the inner and outer radii of the fluid shell is approximately ½. This case simulates convection in the liquid core of the earth when magnetic effects can be neglected. If convective motions do occur in the earth's core it is likely that they generate the earth's magnetic field (*4*). Although the Lorentz forces are dynamically important, it is necessary to investigate the nonmagnetic case in order to understand the origin of the geomagnetic field. The laboratory experiment is well suited for this purpose since it allows for the study of aspects of the problem which are not easily accessible to theoretical analysis, such as a differential rotation caused by the nonlinear interaction of the convection columns.

Figure 4 shows convection in a thin shell. The small thickness of the fluid layer permits the realization of a relatively high Ekman number without lowering the rotation speed of the apparatus below a value of approximately 60 rev/min, where effects of gravity become noticeable. The experiment demonstrates a convection pattern which was proposed in connection with a new theory of the solar differential rotation (*5*). By parameterizing the effects of small-scale motions in the solar atmosphere in terms of an eddy viscosity, it was shown that giant convection cells (*6*) of a form similar to that shown in Fig. 4 give rise to a differential rotation which agrees in all qualitative aspects with that observed on the sun. Although neither theory nor experiment is capable of simulating the detailed structure of solar convection, the strong north-south correlation of large-scale convection is borne out by the phenomenon of "active longitudes" and the north-south coherence of solar magnetic fields (*7*).

Measurements of the onset of convection as a function of rotation rate and temperature difference have been compared with the results of linear theory and will be published separately (*8*). The good agreement with the theoretical predictions indicates that this relatively simple experiment can be valuable for exploring and understanding the large variety of nonlinear processes which confront scientists studying the dynamics of convection in rotating planets and stars.

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11 August 1975

Activity of Nocturnal Primates: Influences of Twilight Zeitgebers and Weather

Abstract. *The time of onset of activity of bush babies* (Galago senegalensis), *slow lorises* (Nycticebus coucang), *and an owl monkey* (Aotus trivirgatus) *living in outdoor enclosures usually fell in certain illuminance ranges of dusk and kept pace with seasonal progressions of sunset time. Influences of cloud cover were variable, but excessive heat and cold were inhibitory. Accurate endogenous timekeeping and reliance on the most stable zeitgeber apparently maintain activities in synchrony with the rhythmically changing environment.*

Under natural conditions, activity rhythms usually become synchronized with (entrained to) the earth's rotational period as a result of responses to certain periodic environmental changes, or zeitgebers, of which illuminance is often the most important. For many animals the photic zeitgebers are believed to involve the twilight periods. Many animals customarily begin or cease activity during twilights (*1–3*), and simulated twilights influence the activity of numerous captive mammals (*4–8*).

It is virtually impossible to determine the isolated influences of twilights through field studies [but see (*3*)] because of the confounding influences of environmental variables, such as cloud cover, temperature, and food availability. The behavioral inconstancy during twilights may obscure functional relationships that only emerge when the naturalist's findings are complemented with results of controlled studies.

We are studying small and medium-sized mammals by monitoring locomotor activity in outdoor and indoor activity-wheel enclosures (*7, 9*). Natural light and weather are the primary variables outdoors, while the chief indoor variable is a cyclic light regime with artificial twilights. We report here briefly our outdoor findings for the activity onset and cessation times of seven individuals belonging to three species of nocturnal primates [see (*8*) for detailed results]. The ability of the animals to maintain entrainment in variable weather confirms certain a priori expectations about the role of twilights in modulating the endogenous physiological clock. We suggest a new role for the duplex retina as a physiological relay between twilight light changes and the endogenous clock.

