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Chronomics: Imaging in time by phase synchronization reveals wide spectral-biospheric resonances beyond short rhythms[1] ("Wenn man über kurze Rhythmen hinausgeht")

In memoriam – lost future[†]: Dr.-Ing. habil. Dr. rer. nat. BARBARA SCHACK: 1952–2003

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Setting the stage

Dr. Barbara Schack is no longer with the authors of this paper, who are her students of all ages. After overcoming the deep shock of her death, so that others may benefit from her contributions, we list her biography and bibliography, and illustrate the fruits of intense research by her during the past 15 months with a series of figures prepared by her in Appendix A, qualifying this appendix by emphasizing that any misinterpretations are ours, not hers. We do this against the background of Appendix B, the latter an abstract, qualified in the light of subsequent one-on-one cooperation. Appendix B was never submitted to a meeting in June 2003, since she rescheduled her trip to Minnesota after she received an invitation by Rodolfo Llinas and Urs Ribary to a workshop on magnetoencephalography (MEG). She very gladly accepted this invitation but could not attend. As a co-worker of Herbert Witte, who defines her methods and concepts mathematically in Appendix C, Dr. Schack was involved for many years in the functional imaging of the human brain. Herein, we consider her recently broadened concepts with the inclusion of chronomes, i.e., a temporal imaging of relations between human myocardial infarctions and solar activity. Her methods are applicable to many aspects of chronomics, the imaging of time structures in and around us.

An immediate reason for this note was to communicate this information to those assembled at a workshop on MEG (Cold Spring Harbor, NY, July 30–August 4, 2003). Urs Ribary, the director of the workshop, writes:

> The goal of the workshop was to discuss the nature and significance of MEG signals, the state-of-the-art analysis tools and its potential applications in basic and clinical research with focus on oscillatory human brain activity.
>
> Over the past years it became evident that the properties responsible for the mental representations underlying all aspects of cognition and memory from linguistic perception and production to thought can be viewed as functional states in the sensory, motor and

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[1] The indefatigable assistance of Mary Sampson in preparing this manuscript is here acknowledged.

associative brain systems. Because such cognitive events are encoded in the temporal domain of neuronal activity, electrical pinpointing of the where and when of such activity provides an unsurpassed window into brain function. In particular, the distributed coherent electrical properties of central neuronal ensembles are considered to be a promising avenue of inquiry concerning global brain functions. The intrinsic oscillatory properties of neurons, supported by a large variety of voltage-gated ionic conductances are recognized to be central elements in the generation of the temporal binding required for cognition. Research in neuroscience further indicates that oscillatory activity can be correlated with both sensory acquisition and pre-motor planning, which are non-continuous functions in the time domain. From this perspective, oscillatory activity is viewed as serving a broad temporal binding function, where single-cell oscillators and the conduction time of the intervening pathways support large multicellular thalamo-cortical resonance that is closely linked with cognition and subjective experience. Temporal conjunction is viewed as a form of mapping where sensory inputs that are related to each other are bound by their electrophysiological coincidence. MEG is a truly non-invasive functional brain imaging technique, monitoring the electrical activity of nerve cells within the human brain. The methodology, using state-of-the-art whole-head MEG scanners, allows the localization and monitoring of human brain functions dynamics in three-dimension with a few mm accuracy and with a fast time resolution of less than 1 msec.

Dr. Schack's work and expertise have already contributed to the field of neuroscience, especially the careful description of coherence between theta and gamma oscillations during memory tasks in humans. In addition, Dr. Schack was collaborating with various clinical and basic research investigators and their important findings were published in numerous journals [1–103; cf. 104–108]. Unfortunately Dr. Bärbel Schack was never able to come to the workshop and her expertise could not be integrated with the ongoing discussions. Dr. Bärbel Schack was deeply missed at the workshop and we will keep her in good memory.

Bärbel's brief biography and her bibliography are pertinent further to a broad community of chronobiologists interested in the science of diversity in time and in chronomics, the mapping of chronomes, i.e., time structures and thus also to mapping brain function by MEG.

Personalia

Dr. Barbara (Bärbel) Schack, assistant professor of medical informatics at Friedrich Schiller University in Jena, Germany, drowned while swimming in Lake Owasso, Roseville, Minnesota, in the early morning of July 24, 2003. Bärbel was a master in analyzing transiently phase-coupled oscillations in processes covering widely differing time scales. It is difficult to conceive that Bärbel is no longer with us in person, but her concepts about various types of phase-synchronization, including processes more or less loosely coupled at multiple not necessarily harmonic frequencies and documented facts noted herein remain a treasure for transdisciplinary science.

