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Time Structures (Chronomes) of the Blood Circulation, Populations' Health, Human Affairs and Space Weather*

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Abstract

We complement an "Extended Consensus" [1], focused on the individual's health, by documenting associations between the human heart and circulation and the environment near and far at the level of local and global populations in both space and time [2, 3]. Life in the atmosphere of the sun [4] mimics its inanimate surroundings; its rhythmic components nearly match in length the cycles of the cosmos [5-15]. Longitudinal records of the human blood circulation reveal heretofore unrecognized aspects of its variability. The view from a very few long and relatively dense series, covering mostly around-the-clock (up to) decades on individuals, reveals variability that cannot readily or necessarily be found in hundreds of thousands of individuals' around-the-clock 24-hour spotchecks and certainly not in single samples, unless the individuals' cycles are synchronized and assessed on a population basis.

Periods, τ, longer than 28 hours, that is infradian variations, like the circadians (with τ tentatively between 20 and 28 hours), have entered the genome and their characteristics await mapping. For those cycles that are already mapped, we consider further the extent to which the parameters and nonparametric endpoints of healthy infradian and circadian variability and their anomalies can become everyday measures of Sir William Osler's wear and tear, i.e., of Hans Selye's and Paul Rosch's stress and strain to the point of becoming gauges of distress (again complementing or replacing single samples or the mean values of dense sampling during single days). Criteria for recognizing and quantifying the alteration indicating when a load changes from benetensive to maletensive have yet to be identified, perhaps by monitoring blood pressure and heart rate in everyday life, replacing spotchecks in the clinic.

The probable role of cosmos-induced loads in pathogenesis, assessed, among others, as an effect of a magnetic storm in laboratory animals [16-18] and in humans [19], awaits study by using superposed epochs and a subtraction and addition approach [2, 3].

* Update on chronomics, the first in a series of presentations at the 3rd International Conference on Advanced Cardiac Sciences "King of Organs 2010" (September 27-30, 2010, Hofuf, Saudi Arabia) from the Halberg Chronobiology Center at the University of Minnesota, Minneapolis, MN, USA

1. Preamble

We set the stage for Paul Rosch, who has devoted a lifetime to problems of stress, as Hans Selye and many others did, without concern for cycles. Rosch also wrote a scholarly treatise on electromagnetism [20], although again a novel spectrum of cycles was not in his focus. Cycles, however, underlie both stress and electromagnetism, much more than is apparent in pertinent papers. Magnetic fields, like electric ones, constitute a usually ignored yet ever-present and greatly varying background to life; they can represent a time-varying stress which can accumulate to unacceptable strain that can eventually harm. By resolving the many aeolian (i.e., nonstationary) frequencies involved, chronobiology, the study of time structures (chronomes) in the biosphere and chronomics, analyzing interactions between internal and external chronomes, are each tools for examining the "subtle energies" that act frequency-dependently and that, from a circadian and lunar viewpoint, were of great interest to Frank A. Brown Jr. [21] and Franklin Barnwell [22] and are currently in the focus of Rollin McCraty, who with Rosch prompted our participation at the meeting; we are indebted to both.

We are at a site where a geomagnetic recording station tuned to the resonances in the ionosphere and geomagnetic field line resonances was just installed by Abdullah al-Abdulgader and Rollin McCraty, which may complement (for a unified science) the systematic monitoring that Gauss, Humboldt and Sabine started in the nineteenth century to measure geomagnetism worldwide, Figure 1A.

Stations yet to be built and aligned on a global scale for the study of congruences among periods in and around us, as one of several approaches used by us, constitute an indispensable step toward an inferential statistical cross-spectral (as well as humanistic) assessment of coherence. In this context, Saudi Arabia could provide a model for the world. A study designed to investigate correspondences in the activity of biosphere with those found in long-term recordings of heart rate variability and blood pressure is planned, which in addition to the geomagnetic and solar indicators intends to include a comparison with the locally collected Schumann Resonance data.

Arabic medicine during the Islamic Golden Age (c. 9^{th} century-c. 16^{th} century CE) has already generated Ibn al-Nafis'[1], Figure 1B, experimental approach to physiology [23, 24]. His endeavor "in determining the use of each organ" led him to discover the pulmonary circulation. His motto, "[W]e shall rely necessarily on verified examination, disregarding whether our opinions will agree or disagree with those of our predecessors", is timely, applying to those who wish to replace a spotcheck medicine that flies blind between office visits, to examine each variable, beginning with heart rate and blood pressure, longitudinally. In al-Nafis' spirit, in this forum we describe some of the reciprocal cycles others and we encountered in and around us, also alluding to ongoing studies and problems. While their amplitudes can be relatively small, these cycles constitute potential tipping factors leading to several hard events, including sudden cardiac death and suicide by individuals as well as crime and terrorism in populations.

2. Method

Figure 1C introduces least squares, used by the extended cosinor to get, in the presence of partly rhythmic time series, a usually more accurate or more precise mean in the case of unequidistant data in particular. Furthermore, in addition to the superiority of the MESOR, M, a **m**idline-**e**stimating **s**tatistic **o**f **r**hythm, as compared to an arithmetic mean, the methodology used also yields for each τ amplitudes, acrophases, Figure 2A, and the (A,ϕ) pairs of harmonics as new endpoints used for diagnosis and treatment [25-27]. With appropriate checks for non-stationarities that can yield spurious spectral peaks (Figures 2B-2D), one or several τs can also be resolved by the extended linear-nonlinear cosinor (Figure 2E) and by other methods, Table 1.

[1] This paper is dedicated to the memory of Ibn al-Nafis (1213-1288), who discovered the movement of blood from the right to the left ventricle of the heart via the lungs. George Sarton (1884-1956), the father of the history of science, wrote: "... his importance will increase enormously, for he must be considered one of the main forerunners of William Harvey and the great physiologists of the Middle Ages" [24].

Table 1. Comparison of Methods Applied to Noisy Test Series with Two Components With Close Periods -- Only Two Approaches (7 and 8) Resolve Both Components†

$Y_i = 100 + 10 \cos(2\pi t/24 - \pi) + 2 \cos(2\pi t/24.8 - \pi) + 5\,R$, where i = 1, …, 336 ($\Delta t$=1 hour; T=14 days) and R is uniformly distributed with zero mean and range =1 (±0.5)

Method		Period (h)#	MESOR	Amplitude	Acrophase (degrees)	Detection		N of components detected
N	Kind					Test	P	
1#	"Cosinor"-SC[1]	24.00	100.18	10.47	-98	F(2,333) = 2951.51	<0.001	1
2#	Cosine_fit	24.00	100.18	11.53	-98	GoodFit = 0.001	<0.001	1
3*	Fourier	23.93					<0.001	1
4*	Lomb-Scargle	24.00				Robustness = 96%	<0.001	1
5*	Enright	24.00				Robustness = 96%	<0.001	1
6	ARIMA.MLE[2] in SPLUS§	24.00	100.15(99.8,100.5)	10.45(10.11,10.80)	-96.5(-94.5,-101)		<0.001	>12
7a	Linear step 1 (L)[3]	24.00	100.18(99.98,100.37)	10.47(10.20,10.74)	-98(-97,-100)	PR=95%	<0.001	
7b	Nonlinear step 2 (NL)	23.97 (23.83,24.10)	100.13(99.83,100.43)	9.75(7.67,11.84)	-91(-78,-105)		<0.05@	
		24.63(24.04,25.21)		2.49(0.34,4.63)	-98(-47,-149)		<0.05@	2
8	Simulated Annealing (GOSA software)[4]	23.96(23.89,24.03)	100.4(100.1,100.7)	9.6(8.4,10.8)	-94(-83,-105)		<0.05	
		24.6(24.3,24.9)		2.5(1.3,3.7)	-94(-60,-128)		<0.05	2
9	Wavelets	24.00	Time evolution noted but not quantified by point-and-interval estimates.					

Acrophase expressed in (negative) degrees, with 360°≡period length, and 0° set to 00:00 at start of series. # Period is anticipated trial period. * Only one peak detected. GoodFit: Goodness of Fit. @ From non-overlap of zero-amplitude by 95% Confidence Interval (CI).

†Items 1-8 from Refinetti R, Cornélissen G, Halberg F. Procedures for numerical analysis of circadian rhythms. Biological Rhythm Research 2007; 38 (4): 275-325. http://dx.doi.org/10.1080/09291010600903692; item 9 courtesy of Prof. S.R. Prabhakaran Nayar, Department of Physics, Kerala University, Kariavattom, Trivandrum, India.

[1]SC: South Carolina: cosinor restricted to 24-hour component, by contrast to Minnesota's cosinor, which includes least squares fit of multiple components consisting of cosine functions with anticipated components not necessarily equal to 24 hours, originally called 'single cosinor' to indicate analyses of individual time series (and NOT of a single component fit), soon thereafter extended to include the chronobiologic serial section and the combined linear-nonlinear rhythmometry, among others; all procedures involving the least squares fit of COSINe curves often displayed vectORially along polar coordinates and checked against chronograms and data stacked for the period(s) found, i.e., as plexograms, for each cosinor-isolated component (periods are estimated with their respective confidence intervals).

[2] Structure of residuals found to be correlated and modeled with an ARMA (1,1) model, with AR coefficient = 0.78 (0.49, 0.89) and MA coefficient = 0.54 (0.23, 0.75). Results reported at fixed anticipated period of 24 hours.

[3]Least squares spectrum detects peak at anticipated period of 24 hours and small sidelobes with periods of 26.7 and 21.8 hours resolved nonlinearly as presence of second component with period slightly longer than 24 hours.

[4] Czaplicki J, Cornélissen G, Halberg F. GOSA, a simulated annealing-based program for global optimization of nonlinear problems, also reveals transyears. J Applied Biomedicine 2006; 4: 87-93. http://www.zsf.jcu.cz/vyzkum/jab/4_2/czaplicki.pdf

6, 7 and 8: 95% CIs in parentheses; 7a and 7b are part of the more extensive, as need be, MN-cosinor.

§Chatfield C. The analysis of time series: an introduction. London: Chapman and Hall; 1984.

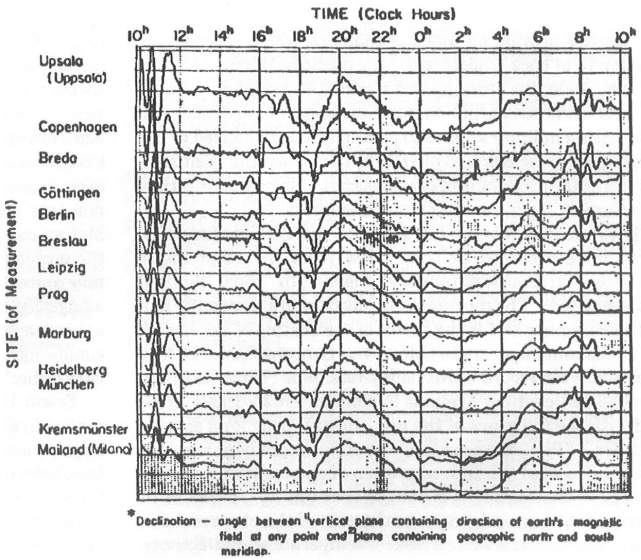


Figure 1A. The "harmony of curves" in itself can definitively be documented but not quantified in instances such as the record presented without any inferential statistics in the pre-computer era by Carl Friedrich Gauss, discoverer of the least-squares method, and Wilhelm Weber in Biermann K-R, editor. Briefwechsel zwischen Alexander von Humboldt und Carl Friedrich Gauß: Zum 200. Geburtstag von C.F. Gauß im Auftrage des Gauß-Komitees bei der Akademie der Wissenschaften der DDR (Berlin: Akademie-Verlag; 1977; 202 pp. + plates).

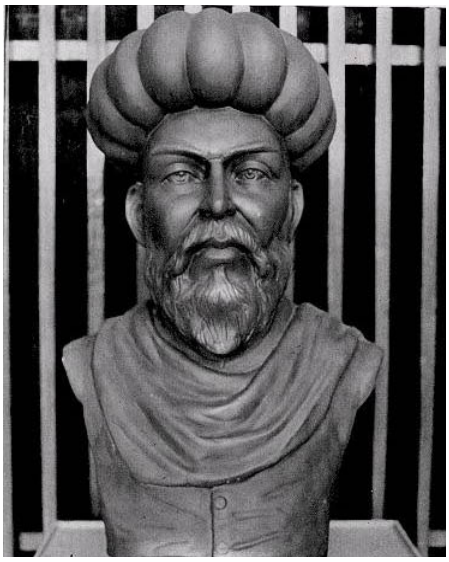


Figure 1B. Ibn al-Nafis (1213-1288), a dominant figure of the Islamic Golden Age (c. 9th century-c. 16th century CE) [23, 24].

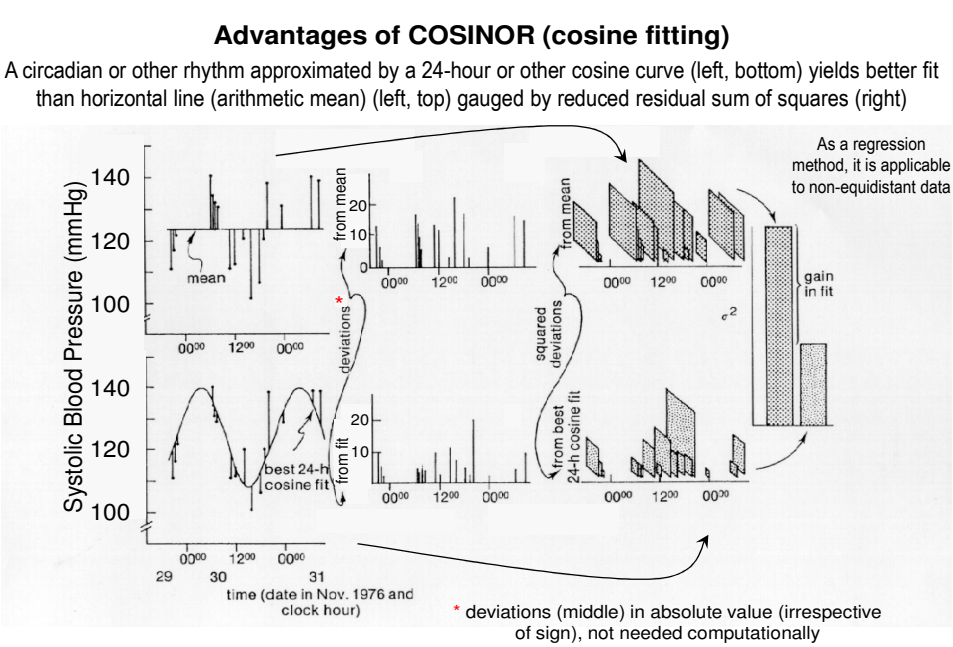


Figure 1C. Gauss' least-squares method in the inferentially extended cosinor [25, 26] provides a usually more accurate and more precise average than the arithmetic mean, a task easily accomplished in the era of computers. © Halberg.

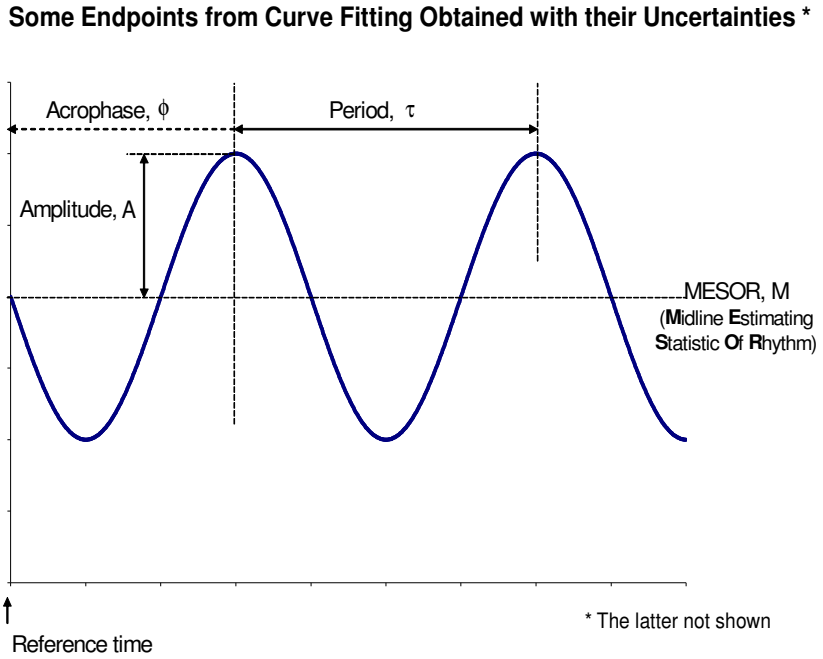


Figure 2A. Diagnostically useful endpoints from the cosinor, each underlying a **v**ascular **v**ariability **a**nomaly, VVA [1]. © Halberg.

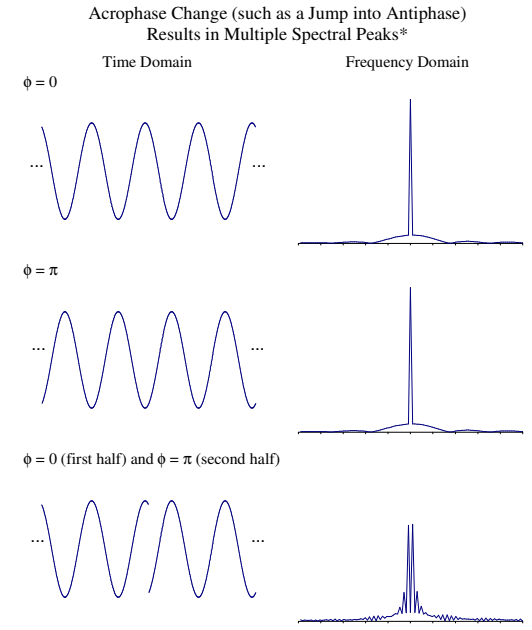


Figure 2B. The presence of a phase jump (e.g., by 180°) of a cosine curve with a fixed period is spuriously associated with two spectral peaks. © Halberg.