Our animals included three African lesser bush babies (*Galago senegalensis*), three Asian slow lorises (*Nycticebus coucang*), and one male South American owl monkey (*Aotus trivirgatus*). All were mature, wild-caught, and fed as described (*6*). Two enclosures were used. The "roof" enclosure (*10*) was our primary data collecting system. It was located above a penthouse on the roof of the Life Sciences Building at the University of California, Los Angeles, and consisted of an activity wheel 122 cm in diameter adjoining a wire-mesh cage with a heated nest retreat. It was housed in a wire-mesh cubical, to the top and sides of which were fastened artificial plants in a very dense arrangement, giving both heavy cover and a seminatural setting.

The "run" enclosure was located nearby but 4 m lower. It contained an activity wheel and a sheltered nest retreat. The wheel in the run received only indirect light when the sun was low on the horizon, and it was more sheltered from both wind and rain than that on the roof. Thirty minutes before sunset the illuminance (all values measured at the bottom of the wheel) in the run was only 15 percent of that in the roof wheel; at sunset it was 44 percent. By 10 minutes after sunset the illuminances were equal.

All individuals adapted to locomotion in wheels as an activity outlet within a few days. Systems controls, monitoring, and data reduction methods have been described (*4, 11*). Digital printers and strip-chart recorders gave the times of initiation, duration, and cessation of activity (wheel revolutions) and half-hourly totals for wheel revolutions in both enclosures. Strip-chart analog records gave the time and instantaneous speed and direction of running in the roof enclosure; we also obtained half-hourly printouts of time spent running. Meteorological variables were recorded simultaneously (*7*) on the analog records from the roof enclosure.

All animals were almost strictly nocturnal [night plus twilights (*12*), Table 1]. An animal usually entered the wheel during dusk and became sustainedly active at times that generally correlated with light level (Fig. 1). Average starting times on the roof (excluding bush baby 3, March and April) ranged from 13.2 to 33.4 minutes after sunset, corresponding to 2.5 to 0.042 lux. The most consistent performance was that of bush baby 3 (Fig. 1, July and August). The mean absolute deviation (M.D.) from its mean emergence time relative to sunset was only 2.5 minutes. Starting times for the slow lorises in the more sheltered run were affected very little by the illuminance differences, whereas bush babies 2 and 3 emerged appreciably earlier in the run than on the roof.

Seasonal progressions in the time of sunset were at the rate of 0 to 94 seconds per day. In many instances the emergence times of all three species kept pace closely with these progressions (Fig. 1 and Table 1). In some instances emergence times varied considerably, but there was not always a correlation with variable weather and cloud cover. Thus, while the lowest variability of emergence times of the bush babies occurred on days with clear mild afternoons, high variability also occurred in such weather.

In some cases, heavily overcast sky engendered little variability, while in others overcast led to the earliest emergence times. There was no apparent systematic effect of variable late afternoon cloud cover over the periods when emergences were variable for the slow lorises and owl monkey, but these animals emerged later in both cool rainy weather and clear, exceptionally hot weather. Sustained activity usually began on first emergence but on some days it commenced later in the evening (Fig. 1).

Retiring times typically had a much greater M.D. than emergence times, and in 10 of the 18 instances (Table 1) the retiring times occurred at night. The 8 that occurred during dawn ranged from 12 to 43 minutes before sunrise, corresponding to illuminances of 0.007 to 3.5 lux. In most instances the animals retired promptly on ceasing sustained activity, but on some occasions there were subsequent brief reemergences. The most consistent retiring times were those of bush baby 3 (Table 1; M.D., 3.4 minutes). There was a notable tendency for bush babies to retire earliest. In several cases, retiring times kept pace with seasonal progressions in sunrise.

The major meteorological variables influencing retiring times were cloud cover, precipitation, and occasional extreme temperatures and wind. In contrast, a sudden shift of slow loris 3 to earlier retiring times (*8*) from May through July (Table 1) did not appear to be related to changing cloud cover, and the relatively variable retiring times of slow loris 2 during July and August occurred on mostly clear nights. The latest and least variable retiring times (bush baby 3, March and April) also occurred in clear weather.

