vostomatitis were tested and predominantly type 1 antibodies developed, although low levels of type 2 neutralizing activity also appeared. These data suggest that antibody activity to the two types of virus could be measured independently by the kinetics of neutralization.

The variability of the test procedure was examined by repeatedly testing four serums that rapidly neutralized both types of virus. The mean K value of 26 determinations made with the type 1 oral isolate was 10.4, with a standard deviation of 2.8; that of 27 determinations made with the type 2 genital isolate was 9.3, standard deviation 2.7. The coefficient of variation of the 53 determinations was 28 percent.

Analysis of serums from various groups of individuals revealed a very high incidence of antibodies to the genital type of herpesvirus in patients with invasive carcinoma of the cervix (Table 2). These patients were from the lower socioeconomic class, and the incidence of type 2 antibodies was higher in women from the same class without the disease than in persons from the higher socioeconomic classes. However, the incidence of antibodies was significantly greater in the carcinoma patients than in the matched control group ($P < .001$). Absence of antibodies in the serums from children and adults from the higher socioeconomic group supports the venereal mode of transmission of the genital type of herpesvirus.

Analysis of three serums, two from women with carcinoma of the cervix and one from patient number 6 (Table 1), by sucrose density gradient centrifugation revealed that the neutralizing activity against type 2 herpesvirus resided with the $7S$ globulins. The kinetics of neutralization of two other lipid-containing enveloped viruses, rubella and measles, was similar for serums from women with carcinoma of the cervix and for serums from their matched controls.

The results of this preliminary study indicate that women with carcinoma of the cervix have a significantly higher incidence of type 2 antibodies than women from the same segment of the population who do not have the disease. In 15 of 18 patients studied, type 2 K values of 4 or greater were found. Type 2 antibody activity was present in three other patients, but it was of such a low level that it may have represented cross reactivity with type 1 antibody. These three patients had systemic metastasis of their malignancy. Type 2 herpesvirus neutralization was found to be associated with $7S$ globulins and was not present with a high frequency in persons with other types of carcinomas. Virus neutralization of two other lipid-containing viruses was not observed in unusual frequency with serums from the patients with carcinoma of the cervix.

The present findings are compatible with a carcinogenic or co-carcinogenic role of type 2 herpesvirus in carcinoma of the cervix. Other evidence suggesting an etiologic role of herpesvirus in carcinoma of the cervix includes the report by Naib (*7*) who found a 7 percent incidence of *in situ* carcinoma among women with genital herpes, while only 0.6 percent of the women without genital herpes was found to have this lesion. The epidemiologic features of carcinoma of the cervix point to a venereally transmitted agent (*1*, *2*). Genital herpesvirus also appears to be venereally transmitted (*8*). An unexplained observation in the epidemiology of carcinoma of the cervix is the low frequency of the disease among women who consort with circumcised males (*1*). Herpes progenitalis is uncommon among circumcised males and occurs primarily in uncircumcised males (*8*, *9*). Thus, the epidemiologic features of genital herpesvirus are in keeping with those of carcinoma of the cervix and complement the serologic data presented in this report.

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Program Clocks in Small Mammals

Abstract. *Complex patterns of time, direction, and speed of running by small nocturnal mammals in activity wheels sometimes are duplicated almost exactly from night to night. These activity pattern repetitions disclose: (i) previously unknown capabilities of biological clocks to act as sequence programmers for behavior; (ii) that animals can retain a record of the sequence and timing of their activities covering an entire night; and (iii) that the activities of one night can bias an animal toward similar behavior on subsequent nights.*

Given access to an activity wheel, small mammals spend almost all their active time running it (*1*, *2*). In effect, this single activity substitutes for most of the locomotor and manipulatory activities of animals in the wild. If the instantaneous speed and direction of running are recorded every few seconds on a moving chart (*1*, *2*), the activity patterns obtained rival sonographs of birdsong in their richness of individual and species detail. Performance properties, such as time spent running, speed, lengths of nonstop sessions, and directional consistency usually depend sensitively on the state of the animal and environmental variables, particularly ambient light (*2*). A chief finding of earlier studies is that the animals often run in the same direction all night, even though they start and stop running hundreds of times. They get their bearing for this orientation chiefly from sightings of nearby objects (*2*).