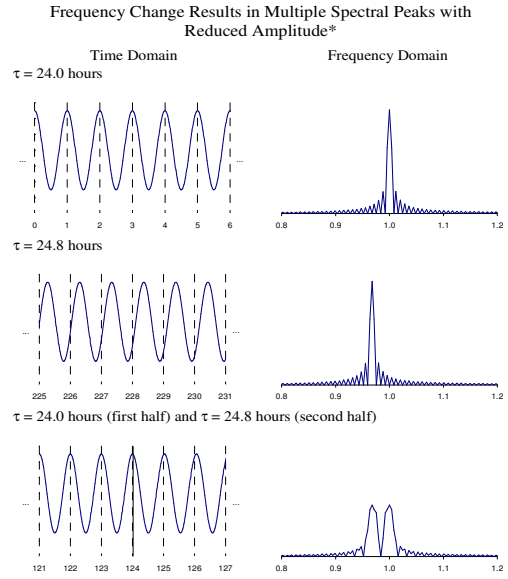


Figure 2C. The occurrence of a change in period length (e.g., from 24.0 to 24.8 hours in mid-course of a 124-day record) of a single cosine component is spuriously associated with two spectral peaks with amplitudes smaller than that of actual signal. © Halberg.

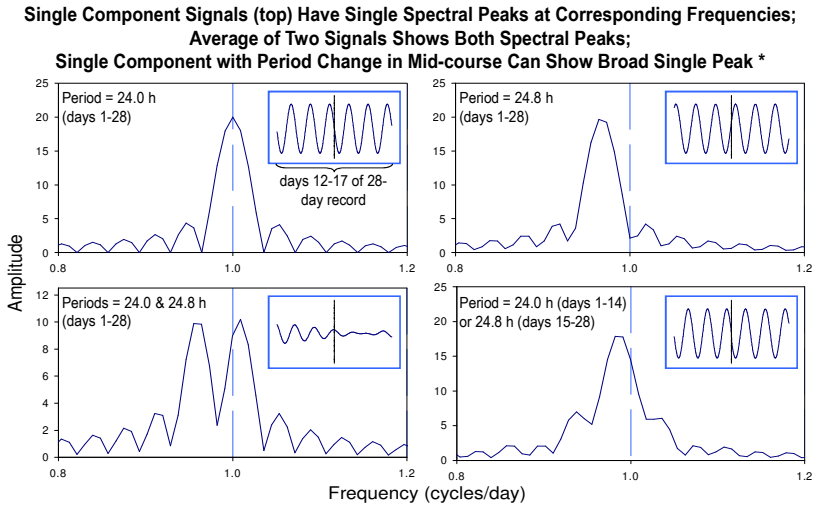


Figure 2D. The occurrence of a change in period length (e.g., from 24.0 to 24.8 hours in mid-course of a 28-day record) of a single cosine component is spuriously associated with a single broad spectral peak with a reduced amplitude and sidelobes. Whether a single broad peak or two spectral peaks are observed depends on the length of the record, the extent of the difference in period length and the time when the switch in period occurs in the record. © Halberg.

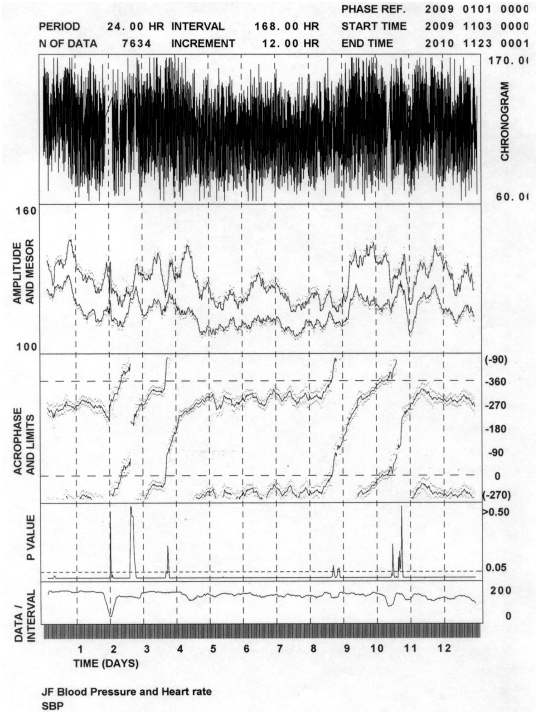


Figure 2E. The systolic blood pressure of JF, a woman 61-62 years of age, suggests alternating 24.0-hour synchronization (up to full moon 2) and circadian desynchronization of acrophases (in row 3) (up to full moon 5), followed by 24.0-hour resynchronization lasting several months, alternating with renewed circadian desynchronization (after full moon 8) and 24.0-hour resynchronization (after full moon 11). This chronobiological serial section shows the dominant behavior but does not reveal the coexistence of two circadian periods, demonstrated in Figure 2F. Vertical dashed numbered lines indicate consecutive full moons. © Halberg.

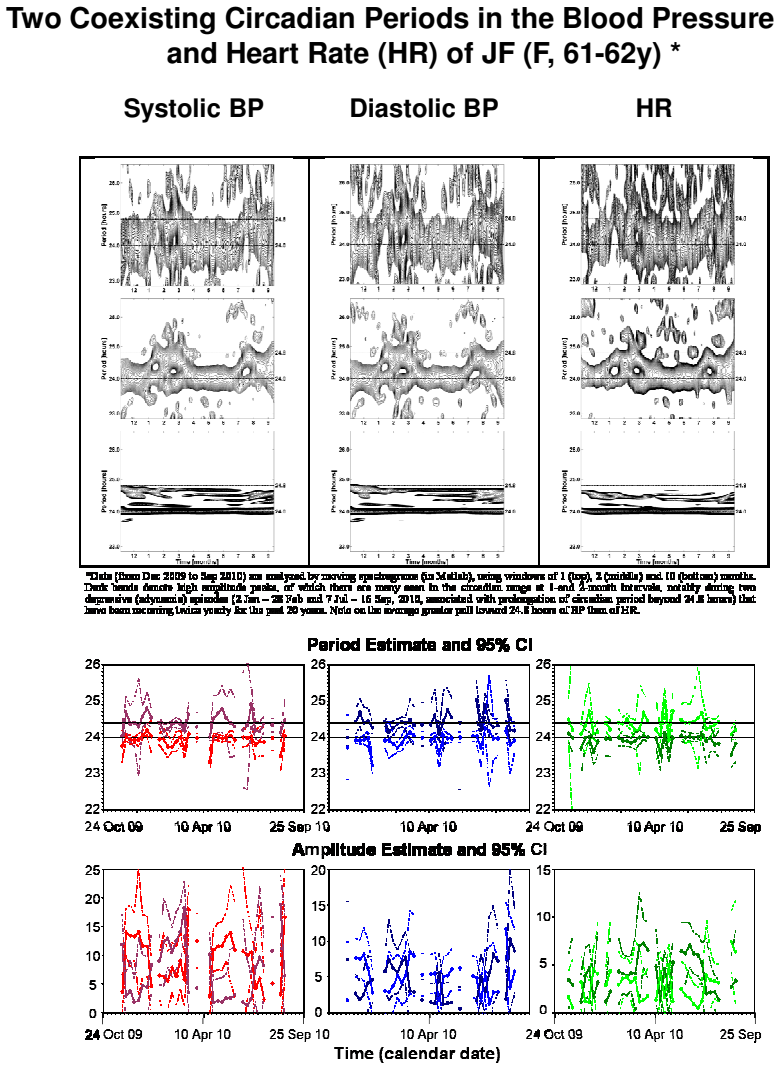


Figure 2F. A change in the relative prominence of two coexisting circadian components has been observed in a 61- to 62-year old woman (JF) who suffers from adynamia episodes lasting 2-3 months and recurring twice a year, using two complementary approaches, namely spectrograms (top section) and nonlinear fit of two components (bottom section). In the third row (top section), components with different frequencies coexist, demonstrating responses to both the solar and lunar day glocally in time, with parameters estimated with their uncertainties in the last two rows. © Halberg.

3. Diverse Cycles in a Unified Science Reinforce Each Other

In 1600 the physician William Gilbert [28] gave physics its first scientific treatise [29]. In 1995, perhaps to return the favor, Juan Roederer [30] asked physicists for "unselfish cooperation" in helping biomedicine so that it can detect "physiological harbingers and their possible correlations with space weather". Elsewhere, Roederer [31] as well as others [2, 3, 32-34] noted cycles in and around us with periods, τ, that are reciprocal by their similar length (not arithmetically). In the interim, old paradecadal (Figure 3A) [35, 36] and novel biospheric spectral components (Figure 3B) [34] mirror environmental quasi-periodicities, among others, in the speed of the solar wind. Some of the τs are shorter than (cis = on this side of) the year or half-year or of other reference

periodicities; others are longer than a year (trans = beyond), i.e., they are transyears [2, 3, 33, 34, 36-43]. In the spectrum of the incidence of sudden cardiac death in Minnesota, USA [37, 43], with hot summers and often-harsh winters, transyears can coexist with and even replace, at least for a while, the effect of the seasons, as they also do in Tokyo, Japan [42].

These nonphotic cycles bear not only on whether one is unaffected by (versus dies from) an electrical accident of the heart (sudden cardiac death) but also whether death is brought about by one's own hand (suicide) [44-46] or by the action of others (crime, terrorism) [3].

The variable sun, interplanetary space, the atmosphere and earth all undergo a spectrum of non-photic and photic cycles, many of them mirrored in the biosphere. Paraphrasing Roederer [30], the physicists' cooperation may also serve their own discipline by transdisciplinarily supporting the reality of questioned or with notable exceptions [47, 48; cf. 49] forgotten periods of weather in space or on earth that are found in living things [50]. Among others [51], an about (~) 35-year or paratridecadal climate cycle, Figure 4 [50; cf. 52] is a case in point. In addition, the case of an ~5-month or quinmensal cycle, Figure 5 [53-55], was predicted [56] and found first by physicists [57]. Further, in transyears, Figure 6 [37-43; cf. 3], the aeolian behavior of both solar wind speed and systolic blood pressure, and the effect of the former on the latter, are seen.

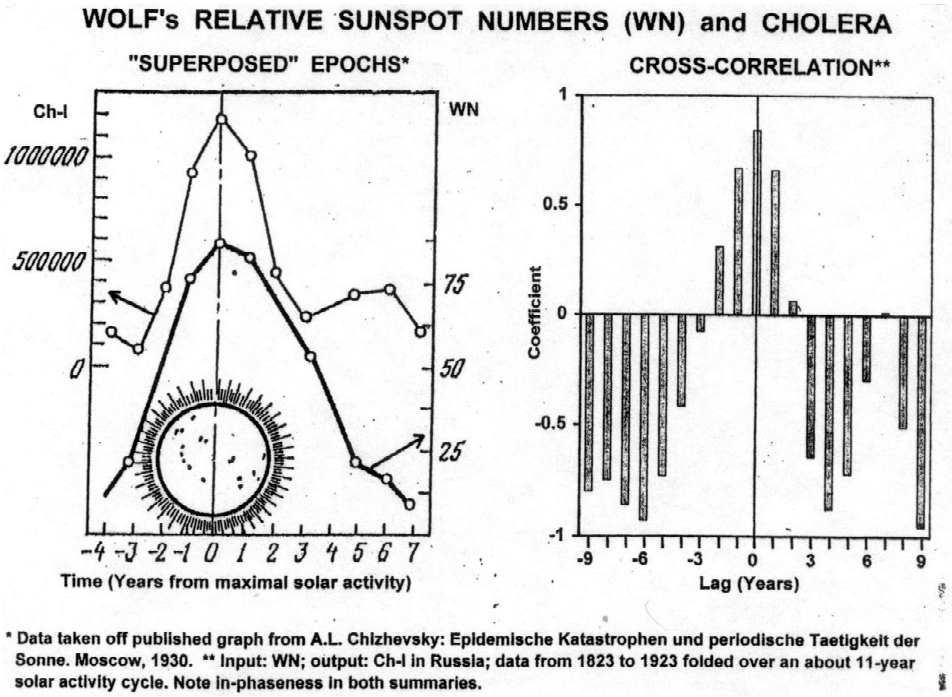


Figure 3A. Cholera in Moscow characterized by a decadal cycle revealed by superposed epochs summarized by Alexander Leonidovich Chizhevsky, according to Sigel [35]. Data from Chizhevsky on cases of cholera recorded in Moscow between 1823 and 1923, originally folded over an ~11-year solar activity cycle, showing a peak incidence coinciding with maximal solar activity (left). Data taken off the published graph, analyzed by cross-correlation, corroborate that the largest correlation corresponds to a lag of zero (right). Should the original 100-year series have been available for analysis, a measure of uncertainty could have complemented the average curves (left). © Halberg.

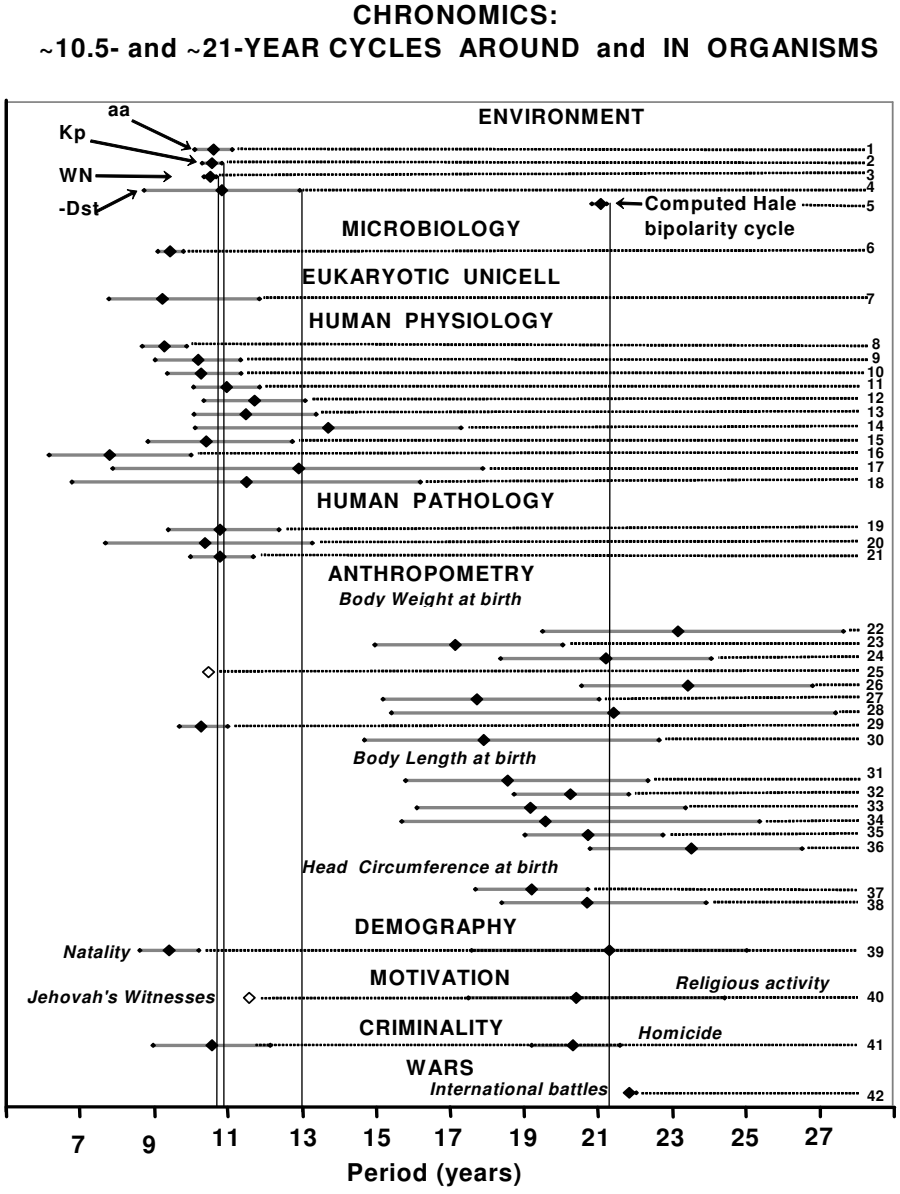


Figure 3B. Paradecadals and paradidecadals, ~10- and ~20-year cycles similar in length to the Schwabe and Hale solar activity cycles characterize a host of biological variables, from micro-organisms to human physiology, pathology, anthropometry and sociology, assessed from population statistics, yet critically dependent upon also-available individual "pilot studies". Such self-experimentation is indispensable for a scrutiny of mechanisms underlying population cycles (see HUMAN PHYSIOLOGY, above, and Figures 2E, 2F, 6-9, 17 and Tables 3 and 4). © Halberg.

The photic changes with day and night and the seasons are unmistakable in the entire biosphere: some degree of endogenicity has been documented by modern molecular biology for what the senior author has called circadians over half a century ago [51]. Partly built-in 7-day cycles are also documented by their desynchronization for 3 years -- after prior 7-day societal synchronization for the preceding 12 years, of the urinary 17-ketosteroids, breakdown products of steroidal hormones (essential for survival and reproduction) [58]. Desynchronization occurred from both the societal week, to which urine volume remained synchronized, and from a 6.75-day component of the earth's magnetism [33]. The biospheric cycles with novel or forgotten environmental nonphotic counterparts bear on physiology, as shown in Figure 5 for ~5-month cycles

(quinmensals or cis-half-years) and on many other human affairs, as in the case of ~10-, ~21- and ~35-year cycles, Figures 3 and 4 [50].

