tained in a number of animals. Figure 1 shows the cortical potentials (two electrodes) evoked by a flash of light (i) before ultrasonic irradiation, (ii) at the termination of the ultrasonic exposure period, and (iii) subsequent to irradiation. At the termination of the ultrasonic irradiation period the amplitude of the primary response (upper record) was reduced to less than one-third of its original value. The amplitude of the secondary response (upper record) was reduced to practically zero. Complete recovery of the primary and secondary response was apparent 30 minutes after exposure.

Experiments are in progress to quantify further the conditions for producing controlled reversibility and to determine the site or sites (synapses, axons, cell bodies) of action of the sound (*3*).

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* The name of the Bioacoustics Laboratory was recently changed to Biophysical Research Laboratory of the College of Engineering.

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Effects of Caffeine and Chlorpromazine on the Sexual Behavior of Male Rats

Although the effects of stimulant and tranquilizing drugs on sexual behavior are of considerable importance, the amount of systematic research on this problem has been negligible. Soulairac and Coppin-Monthillaud (*1*) have reported that after an injection of 30 mg of caffeine (and sodium benzoate) per kilogram, male albino rats decreased their latency to first sexual activity and increased their rate of copulation. The study described in this report (*2*) compares the effects of moderate doses of caffeine and chlorpromazine on the sexual performance of 17 150-day-old male hooded rats. The previous sexual behavior of the rats varied from complete impotence to extreme vigor.

Table 1. Average performance for various criteria of sexual behavior. (Not included are two subjects which did not perform at all on any of the trials.)

Behavioral measures	No.	Caffeine	No drug	Chlorpromazine	Friedman analysis of variance
Latency to:					
(i) first mount	9	13.4	26.4	69.7	$\chi^2 = 10.1$*
(ii) first copulation	9	13.4	28.3	71.3	$\chi^2 = 9.5$*
(iii) ejaculation	6	436.7	589.2	528.3	$\chi^2 = 7.0$†
Frequency of:					
(i) mounts	15	4.1	4.7	3.9	Not significant
(ii) copulations	15	16.1	15.1	12.0	$\chi^2 = 7.4$†
Percentage of group that:					
(i) copulated	15	80	87	87	Not significant
(ii) ejaculated	15	47	50	47	Not significant
Copulatory rate:					
(i) for subjects that copulated	9	2.41	1.87	1.45	$\chi^2 = 8.7$*
(ii) for subjects that ejaculated	6	2.80	1.64	1.63	$\chi^2 = 9.2$*

* Significant beyond the 0.01 level of probability. † Significant beyond the 0.05 level of probability.

Each male was given four 15-minute tests, spaced at least 2 days apart. Males were injected with 20 mg of caffeine (and sodium benzoate) per kilogram before one test, with 1 mg of chlorpromazine per kilogram before another test, and with isotonic saline (no drug) before two tests (*3*). Drug tests were alternated with no-drug tests. All injections were given intraperitoneally, between 15 and 60 minutes before the start of the test; this time-interval was within the effective range of the drugs. The drugs were dissolved in the same volume of isotonic saline (1 ml/kg) that comprised the no-drug injections. The rats were randomly assigned to one of four groups, which differed in the sequence of drug and no-drug tests. During each of the four test sessions one group was under caffeine, one group was under chlorpromazine, and two groups were under no drug. By these procedures, the order of drug conditions was counterbalanced, and each drug condition was tested in each session.

The tests were conducted in a circular observation cage 30 in. in diameter. Each male was given 2 minutes alone in the cage before the introduction into the cage of a female which was in full behavioral heat. The sexual behavior of male rats consists of mounting the female and making a brief intromission (copulation). On some occasions the male may mount without accomplishing an intromission. After a number of intromissions, generally between 10 and 20, ejaculation occurs. The male withdraws from the female and shows no sexual interest for at least 15 seconds after each intromission and for at least several minutes after ejaculation.

Table 1 shows these measures of sexual activity, presented in terms of (i) latency in seconds of first occurrence after introduction of the female; (ii) frequency of occurrence during the 15-minute test; (iii) percentage of group performing the response; and (iv) copulatory rate. Copulatory rate is the average number of copulations per minute to ejaculation (or, if no ejaculation occurs, from the first copulation to the end of the test). These measures and the procedures are more fully described elsewhere (*4*). As is shown in Table 1, caffeine decreased the latencies to mount, copulate, and ejaculate and increased the frequency and rate of copulation. Chlorpromazine had opposite effects on all these measures except latency to ejaculation. Of interest is the failure of both drugs to alter significantly the percentage of subjects which copulated or ejaculated.

In order to test for the effects of the drugs on subsequent no-drug sessions, the tests following administration of caffeine were compared with the tests following administration of chlorpromazine. An additional 15-minute no-drug test was given to animals whose last regular test was with one of the drugs, in order to complete this procedure. The animals made more than twice as many mounts and 24 percent more copulations during the no-drug session following administration of chlorpromazine than during the no-drug session following administration of caffeine. The difference in number of mounts is statistically significant ($p < 0.05$ by Wilcoxon matched-pairs rank test). There were no reliable differences in the other measures of sexual behavior. Since the time interval between sessions was ample to allow the drug effects to dissipate, these results apparently point to differences in behavior learned under the two drugs. A more strenuous sexual response may have been learned under chlorpromazine to over-

come the depressant effects of the drug.

