

The solid curves represent the dependence of CO concentration on the time as obtained from the results of the following calculations. If x is the mole fraction of CO in a bulb (of volume V cc.) at a time t , then with a convective transport rate of T cc./minute upwards through the converter, the flow of CO_2 into the converter at time t is $T(1-x)$ cc./minute. Assuming complete conversion of the CO_2 in the mixture to CO, $T(1-x)$ also represents the increment in the flow of CO leaving the top of the converter at time t . The net increase in the number of cubic centimeters of CO in the vessel is then given by:

$$V \frac{dx}{dt} = T(1-x).$$

The solution of this equation for the boundary condition, $x = 0$ at $t = 0$, gives the following expression for the time dependence of the concentration of CO in the vessel:

$$x = 1 - e^{-Tt/V}.$$

The two solid curves in Fig. 3 were obtained by substituting convective flow rates of $T = 35$ cc./minute and $T = 40$ cc./minute in the above equation. It is therefore evident that the convective flow in the converter was approximately 35–40 cc./minute. Using this value for T , the percentage conversion at any time, t , can be calculated. It can be seen that

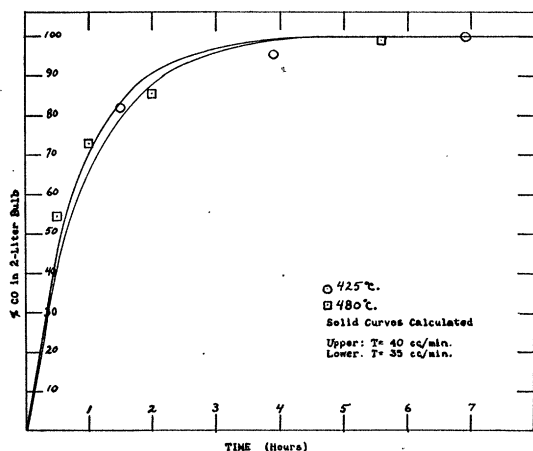


FIG. 3. Rate of conversion of CO_2 to CO in a closed system.

this method may readily be adapted to the determination of convective transports through different types of packed columns for engineering experiments.

To test the method for conversion of small samples, a 5-cc. reaction vessel containing about 1 gram of the powdered zinc-asbestos mixture, as illustrated in Fig. 2(C), was used in connection with a standard system (2) for obtaining CO_2 from BaCO_3 . Carbon dioxide was liberated from 40 mg. of BaCO_3 ,² in which a mass spectrographic analysis showed 3 per cent of the carbon atoms to be C^{13} . After the sample was transferred to the reaction vessel, the zinc was heated to about 425° C. for two hours. Analysis with the microgas analysis apparatus showed 99 per cent conversion to CO. Mass spectrographic analysis showed that it contained 3 per cent C^{13}O .³

² The authors are indebted to Dr. A. V. Grosse of the Houdry Process Corporation for the barium carbonate enriched in C^{13} .

³ Thanks are due to E. H. Mosbach for assistance with the mass spectrographic and gas analyses and to Miss M. Lamson for help with the spectrographic analyses.

The carbon monoxide may be converted back to carbon dioxide, if desired, by passing it through copper oxide heated to 400° C.

References

1. NOACK, E. *Ber.*, 1883, 16, 75.
2. RITTENBERG, DAVID. In *Preparation and measurement of isotopic tracers*. Ann Arbor: Edwards, 1946. P. 31.
3. TAYLOR, T. I., and BERNSTEIN, R. B. *J. Amer. chem. Soc.*, 1947, 69, 2076.

A Kinesimeter for Studying the Spontaneous Activity of Small Animals

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With the increase in number of sympathomimetic amines in use and under investigation for their circulatory effects, it has become necessary to study their effects on central stimulation with ever-increasing accuracy.

Many types of activity recorders have been employed for this purpose and with varying degrees of results.

As early as 1898, Stewert (6) tested the effects of alcohol, diet, and changes in barometric pressure on the spontaneous activity of small animals. His method consisted of a squirrel cage made of wire mesh 18 inches in diameter and 20 inches in length. The animal's movements caused the cage to rotate. An eccentric coupled to the escapement mechanism of an alarm clock caused the revolutions to be registered by the second hand. Slonaker (5), using a slight modification of the same technique, studied the normal activity of the white rat at different ages. His findings showed that the greatest activity of the rat occurred when the animal was 87–120 days old.