After a few days of full-time and overtime tête-à-tête discussion and an extensive cooperation for some of the preceding 15 months, Bärbel will be warmly remembered beyond Minnesota by the worldwide group of investigators on problems of the BIOsphere and the COsmos (BIOCOS), as well as, among others, by her collaborators in Jena, Vienna, Salzburg and Berlin. For the Minnesotans, just as for her institute head Prof. Dr. Herbert Witte and her fellow Wolfram Hesse in Jena when they received the news, it proved to be very hard to realize her passing. It must be even more difficult for her family, who wish to make their own arrangements in her memory in private.

To her academic family, the size of which is apparent from the many co-authors in her bibliography (1–103), we are also the bearers of professional developments and findings. Her concepts and results to be further documented were that relations among certain events and processes are so intimately interwoven that they can be mathematically expressed across very broad ranges of frequencies.

Bärbel Schack was born on March 15, 1952, in Waren–Müritz, Seeplatte, a region known for its many lakes, not unlike the state of Minnesota in which she spent the last four days of her life. After finishing high school, she studied mathematics at the University of Yerevan, Armenia, for five years. She earned a diploma in mathematics at Yerevan in 1975, a PhD in mathematics at the Friedrich Schiller University of Jena, in 1980, and a doctorate in engineering (with habilitation, a title and academic level conveying the right to lecture) from the Technical University of Ilmenau, Thüringen, Germany.

Bärbel also earned habilitation from the University of Jena, and was considered the leading candidate for a professorship in "Biosignal Analysis" at the Institute of Biomedical Engineering and Informatics in Ilmenau. Bärbel was a member of the German Society for Biomedical Engineering (DGBMT), the German Society for Medical Informatics, Biometry and Epidemiology (GMDS), the International Organization of Psychophysiology, and the Commission for Scientific Visual Imaging of the Austrian Academy of Sciences. She served as a reviewer for the journals Biological Cybernetics; International Journal of Bifurcation and Chaos; International Journal of Psychophysiology; Psychophysiology; Biometrical Journal; Anesthesiology; Theory in Biosciences, and IEEE Transactions in Biomedical Engineering, and was a member of the Editorial Board of the International Journal of Psychophysiology.

Bärbel arrived in Minnesota in the mid-afternoon of July 20, 2003, with two heavy pieces of luggage. The senior author so valued her coming that he obtained special permission to go to the gate; at the gate he persuaded an employee to go into the plane, where he called her by name and helped her off with her bag. We went to a club, had refreshments, and began a very interesting professional talk. Before we left the airport, Bärbel was offered a choice of staying at a three-star hotel near the University, at a townhome or at a lakeshore home. She emphatically preferred the home on the lake, and when she saw the view, repeated that she much preferred the lake home to a hotel or to anything else in town. The same evening, we continued our professional discussions over dinner, as we did during all other meals except for breakfast, for which Germaine Cornélissen, the director of our center, had stocked the refrigerator. Dr. Cornélissen looked after Bärbel, picked her up in the morning and brought her home at night. Her computer ran most of the day, and she received free access for the future to the University of Minnesota's supercomputer. On the evening before her scheduled afternoon seminar in the department of statistics, she introduced the senior author to some of her methods, and completed further analyses that yielded new findings for all of us. Bärbel was very proud of her good physical shape, emphasized her membership in a fitness club *(Turnverein),* and on each of three mornings she swam back and forth across the lake (a round-trip distance of about two-thirds of a mile). Sadly, on the fourth morning she did not return alive from her swim.

For Hellmuth Petsche, Emeritus Professor of the Institute for Neurophysiology at the University of Vienna, as he writes in a letter translated from his original German at his request, Bärbel was a scientific daughter. Early on, he also learned first-hand of her basic professional competence, sincerity, unusual ability to work, and above all, of her creativity. He came to esteem her unusual character very highly, using the old German word *Lauterkeit,* conceivably "unblemishedness", to characterize her. He was very pleased to be allowed to become her mentor, and was grateful that she allowed him very intensively to participate in her scientific development. Foremost, it was his endeavor to fortify her belief in herself and to help her become convinced of her own worth. Thanks to her, he could think along with her at the frontier of his science for many years after his becoming emeritus. Prof. Petsche writes further that he also encouraged Bärbel to devote herself fully to endeavors in chronomics, and Bärbel did so even overtime. He and Bärbel were convinced that the work on the diverse Minnesotan time series, which she analyzed with feverish enthusiasm, would become a decisive new and successful step for her better understanding of the complex relations among seemingly independent areas. He describes Bärbel's interest in enlarging her perspective (by chronobiology and chronomics) by coining the neologism *Entgegenfieberte,* meaning "enthusiastic fever", in a positive sense.

