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186. PHASE RELATIONS OF CIRCADIAN RHYTHMS: ANIMALS

Some information provided herein is limited in value since the original articles neither reported on sampling variability nor provided numerical data for a statistical estimation of rhythm parameters, as indicated in the table by the lack of confidence limits for phase and amplitude values. **Phase Marker:** that feature of circadian rhythm chosen for indication of phase relations--e.g., marker can be crest (high point) of rhythm. Crest is italicized when determined by harmonic analysis--e.g., the "cosinor" method (*see* Part I, reference 23); any effect of a nonsinusoidal shape of circadian rhythmic function then remains unevaluated. Unless otherwise stated in the literature, the crest-phase estimate or sample phase, φ, is a statistical average computed from data covering an appropriate number of circadian cycles. The data may be obtained "longitudinally" from one individual, and/or "transversely" from a group of comparable individuals during one or a few cycles. *Abbreviations and Symbols:* φ = sample phase (*see* above); $\Delta\varphi$ = any consistent change in φ, unless otherwise stated in the reference; $-\Delta\varphi$ = delaying change (one or a few periods lengthened); $+\Delta\varphi$ = advancing change (one or a few periods shortened); $\sim$ = approximately; Δt = time interval between

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consecutive observations; L = light; D = dark; LL = continuous light; DD = continuous dark; L_f = fluorescent lamps; L_i = incandescent lamps. Figures in parentheses after L give intensity in lux (values originally reported in footcandles have been multiplied by 10.8). Figures in brackets after L or D give either duration, or span of clock hours in local time--e.g., L[12 hr]:D[12 hr] = a cycle of 12 hours of light alternating with 12 hours of darkness; $L_i(50)[06^{00}-18^{00}]$: $D[18^{00}-06^{00}]$ = a cycle of light at an intensity of 50 lux (incandescent source) from 6:00 a.m. to 6:00 p.m., alternating with darkness from 6:00 p.m. to 6:00 a.m.

Part I. REGULARLY ALTERNATING LIGHT: DARK CYCLE

No. of Days: time span covered by observations. **Synchronizer Schedule:** lighting regimen. **Series Average:** the mean from all subjects and sampling times; "$\bar{X}$ = 100%" indicates data were reported only as percentage deviations, at different time points, from the overall mean value. **Circadian Amplitude:** the difference between the highest (or lowest) value and mean value in a sinusoidal oscillation; determined by harmonic analysis. Values in parentheses are confidence limits roughly equivalent to estimate "b" (*see* Introduction). Values in brackets give one-half the range of group means over the circadian period, and were included as an approximation of circadian amplitude when only group means at different clock hours were available. **φ of Rhythm from Different Origins** is given redundantly in several units: in degrees from "Mid-D" or "Mid-L" (with 360° = period of rhythm--e.g., 24 hr); in hours from "light on" (L-on) or "light off" (L-off); and in local clock time (only for the 24-hour synchronized rhythm of man). A minus value denotes that the phase marker, on the rhythm, occurred later (by the span specified--e.g., in degrees) than the temporal reference point or time origin. Values in parentheses are approximate confidence limits, 95% or 99%, indicated by one or two asterisks, respectively.

	No. of Subjects	No. of Days [Δt, hr]	Synchronizer Schedule	Biological Variable [Phase Marker]	Series Average	Circadian Amplitude	φ of Rhythm from Different Origins	Reference
				Diurnally Active[1]				
	Homo sapiens[2]							
1	193♂, ~20 yr[3]			Epidermal mitoses, % of cells [*Crest*]	1.9	1.3(0.6-2.0)	Local 00^{00}: 00^{44} (22^{50}-02^{38})*	41
2	6	1+ [4]	L[08^{00}-23^{00}]: D[23^{00}-08^{00}]	Skin reactivity to histamine [*Crest*]	$\bar{X}$ = 100%	24(16-33)	Mid-D: -290° Local 00^{00}: 22^{52}	38
3	13♂, 18-35 yr[4]	1 [~3]	L[07^{00}-23^{00}]: D[23^{00}-07^{00}]	17-Hydroxycorticosteroid, μg/100 ml plasma [*Crest*]	14	4(2-6)	Mid-D: -100° (-45 to -144)** Local 00^{00}: 09^{42} (06^{00}-12^{36})*	22
4	16♂, 18-35 yr[4]	1 [~3]	L[07^{00}-23^{00}]: D[23^{00}-07^{00}]	Electrocortical activity, arbitrary units [*Crest*]	49	5(2-8)	Mid-D: -159° (-123 to -193)** Local 00^{00}: 13^{36} (11^{14}-15^{53})*	9
5	4♂, 20-42 yr[4]	1 [~6]	L[06^{45}-23^{15}]: D[23^{15}-06^{45}]	Testosterone, μg/100 ml plasma [*Crest*]	0.72	0.11(0.04-0.18)	Mid-D: -128° (-61 to -210)** Local 00^{00}: 11^{32} (07^{05}-17^{00})*	7
6	11♂, 21-25 yr[4]	1 [~1.5]	L[07^{30}-23^{30}]: D[23^{30}-07^{30}]	Oral temperature, °C [*Crest*]	36.6	0.4(0.3-0.5)	Mid-D: -200° (-181 to -221)** Local 00^{00}: 16^{49} (15^{34}-18^{13})*	19
7				Eosinophils, cells/mm³ blood [*Crest*]	347	61(40-82)	Mid-D: -324° (-286 to -346)** Local 00^{00}: 01^{07} (22^{33}-02^{33})*	
8	1♂, 37 yr[4]	34 [~3.3]	L[06^{45}-23^{15}]: D[23^{15}-06^{45}]	Oral temperature, °C [*Crest*]	36.7	0.33(0.27-0.39)	Mid-D: -191° (-183 to -199)** Local 00^{00}: 15^{44} (15^{12}-16^{17})*	27
9				Urine volume, ml/hr [*Crest*]	45	9(6-12)	Mid-D: -88° (-62 to -118)** Local 00^{00}: 08^{54} (07^{10}-10^{54})*	
10				Urine sodium, mEq/hr [*Crest*]	8	2.09(1.27-2.91)	Mid-D: -94° (-71 to -120)** Local 00^{00}: 09^{16} (07^{44}-11^{02})*	
11				Urine potassium, mEq/hr [*Crest*]	4	1.07(0.64-1.50)	Mid-D: -141° (-117 to -164)** Local 00^{00}: 12^{26} (10^{47}-13^{54})*	

[1] Or active at undefined times. [2] Approximate rest or sleep span of the daily regimen corresponds roughly to the D span of the synchronizer schedule. [3] Observations on different subjects. [4] Repeated observations.