Precipitation inhibited the species to different degrees. The bush babies were the most sensitive, sometimes being inhibited by heavy mist alone. The owl monkey (March through June) was sometimes active in light rain, but its earliest retiring times occurred in rainy weather. A single exposure to light rain did not notably affect slow loris 1. The other two slow lorises were not inhibited even by heavy rain on very cool nights and mornings. In fact, rain sometimes prolonged activity until after sunrise (slow loris 3, November and December).

Weather extremes had notable effects. Slow loris 3 retired as early as 314 minutes before sunrise on exceptionally cold nights (2° to 7°C, November and December). Slow loris 2 retired from 113 to 215 minutes before sunrise on several windy nights (October). Both the owl monkey and slow loris 3 emerged very late after very hot days, and the latter also retired very early the next morning (186 minutes before sunrise).

Our findings for nocturnal phasing of these animals agree with limited observations in the wild (*13*), none of which yielded systematic data on seasonal progressions of onset or cessation times. The endogenous clock is capable of timekeeping accuracy to within a fraction of a minute in rodents (*9*) and to within 1 to 3 minutes in these primates (*6*). Yet even in clear, mild weather, emergence times often varied considerably, which demonstrates that other factors, both meteorological and physiological, can override direct influences of the endogenous clock, the photic zeitgeber, and the nonzeitgeber ranges of dim light. However, there was no tendency to compensate for weather-induced inactivity by becoming active during the normal rest period.

The difference in light environment in the run (shielded from sunlight near the horizon) as opposed to the roof enclosure would be similar to that occurring in lower (stronger light-filtering) as opposed to higher (weaker light-filtering) levels of a vegetation canopy. Accordingly, in the run compared to on the roof, the advanced emergence times of bush babies but not of

Table 1. Emergence and retiring times relative to sunset and sunrise, and percentages of night and twilight activity. Abbreviation: M.D., mean absolute deviation.

Animal*	Months studied	Days studied (No.)	Emergence time after sunset (minutes)		Retiring time before sunrise (minutes)		Night activity (%)	Twilight activity (%)		
			Mean	M.D.	Mean	M.D.		Dusk	Dawn	Total
Bush baby 1	Mar.	16	26	9.4	63	32.7	91.7	6.5	1.8	8.3
	Sept.–Oct.†	21	33	6.2	35	14.2				
Bush baby 2	Apr.–May	18	13	4.2	220	59.2	86.5	13.5	0.1	13.6
	June–July†	32	–5	4.0	59	34.8				
	Aug.–Sept.†	32	5	3.2	100	51.1				
Bush baby 3	Mar.–Apr.	14	110	100.0	12	3.4	85.8	1.0	13.2	14.3
	Apr.–May†	34	4	8.4	110	42.8				
	July–Aug.	28	18	2.5	59	23.1	90.4	8.3	1.3	9.6
Slow loris 1	Aug.–Sept.	18	18	5.5	19	4.6	94.1	2.9	3.1	6.0
	Oct.–Nov.†	21	36	7.6	51	34.1				
Slow loris 2	July	14	21	8.7	9	8.5	91.6	3.5	4.5	8.0
	July–Aug.†	16	37	36.9	34	12.2				
	Oct.–Nov.†	19	20	6.8	54	40.6				
Slow loris 3	Sept.–Oct.	38	25	4.8	26	19.9	94.7	3.1	2.3	5.4
	May–July†	65	11	7.4	16	20.8				
	Nov.–Dec.†	28	30	9.6	130	73.8				
Owl monkey 1	Nov.–Dec.	30	23	5.2	110	23.1	96.4	3.6	0	3.6
	Mar.–June	100	23	4.5	43	8.7				

*Odd-numbered animals were males, even-numbered ones were females. †Experiments carried out in run without recording data on percentages of night and twilight activity.

slow lorises suggest possible differences between these species' twilight responses to light or their reliance on activity-onset signals from the endogenous clock.

