FUNCTIONAL INTERCONNECTIONS OF CAT VISUAL CORTICAL AREAS (V1 AND V2) AS EXAMINED BY CORTICAL HYPOTHERMIA

by

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ABSTRACT

The effects of cooling cat V1 or V2 cortex on its response to a single LGB shock, or to three successive Pul shocks, were investigated at both gross and unit levels using a specially designed cryogenic unit. Thirty-five locally anesthetized, adult male cats were used, each maintained on a mixture of N_2O analgesia plus metabolic O_2. The cryogenic unit enabled either V1 or V2 cortex to be cooled while maintaining the adjacent V2 or V1 cortex at normal temperature. Two on-line thermistor readouts permitted the monitoring of temperature. Built-in gross electrodes and a microelectrode detected cortical activity which was amplified and displayed on a storage scope. Unit activity was temporally analyzed using a histogram computer and the output displayed on the storage scope. In most cases, the cortical response was recorded in the adjacent region of cortex kept at normal cranial temperatures, and from the area being cooled.

Results showed: (1) Cooling the area adjacent to either V1 or V2 cortex (V2 or V1 cortex respectively) produced an enhancement in the amplitude of the gross response to LGB shock with a maximum in the range 25 - 29°C. The summated unit response above the spontaneous level elicited by LGB shock also showed an enhancement; a maximum being obtained in the range 25 - 30°C. The secondary (delayed) unit discharge exhibited a greater relative enhancement than the primary (initial) unit discharge. (2) Local cooling of

either V1 or V2 cortex again produced an enhancement both of the gross and unit response to LGB shock in the area being cooled, with a maximum in the range 25 - 29°C for the gross response and in the range 26 - 30°C for the unit response. (3) No change in the enhancement effect was obtained on subpial aspiration of the gray matter along the boundary between V1 and V2 cortex. (4) Cooling V1 cortex produced no systematic change in the gross cortical responses elicited by Pul shocks, either locally in V1 cortex, or in the adjacent V2 cortex. (5) Cooling V2 cortex, on the other hand, produced a consistent general decline in relative amplitude (although small maxima were obtained in some cases) in the gross cortical response elicited by Pul shocks, not only locally in V2 cortex but also in the adjacent V1 cortex. (6) Unit responses to the train of three pulvinar shocks were studied in only four units and no reliable results were obtained on cooling either V1 or V2 that were comparable to those seen in the gross responses.

The findings obtained by cooling adjacent cortex provide support for the existence both of reciprocal functional interconnections between V1 and V2 cortex associated with the LGB projection, and of functional connections from V2 back to V1 cortex associated with the pulvinar projection, thus extending concepts of cortical functioning based upon prior anatomical studies. The existence of the enhancement effect obtained in this study was discussed in terms of possible cortical mechanisms of excitation and inhibition.

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TABLE OF CONTENTS

LIST OF FIGURES

INTRODUCTION

Since the experimental work of Flourens (1823) it has been known that normal visual function depends upon the integrity of cerebral cortex. Panizza in 1885 further localized visual function to the occipital lobes (Fulton, 1943). Clinical observations in man (Holmes, 1918) and experimental studies in dog (Minkowski, 1911) and monkey (Polyak, 1933) further defined the cortical region associated with vision as the area striata, a region cytoarchitectonically designated by Brodmann (1905) as area 17. On the basis of findings obtained by perimetry this area was clinically recognized as the primary projection of the visual fields (Holmes and Lister, 1916), lending support to the work of Henschen in 1890 who considered the visual field to project topologically onto striate cortex ("cortical retina"). After the work of Flechsig (1876) on association cortex and Munk (1880) on the "psychic" areas, the region surrounding area striata, i.e., Brodmann's areas 18 and 19, was thought to be concerned with higher visual functions. For example, Holmes (1918) put forward the idea that area 18 was immediately concerned with the organization of the visual image, and Horrax (1923) thought that area 19 was concerned with visual associations involving other sensory modalities and the motor cortex. Thus evolved the concept of serial processing of visual information, the visual input first received by area 17 being elaborated in area 18 and then in area 19.

Von Bonin, Garol and McCulloch (1942) using strychnine neuronography showed functional connections from area 17 to area 18. After applying strychnine to a small region of area 17 strychnine spikes were recorded locally and also in ipsilateral area 18, thus providing physiological support for the concept of serial processing. Using the same method, they also provided evidence for functional connections from the border area between 18 and 19 back to area 17 showing in the monkey at least that there were reciprocal functional interconnections. Hubel and Wiesel (1965) using microelectrodes mapped out receptive fields for cells in areas 17, 18 and 19 in the cat. Their results suggested that there is a progression of complexity in receptive field characteristics recorded from areas 17, 18 and 19 respectively. They tentatively proposed that information from the LGB was processed in area 17 first by simple cells and then by complex cells. Projections carry this processed information to area 18 where other complex and hypercomplex cells further process the information. The results obtained from the latency studies of Denny, Baumgartner and Adorjani (1968) lend support to this theory.

In contrast to the concept of serial processing other studies have suggested the possibility of parallel processing of visual information. Landau, Bishop and Clare (1961) using gross electrode recordings showed that the evoked response recorded at any locus in cortex, including visual cortex, was made up of two components. The first component was thought to be produced by direct primary input of the specific sensory

modality while the later components arose from other cortical areas. These data suggested that processing of sensory information occurred simultaneously at all cortical loci.

By themselves, however, neither the concept of serial nor that of parallel processing my be sufficient to explain the full complexity of cortical functioning. Experimental studies by Talbot and Marshal (1941) demonstrated by evoked potential recordings two representations of the visual field that were topologically organized in the cat's visual cortex. One was situated at least in part on the postero-medial portion of the marginal gyrus (V1) and the second was located lateral to this on the marginal and suprasylvian gyri (V2). Later these areas were found to coincide with Brodmann's area 17 and 18 respectively as defined cytoarchitectonically for the cat by Otsuka and Hassler (1962). Bilge, Bingle, Seneviratne and Whitteridge (1967) used microelectrodes to map the visual field projection onto the mesial surface of the cat's hemisphere and Woolsey (1971) has provided data in other species including lower lissencephalic primates.

More recently, anatomical (Wilson and Cragg, 1967; Rosenquist, Edwards and Palmer, 1974) and electrophysiological (Vastola, 1961) studies in cat have demonstrated independent projections from the lateral geniculate nucleus directly to area 18 as well as 17, that is, there is a primary projection onto both visual cortical areas. Such studies support and extend the concept of parallel processing and add to the

traditional concept of serial processing.

Cowey (1964) using direct cortical stimulation demonstrated a functional connection between V1 and V2 in squirrel monkey. Since the effects of antidromic stimulation were not controlled for, the direction of conduction could not be determined from his study (see Von Bonin et al, 1942). Cowey also made cuts of varying depths along the boundary between areas V1 and V2 and was able to show that connectivity depended upon the white and not the gray matter. He was unable to show the existence of V2 in the rhesus monkey using photic stimulation, but Allman and Kass (1971) using the same method were able to find V2 in the depths of the lunate fissure in one rhesus monkey. Recently, Tigges, Spatz and Tigges (1973) have demonstrated anatomically that there are topologically organized reciprocal connections between areas 17 and 18 in the squirrel monkey. Wilson (1968) and Kawamura (1973) have shown that V1 and V2 cortex in the cat are also reciprocally interconnected in topological fashion. Together the above studies suggest that visual cortical function depends at least upon parallel inputs from LGB to V1 and V2 in cat and also reciprocal interconnections between V1 and V2 in both cat and primate.

Yet another complication is that visual cortical function may depend upon the influence of extrageniculo-striate structures. The reticular formation, superior colliculus and pulvinar are known to modify the potential evoked in cortex, both by geniculate shock (Chalupa, Battersby

and Frumkes, 1973) and photic stimulation (Battersby and Oesterreich, 1963; Brown and Marco, 1966; 1967). Furthermore, low frequency stimulation of pulvinar produces an augmenting response in visual cortex (Morison and Dempsey, 1942). Graybiel (1972) using anterograde degeneration methods has described direct projections from pulvinar to area 18 and 19 ("rim-areas"), while Burrows and Hayhow (1971) have shown Pul connections to the lateral bank of the suprasylvian gyrus. These findings suggest that visual cortical function may depend upon pathways outside the classical retino-geniculo-cortical system.

Traditionally, the ablation method has been widely used in the study of cortical function (eg., Flourens, Minkowski, and Polyak), the resulting deficits being ascribed to the effects of the lesion itself. One weakness of the ablation method is its lack of reversibility resulting in the need for numerous control studies before positive conclusions can be drawn. Two methods for producing reversible cortical lesions, the application of KCl (Leao, 1944) and cooling (Trendelenburg, 1910) have been described. The difficulty of using KCl is that of controlling both the spread of the KCl depression and its effective concentration on cortex, and hence the variability of its action. Another difficulty in working with KCl in unit studies is that the mechanical disturbance caused by the application of KCl frequently results in the loss of unit activity. Hypothermia, on the other hand, does not suffer from these disadvantages

but does require the use of more elaborate equipment.

Hypothermia has been used in human surgery as a reversible method for identifying structures associated with motor disturbances such as those seen in Parkinson's Disease (Cooper and Lee, 1961). Structures identified by such a method, would then be permanently destroyed by a further reduction in temperature. Experimental studies have used cortical cooling as a means of producing reversible changes in behavior (Trendelenburg, 1910; Kuvatov and Mutly, 1936; Rougeul and Buser, 1962; Byck and Dirlik, 1963; Shacter, 1966). For example, Rougeul and Buser (1962) found that cooling visual cortex in cat produced deficits in response to a light flash but not an auditory stimulus, and Shacter (1966) observed reversible deficits in delayed response performance in monkeys following cooling of the frontal cortex. Recently, other studies have examined the effects of cortical cooling on the electrical activity within the central nervous system; Calma (1965) cooled occipital cortex in cat and observed a depression of responses to visual stimuli within the posterior thalamus; Kalil and Chase (1970) in the cat and Hull (1968) in the monkey described a decrease in the responsivity of LGB neurons following cortical hypothermia; and, Chalupa, Anchel and Lindsley (1972) found that cooling the suprasylvian gyrus of the cat produced a reduction in the amplitude of the negative component of the pulvinar response to light flash. While the above studies described a decrease in activity on cortical cooling, other results show that cooling can produce

an increase in electrical activity. For example, Hull (1968) found that the unit responsivity of some LGB neurons was increased following cortical cooling. Also, Bindman (1963), recording from cortex, obtained an enhancement of both evoked response and spontaneous acitivty after local cooling of motor cortex and Peacock, Langfitt and Koff (1965) observed a transient increase in the cortical evoked response to optic tract shock on cooling visual cortex with ethyl chloride spray. Recently, Reynolds, Ojemann and Ward (1975a,b) recording intracellularly, were able to show both increased rate of firing and also an increase in the magnitude of the action potential (maximum at 27°C) of cortical neurons in the pericruciate cortex after local cortical cooling. Collectively the foregoing results suggest that cortical cooling may selectively affect excitatory and inhibitory mechanisms in the central nervous system, and if true, would provide a powerful technique for analyzing the functional interrelationships between cortical areas.

The purpose of the present study was to investigate further the functional interconnections between V1 and V2 cortex in the cat using a specially designed cryogenic unit to produce reversible suppression of local cortical regions. The cryogenic unit included a pair of thermal probes, each capable of cooling or maintaining normal temperatures and of recording cortical electrical activity within the temperature controlled area. Specifically, the effects of cooling either V1 or V2 cortex on the potential elicited by lateral geniculate

or pulvinar shock were examined both in V1 and V2 at the unit and gross electrode level. Thus, by recording from the cortical region (maintained at normal temperature) adjacent to the area being functionally suppressed by cooling, the basis of cortico-cortical interaction, i.e., excitation, inhibition and direction of information flow could be evaluated.

METHODS

Preparation Observations were made on a total of 35 male adult cats. Eight were used in early investigations of a qualitative nature, the remaining 27 preparations provided parametric data. Twenty-five preparations provided data on LGB stimulation while 10 preparations (many the same) provided Pul data. A total of 22 units were held for the 30 min duration required for each experiment. Anesthesia was induced in each animal with diethyl ether and a tracheotomy performed. The ether was then withdrawn and replaced by a mixture of Halothane (concentrations being adjusted by reference to physiologic signs such as pupil size and muscle tone), nitrous oxide (1000 ml/min) and metabolic oxygen (600 ml/min). The animal was mounted in a stereotaxic instrument (Kopf), the saphenous vein was cannulated and connected to a gravity fed microdrip supplying a 5% solution of dextrose in physiological saline (10 drops/min).

Surgery The scalp was incised along the midline and the left temporal muscle reflected laterally uncovering the dorsal and lateral parts of the cranium. A craniectomy was made to expose the marginal and suprasylvian gyri from A+15 to P-5 and from the midline to L+10. A second craniectomy was made so that electrodes could be directed horizontally towards LGB and pulvinar. The dura was reflected and the cortex kept moist with warm saline. The dorsal neck muscles were reflected and the cisterna magna punctured, to help

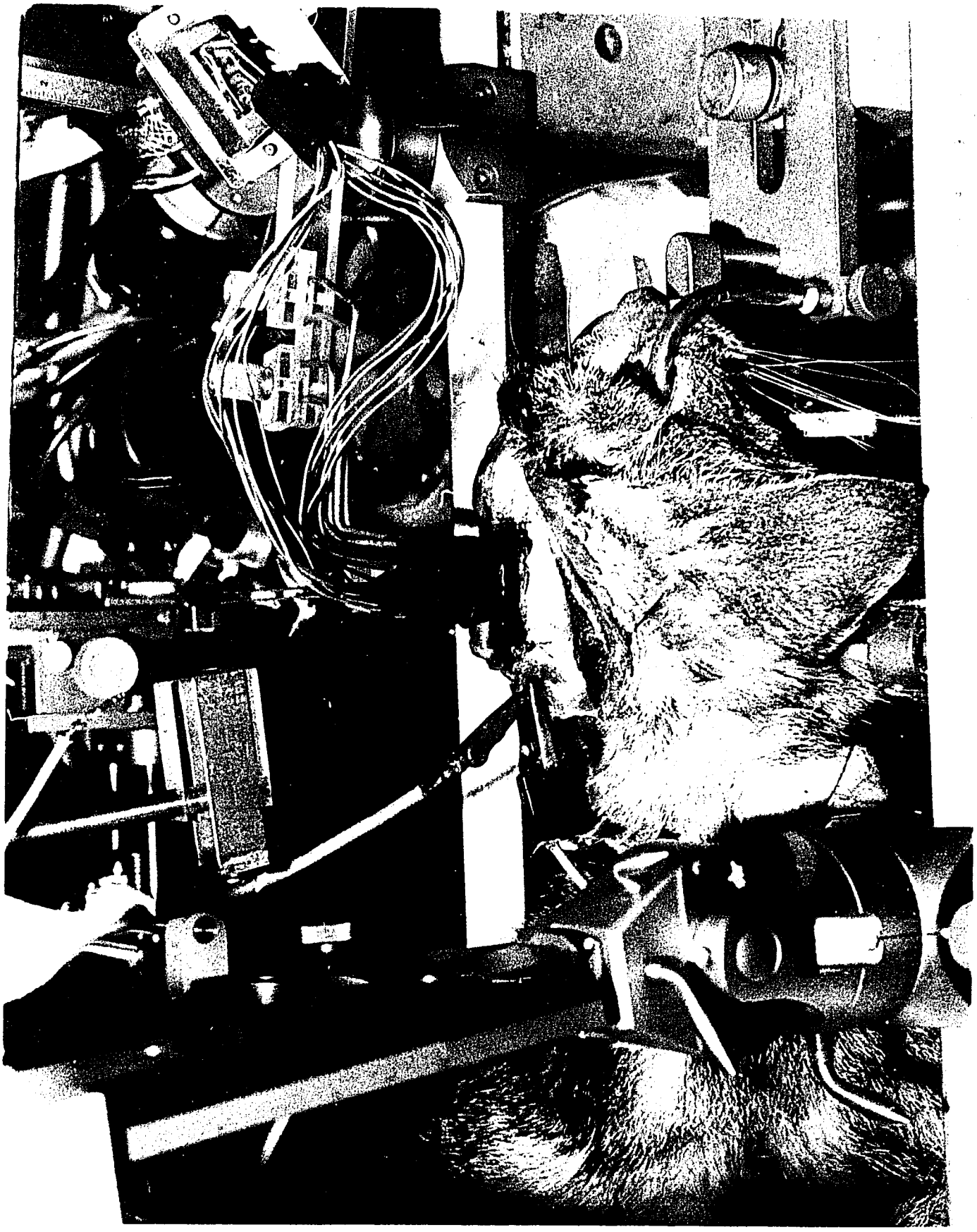
mechanically stabilize the cortex.

General Procedure An array of six parallel stimulating electrodes (two above and four below) was advanced horizontally and medially through the trephine hole towards the left LGB and pulvinar. Coordinate values were determined using the cat brain atlas of Jasper and Ajmone-Marsan (1954). Before each experiment the impedances of the stimulating electrodes were measured while the tips were immersed in normal saline to check that their values were in the range of 50-100 kohms. In some experiments the value of the stimulating current being passed through either the LGB or pulvinar electrodes was measured using an inductively coupled current probe (Tektronix 134) to check that it was in the range of 100 to 200 microamperes.

The two thermal probes (see Fig 1) were carefully lowered until they just touched the cortical surface. One probe was situated on the medial part of the marginal gyrus (V1) and the other on the medial suprasylvian gyrus (V2). Both probes rested on the cortical surface in a position extending from A+10 to P-5.

At this point all wound edges and pressure points were liberally infiltrated with propitocaine (Citanest), isotonic methyl cellulose (Lacaryl) was placed on the conjunctivum of the eyes, and a muscle relaxant, gallamine triethiodide (Flaxedil), infused via the cannulated saphenous vein and the animal immediately placed on artificial respiration (35cc/stroke, 26 strokes/min). Infusions of gallamine

Fig. 1 A view of the pair of thermal probes on the cat's visual cortex together with the micro-electrode assembly.



triethiodide were repeated as necessary. Halothane was then completely withdrawn, the animal thereafter being maintained on the mixture of nitrous oxide and oxygen (30% by volume). Every 3 hours the propitocaine and eye drops were readministered. A DC powered heating blanket wrapped around the animal's body maintained rectal temperature at 36°C, this value being periodically checked during each experiment using a thermometer. Periodically the trachea was aspirated to remove any accumulations of mucous.[1]

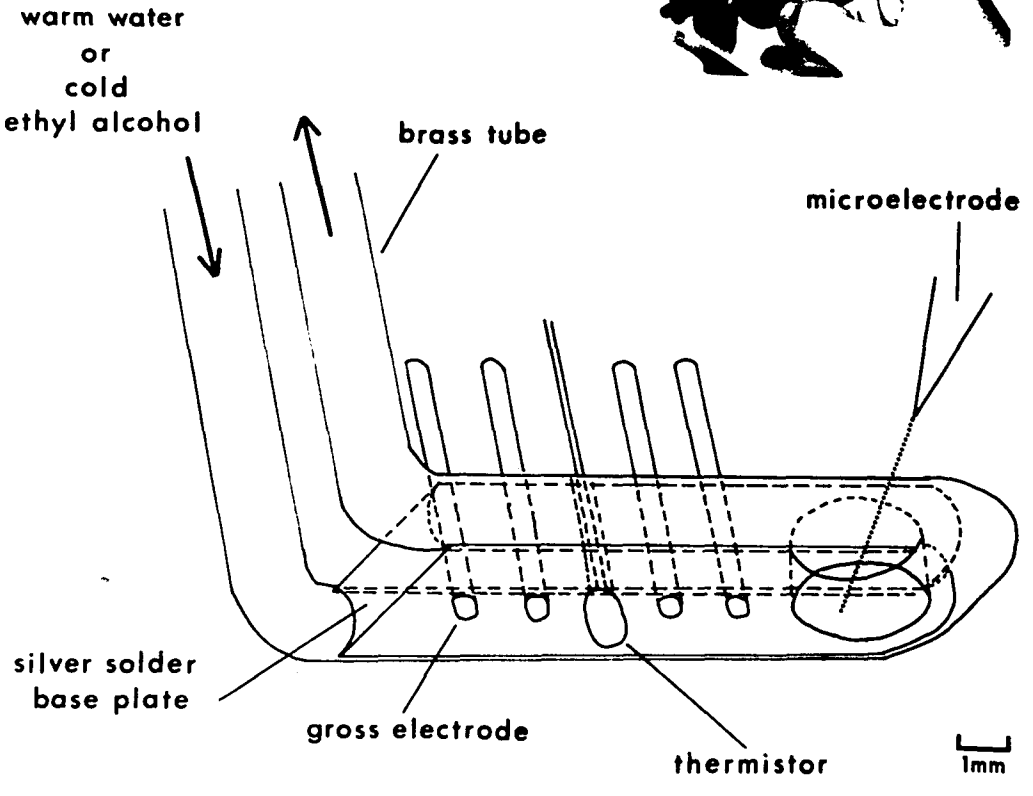
At the end of each experiment the animal was killed with an overdose of sodium pentobarbital (Nembutal) via the cannulated saphenous vein. In some experiments the positions of the electrode tips in LGB and/or pulvinar were electrolytically marked and the head removed and stored in 10% formalin for later histological analysis. The brains were blocked and cut in frozen coronal sections at 50μm. Every fifth or tenth section was saved and stained according to the Klüver-Barrera method (1953).

Apparatus The cryogenic unit was designed for this study and consisted of two probes, their associated bridge circuits, a heat exchanger and a Harvard infusion pump (see Fig 2). The two probes were set adjacent and parallel to

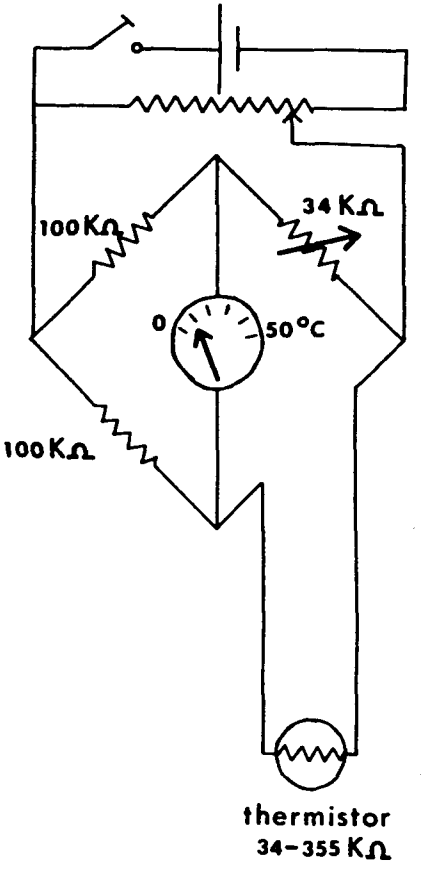
1 In order to help prevent stasis the rear of the animal was raised in a few early experiments, but the technique was later abandoned when it was found to cause pulsations of the cortex and a consequent inability to hold a unit with a microelectrode.

Fig. 2 Cryogenic Unit--Probe and Bridge Circuit.