Chronomics: ~10.5- and ~21-year cycles in and around us											
					Period (years)						
					Lower	**Best**	Upper	Series duration		Number	Geographic
	Line				limit*	**Fit**	limit*	Dates	Years	of data	site
Environment	1	aa = Antipodal Geomagnetic Index			10.12	**10.63**	11.13	1890-1999	110	1 / year	
	2	Kp = Planetary Geomagnetic disturbance			10.32	**10.58**	10.85	1932-1999	68	1 / month	
	3	WN = Wolf relative sunspot number			10.37	**10.54**	10.70	1890-1999	110	1 / year	
	4	-Dst = Equatorial geomagnetic disturbance			8.75	**10.85**	12.96	1973-1999	27	"	
					10.48	**10.51**	10.55	1700-1999	300	"	
	5	Bipolarity "Hale Cycle" **			20.86	**21.10**	21.26	1890-1999	110	"	
					21.42	**21.428**	21.43	1700-1999	300	"	
Biology	6	Prokaryotes: Air Bacterial Sectoring			9.12	**9.45**	9.81	1970-1982	13	3,744	Italy
	7	Eukaryotes: Unicellular Algal O_2 Production			7.79	**9.24**	11.87	1980-1991	11	324	Germany
Physiology* **	8	Mood (RBS)			10.11	**11.50**	13.41	1966-1998	33	~5 / day	USA
	9	Time (1-Minute) Estimation (RBS)			9.38	**10.29**	11.37	1966-1998	33	"	"
	10	Urinary 17-ketosteroid excretion (CH)			8.70	**9.30**	9.90	1948-1963	15	1 / day	Denmark
	11	Peak Expiratory Flow (RBS)			10.36	**11.74**	13.11	1966-1998	33	~5 / day	USA
	12	Respiratory Rate (RBS)			10.13	**12.50**	17.32	1966-1998	33	"	"
	13	Systolic Blood Pressure - SBP (RBS)			9.05	**10.21**	11.36	1966-1998	33	"	"
	14	Standard Deviation of SBP (YW)			8.85	**10.43**	12.76	1987-1998	11	~48 / day	Japan
	15	Diastolic Blood Pressure - DBP (RBS)			10.09	**10.98**	11.87	1966-1998	33	~5 / day	USA
	16	Standard Deviation of DBP (YW)			6.18	**7.82**	10.02	1987-1998	11	~48 / day	Japan
	17	Heart Rate - HR (YW)			9.54	**12.93**	17.91	1987-1998	11	"	"
	18	Standard Deviation of HR (YW)			8.27	**11.52**	16.22	1987-1998	11	"	"
Pathology	19	Myocardial Infarction			10.00	**10.80**	11.70	1960-1996	37	129,205	USA
	20	Leptospirosis			9.40	**10.80**	12.40	1949-1995	47	2,907	Slovakia
	21	Diabetes			7.70	**10.40**	13.30	1985-1995	11	1,369	"
Anthropo-		***Body Weight***	***Boys***								
metry	22		Minnesota		19.53	**23.19**	27.67	1963-1998	36	2,136,745	USA
at birth	23		Alma-Ata Russians		14.99	**17.17**	20.07	1946-1998	53	9,056	Kazakhstan
	24		" Kazakhs		18.39	**21.24**	24.05	1946-1998	53	3,459	"
	25		Moscow			**10.49**		1874-1985	112	5,987	Russia
			Girls								
	26		Minnesota		20.58	**23.46**	26.83	1963-1998	36	1,039,464	USA
	27		Alma-Ata Russians		15.21	**17.75**	21.06	1946-1998	53	9,105	Kazakhstan
	28		" Kazakhs		15.44	**21.45**	27.45	1946-1998	53	3,448	"
	29		Moscow		9.70	**10.29**	11.01	1874-1985	112	5,840	Russia
			Both genders								
	30		Denmark		14.71	**17.94**	22.68	1973-1994	22	1,166,206	Denmark
		Body Length	***Boys***								
	31		Alma-Ata Russians		15.82	**18.58**	22.38	1946-1998	53	9,026	Kazakhstan
	32		Moscow		18.76	**20.28**	21.86	1874-1985	112	5,976	Russia
			Girls								
	33		Alma-Ata Russians		16.13	**19.20**	23.39	1946-1998	53	9,105	Kazakhstan
	34		" Kazakhs		15.72	**19.60**	25.40	1946-1998	53	3,485	"
	35		Moscow		19.05	**20.76**	22.78	1874-1985	112	5,976	Russia
			Both genders								
	36		Denmark		20.81	**23.55**	26.55	1973-1994	22	1,166,206	Denmark
		Head Circumference									
	37		***Boys***	Moscow	17.71	**19.23**	20.75	1874-1985	112	5,976	Russia
	38		***Girls***	"	18.42	**20.73**	23.95	1874-1985	112	5,820	"
Demography	39	Birth rate			8.63	**9.43**	10.23	1940-1996	57	57	USA
					17.61	**21.33**	25.05	1940-1996			
Motivation	41	Religious activity of Jehovah's Witnesses			17.52	**20.44**	24.45	1950-1999	50	328,572#	Worldwide
										5,653,987##	
Criminality	40	Homicide			8.99	**10.58**	12.16	1900-1998	99	99	USA
					19.23	**20.35**	21.62				
Wars	42	International battles			21.87	**21.96**	22.06	599BC-1957	2556	2556	Worldwide
* 95% confidence limit; not shown if cycle is not statistically significant.											
** Computed by changing the sign of WN at each WN minimum.											
***RBS - Dr. Robert B. Sothern, CH - Dr. Christian Hamburger, YW - Dr. Yoshihiko Watanabe.											
# in 1950, ## in 1999, pool of 103 plus other unspecified number of sites.											

Figure 3C. Key to Figure 3B. © Halberg.

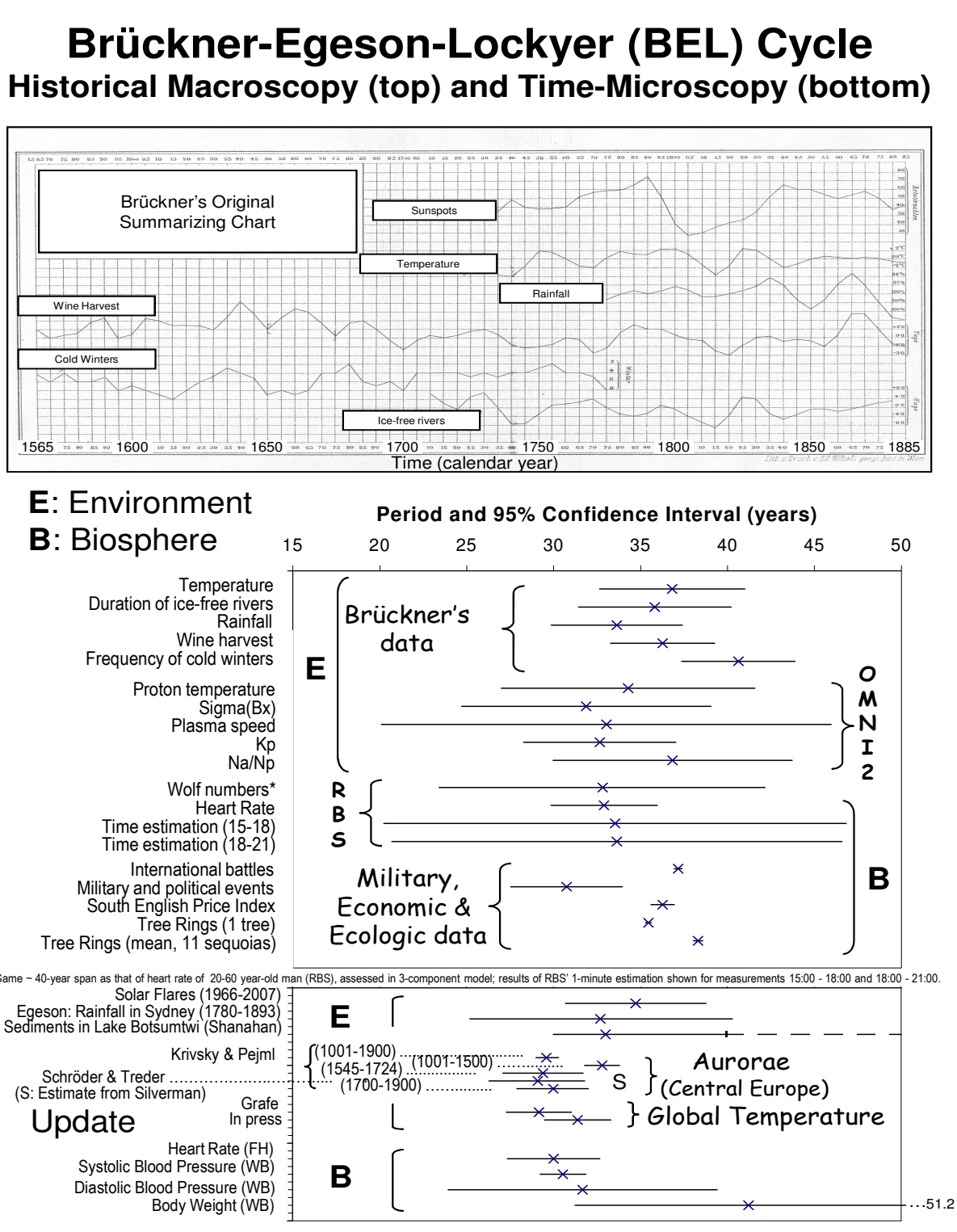


Figure 4. Paratridecadal BEL (**B**rückner-**E**geson-**L**ockyer) cycles, defined by a confidence interval of their period approaching or overlapping the 30-40-year range. © Halberg.

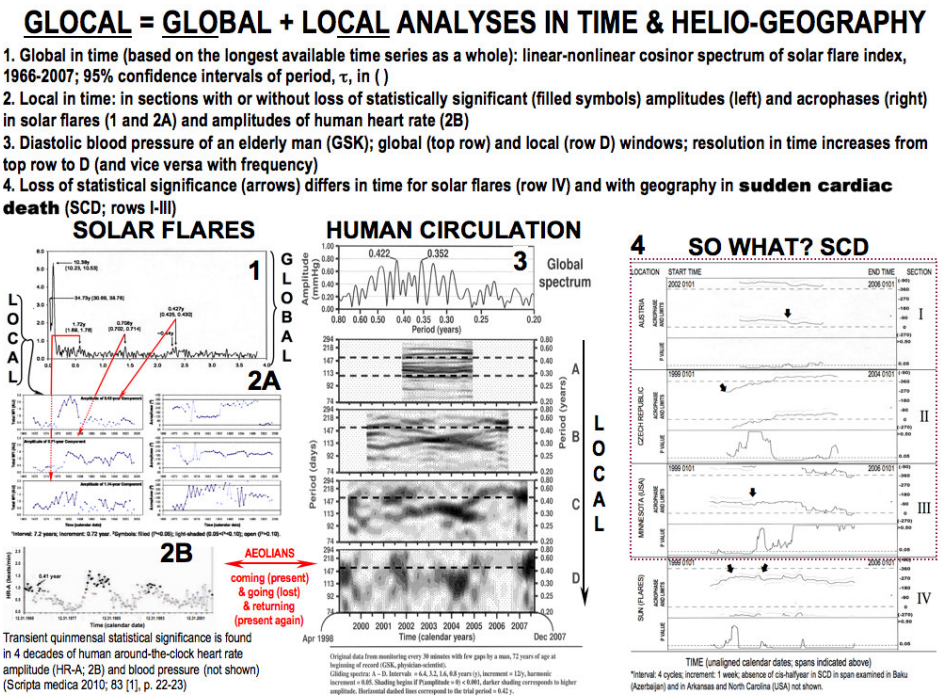


Figure 5. Quinmensals, ~5-month periods predicted by Charles Wolff [56] documented by Rieger et al. [57] in solar flares and found in the human circulation [53], in the excretion of 17-ketosteroids [54] and in the incidence pattern of sudden cardiac death [37-43]. © Halberg.

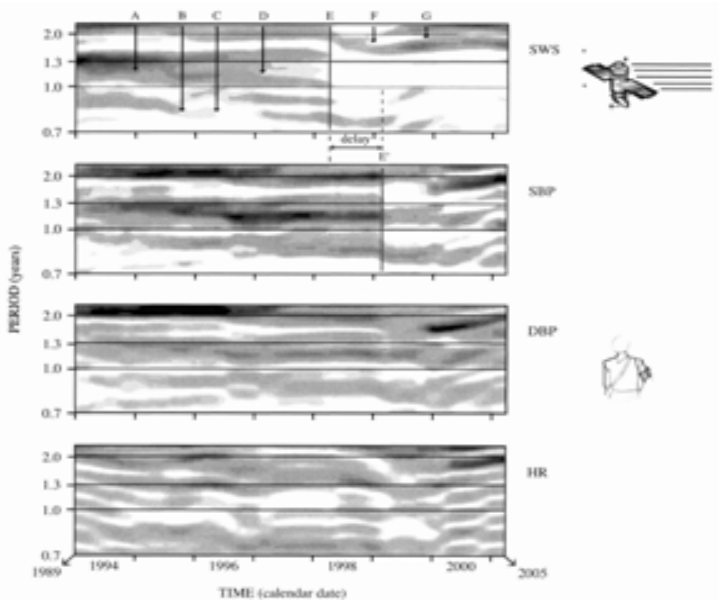


Figure 6. Time courses of the para-annual frequency structures in solar wind speed (SWS) (top) and of an elderly man's (FH) systolic and diastolic blood pressure and heart rate, SBP, DBP and HR (rows 2-4, respectively), examined by gliding spectral windows, constitute an example of the subtractive or "remove" approach. The aeolian behavior shared by SWS and SBP (drifting, bi- or trifurcation, disappearance and reappearance of a frequency and, when present, the waxing and waning of its amplitude) and the fading and narrowing, but persistence, of an ~1.3-year component are in keeping with external driving of a built-in (since dampened but persisting) component in the individual. © Halberg.

Table 2. Brückner-Egeson-Lockyer (BEL) cycle in heliogeomagnetics*

Variable	Period (years) [95% CI]	Amplitude (%M)** [95% CI]
Interplanetary magnetic field		
ProtonTemperature	34.28 [26.99, 41.57]	13.62 [6.56, 20.68]
sigma(Bx)	31.87 [24.70, 39.04]	6.81 [3.41, 10.71]
PlasmaSpeed	33.04 [20.10, 45.97]	2.47 [0.10, 4.83]
Planetary geomagnetic index		
Kp	32.65 [28.27, 37.03]	12.74 [8.58, 16.86]

*Monthly means from 1963 to 2003 (41 years), analyzed by extended cosinor with nonlinear least squares, using 33.0 years as a trial period. By the criterion of a CI of the period overlapping the 30-40-year range and, if so, of a positive CI of the amplitude, five time series in the OMNI2 database qualify as compatible with a BEL cycle. Na/Np (alpha/proton ratio: http://nssdcftp.gsfc.nasa.gov/spacecraft_data/omni/omni2.text) also had a period of 36.84 years [29.97, 43.72]; 22 other variables converge to periods shorter than 30 years or longer than 40 years; three others do not reach statistical significance, and the remaining 10 do not converge, i.e., do not allow a period estimate with the trial period used. Zürich (Wolf) sunspot numbers for the span from 1745 to 2003 yield a period of 29.068 [27.92, 30.22] years.

**%M: percentage of MESOR.

Multiple cycles of similar length are said to be congruent by overlying or even only overlapping uncertainties, CIs (95% confidence intervals) of their τs. By not insisting on identical point estimates of their τ, one allows for measurement and other error. Congruences in τ (not necessarily in phase) are also found among biospheric and environmental 7-day periods (circaseptans) and at multiples and submultiples of 7 days (multiseptans), at ~5 (and/or ~6) months, the quinmensals perhaps related to a beat of rotations at different solar latitudes [56; cf. 57] and the semiannuals to geomagnetics [29, 59]. Congruent near-transyears (1.0 year < [τ - CI] < [τ + CI] < 1.2 years) and far-transyears (1.2 years < [τ - CI] < [τ + CI] < 1.9 years) have wide ranges of period. The ranges of τ depend on the extent of the τ's drifting in time on the one hand and on wide concurrent differences in period length in various geographic locations of the same biospheric reciprocal counterpart to a component of the solar wind's speed such as sudden cardiac death [37, 43] on the other hand. Many biospheric cycles of ~11 or ~22 years (decadals and didecadals), Figure 3, and longer ones approaching or exceeding 30 years (paratridecadals), Figure 4, have their approximate counterparts in sunspots, in variables of the interplanetary magnetic field, Table 2[2] and/or in geomagnetics.

A selective assortment of biospheric-cosmic pairing is found in an individual's heart rate with a transtridecadal environmental cycle and for his blood pressure with an image of a didecadal Hale cycle of sunspot bipolarity, Figure 7.

A pull by the geomagnetic planetary index Kp of the heart rate's, but not of the blood pressure's ~7-day (circaseptan) phase [60], constitutes a selective assortment, as does, for the quinmensal, the parallelism of phases in 17-ketosteroid excretion and of Kp [59]. Some statistically significant environmental-biospheric congruences, Tables 3 and 4, are not likely due to chance, Figure 8 [61, 62]; their selective assortment is reminiscent of Mendel's laws of segregation and of the independent assortment of what became genes [63].

2 It is always desirable in time series analyses to cover more than several cycles of a given rhythm investigated. Extrapolating from a few cycles or just one, or even from part of a cycle, has indeed led to controversy. Inferences from very extensive data in the USA regarding the lack of an effect of geomagnetics indeed were drawn [86-87, cf. 88] when they did not detect any effect of magnetic storms upon the cardiovascular system based on data covering less than a circadecadal solar cycle. Classic statistical methods were used on very large samples, one totaling an estimated 1 million and another over 14 million cases. The controversy, however, can be readily resolved by the use of chronomics, combining inferential statistical time series analyses with a subtractive and an additive (remove-and-replace) approach on longer series from the USA and elsewhere, once we realize that basing a study on less than a single solar cycle is equivalent to taking the pulse for one second! Nonetheless, there are occasions when, with emphasis on necessary caution, extrapolation as-one-goes becomes desirable before the data cover a full cycle, as in the case of FH when, in ~23 years of data, the output of computer analyses yielded an ~30-year cycle in heart rate that was not part of the input. For another person, RBS, an ~50-year cycle was discovered in ~5-6 self-ratings per day of mood recorded during ~43.5 years, since he was ~20.5 years of age. Waiting for a maximum of 3 covered cycles would mean waiting until RBS reaches 170 years of age. This may be highly desirable since he is a motivated, useful scientist, but may not be assuredly possible.