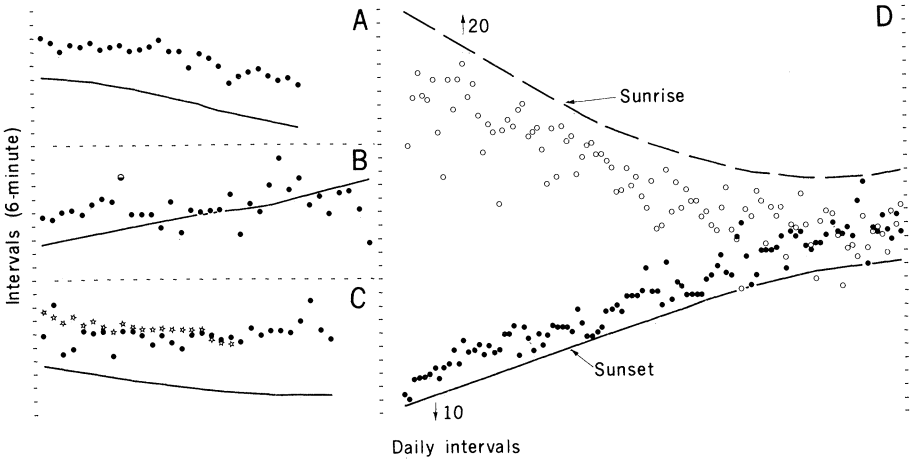

Fig. 1. Day-by-day activity onset (closed circles) and cessation (open circles) times of bush baby 3 (A and B) and owl monkey 1 (C and D) relative to times of sunset (solid lines) and sunrise (dashed line). The half-filled circle (B) denotes a brief emergence not followed immediately by sustained activity. The night period for owl monkey 1 has been omitted, and the sunset and sunrise curves have been displaced 10 and 20 minutes, respectively, relative to the onset and cessation points, to conserve space (small arrows with adjacent numbers indicate proper locations of the curves). Stars (C) denote the times of 2.3-lux illuminance for a period of 20 days of variable cloudy weather. Bush baby 3 was in the roof enclosure during July and August (A), and in the run during April and May (B). Owl monkey 1 was on the roof during November and December (C), and on the roof from March through June (D).

A priori, we entertain certain expectations for twilight zeitgebers. We consider only nocturnal animals, but similar reasoning may be applied to others. One expects some aspect of dusk to be the "primary" zeitgeber for many nocturnal animals, because becoming active as soon as evening light conditions allow might confer advantages for survival (*5*). Similar advantages would not necessarily accrue to animals active during dawn; for individuals that had obtained sufficient food during the night, it would usually be advantageous to avoid needless dawn exposure. For many nocturnals, though, some aspect of dawn must be a "secondary" zeitgeber, since only by coordinating both dawn and dusk zeitgebers could changes in day length be detected.

A second expectation is that selection would usually favor individuals that reset their endogenous clocks by the twilight phases most stable on a day-to-day basis, that is, with the sun below the horizon, for under these conditions ambient light is least affected by inclement weather (*8, 14*). For example, 20 minutes before sunset illuminance may vary from 300 to 3000 lux. However, 20 minutes after sunset (sun 4° to 5° below horizon) the light is indirect and more diffuse, with markedly less temporal variability, regardless of cloud cover (see plot for owl monkey, November and December, Fig. 1). Furthermore, the three to four times greater rate of decrease of illuminance 20 minutes after sunset compared to 20 minutes before sunset would facilitate detection of dusk illuminance changes (*15*).

Our findings for carnivores (*7*) and primates, and other data (*1, 3*) act as guides to the specific twilight zeitgeber illuminance ranges. But an a priori consideration offers a clue consistent with these data; the immediate physiological "relay" of the photic zeitgebers in many vertebrates with duplex vision [even where one type of visual cell vastly predominates, as is the case for the animals of this study (*16*)] may be the shift between adaptations for bright-light and dim-light vision (*8*). Accordingly, the zeitgebers would be the specific twilight periods when this shift (*17*) takes place (the rod threshold, the cone threshold, or the region of functional overlap).