CRYOGENIC UNIT — PROBE AND BRIDGE READOUT



THERMISTOR
BRIDGE CIRCUIT



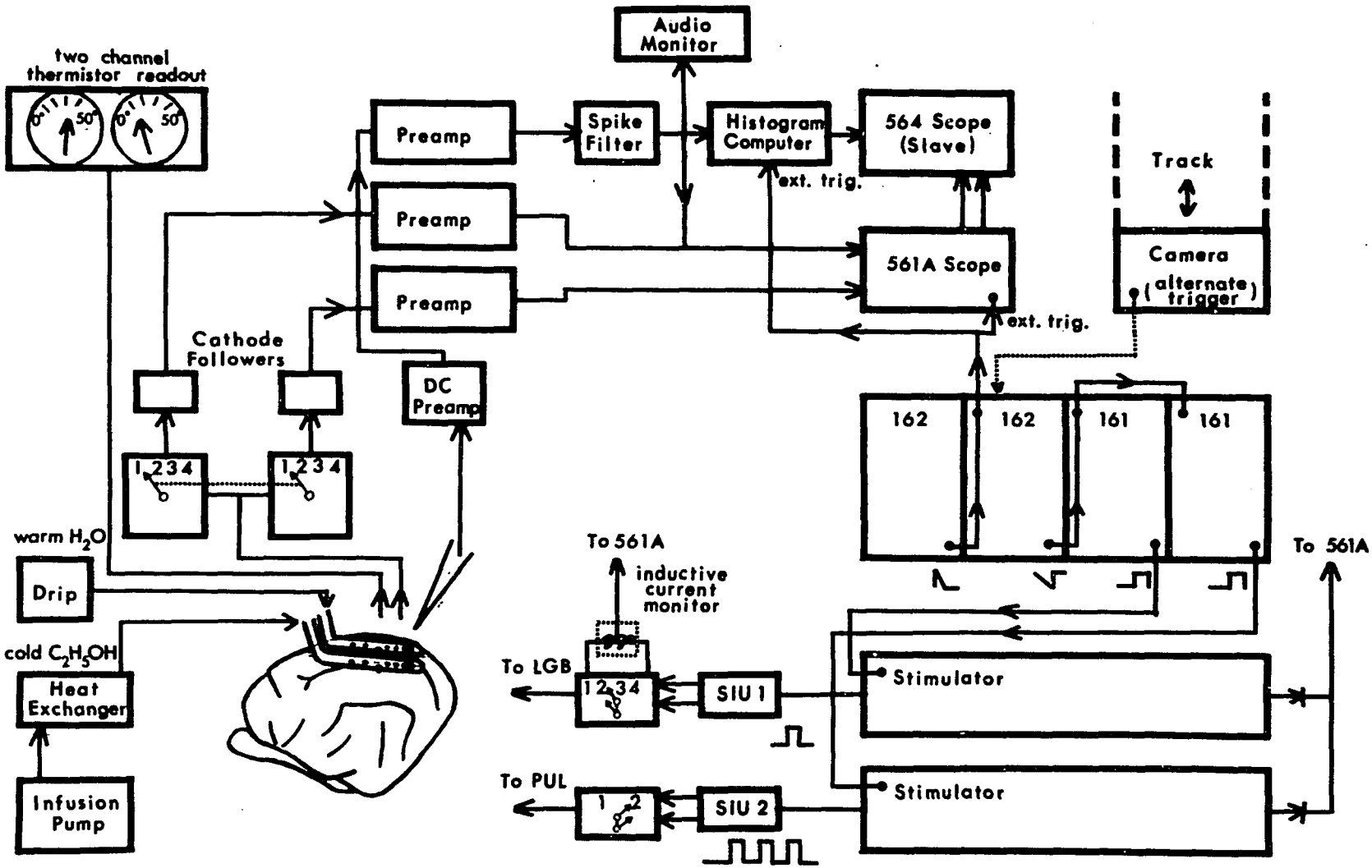
each other, each being fabricated from brass tubing 1 mm outside diameter, shaped into a "U", the gap within the "U" being filled with silver solder in order to produce a uniform thermal gradient. Along the center-line of each solder plate were drilled four holes to receive insulated silver cortical recording electrodes, the tips of which were rounded, uninsulated, and projected 0.5 mm beyond the bottom surface of the plate. A fifth hole was drilled on the center-line in the middle of each plate to receive the insulated leads from a glass-coated bead thermistor (Fenwal Electronics Inc., type 6-A52L1) cemented 1 mm below the bottom surface of the plate. A sixth hole was drilled on the center-line, 1 mm from the distal end of each probe, to allow passage of a tungsten microelectrode. The thermistor of each probe formed one arm of its associated bridge circuit. After calibration of the thermistor, using melting ice as a reference, the unit provided direct centigrade temperature on-line readout, linear from 0 C to 50 C as calibrated (see Fig 2). The Harvard infusion pump was used to pass ethyl alcohol at a constant velocity using a preselected gear ratio through a heat exchanger where it was cooled and then passed on through either one of the two thermal probes selected. The heat exchanger was composed of a coil of 60 cm of brass tubing, 1 mm in diameter, immersed in a mixture of ethyl alcohol and solid carbon dioxide, contained in a thermally insulated 500 cc beaker. Using a gravity drip feed bottle, warm water was passed through the other thermal probe, at a rate set by the adjustment of a flow valve.

Overall timing for stimulation and recording was centralized using a Waveform Generator (Tektronix type 162). Every four sec. this generator triggered another waveform generator (Tektronix type 162), which in turn provided the time base for two pulse generators (Tektronix type 161). The first pulse generator gated on a stimulator (Grass S-4) which could be switch-selected to stimulate any one of four loci in LGB. The onset of this gate was also used to provide a delayed trigger to the CRO time base. The second pulse generator gated another stimulator (Grass S-4) to produce stimulation of either one of two loci in pulvinar (see Fig 3).

The LGB stimulus was a 0.1 msec duration square pulse of 6 v amplitude and the pulvinar stimulus also 6 v in amplitude consisted of three 0.1 msec duration square pulses separated by 100 msec intervals. Stimulus isolation units (Grass SIU-B) were used to couple each stimulator to the selected electrode.

The stimulating array of LGB and pulvinar electrodes were all mounted on a common electrode carrier (in the earlier experiments only the four LGB electrodes were used). Each of the LGB concentric electrodes was formed of a central insulated 0.005 in tungsten wire inserted into a 24 gauge insulated hypodermic tubing so as to project 0.5 mm beyond the end of the tube. The tip of both the wire and the tube were bare of insulation. The two pulvinar stimulating electrodes consisted of two 0.005 in insulated tungsten

Fig. 3 Flow diagram of the stimulating, recording and cooling equipment.


two channel thermistor readout
0 50
0 50
Audio Monitor
Preamp
Spike Filter
Histogram Computer
564 Scope (Slave)
ext. trig.
Track
Camera
(alternate trigger)
Preamp
561A Scope
Preamp
ext. trig.
Cathode Followers
DC Preamp
1 2 3 4
1 2 3 4
162
162
161
161
warm H_2O
Drip
To 561A
inductive current monitor
To 561A
cold C_2H_5OH
Heat Exchanger
To LGB
1 2 3 4
SIU 1
Stimulator
Infusion Pump
To PUL
1 2
SIU 2
Stimulator

wires, passed through insulated hypodermic tubing, the bare wire tips again 0.5 mm from the end of the tubes.

The cortical monopolar electrodes within the cryogenic unit were used to record the gross evoked response from cortex, with the bone at the occipital ridge serving as a reference. Pairs of adjacent recording electrodes one on V1 and the other on V2, were selected using a double-pole 4 position switch box with make-before-break contacts. Cortical activity was fed via cathode followers to two differential AC preamplifiers (Grass P-50; -3db at 7 Hz to 10 kHz) and displayed on a split-beam oscilloscope (Tektronix 561A) and a slave storage scope (Tektronix 564). Five superimposed traces of the gross response were recorded on the slave storage scope and photographed (Grass Kymograph camera).

In unit studies a tungsten microelectrode (Frederick Haer and Co.; impedance 15-25 megohms at 1000 Hz; tip diameter less than 1 μm, tip length 5 μm) was used to record extracellularly from the cortex via a DC negative capacitance probe head (Transidyne MPA-6) feeding into an AC preamplifier (Grass P-50), with a band pass of 35 Hz to 10 kHz (-3db). The amplified signal was then passed through a spike filter (David Kopf EFA-12), to an audio monitor, a histogram computer (Synax) and a CRO (Tektronix 561A). The output (200 bins/sweep) from the histogram computer was displayed on the storage scope as a time latency histogram formed from 16 sweeps. The CRO displays were photographed with a Kymograph camera and the results stored on 35 mm film.

Experimental Procedure The experiments were begun about one hour after Halothane was withdrawn. All experiments were conducted under low ambient illumination. The classical LGB evoked potential was obtained by advancing the array of LGB stimulating electrodes medially in 0.3 mm steps until a pair of adjacent cortical electrodes, one on V1 and the other on V2, recorded a large stable response to stimulation of at least one of the 4 LGB stimulating electrodes. In experiments where the pulvinar was also stimulated a similar procedure was used to obtain the augmenting response.

In experiments where unit recording was made from cortex, the LGB stimulating electrodes were advanced until a maximal cortical response to LGB shock was obtained at those pair of gross electrodes immediately adjacent to the microelectrode. Before advancing the microelectrode tip towards the cortical surface, a 1 megohm shunt resistor was switched across the input to the DC negative capacitance probe head in order to prevent high current densities from damaging the tip of the electrode. The microelectrode was advanced using a microdrive (David Kopf) until a loud click was obtained on the audio monitor, indicating contact with the cortical surface. The shunt resistor was then switched out and the microelectrode was further advanced into the cortex until a unit could be identified either by its spontaneous activity or its response to a flash of light in the eyes.

Either V1 or V2 cortex was cooled by passing cold ethyl alcohol through the selected thermal probe. Adjacent cortex, either V2 or V1 was maintained at normal temperature by passing warm water through the other thermal probe. Cortical responsivity to LGB and pulvinar shock was examined systematically as a function of temperature in the range 34 - 20° C.

It is possible that cortical cooling could produce changes in the temperature of subcortical structures, including the LGB and pulvinar. The effects of such cooling could then be attributed to changes in stimulating current produced by variations in contact resistance between the stimulating electrodes and thalamic tissue. To control for this possibility the temperature of the LGB and pulvinar region was measured during cortical cooling at the conclusion of two experiments and was found to remain constant at 35°C.

In some cats a lesion was made along the approximate boundary between V1 and V2 cortex (Woolsey, 1971). In the first stage the gray matter only was aspirated using a 20 gauge needle and the effects of cooling first one visual area and then the other were examined. In the second stage the white matter was also aspirated using an 18 gauge needle and the cooling experiments repeated.

Analysis of the data The peak to peak amplitude of the gross response to LGB and Pul shock was read from filmed data of five superimposed tracings as a function of

temperature. This peak to peak amplitude corresponds to the amplitude of the peak positive to peak negative deflection (components 4-5 of Malis and Kruger, 1956 in the case of LGB). Amplitude of response at any given temperature was then expressed as a per cent of control amplitude; i.e., the amplitude at "normal" temperature, where normal was defined as the response at 32-34°C (see below).

To quantify the unit data, the response areas underlying the histograms of unit discharges were measured with an electronic graphic calculator (Numonics Corp.), with digital readout, and expressed as a function of temperature. At each temperature, the spontaneous level of activity ("noise") prior to LGB or pulvinar shock was measured and its possible contribution to the responses was subtracted to yield an adjusted estimate of magnitude of the response (the "signal"). Such integrated response areas were then expressed as a per cent of control; i.e., the unit discharge at "normal" temperature, as defined above.

RESULTS

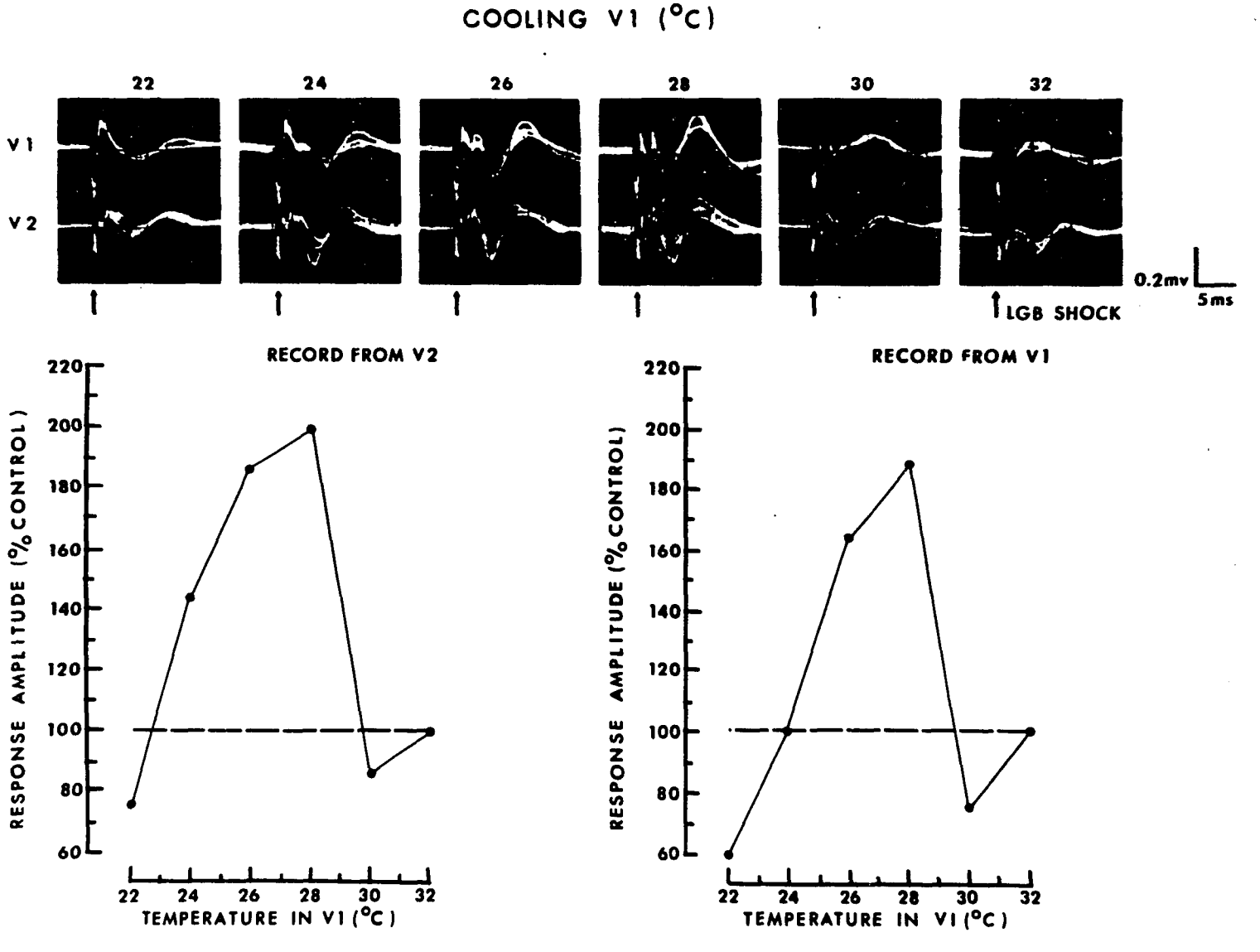
(1) Gross Evoked Response to LGB Shock In both V1 and V2 cortex the response from a given macroelectrode to a single LGB shock was the classic sequence of four positive waves followed by one later negative wave as previously described (Clare and Bishop, 1955; Malis and Kruger, 1956). The effects of cooling either V1 or V2 cortex on this response were studied in 25 animals.

(a) Effects of cooling V1 The results for Cat 419 in Fig 4 are representative of the findings. As indicated by the oscilloscope tracings at the top of the figure, cooling V1 cortex produced a marked enhancement in the later cortical components of the geniculate shock evoked potential (components 4 to 5 of Malis and Kruger, 1956) in both V1 and V2 cortex (top and bottom traces respectively). This enhancement effect was maximal at about 28°C. Below this temperature the cortical response to LGB shock dropped rapidly on further cooling and at 22°C had a value less than the response at normal temperatures (32 - 34°C).[1] The early components of the geniculate shock evoked potential were found to be uneffected by cooling in the range 20 - 34°C. This effect is illustrated in the graphs at the bottom of Fig 4 where response amplitude (in per cent of control at

1 The somewhat low temperatures (32 - 34°C) found for the cortex compared with the body temperature of 36°C was thought to be caused by stasis. This condition was a result of using an immobilized preparation.

Fig. 4 Effects of cooling V1 cortex on the LGB shock evoked potential recorded in V1 and V2 cortex for cat 419. The oscilloscope tracings at the top show a maximum enhancement at 28°C for components 4 and 5 of Malis and Kruger (1956) in V1 and V2 cortex. The graphs at the bottom show that the enhancement in both cases was approximately 200 per cent.

CAT 419 - AMPLITUDE CHANGES DUE TO HYPOTHERMIA



32°C) is expressed along the ordinate as a function of temperature along the abscissa. The graphs show that response amplitude was enhanced approximately 200 per cent in both V1 and V2 cortex, on cooling V1.

(b) Effects of cooling V2 Fig 5 illustrates the effects obtained by cooling V2 on the LGB shock elicited response in both V1 and V2 cortex. These results are for the same animal, Cat 419, previously illustrated in Fig 4. The oscilloscope tracings at the top show that cooling V2 again produced a marked enhancement in the components 4 and 5 of the shock response in V1 cortex (top trace). This enhancement effect was maximal at about 24 - 26°C. In V2 cortex (bottom trace) a similar enhancement effect was also obtained, but the magnitude of this effect was smaller in this particular animal. At both cortical locations there was a rapid drop in response amplitude at lower temperatures, and in V2 cortex response amplitude fell below control level.

(c) Group data on the effects of cooling V1 or V2 cortex Fig 6 presents a summary of the group results obtained upon cooling either V1 cortex (N=15) or V2 cortex (N=17 cats). The graphs present median response amplitude (per cent of control) plotted as a function of temperature; the length of the vertical bars representing the interquartile range. In the four combinations of the two cooling conditions (cooling either V1 or V2) and the two recording loci (V1 or

Fig. 5 Effects of cooling V2 cortex on the LGB shock evoked potential recorded in V1 and V2 cortex for cat 419. The oscilloscope tracings along the top show an enhancement in the later components, maximal in the range 24-26°C in V1 and V2 cortex. The graphs below show that at lower temperatures a rapid drop in relative response amplitude occurred in both cortical locations.

CAT 419 - AMPLITUDE CHANGES DUE TO HYPOTHERMIA

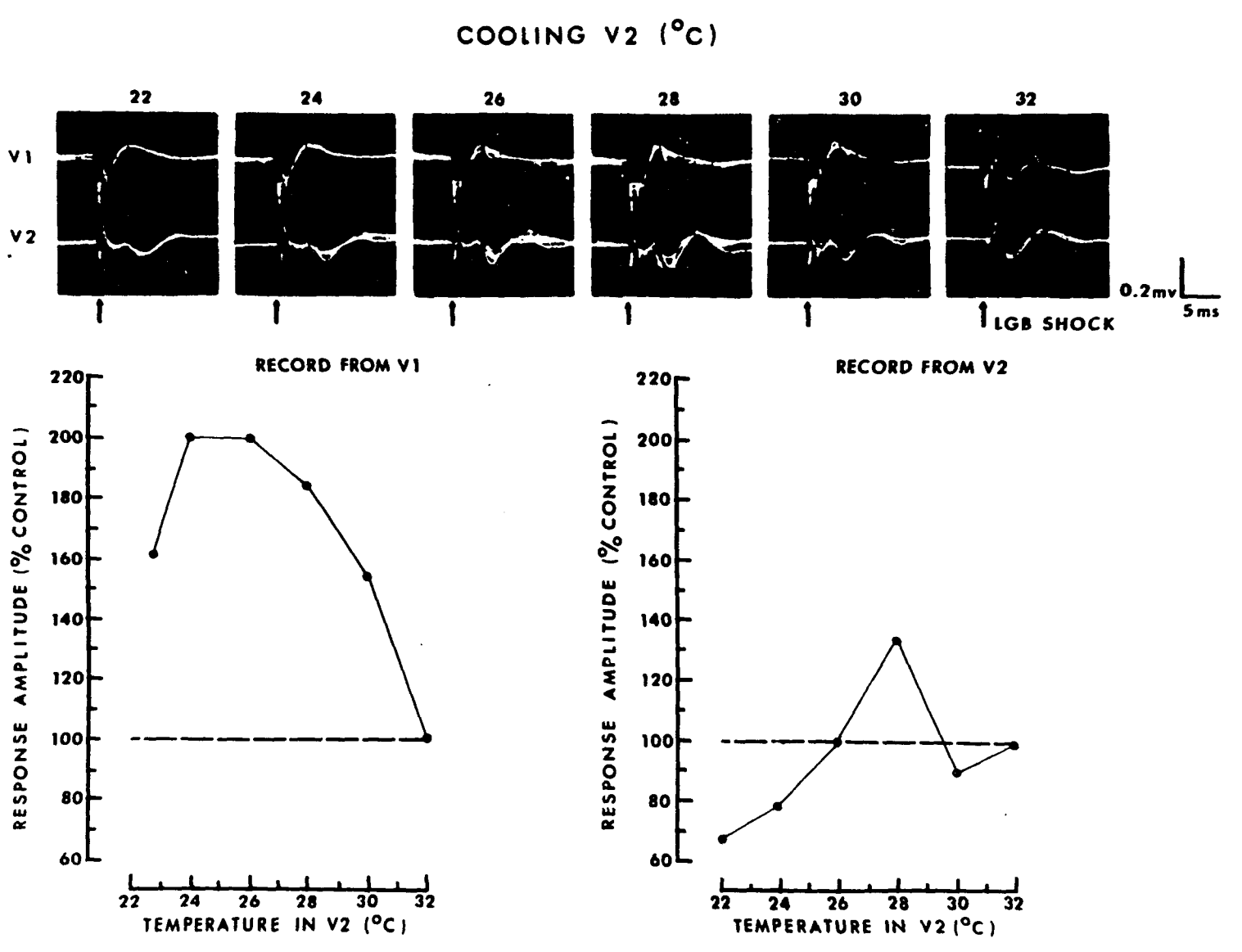
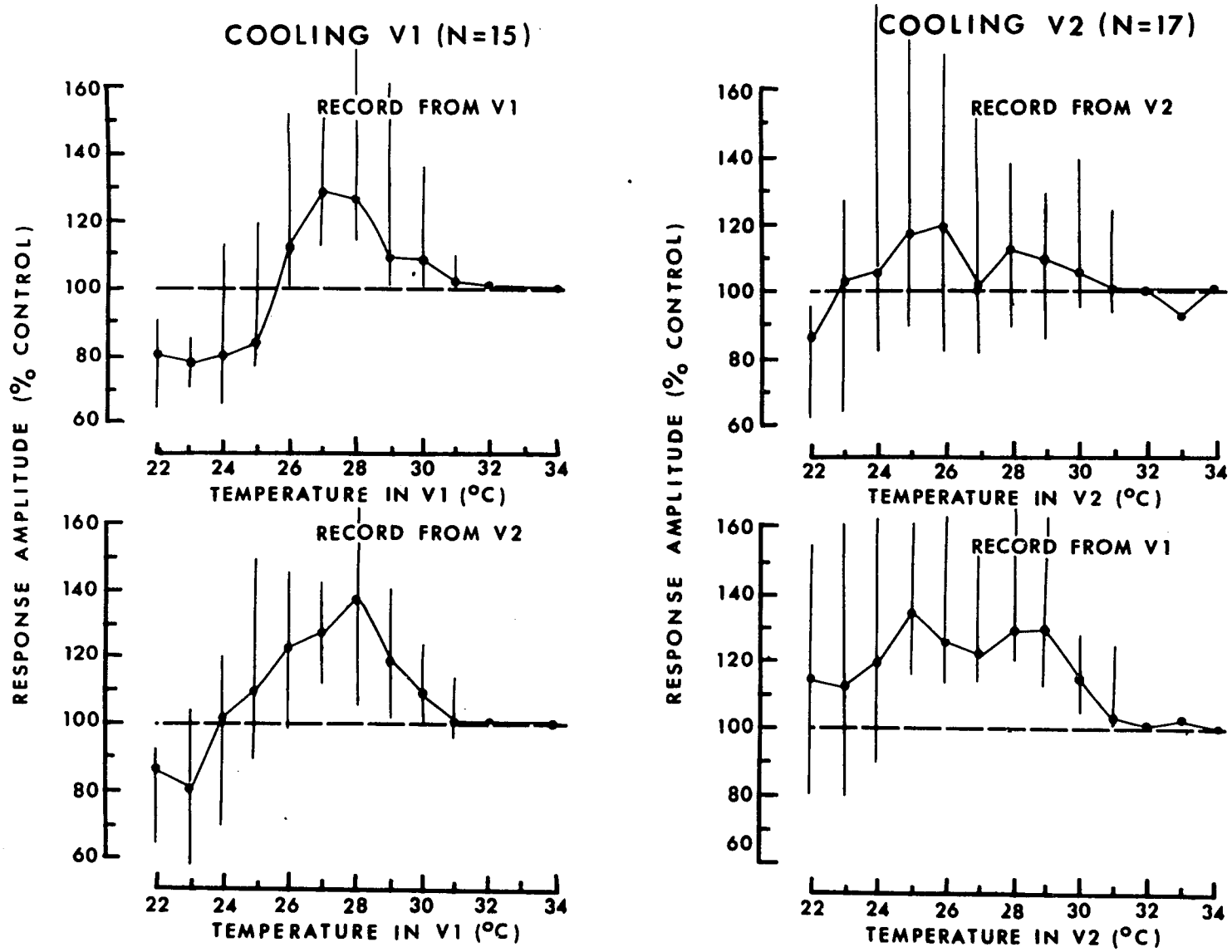


Fig. 6 Group Data: Relative response amplitude changes of the LGB shock evoked potential due to cortical cooling. Solid circles represent medians and vertical bars give the value of the interquartile range. The graphs show that the greatest percentage increase occurred in the temperature range 24-26°C.