The above method, of course, is suitable only for the type of research in which activity is studied for many days or weeks. For studies of activity due to the central nervous excitability of various drugs, involving only a few hours, a much more sensitive apparatus had to be developed.

Schulte, *et al.* (4) used a cage and spring suspension, coupled to a work adder by a string. As the animal's motions moved the cage, the work adder revolved. A signal magnet recorded these motions on a kymograph. This method has a decided advantage in that it takes into account both large and small motions and accumulates them. However, the cage is undamped and is free to oscillate in any direction.¹

Abreu (1) used a cage suspended by a spring in which the movements were transmitted by a tambour-air system to a kymograph.

The above types of apparatus are best described by the term "jiggle" cages. Since they are all suspended on coiled springs, one movement of the animal results in from one to several movements of the cage. Both vertical and pendular movements may be transmitted to the recording devices.

¹ C. W. Geiter, of Frederick Stearns & Company, developed a method whereby a cage was suspended on a spring. As the animal's motions caused the cage to move up and down, a flag cut a beam of light, causing a photocell to operate a counter (unpublished).

Ross E. Hart, of Jefferson Medical School, Philadelphia, studied activity by means of transmitting the motions of an activity cage coupled to an air tambour writing on a kymograph. By this method activity can be judged roughly by inspection of the records (unpublished).

These types of apparatus serve very well for screening work, but for more accurate work a type in which the spring is damped sufficiently to eliminate the "jiggle" is required. It is also desirable to eliminate any pendular movements which might record.

The apparatus herein described (Fig. 1) consists of a Lucite cage. The advantages of Lucite are its lightness in weight and its rigidity, which imparts the full force of the animal's motions to the upper electrode. The closed bottom of the cage

resting upon a sheet of metal which forms another (lower) electrode. By this means a variable resistance is formed which is connected in series with a series wound fractional horsepower motor. A speed reducer of variable ratio at the end of the motor drives a revolution counter. This assembly is supported by a $\frac{1}{8}$ -inch coiled spring, the tension of which may be varied according to the weight of the rat.

The upper electrode is so mounted that its height can be adjusted independently of the rest of the apparatus and so