In locomotion studies in complex burrow-simulating mazes, white-footed mice, genus *Peromyscus*, readily learned their way back and forth along routes having hundreds of turns and blind alleys (*3*). Together, these studies of locomotion reveal a strong tendency toward conservatism or stereotypy of movement patterns and an impressive ability to learn complex sequences of movements and to keep track of surroundings, position, and direction. Presumably, the more conservative its movement patterns, the more readily an animal can keep track of its position. These findings complement other studies that suggest a strong propensity of small mammals to construct a "cognitive map" or "mind's eye view" of the terrain and to keep track of their position in it, whether in the home range or the laboratory enclosure (*4*). Our most recent studies show (i) that small nocturnal mammals have a remarkable ability to adhere to complex internally programmed schedules of time and direction of movements and (ii) that during one night's activity an animal's behavior sometimes is biased toward repeating activities of previous nights.

The strong tendency toward unidirectional running does not develop until after several days or even weeks of adaptation to the experimental situation, including learning to run the wheel (*2*). Changes of running direction usually occur frequently in the first few days but gradually become less frequent. During this early period, the direction reversal patterns of white-footed mice sometimes showed many similarities on successive nights. Pattern similarities were most marked for a few animals whose directional habits remained variable. We report one of these cases here, that of a female old-field mouse, *P. polionotus*, born in captivity, which was being used in a study of the effects of natural dawn on activity (*5*).

The enclosure (*6*) was housed in a light-proof cabinet having one side open to a windowpane with an eastern exposure. From 10:00 a.m. to midnight a discrete incandescent light source yielding an illuminance of 43 lux supplemented natural light (*7*). A 1-hour artificial dusk of variable color temperature provided by this source began at midnight (*1, 2*). The light increase of natural dawn (astronomical dawn) began at the times marked by the bases of the dawn arrows in Figs. 1 and 2. The responses of the old-field mouse to this light change consisted of increases in running speed followed by abrupt cessation of activity (curved brackets, Figs. 1 and 2). Since artificial dawns induce the same responses (*1, 2*), this finding supports the view that twilight light changes are the chief factor influencing the time of onset or cessation (or both) of activity of many small mammals (*2*).

The repetitions of the pattern given by this animal did not occur until after the 7th week of the experiment. Of these, the two most striking pairs are shown in Figs. 1 (15 and 16 November) and 2. On 15 and 16 November the first bout of sustained running began during artificial dusk and was eastward (Fig. 1). On both nights the first reversal of running direction occurred within a few seconds of 54 minutes after the starting