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186. PHASE RELATIONS OF CIRCADIAN RHYTHMS: ANIMALS

Part I. REGULARLY ALTERNATING LIGHT: DARK CYCLE

	No. of Subjects	No. of Days [Δt, hr]	Synchronizer Schedule	Biological Variable [Phase Marker]	Series Average	Circadian Amplitude	φ of Rhythm from Different Origins	Reference
				Diurnally Active[1]				
12	*H. sapiens*[2] 1♂, 37 yr[4]	34 [~3.3]	L[06^{45}-23^{15}]: D[23^{15}-06^{45}]	Urine 17-hydroxycorticosteroid, mg/hr [*Crest*]	0.4	0.17(0.13-0.20)	Mid-D: -130° (-117 to -144)** Local 00^{00}: 11^{38} (10^{47}-12^{33})*	27
13				Urine 17-ketosteroid, mg/hr [*Crest*]	0.5	0.1(0.07-0.14)	Mid-D: -99° (-78 to -126)** Local 00^{00}: 09^{38} (08^{14}-11^{28})*	
14	*Fringilla coelebs*, 3[4]	4	L(400)[12 hr]: L(0.4)[12 hr]	Activity [Onset]			Mid-D: -90°; L-on: 0 hr	1
15	*Gallus domesticus*, 190♂, 14 days[5]	1 [2]	L[03^{00}-21^{00}]: D[21^{00}-03^{00}]	Liver glycogen, % [Crest]	2.3	[1.2]	Mid-D: ~-255°; L-on: ~-14 hr	42
16	*Passer domesticus*, 32	[0.25-3][6]	Natural lighting (March)	Mitoses in testes [Crest]			Mid-D: ~-45°; L-on: ~-21 hr	39
17	*Tetranychus urticae*, 4500[5]	[3-4]	L[08^{00}-22^{00}]: D[22^{00}-08^{00}]	Susceptibility[7] to ether, chloroform, & carbon tetrachloride; minutes recovery time[8] [Crest]	25	[3]	Mid-D: ~(-75 to -120°); L-on: ~0.3 hr	33
18	*Drosophila pseudoobscura*, cultures		L[2 hr]:D[22 hr]	Eclosion [Median]			Mid-D: ~-135°; L-on: -22 hr	36
			L[8 hr]:D[16 hr]	Eclosion [Median]			Mid-D: ~-120°; L-on: 0 hr	
			L[12 hr]:D[12 hr]	Eclosion [Median]			Mid-D: ~-200°; L-on: -3.3 hr	
			L[16 hr]:D[8 hr]	Eclosion [Median]			Mid-D: ~-120°; L-on: -4 hr	
			L[20 hr]:D[4 hr]	Eclosion [Median]			Mid-D: ~-75°; L-on: -3 hr	
19			Skeleton photoperiods: 1-12 hr, with L:D span = 24 hr[9]	Eclosion [Median]			φ from first L signal similar to that observed with complete photoperiods (*see* entry 18)	
20			L[15 min]:D[20 hr, 45 min]	Eclosion [Median]			Mid-D: -270°; L-on: -5.5 hr	
			L[15 min]:D[22 hr, 15 min]	Eclosion [Median]			Mid-D: -200°; L-on: -1.4 hr	
			L[15 min]:D[23 hr, 25 min]	Eclosion [Median]			Mid-D: -180°; L-on: -23.3 hr	
			L[15 min]:D[24 hr, 45 min]	Eclosion [Median]			Mid-D: -60°; L-on: -16.9 hr	
				Nocturnally Active				
21	*Mesocricetus auratus*, 3[4]	10 [1]	L[12 hr]:D[12 hr]	Activity [Onset]			Mid-L: ~-90°; L-off: ~0	1
22	*Mus musculus* ♂	1 [~4]	L[08^{00}-20^{00}]: D[20^{00}-08^{00}]	Susceptibility[7] to pentobarbital anesthesia, duration [Crest]	$\bar{X}$ = 100%	30%	Mid-L: ~0; L-off: ~-18 hr	5
23	84♂, 5 wk	1 [4]	L$_f$[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Mitoses in liver parenchyma [*Crest*]	$\bar{X}$ = 100%	"147"% (37-257)	Mid-L: -13°(-330 to -56)*; L-off: -18.8 hr	12
24	84	1 [4]	L$_f$[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Mitoses in pinnal epidermis [*Crest*]	$\bar{X}$ = 100%	44% (26-62)	Mid-L: -21°(-359 to 43)*; L-off: -19.4 hr	11

[1] Or active at undefined times. [2] Approximate rest or sleep span of the daily regimen corresponds roughly to the D span of the synchronizer schedule. [4] Repeated observations. [5] Single observations. [6] Each bird was studied on the day after capture, at a single time point which varied among birds. [7] Susceptibility rhythms refer to physiological changes dependent on the times (circadian system phases) at which exposure to the noxious agent occurred. [8] Evaluation based on recovery time of 50% of subjects. [9] e.g., L[15 min]:D[11.5 hr]:L[15 min]:D[12 hr].

