freezing point of brain is about −1.5°C and temperatures for permanent damage of peripheral nerve and of brain appear to be in the range of 0° to 8°C (*13*).

Suitable cooling forks and other devices can be designed to block off almost any mass of tissue within the brain. Further extensions of the principle of cooling in two and three dimensions in the depths of the brain should allow analysis of the behavioral effects of ablations and of sections in the (relatively) intact animal. The technique shows promise of usefulness in the analysis of brain mechanisms of learning and memory, in the determination of sites of action of behaviorally active drugs, and in providing the potential for reversible "trial" neurosurgery of mass lesions in man (*14*).

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Cyanogenic Glandular Apparatus of a Millipede

Abstract. *The cyanogenic secretion of the polydesmoid millipede* Apheloria corrugata *(Wood) is discharged from paired, serially arranged glands, each consisting of two compartments. In one compartment is stored an undissociated cyanogenic compound, and in the other, a chemical factor that triggers cyanogenesis. The gland is constructed in such a way that the contents of the two compartments are mixed, and cyanogenesis is initiated, at the very instant of discharge. The stored cyanide precursor may be mandelonitrile.*

Certain polydesmoid millipedes produce a cyanogenic secretion (*1–3*). The glands are unquestionably defensive in function. A discharge occurs only in response to traumatic stimuli, and the secretion is strongly repellent to ants and some other predators (*2, 4*). Neither the structure of the glands nor the mechanism controlling cyanide emission has been properly understood. The purpose of this note is to present experimental evidence for the hypothesis (*2*) that the glands store an undissociated cyanogenic precursor, and that cyanide emission is triggered at the moment of discharge by addition of a catalyst (*5*).

Apheloria corrugata (Wood) is an aposematically colored polydesmoid millipede. The glands, like those of other polydesmoids (*2, 6*), are serially arranged in pairs, one pair to each of most body segments. Their openings are visible as tiny pores on the notal lobes. Each gland has two compartments: an inner relatively large membranous reservoir, and an outer rigid vestibule (Figs. 1–4). The reservoir leads into the vestibule by way of a narrow duct, the terminal portion of which is tightly occluded by a spring-like valvular infolding of the duct wall (see *d*, Figs. 3 and 4). A muscle, originating on the body wall, inserts on this infolding (see *e*, Figs. 2 and 4) and serves to open the valve, thus clearing the duct lumen when the contents of the reservoir are discharged. The vestibule leads directly to the outside through a permanently opened orifice (see *c*, Figs. 1, 3, and 4). The entire glandular apparatus is lined with cuticle. The cuticle is overlaid with a variously modified secretory epithelium. There are no compressor muscles around the reservoir, so that the discharge must be effected by other means (*7*).

To test the supposition that the reservoir holds a stored undissociated cyanogenic compound, and the vestibule supplies an agent that initiates cyanogenesis at discharge, a series of qualitative tests were made on the contents of individual excised glands which had been spotted on filter paper. Several millipedes were killed by freezing, and while frozen, the cuticle of the body wall was chipped away, to expose