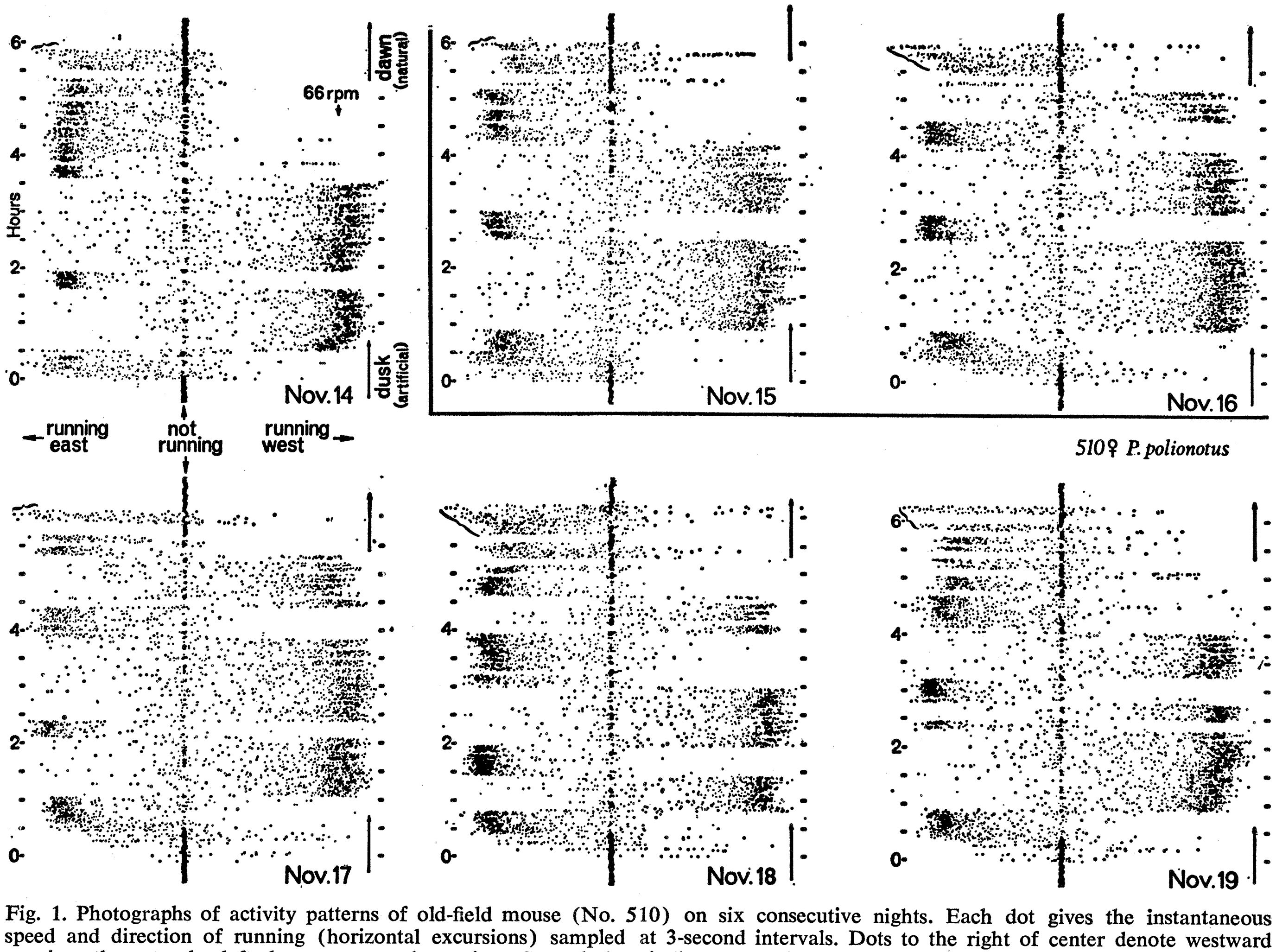

Fig. 1. Photographs of activity patterns of old-field mouse (No. 510) on six consecutive nights. Each dot gives the instantaneous speed and direction of running (horizontal excursions) sampled at 3-second intervals. Dots to the right of center denote westward running; those to the left denote eastward running. Central dots indicate a stationary wheel. The horizontal scale is linear, with the 66 rev/min point indicated (14 November). Time is marked off in the margins in half-hour intervals running from bottom to top and beginning at the time when running began. A 1-hour artificial dusk is indicated by the arrows at the lower right for each day. Natural dawn began at the time indicated by the base of the arrows at the upper right; the length of the arrows denotes only its first hour. The curved brackets at the upper left indicate the high-speed running response evoked by natural dawn. The mouse usually did not run at high speed during artificial dusk in the fashion more or less typical of white-footed mice (*1, 2*), including other old-field mice.

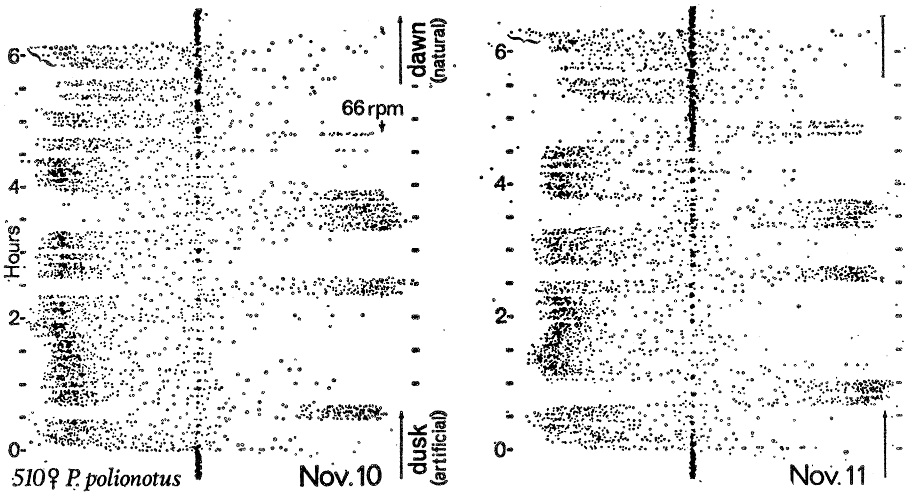

Fig. 2. Photographs of a repetition of activity pattern by No. 510 old-field mouse on 10 and 11 November. All conditions are the same as for Fig. 1.

time, the next within a few seconds of 150 minutes, the third within 30 seconds of 79.5 minutes, and the fourth within 120 seconds of 248 minutes. Running ceased within 2 minutes of 6 hours after starting time. Thus, the elapsed times after which reversals occurred on the two nights differed from the mean by at most 0.8 percent, with the duration of the activity periods differing by only 0.5 percent. The amount of time actually spent running was within a few seconds of 240.2 minutes. The only notable difference between the running patterns was the third sustained westward bout that occurred on 16 November but not on 15 November. A striking repeat of a different pattern on 10 and 11 November is shown in Fig. 2.