AMPLITUDE CHANGES DUE TO HYPOTHERMIA



V2) investigated, cortical cooling below 30°C always produced enhancement of response amplitude, with the greatest percentage increase (130-140 per cent gain) occurring at 26 - 28°C. Under all conditions, relative response amplitude declined following maximal enhancement, and also in all conditions except that of cooling V2 cortex and recording from V1, fell below control level at about 22°C. It appears from the group data that the enhancement effect was slightly greater in the cortex adjacent to that being cooled (compare the bottom set of graphs with the top set of graphs) but the difference was slight and of questionable reliability. The values of the interquartile range suggest that the scattering of the data was somewhat greater for responses obtained in locally cooled cortex, as opposed to that in the adjacent cortex.

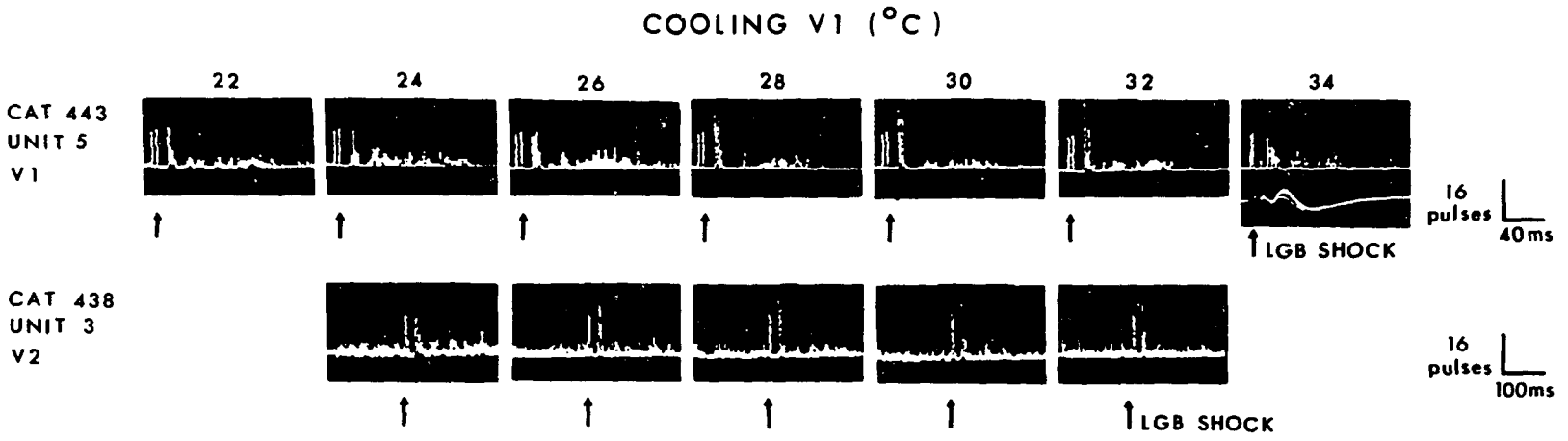
(2) Unit Response to LGB Shock The unit discharge pattern to geniculate shock recorded in either V1 or V2 cortex can be described by three components: The first component, the primary discharge, was an intense burst of unit activity of 5 msec duration which occurred about 3 msec after shock onset, and was correlated in time with the positive going components of the gross shock response. Following this initial burst there was a period of suppression lasting 20 - 40 msec which was correlated with the negative going components of the gross response and was characterized by a rate of discharge less than the spontaneous level. Finally, there was a less intense secondary discharge lasting

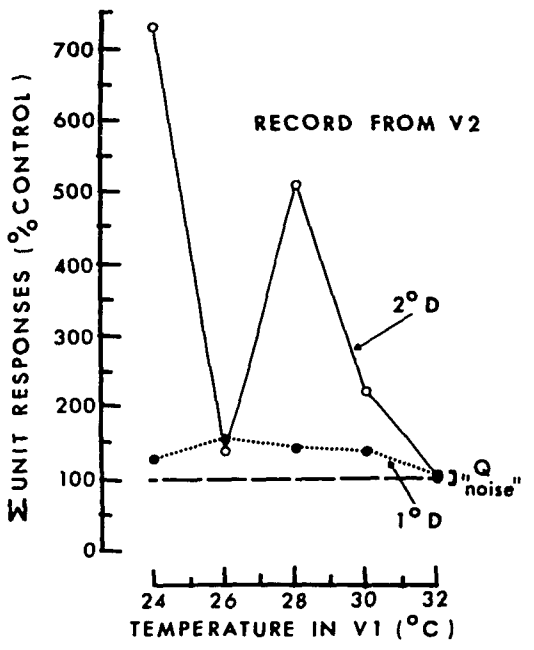
50 - 100 msec which was correlated with the return to baseline of the gross evoked potential (see top right histogram in Fig 7).

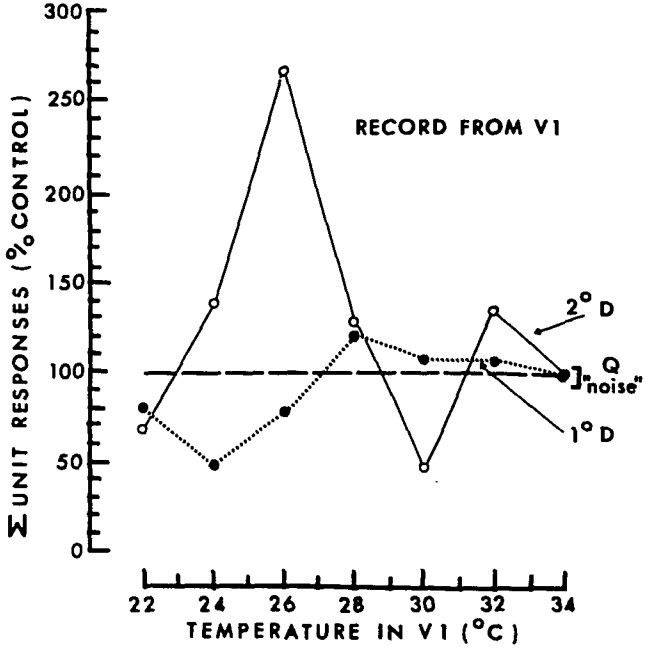
(a) Effects of cooling V1 cortex In six animals the effects of cooling V1 cortex on the unit response to LGB shock were investigated in both V1 and V2 cortex. In Fig 7 are given the results obtained for two illustrative units, one in V1, the other in V2 cortex, taken from two different cats (cats 443 and 438 respectively). Time latency histograms at the top of the figure show that cooling V1 increased the primary and secondary unit discharge activity in both V1 and V2 cortex. The maximum effect in V1 was obtained at 26°C; the maximum in V2 showed two peaks, one at 28°C, the other at 24°C. This latter double maxima was not obtained in most animals, (see section 2c for group data). The graphs at the bottom of Fig 7 present quantified data where planimetric areas of the two major response components less spontaneous level ("noise") are plotted separately as a per cent change from the control level at normal temperature. For both units enhancement of the secondary discharge is relatively much greater than that of the primary discharge, however both were above the level of spontaneous activity (the small bracket at the right of each abscissa represents the value of the semi-interquartile range of the spontaneous activity). In V2 cortex a maximum enhancement was shown at 26°C for the primary discharge and at 28°C for the secondary, whereas in V1 cortex, the maximal

Fig. 7 Effects of cooling V1 on primary (1^{o}) and secondary (2^{o}) unit discharge (D) elicited by LGB shock for a unit recorded in V1 (cat 443, unit 5) and a unit recorded in V2 (cat 438, unit 3). Oscilloscope tracings at the top show time latency histograms. Trace at right (34^{o}C) compares histogram (top) with gross evoked potential (bottom). Bracket labeled Q "noise" represents the semi-interquartile range of the spontaneous activity measured over all temperatures. Histogram (top and bottom trace) bin width is 5 msec.

EFFECTS OF HYPOTHERMIA ON 1° AND 2° UNIT DISCHARGE (D)







enhancement of the primary discharge occurred at 28°C and of the secondary discharge at 26°C.

(b) Effects of cooling V2 cortex The effects of cooling V2 cortex on unit activity in V1 and V2 cortex were examined in six animals. Fig 8 presents representative data for two such units; one set from V1 (cat 443, unit 2) and the other from V2 (cat 438, unit 4). Time latency histograms at the top show that cooling V2 produced an increase in unit activity in both V1 and V2 cortex, with the major effect being on the primary and secondary discharge. These effects are presented in quantifiable terms (per cent change in summated area versus temperature) in graphical form. The graph at the left shows that there was no increase above "noise" level of the primary discharge in the V1 unit. The secondary discharge in V1, on the other hand, was substantially increased with a maximum effect at 28°C, and another smaller peak at 32°C. The unit in V2 (graph on the right) shows an increase above the spontaneous level for both the primary and secondary discharges, with a maximum at 30°C, the increase in the secondary discharge, however, being considerably greater.

(c) Group data on the effects of cooling V1 or V2 cortex Fig 9 presents a summary of group results obtained from unit activity upon cooling V1 cortex (N=10 units) or V2 cortex (N=8 units). Generally, an increase in summated unit responses above the spontaneous level occurred for both the primary and secondary discharge under the four combinations

Fig. 8 Effects of cooling V2 on primary (1^{o}) and secondary (2^{o}) unit discharge (D) elicited by LGB shock for a unit recorded in V1 (cat 443, unit 2) and a unit recorded in V2 (cat 438, unit 4). Histogram (top and bottom trace) bin width is 5 msec.

EFFECTS OF HYPOTHERMIA ON 1° AND 2° UNIT DISCHARGE (D)

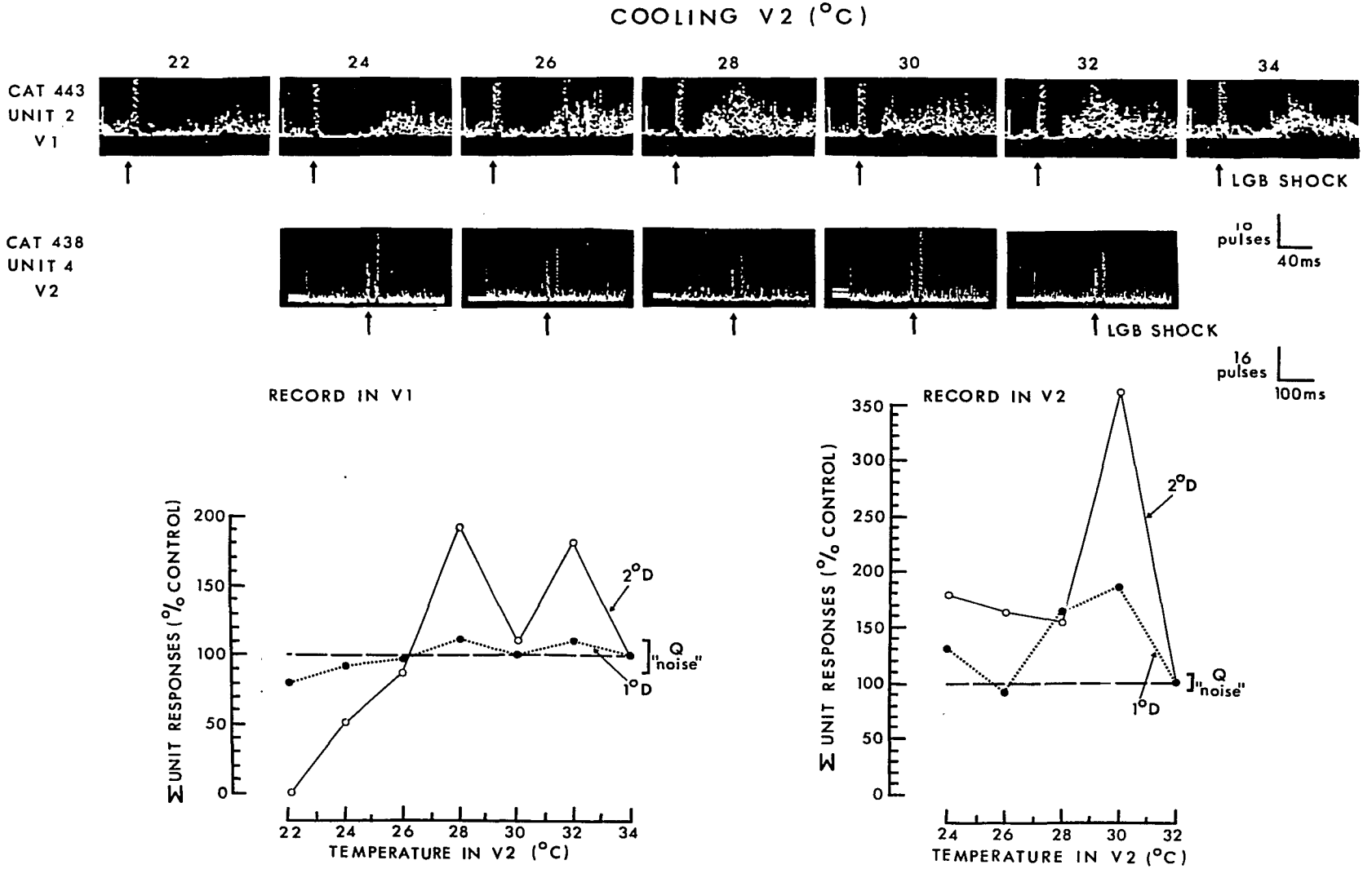
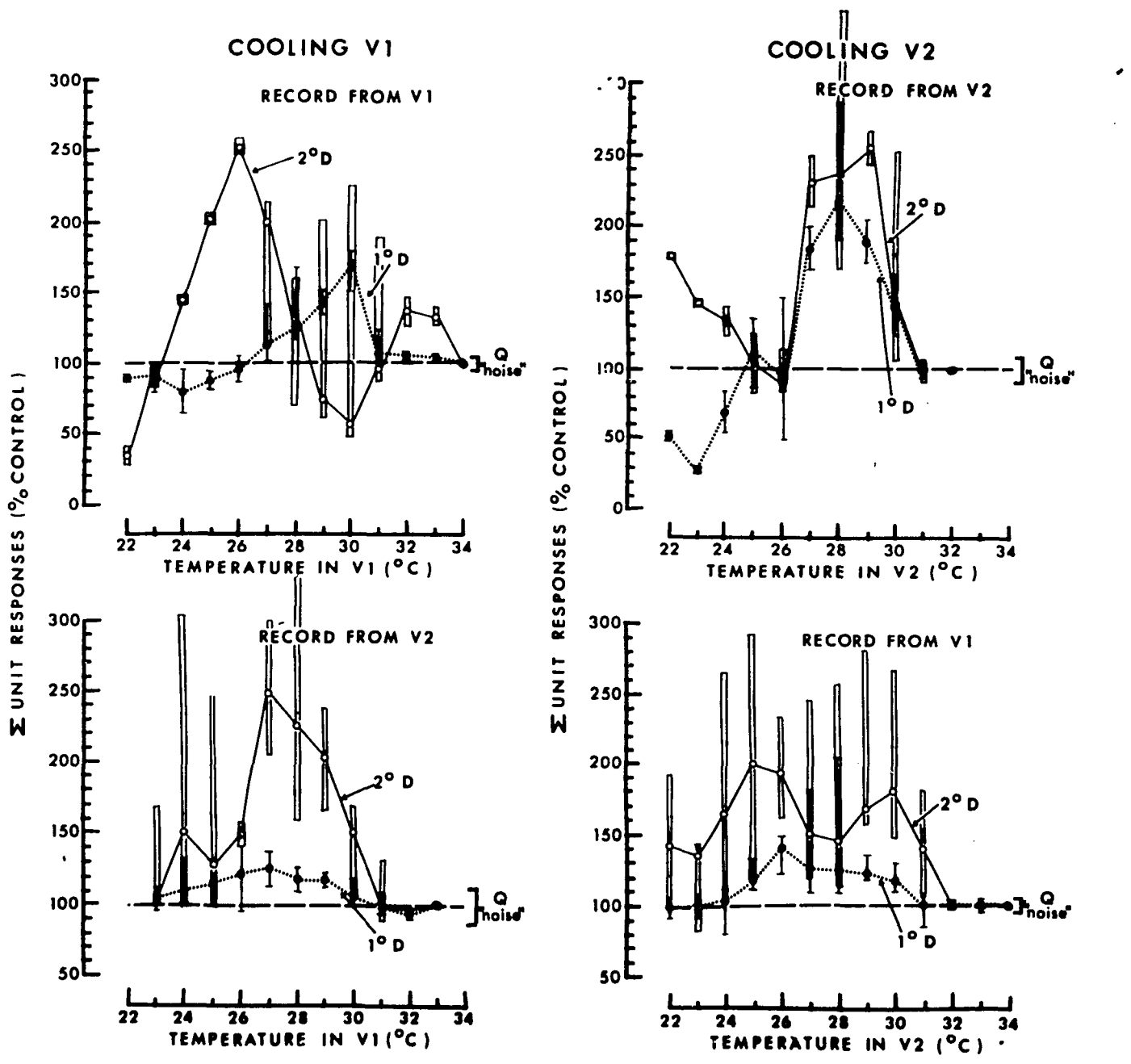


Fig. 9 Group Data: Effects of cortical cooling on the primary (1^o) and secondary (2^o) unit discharge (D) elicited by LGB shock. Median values of relative summated unit responses are given by the solid circles for the 1^o and the open circles for the 2^o. The interquartile range is given by the vertical lines for the 1^o and the vertical bars for the 2^o.

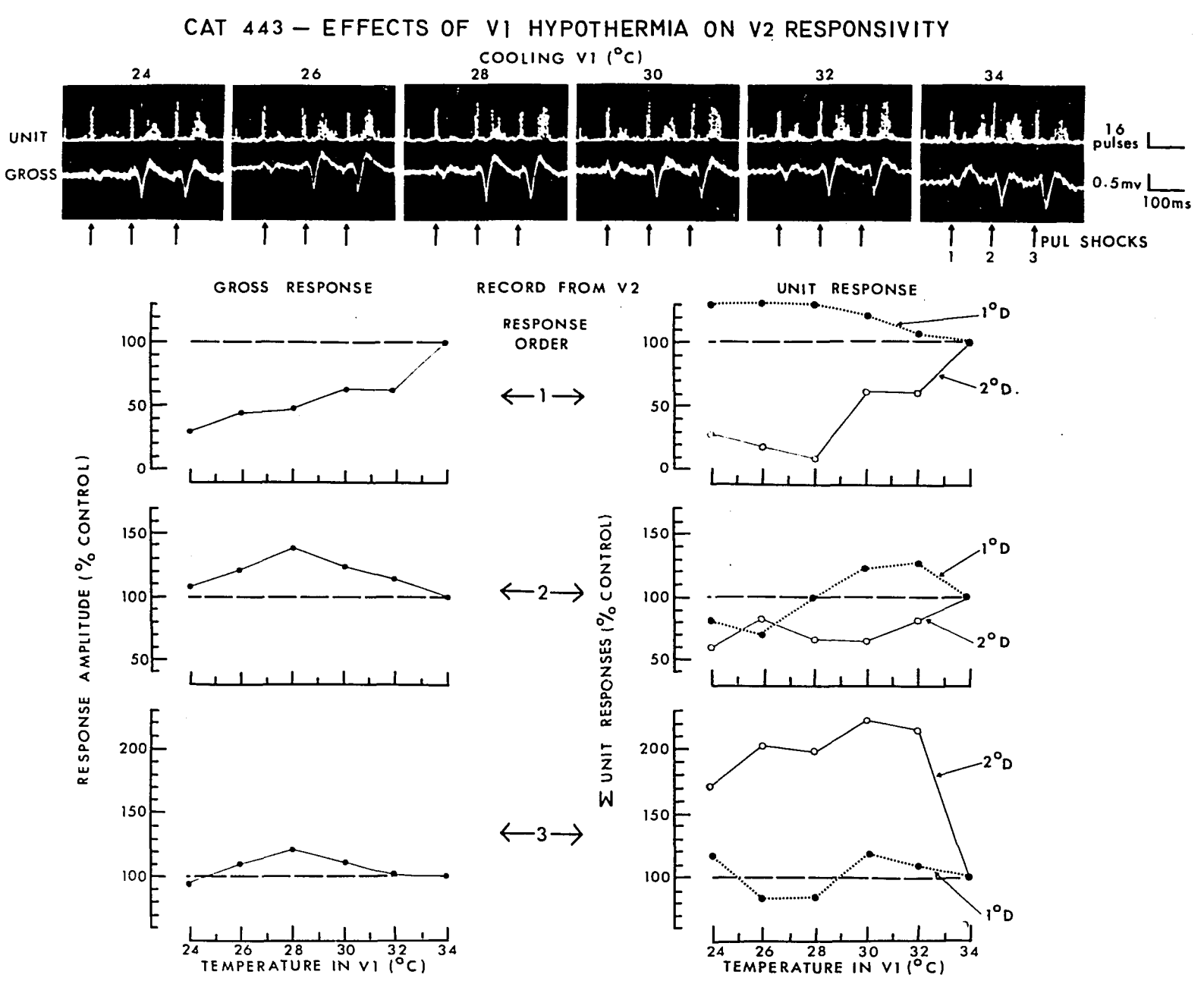

EFFECTS OF HYPOTHERMIA ON 1° AND 2° UNIT DISCHARGE (D) (N=18)
COOLING V1
RECORD FROM V1
2°D
1°D
Q noise
Σ UNIT RESPONSES (% CONTROL)
TEMPERATURE IN V1 (°C)
RECORD FROM V2
TEMPERATURE IN V1 (°C)
COOLING V2
RECORD FROM V2
TEMPERATURE IN V2 (°C)
RECORD FROM V1
TEMPERATURE IN V2 (°C)

of cooling (V1 or V2) and recording (V1 or V2) investigated. A maximal enhancement of unit responses in the range of 25 - 29°C for both the primary and secondary discharge was obtained, the enhancement of the secondary discharge being the greater. In most cases, there was a decline in unit discharge from the maximum below 25°C, but a rise was seen in V2 cortex, upon cooling V2 at low temperatures.

(3) Gross Evoked Response to Pulvinar Shock In both V1 and V2 cortex the responses from a given macroelectrode to a train of three pulvinar shocks (each separated by 100 msec) were typically biphasic waveforms, (although occasionally triphasic responses were seen), with the positive phase leading. These responses occurred 5 msec after shock onset and lasted for about 40 msec. The responses to the second and third pulvinar shocks were always augmented. The effects of cooling either V1 or V2 on this response pattern were investigated in a total of nine cats.

(a) Effects of cooling V1 The results in Fig 10 obtained for cat 443 are illustrative of the findings. As shown by the lower oscilloscope tracings at the top of the figure, cooling V1 produced a gradual reduction in amplitude of the first response, and an increase in the relative amplitude of the second and third responses in V2 cortex. The left set of graphs at the bottom of Fig 10 present response amplitude (in per cent of control at 34°C) versus temperature. These plots show that the relative amplitude of response 1 continually declined as temperature was decreased. Responses

Fig. 10 Effects of cooling V1 cortex on the pulvinar shock evoked potential recorded at both the gross and unit level from V2 cortex for cat 443. Histogram (top trace) bin width is 5 msec.