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186. PHASE RELATIONS OF CIRCADIAN RHYTHMS: ANIMALS

Part I. REGULARLY ALTERNATING LIGHT: DARK CYCLE

	No. of Subjects	No. of Days [Δt, hr]	Synchronizer Schedule	Biological Variable [Phase Marker]	Series Average	Circadian Amplitude	φ of Rhythm from Different Origins	Reference
				Nocturnally Active				
	M. musculus							
25	>60	1 [4]	L_f[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Mitoses in adrenal cortical parenchyma [*Crest*]	$\bar{X}$ = 100%	39% (23-55)	Mid-L: -150° (-127 to -174)*; L-off: -4.0 hr	16
26				Mitoses in adrenal cortical stroma [*Crest*]	$\bar{X}$ = 100%	30%	Mid-L: -165° (-106 to -224)*; L-off: -5.0 hr	
27	>60[4,10]	1 [4]	L_f[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Gross motor activity [*Crest*]	$\bar{X}$ = 100%	65% (23-107)	Mid-L: -160° (-123 to -198)*; L-off: -4.7 hr	16
28	>60[5,10]	1 [4]	L_f[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Blood eosinophils [*Crest*]	$\bar{X}$ = 100%	98%	Mid-L: -359° (-340 to -378)*; L-off: -17.9 hr	18
29	>60[5,10]	1 [4]	L_f[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Colonic temperature, °C [*Crest*]	36.4	1.2(1.0-1.4)	Mid-L: -171° (-162 to -179)*; L-off: -5.4 hr	20
30	>60[10]	1 [4]	L_f[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Adrenal corticosterone [*Crest*]	$\bar{X}$ = 100%	21% (9-33)	Mid-L: -85°(-54 to -117)*; L-off: -23.7 hr	15
31	>60[10]	1 [4]	L_f[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to ethanol, % mortality[11] [*Crest*]	39	16(9-23)	Mid-L: -107° (-80 to -134); L-off: -1.1 hr	26
32	B6, 270♂	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to acetylcholine, % mortality[12] [Crest]	~76	[14]	Mid-L: ~-120°; L-off: ~-2 hr	25
	Bagg albino							
33	360	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Adrenal reactivity to ACTH, in vitro [Crest]	$\bar{X}$ = 100%	[75%]	Mid-L: -240°; L-off: -10 hr	43
34	120♂, 10-15 wk	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Inorganic phosphorus, μg/ml plasma [*Crest*]	69	10.1(8.2-12.1)	Mid-L: -326°; L-off: -15.7 hr	32
35	120♂, 4-5 mo	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to ouabain, % mortality[13] [Crest]	45	[18]	Mid-L: ~-300°; L-off: ~-14 hr	17
36	104♂♀[5]	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Change in serum corticosterone after ACTH injection, %[14] [Crest]	~210	[110]	Mid-L: ~-180°; L-off: ~-6 hr	25
37	120♂♀, mature	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to endotoxin, mortality[15] [*Crest*]	$\bar{X}$ = 100%	71%(47-95)	Mid-L: -37°(-18 to -57)*; L-off: -20.5 hr	21
38	340♀, 2-3 mo		L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Hypophyseal adrenocorticotropic function, in vitro[16] [Crest]	$\bar{X}$ = 100%	[30%]	Mid-L: ~0°; L-off: ~-18 hr	44
	Bagg albino & D8							
39	120♂, mature	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Kidney transamidinase [Crest]	$\bar{X}$ = 100%	[10%]	Mid-L: ~-60°; L-off: ~-22 hr	45
40	~60♂♀[5,17]	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Serum corticosterone [*Crest*]	$\bar{X}$ = 100%	45%(34-56)	Mid-L: -48°(-34 to -62)*; L-off: -21.2 hr	16
	Bagg albino & other strains							
41	120♂, 4 mo	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Adrenal succinic dehydrogenase [Crest]	$\bar{X}$ = 100%	[25%]	Mid-L: ~-60°; L-off: ~-22 hr	10
42	440♂, mature	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to methopyrapone, mortality[18] [Crest]	$\bar{X}$ = 100%	[90%]	Mid-L: ~-60°; L-off: ~-22 hr	8
43	C57BL, ~100♂	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to Fluothane, % mortality[19] [Crest]	~17	[13]	Mid-L: ~-180°; L-off: ~-6 hr	31

[4] Repeated observations. [5] Single observations. [7] Susceptibility rhythms refer to physiological changes dependent on the times (circadian system phases) at which exposure to the noxious agent occurred. [10] *See also* Part IV. [11] Evaluation 4 hours after intraperitoneal injection. [12] Evaluation within minutes after injection. [13] Evaluation 10 minutes to 1 week after injection. [14] Evaluation 15 minutes after injection. [15] Evaluation 1 week after injection. [16] Adrenals removed at 04^{00} and incubated with hypophyseal glands removed at different clock hours. [17] Various ages. [18] Evaluation 6 hours after injection. [19] Evaluation 7 minutes after exposure to vapor.