The wide range in sexual potency of our subjects was in part the result of antecedent conditions to which they were subjected in an experiment by one of us (P. G. Z.) (*5*). After weaning, 11 of the rats had been reared under unfavorable conditions (that is, they had been given electric shock for approaching a receptive female and had been subsequently reared in isolation, or they had been reared entirely in isolation). Six rats had been reared under more favorable conditions (that is, they had been given no electric shock when they were with a receptive female and had been reared in cohabitation with other males or with females). In order to increase the number of subjects in testing the differential effects of previous sexual experience, eight pretest rats were added to this comparative study. These animals had been reared under the same conditions as the others (five under favorable conditions, three under unfavorable ones) but were given four *ten*-minute tests and were not given a no-drug test between the two drug tests.

In the various measures of sexual performance, the depressant effects of chlorpromazine were found to be approximately equal among animals reared under these two sets of conditions. On the other hand, the stimulating effects of caffeine were evident only among animals reared under the more favorable conditions. These animals copulated almost twice as many times when they were under caffeine as when they were under no drug and showed an increment, under caffeine, in number of mounts, in copulatory rate, and in percentage that copulated and ejaculated. Among the animals reared under unfavorable conditions, caffeine produced only a slight increment in copulatory rate and a slight decrement in all of these other measures. The effect of rearing conditions on the caffeine-versus-no-drug difference was statistically significant for number of copulations ($p < 0.02$) and almost significant for number of mounts ($p < 0.10$), according to the Mann-Whitney rank test. The different effects of caffeine might be explained by the hypothesis that the stimulating effects of caffeine enhance whatever behavior tendency is dominant in the situation. If the conditions of rearing have been favorable, positive sexual responses will generally be dominant; if the conditions of rearing have been unfavorable, inhibitory or incompatible responses may be dominant.

The study described in the present report confirms and extends the finding by Soulairac and Coppin-Monthillaud of the stimulating effect of caffeine on sexual behavior—even of a smaller dose. A depressant effect of chlorpromazine was also found. The use of non-drug tests and of animals with variation in previous sexual experience permitted further observations on effects of the drugs.

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2. This study was conducted while we were under predoctoral and postdoctoral fellowships, respectively, from the National Institutes of Health, U.S. Public Health Service. The costs for equipment and rats were financed in part by a National Science Foundation research grant.
3. Helpful advice on doses and injection procedures was given by N. J. Giarman of the department of pharmacology, Yale University.
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Electromigration on Filter Paper of Uric Acid from Serum and Synovial Fluid

It has long been a matter of discussion whether uric acid is present in human serum as a free molecule or is bound to other components such as proteins. Ultrafiltration and dialysis have given controversial results in this connection (*1*). Zone electrophoresis on filter paper offers a new approach to the study of the problem.

Previous reports from our laboratory (*2*) have shown that several techniques can be followed for identification and evaluation of uric acid on the strip of filter paper. The most practical technique proved to be direct treatment of the strip with silver nitrate and sodium lactate; uric acid appears, then, as a brown band on a white background. While this method is suitable for detecting the position of the spot of uric acid, quantitative data are more readily obtained by elution and chemical (*3*) or ultraviolet absorption analysis.

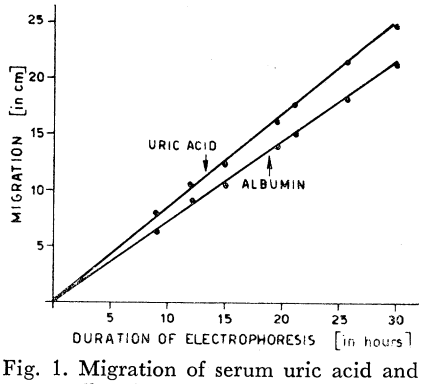

Fig. 1. Migration of serum uric acid and serum albumin as a function of duration of electrophoresis, in standard conditions of potential gradient (2.5 v/cm) and temperature (15°C), in Veronal at pH = 8.6, $\Gamma/2 = 0.05$. Each point represents an average of four experiments. In calculating distance of migration, it has been assumed that the starting point corresponds to the band of gamma globulin.

Paper electrophoresis was performed in accordance with the method of Durrum, as modified by Flynn and De Mayo (*4*). Different buffer solutions were tried: Veronal at pH = 8.6, $\Gamma/2 = 0.10$, 0.05, and 0.025, respectively; phosphate at pH = 7.2, $\Gamma/2 = 0.05$; acetate at pH = 5.4, $\Gamma/2 = 0.05$; glycine-NaOH at pH = 9.7, $\Gamma/2 = 0.05$. The best results, as far as resolution of protein components and uric acid is concerned, were obtained with Veronal buffer at pH = 8.6, $\Gamma/2 = 0.05$. Whatman No. 31 extra-thick filter paper was used.

Forty-two sera from normal subjects and from hyperuricemic patients with gout, nephritis, and leukemia and ten samples of synovial fluid from gouty and rheumatic subjects were studied. Control experiments were run with pure uric acid solutions of different concentration (from 3 to 20 mg percent). The results obtained can be summarized as follows:

1) Uric acid present in serum and synovial fluid showed the same electrophoretic behavior as uric acid in free solution, in all the conditions of pH, ionic strength, potential gradient, temperature, and duration of migration that were tried. A single band was always obtained for this substance. Though we cannot rule out entirely the possibility that there was a dissociation of labile bonds between uric acid and other serum components, it is not likely that such a dissociation would have occurred under the mild conditions of our experiments.

2) The mobility of uric acid, as judged from the electrophoretic migration on filter paper, proves to be slightly higher than that of serum albumin, being about 15 percent greater (Fig. 1).

3) No change of the electrophoretic behavior of uric acid was observed after general or intra-articular administration of drugs that are active in modifying uricemia (prednisone, phenylbutazone, probenecid, pyrazinamide).

Our results seem to indicate that uric acid is not bound to other serum components and is not present in a particular chemical form; several drugs that act on uric acid metabolism and excretion fail to modify the physical or chemical properties of this substance in the blood.

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