Table 3. Some congruent* periods of helio-geomagnetics (columns 1 and 2), the estimation of 1-minute by a healthy man over 3.5 decades (column 3) and terrorism (bottom, bold)

	Period (years) (CI=95% confidence interval)			
Variable:	solar wind	aa	1-min estimation	
	15.6 (15.2, 16.0)			
		10.85 (10.78, 10.92)		
	9.54 (9.38, 9.70)			
			8.71 (8.52, 8.90)	
		5.31 (5.38, 5.35)		
	3.56 (3.52, 3.60)		4.11 (4.06, 4.16)	
			2.81 (2.76, 2.84)	
	2.17 (2.15, 2.19)			
		1.92 (1.89, 1.95)*	1.98 (1.94, 2.01)*	E
			1.85 (1.82, 1.88)*	
	*1.69 (1.67, 1.72)**	*1.71 (1.69, 1.74)**	*1.71 (1.68, 1.74)**	*SE*
	1.60 (1.58, 1.62)*			
	*1.52 (1.50, 1.54)**		*1.54 (1.52, 1.56)**	*S*
	*1.39 (1.37, 1.41)**	*1.39 (1.37, 1.41)**		
	*1.32 (1.31, 1.34)**			
	1.24 (1.23, 1.26)*		*1.26 (1.25, 1.27)**	S
			1.16 (1.15, 1.18)*	
	*1.06 (1.05, 1.07)**	*1.06 (1.04, 1.07)*	*1.06 (1.05, 1.07)**	*SE*
		0.99 (0.98, 1.01)*	*0.99 (0.98, 1.01)**	*SE*
	0.91 (0.90, 0.92)*			
	0.83 (0.82, 0.84)*		*0.82 (0.81, 0.83)**	**S**
	*0.72 (0.71, 0.73)**	*0.72 (0.71, 0.73)**	*0.713 (0.708,0.719)*	*SE*
		0.599 (0.598,0.600)		
	0.559 (0.557,0.561)		0.561 (0.558,0.564)	S
		0.548 (0.547,0.549)		
	0.524 (0.522,0.526)			
	0.500 (0.499,0.501)	0.500 (0.499,0.501)		
		0.437 (0.436,0.438)	0.440 (0.438,0.442)	E
	0.485 (0.483,0.487)			
	0.425 (0.423,0.427)			
	0.409 (0.407,0.411)			
	0.355 (0.354,0.356)			
		0.341 (0.340,0.342)	0.339 (0.338, 0.340)	

*Based on weekly, otherwise on daily measurements. Congruence defined by overlying or overlapping 95% confidence intervals, given in ( ). Congruence in the last column is designated as pertaining to the Sun (S) or Earth (E).

The transyear of 1.34 years, with CI [1.31, 1.37], of terrorism worldwide is congruent with environmental periods and time courses show similarities that are resolved with hypothesis testing and estimation of the uncertainty of the acrophase in Figure 3c. When more data on terrorism are analyzed, the transyear period (in the footnote to Table 2) is of 1.28 [1.26-1.29] year length overlapping with a period of 1.26 years in 1-minute estimation and solar wind speed.

Table 4. Spectral components in human violence (MIPT) and in (possibly involved) solar (SWS), terrestrial (aa) and psychophysiological variables*

Trial period (y)	MIPT**			SWS			aa			1MTE			HR		
25	27.81	25.54	30.08	NS			NS			25.92	23.68	28.16	NS		
11	9.67	9.17	10.17	9.48	9.24	9.73	9.40	9.09	9.70	NS			NS		
3	2.88	2.82	2.94	2.90	2.83	2.97	NS			2.82	2.76	2.87	2.75	2.68	2.83
1.7	1.69	1.67	1.72	1.69	1.66	1.72	1.71	1.69	1.74	1.71	1.68	1.74	NS		
1.3	1.34	1.32	1.37**	1.32	1.31	1.34	1.32	1.30	1.33	1.26	1.24	1.27	1.25	1.23	1.27
1	NS			0.998	0.985	1.012	0.989	0.979	0.999	0.994	0.982	1.007	0.994	0.987	1.001
0.5	0.496	0.493	0.498	NS			0.500	0.499	0.502	NS			0.502	0.499	0.505
Trial period (y)	SBP			DBP			Mood			Vigor			Oral Temp		
25	24.20	23.02	25.38	21.22	20.12	22.32	23.06	19.11	27.02	NS			NS		
11	11.01	10.65	11.37	10.54	10.15	10.93	11.27	10.81	11.73	8.91	8.60	9.22	11.00	10.50	11.50
3	3.02	2.94	3.10	3.22	3.12	3.33	2.71	2.63	2.78	2.97	2.86	3.08	2.85	2.77	2.94
1.7	1.68	1.65	1.71	1.69	1.66	1.73	1.74	1.71	1.77	1.71	1.68	1.74	NS		
1.3	1.31	1.29	1.33	NS			1.38	1.36	1.40	NS			NS		
1	1.002	0.998	1.006	1.007	1.002	1.012	1.018	1.007	1.029	1.032	1.019	1.044	1.015	1.007	1.023
0.5	0.500	0.498	0.502	0.500	0.497	0.504	0.502	0.499	0.504	0.502	0.498	0.504	0.504	0.500	0.508

*MIPT: Memorial Institute for the Prevention of Terrorism (the presence of counterparts of statistically significant components in MIPT is investigated in other time series); SWS: solar wind speed; aa: antipodal geomagnetic index; 1MTE: 1-minute time estimation; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure

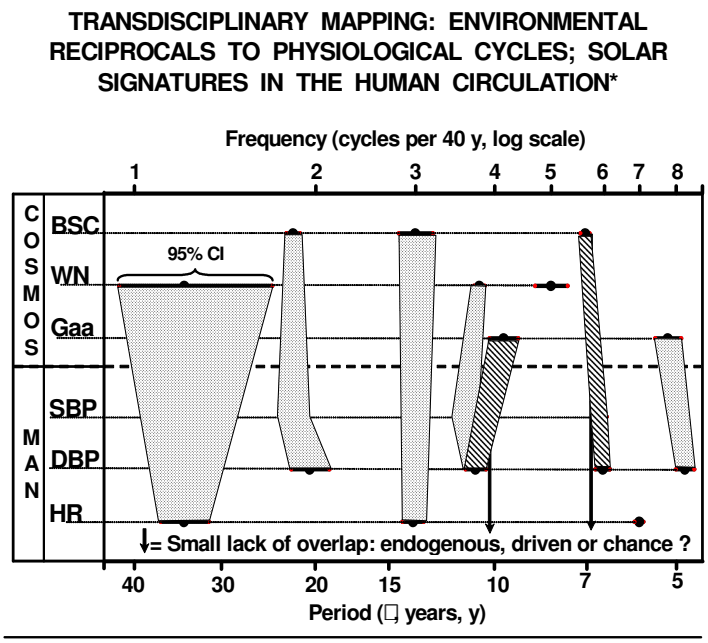
[1]MTE, HR, SBP, DBP, mood, vigor and oral temperature from RBS, a clinically healthy man, ~20.5 years old at the start of record of ~5-6 daily self-measurements on May 11, 1967, and continuing for over four decades to the present day.

When found, counterparts are listed here.

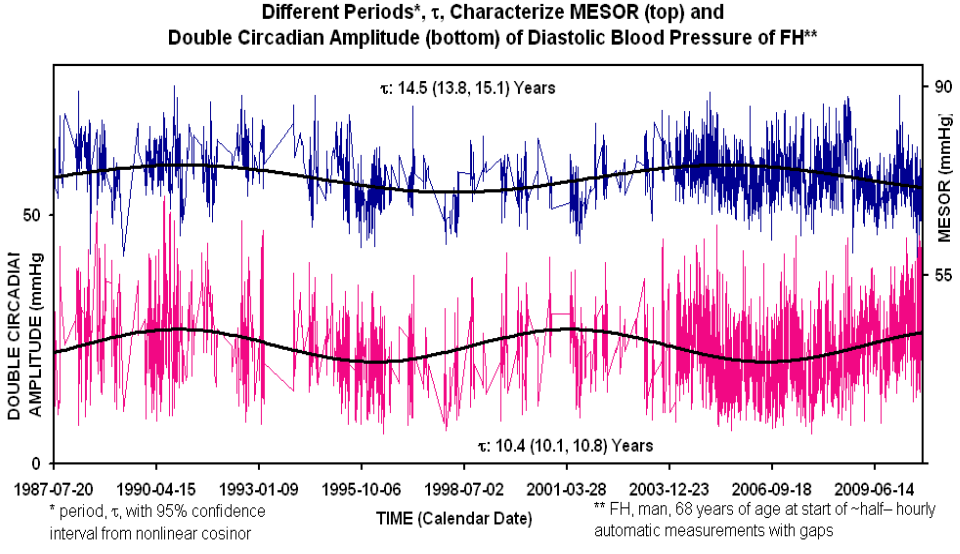
**When added daily data were accessed in MIPT and analyzed 3 months after our first use of the MIPT database (in January 2008 rather than October 2007), the about 1.3-year period changed to 1.28 [1.26-1.29] years length for MIPT, becoming congruent with 1MTE and HR. Second decimals are computational results to which no importance is necessarily implied in view of the drifting of the periods.

Analyses (not tabulated above) of much shorter time series of a) helioseismologic probing of the solar interior at the sun's equator yield a period of 1.36 [1.27, 1.45] years and b) of Gallup Poll's approval ratings of George W. Bush from February 2001-December 2007 (A: approval; D: disapproval; N: no opinion) show for A, a period of 1.46 [1.33, 1.58] years, for D one of 1.42 [1.29, 1.54] years and for N one of 1.75 [1.51, 1.99] years. These findings hint at the importance of the about 1.3-year component, while the about 1.7-year component is also seen in cosmic rays. The finding in polls (b) supports the pervasive influence of the cosmos, overriding the influence of the seasons, since a calendar-yearly component is absent.

Subtractions, Figure 6, from the transdisciplinary spectrum of an environmental ~1.3-year or 7-day component, or their addition or both, Figure 9, may entail corresponding damping (but not loss) or amplification in the biosphere. Such observations validate biospherically the long-term occurrence of an environmental cycle to the point that it became genetically coded [63]. Damped persistence of the biospheric cycle upon removal of the environmental counterpart is hence a transdisciplinary tool in the service of physics, biology and beyond for an eventual unified science. Among others [64], Alexander Leonidovich Chizhevsky [65; cf. 35], Figure 10, Frank A. Brown Jr, Figure 11, Düll and Düll [89] and Stetson [90] foresaw all of this: Chizhevsky found the circadecadal sunspot cycle of ~11 years in military-political affairs [35, 65] and folded cases of cholera in Moscow from 1823 to 1923 over an 11-year cycle; a peak cholera incidence coincided with maximal solar activity, corresponding (in our metaanalysis) to maximal cross-correlation [36], Figure 3A. Breus and Chibisov have updated heliobiology [18, cf. 91].



A



B

Figure 7. Selective environmental-psychophysiological pairing of variables (A) in a clinically healthy man, RBS, and of circadian characteristics, MESOR vs. circadian amplitude (B) in an elderly man on antihypertensive medication (FH). © Halberg.

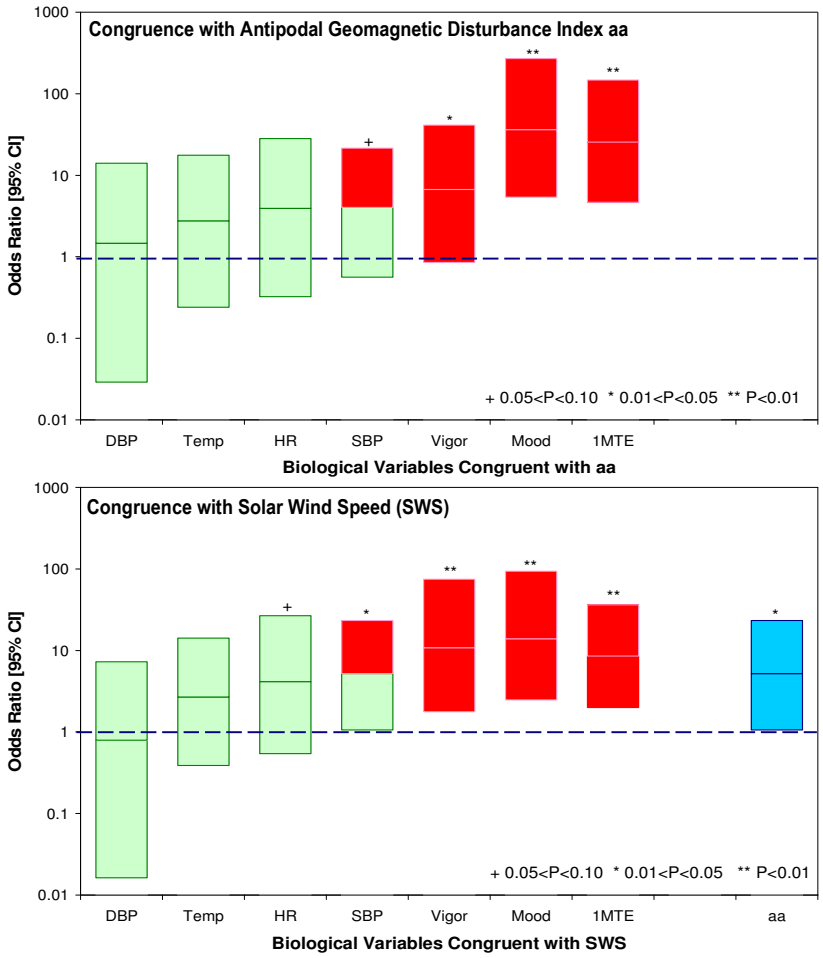


Figure 8. The association of RBS's psychophysiology with a true terrestrial or interplanetary magnetism more than matches the association of the latter two sharing common para-annual spectral components [61, 62] (see also Figure 17). © Halberg.

The extension of the mapping of the resonances in the human heart and mind of helio-, interplanetary and geomagnetics is part of an international transdisciplinary effort on The BIOsphere and the COSmos (BIOCOS) [2, 3].

The question thus arises: Can environmental influences, whether direct ones or exerted via the weather in space acting upon terrestrial conditions, be monitored and thus investigated in human individuals, and if so, can a cost-effective self-surveillance be implemented for the goals of both the individual and society at large? In the case of the given proverbial person on the street or at home, the aim is to avoid massive brain attacks as well as transient ischemic attacks. In the case of the population, we aim at the prevention of terrorism and war as well as crime. The unseen factor "cosmos" can perhaps be assessed as a dividend from self-help by computer-implemented self-surveillance.

For an automatic analysis of the data of individuals, a website manned for special tasks arising in the course of the care or cure of individuals could provide the accumulating data for many aspects of research; its combination could be a first step toward a worldwide surveillance of how we are affected by the sun in whose atmosphere we live, starting at birth [92], Figure 12. Photic and non-photic spectral components determine both the deep history of the origins of living matter and the more recent past. During the current lifetimes of individuals, we should strive to optimize not only the habitat's temperature and light, but also more subtle factors that impinge upon us and can constitute loads that are best recognized so that we can develop countermeasures for associations that started with the changing

resistance to cholera (Figure 3A) and more broadly to infection [66, 67; cf. 35] and with revolutions [65, 68] and have become apparent by the patterns of sudden cardiac deaths, Figure 13, suicides, Figure 14, and terrorism, Figures 15 and 16.

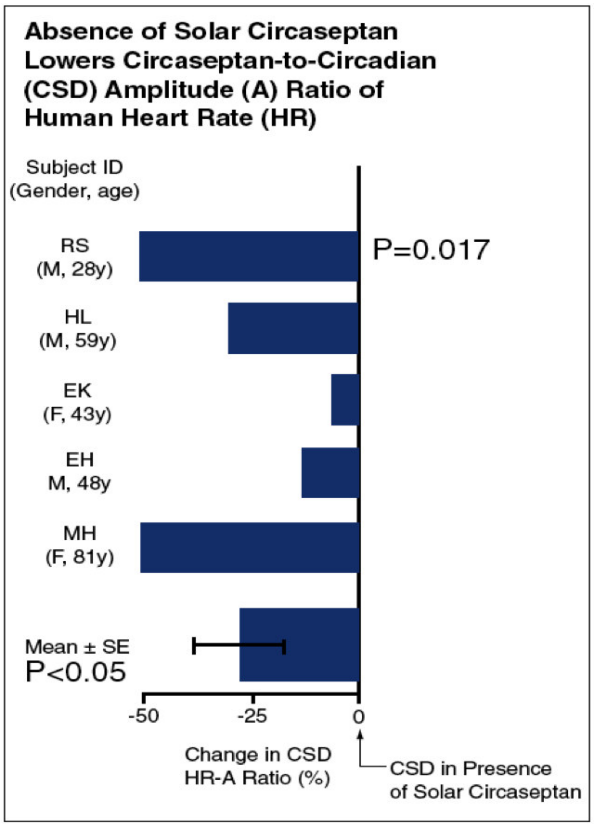


Figure 9. An ~7-day spectral component in the heart rate of five men is less prominent when the solar wind loses its counterpart of corresponding length. Implied, but not shown, is the persistence in the biosphere of an ~7-day component that can be amplified (driven) by a reciprocal component in solar activity [62, 63, 93]. © Halberg.

The criterion used herein to examine environmental-physiological associations based on congruence, defined by overlapping CIs, can be used to inquire about the extent to which the results may be due to chance, as compared to the reference standard of an association between interplanetary and terrestrial magnetism with long-sought results. The biological associations of the interplanetary (solar wind speed, SWS) or the terrestrial (antipodal index aa-gauged) magnetism more than match the relation of the chosen standard of interplanetary and terrestrial magnetism, Figure 17 [61, 62].

Chizhevsky (1897-1964) who demonstrated in descriptive statistical terms a circadecennian cycle in the ravages of an infectious disease (validation in Fig. 3A).

Figure 10. Alexander Leonidovich Chizhevsky (1887-1964).

Figure 11. **Frank A. Brown Jr. (1908-1983)**.