Our present findings are consistent with these expectations. Apparently the endogenous clock usually aroused our primates at about the time of sunset but well before the zeitgeber. If light conditions were favorable, the evening's activity commenced. If the illuminance was too great, only a brief emergence was recorded (*18*); the animal rested, entered or left the wheel, groomed, or ate before eventually commencing sustained locomotion.

Unless our animals had built-in twilight schedules or continuously monitored light during deep sleep, the many cases in which they emerged and retired in pace with seasonal sunset and sunrise progressions provide almost conclusive evidence that some aspects of twilights are the photic zeitgebers. In particular, since bush baby 3 (fig. 1, July and August) began activity in the range of 0.2 to 2.8 lux (12 to 24 minutes after sunset), it seems likely that the primary zeitgeber for this individual was in or somewhat below this range [in man, the cone threshold is 0.25 lux (*20*)]. The dawn zeitgeber may have been without effect when animals retired very early, whereas when activity continued through dawn, it doubtless was registered. But it was not unusual for an animal to continue activity after sunrise in overcast weather. Occasional brief dawn reemergences after early activity cessations suggest that retired animals continued, for a time, to maintain awareness of ambient illuminance.

Highly consistent emergence and cessation times during some periods of markedly variable day-to-day cloud cover support our suggestion that specific stable postsunset and presunrise twilight segments are the photic zeitgebers for these primates. This evidence is most convincing for cases of rapid day-to-day progression of sunset and sunrise times. With small or zero progression rates, the findings might be explained equally well by assuming that activity-onset signals from the circadian endogenous clock took precedence over light conditions. Our indoor studies of these primates using around-the-clock 4-hour light cycles (*6*) have shown that this can occur.

The seasonal changes in sunset and sunrise times in Los Angeles occur 2 to 3 times faster than in the subtropics and tropics, while the corresponding changes in daylength are greater and the twilights last longer. Accordingly, the animals had to make much greater seasonal adjustments using twilight cues that were more gradual and difficult to detect. In view of the fact that the ancestors of these primates were not exposed to temperate latitude conditions since at least the Miocene, our findings suggest a high degree of efficiency of entrainment of biological clocks by photic zeitgebers.

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15. Current parallel telemetric field studies of several rodent species by L. Shields, from this laboratory, suggest the generalization that times of onset and cessation of activity (or bouts of activity) tend to center on the most abruptly occurring light changes that the animals experience, whether these be deep twilights or merely local sunset and sunrise. In this connection, Pariente (*3*) noted that most returns of the Malagasy lemur, *Phaner furcifer*, to the nest took place at a time when the rate of increase of dawn illuminance was maximal.
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17. In this connection, Pariente (*3*) noted that *Phaner furcifer* in the wild become highly active at just the time when human vision is shifting from light-adapted to dark-adapted, and he noted that "it is conceivable" that the mechanism for discriminating a specific illuminance level "would call for a duplex cone-rod system."
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15 September 1975; revised 28 October 1975

Breast Cancer Patients: Substance in Blood Causing Acceleration of Erythrocyte Sedimentation Rate

Abstract. The frequency distribution curve of the erythrocyte sedimentation rates obtained from a population of 3523 normal females was compared with the distribution found in 544 patients with benign breast disease and that for 385 patients with carcinoma of the breast. No significant difference was found between the normal female population and patients with benign lesions of the breast. This was in contrast to the distorted distribution curve of erythrocyte sedimentation rates exhibited by the population of patients having malignant breast lesions. An unknown substance present in the blood plasma of the cancer patients appears to be responsible for the abnormal sedimentation rate phenomenon.