Records for six successive nights (Fig. 1) show that running patterns may remain similar for several days and illustrate how the patterns evolve. Four reversals occurred on the first two nights (14 and 15 November), when the patterns differed mostly in timing. As mentioned above, the third night's pattern was almost an exact duplicate of that of the second, except for the additional bout of westward running. Bout timing changed somewhat on the fourth and fifth nights (17 and 18 November) but the reversal patterns were very similar. Intermediate bout timing changed very much from the fifth to the sixth nights. Although these six records show considerable similarities, they are quite different from those of 10 and 11 November (Fig 2).

On one occasion the patterns for two successive nights were almost mirror images, just as if the timing of the reversal sequence had been programmed "correctly" but a "mistake" was made in the polarity. In other words, the animal started running in the "wrong" direction but changed directions at the "right" times. Pattern repetitions often involve duplication of the speed and degree of sustained running during a bout, as well as the time and direction (Fig. 1).

Similar results have been obtained in purely artificial light. The same old-field mouse gave several other noteworthy pattern repetitions, as did a male least weasel [*Mustela rixosa* (*8*)] caught in the wild, a female mouse opossum, (*Marmosa mitis*) caught in the wild, and a canyon mouse (*P. crinitus*) born in captivity. The mouse opossum also repeated patterns on nonsuccessive nights that were separated by nights for which the patterns and light program were different. Another female old-field mouse, caught in the wild, repeated a directionally complex pattern three nights in succession. Repetitions of a temporal pattern were given by a male California mouse (*P. californicus*) and a female cactus mouse (*P. eremicus*) caught in the wild. Their running was unidirectional but broken into several bouts of different durations that occurred in the same sequence on successive nights and tended to begin and end at the same time.

The existence of these strong tendencies toward repetition of running patterns from night to night enables us to expand on conclusions drawn only from the occurrence of strongly unidirectional wheel running: (i) The ability of small mammals to keep close track of running direction extends far beyond merely being able to adhere to a habit of running in the same direction all night; and (ii) small mammals not only tend to be highly conservative or stereotyped in their behavior during activity periods, but also from one period to the next. When an animal has strong tendencies toward stereotypy both during the night and from one night to the next, running is in a single same direction every night. When the night-to-night tendency is strong and the tendency during the night is weak, the patterns are not unidirectional but they do tend to repeat on successive nights. When the converse is the case, running is highly unidirectional during a given night but the direction may change from one night to the next, and so forth. All of these variations have been observed.

It should be noted that running in a new direction involves memory of the most recent direction reversal, for the animals maintain the new direction all through a bout, even though they start and stop running many times. Moreover, the actions of the animals during the replaying of a pattern show that the directional performance is subject to continual "review and correction." Thus, after a pause during a "scheduled" unidirectional bout, the animals sometimes begin to run again in the "wrong" direction. But they usually "correct" themselves promptly and revert to the scheduled direction (Figs. 1 and 2). Of course, variation and evolution of the patterns from night to night imply considerable flexibility of the processes of review and correction.

Studies of rhythmicity and sun-compass navigation have shown that many animals have an internal physiological clock that can be read at any time and can be used as a periodic timer, signaling the time to begin or end activity (*9*). In addition, numerous animals in the wild have been observed doing the same things at the same times and places day after day (*10*). Our results complement these observations by showing that internal physiological clocks can serve as sequence programmers, giving animals a series of accurately timed signals at preset intervals.

The selective advantages of possessing refined time- and space-tracking mechanisms and the ability to transcribe and recall activity programs probably are manifold. Selection clearly would favor animals that maintained continual awareness of time and their position relative to key regions of the home range, while animals that repeated today the patterns of interaction with the environment which were successful yesterday generally would have the best chance of surviving until tomorrow. For example, as different regions of the home range became productive, selective advantage probably would accrue to animals that developed and made repeated use of activity routines that effected systematic exploitation of the resources of these regions. Studies of old-field mice in the wild probably reveal some of these processes at work. Thus, the nightly wanderings of these mice were confined primarily to certain well-worn paths—usually to and from seasonal food sources, such as fruiting weeds and grasses (*11*). Most trips involved collecting food and transporting it to storage depots.

One also could make a strong case for the selective advantages of not holding to exactly the same space-time patterns of activity night after night, since predation and variability of environmental factors would lead to selection against absolute stereotypy. A balance would have to be struck between the advantages of adherence to stereotyped activity patterns as opposed to those of plasticity of behavior, with an animal being able to abandon stereotypy as required. However, even in an emergency, such as a predator encounter, a selective advantage probably would be conferred on an animal engaged in a familiar nightly routine.