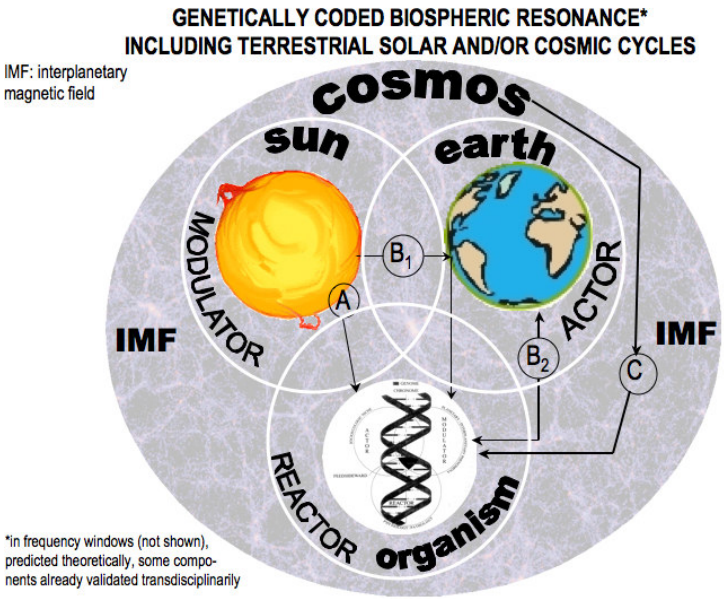


Figure 12. We need not ignore the many signatures of the cosmos with validated statistical significance of anticipated periods that characterize: a. dozens of decades-long time series of human blood pressure and heart rate; b. other physiology and psychology, including human mental functions; c. religious proselytism; d. suicide; e. sudden cardiac death; f. terrorist activity for the past 39 years; g. 2,556 years of international battles compiled by Raymond Holder Wheeler; h. military expenditures for training in non-medical science; i. non-medical (scientific) degrees earned; j. Gallup Polls; and k. political and military actions in nearly 200 years, meta-analyzed from the much broader treasure of data compiled by Alexander Leonidovich Chizhevsky. While chance can never be ruled out, it would be further greatly reduced by systematic lifetime monitoring of physiology in health, of pathology and disease, notably in archives to separate effects of sun and earth, many of which are beneficial. Other effects such as extreme cold and heat or extreme light can be met by countermeasures such as housing, heating and air conditioning. The task remains to develop countermeasures to those nonphotic effects that can be documented as harmful. While the earth is the immediate actor, and for that action the sun is the modulator, the biosphere reacts directly (Figure 17) to both terrestrial and solar factors; the roles of actor, reactor and modulator are continuously changing. In the greenhouse effect, organisms are the actors, as shown by a double-headed arrow (B_2). There may be other more subtle effects of synchronized human action upon the earth. Effects of the moon also are demonstrated [94]. Original drawing by Mary Sampson. © Halberg.

Everybody's task is to do preventive maintenance for one's own health, donating the data (deidentified when desired to protect privacy) to contribute to the maintenance of societal health. For these purposes, just as we learn geography from maps, imaging in time seems essential, the sooner and the earlier in life the better, all within the scope of a website for these purposes, Figure 18.

A Chronobiologic-Chronomic Website

Chronobiology, the study of the time structures of living things (chronomes), including predictable rhythms, along with chaos and trends, and chronomics, the investigation of links between cycles in organisms and their environment, near and far, seen and unseen, can be taught early in life [69, 70]. Chronobiology and chronomics image in time, revealing alterations of variability that currently go unrecognized and concern many millions of people, including all those with high blood pressure.

There is a need to change from a current spotcheck-based health care to one based on time series for educated self-help by self-surveillance [95]. Cybercare [71] could use modern technology not only to enable what we do today with blood pressure and heart rate (spotchecks and around-the-clock 24-hour profiles) more readily and on a larger scale. Instead, it could also lead to great improvements (from a minimal 7-day to continuous surveillance around-the-clock and as-one-goes analyses) by new diagnoses that recognize and treat disease risks (revealed by altered variability) rather than established illness only.

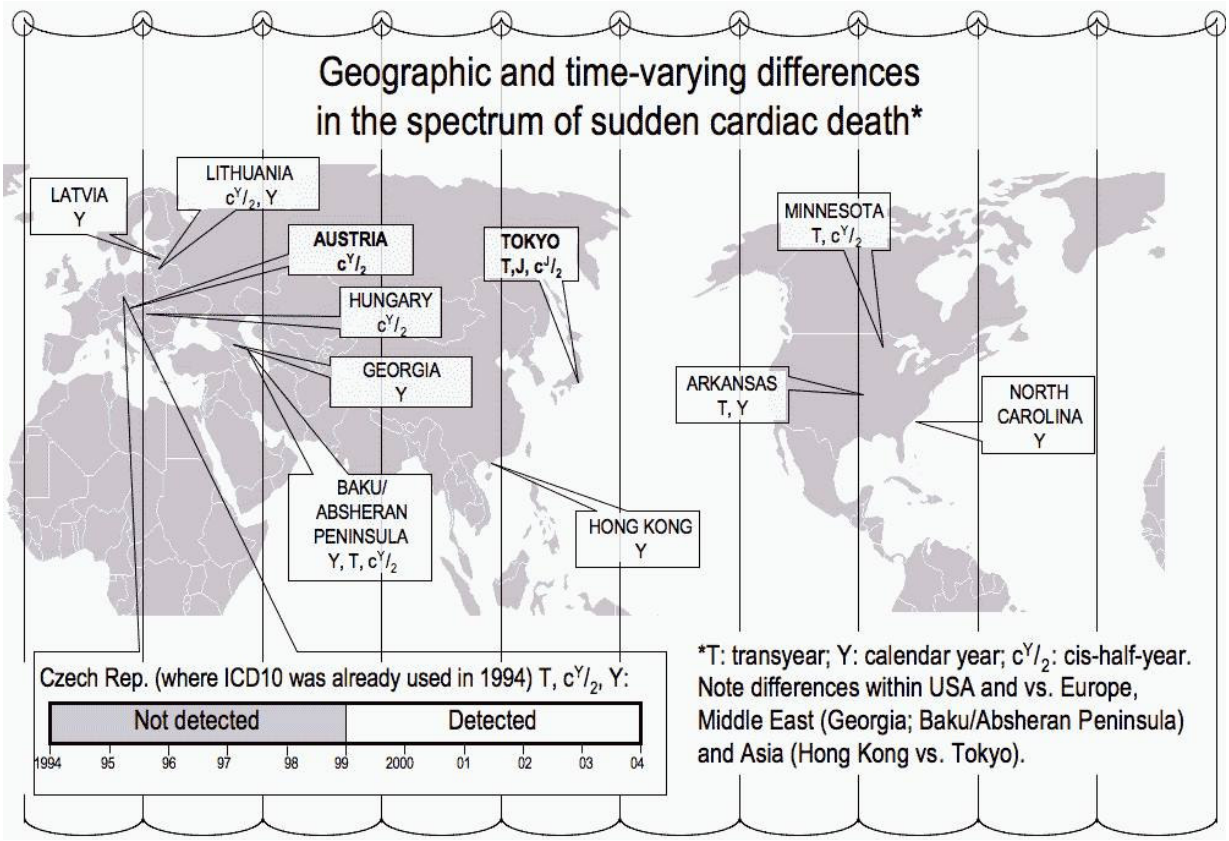


Figure 13. A curtain of uncertainty, because of limited available data, hides any time- and geographic (geomagnetic or dip-magnetic) site-specificity of various spectral aspects of sudden cardiac death. Thus, we find a transyear in Minnesota with a cis-half-year (cY/2) and both a calendar year and a transyear in Arkansas and the Czech Republic: at the latter site a cis-half-year, corresponding in length to an also-transient period of hard solar flares, is detected after but not before 1999. Whether other geographic differences in sudden cardiac death may also relate to any magnetic latitude deserves scrutiny. It is noteworthy in any event that cardiac arrhythmias can also transiently reveal a transyear or a cis-half-year, each in a different solar Schwabe cycle stage, as seen from the limited data in [37]. In 1998, Peter V. Minorsky (Annals of Botany 1998; 82: 133-140) re-evaluated "Latitudinal differences in coconut palms' foliar spiral direction" (FSD); he hypothesized that latitude-dependent biases in FSD, a non-Mendelian trait, will be associated with a temporally-varying component of the earth's magnetic field. Earth currents, which are measurable in trees, bias the difference of auxin (or auxin transport proteins) in young embryos, such that left-handed palm trees (LHP) are produced preferentially in the Northern Hemisphere and right-handed ones (RHP) in the Southern Hemisphere. He built his observations on a previously collected data base by Davis and Davis, revealing that the ratio of (LHP – RHP)/Total was better correlated with magnetic (dip) latitude than with geographic or geomagnetic (centered dipole) latitude. Most recently, Minorsky and Bronstein (Natural experiments indicate that geomagnetic variations cause spatial and temporal variations in coconut palm asymmetry. Plant Physiol 2006; 142: 40-44) referred to this classical case of morphological antisymmetry in which dextral and sinistral forms are not inherited and are equally common within a species, proposing that Pc1-induced earth currents may bias the diffusion of morphogens in coconut palm embryos, thereby giving rise to asymmetries of FSD. © Halberg.[3]

3 Thus far analyses were on data from Argentina, Armenia, Austria, Azerbaijan, Belgium, Bulgaria, Canada, China, the Czech Republic, Denmark, the Republic of Georgia, Hong Kong, Hungary, India, Italy, Japan, Kazakhstan, Mexico, Poland, Peru, Romania, Russia, Saudi Arabia, Slovakia, Spain, Sweden, Ukraine and the USA.

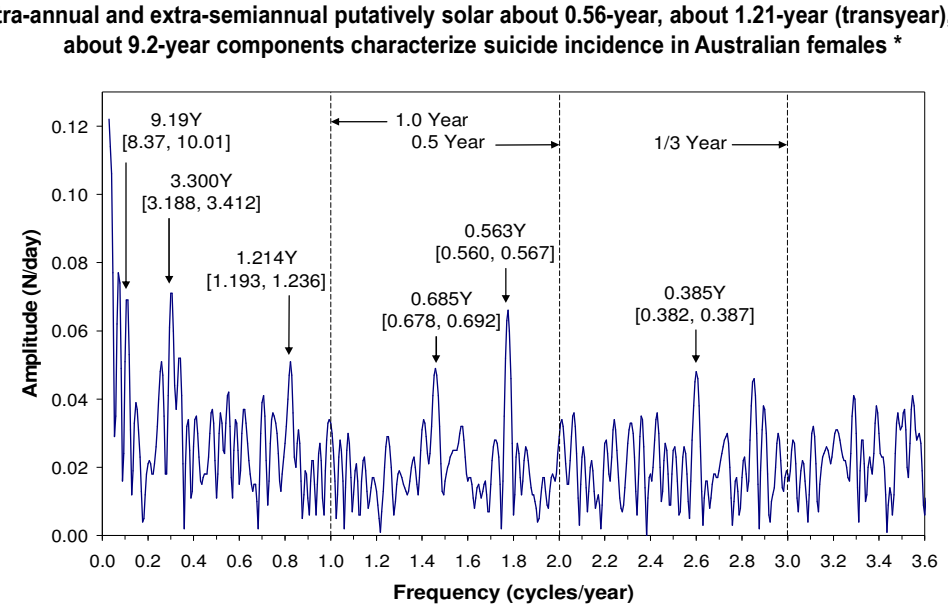


Figure 14A. Nonphotic para-annual prominence in the incidence spectrum of suicides by females in Australia. © Halberg.

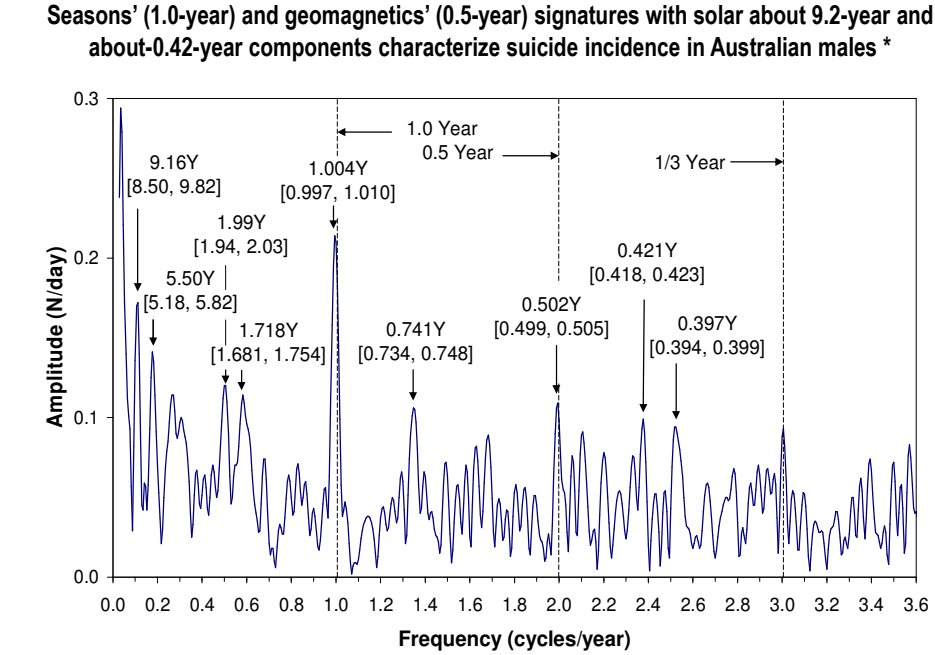
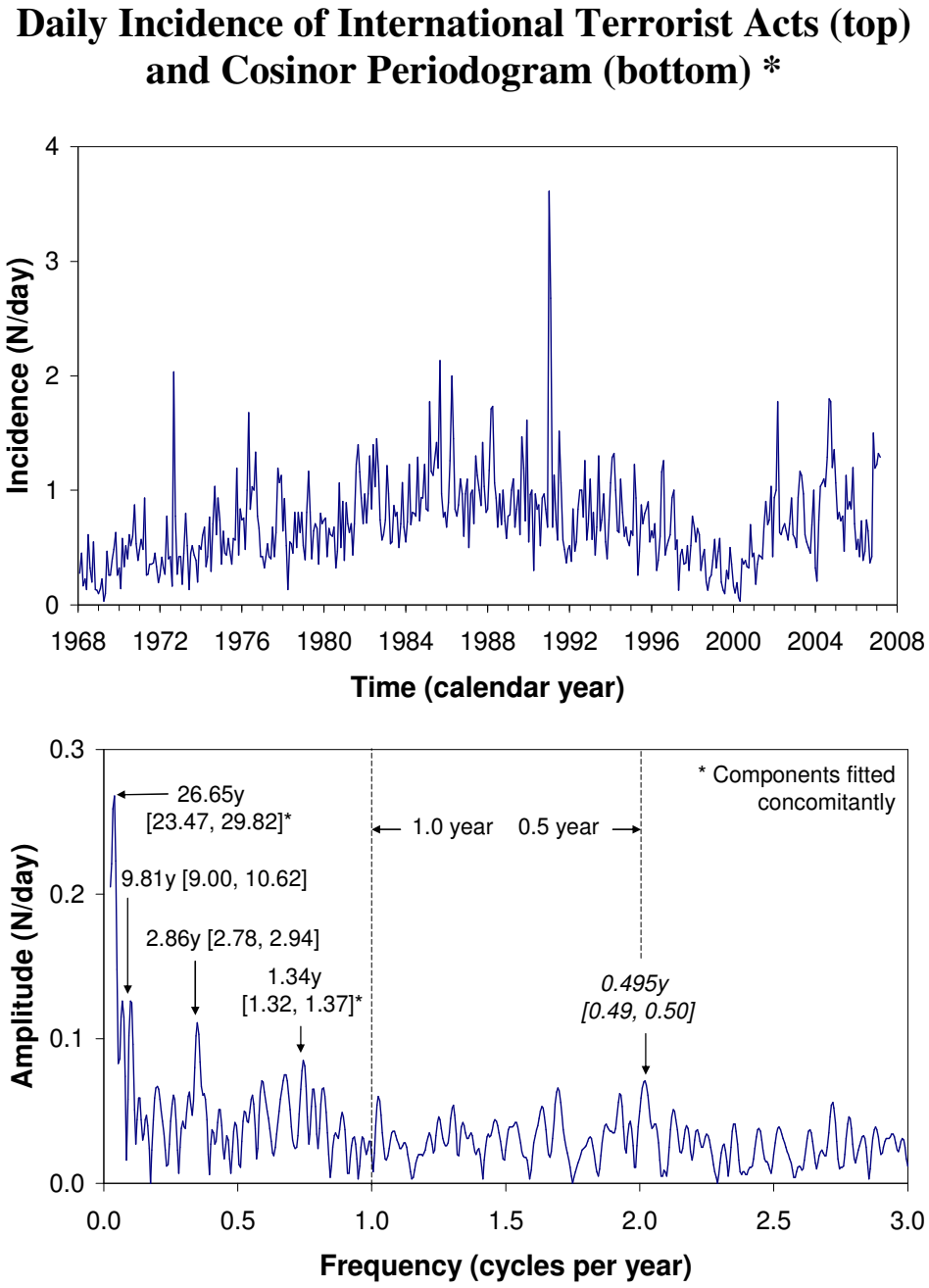


Figure 14B. Coexisting photic and nonphotic components in suicides by males in Australia. © Halberg.



* From February 1968 to March 2007, daily incidence computed from monthly totals (adjusted for differences in the number of days per month). Data from MIPT Terrorism Knowledge Base (http://www.tkb.org/).

Figure 15. In data from the Memorial Institute for the Prevention of Terrorism's (MIPT) Terrorism Knowledge Base (1968-2008) (http://www.tkb.org/) (top), a transyear of ~1.3 years is detected in the absence of a calendar yearly component. © Halberg.