continued

Part I. REGULARLY ALTERNATING LIGHT: DARK CYCLE

	No. of Subjects	No. of Days [Δt, hr]	Synchronizer Schedule	Biological Variable [Phase Marker]	Series Average	Circadian Amplitude	φ of Rhythm from Different Origins	Reference
	Nocturnally Active							
	M. musculus D8							
44	~120, 5 wk[5]	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to audiogenic convulsions[20] [*Crest*]	$\bar{X}$ = 100%	67% (31-103)	Mid-L: -128° (-98 to -159)*; L-off: -2.6 hr	13
45	384♀	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to dimethylbenzanthracene, % with breast cancer[21] [Crest]	~36	[9]	Mid-L: ~-60°; L-off: ~-22 hr	14
46	D8 & C57BL, 260♂, mature	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to librium[22] [Crest]	$\bar{X}$ = 100%	[30%]	Mid-L: ~-180°; L-off: ~-6 hr	30
47	DBA/2, ~200♂, 5-11 wk[5]	3 [4]	L[08^{00}-20^{00}]: D[20^{00}-08^{00}]	Susceptibility[7] to hexafluorodiethyl ether, sec for convulsions [Crest[23]]	~380	[40]	Mid-L: ~-150°; L-off: ~-4 hr	6
48	Swiss-Webster & C3H, 60♂	1 [4]	L[07^{00}-19^{00}]: D[19^{00}-07^{00}]	Susceptibility[7] to whole body X-irradiation, days for 50% mortality [Crest[23]]	~8	[2.5]	Mid-L: ~-195°; L-off: ~-7 hr	37
	ZBC3							
49	120♂, 4-5 wk	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Liver glycogen, mg/g [*Crest*]	17.1	15.8(14-17.6)	Mid-L: -294° (-288 to -300)*; L-off: -13.6 hr	3
50	84♂, 4-5 wk	1 [4]	L_f(10-150)[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Liver DNA uptake of P^{32} [*Crest*]	$\bar{X}$ = 100%	48%	Mid-L: -270° (-196 to -346)*; L-off: -12 hr	
51				Liver RNA uptake of P^{32} [*Crest*]	$\bar{X}$ = 100%	14% (9-19)	Mid-L: -177° (-156 to -199)*; L-off: -5.8 hr	
52				Liver phospholipid uptake of P^{32} [*Crest*]	$\bar{X}$ = 100%	13% (9-17)	Mid-L: -164° (-146 to -182)*; L-off: -4.9 hr	
	Rattus norvegicus							
53	36	1 [4]	L_f[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Adrenal pantothenate, mμg/mg fat-free dry wt [Crest]	~140	[20]	Mid-L: ~-180°; L-off: ~-6 hr	10
54	97♀	1 [2]	L[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Hypophyseal prolactin, I.U./mg [Crest]	~0.05	[0.05]	Mid-L: ~-60°; L-off: ~-22 hr	4
	Sprague-Dawley							
55	40, 6-10 mo	1 [6]	L_f[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to pentobarbital, % mortality [Crest]	48	[25]	Mid-L: ~-150°; L-off: ~-4 hr	34
56	90, 6-10 mo	2 [2-6]	L_f[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Susceptibility[7] to tremorine, % mortality [Crest]	58	[30]	Mid-L: ~-180°; L-off: ~-6 hr	
57	60♂	2 [1-6]	L[08^{00}-20^{00}]: D[20^{00}-08^{00}]	Thyroid-stimulating hormone, U.S.P. milliunits/hypophysis [Crest]	~160	[57]	Mid-L: ~-270°; L-off: ~-12 hr	2
58	~190♂, 350-400 g[5]	1 [2]	L[06^{00}-18^{00}]: D[18^{00}-06^{00}]	Neutrophils/mm³ blood [*Crest*]	2220	626(328-924)	Mid-L: -304° (-277 to -331)*; L-off: -14.3 hr	35
59				Eosinophils/mm³ blood [*Crest*]	293	96(51-141)	Mid-L: -318° (-291 to -345)*; L-off: -15.2 hr	
60				Lymphocytes/mm³ blood [*Crest*]	12,200	2820 (2020-3620)	Mid-L: -305° (-289 to -321)*; L-off: -14.3 hr	

[5] Single observations. [7] Susceptibility rhythms refer to physiological changes dependent on the times (circadian system phases) at which exposure to the noxious agent occurred. [20] Evaluation within 60 seconds after exposure to noise. [21] Evaluation several months after oral administration. [22] Evaluation based on mean survival time. [23] Crest refers to maximum susceptibility, interpreted as the inverse of response latency.

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Part I. REGULARLY ALTERNATING LIGHT: DARK CYCLE

	No. of Subjects	No. of Days [Δt, hr]	Synchronizer Schedule	Biological Variable [Phase Marker]	Series Average	Circadian Amplitude	φ of Rhythm from Different Origins	Reference
	Nocturnally Active							
	R. norvegicus Sprague-Dawley							
61	14♀, 6 mo[4]	18 [~1]	$L_f(400)[06^{00}-18^{00}]$: $D[18^{00}-06^{00}]$	Intraperitoneal temperature, °C[24] [*Crest*]	37.3	0.6(0.5-0.7)	Mid-L: -184° (-178 to -190)**; L-off: -6.3 hr (-5.9 to -6.6)*	24
	Wistar[25]							
62	104♂, 24 days	1 [2]	$L[06^{00}-16^{00}]$: $D[16^{00}-06^{00}]$	Mitoses in liver/1000 cells [Crest]		[6]	Mid-L: ~-315°; L-off: ~-16 hr	29
63	1♂, 200 days[4]	8 [1]	$L_i(130)[07^{00}-19^{00}]$: $D[19^{00}-07^{00}]$	General activity [Crest]			Mid-L: ~-165°; L-off: ~-5 hr	28
64	4♀, 250 g	2 [4]	$L[05^{30}-21^{30}]$: $D[21^{30}-05^{30}]$	Urine volume, ml/4 hr [*Crest*]	3.9	1.8	Mid-L: -198° (-185 to -211)*; L-off: -5.2 hr	46
65				Urine histamine, μg/4 hr [*Crest*]	21.7	8.2	Mid-L: -154° (-127 to -181)*; L-off: -2.3 hr	
66	*Acheta domesticus (Gryllus domesticus*[26]*)*, 2500[5]	[3]	$L[08^{00}-20^{00}]$: $D[20^{00}-08^{00}]$	Susceptibility[7] to ether, chloroform & carbon tetrachloride; minutes recovery time[8] [Crest]	~40	~[3]	Mid-L: ~-135°; L-off: ~-3 hr	33
67	*Leucophaea maderae*		L[23 hr]:D[1 hr]	Activity [Onset]			Mid-L: ~-170°; L-off: ~0	40
			L[16 hr]:D[8 hr]	Activity [Onset]			Mid-L: ~-120°; L-off: ~0	
			L[12 hr]:D[12 hr]	Activity [Onset]			Mid-L: ~-90°; L-off: ~0	
			L[7 hr]:D[17 hr]	Activity [Onset]			Mid-L: ~-50°; L-off: ~0	
			L[1 hr]:D[23 hr]	Activity [Onset]			Mid-L: ~-10°; L-off: ~0	

[4] Repeated observations. [5] Single observations. [7] Susceptibility rhythms refer to physiological changes dependent on the times (circadian system phases) at which exposure to the noxious agent occurred. [8] Evaluation based on recovery time of 50% of subjects. [24] Determined by telemetry from implanted transensors. [25] Food and water at will. [26] Synonym.