Like all of us, Wolfgang Klimesch, Professor of the Institute of Psychology at the University of Salzburg, was moved deeply by Bärbel's death. He wrote:

I bec[a]me acquainted with her via Prof. Petsche with whom we both had/have a close personal and scientific relationship. In the many discussions with Hellmuth Petsche, he was emphasizing repeatedly that Bärbel has those mathematical tools developed that are badly needed for a better understanding of brain oscillations. I was very happy that Bärbel became interested in the idea that even ERP's can be explained by evoked oscillations. Highly important research was carried out already by other [investigators], but what was needed was a comprehensive program focusing on the development of appropriate methods to analyse phase relationships within and [among] different frequency domains. She was working on that pioneering edge of research. Her paper about n:m phase synchronization in a short-term memory task (published in 2002) is – to my knowledge – the first of its kind demonstrating phase coupling between theta and gamma [rhythms] in the human EEG. We were currently working on a manuscript about theta : upper alpha phase synchronization when her death suddenly ended our research. Her emails from her last days in the US were so much emphasizing how excited she is about the kind hospitality and the joy of swimming in the morning.

Bärbel was a gentle friend to me, so interested showing me the application of the complex and elegant mathematical tools she has developed. She was fascinated – as I was – by the idea that these tools allowed completely new insights for a better understanding of the EEG and brain oscillations in particular. I am so grateful that I could join her on her scientific path for almost a year.

With gratefulness and great respect for Bärbel as a friend and scientist, …

Bärbel Schack was pleased by her stay in Minnesota, according to a letter written to Sabine Weiss and another note which describes her experience in Minnesota as "extremely interesting". "Away from conventional provincialism, there are findings about rhythms of many kinds with insight into their coupling. We tried to sort out the results found thus far for a relation with solar activity of the heart and circulation in disease. The interaction is unbelievable and very clear if one broadens one's perspective beyond the short [period] rhythms." Her German text follows. (The insert in [ ] is ours.)

Lieber Prof. Geissler … Der Aufenthalt hier in seinem [Halberg's] *Labor ist hoechst interessant. Weg aus der Provinzialitaet, neue Sachverhalte ueber Rhythmen aller Art und Einsichten in deren Verschaltung. Wir versuchen, die bisherigen Ergebnisse (Zusammenhaenge zwischen Sonnentaetigkeit und Herz-Kreislauf-Krankheiten) zu sortieren. Die Interaktion ist unglaublich und sehr klar, wenn man ueber kurze Rhythmen hinausgeht. Herzliche Gruesse aus Minneapolis, Baerbel Schack*

With the shock of her death, Hans-Georg Geissler referred first to Rilke's "lost future" (109):

Klage

Wem willst Du klagen, Herz? Immer gemiedener
ringt sich dein Weg durch die unbegreiflichen
Menschen. Mehr noch vergebens vielleicht,
da er die Richtung behaelt,
Richtung zur Zunkunft behaelt,
zu der verlorenen.

Früher. Klagtest? Was wars? Eine gefallene
Beere des Jubels, unreife.
Jetzt aber bricht mir mein Jubelbaum,
bricht mir im Sturme mein langsamer
Jubelbaum.
Schoenster, in meiner unsichtbaren
Landschaft, der du mich kenntlicher
machtest Engeln, unsichtbaren.

Complaint

To whom shall you complain, heart? Ever more / shunned
your way wrestles through the impenetrable
people. The more to no avail perhaps,
because it holds to the direction,
holds to the direction of the future,
to the lost ones.

In the past. You complained? What was it? A fallen
berry of Joy, unripe.
But now my whole Tree of Joy is breaking,
in the storm my slowly grown Tree of Joy
is breaking.
Most beautiful thing in my invisible
landscape, you who made me more knowable
to angels, invisible ones.