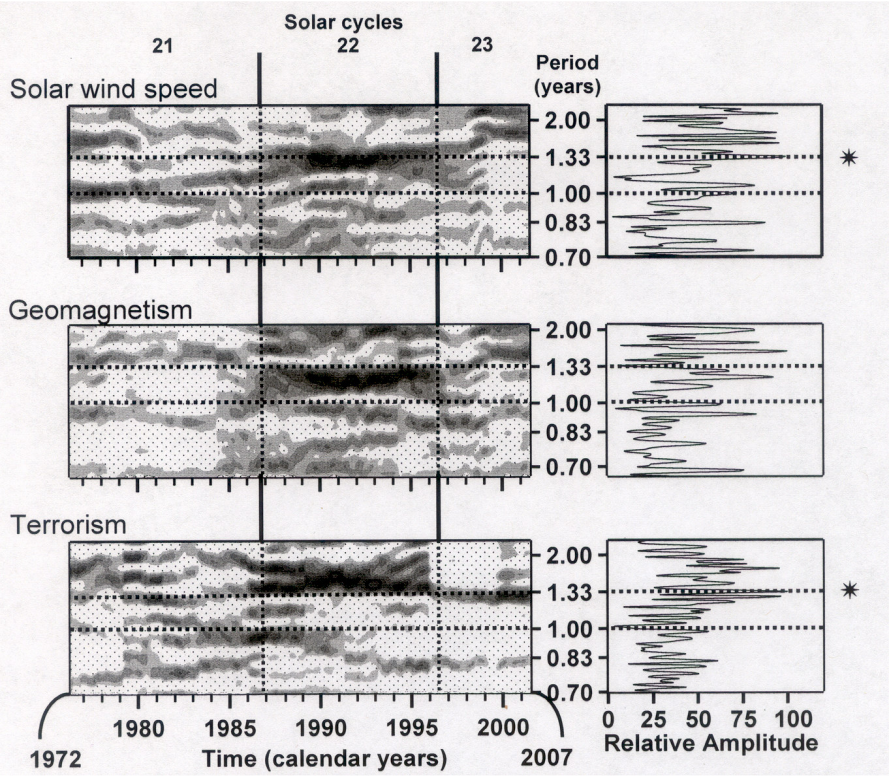


Figure 16. Just as removal and replacement of a gland led to endocrinology, so biological consequences of the loss of environmental spectral components are critical to chronomics, the study of chronomes (time structures) in and around us. Note neighboring frequencies waxing at or near a transyear component in solar wind speed (top row), geomagnetism (second row, aa), and in 39 years of terrorist activity (bottom row), an association supported by an independent method (by the statistical significance of the fit of a 1.3-year far-transyear to interplanetary (SWS) and terrestrial (aa) magnetism and to terrorism. © Halberg.

Ever-refined, miniaturized, affordable, instrumentation for data collection and transfer, to replace current functional tools and the development of a smart phone as a diary, psychological test device and data storer and transmitter, in combination or as a complement to an international multilingual chronobiologic-chronomic website, could be the first two steps toward this goal, for self-health service, education and multipurpose research.

Background

During the past decade in particular and in some cases for much longer, the Halberg Chronobiology Center at the University of Minnesota has served all comers from different continents[2] with cost-free analyses of time series, including sphygmochrons, summaries of blood pressure and heart rate for diagnostic purposes and more recently control charts, Figure 19 (cf. Figure 20), to assess changes in time series as a function, among others, of the timing of medication [1; cf. 72-74]. The Phoenix Study Group, composed of volunteering members of the Twin Cities chapter of the Institute of Electrical and Electronics Engineers (http://www.phoenix.tc-ieee.org) has developed scenarios [75] on how this current activity, on the international scale (on different continents) could be enlarged.

As hardware and software technologies advance, Larry A. Beaty of Phoenix [76, 77] expects to see improvements in the convenience, cost, sensitivity of sensors, and network connectivity of blood pressure monitors, to which he already contributed [78]. He continues to investigate a change from the current desideratum of 7-day/24-hour monitoring preferably to continued surveillance by an unobtrusive, affordable instrument, possibly on the wrist. He also started a website for use of the currently available

analysis software by self-helpers in their homes, interested in self-surveillance-based, preventive health care. A manned international website would save the (if necessary de-identified) data for ongoing multipurpose research.

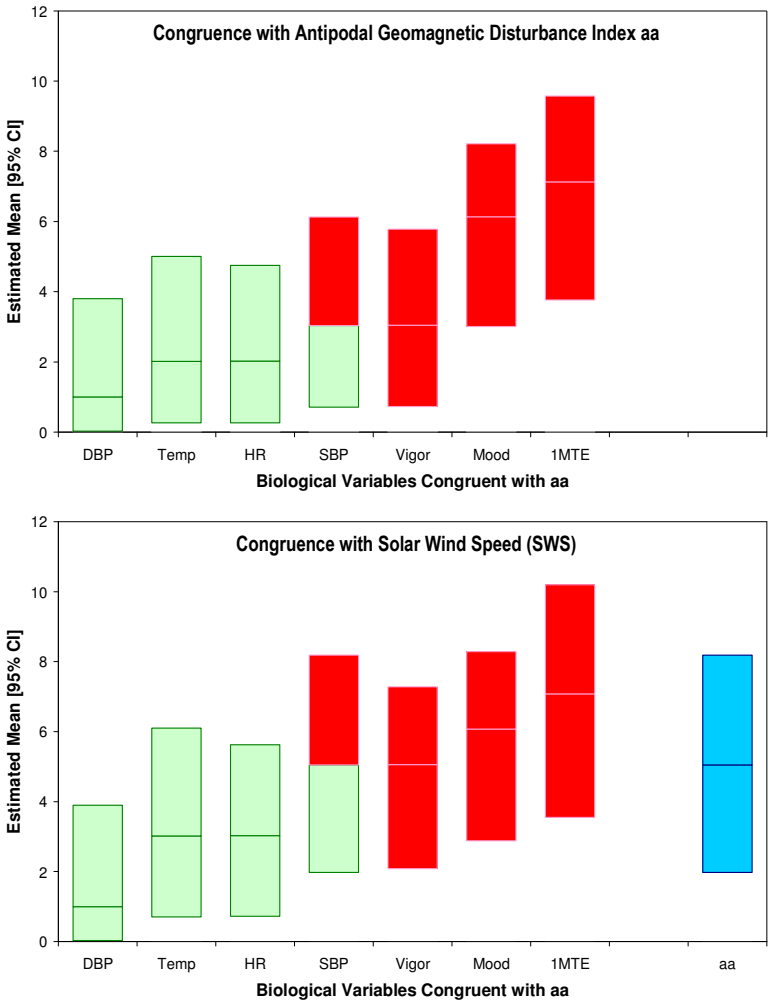


Figure 17. Some inferentially statistically validated congruences of human somatic and mental functions with the environment, gauged by the antipodal geomagnetic disturbance value (aa) (top) and solar wind speed (SWS) (bottom). While limited to a single clinically healthy case, RBS, a man aging during the study from ~20 to ~60 years of age, discussed in detail elsewhere (Tables 2 and 3 and Figure 8), the number of congruences found for the estimation of 1-minute and for mood in the spectral range investigated (from one cycle in 2.5 years to 3 cycles per year) more than equals that of the known association of helio- and geomagnetism, commented upon in 1852 by Gen. Sir Edward Sabine (on the basis of too few data) -- "... it is certainly a most striking coincidence, that the period, and the epochs of minima and maxima, which M. SCHWABE has assigned to the variation of the solar spots, are absolutely identical with those which have here been assigned to the magnetic variations" -- and extended to the solar wind by Marcia Neugebauer (Large-scale and solar-cycle variations of the solar wind. Space Science Reviews 1975; 17: 221-254) and qualified by Gordon Rostoker and Carl-Gunne Falthammar (Relationship between changes in the interplanetary magnetic field and variations in the magnetic field at the earth's surface. J Geophys Res 1967; 72, 5853-5863) and by Wolfgang Baumjohann and Gerhard Haerendel (Magnetospheric convection observed between 0600 and 2100 LT: solar wind and IMF dependence. J Geophys Res 1986; 90 [A7]: 6370-6378). When congruence is assessed by means of the odds ratio based on the non-central hypergeometric distribution (see Figure 8), mental functions show higher congruence than somatic functions; among the latter, systolic blood pressure is responsive, perhaps constituting a seemingly acceptable approximation for the mental functions. © Halberg.

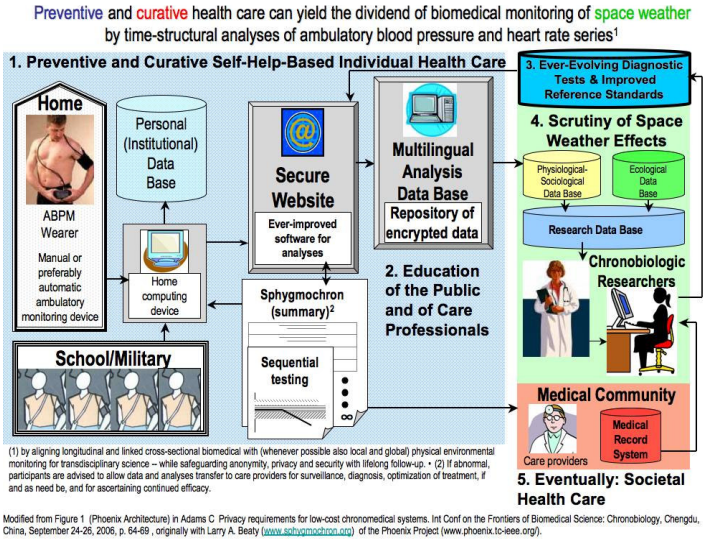


Figure 18. The Phoenix Group of volunteering electrical and electronic engineers from the Twin Cities chapter of the Institute of Electrical and Electronics Engineers (http://www.phoenix.tc-ieee.org) is planning on developing an inexpensive, cuffless automatic monitor of blood pressure and on implementing the concept of a website (www.sphygmochron.org) for collection and analysis of data collected with these instruments. © Halberg.

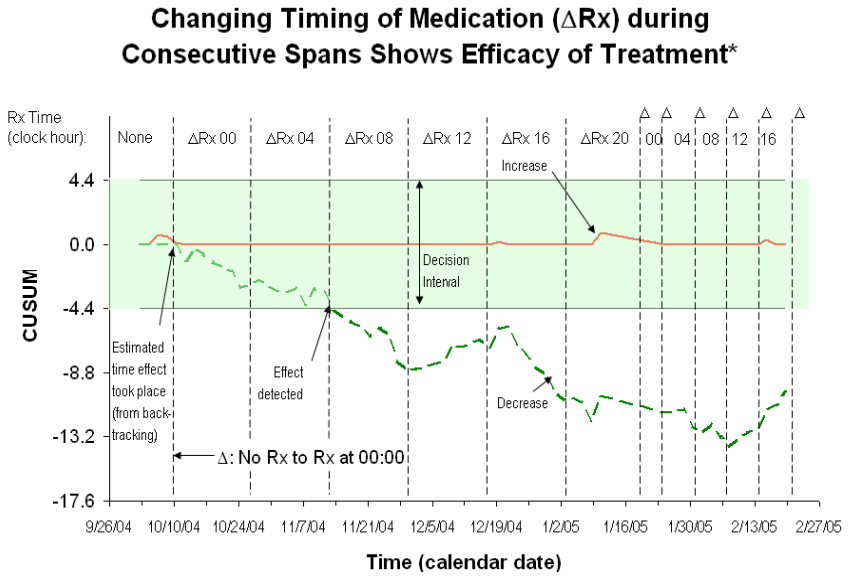


Figure 19A. Changing timing of medication (ΔRx) during consecutive spans shows whether and, if so, when treatment is most effective as an empirical approach to chronotherapy. Immediately after the diagnosis of MESOR-hypertension, one should ascertain that the treatment is effective. Optimization of treatment effects by timing can be achieved for the individual patient by systematically changing, e.g. advancing the time of treatment. Successful treatment of MESOR-hypertension can thus be assessed by a self-starting cumulative sum control chart to be offered by the website. To optimize his hypotensive treatment (Rx), a just-diagnosed 24-year-old individual (TT) switched his Rx first every 17 days by 4 hours and then mostly at shorter intervals. Note statistically significant decrease in MESOR, evidenced by the breakout outside the decision interval of the negative CUSUM line. With continued Rx, the blood pressure MESOR leaves the decision interval, indicating a statistically significant decrease but Rx-time-dependent in overall blood pressure. © Halberg.

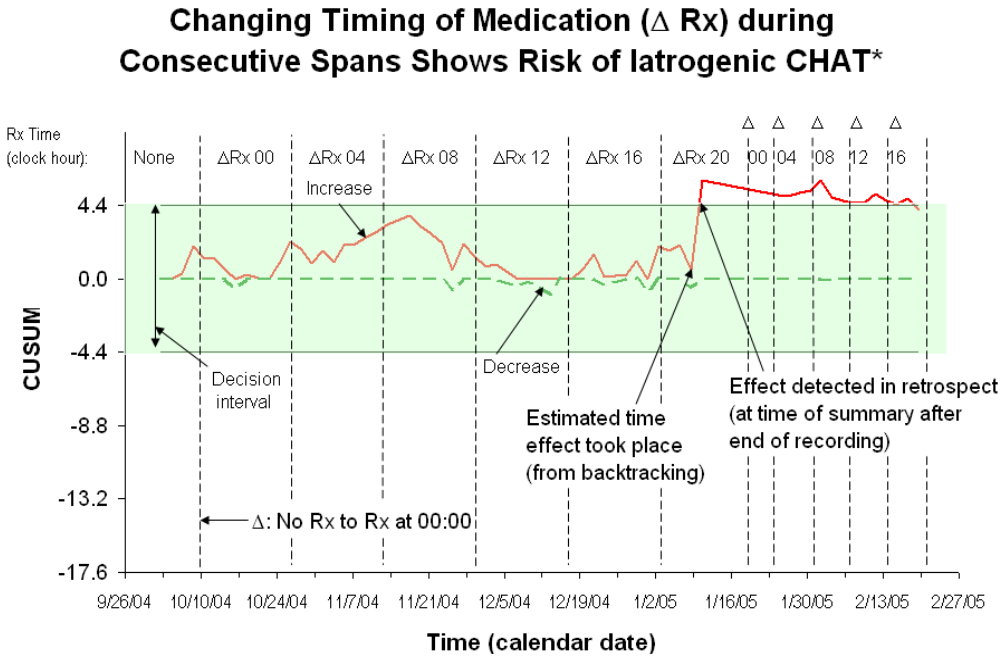


Figure 19B. Changing timing of medication (ΔRx) during consecutive spans shows risk of iatrogenic CHAT. An empirical approach to chronotherapy: immediately after diagnosis, one should ascertain that one does not induce circadian hyper-amplitude-tension (CHAT) by inappropriate timing of anti-hypertensive medication. In this 24-year old man (TT) who advanced the time of treatment by 4 hours every 17 days initially and at shorter intervals thereafter, treatment in the evening was associated with iatrogenic CHAT, raising the question whether the risk of MESOR-hypertension may not have been traded for the sometimes even higher risk of stroke that CHAT represents. Iatrogenic circadian hyper-amplitude-tension, CHAT, induced by treatment at 20:00 daily, was silent to office visits. TT may have traded benefit (lowering of the MESOR of blood pressure) for something worse (circadian overswinging of blood pressure). This danger applies to some hypertensives (who tend to have a large circadian amplitude of blood pressure) to whom treatment time is not specified by the care provider, as was the case for TT (or is specified for bedtime). A few others who took hypertensive medication at bedtime were also found to have CHAT. The figure also shows the assessability of otherwise undetected harm by as-one-goes sequential analysis. © Halberg.

What is needed

We propose beginning implementation and manning of an international website that could serve the multiple purposes of 1) automatic service to healthy or sick self-helpers as well as to the health care professionals, 2) personnel preparing materials and interesting subjects in life-long self-help in their self-surveilled health care, for 3) teaching how to interpret results of analyses that detect novel indicators of risk [1, 72] or disease, for 4) guiding any treatment, for 5) continuing research on improving reference standards and 6) on refining the procedures that now detect treatable conditions, some with risks greater than a high blood pressure in certain populations and, on the same data pool, as it already accumulates in some subjects for decades, 7) to monitor the Sun, in whose atmosphere we live and the broader cosmos to map on a population the many environmental cycles reflected in their biospheric counterparts, and 8) to investigate in continuously monitored individuals, any alterations with focus on any undesired consequences of environmental events and, as necessary, 9) for the development of countermeasures.

Specific components of the first website design addressed by Larry Beaty [76-78] are:

- making the sphygmochron analysis available to home users, and their health care providers,
- making blood pressure data from home users available to researchers,

- updating the analysis software in the light of results of new research as time progresses,
- providing a library of educational materials for home users and health care providers, and
- building a community of self-helping users consisting of those engaged in preventive health care as well as those being treated by health care providers.