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References: [1] Aschoff, J. 1960. Cold Spring Harbor Symp. Quant. Biol. 25:11. [2] Bakke, J. L., and N. Lawrence. 1965. Metabolism 14:841. [3] Barnum, C. P., C. D. Jardetzky, and F. Halberg. 1958. Am. J. Physiol. 195:301. [4] Clark, R. H., and B. L. Baker. 1964. Science 143:375. [5] Davis, W. M. 1962. Experientia 18:235. [6] Davis, W. M., and O. L. Webb. 1963. Med. Exptl. 9:263. [7] Dray, F., A. Reinberg, and J. Sebaoun. 1965. Compt. Rend. 261:573. [8] Ertel, R. J., F. Halberg, and F. Ungar. 1964. J. Pharmacol. Exptl. Therap. 146:395. [9] Frank, G., et al. 1961. Proc. Ann. Meeting Am. Electroencephalog. Soc., 15th, p. 24. [10] Glick, D., et al. 1961. Am. J. Physiol. 200:811. [11] Halberg, F. 1959. Z. Vitamin. Hormon. Fermentforsch. 10:225. [12] Halberg, F. 1960. Perspectives Biol. Med. 3:491. [13] Halberg, F. 1964. In K. E. Schafer, ed. Bioastronautics. Macmillan, New York. p. 181. [14] Halberg, F. 1964. Monatsk. Aerztl. Fortbild. 14(2):67. [15] Halberg, F., P. G. Albrecht, and J. J. Bittner. 1959. Am. J. Physiol. 197:1083. [16] Halberg, F., R. E. Peterson, and R. H. Silber. 1959. Endocrinology 64:222. [17] Halberg, F., and A. N. Stephens. 1959. Proc. Minn. Acad. Sci. 27:139. [18] Halberg, F., M. B. Visscher, and J. J. Bittner. 1953. Am. J. Physiol. 174:313. [19] Halberg, F., et al. 1951. J. Lancet 71:312. [20] Halberg, F., et al. 1959. Publ. Am. Assoc. Advan. Sci. 55:803. [21] Halberg, F., et al. 1960. Proc. Soc. Exptl. Biol. Med. 103:142. [22] Halberg, F., et al. 1961. Experientia 17:282. [23] Halberg, F., et al. 1965. Acta Endocrinol. 50(Suppl. 103). [24] Halberg, F., et al. 1966. Physiologist 9:196. [25] Haus, E. 1964. Ann. N. Y.

continued

Part I. REGULARLY ALTERNATING LIGHT: DARK CYCLE

Acad. Sci. 117:292. [26] Haus, E., and F. Halberg. 1959. J. Appl. Physiol. 14:878. [27] Haus, E., and F. Halberg. 1966. Acta Endocrinol. 51:215. [28] Hunt, J. M., and H. Schlossberg. 1939. J. Comp. Psychol. 28:23. [29] Jackson, B. 1959. Anat. Record 134:365. [30] Marte, E., and F. Halberg. 1961. Federation Proc. 20:305. [31] Matthews, J. H., E. Marte, and F. Halberg. 1964. Can. Anesthesiol. Soc. J. 11:280. [32] Nelson, W. 1964. Am. J. Physiol. 206:589. [33] Nowosielski, J. W., R. L. Patton, and J. A. Naegele. 1964. J. Cellular Comp. Physiol. 63:393. [34] Pauly, J. E., and L. E. Scheving. 1964. Intern. J. Neuropharmacol. 3:651. [35] Pauly, J. E., and L. E. Scheving. 1965. Anat. Record 153:349. [36] Pittendrigh, C. S. 1965. In J. Aschoff, ed. Circadian clocks. North Holland, Amsterdam. p. 277. [37] Pizzarello, D. J., et al. 1964. Science 145:286. [38] Reinberg, A. 1965. In J. Aschoff, ed. Circadian clocks. North Holland, Amsterdam. p. 214. [39] Riley, G. M. 1937. Anat. Record 67:327. [40] Roberts, S. K. 1962. J. Cellular Comp. Physiol. 59:175. [41] Scheving, L. 1959. Anat. Record 135:7. [42] Sollberger, A. 1964. Ann. N. Y. Acad. Sci. 117:519. [43] Ungar, F., and F. Halberg. 1962. Science 137:1058. [44] Ungar, F., and F. Halberg. 1963. Experientia 19:158. [45] Van Pilsum, J. 1964. Ann. N. Y. Acad. Sci. 117:337. [46] Wilson, C. W. M. 1965. Intern. Arch. Allergy Appl. Immunol. 28:32.