CAT 443 — EFFECTS OF V1 HYPOTHERMIA ON V2 RESPONSIVITY
COOLING V1 (°C)
24
26
28
30
32
34
UNIT
GROSS
16 pulses
0.5mv
100ms
1
2
3
PUL SHOCKS
GROSS RESPONSE
RECORD FROM V2
UNIT RESPONSE
RESPONSE ORDER
←1→
←2→
←3→
1°D
2°D
RESPONSE AMPLITUDE (% CONTROL)
Σ UNIT RESPONSES (% CONTROL)
TEMPERATURE IN V1 (°C)

2 and 3, in contrast, showed a slight enhancement effect at about 28°C, and then declined to control level.

(b) Effects of cooling V2 Fig 11 illustrates the effects produced by cooling V2 on the responses elicited in V1 cortex by a train of three pulvinar shocks, again for cat 443. The bottom oscilloscope tracings at the top of the figure show that the amplitude of the responses was much reduced compared with the amplitude of the responses in V2 cortex. Graphs at bottom show that responses 1 and 3 generally declined while response 2 showed a minimal enhancement in the range of 26 - 32°C. Below 24°C all responses declined markedly.

(c) Group data on the effects of cooling V1 Group results are given graphically for the effects of cooling V1 cortex (N=8) in Fig 12. The graphs present median response amplitude (per cent of control) plotted against temperature; the length of the vertical lines representing the value of the interquartile range. The graphs at the left present the relative amplitude of responses 1, 2 and 3 (top to bottom) as recorded in V2 cortex. These results show no reliable change of relative amplitude in responses 1 and 3, but for response 2 there is some slight enhancement, maximal in the range 25 - 28°C. Graphs at the right show that in V1 cortex, no effect was produced in response 3 but a questionable enhancement occurred to response 2 and a more definite enhancement effect occurred for response 1 at low temperature (22°C). However, the absolute magnitude of

Fig. 11 Effects of cooling V2 cortex on the pulvinar shock evoked potential recorded at both the gross and unit level from V1 cortex for cat 443. Histogram (top trace) bin width is 5 msec.

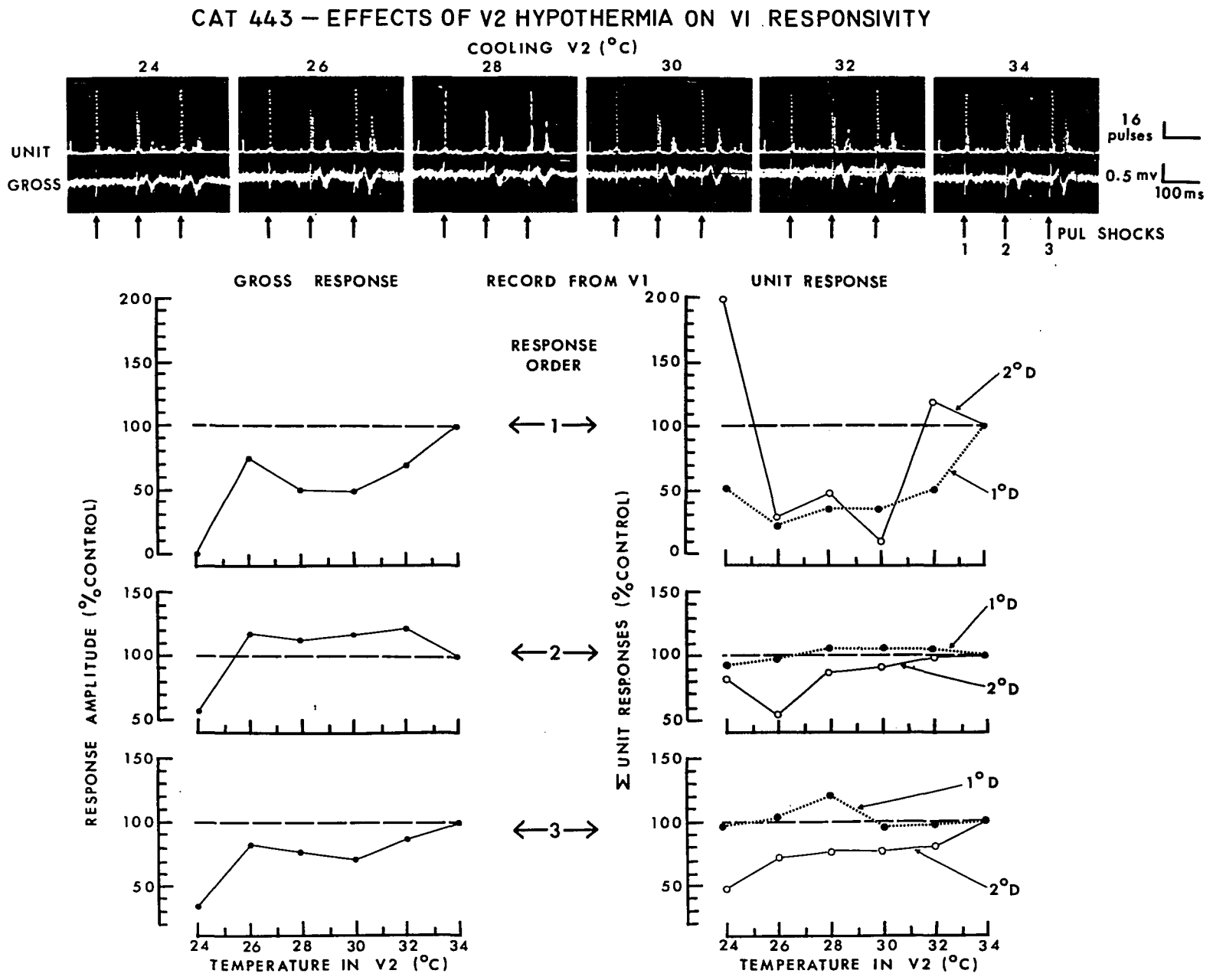
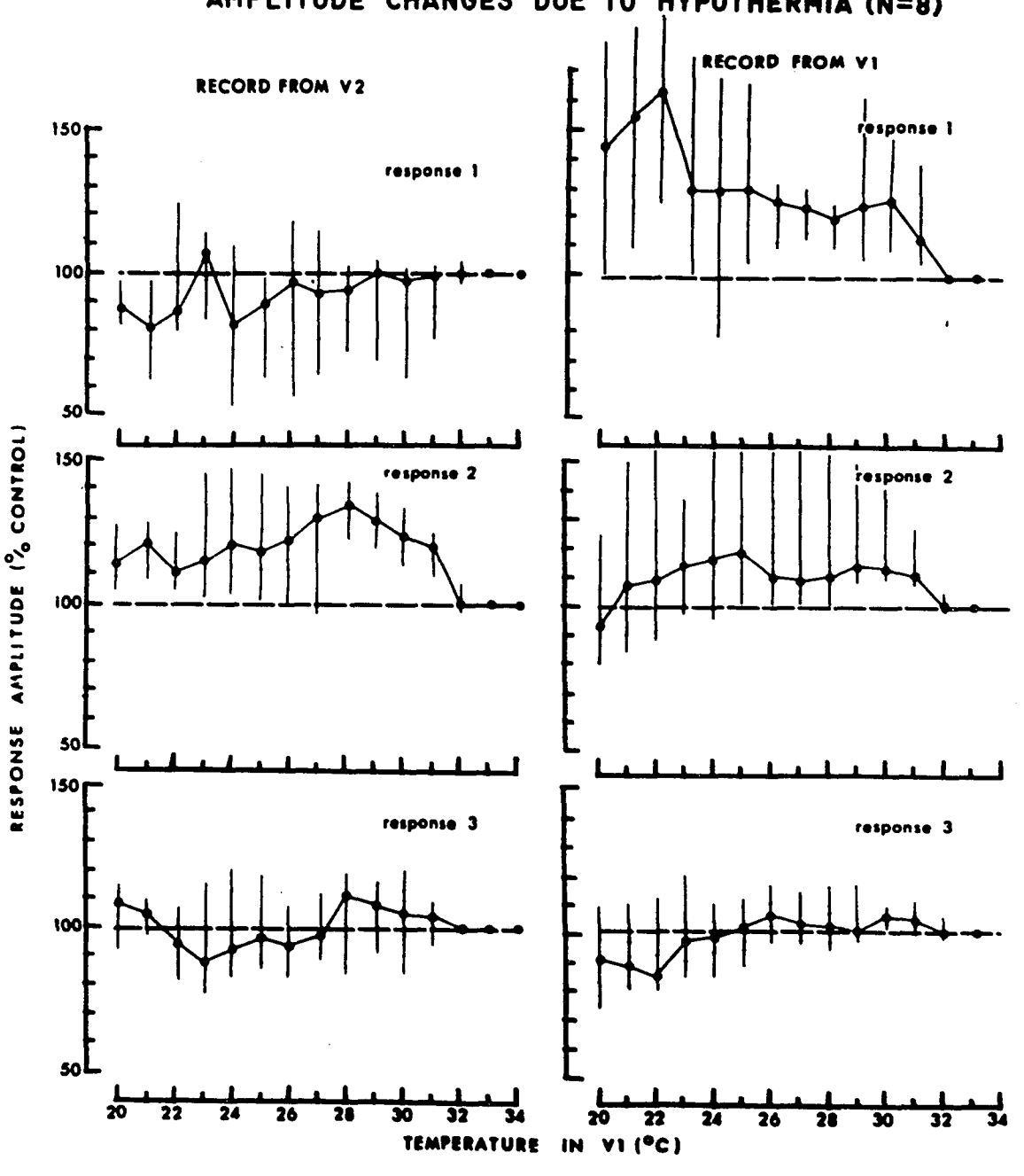

CAT 443 — EFFECTS OF V2 HYPOTHERMIA ON V1 RESPONSIVITY
COOLING V2 (°C)
24
26
28
30
32
34
UNIT
GROSS
16 pulses
0.5 mv
100 ms
1
2
3
PUL SHOCKS
GROSS RESPONSE
RECORD FROM V1
UNIT RESPONSE
RESPONSE ORDER
←1→
←2→
←3→
2°D
1°D
RESPONSE AMPLITUDE (%CONTROL)
Σ UNIT RESPONSES (%CONTROL)
200
150
100
50
0
TEMPERATURE IN V2 (°C)

Fig. 12 Group Data: Relative amplitude changes of the evoked responses (responses 1. 2 and 3) to a train of three pulvinar shocks, due to cooling of V1 cortex. Solid circles indicate median values and vertical lines the interquartile range.


AMPLITUDE CHANGES DUE TO HYPOTHERMIA (N=8)
RECORD FROM V2
RECORD FROM V1
response 1
response 2
response 3
RESPONSE AMPLITUDE (% CONTROL)
150
100
50
20
22
24
26
28
30
32
34
TEMPERATURE IN V1 (°C)

these low level responses was so small as to make any measurement of changes inaccurate and therefore the percentage plots are unreliable.

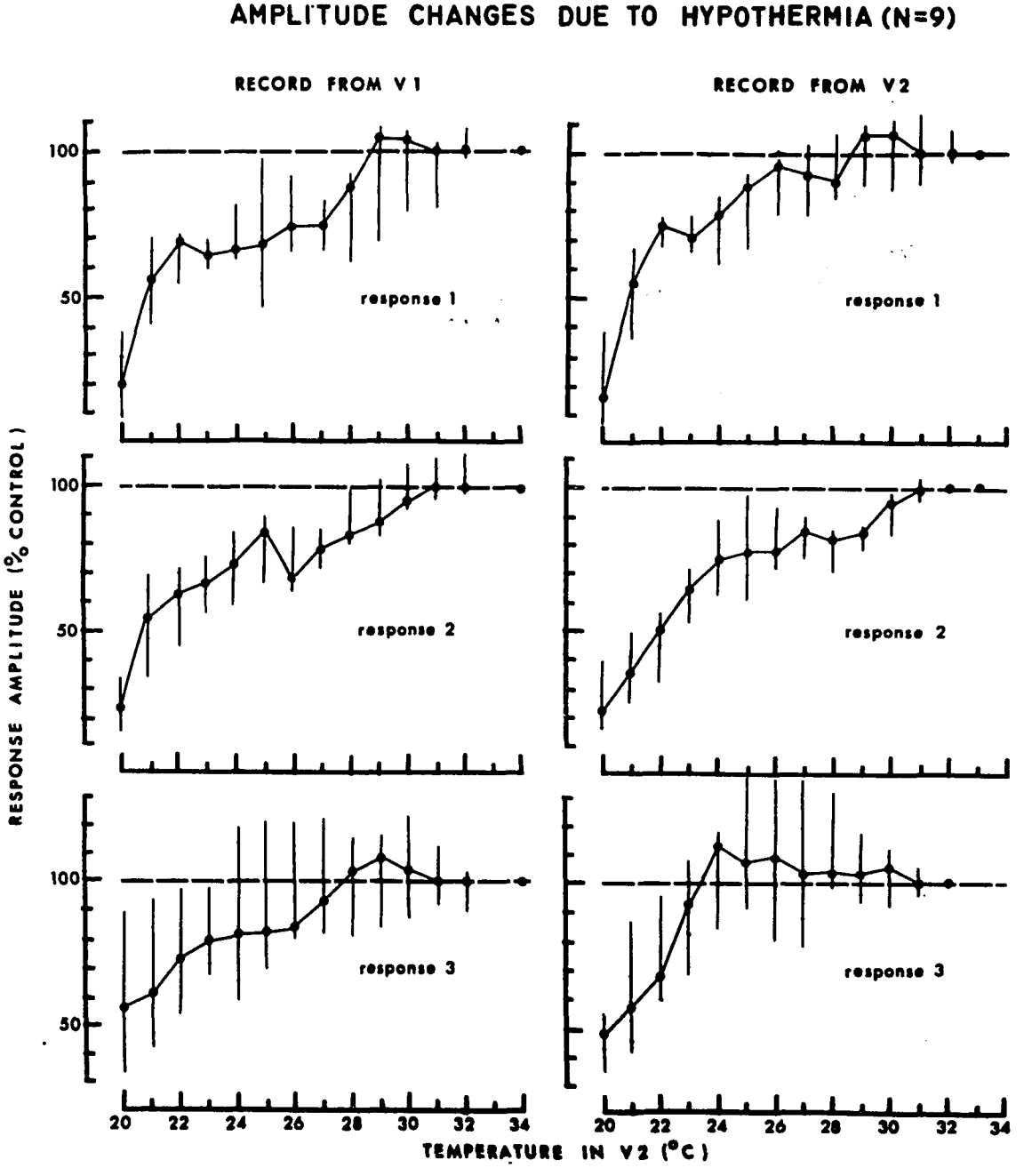
(d) Group data on the effects of cooling V2

Group results for cooling V2 cortex (N=9) are given in Fig 13. Graphs on the left present median relative amplitude of responses 1, 2 and 3 (top to bottom) as recorded in adjacent V1 cortex versus temperature. These results show, in contrast to cooling V1, a consistent general decline in relative amplitude with small maxima at 29°C for responses 1 and 3 and at 25°C for response 2 (in this case the maximum was below the control level). The graphs at the right present median relative amplitudes recorded locally in V2 cortex and again show a general decline with small maxima. The maximum for response 1 was at 30°C, for response 2 at 27°C (below control level) and for response 3 at 24°C.

(4) Incidental Observations

(a) Unit response to pulvinar shock The pattern of unit discharge in either V1 or V2 cortex to each of three pulvinar shocks can be described for each of the responses as two bursts of unit activity. A primary discharge 5 msec in duration occurs during the initiation of the positive going phase of the gross evoked potential, about 5 msec after shock onset. Following this there is a variable period of suppression (decreased unit discharge) of variable duration lasting from 10 to 30 msec and correlated with the peak positive deflection of the gross evoked potential. A secondary

Fig. 13 Group Data: Relative amplitude changes of the evoked responses (response 1, 2, and 3) in V1 and V2 cortex, to three pulvinar shocks, due to cooling V2. Solid circles indicate median values and vertical lines, the interquartile range.


AMPLITUDE CHANGES DUE TO HYPOTHERMIA (N=9)
RECORD FROM V1
RECORD FROM V2
response 1
response 2
response 3
RESPONSE AMPLITUDE (% CONTROL)
100
50
20
22
24
26
28
30
32
34
TEMPERATURE IN V2 (°C)

discharge of relatively high intensity and lasting 30 to 50 msec follows the period of suppression. This secondary discharge is correlated with the peak of the negative going phase of the gross evoked potential (see oscilloscope tracings at the top of Fig 10 or 11).

Only two units were held in the two preparations used during the investigation of the effects of cooling V1 cortex on the unit responses to a train of three pulvinar shocks in V2 cortex. The time latency histograms in the top trace of Fig 10 illustrate for cat 443 the results of cooling V1 cortex. The graphs on the right side of Fig 10 present quantified data where the areas of the primary and secondary discharges less the level of spontaneous activity are plotted (as per cent change from the control level at normal temperature) against temperature. The effect on the primary discharge for response 1 showed little consistent change, while responses 2 and 3 exhibited questionable enhancement and reduction effects respectively in their unit activity. In contrast, the secondary discharge showed a precipitous and marked decline in unit activity for responses 1 and 2 while response 3 showed a marked enhancement effect, maximum in the range 28 - 32^{o}C.

In an additional two units for the same two animals the effects of cooling V2 cortex on unit activity in V1 cortex were examined. Fig 11 provides illustrative data again for cat 443 in terms of time latency histograms. The graphs at the right show that the primary discharge had no

enhancement in unit activity for response 2, a questionable amount for response 3 and a decline for response 1. The secondary discharge exhibits a general decline in all responses with the exception of response 1 at low temperature (24°C) where a marked enhancement occurs. The apparent variability of the secondary discharge of response 1 may be the result of the small absolute magnitude of the changes of area in the histogram produced by this discharge; this would have the effect of making percentage plots unreliable.

In general, the small number of observations precludes any generalization, and hence no group data could be presented. On the other hand, the consistent decline in all responses in V1 cortex upon cooling the adjacent V2 cortex is well illustrated in the gross electrode group data (see Fig 13, left). This effect, however, is not clearly paralleled by the unit data mentioned above. The results from two additional units in another preparation (cat 444) were also parametrically tested and again gave results essentially the same as those shown in the graphs above (Figs 12 and 13).

(b) Effects of a lesion placed along the boundary of V1 and V2 cortex No change in the enhancement effect of the response in either V1 or V2 cortex to LGB shock upon cooling V2 or V1 cortex respectively, was obtained after a subpial aspiration of the gray matter only, along the boundary between V1 and V2 cortex. Two preparations were used, in one case the aspirated cortex was replaced by an insulating plastic tube. Further deeper subpial aspiration

to include the white matter caused excessive bleeding, and a loss of the LGB shock evoked response in both cortices, thus precluding any significant test for temperature effects.

DISCUSSION

The results of the present study show that cooling either V1 or V2 cortex produced enhancement of gross and unit responsivity to LGB shock recorded locally (in the area being cooled), and also in the adjacent cortex even though this cortex was maintained at basal temperature (32 - 34°C). These enhancement effects were either the same or greater in the cortex adjacent to the area being cooled, were maximal in the range 25 - 29°C, and survived subpial resection of a strip of gray matter along the boundary between V1 and V2 cortex, even when insulating material was inserted in place of aspirated cortex. In contrast, the gross evoked response to pulvinar shock recorded in V1 or V2 upon cooling V2 showed, after a small initial rise, a continuous decline, while cooling V1 produced a slight enhancement, with little evidence of decline at lower temperatures.

The amplitude changes in the LGB gross evoked potential can be attributed mainly to intracortical activity because it was the later cortical components (Denney et al, 1968) that were primarily affected by cooling. Further, at the unit level the longer latency secondary discharge, which is indicative of purely cortical activity, was increased by cortical cooling more than the short latency primary discharge.

The above findings in which cooling cortex, either V1 or V2, produced a change in cortical responsivity to LGB shock in adjacent V2 or V1 respectively are consistent with the

known projections of LGB to V1 and V2 cortex (Burrows and Hayhow, 1971). The author has found no electrophysiological studies showing an interaction between V1 and V2 cortex in the cat although anatomical studies (Wilson, 1968; Garey, Jones and Powell, 1968; Kawamura, 1973) show that reciprocal cortico-cortical connections exist. Since in this study no change in interaction effects was observed when the gray matter along the boundary between V1 and V2 cortex was sectioned and separated by insulating material, the interaction effects are most probably mediated by fibers coursing through the underlying white matter. A U-fiber system entering the white matter and connecting area 17 to area 18 has been described in the squirrel monkey (Tigges, Spatz and Tigges, 1973; see also Cowey, 1971). On the other hand, interaction effects may be mediated in part by cortico-fugal fibers to LGB and fibers back to cortex via the geniculo-cortical pathway. Connections from visual cortex to LGB have been described (Kalil and Chase, 1970; Hollander, 1972).

The cortical response to Pul shock showed a much greater amplitude in V2 cortex than in V1, a result consistent with the anatomical studies of Graybiel (1972), who described projections of Pul to area 18. The finding that cooling V2 cortex produced an effect in V1 whereas cooling V1 cortex apparently produced no consistent effect in V2 indicates that the cortico-cortical projection mediating Pul information is not reciprocal; i.e., information flows in the direction from V2 to V1 cortex only.

The differing results obtained by cooling, on cortical responsitivity to LGB and Pul shock, indicate that there is more than one cortico-cortical system interconnecting V1 cortex and V2.

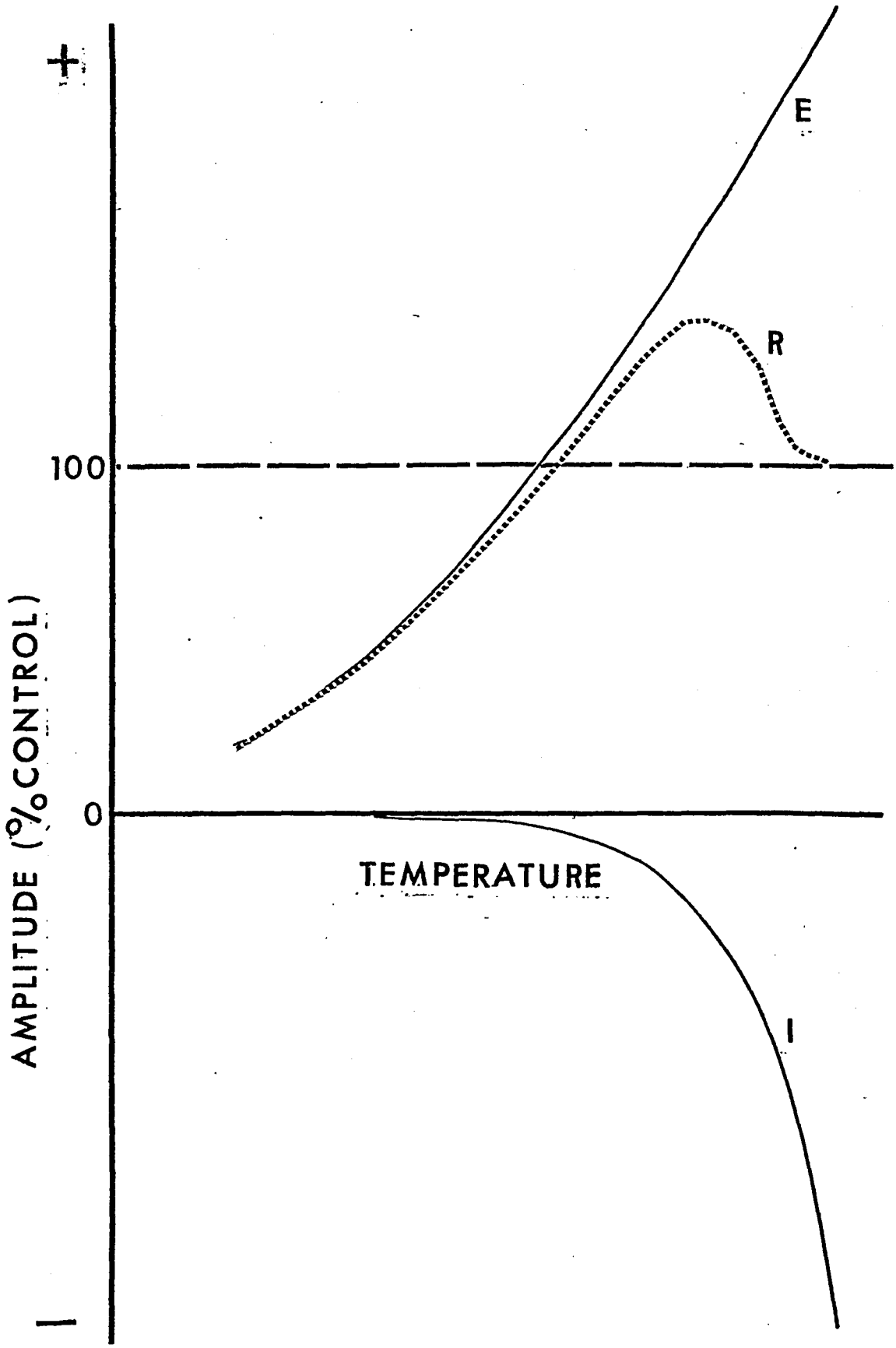
The above interaction effects due to cooling cannot be attributed to a transcortical thermal conduction or to changes in blood circulation within the visual cortex because the temperature of the adjacent area was monitored and maintained at normal levels. Changes in contact resistance between recording electrodes and the cortex due to cooling cannot explain the enhancement produced in adjacent cortex since, again, this was always maintained at normal temperature. Effects on the stimulating electrodes can also be ruled out since Kalil and Chase (1970) have shown that cortical cooling produces no change in the temperature or blood oxygen level in LGB.