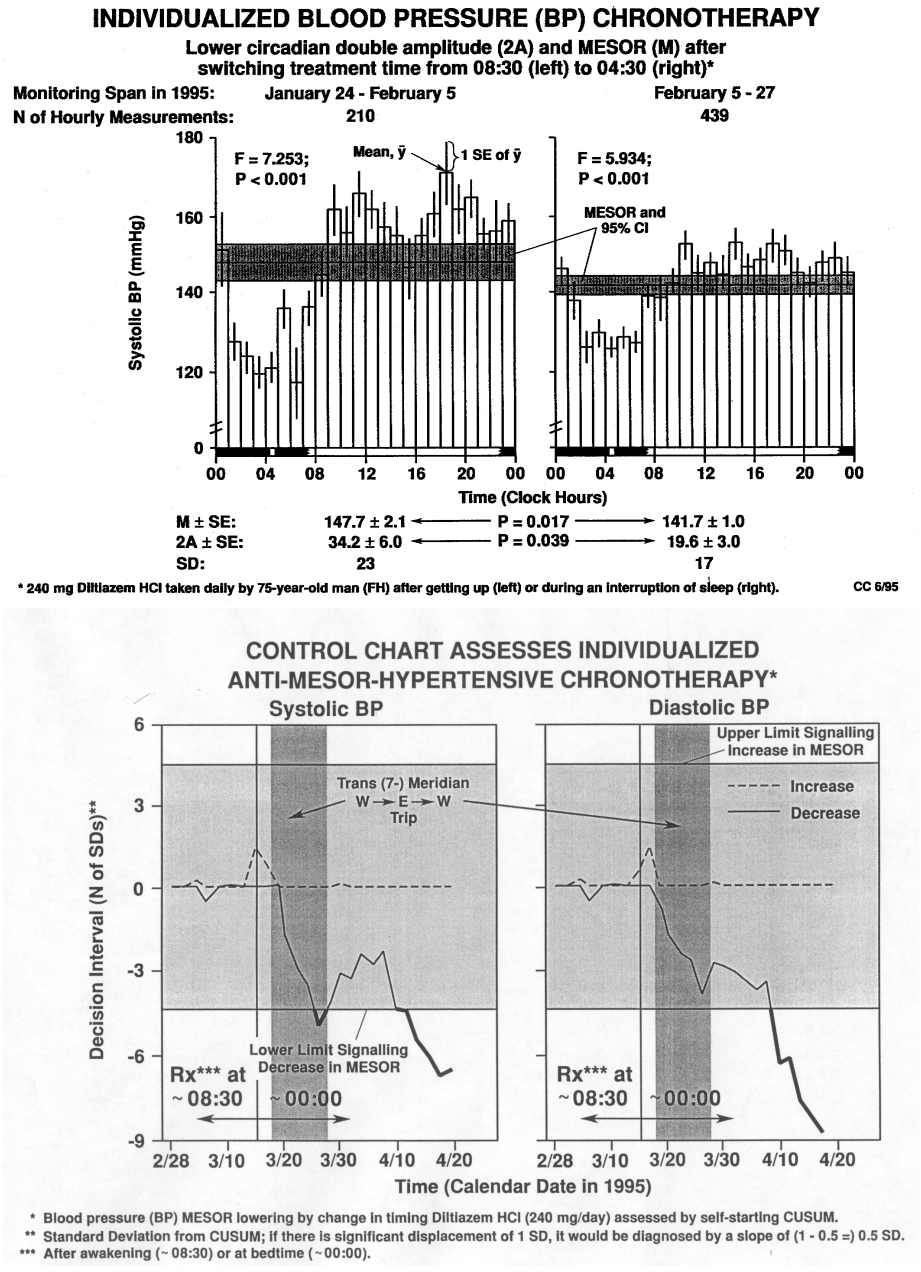


Figure 20. The usefulness of a chronobiologic approach is supported by the demonstration that treatment with antihypertensive drugs can be optimized by timing. The same dose of the same drug can have different effects on the MESOR and circadian amplitude of the same patient's blood pressure when it is administered daily at a different circadian stage as seen by the naked eye in the top graph. The practicality of a chronobiological approach lies in the availability of inferential statistical methods for the rigorous assessment of intervention effects applicable to the individual patient as shown in the bottom graph by using CUmulative SUM (CUSUM) control charts for personalized sequential testing. © Halberg.

Another larger set of website components yet to be developed aims at

- further temporally and spatially global and local (glocal) spectral and cross-spectral analyses of time-varying coherence among environmental, psychophysiological and epidemiological variables, including multiple component serial sections of these sets of multidisciplinary time series,
- at each of the known shared frequencies, by
- programs for automatically repeated multiple passes over each of the accumulating time series and of their coherence, if any, and
- subtraction and addition approaches.

Discussion

The website would contribute advanced transdisciplinary basic biological as well as medical research data bases, with the biological data base aiming at a clarification of biological associations of solar and terrestrial effects in human physiology. The medical data base would serve to gradually improve the service rendered by the website to self-care recipients by a refinement of the reference standards and of the harbingers of elevated risk of severe disease. Several updates to the existing sphygmochron software and additional analysis programs are planned for use by those who do continuous monitoring with repeated passes over the accumulating series and of those who do intermittent surveillance, repeating monitoring sessions (annually, on some other schedule and/or as warranted by analysis). To support users retrieving data directly from blood pressure monitors, the website will have to accept files as produced by many commercially-available devices and manufacturer-supplied analysis software, just one of several problems [76-78].

The user of the website must be computer-literate and able to perform analyses for multiple people, including those who need help with tasks involving computers. The first major scenario to be supported includes a computer-savvy friend or preferably family member accessing the website for his/her spouse, children, aged parents, people with disabilities, or others who fall within the individual's guardianship. The second scenario is for health care professionals or their staff members to be taught why and how to log in and submit data from patients. In the near term, the website supports running the sphygmochron analysis. In the long term, comparative analysis programs currently used at the Halberg Chronobiology Center at the University of Minnesota can also be run, improved and extended on the basis of ongoing experience.

The comparative analysis programs need two or more files of blood pressure data taken at different times in the person's life, or preferably a more or less continuous record, such as that taken by hypertensive opinion leaders from the time of diagnosis to their life's end. For instance, a former head of the then Hypertension/Endocrinology section of the U.S. National Institutes of Health who thereafter became director of that institution's Clinical Center believed that when hypertension is involved, one should not "fly blind" [79] (without continued surveillance by monitoring) [80].

Two major components already available as modules to be added to the website for comparative analyses of an individual accumulating continuous or intermittent record consist of parameter tests [81] and control charts [74, 82], the former triggered by the latter, Figure 18. Parameter tests can tell whether a change in (rhythm-adjusted) mean value or in the circadian dynamics has taken place with statistical significance. Diaries have yet to be developed to record times of getting up, going to bed, onset and end of exercise, meals and emotional events. They could perhaps be smart phones that also allow carrying out psychophysiological tests such as 1-minute estimation, eye-hand coordination, a positive and negative affect and vigor rating, along with transient storage and eventual transfer of data to the website. This desirable two-way tool may provide information to the participant, prompted by a statistically significant change in the record for which its clinical significance must be resolved as a function of whether it occurs spontaneously, in relation to a load, or in response to an intentional intervention such as the institution or modification of treatment. When data are collected continuously, cumulative sum (CUSUM) control charts can further help determine whether detected changes in circadian rhythm characteristics are temporally if not causally related to

the given intervention, thereby enabling a rigorous assessment of treatment efficacy and safety.

Beaty writes that:

"A small, well-focused library of materials related to sphygmochron analysis, heart and blood vessel physiology, cardiac and eventually other diseases, and treatments will be kept on the website. The library will contain sections for different types of users, including children, high school and college students, adult home users, and medical and health care students and professionals. The most important section might be the one for adult home users. It supports the desires of users with different backgrounds and levels of education to:

- "Learn advanced interpretation of sphygmochron reports, and
- "Research medical conditions, diseases, and treatments beyond the level of everyday 'household' words [76, 77].

"To support building a community of self-helped home users interested in preventive and curative health care, a popular web mechanism currently employed by some internet users in self-help or self-directed educational situations is 'forum' software, which lets users communicate with each other via leaving publicly available messages directly on the website. The envisioned website will have such forums available early in its lifetime. The concept of community-building on the Internet still seems to be undergoing considerable change. We expect to watch for new trends in this area and adapt the website accordingly to accommodate desires of the users.

"The website will make available information about obtaining a blood pressure monitor for ambulatory use (often called an Ambulatory Blood Pressure Monitor, ABPM, where 'ambulatory' means only that the instrument also functions during briefly interrupted walking), since many home users, especially those interested in the self-help style of medical care, might not know how to obtain ABPMs at reasonable cost, and will have questions about ABPM quality, testing and calibration, data off-loading software, and the logistics of wearing an ABPM around the clock for a week or much longer. A common question will be along the lines of 'This is different from current practice. How can this information help me, and how can my care provider use it?' We plan to encourage home users to monitor themselves for longer and longer time spans to get more and more basic and applied information from the analyses available on the website....

"As additional models and categories of ABPMs become available over the next few years, the website will be updated with descriptions and other appropriate information, to help its users capitalize on those improvements in the convenience, cost, sensitivity of sensors, and connectivity of blood pressure monitors that will affect how 7-day/24-hour monitoring, or preferably much longer surveillance, analyzed as-one-goes, is done.

"By 1880, Ignaz Zadek [83] had sufficient data to allow the demonstration in a meta-analysis of about-24-hour, about 84-hour and about-7-day changes in blood pressure [84]. In 1904, Janeway at Johns Hopkins Hospital insisted, before seeing a patient, on having enough data to evaluate periodic variations (note: variations is plural) [85]. He could do so on the basis of Zadek's record which allowed the demonstration of circadian and two infradian components of variability, Figure 21. In 2011, signatures of the about-10.5-year Schwabe cycle and 21-year Hale cycle, and even of the paratridecadal BEL cycle, are demonstrated in the human circulation, along with many other non-photic cycles, probably magnetoperiodisms, some of which also have signatures in sudden cardiac death [37], an association speaking for their importance."

Another important module of the website that needs development is an automated mechanism of several passes of data analyses aimed at assessing cycles with increasingly longer periods. On a short-term basis, ultradians and circadians can be determined. For ongoing analyses, rather than storing all original data, the salient rhythm characteristics are stored instead, serving for the determination of components with the next lower frequencies and for an assessment of changes with time in these components' characteristics. Such ongoing monitoring, analyzing and recycling could be the larger-scale supplement to the ongoing systematic mapping of rhythms of several frequencies in a few individuals. The examination of congruences with cycles in solar, interplanetary and other magnetics could yield a better understanding of environmental factors impacting human health. Studies by a subtraction-addition approach can be included opportunistically, triggered by concomitant environmental geomagnetic monitoring, preferably glocal (*global and local*) in geography and in time, by examining both the entire time series available at a given time (globally) and in its sections (locally in time).

Beaty concludes:

Assessment of these different periodicities in long populations' and individual's records will be a dividend in basic science and space weather monitoring from self-help

in health care that continuously assesses variability. This longitudinal surveillance could start for many hypertensives at the time of a chronomic diagnosis of abnormality to the time of life's end. The benefit for the individual involved would be a reduction in the number of episodes of variability disorders by their prompt detection and treatment (while otherwise an anti-hypertensive treatment might constitute the trade of a lesser risk such as hypertension for greater risk such as a circadian blood pressure overswing). In some cases, control of a silent disease (hypertension) cannot currently be achieved without bringing about an even greater also silent risk (overswing). The putative benefit of continuous surveillance is a critical remaining problem awaiting studies on populations. Every person with alterations in the variability of blood pressure and heart rate should continuously monitor and analyze, and thus serve his or her own health care as well as science. The website could, in combination with existing and preferably improved blood pressure monitors, mood and vigor assessment enable the public at large to determine the need for self-surveillance, and then implement continuous monitoring, individual-by-individual.

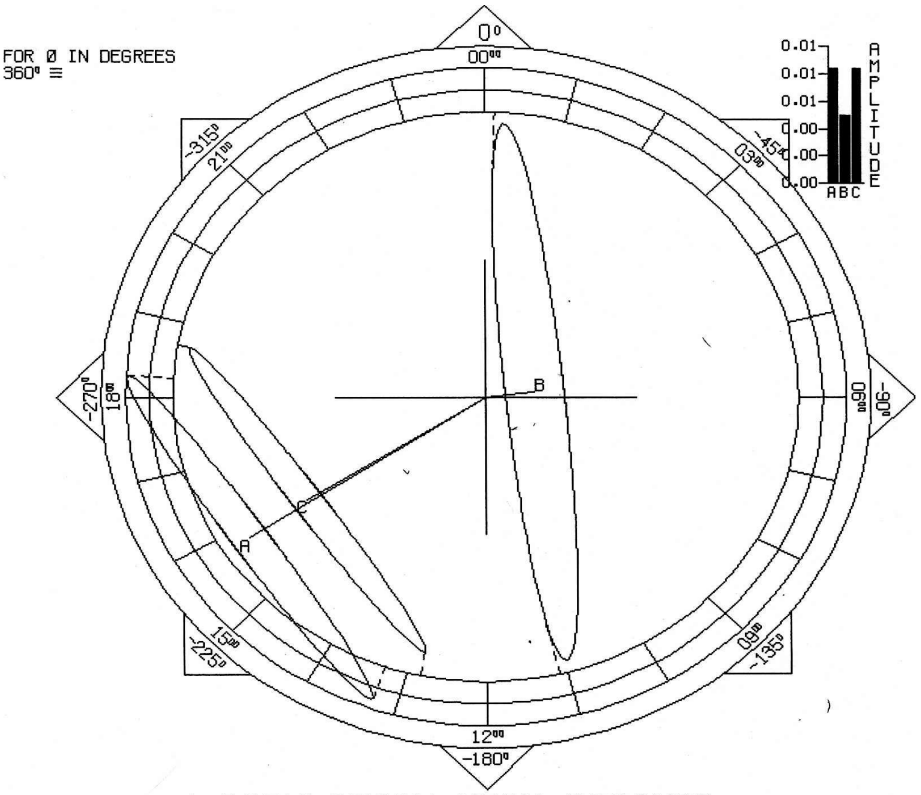
Problems

Larry Beaty, speaking for the Phoenix Study Group, composed of volunteering members of the Twin Cities chapter of the Institute of Electrical and Electronics Engineers (http://www.phoenix.tc-ieee.org), has well described the problem in advocating only 7-day/24-hour chronobiologic monitoring of blood pressure and heart rate in the USA. He notes that

> When we advocate that "healthcare should change with the help of modern technology", specifically talking about "a relatively inexpensive, largely self-implemented, continuous computer-aided surveillance" and associated website, and then suggest that people need to be routinely monitored for Vascular Variability Disorders (VVDs), notably those with a high blood pressure, a VVD in its own right, we are compelled to describe the current situation in the USA, since the implementation of these goals meets a major problem, namely that of fighting the current business model of the health care industry. This leads to the necessity of convincing "everybody" that it is all worthwhile.
>
> ... having inexpensive new technology is not enough to make a medical device successful in the market, no matter how novel or effective the device. The industry is rife with stories of technically successful devices that failed due to "poor marketing". What this phrase usually means is that there was not enough recognition that, at least in the USA, the marketing did not take the care providers' (and the companies that control them) business (read: profit) models into account well enough. Given a choice between two devices for diagnosis or treatment that are of equal merit in the USA, a care provider will often choose the device that generates more profit for him (or the company that controls his choices), regardless of which device is more costly [and, perhaps, some differences in quality will be ignored].
>
> In this atmosphere, merely putting out for display to the public new, inexpensive devices or systems that can detect vascular variability disorders, VVDs, or other conditions might not be enough to push a new device into use in everyday health care. Convincing government officials to make it a mandate might also not be enough, and the attempt to convince them might not even work as the competition for the attention of politicians is large.
>
> When one walks down the aisle of a local pharmacy and looks at the medical devices there, one sees eyeglasses, glucose meters and A1C diabetes tests, pregnancy tests, certain drugs, and of course blood pressure monitors. But while all these medical devices share the characteristic of now being directly available to the consumer after having once been largely exclusively in the domain of prescription-controlled healthcare, they also share another characteristic, which is that they are used in the home essentially the same way as they are used by clinicians.
>
> Here we are talking about using blood pressure monitors (those now available for home use, and those dependent on new technology still under development) in an importantly different way. The need to have blood pressure data for at least 7 days to detect VVDs and preferably for much longer for the validation of pre-hypertension of an altered circadian period or of chronobiologic pre-hypertension (rather than a single measurement of systolic blood pressure between 128-139 and/or of diastolic blood pressure of 80-89 mm Hg) is not currently recognized by the profession, notwithstanding the fact that it was advocated over a century ago by opinion leaders such as Theodore C. Janeway. The history of medical devices becoming widely used at home in a significantly different way from that in which they were used by clinicians may yet have to be written.
>
> Similarly, when one looks at the history of convincing politicians to enact healthcare mandates based on their own experiences, successful examples again seem sparse, and attempts seem prone to failure. Thus, an enthusiastic mayor of Roseville, a suburb of Minneapolis and St. Paul, ordered a set of automatic blood pressure and heart rate monitors, convinced of both the need for their use in the community at large as such and for a 7-day record to start with. He had seen that he himself, on one of 7 days, had been very

abnormal when he had to keep time in an ice hockey game and did not satisfy some husky players. By the time the instruments arrived, however, the mayor was no longer in office and his successor was not interested in the project. Fortunately for people in Japan, the project was picked up and has now been running in two cities there (Urausu, on the island of Hokkaido, and Tosa City, in Kochi on the island of Shikoku) for over 10 years.

... If the health care providers, politicians, educators, religious leaders, and others that we appeal to first do not see any obvious benefits in the short term (meaning, if they and their families are not affected by and cured of health problems such as chronobiologic pre-hypertension, a pre-metabolic syndrome, or another VVD or a combination thereof leading to a Vascular Variability Syndrome, VVS), then the idea of screening them for these conditions and for other diseases as a way of educating them and working towards a mandate for all to be screened in that way, will fail as they lose interest and go back to working on more short-term, tangible concerns in their lives.



KEY	P	N	PR	MESOR +-SE	AMPLITUDE *			ACROPHASE (Ø) *		
A 168 HOURS	<.001	4	6	117.75	12.08	0.98	(.92	1.05)	-237°	(-199 -274)
B 84 HOURS	.018	4	11	117.56	12.09	0.59	(.24	3.56)	-83°	(-2 -166)
C 24 HOURS	<.001	4	30	115.81	12.38	0.98	(.91	1.39)	-238°	(-192 -280)

Figure 21. Blood pressure on four patients of Ignaz Zadek in the 1880s. Error ellipses around directed lines (representing by their length half the extent of rhythmic change (amplitude) and by their angle the timing of overall high values recurring in each cycle) are 95% confidence regions that indicate statistical significance at the 5% probability level when they do not overlap the pole (center of the graph). © Halberg.

Figure 22. "Flying blind" between office visits and the (false) platinum standard of a (chronobiologically-uninterpreted) 24-hour blood pressure trace does not allow the diagnosis of Vascular Variability Disorders, VVDs, which remain unrecognized by both those administering treatment and those receiving it. The latter can hence gain greatly from self-help in computer-aided surveillance by a website (see Figure 18). Pieter Breughel's painting "The Parable of the Blind Leading the Blind", which may be the appropriate description of the status quo, is reproduced by kind permission of the Fototeca della Soprintendenza of the BAS PSAE and of the Polo Museale of the City of Naples. © Halberg.