Part II. PHASE CHANGE OF LIGHT: DARK CYCLE

	No. of Subjects	Biological Variable [Phase Marker]	Change in Lighting Regimen	Response of Rhythm	Remarks	Reference
	Homo sapiens					
1	8	Axillary temperature [Pattern]	L[07^{00}-22^{30}]:D[22^{30}-07^{00}] changed abruptly to D[10^{30}-19^{00}]:L[19^{00}-10^{30}]↳	Resynchronization in all subjects in 3-4 days after change	Abrupt reversion to previous regimen resulted in similar rate of φ shift	15
2	8	Urine volume; urine pH & specific gravity [Pattern]	L[07^{00}-22^{30}]:D[22^{30}-07^{00}] changed abruptly to D[10^{30}-19^{00}]:L[19^{00}-10^{30}]↳	Resynchronization in ~6(4-8) days	Abrupt reversion to previous regimen resulted in similar rate of φ shift	16
3	12	Oral temperature [Pattern]	24-hr periodic routine changed to 21- or 27-hr periodic routine	Resynchronization in 1-2 days in 11 of 12 subjects (apparently similar for 21- & 27-hr routines)		14
4	12	Urine volume; urine sodium, chloride, & potassium [Crest]	24-hr periodic routine changed to 21- or 27-hr periodic routine	Resynchronization in 1-2 days in 3 of 12 subjects; 8 subjects required 4 wk or more for resynchronization of potassium rhythm		13, 14
5	*Mesocricetus auratus*, 1	Running-wheel activity [Onset]	L[09^{00}-21^{00}]:D[21^{00}-09^{00}] changed abruptly to D[09^{00}-21^{00}]:L[21^{00}-09^{00}]	Resynchronization in ~3 wk (by +$\Delta\varphi$)	Rate of φ shift typical of most hamsters	5
	Mus musculus					
6	3	Total activity [Weighted midpoint of maximum]	L[12 hr]:D[12 hr] period gradually lengthened or shortened (in steps of 1 hr at Δt of a few days), with L and D spans equal	No resynchronization with periods shorter than 21 hr or longer than 27 hr (φ drifting occurred beyond these extremes)		17
7		Total activity [Weighted midpoint of maximum]	L[12 hr]:D[12 hr] changed abruptly (in steps of at least 4 hr) to L:D periods of 20,16,28, & 22 hr, with L and D spans equal	No resynchronization		
8	600	Liver glycogen [Pattern]	L_f(10-150)[06^{00}-18^{00}]:D[18^{00}-06^{00}] changed to D[06^{00}-18^{00}]:L_f(10-150)[18^{00}-06^{00}] by single 24-hr D span	Resynchronization in ~8 days (by -$\Delta\varphi$)	20 mice at Δt of 4 hr during 24-hr spans before, and 5,6,8, & 9 days after, change in lighting regimen; rate of $\Delta\varphi$ slower during first 4 days than during last 4 days	6

↳ Blindfold used for D span.

continued

186. PHASE RELATIONS OF CIRCADIAN RHYTHMS: ANIMALS

Part II. PHASE CHANGE OF LIGHT: DARK CYCLE

	No. of Subjects	Biological Variable [Phase Marker]	Change in Lighting Regimen	Response of Rhythm	Remarks	Reference
	M. musculus					
9	480	Liver RNA uptake of P^{32} [Pattern]	$L_f(10\text{-}150)[06^{00}\text{-}18^{00}]:D[18^{00}\text{-}06^{00}]$ changed to $D[06^{00}\text{-}18^{00}]:L_f(10\text{-}150)[18^{00}\text{-}06^{00}]$	Resynchronization complete in 8-9 days	20 mice at Δt of 4 hr during 24-hr spans before, and 4,8, & 21 days after, change in lighting regimen	2
10	150	Kidney transamidinase [Pattern]	$L_f(10\text{-}150)[06^{00}\text{-}18^{00}]:D[18^{00}\text{-}06^{00}]$ changed abruptly to $D[06^{00}\text{-}18^{00}]:L_f(10\text{-}150)[18^{00}\text{-}06^{00}]$	Resynchronization in ~2 wk	12 or more mice at Δt of 4 hr during 24-hr spans	18
11	428	Susceptibility to ethanol[2], % mortality [Pattern]	$L_f(10\text{-}150)[06^{00}\text{-}18^{00}]:D[18^{00}\text{-}06^{00}]$ changed to $D[06^{00}\text{-}18^{00}]:L_f(10\text{-}150)[18^{00}\text{-}06^{00}]$	Resynchronization in ~2 wk	15 mice at Δt of 4 hr before, and 4,8, & 16 days after, change in lighting regimen	9
12	*M. musculus*, D8	Mitoses in epidermis [Differences at 12^{30} & 00^{30}]	$L[06^{00}\text{-}18^{00}]:D[18^{00}\text{-}06^{00}]$ changed abruptly to $D[06^{00}\text{-}18^{00}]:L[18^{00}\text{-}06^{00}]$	Resynchronization in >9-<23 days	Separate groups of mice studied before, and 3,9, & 23 days after, change in lighting regimen	7
13	*Peromyscus maniculatus*, 1	Running-wheel activity, food consumption & water consumption [Pattern]	$L_i(43)[16\ hr]:L(0.009)[8\ hr]$ changed to $L_i(43)[8\ hr]$:Dusk [1 hr]: $L_i(0.009)[6\ hr]$:Dawn [1 hr][3]	All 3 rhythms synchronized with the 16-hr regimen after ~4 days		12
	Rattus norvegicus					
14	1	Running-wheel activity [Pattern]	$L[08^{00}\text{-}16^{00}]:D[16^{00}\text{-}08^{00}]$ changed to $D[08^{00}\text{-}20^{00}]:L[20^{00}\text{-}08^{00}]$ by single 28-hr D span	Resynchronization in 7-10 days		10, 11
15	3	Intraperitoneal temperature [Crest]	$L_f(200)[06^{00}\text{-}18^{00}]:D[18^{00}\text{-}06^{00}]$ changed to $D[06^{00}\text{-}18^{00}]:L_f(200)[18^{00}\text{-}06^{00}]$ by single 24-hr L span	Resynchronization in ~8 days (by $-\Delta\varphi$)	Temperature determined by telemetry from implanted transensors	8
16	3	Intraperitoneal temperature [Crest]	$L_i(25)[06^{00}\text{-}18^{00}]:D[18^{00}\text{-}06^{00}]$ changed to $D[06^{00}\text{-}18^{00}]:L_i(25)[18^{00}\text{-}06^{00}]$ by single 24-hr D span	Resynchronization in ~8 days (by $-\Delta\varphi$)	Temperature determined by telemetry from implanted transensors	8
17	7	Intraperitoneal temperature [Crest]	$L_i(2)[06^{00}\text{-}18^{00}]:D[18^{00}\text{-}06^{00}]$ changed to $D[06^{00}\text{-}18^{00}]:L_i(2)[18^{00}\text{-}06^{00}]$ by single 24-hr L span	Resynchronization in ~8 days (by $-\Delta\varphi$)	Temperature determined by telemetry from implanted transensors	8
18	9	Intraperitoneal temperature [Crest]	$L_i(2)[06^{00}\text{-}18^{00}]:D[18^{00}\text{-}06^{00}]$ changed to $D[06^{00}\text{-}18^{00}]:L_i(2)[18^{00}\text{-}06^{00}]$ by single 24-hr D span	Resynchronization in ~8 days (by $-\Delta\varphi$)	Temperature determined by telemetry from implanted transensors	8
19	*Coturnix japonica*, 6	Intra-abdominal temperature	$L_i[06^{00}\text{-}20^{00}]:D[20^{00}\text{-}06^{00}]$ changed abruptly to $D[10^{00}\text{-}20^{00}]:L_i[20^{00}\text{-}10^{00}]$	Resynchronization within 24 hr	Temperature determined with implanted thermocouple	19
	Fringilla coelebs					1
20	13	Activity [Onset]	$L(250)[12\ hr]:L(0.5)[12\ hr]$ inverted by single 24-hr L(0.5) span	Average of 5-6 days required for resynchronization (by $-\Delta\varphi$)		
21	9	Activity [Onset]	$L(250)[12\ hr]:L(0.5)[12\ hr]$ inverted by single 24-hr L(250) span	Average of 5-6 days required for resynchronization	Masking effect of light resulted in initial $+\Delta\varphi$ in some birds	
22	9	Activity [Onset]	$L(250)[12\ hr]:L(0.5)[12\ hr]$ shifted by single subtraction of either 6 hr L(250) or 6 hr L(0.5)	Average of 2-3 days required for resynchronization (by $+\Delta\varphi$)		
23	8	Activity [Onset]	$L(250)[12\ hr]:L(0.5)[12\ hr]$ shifted by single addition of either 6 hr L(250) or 6 hr L(0.5)	Average of 4-5 days required for resynchronization (by $-\Delta\varphi$)		
	Uca sp.					
24	10[4]	Chromatophore [Pattern]	$L(\sim430)[06^{00}\text{-}18^{00}]:D[18^{00}\text{-}06^{00}]$ changed to $D[09^{00}\text{-}21^{00}]:L(\sim1600)[21^{00}\text{-}09^{00}]$ by single 27-hr L span	Resynchronization apparent on 2nd day		4