An interesting and unexpected finding in this study were the changes observed in cortical responsivity due to local cooling of cortex. Bindman et al (1963) showed that cooling the somatosensory cortex in rats produced an enhancement in the same cortical area of the evoked potential to forepaw stimulation. Peacock et al (1965) reported a transient facilitation of the evoked response in visual cortex to optic tract stimulation upon cooling the same cortical area with a topical application of ethyl chloride. Recently, Reynolds et al (1975a) have shown that cooling the cat's pericruciate cortex to 28°C increased the spontaneous

discharge frequency of pericruciate neurons. These findings are consistent with those of the present study and indicate that local enhancement effects due to cortical cooling may represent a general phenomenon.

One possible mechanism to explain the enhancement produced by cooling could be a suppression of intracortical inhibition resulting in a release-type phenomenon. This "disinhibition" would be superimposed on a general reduction of cortical excitation also produced by cooling. Fig 14 illustrates this hypothetical model in more detail. The diagram shows two components; E, an excitatory component, and I, an inhibitory component both drawn as a function of temperature. It is postulated that the inhibitory component approaches zero amplitude more rapidly than the excitatory component as the temperature is reduced. When these two components are algebraically summated the resultant, R, will show a maximum amplitude. This maximum amplitude would correspond to an enhancement effect due to disinhibition. It is possible that different thalamo-cortical systems may respond to temperature decrements with different peaks of maxima and minima depending on the two temperature constants. Thus, the different results obtained using LGB and pulvinar stimulation with cortical cooling can be explained by one mechanism. Anatomical evidence indicates that many of the neurons in visual cortex are short axon, Golgi type 2 interneurons (category 11 of Szentágothai, 1973) which on the basis of studies of other parts of the nervous system

Fig. 14 Theoretical model to explain enhancement effect due to cortical cooling. Excitatory (E) and inhibitory (I) component curves are drawn as a function of temperature. The resultant (R) represents the algebraic summation of the amplitudes of E and I (R=E-I).


+
E
R
100
0
AMPLITUDE (% CONTROL)
TEMPERATURE
I
—

are thought to be inhibitory in nature (Eccles et al, 1966). Li and Chou (1960) recording intracellularly have shown that suprathreshold electrical stimulation of the cortex results in hyperpolarization of cells. These studies provide evidence that inhibition as well as excitation is operating in cortex.

In the present study cooling V1 or V2 cortex has been shown to produce an enhancement of the cortical response to LGB shock in the adjacent cortex; i.e., at a distance from the site of cooling. If the above explanation of the enhancement phenemenon is correct then the fibers interconnecting V1 and V2 cortex mediating LGB information flow would be largely inhibitory. This would be in agreement with the findings of Toyama, Matsunami, Ohno and Tokashiki (1974) who demonstrated, via intracellular recordings, that multi-synaptic inhibitory pathways existed within the cat visual cortex.

Cooling V2 cortex produced a small initial enhancement of the V1 cortical response to Pul shock followed by a decline in the amplitude of the response. This implies that the fibers connecting V2 cortex with V1, mediating Pul information flow, are largely excitatory.

One way of testing the hypothesis of disinhibition due to cooling would be to map the receptive field of a simple cell in cortex and then cool the cortex in the region of the microelectrode and observe the changes, if any. The size of the receptive field would be expected to increase due to disinhibition of excitatory neurons in a surrounding cortical

zone. Moreover, the use of intracellular methods would show directly the effects of cooling on membrane potentials, i.e., changes in epsp's and ipsp's (see Reynolds et al, 1975b).

The explanation for the specific finding that the maximal enhancement effect due to cooling is obtained in the range between 26 - 28°C may involve more basic mechanisms. Reynolds et al (1975b) found that cortical cooling to 27°C produced maximal enhancement of the action potential, suggesting that changes at the membrane level do underly this effect. A sudden decrease in inhibitory activity at about 28°C as postulated above (see Fig 14), could be the result of one or both of the following: (1) A rapid change in the activity of an enzyme associated with GABA metabolism (for example, an increase in GABA glutamic transaminase, or a decrease in glutamic decarboxylase activities); (2) A phase transition in the membrane (Hogg, personal communication) that affects the rate of Ca^{++} ion diffusion across the membrane.

Earlier studies have used cooling as a means of producing a reversible lesion in order to observe marked changes in behavior (see Introduction). The present findings suggest that behavioral function dependent at least in part upon cortical processes should be altered by a small reduction (5-6°C) in cortical temperature. Furthermore, the cortical contribution to Mach band, CFF and other contrast phenomena could be evaluated under such experimental conditions. This would require implanting a thermal probe in a chronic animal trained to make the appropriate discriminations.

The cryogenic probe used in this study has design features which make it readily adaptable to different types of experiments, such as those described above. The brass tubing used can easily be fashioned to conform to the shape of the cortical surface. The U-shape construction enables electrodes and thermistors to be inserted into the probe and easily positioned over the cortex being cooled, and together with the silver solder plate, is of such a geometry as to provide a uniform temperature along the midline where the electrodes and thermistors are placed.[1]

In both acute and chronic preparation the cryogenic technique offers a new way of looking at cortico- and thalamocortical interactions. It is the author's contention that application of this technique could materially advance our understanding of cerebral function.

1 Modifications in the design of the cryogenic unit to improve accuracy would be the addition of a guard ring to restrict the area being cooled, and a negative feedback system to control temperature. Temperature control would have the advantage of reducing the variability and would also be more convenient to operate.

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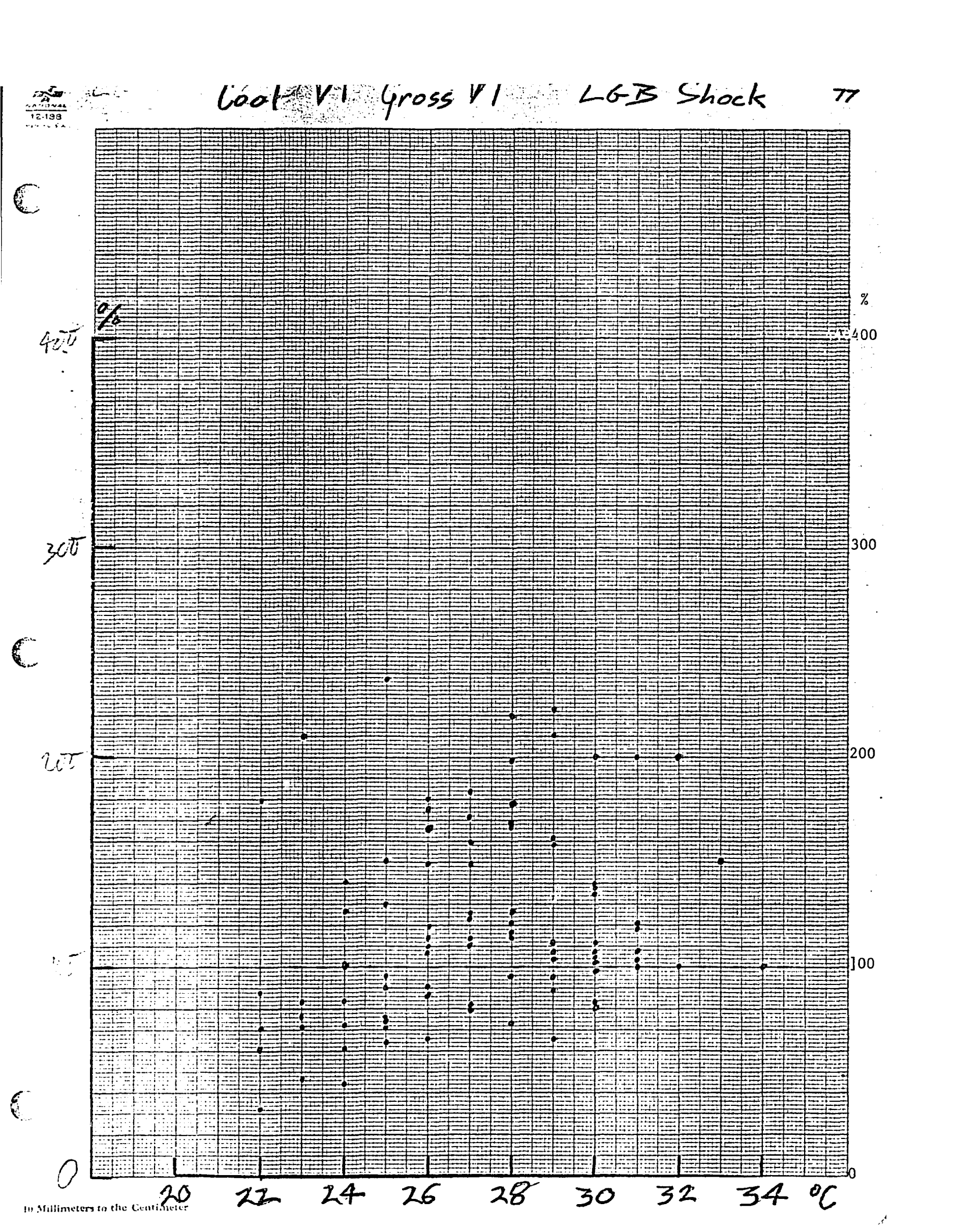
APPENDIX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10 Millimeters to the Centimeter

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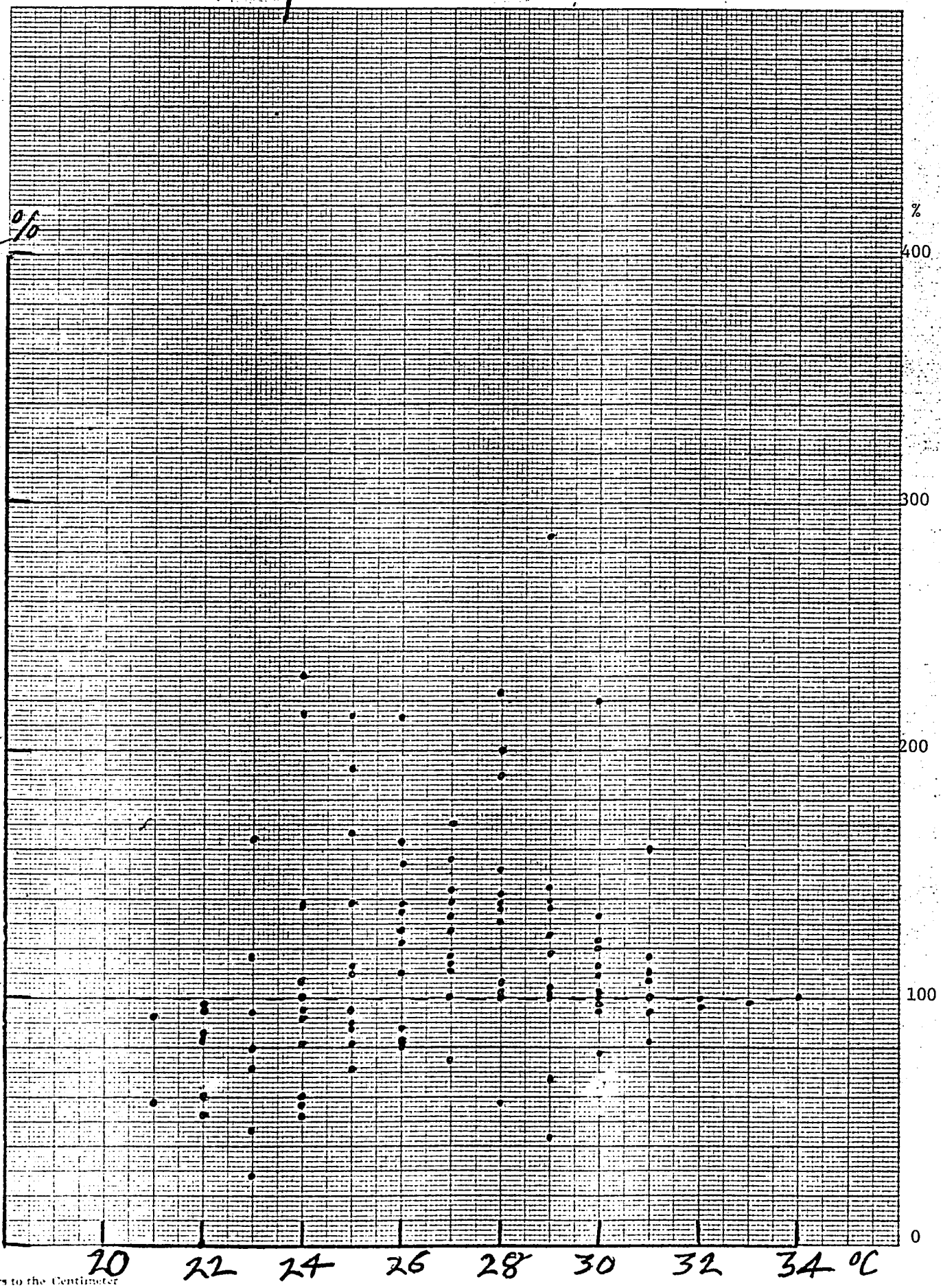

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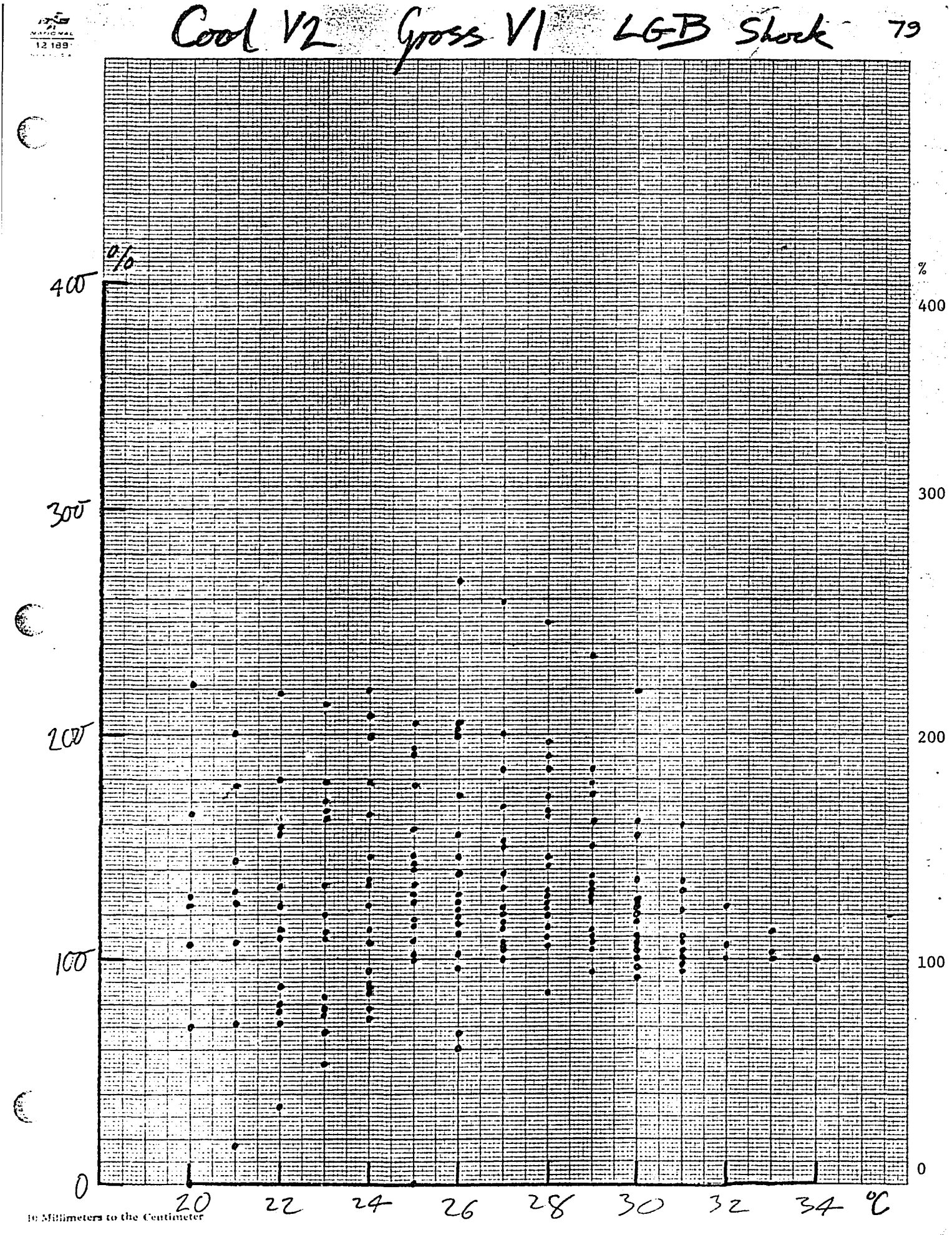
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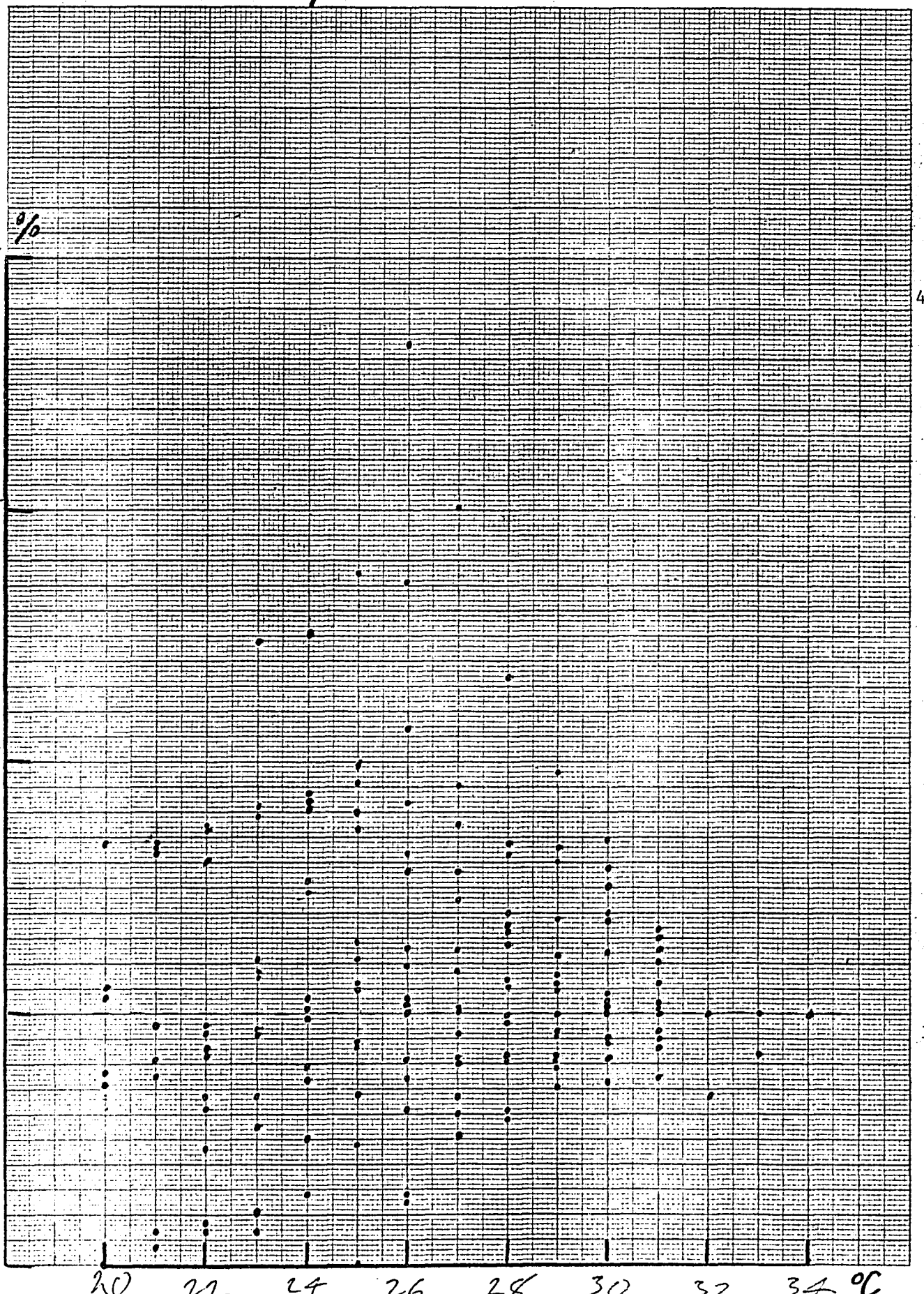