This report describes the presence of an unknown substance in the blood of patients with breast cancer that is not exhibited by large populations of either normal females or patients with a variety of benign breast lesions. The existence of this component is inferred and detected through its influence in causing a significant acceleration in the erythrocyte sedimentation rate (ESR) of specific cancer patients. The ESR differences were established through a comparison of the frequency distribution of ESR data obtained from several thousand individuals.

The data of this report are not offered in their present form for clinical application to either diagnosis or prognosis of mammary carcinoma. Of more relevance to the cancer process are the physiological implications of an unknown substance in the plasma of patients having early malignant breast lesions. Inasmuch as this substance was not detected in a population of patients having benign breast nodules that were clinically indistinguishable from the malignant lesions, its characterization is pertinent in furthering an understanding of specific physiological aspects of neoplasia.

Double-blind ESR tests were run on large populations of normal females and various patients examined in a cancer clinic (*1*). Most of those exhibiting breast nodules and other suspected malignant lesions were admitted to the hospital for further tests and possible surgery. Reported here are the analyses of the comparative ESR findings for the patients that were diagnosed following biopsy or surgery as having either benign or malignant breast lesions. The generous size of both the normal and patient populations examined permitted the resulting data to be analyzed as ESR frequency distribution curves of the normal and disease categories rather than as simple averages of the individual values found in each patient group. This type of analysis provides a more sensitive and reliable basis for detecting significant ESR differences between sizable populations.

The ESR baseline data for normal females were obtained from a population of presumed healthy women who voluntarily submitted themselves for a standard physical and hematological examination at a cancer detection clinic (*1*). This "normal" ESR distribution curve was derived from a population of 3523 women of various ages, and is depicted by the shaded areas in Figs. 1 and 2. The only consecutive blood samples that were not included in the composition of this "normal" curve were those from the small number of individuals whose examination revealed a suspected malignancy or other serious pathologies, and who thus were referred to the hospital for further examination. Such sample discards represented less than 1 percent of the women examined (*1*).

The two shaded areas of Figs. 1 and 2 show the relatively minor differences in the distribution of ESR values with and without hematocrit correction. The theoretical purpose of such correction of the observed ESR rate lies in the potential influence of the blood hematocrit, or percentage of packed erythrocytes, upon the sedimentation rate of the red blood cells. All other factors being equal, the higher the percentage of erythrocytes in the blood, the slower the ESR. With conspicuous anemia the ESR thus tends to be faster, while it is slower in patients with polycythemia. Correction of the observed ESR for hematocrit differences therefore tends to nullify this variable, yielding ESR values that are unaffected by alterations in blood viscosity and related physical factors associated with tendencies toward polycythemia or anemia (*2*).

It follows that if there were a systematic difference in the hematocrits of any of the normal or patient populations tested, its effect would be exhibited in the uncorrected ESR curves and remedied in the corrected ESR values. This is not a significant factor in any of the groups examined (Figs. 1 and 2), and the accelerated ESR values observed in the patients with malignant breast lesions cannot therefore be ascribed to anemia or other systematic hematocrit alterations (*3*).

The similarity of the distribution of both the corrected and uncorrected ESR values of women having benign breast lesions to those of women in the normal population is shown in Fig. 1. The benign lesions were detected by clinical examination and could not be distinguished with certainty, at that point, from carcinoma. The final diagnosis was established by surgical removal or biopsy of the lesion or nodule and microscopic examination by experienced pathologists (*4*). The following breast lesions were among those diagnosed as benign: cysts, abscesses, mastitis, duct papilloma, fibroadenoma, fat necrosis, lipoma, and fibrocystic tumors. Patients with these conditions were combined to produce the ESR frequency distribution curve in Fig. 1.

The ESR data obtained from the patients who were subsequently shown to have some variety of breast carcinoma are depicted in Fig. 2. There was a significant shift in the ESR values to the right of the normal distribution curve, which demonstrates that a sizable percentage of the patients with mammary carcinoma had higher ESR values. These differences are