[2] Administered intraperitoneally. [3] Using "twilight transitions." [4] Repeated observations.

continued

Part II. PHASE CHANGE OF LIGHT: DARK CYCLE

	No. of Subjects	Biological Variable [Phase Marker]	Change in Lighting Regimen	Response of Rhythm	Remarks	Reference
25	*Uca* sp. 10[4,5]	Chromatophore [Pattern]	L:D (natural) changed to L_i(1080)[19⁰⁰-07⁰⁰]:D[07⁰⁰-19⁰⁰] for 6 days, then to DD; observations made for 1st 5 days in DD	φ in DD shifted ~12 hr from φ in L:D (natural)		3
26		Chromatophore [Pattern]	L:D (natural) changed to L_i(22)[19⁰⁰-07⁰⁰]:D[07⁰⁰-19⁰⁰] for 6 days, then to DD; observations made for 1st 5 days in DD	φ in DD shifted ~6 hr from φ in L:D (natural)		

[4] Repeated observations. [5] At Δt of 6 hours.

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References: [1] Aschoff, J., and R. Wever. 1963. Z. Vergleich. Physiol. 46:321. [2] Barnum, C. P. 1961. Rept. Ross Pediat. Res. Conf. 39:79. [3] Brown, F. A., M. Fingerman, and M. N. Hines. 1954. Biol. Bull. 106:308. [4] Brown, F. A., and H. M. Webb. 1949. Physiol. Zool. 22:136. [5] Bruce, V. G. 1960. Cold Spring Harbor Symp. Quant. Biol. 25:29. [6] Halberg, F., P. G. Albrecht, and C. P. Barnum, Jr. 1960. Am. J. Physiol. 199:400. [7] Halberg, F., J. J. Bittner, and D. Smith. 1957. Z. Vitamin. Hormon. Fermentforsch. 9:69. [8] Halberg, F., et al. Unpublished. Univ. Minnesota, Dept. Pathology, Minneapolis, 1965. [9] Haus, E. 1964. Ann. N. Y. Acad. Sci. 117:292. [10] Hemmingsen, A. M., and N. B. Krarup. 1937. Kgl. Danske Videnskab. Selskab. Biol. Medd. 13(7):1. [11] Holmgren, H., and Swenson. 1953. Acta Med. Scand., Suppl. 278:71. [12] Kavanau, J. L. 1962. Experientia 18:382. [13] Lewis, P. R., and M. C. Lobban. 1957. Quart. J. Expt. Physiol. 42:356. [14] Lewis, P. R., and M. C. Lobban. 1957. Ibid. 42:371. [15] Sharp, G. W. 1961. Nature 190:146. [16] Sharp, G. W. 1962. Ibid. 193:37. [17] Tribukait, B. 1956. Z. Vergleich. Physiol. 38:479. [18] Van Pilsum, J. 1964. Ann. N. Y. Acad. Sci. 117:337. [19] Woodard, A. E., and F. B. Mather. 1964. Nature 203:422.

Part III. SINGLE PERTURBATIONS OF ILLUMINATION

L between slashes indicates light perturbation of an otherwise continuous regimen--e.g., DD/L_f(1080)[15 min]/DD = a 15-minute interruption of continuous dark by light, at an intensity of 1080 lux, from a fluorescent lamp.