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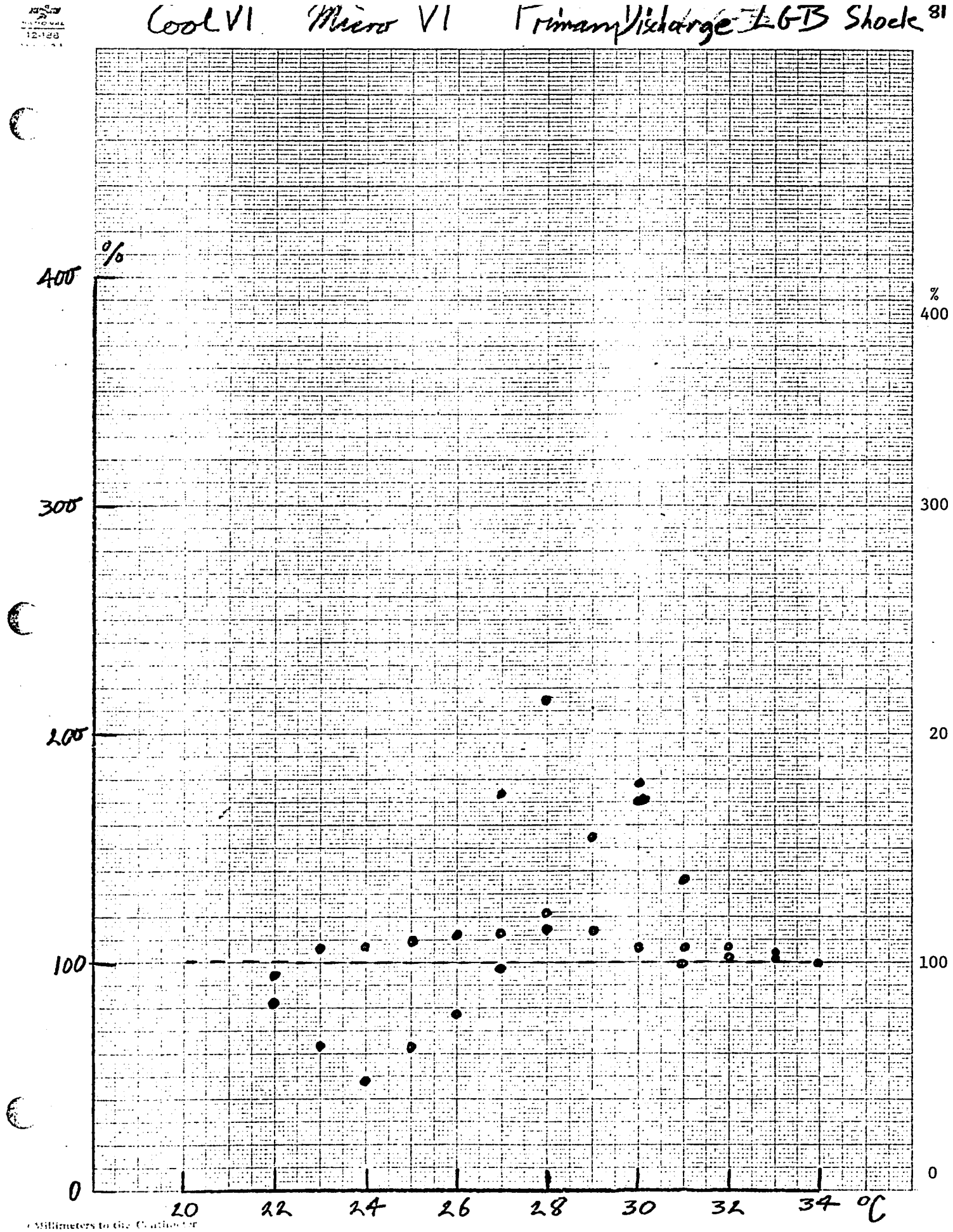
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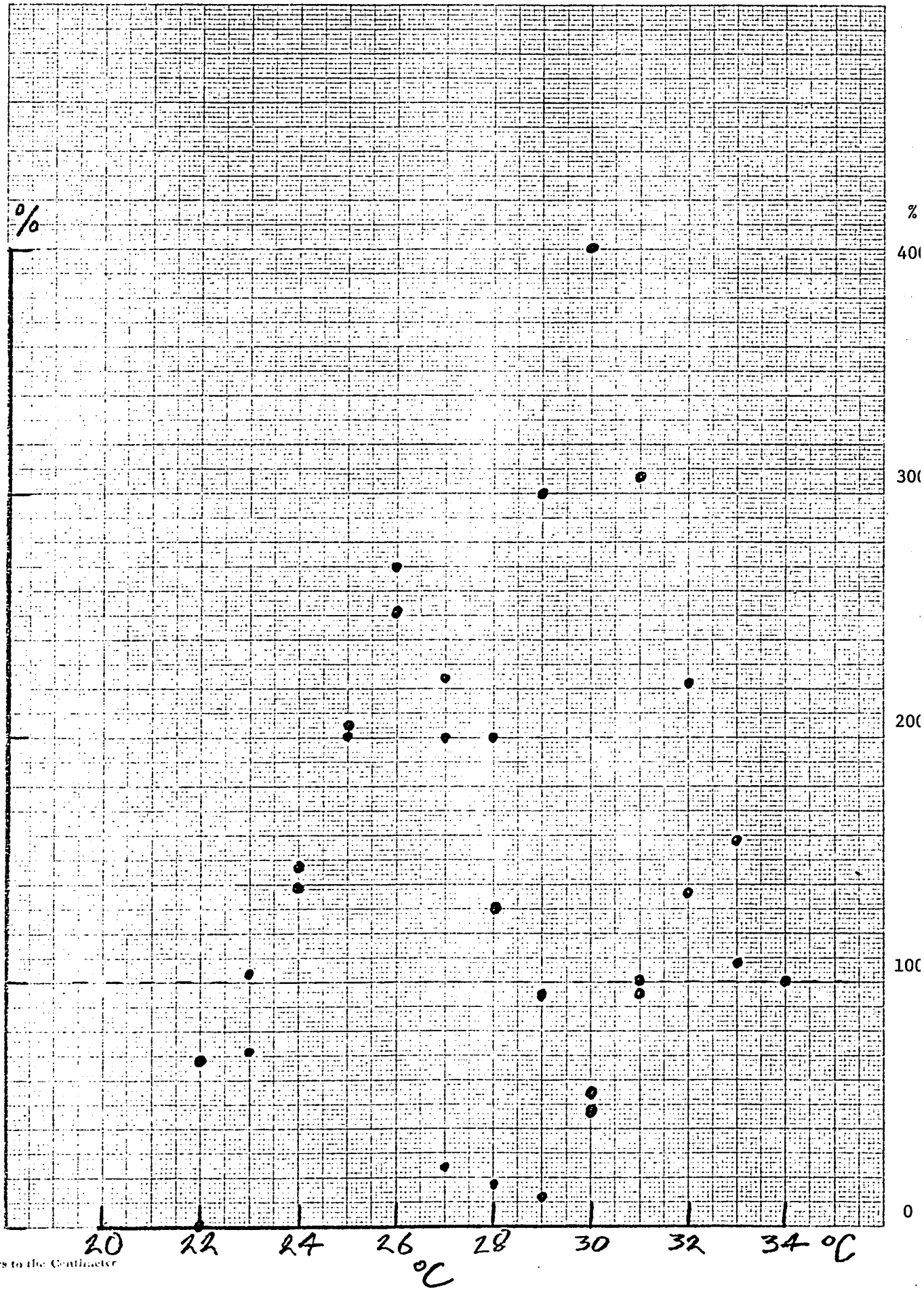

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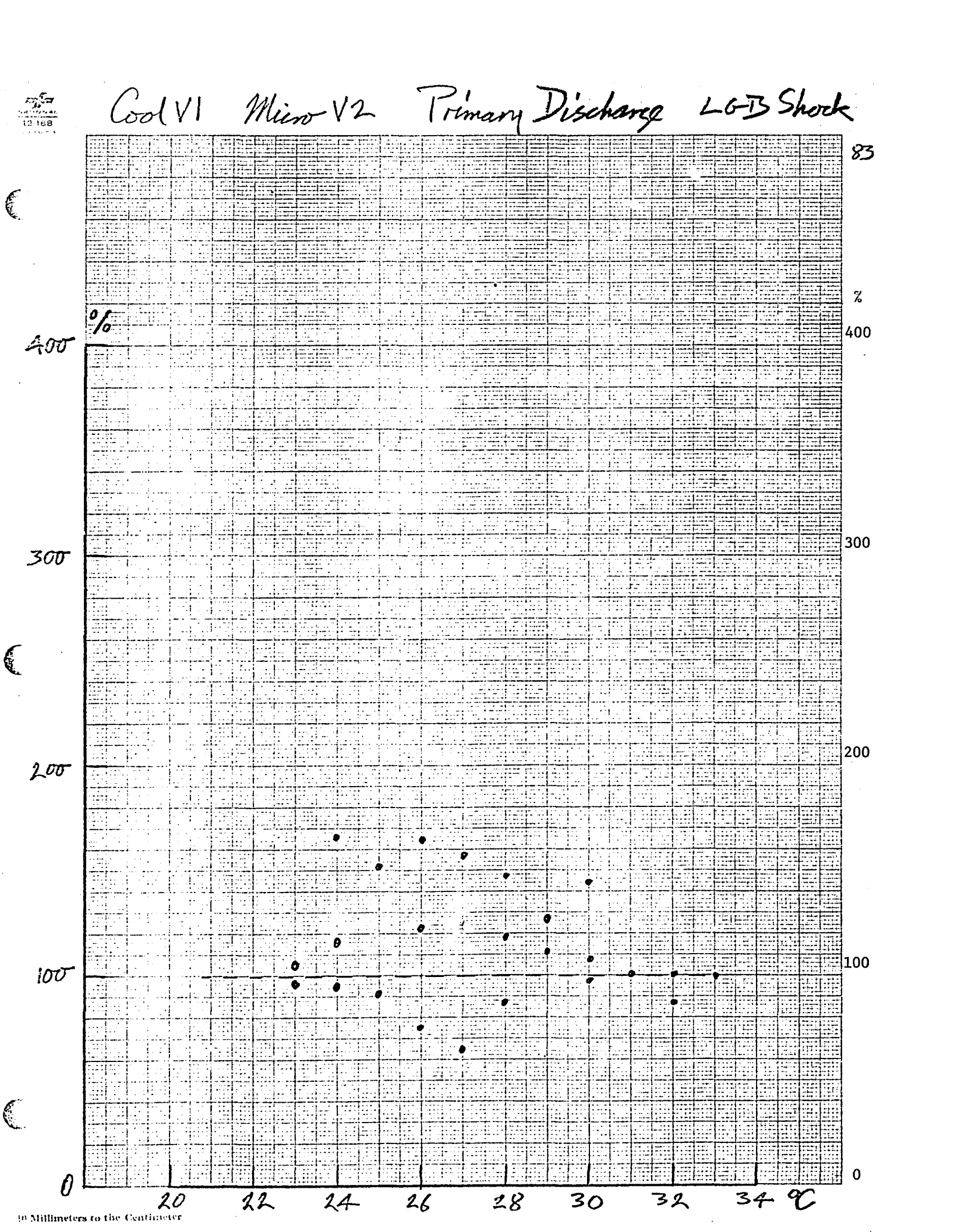
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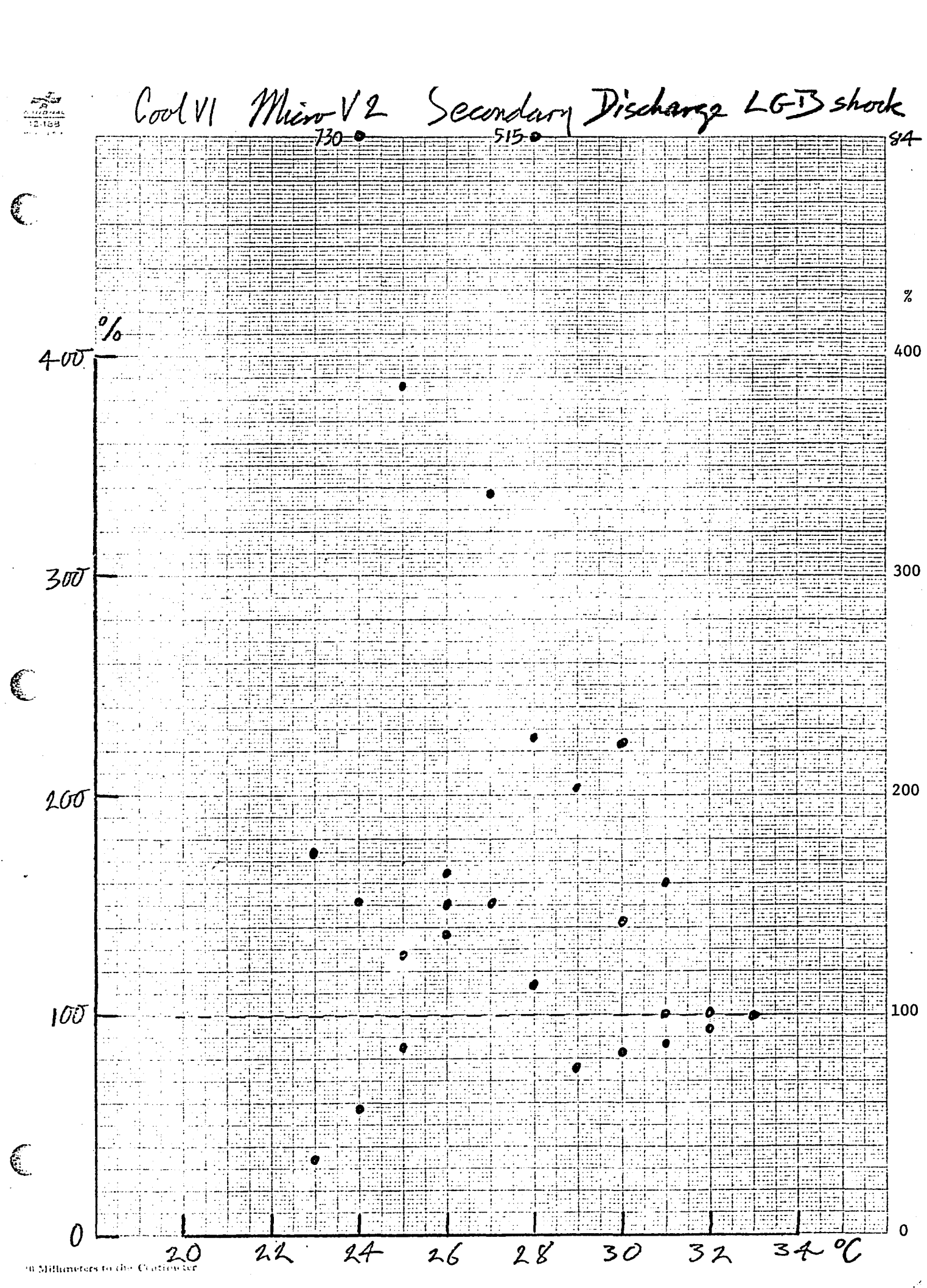
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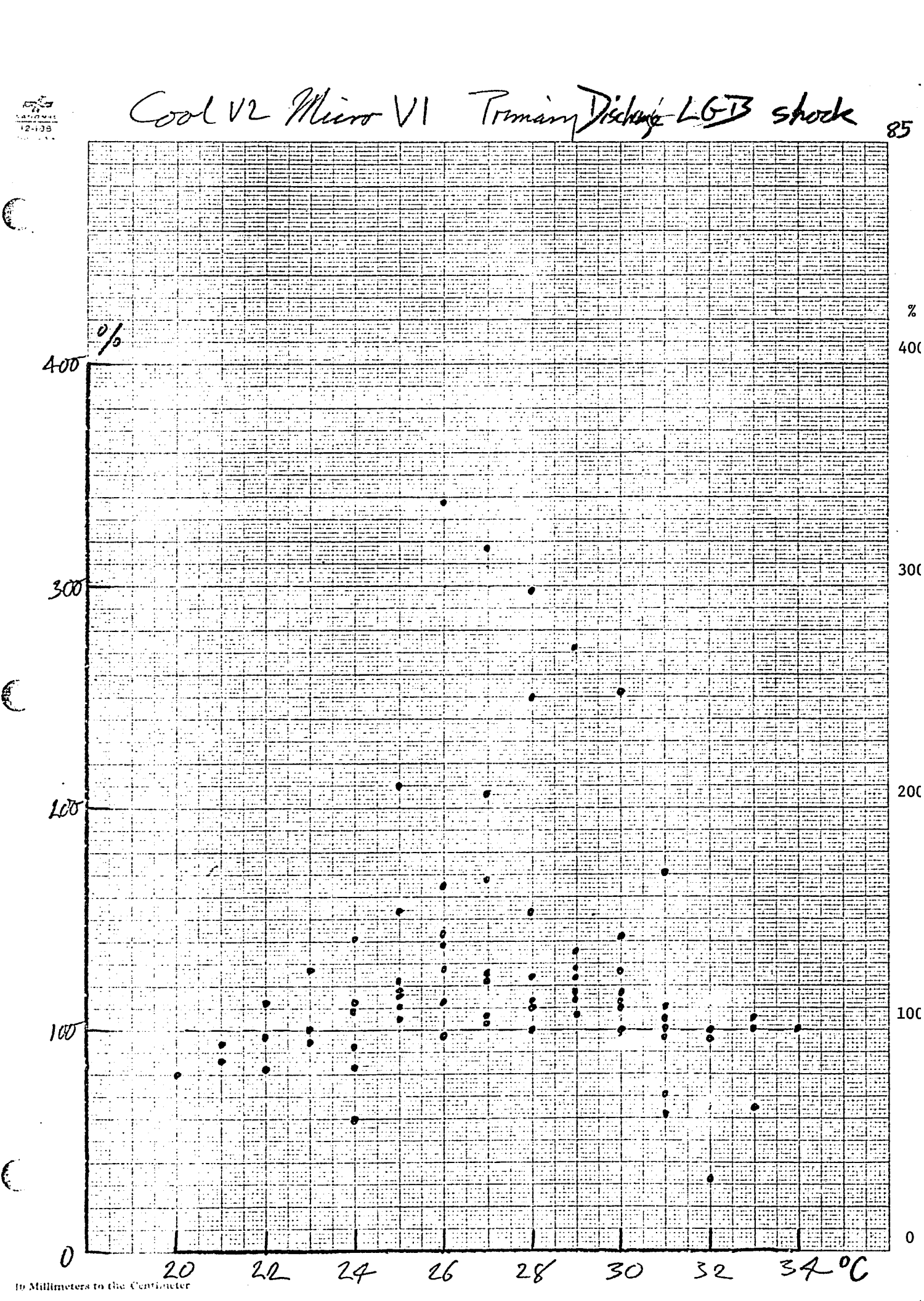
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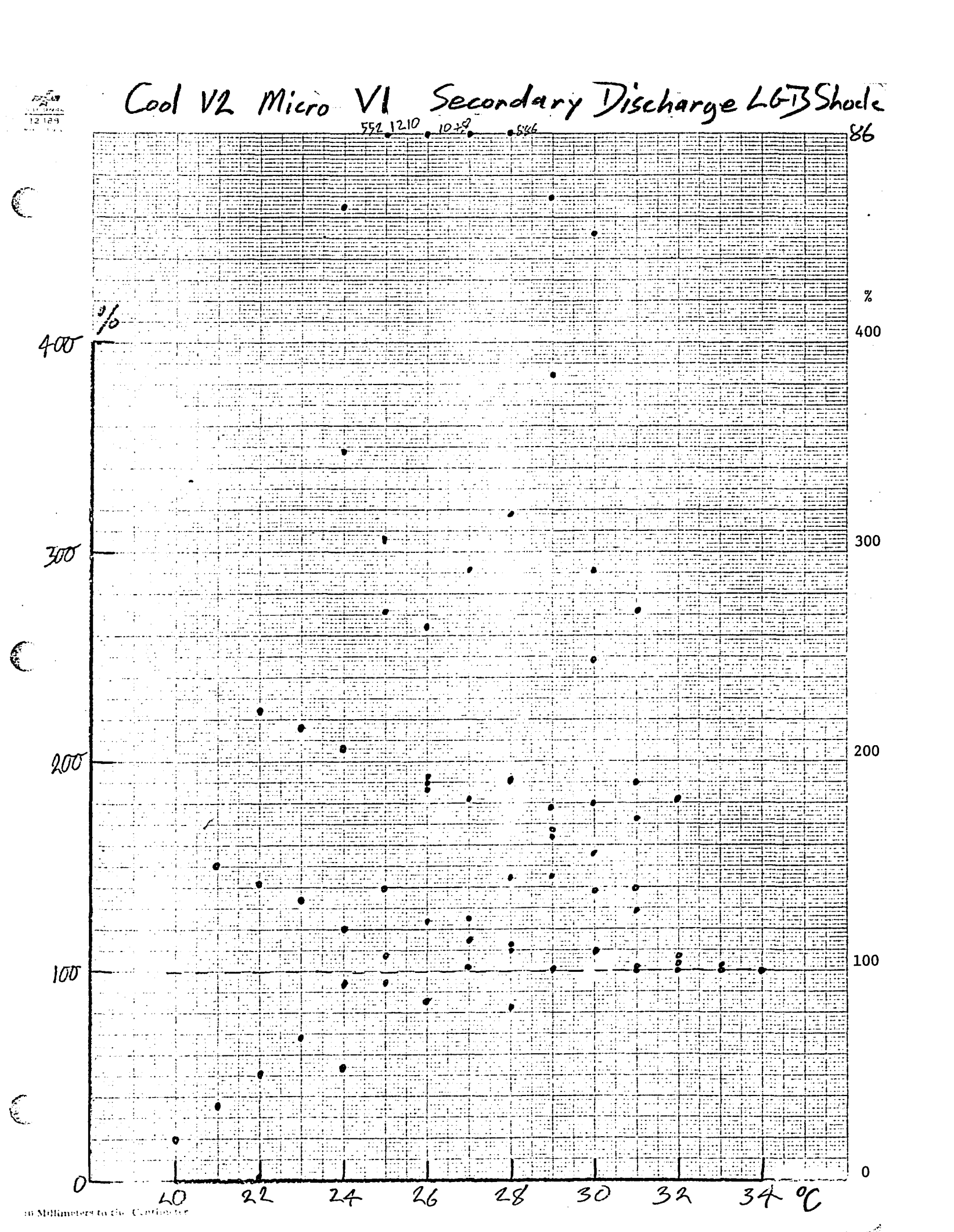
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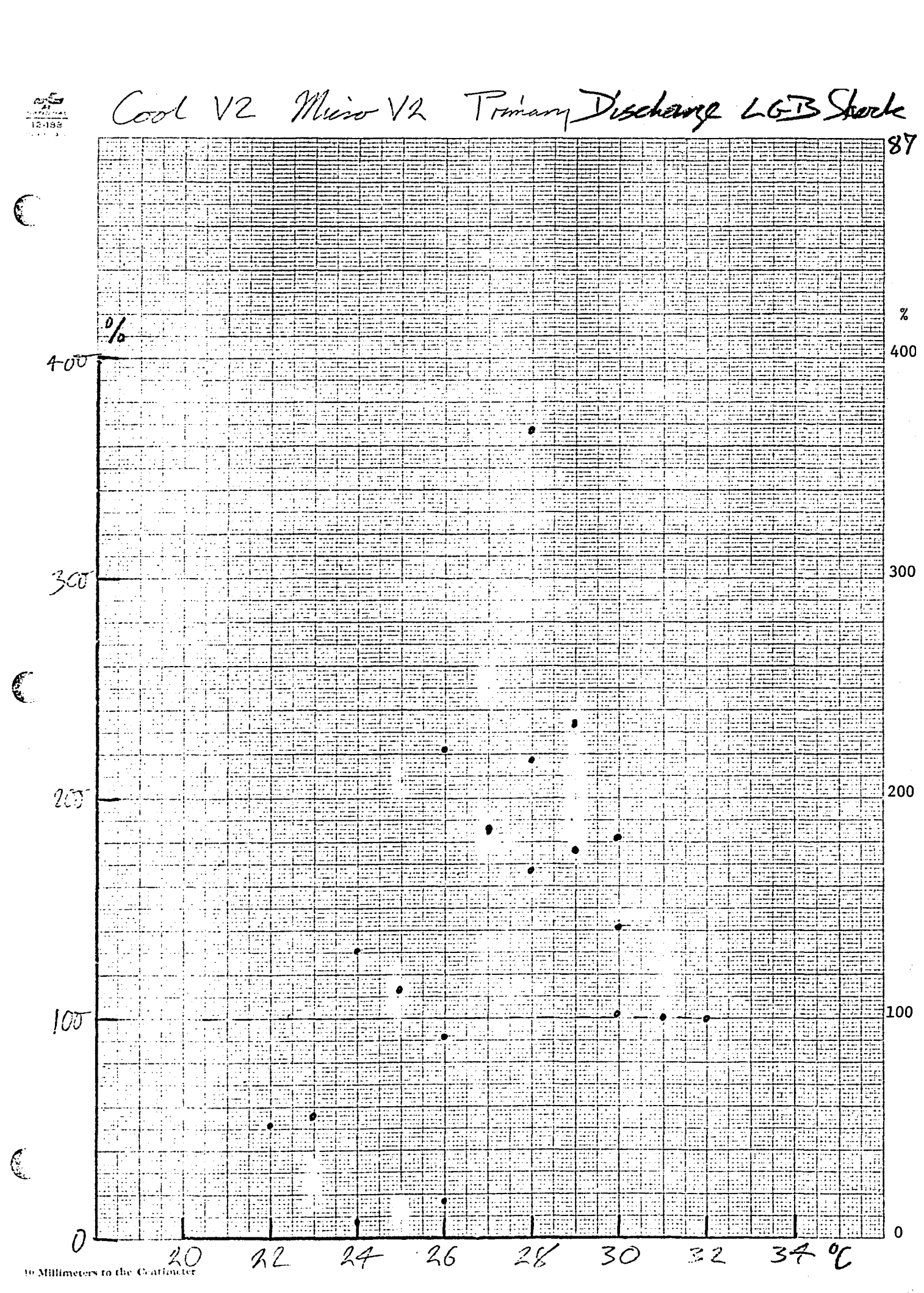
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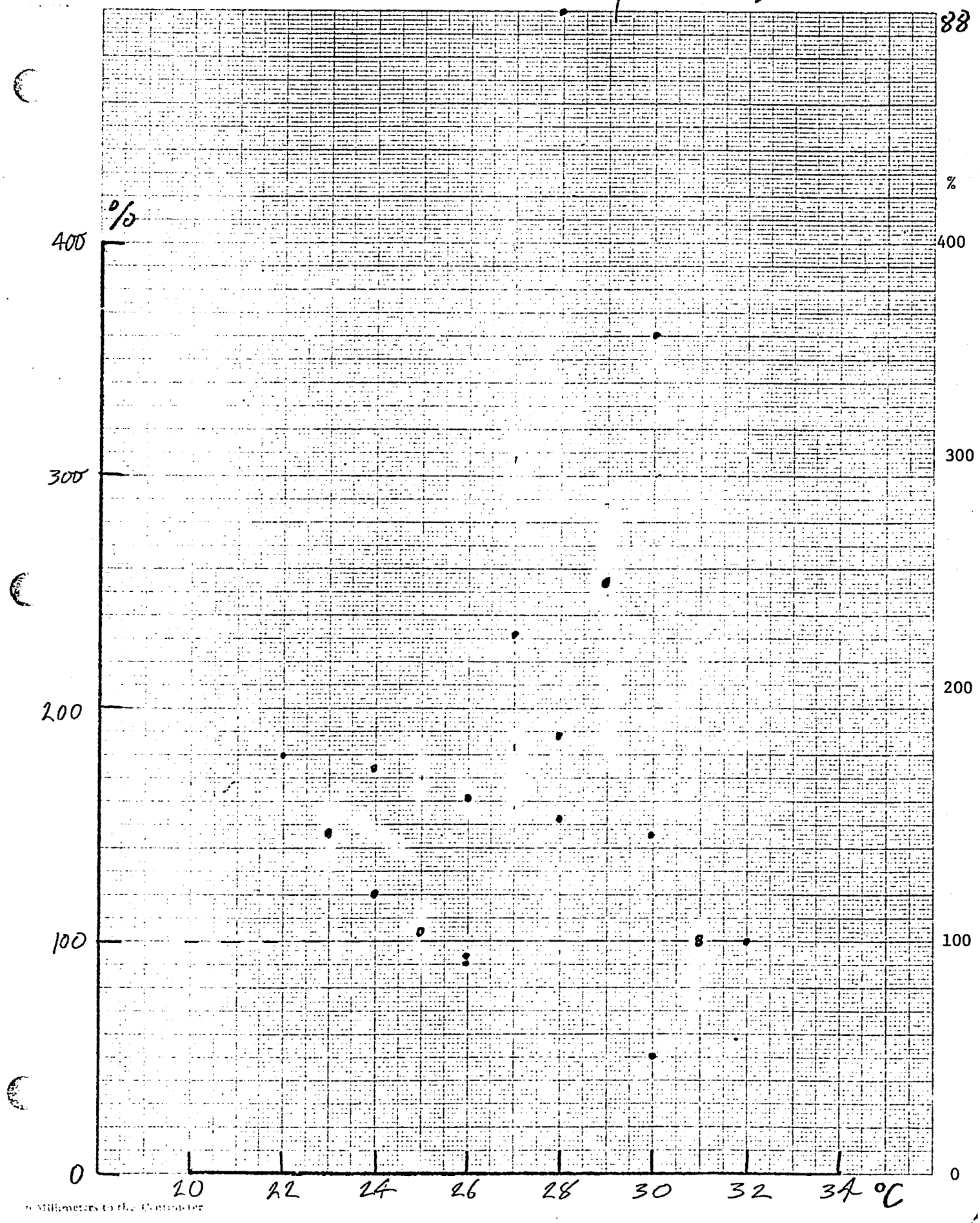