On a happier earlier note, the senior author wrote to Hans-Georg Geissler (who had introduced him to Bärbel through his publication with her [40]):

Hier sind wir versammelt aum löblichen Tun
Weil die Bärbel Schack kann nicht ruhn
Sie ist unser lieber Lehrer und Gast
Und wir haben so manches von Ihr erfasst
Es verschwinden interdisziplinäre Schranken
Dafür wollen wir Ihnen allerherzlichst danken

Geissler replied:

Wie sehr mich diese Botschaft erfreute;
denn nichts ist besser für ältere Leute
als sich am Schaffen anderer zu freuen
und damit die eigene Kraft zu erneuen.

Bleibt Euch beim löblichen Tun eine Luecke,
solltet ihr Eure scharfen Röntgenblicke
mal auf die schnellen Rhythmen lenken
und deren Beziehung zu Euren bedenken.

In this sense, we wish to do what Hans-Georg wanted, and it remains our challenge with the modified title of "Future history" rather than concluding as we did above, as an immediate response to the news of Bärbel's death, with Rilke's "Complaint" or "lost future".

Verlorene Zukunft oder eher Zukünftige Geschichte

Bärbel Schack war in Minnesota hoch willkommen
Davon haben Ihre Freunde direkt von Ihr vernommen.
Den Owasso-See hatte Sie dreimal überquert
Ein viertes Mal war Ihr nicht beschert.
Der liebe Gast hat uns so jäh verlassen
Wir alle konnten es zunächst nicht fassen
In der transdisziplinären Wissenschaft
Hatte Sie überaus produktiv geschafft
Sie hat jedem von uns so sehr Viel geschenkt
Davon unabhängig, auch als Freund, man Ihr gedenkt.
Aber ist die aufrichtigste tiefste Trauer
Wirklich in Bärbel's Sinne auf die Dauer?

Oh jeh ! würde die Bärbel selbst sicher sagen
Wenn wir über Sie als Verlorene Zukunft *klagen !*
Diese Fassung von Hans-Georg Geissler adaptiert,
Als erste Reaktion, nach Rilke treffend modifiziert,
Gibt Raum einer gewonnenen Geschichte
Sonst kommt Bärbel's Schaffen zunichte.
Die Hoffnung die wir hier entschieden hegen:
Ihr Nachlass soll noch lange in unserer Mitte leben,
Ihre Lektionen die wir so gerne vernommen
Sollen erweitert in transdisziplinäre Lehrbücher kommen

Bärbel besass Kompetenz und Lauterkeit
Diese Bezeichnungen hatte Helmuth Petsche bereit
Als Herbert Witte's Mitarbeiter hat Sie schön belegt
Was über 10 Grössenordnungen von Frequenzen geht
Ob in Jena, Wien, Minnesota oder Salzburg
Ihr Gedenken ist eine sehr feste Burg
Es ist eine Basis für fieberhaftes Überbrücken
Der vielen heute existierenden Lücken
Das Gehirn mit seinen etlichen/vielen Hertz
Hängt eng zusammen mit dem wetteifernden Herz
Die Atmung hinkt dann langsamer danach
Circadiane Rhythmen sind in jedem Gemach
Dann kommen biologische Wochen und ein Halbjahr
Die beide uns die jahrlose Geomagnetik gebar
Winter-Sommer folgen und sind drastisch beim Katzenhai
Aber viel weniger regulär in uns selber dabei
Das humane Circannualsystem wurde uns erst klar
Als uns der Sonnenwind das 1.3-Jahr-lange Transjahr gebar
Wir finden das Transjahr in 52 von 52 auch Jahrzehntelangen Zeitreihen
Die uns Kollegen als Puls und Blutdruck leihen
Dank Wissenschaftern die von der Chronomik versessen
Noch immer enthusiastisch sich rund um die Uhr messen.
Wiederholt das Transjahr die Ubiquität vom Circadiansystem
Aber endogene Aspekte aufzudecken ist nicht so bequem
Sich nicht überlagernde Konfidenzintervalle sind ein Kriterion
Diese finden wir im Transjahr und freuen uns schon.
Wenn ohne es zu wissen das biologische Jahr und Transjahr schweben
Und dies Schweben missachtet wird kann es Probleme geben.
All dies und Dimensionen von Schwabe in Jahrzehnten
wir der Bärbel als Sonnenflecken-Rhythmen erwähnten
So hat Sie den Minnesotesischen Myokardinfarkt
Mit Schwabe-Rhythmen zur Phasensynchronisation gebracht.
Manch anderes zeigen Abbildungen
So vieles ist der Bärbel gelungen
Bevor Sie uns verliess machte Sie Geschichte
Und diese zu schreiben wurde zu unserem Pflichte
Wonach sich jeder Chronomiker nun unverzüglich richte.