	No. of Subjects	Biological Variable [Phase Marker]	Light Perturbation: Kind	Light Perturbation: Timing	Approximate Maximum $\Delta\varphi$	Remarks	Reference
1	*Glaucomys volans*, 6	Running-wheel activity [Onset]	DD/L_i(5.4)[10 min]/DD; at intervals of several days to several weeks	~1 hr before, to ~7 hr after, onset	-75 min	-$\Delta\varphi$ complete at first onset after perturbation; $\Delta\varphi$ varied up to twofold among individuals	3
2				~7-12 hr after onset	+25 min	+$\Delta\varphi$ required days or weeks for completion	
3	*Mesocricetus auratus*, 1	Running-wheel activity [Onset]	DD/L_i(5.4)[10 min]/DD; at intervals of 10 days	~0-4 hr after activity onset	-70 min	-$\Delta\varphi$ maximum at first subsequent onset	4
4				~4-12 hr after activity onset	+140 min	+$\Delta\varphi$ maximum after several transient cycles	
5				~12-24 hr after activity onset	0		

continued

186. PHASE RELATIONS OF CIRCADIAN RHYTHMS: ANIMALS

Part III. SINGLE PERTURBATIONS OF ILLUMINATION

	No. of Subjects	Biological Variable [Phase Marker]	Light Perturbation: Kind	Light Perturbation: Timing	Approximate Maximum $\Delta\varphi$	Remarks	Reference
6	*Fringilla coelebs*, 3-13	Activity [Onset]	L(200)[12 hr]:L(0.5)[12 hr] changed to LL(200)	Last change of L(0.5) to L(200) at 5 hr after activity onset	-3 hr	$\Delta\varphi$ determined by extrapolation from "free-running" onsets	1
7				Last change of L(0.5) to L(200) at 20 hr after activity onset	+6 hr		
8			L(200)[12 hr]:L(0.5)[12 hr] changed to LL(0.5)	Last change of L(200) to L(0.5) at 4 hr after activity onset	+1 hr	$\Delta\varphi$ for L-to-"D" transition opposite to that observed for "D"-to-L transition	
9				Last change of L(200) to L(0.5) at 21 hr after activity onset	-6 hr	$\Delta\varphi$ for L-to-"D" transition opposite to that observed for "D"-to-L transition	
10	*Uca* sp. 10	Chromatophores [Pattern]	LL(860) changed to DD	07^{00}	-6 hr		2
11				13^{00} or 19^{00}	0		
12	10	Chromatophores [Pattern]	DD/L_f(1000)[6 hr]/DD	Beginning ~7 hr after start of night phase of rhythm	+6 hr		8
13			DD/L_f(1000)[16,20, or 24 hr]/DD	Ending ~1 hr after start of day phase of rhythm	-6 hr		
14	*Drosophila pseudoobscura*, cultures	Eclosion [Distribution median]	DD/L_f(1080)[15 min]/DD	11-16 hr after eclosion median	-11 hr	$-\Delta\varphi$ nearly maximum at first eclosion after perturbation	6
15				17-23 hr after eclosion median	+11 hr	$+\Delta\varphi$ requires ~6 transient cycles to become maximum	
16		Eclosion [Distribution median]	DD/L(high)[0.0005 sec]/DD	10-17 hr after eclosion median	-6 hr		5
17				0-1 hr & 18-24 hr after eclosion median	+7 hr		
18	*Leucophaea maderae*, 1	Running-wheel activity [Onset]	DD/L(2160)[12 hr]/DD	Beginning ~7 hr before onset	-2 hr		7
19				Beginning ~7 hr after onset	+1 hr		
20			DD changed to L_i(270)[12 hr]:D[12 hr]	0-12 hr after activity onset	-		
21				12-24 hr after activity onset	+		

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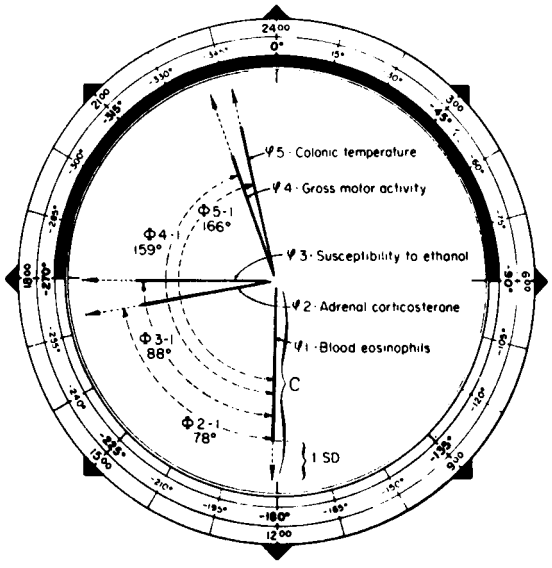
References: [1] Aschoff, J. 1965. In J. Aschoff, ed. Circadian clocks. North Holland, Amsterdam. p. 95. [2] Brown, F. A., and H. M. Webb. 1949. Physiol. Zool. 22:136. [3] DeCoursey, P. 1961. Z. Vergleich. Physiol. 44:331. [4] DeCoursey, P. 1964. J. Cellular Comp. Physiol. 63:189. [5] Pittendrigh, C. S. 1960. Cold Spring Harbor Symp. Quant. Biol. 25:159. [6] Pittendrigh, C. S., and D. H. Minis. 1964. Am. Naturalist 98:261. [7] Roberts, S. K. 1962. J. Cellular Comp. Physiol. 59:175. [8] Webb, H. M. 1950. Physiol. Zool. 23:316.

continued

186. PHASE RELATIONS OF CIRCADIAN RHYTHMS: ANIMALS

Part IV. INTERNAL TIMING: MOUSE

Values for Part IV were obtained from analysis of all available data, whereas values for Part I are from data for an integral cycle. Small discrepancies therefore occur in φ's (sample phases) between the figure in Part IV and corresponding functions in the preceding tables. The figure was derived from external-timing estimates of 24-hour synchronized circadian rhythms and illustrates the phase difference between two circadian crests, i.e., internal timing. φ, as delay of 24-hour synchronized circadian crest from local 24^{00}, is given in clock hours and degrees on outer and middle scales, respectively. Light-dark regimen (white for light and black for dark) is indicated on inner scale. Φ = internal timing, given in degrees. C = circadian amplitude; SD = standard deviation, expressed as % of circadian amplitude. For further information on internal timing, consult reference 1; on methodology, references 2 and 3.



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References: [1] Halberg, F., et al. 1960. Proc. Minn. Acad. Sci. 28:53. [2] Halberg, F., et al. 1965. Acta Endocrinol. 50(Suppl. 103). [3] Halberg, F., et al. 1965. Intern. Congr. Anatomists, Proc. (in press).