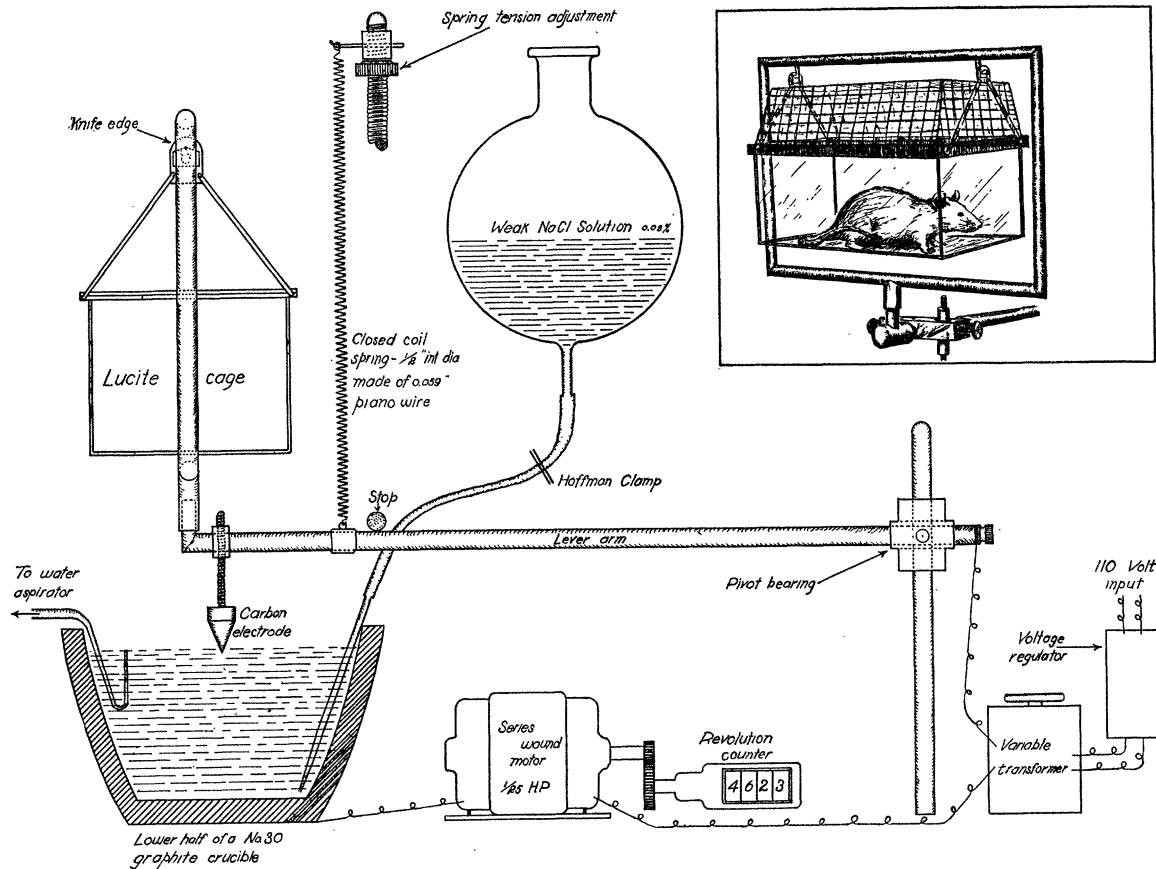


FIG. 1. Semidiagrammatic drawing of kinesimeter. Cage suspension is shown in insert.

keeps the animal's urine from getting into the electrolyte solution. The lid is made of $\frac{1}{4}$ -inch mesh screen wire in the form of an inverted box, so that the animal's movements are completely unhampered. The cage is suspended on knife edges mounted rigidly to one end of a horizontal brass tube 20 inches long. The other end of this tube is attached to an upright by pivot bearings. It is very important that the cage be suspended on knife edges, since direct attachment of the cage to the horizontal lever arm changes the arm's length as the rat shifts its position from side to side. If the rat went to sleep on the side of the cage distal to the pivot of the horizontal arm, the motor would turn and thus faultily register activity. The whole assembly is suspended on a damped coiled spring. Directly under the plastic cage is mounted a pointed carbon electrode. This upper electrode dips into a weak solution of sodium chloride (.08 per cent) contained in a No. 30 graphite crucible

regulated that it barely makes contact with the salt water. The current is decreased by a variable transformer or rheostat until the motor armature just ceases turning. This causes the motor as well as the spring to be heavily damped.

The slightest movement of the animal which results in a downward thrust will push the pointed (upper) electrode downward in the salt water, which in turn decreases resistance in the circuit and causes the motor armature to turn. Due to the conical shape of the electrode, the further it is thrust into the salt water, the faster the motor will revolve. Since the spring supporting the apparatus follows Hooke's law, the slope of the electrodes can be adjusted to cancel, or at least minimize, the effect of the spring. Thus, the counter registers only the downward thrust of the rat.

The instrument can easily be made self-recording. The revolution counter is removed, and the speed reducer shaft is

extended several inches. At the end of the shaft is mounted a 2-inch writing point which describes arcs on a slowly moving kymograph. A 15-minute-interval time signal is included with the assembly.

In our studies only male white rats were used, thus eliminating any behavior which might be due to various phases of the oestrus cycle of the female. The animal is first placed in the cage, and the apparatus is adjusted to its weight. It is then removed and injected with the solution under investigation. Twenty-eight animals injected with normal saline were used as controls. The amount of saline injected was made to correspond with the volume of the drug injected. As soon as the injected animal was placed in the cage the initial reading was

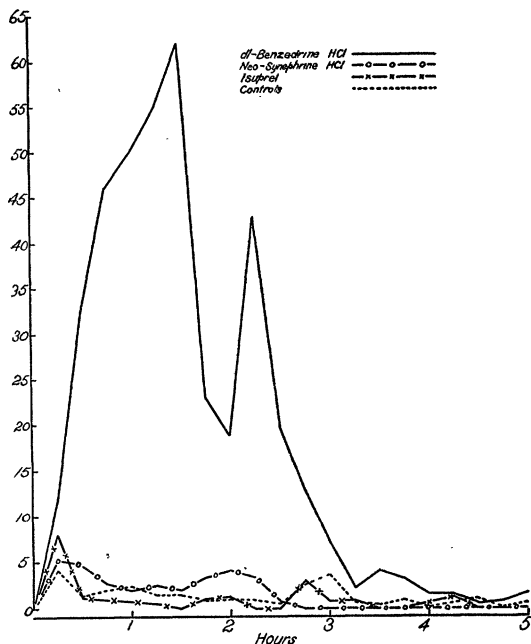


FIG. 2. The effect of dl-benzedrine hydrochloride, Neosynephrine hydrochloride, and Isuprel upon the spontaneous activity of albino rats

taken. Subsequent readings were taken at 15-minute intervals the increments between readings being recorded and plotted on graph paper.