Rhythms with frequencies above 1 Hertz

According to Sabine Weiss, with whom Bärbel worked enthusiastically shortly before she left for the USA: "One of Bärbel's major interests was the investigation of cerebral oscillations related to human cognitive processing based on electro- and magnetoencephalographic data. [Schack and Weiss extended and adapted] state-of-the-art techniques and developed several new approaches [to gain] new insights into the brain's activity during different high level cognitive processes, such as thinking, music perception, memory processes and language comprehension (e.g., 26, 29, 34, 47, 54, 92, 102). In particular, she was engaged in developing methods based on the application of an adaptive fit of bivariate autoregressive moving average (ARMA) models. With this approach she was able to investigate dynamic neuronal interaction with high time and frequency resolution. Her coherence and cross phase analyses during memory and language processing revealed a new picture of brain activity accompanying these processes, showing that the engagement of different neuronal networks changes very dynamically during the ongoing cognitive process.

"Beyond the study of many new measures and variables to determine the meaning of neuronal oscillatory activity within different frequencies, [Schack and Weiss'] most promising step was the application of 1:1 phase synchronization and in particular n:m phase synchronization on EEG data during verbal memory encoding. These results are adding a new dimension towards a theory on the meaning of brain oscillations and the functional interplay among neural networks" (according to Sabine Weiss).

Phase in chronobiology

In a glossary in 1977 (110), focusing primarily but not exclusively on circadian rhythms (111), we defined "phase" as the "instantaneous value of a biologic variable at a fixed time" and noted that phase usually is considered only as an indication of time (e.g., within a cycle), without indicating the actual value of the variable associated with a phase, i.e., as an abbreviation for phase angle. Such an instantaneous phase within a cycle may be considered in relation to some (e.g., angular) transformation of time, with 1 cycle or period equated to 360°.

We defined "phase angle" as "a time point in a periodicity considered in relation to another specified time point", as the acrophase, namely as the phase angle referring to the crest time of the [single] cosine curve fitting the data in relation to a specified reference time, such as local midnight or the middle of the rest span. In chronobiology, a meaningful phase angle reference is essential, and the nature of this reference can be made obvious by the notation of one of several (computative, external and internal) acrophases [110]. Use of the term *phase angle* in biology may thus be limited at best to consideration of macroscopic data. Since the term is unspecific with respect to reference point, it should be replaced by *acrophase* in any discussion of [time-]microscopic analyses. In composite words such as acrophase, the component phase actually denotes phase angle (the word *angle* being omitted for the sake of brevity when the prefix *acro* is used). We refer to an orthophase when a model consisting of a combination of two or more harmonics is used to estimate a rhythm's timing as the lag from a defined reference time, the orthophase reference, to the crest.

> "Acrophase" (ϕ, φ, Φ) is defined as a
> measure of timing; the lag from a defined reference timepoint (acrophase reference) of the crest time in the function appropriately approximating a rhythm; the phase angle of the crest, in relation to the specified reference timepoint, of a single best-fitting cosine (unless another approximating function is specified).

Units for an acro- or orthophase are angular measures such as degrees and radians; time units: seconds, minutes, hours, days, months, years or decades; or physiological episodic units: number of heartbeats, respirations, etc. Angular measures are directly applicable to any cycle length and hence are proposed for general use because of greater familiarity; degrees (with 360° ≡ period of rhythm) are preferred over radians.

The acrophase and orthophase are microscopic measures of timing and are hence not to be confused with the peak macroscopically determined as the highest point of a recurrent pattern. Three types of acrophases have been considered: the computative, external and internal ones (Figures 1 and 2 in ref. 110, pp. 116 & 117). For example, the circadian acrophase, ϕ, may be given in clock hours and minutes on a 24-hour cycle, with midnight as reference timepoint, or the circannual acrophase may be given in months and days on a one-year cycle with December 22nd or June 22nd of the previous year as acrophase references on the northern or southern hemispheres, respectively. This practice is not recommended in itself. It should be accompanied by an indication of timing in degrees (or radians) allowing for direct comparison of acrophases on different cycle lengths.