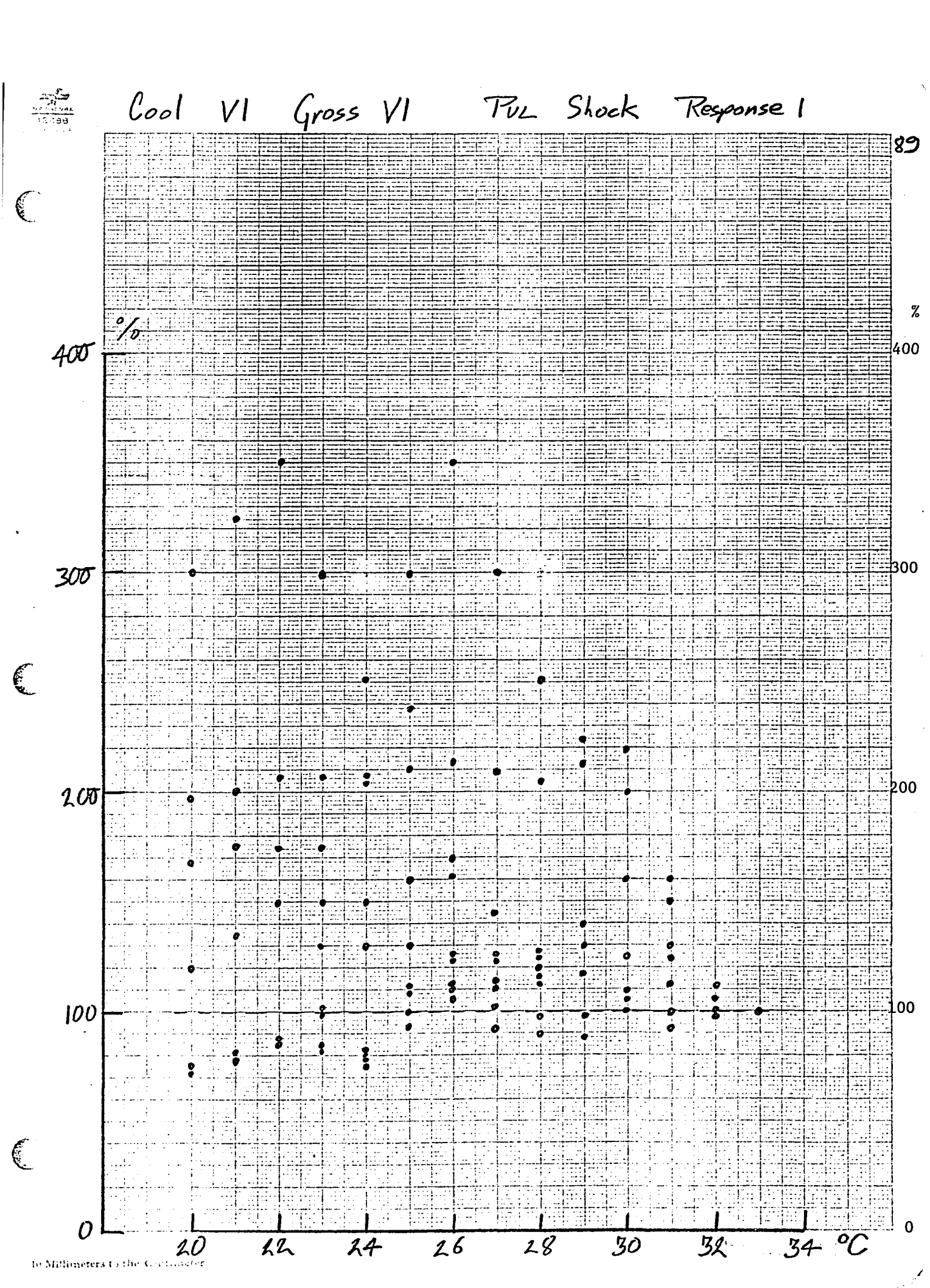
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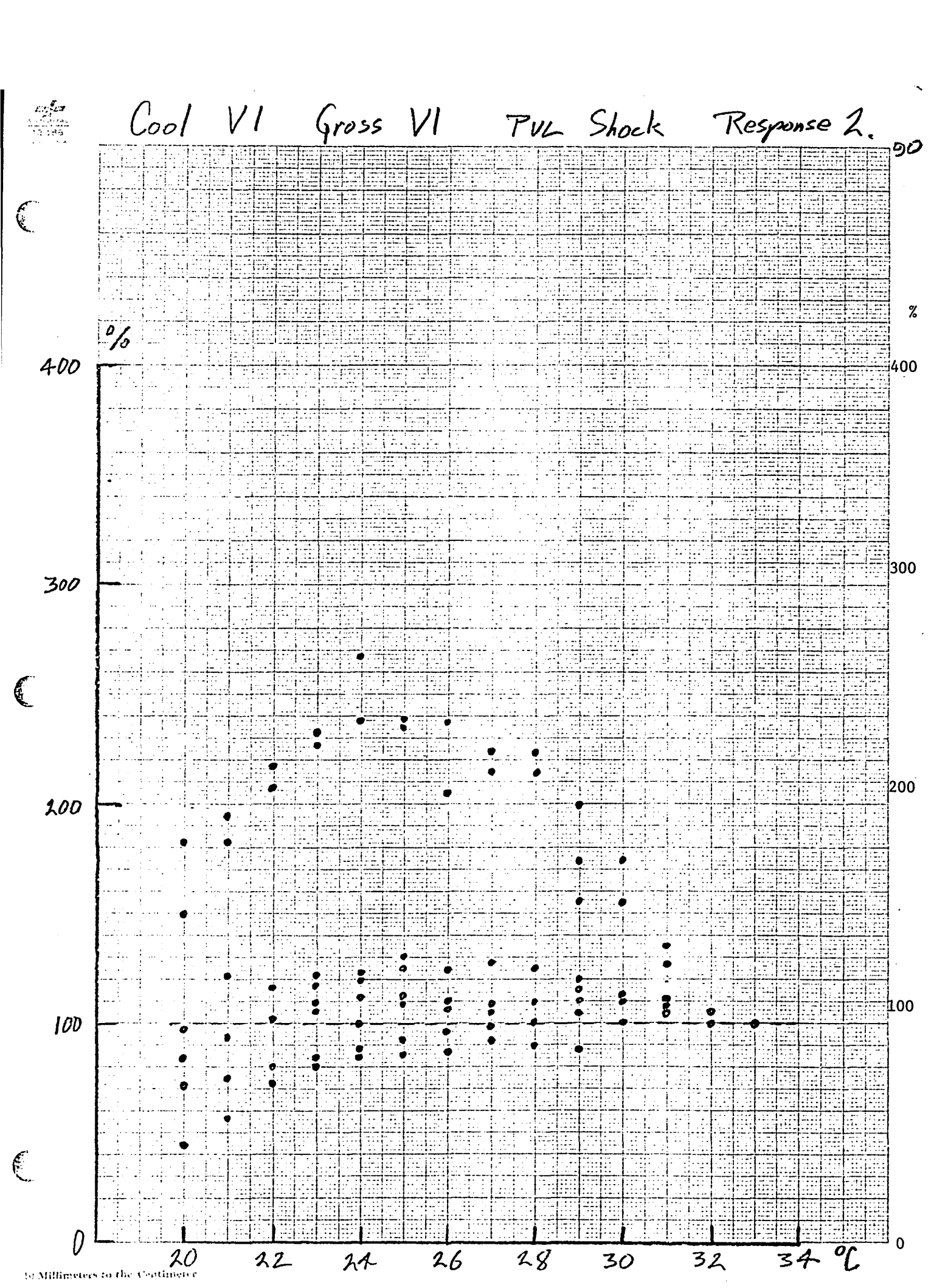
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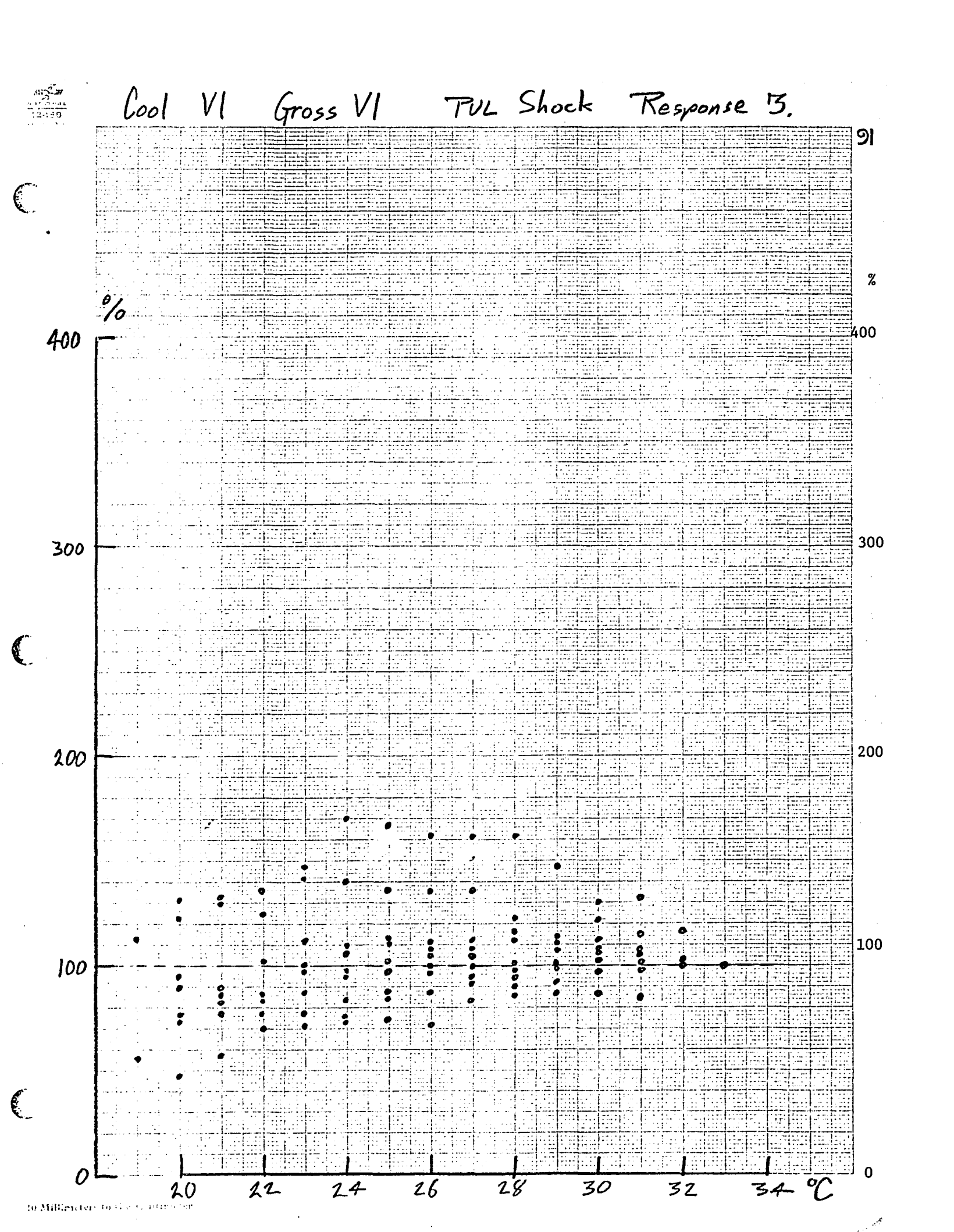
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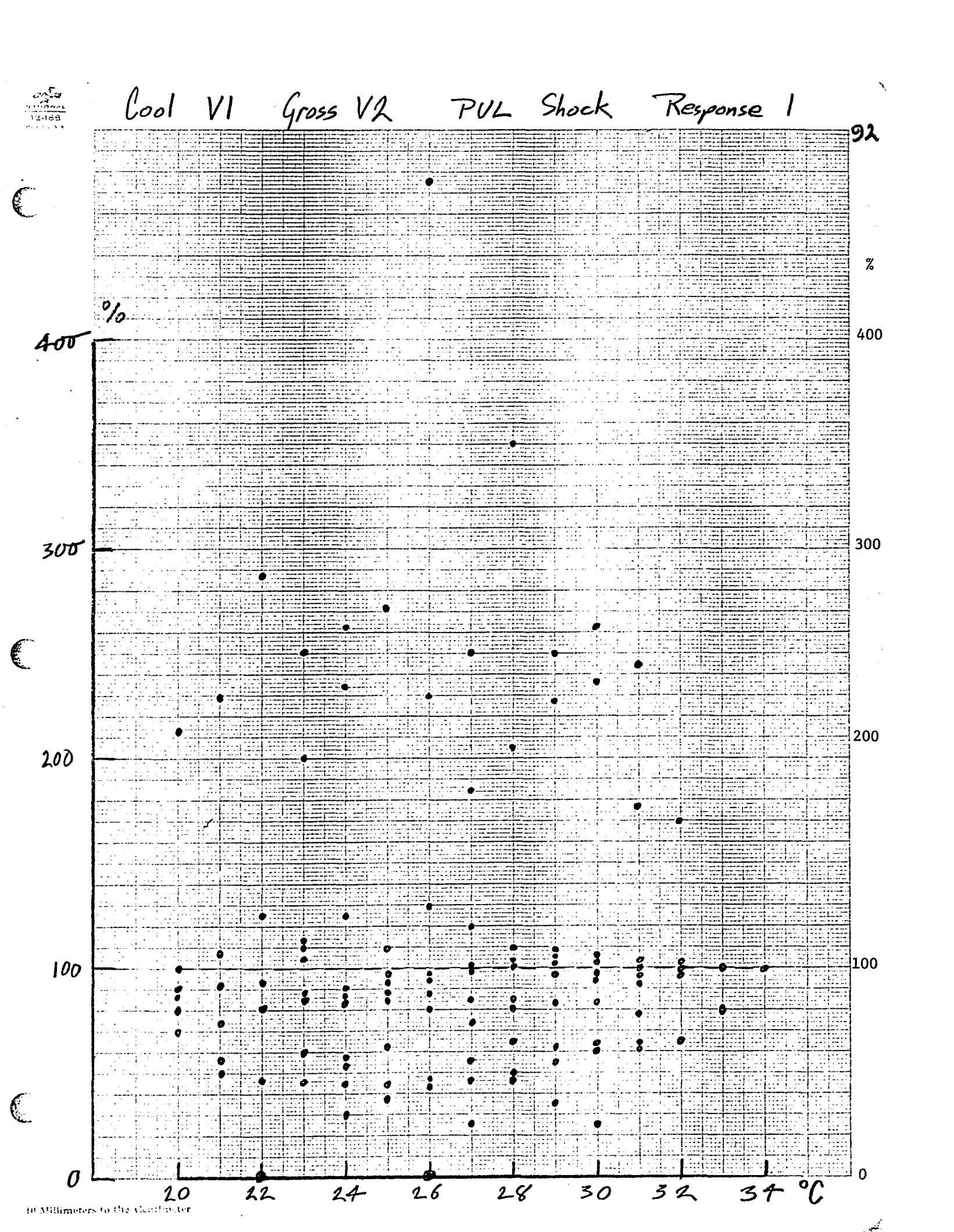
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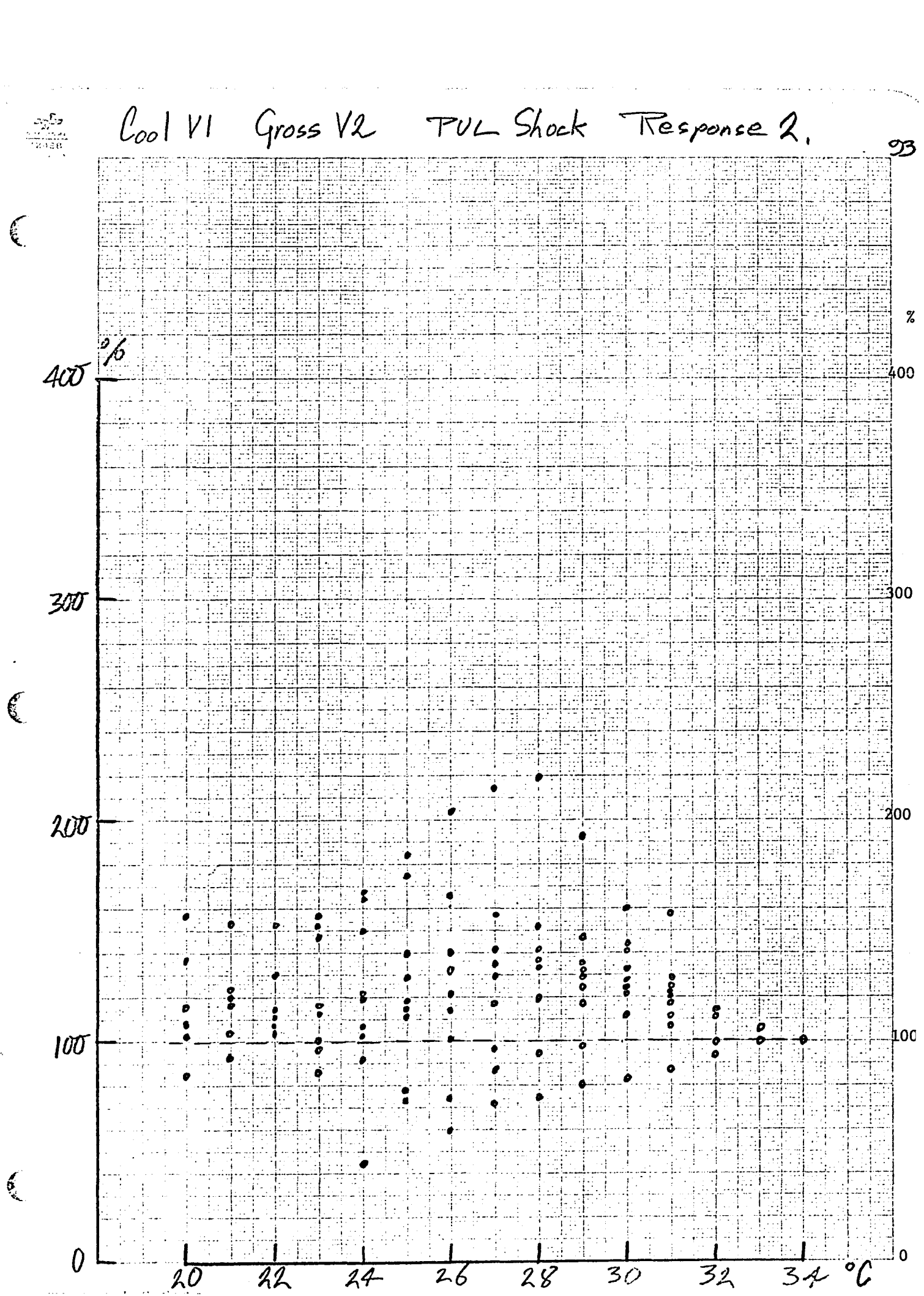
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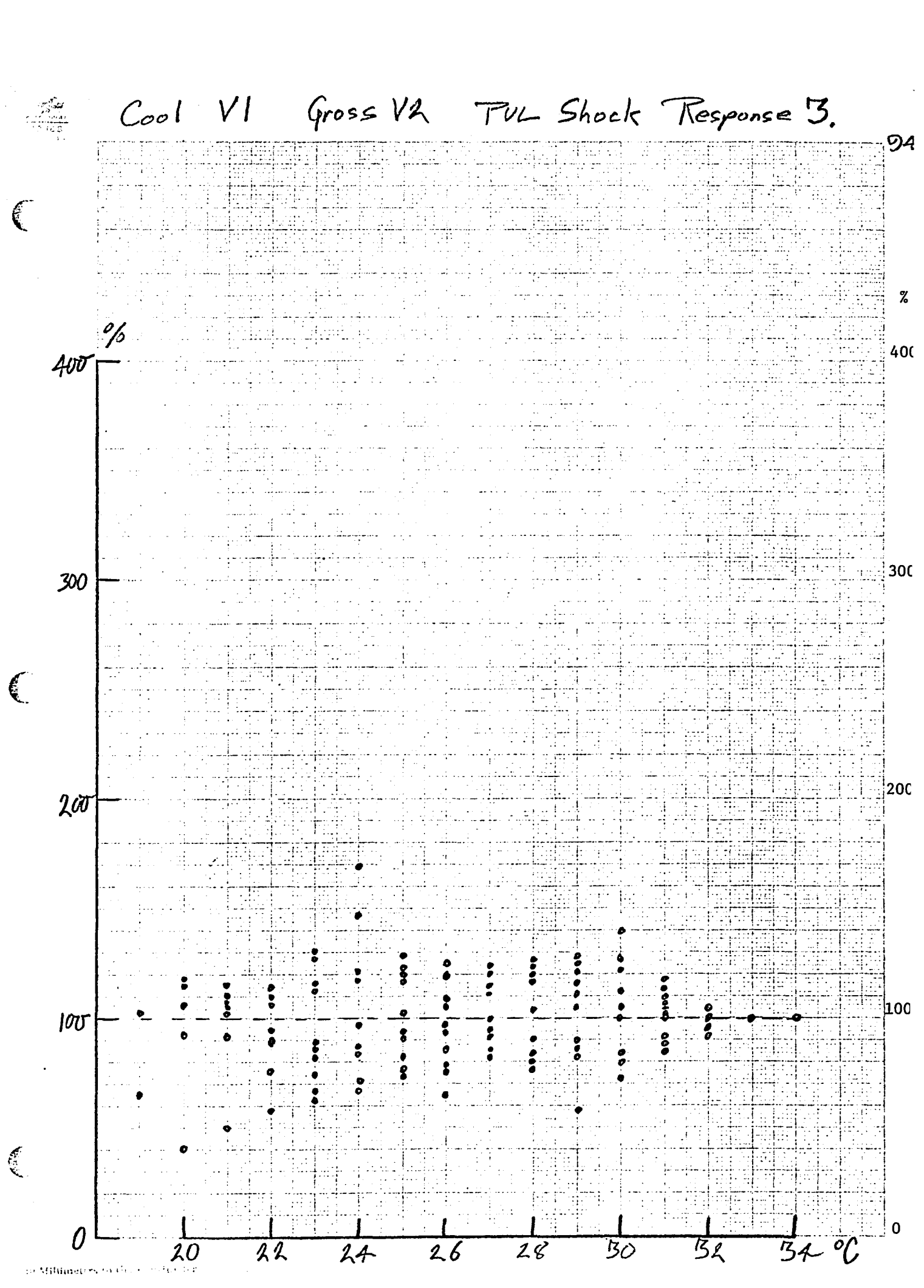
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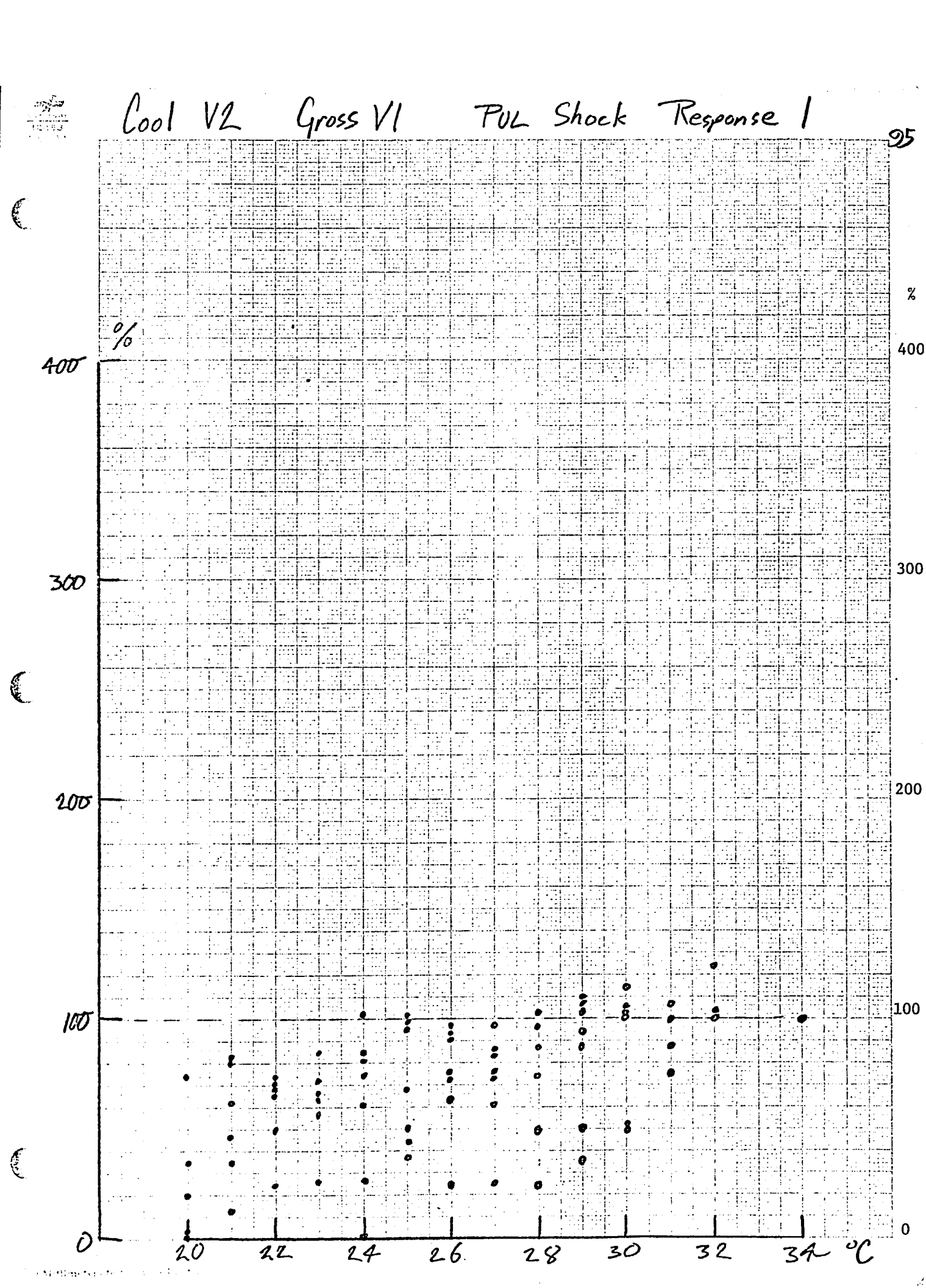