The number of rats and the dosage used in the case of each compound tested were as follows:

	No. of rats	Dosage (mg./kg.)
dl-Benzedrine HCl.....	6	5.0
Neosynephrine HCl.....	6	1.75
1(3', 4'-Dihydroxyphenyl)-2-isopropylamino-ethanol HCl (Isuprel).....	6	1.0
N-Methyl-β-cyclohexylisopropylamine HCl		
d-isomer.....	9	20.0
d-isomer.....	12	5.0
l-isomer.....	15	5.0

The results of the tests with the first three compounds, (Fig. 2) which are in agreement with other workers in the field, clearly show that dl-benzedrine hydrochloride is extremely

exciting to the central nervous system, whereas Neosynephrine hydrochloride and Isuprel show no appreciable stimulating properties.

Both of the two other compounds studied, l-N-methyl- β -cyclohexylisopropylamine hydrochloride and d-N-methyl- β -cyclohexylisopropylamine hydrochloride, showed only a small amount of stimulation of the central nervous system. The d-isomer exhibited about twice the stimulating effect of the l-isomer. This is not in agreement with the results obtained by Frick and Becker, as reported by Lands, *et al.* (3). These investigators found the l-isomer somewhat more stimulating than the d-isomer. However, the writer's findings are in substantial agreement with that of Fellows and his workers, whose preliminary results show that 5 mg./kg. of the l-isomer induces less activity than 20 mg./kg. of the d-isomer (2).

Since the two isomers had not been given in comparable doses, it was thought advisable to do so. Accordingly, attempts were made to inject 20 mg./kg. of the l-isomer. The animals

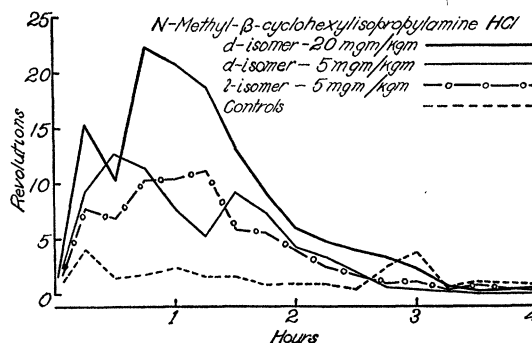


FIG. 3. The effect of d- and l-isomers of N-methyl- β -cyclohexylisopropylamine hydrochloride on the spontaneous activity of albino rats.

showed evidence of toxicity, and no activity resulted. The d-isomer was then injected at a dose level of 5 mg./kg., and the animals responded immediately with increased activity. These results are shown in Fig. 3.

The theoretically ideal kinesimeter would be one which records the motions of an animal directly and does not depend upon any moving parts for its operation. Thus, errors caused by pendular movements and "jiggle" of the machine would be eliminated. This recorder should be extremely sensitive to all movements of the animal's body, including small motions of the head. The apparatus, in addition, should integrate these small movements with large body movements. It would also be desirable if the machine would record in absolute units such as gram-centimeters of work per unit of time, instead of revolutions of a wheel, the pumping of a quantity of water, or the turning of a motor armature.

References

1. ABREU, B. E., TUFTS, R. J., and COUTOLENE, M. E. *Fed. Proc.*, 1946, 5, 161.
2. FELLOWS, EDWIN J. Personal communication.
3. LANDS, A. M., NASH, V. L., GRANGER, H. R., and DERTINGER, B. L. *J. Pharm. exp. Therap.*, 1947, 89, 382.
4. SCHULTE, J. W., REIF, E. C., BACHER, J. A., JR., LAWRENCE, W. S., and TAINTER, M. L. *J. Pharm. exp. Therap.*, 1941, 71, 62.
5. SLONAKER, J. R. *J. comp. Neurol.*, 1907, 17, 342.
6. STEWERT, C. C. *Amer. J. Physiol.*, 1898, 1, 40.