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5. This animal was descended from wild stock captured by Dr. Paul Pearson in 1951 in the Ocala National Forest, Florida, and kindly made available to us by Dr. J. A. King.
6. The enclosure was similar in design to those described in (*1*) except that the wheel was 20 cm in diameter.
7. The light source was mounted to the east (*2*) and consisted of a cluster of four General Electric No. 44, miniature, 6.3-volt incandescent bulbs.
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Determination of Lateral Pharyngeal Wall Motion during Connected Speech by Use of Pulsed Ultrasound

Abstract. *Variations in the position of a point on the lateral pharyngeal wall relative to the external neck wall can be monitored by time-motion display of pulsed ultrasound. Such a portrayal is used to evaluate the lateral pharyngeal wall motion in normal and pathologic speakers during connected discourse.*

In normal speech production the lateral pharyngeal walls contribute to closure of the velopharyngeal port. The integrity of this closure is dependent upon a complex flap-valve sphincter involving the velum and the posterior and lateral walls of the pharynx. In some individuals, notably those with cleft palates, inadequate velopharyngeal closure may result from minimal lateral pharyngeal wall (L.P.W.) motion. The consequence of inadequate closure of the velopharyngeal valve may include hypernasality and an inability to impound sufficient intraoral breath pressure for normal speech production.

We have been developing a procedure to measure the motion of the L.P.W. by the use of pulsed ultrasound. Such a procedure can provide information on articulatory changes within the pharyngeal tube during speech production without extraneous devices in the vocal tract or exposure to radiation. In our procedure a 2.25-Mhz ultrasonic generator is used to produce pulsed ultrasound. Pulses from a transducer 1 cm in diameter are directed toward the L.P.W. from a point on the external neck wall approximately 1 cm below the angle of the mandible. The same transducer is used to send and receive ultrasonic signals and is moved through small angles until a signal from the L.P.W. is obtained. Essentially all of the ultrasonic energy is reflected at the tissue-air interface of the L.P.W. because the transmission of ultrasound in air is negligible for frequencies greater than 1 Mhz. The information contained in the reflected ultrasound beam is recorded on a storage oscilloscope using a time-motion method of display (see Fig. 1). Such a display presents distances between reflecting interfaces as a function of time. Distance calibrations are made by using known displacements in a water bath. With our unit under typical operating conditions it is possible to observe displacements of less than 1 mm.

Simultaneous motion pictures of the L.P.W. and the time-motion display during passive and active displacement of the pharyngeal wall have demonstrated that the displacements actually arise from motion of the L.P.W. External wall motion has been assessed by using a specially constructed water path extender which permitted recording of both external neck wall and the L.P.W. positions. The actual contribution of external neck wall to the motion recorded by the time-motion display is probably less than 1 mm.

Small intrasubject differences in recorded time-motion data are expected, owing to variations in probe angulation and placement. Tests were conducted to investigate the reproducibility of the static pharyngeal wall data obtained with our procedure. Data were obtained from one subject on separate days over a period of 2 months. The mean depth of the static pharyngeal wall of this subject was 27.7 mm with a standard deviation of 1.8 mm. The relative standard deviation of less than 7 percent is interpreted as satisfactory reproducibility.

The effect of connected speech on L.P.W. motion was determined by measurements taken from Polaroid pictures of the time-motion display. Displacements during the production of each phoneme were measured from the static pharyngeal wall position defined as the average of the pre- and post-utterance measures. At the level monitored, L.P.W. displacements as great as 5 mm

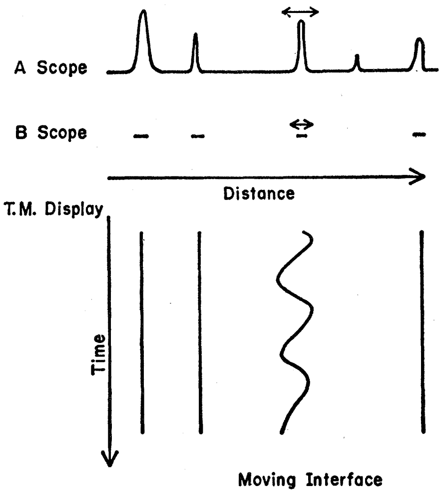

Fig. 1. Schematic representation of three types of ultrasonic display. Upper third of the figure illustrates the appearance of an A scope display, middle third shows a B scope display, and a time-motion display is presented in the lower third of the figure.