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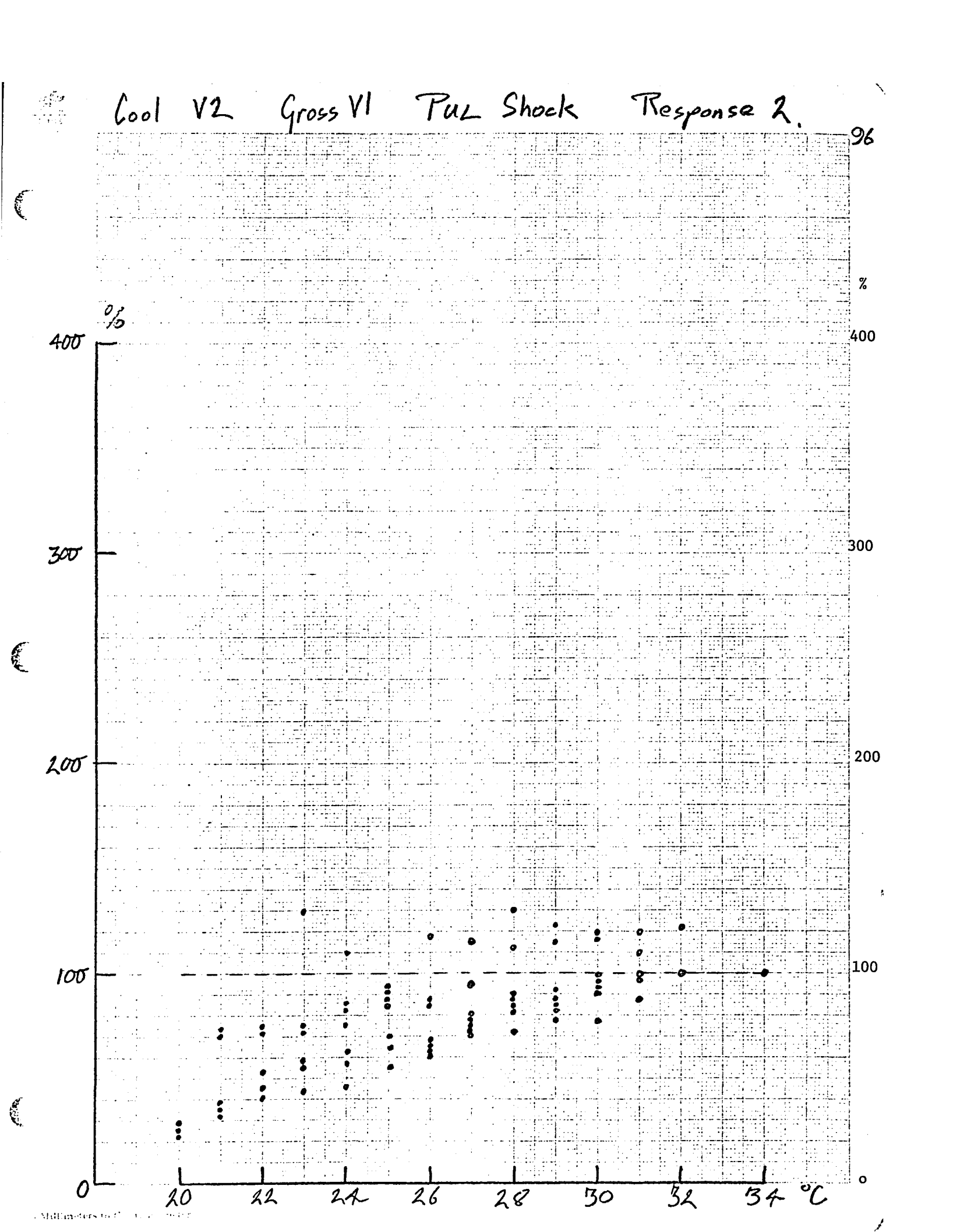
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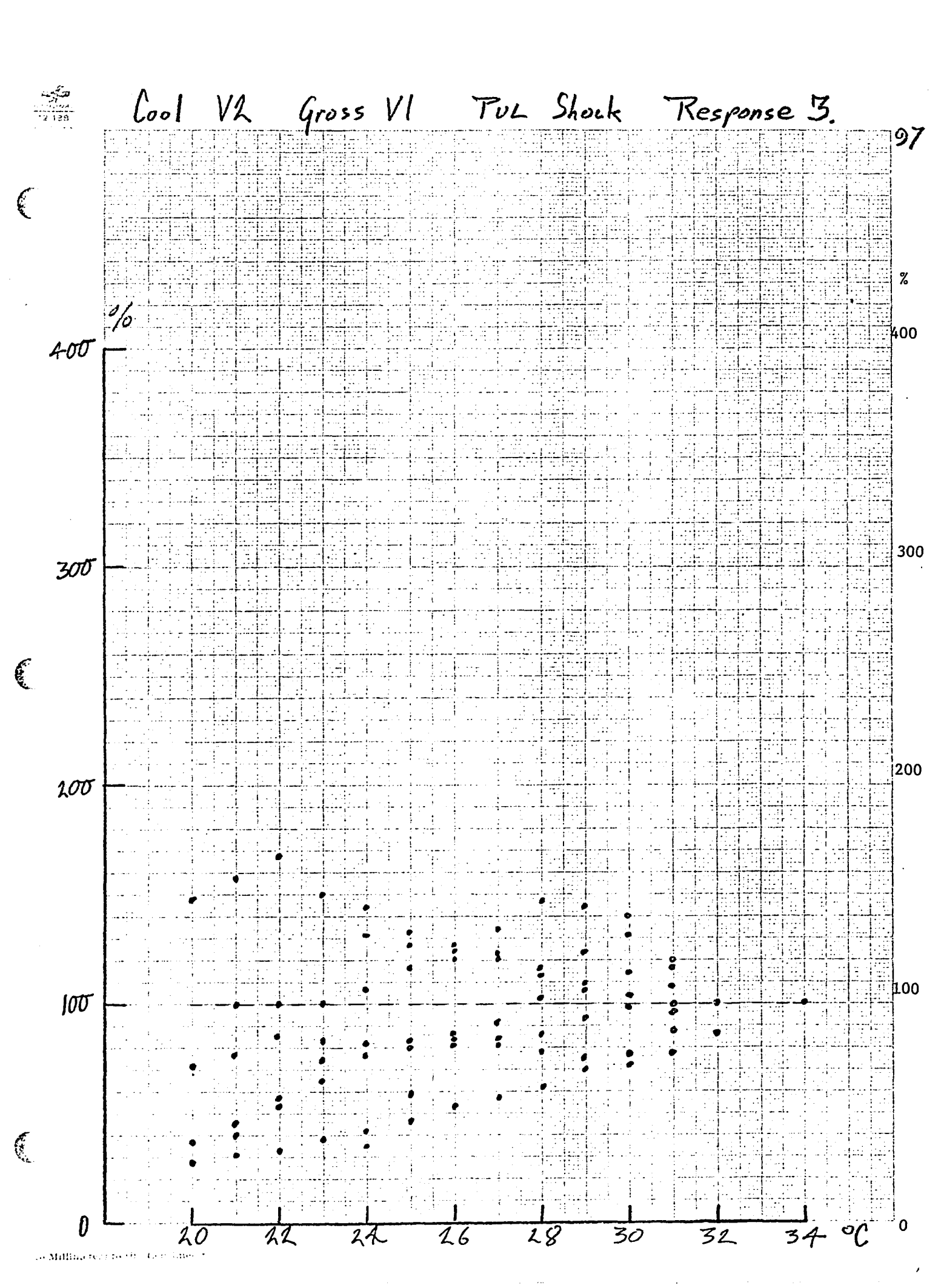
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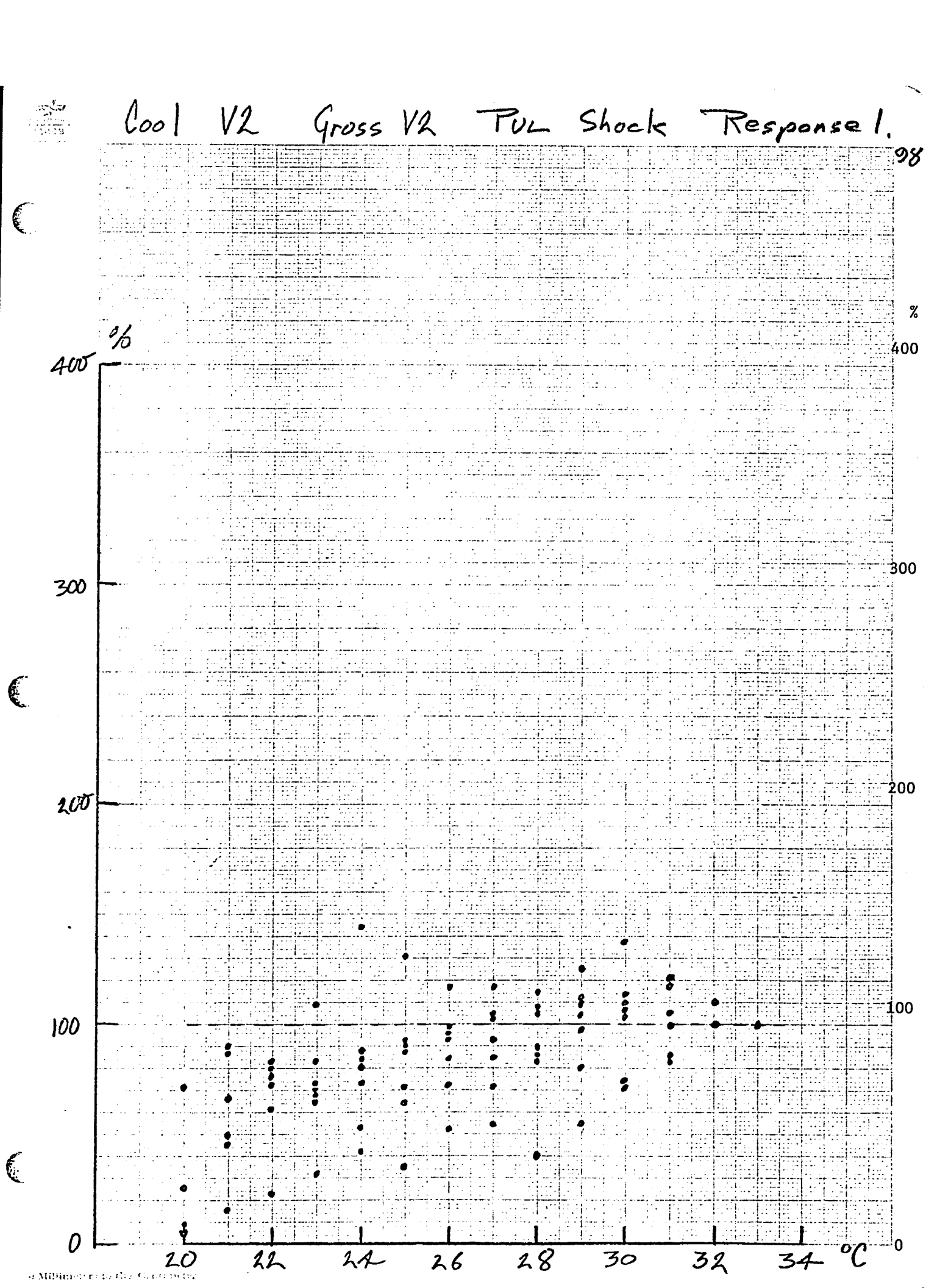
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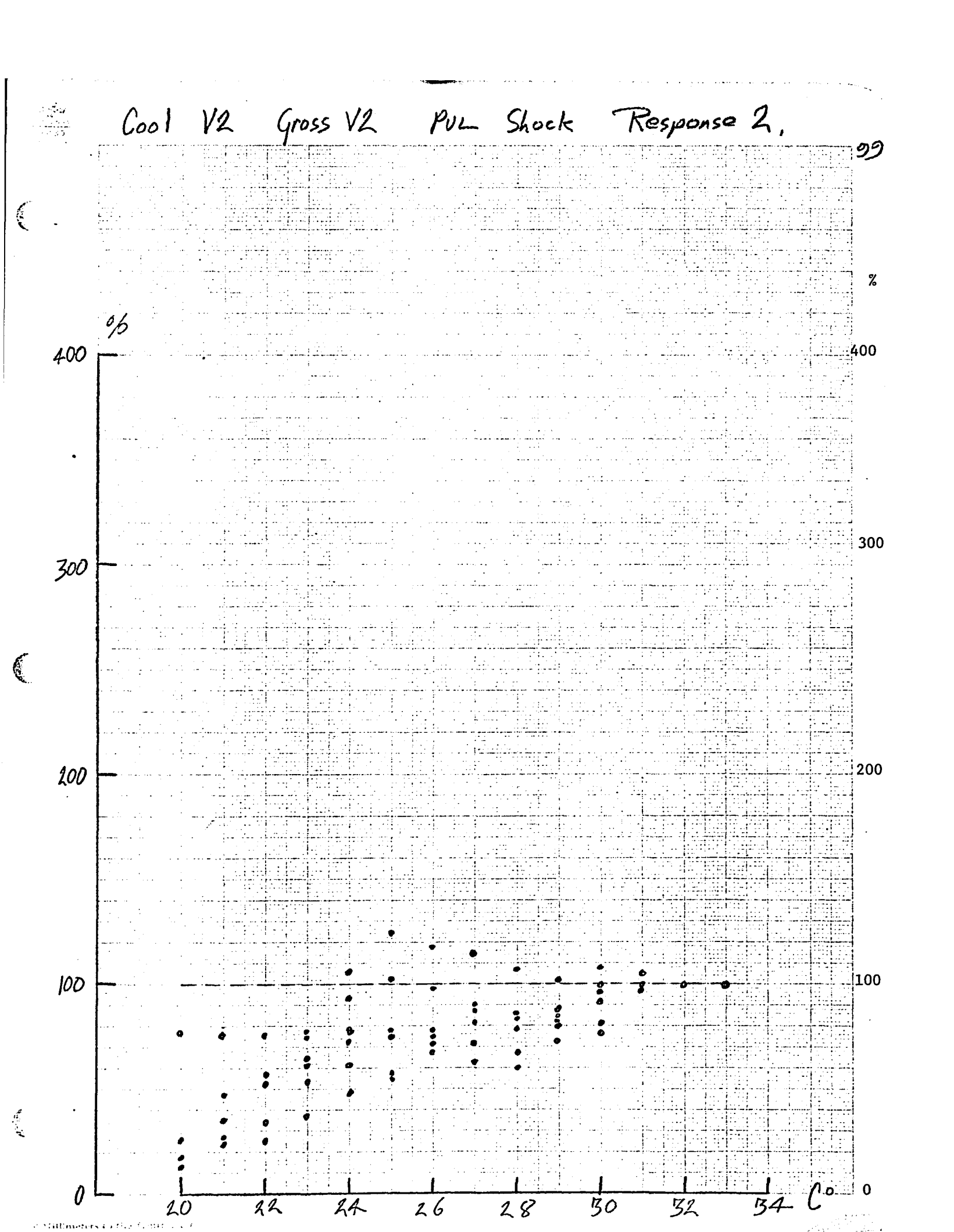
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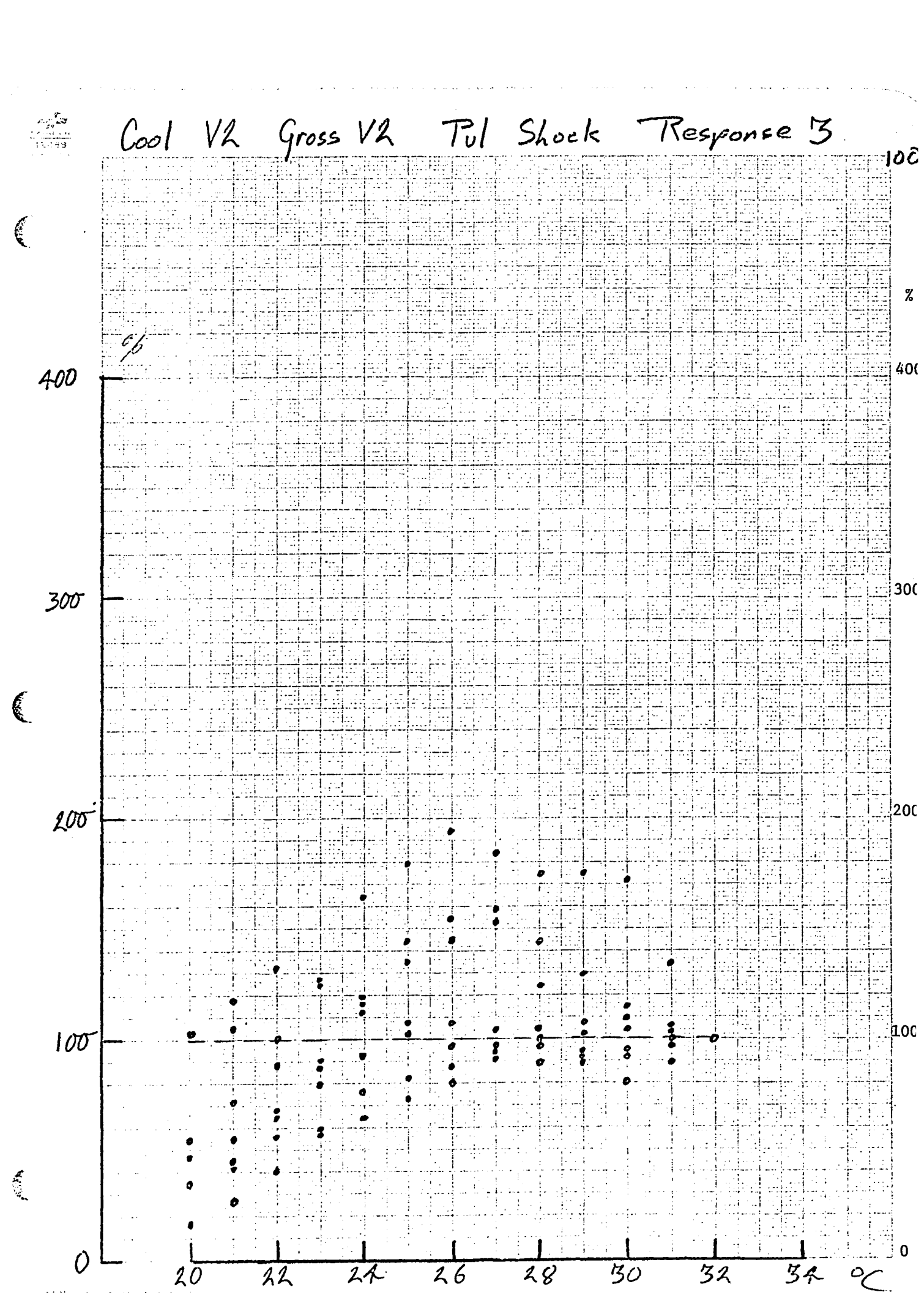
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