Figure 23A. Henri Marie Joseph Vallot (1854-1925) is described in Wikipedia as a French astronomer, geographer and Maecenas (i.e., philanthropist). He came from a rich family who never had financial problems; his wealth allowed him to cover a great deal of the cost of the construction of his observatory (refuge) on Mont Blanc, which he discovered in 1875. "Nonetheless, scientists never considered him as one of their own, even when his work in different fields -- botany, glaciology, construction, geology, photography, medicine, physiology, cartography, alpinism, meteorology, etc. -- was recognized as being of important scientific interest. We wish to show herein that he was indeed a pioneer of the study of clinical symptoms associated with sunspots (see Figure 23B)."

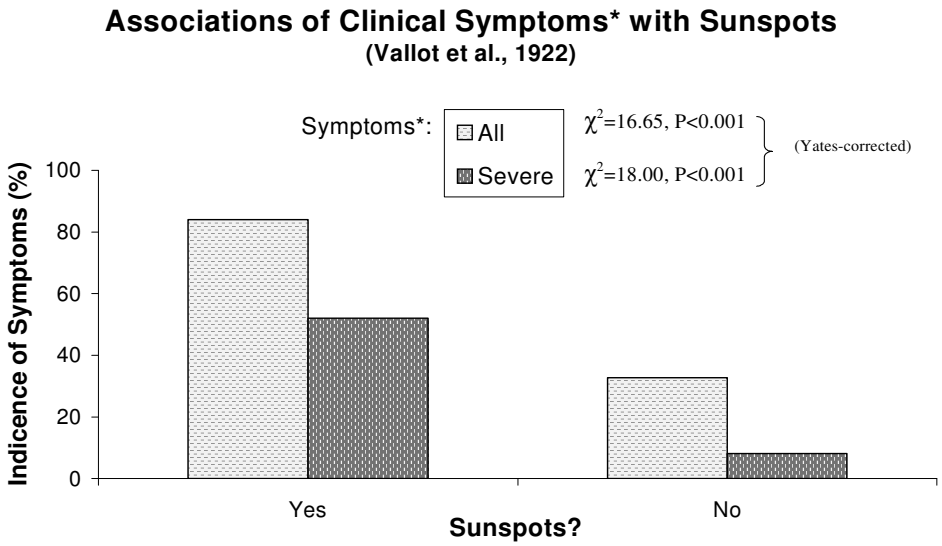


Figure 23B. Meta-analysis of what thoughtful and observant clinicians reported as an association of symptoms with solar activity over 80 years ago. Even mild symptoms, such as excitability, insomnia, tiredness, aches, muscle twitches, etc., have long been associated with sunspots (Vallot J, Sardou G, Faure M. De l'influence des taches solaires sur les accidents aigus des maladies chroniques. Académie de Médecine-Gazette des Hôpitaux 1922; 56: 904-905). We stand on the shoulders of many others who noted a lead in phase by a day of symptoms vs. sunspots.

We assume that these realistic problems, noted by Beaty for the USA, can be overcome in health care systems provided by the state or by others who do not wish to fly blind between office visits, i.e., most of the time, Figure 22.

We are reminded of mountaineers who risked their lives "because it's [the mountain] there". VVDs are here and there, and Joseph Vallot contributed more generally to the recognition that solar activity, reflected by the number of sunspots, can harm, Figure 23 [64].

Glossary

(modified or amplified from Chronobiology glossary cf. Halberg F, Carandente F, Cornélissen G, Katinas GS. Glossary of chronobiology. Chronobiologia 1977; 4 [Suppl. 1], 189 pp) where more information ($^{\Delta}$) can be found.

Large ongoing international cooperative projects such as those revolving around chronobiologic self-help in health care often pose semantic problems that jeopardize the implementation of the work and lead to waste. This glossary should reduce, if not eliminate, semantic misunderstandings and thus contribute to the success of ongoing projects such as that on The BIOsphere and the COSmos, BIOCOS. Steps being implemented toward international cooperation require a selection of comparable if not unified reference standards. Only thus can the definition of certain rhythm (cycle) characteristics become meaningful. By the same token, there is the need for using comparable analytical procedures that are generally applicable to systematically collected and stored data on blood pressure, heart rate and other time series. Broad international agreements can be reached toward the factual as well as semantic standardization of information capture, transfer, storage, analysis and updating from appropriate (data) bases: the characteristics of rhythms, estimated at different times and in different localities, will become amenable to a more facile and meaningful, direct comparison and integration. These are challenges and opportunities for the development of a serially updated individualized health form, card, booklet or equivalent, such as a cellphone, containing the information necessary for the precise early recognition of risk and thus for

endeavors toward the prevention of diseases of individuals and (when data are pooled from many individuals) for learning about solar effects upon societal ills, for the development of countermeasures. In this glossary, the as-yet uninitiated reader may also find a stimulus toward gaining an interest in the time dimension necessary to reach a more dynamic understanding of the entire field of biology and broader science as it relates, beyond personal health, to society's ills and to our environment, in the atmosphere of the sun as a whole in which we happen to live.

ACROPHASE θ, ϕ, Φ

measure of timing; the lag from a defined timepoint (acrophase$^{\Delta}$ reference) of the crest time in the function$^{\Delta}$ appropriately approximating a rhythm$^{\Delta}$; the phase$^{\Delta}$ angle of the crest, in relation to the specified reference timepoint, of a single best-fitting cosine (unless another approximating function is specified).

Units: angular measures: degrees, radians; time units: seconds, minutes, hours, days, months, years, decades, centuries etc.; or physiological episodic units: number of heart beats, respirations etc. Angular measures are directly applicable to any cycle$^{\Delta}$ length and hence are proposed for general use because of greater familiarity; degrees (with 360° equated to period of rhythm) are preferred over radians.

AMPLITUDE, A

measure of one half the extent of rhythmic change in a cycle$^{\Delta}$ estimated by the sinusoidal (or other) function used to approximate the rhythm$^{\Delta}$, e.g., difference between maximum$^{\Delta}$ and MESOR$^{\Delta}$ of a best-fitting cosine.

Units: original physiological units, e.g., number of heart beats, mmHg in blood pressure, etc.

ANGULAR FREQUENCY, ω

special case of frequency$^{\Delta}$ of a periodic process expressed in degrees or radians per unit of time obtained by equating one cycle$^{\Delta}$ to 2π, e.g., ω in equation

$$y(t) = M + A \cos(\omega t + \phi)$$

used to approximate a rhythm$^{\Delta}$. Observe relation between angular frequency and frequency:

$$\omega = 2\pi/\tau = 2\pi f$$

since frequency is the reciprocal of the period$^{\Delta}$:

$$f = 1/\tau$$

Note: equivalent to angular velocity, usually visualized on polar coordinates.

CHAT

Circadian hyper-amplitude-tension or circadian overswing, with circadian double amplitude exceeding the upper limit(s) of reference value(s) derived from clinically healthy peers matched by gender, age, and eventually ethnicity and geographic location.

CHRONODESM

time-qualified reference interval, e.g., time-qualified prediction or tolerance interval.

CHRONOBIOLOGY

Computer-aided study in the biosphere of time structures, chronomes consisting of cycles, trends (that can be parts of cycles longer than a time series) and deterministic (and other) chaos (that can generate cycles).

CHRONOMICS

Computer-aided study of interacting time structures in the biosphere and in its environment.

CIRCADIAN

Relating to biologic variations or rhythms$^{\Delta}$ with a frequency$^{\Delta}$ of 1 cycle$^{\Delta}$ in 24 ± 4 h; circa (about, approximately) and dies (day or 24 h).

CIRCASEMISEPTAN

half-weekly variation. Circasemiseptans characterize widely differing phenomena, such as the behavior on different lighting regimens of an enucleated giant green alga, or an aspect of the biochemistry of (anucleate) platelets and even sudden human death. Thus, in the last few decades in Canada, most sudden human cardiac deaths peak on Mondays, with a second peak on Thursdays. A 3.5-day cosine curve fits such data better than a 7-day cosine curve.

CIRCASEPTAN

about-weekly variation. Some human hormonal bioperiodicities, including rhythms$^{\Delta}$, follow a roughly weekly pattern, such as those in circulating cortisol. Circaseptans are also found to characterize death from a mouse malaria or the rejection of allografts of heart, pancreas or kidney in untreated rats. Human kidney transplant rejection episodes are also more likely to occur around the 7th, 14th, 21st and 28th days after operation, or near other multiples of 7 post-operative days.

CIRCATRIGINTAN

variation, such as the human menstrual cycle, that approximates a month in duration; such bioperiodicities, including rhythms$^{\Delta}$, are also found before menarche and after menopause, and in men.

CONGRUENCE

overlying or overlapping uncertainties (e.g., 95% confidence intervals) of two or more periods$^{\Delta}$ estimated in a time series$^{\Delta}$, given that the confidence interval of their amplitudes do not cover zero.

COSINOR

statistical summary preferably with display of a biologic rhythm's$^{\Delta}$ amplitude$^{\Delta}$ and acrophase$^{\Delta}$ relations, on rectangular or polar coordinates; along the latter, by means of the length and the angle of a directed line, shown with a bivariate 95% or other statistical confidence$^{\Delta}$ region computed (at chosen trial period$^{\Delta}$) 1. to detect a rhythm$^{\Delta}$ (by a confidence$^{\Delta}$ region not overlapping zero, along rectangular coordinates, or the center of the plot, the pole, along polar coordinates) and 2. to estimate rhythm parameters$^{\Delta}$ with their uncertainties (confidence$^{\Delta}$ intervals).

Notes: among procedures for the analysis, mostly, of short time series$^{\Delta}$, three kinds of cosinor have been designed in an integrated routine, each appropriate to a different situation:

1. Single cosinor, cosinor-S procedure applicable to a single biologic time series$^{\Delta}$ (from an individual or group);
2. Group mean-cosinor, cosinor-G: a cosinor procedure applicable to data from two or more individuals for characterizing a rhythm$^{\Delta}$ in that particular group only;
3. Population mean-cosinor, cosinor-P: the original cosinor procedure applicable to parameter$^{\Delta}$ estimates from three or more biologic series for assessing the rhythm$^{\Delta}$ characteristics of a population. All three cosinors use a cosine function: $g(t) = M + A \cos(\omega t + \theta)$.

DEFICIENT HEART RATE VARIABILITY (DHRV)

a standard deviation of heart rate (determined around-the-clock for 7 days at 1-hour or shorter intervals) below the threshold of 7.5 beats/minute, a criterion to be further qualified for gender, age, and eventually ethnicity and geographic location.

DESYNCHRONIZATION

state of two or more previously synchronized rhythmic variables that have ceased to exhibit the same frequency$^{\Delta}$ and/ or the same acrophase$^{\Delta}$ relationships and show changing time relations.

ECPHASIA

odd acrophase outside reference values of gender and age-matched peers.

ECFREQUENTIA

odd frequency outside reference values of gender and age-matched peers.

ENTRAINMENT

interaction between two or more organismic rhythms$^{\Delta}$ or the effect upon rhythm(s) of an (external) synchronizer$^{\Delta}$ resulting in identical frequencies among interactions or in frequencies constituting integral multiples of one another (frequency$^{\Delta}$ -- multiplication or demultiplication).

EXCESSIVE PULSE PRESSURE

above the threshold of 60 mmHg (determined in a record of 7 days at 1-hour or shorter intervals), a criterion to be further qualified for gender and age.

FREE-RUNNING

pertaining to continuance of bioperiodicity$^{\Delta}$ with a natural frequency$^{\Delta}$ usually at least slightly

different from any known environmental schedule.

FREQUENCY, f

the number of occurrences of a given type of event in a given unit of time or the number of members in a population falling into a specified class.

Note: in the study of periodicity$^{\Delta}$ it is the number of cycles occurring per time unit, i.e., f is the reciprocal of the period (τ)

$f = 1/\tau$.

GLOCAL and GLOCALITY

adjective and noun, respectively, beginning with the first syllable of GLObal and ending with the last syllable of loCAL, as "smog" is formed from SMoke and fOG. "Glocal" is proposed to designate, in principle and as method, an approach that is global and local both in time and in space. It is 1. global, both a. in time, insofar as it relates to the structure (or chronome) of a time series$^{\Delta}$ as a whole (in the longest available data series) and b. in space, insofar as it wishes to do so from the earth and other locations, such as the solar system, as a whole, as possible and reasonable and 2. local, again a. in time, insofar as it wishes to examine separately a set of intervals of different lengths and b. in space, namely separately from each of several terrestrial and other locations. As an example the incidence pattern of natality, morbidity or mortality can be studied in global and local statistics by spectra of entire time series and in intervals of each of the series of different length. In combination with spectral windows of an entire series, aligned gliding spectral windows, focusing on a given frequency region, and chronobiologic serial sections, focusing upon a single or few frequencies and their time course, are glocal procedures. The slogan "think globally, act locally" can thus be extended spatio-temporally.

INFRADIAN

relating to certain biologic variations or rhythms$^{\Delta}$ with a frequency$^{\Delta}$ lower-than-circadian$^{\Delta}$.

LEAST-SQUARES METHOD

estimation technique for determining quantities by minimizing the error (or residual) sum of squares. In a linear model, this method produces the best linear unbiased estimate (b.l.u.e.) in terms of variance. Note: two types of least-squares methods are considered: linear or nonlinear. The trial period is fixed in the former, allowed to vary in the latter.

MARKER RHYTHM

rhythm$^{\Delta}$ of use in practical monitoring and, where appropriate, decision-making -- in applied or basic physiologic or pharmacologic work, in preventive health maintenance (prophylactic marker rhythm), risk monitoring (risk marker rhythm), for diagnostic purposes (diagnostic or screening marker rhythm), for timing therapy (chronotherapeutic marker rhythm) or for assessing therapeutic response (response marker rhythm) without any implication of necessarily causal relations between the process and its rhythmic marker.

MESOR, M

rhythm-determined average of Midline Estimating Statistic of Rhythm, e.g., in the case of a single cosine approximation, the value midway between the highest and lowest values of function$^{\Delta}$ used to represent a rhythm$^{\Delta}$.

MESOR-HYPERTENSION, MH

for systolic and/or diastolic blood pressure, a transient$^{\Delta}$ or lasting elevation of the circadian$^{\Delta}$ (about-24-h) rhythm-adjusted mean (MESOR$^{\Delta}$, M) as validated statistically against the person's (patient's) own MESOR at another time in clinical health and/or against a peer reference standard.

PERIOD (τ)

duration of one complete cycle$^{\Delta}$ in a rhythmic variation.

Note: biologic rhythms can be analyzed in terms of a spectrum$^{\Delta}$ with statistically significant components in several spectral$^{\Delta}$ domains. Period notation is customary within a given region or (e.g., circadian$^{\Delta}$) domain of the spectrum.

Frequency$^{\Delta}$ (defined as the inverse of the period$^{\Delta}$ $f=1/\tau$) notation facilitates discussions of phenomena involving several broad spectral domains.

PREDICTION INTERVAL
a range of values expected to contain, on the average, a specified proportion of a population or of a distribution (of values) from an individual.

RESONANCE
property of a system oscillating (or capable of oscillating) with some natural frequency$^{\Delta}$ (or rhythm$^{\Delta}$) to exhibit an increased amplitude$^{\Delta}$ (or to begin oscillating) when subjected to an external periodic influence or force with a frequency similar to that of the system, the amplitude of the resonant frequency increasing as the outside periodic influence approaches the natural frequency of the system.

RHYTHM
a periodic component of (biologic) time series$^{\Delta}$, demonstrated by inferential statistical means, preferably with objectively quantified characteristics (i.e., frequency$^{\Delta}$ f, acrophase$^{\Delta}$ [θ], amplitude$^{\Delta}$ A, MESOR$^{\Delta}$ M, and/or waveform$^{\Delta}$).

SYNCHRONIZER, Sy
environmental periodicity determining the temporal placement of a given biologic rhythm$^{\Delta}$ along an appropriate time scale, by impelling the rhythm to assume synchronization$^{\Delta}$, i.e., its frequency$^{\Delta}$ or an integer multiple or submultiple of its frequency and a specifiable acrophase$^{\Delta}$ Note: also called zeitgeber, a time-giver, entraining agent (even though the environmental cycle does not give time), clue or cue. Adjectives, primary, dominant and secondary, describe relative roles played by different environmental synchronizers. In several strains of inbred mice fed ad libitum, the lighting regimen is the primary synchronizer of the blood eosinophil rhythm. Adjectives dominant and modifying also can be used to describe the effect of a given environmental factor in relation to a given rhythm. Under unusual circumstances a secondary synchronizer may become dominant. Thus in C_3H (Minnesota) mice subjected to a 50 percent restriction in dietary calories, the feeding time (of a diet restricted in calories) may be dominant over the lighting regimen. Moreover, under conditions of time-restricted access to food, synchronization by the lighting regiment may be largely though not fully overridden by meal timing. Thus, limited access time to food can be largely but not entirely dominant over lighting regimen with respect to the synchronization of the rhythm in telemetered intraperitoneal temperature. A secondary effect of the lighting regimen remains apparent as the result of interference among synchronizers. Finally, a rhythm can be influenced by secondary synchronizers and modifying factors, modulators, or, more generally, influencers.

ULTRADIAN
a variation with a frequency$^{\Delta}$ higher than 1 cycle in 20 h, i.e., with a period$^{\Delta}$ of less than 20 h. An example of an ultradian is the sleep-wake cycle of patients with narcolepsy, a sleep disorder in which patients fall asleep several times daily, e.g., with average periods of 1.7 h.

VASCULAR VARIABILITY ANOMALY (VVA):
an alteration of variability as compared to that of healthy peers, found in a 7-day record of measurements at hourly or shorter intervals analyzed as a whole, of blood pressure or heart rate. Examples are MESOR-hypertension; CHAT$^{\Delta}$ (circadian hyper-amplitude-tension); odd timing, or ecphasia; odd frequency$^{\Delta}$, or ecfrequentia; excessive pulse pressure and deficient heart rate variability.

VASCULAR VARIABILITY DISORDER (VVD)
a VVA replicated in at least three 7-day profiles at hourly or shorter intervals, each analyzed as a whole.

VASCULAR VARIABILITY SYNDROME (VVS)
two or more kinds of VVDs present simultaneously in the same patient replicated in three 7-day/24-h records.

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