For some episodic time scales, as well as for, e.g., free-running rhythms with different frequencies, the distance between two physiological events or the period can be equated with 360°. In relation to those two events, one may then express the location of another kind of event (to be studied in relation to events of the first kind).

Other episodic time scales serve students of cardiorespiratory interactions who may express the number of heartbeats not in relation to certain time units but rather to the span elapsed between two consecutive inspirations, whatever the length of that span may be (e.g., 2 heartbeats after start of a given inspiration). By the same token, one may relate the frequency of other physiological phenomena, including changes in mental or physical performance, to the span elapsed between two consecutive awakenings or two consecutive onsets of menstruation or two consecutive events with even lower frequency.

Acrophase from single and population-mean cosinors below 1 Hertz

Clinicians have known for over a century and a half that in some patients with convulsive disorders, seizures occur rather consistently at one or another time of day. When each seizure in such patients is assigned to the time of day when it occurred – such data were then available, thanks to the perspicacity of the superintendent of a state hospital for persons with epilepsy – some clearly apparent time-macroscopic patterns are seen, as reported by others earlier and reviewed in 1953 (112). By 1952, we had also determined either the percentage time in which paroxysmal discharge dominated the record or the number of spikes, one or the other in hard copies of 5-minute-long electroencephalograms (EEGs) repeated every 90 minutes for 24 hours during many sleepless 24-hour days (113–116). It seemed of interest to view these time-macroscopic records objectively as rhythms with phases estimated with their uncertainties. Before us, Ed Batschelet – also then concerned with phase at a given fixed single frequency (118) – found some useful information in the domain of phase on other topics and without usually weighting by the amplitude. The cosinor in its broadest sense, had followed Ed with an amplitude-weighted phase that could also be considered as a phase-weighted amplitude (119–126). After that came the cosinor spectrum and the combination of this linear method with nonlinear least squares to estimate confidence intervals for the period to result in a gliding spectral window, all placed with parameter tests on an inferential statistical basis and thanks to least squares, applicable to unequidistant data.

Figures 1–5 illustrate rhythmicity, called "circadian" (111) along the 24-hour scale in seizure incidence, Figures 1–4, and in paroxysmal EEG discharge, Figure 5 (116, 117; cf. 113–115). The left side of Figure 1 shows that on the average, the number of seizures stacked per unit time and expressed as percentage of series mean can vary greatly in two clinically constituted groups. The data of 6 patients, 4 male and 2 female, with a nocturnal incidence of 11,945 seizures are compared with those from 5 patients, 4 male and 1 female, with a diurnal incidence of 1,997 seizures. By clinical definition they are in antiphase; yet to quantify this time relation, the population-mean cosinor method is applied on the right, to the time-macroscopically displayed data on the left. The 95% confidence intervals non-overlapping the pole (center) provide an estimate of the uncertainties involved. Figure 2 is a summary of seizure incidence for each of 2 patients again based on abundant data. Both Figures 1 (right) and 2 show amplitude-weighted phases as point and interval estimates. In these cases, the hypothesis of "no circadian rhythm" was rejected, a result serving to establish the group rhythm in Figure 1 and the individuals' rhythms in Figure 2.

Figure 3 plots only phases, but again these are derived with amplitude weighting by the cosinor (119–126) and again the individual's 95% confidence interval is provided when the zero-amplitude hypothesis is rejected. Because of nonsinusoidality in some cases the hypothesis of no-rhythm cannot be rejected. In these cases, only point estimates are provided, notably in cases with a peak in seizure incidence around arousal. Figure 4 shows again a quantification of the seizure incidence in 6 individuals, including one (subject A) for whom the 95% confidence interval overlaps the pole (center) of the graph, and in such a case, again (only) a point estimate of parameters is given, the failure of hypothesis testing notwithstanding. Figure 5 in turn summarizes EEGs performed about 54 years ago using up bushelbaskets of recording paper (113–117). By inspection of the record on a hard copy, the percentage of time in paroxysmal discharge was measured and different patterns clearly emerge with the rejection of the no-rhythm hypothesis. In all of the single cosinors and in a population-mean cosinor in Figures 1–5, the phases are estimated at a single fixed frequency of 1 cycle in 24-hours.

In other cases, in phase charts one can use "rubbery" time when, for instance, phases are summarized at physiologically similarly meaningful but numerically different frequencies such as a free-running circadian

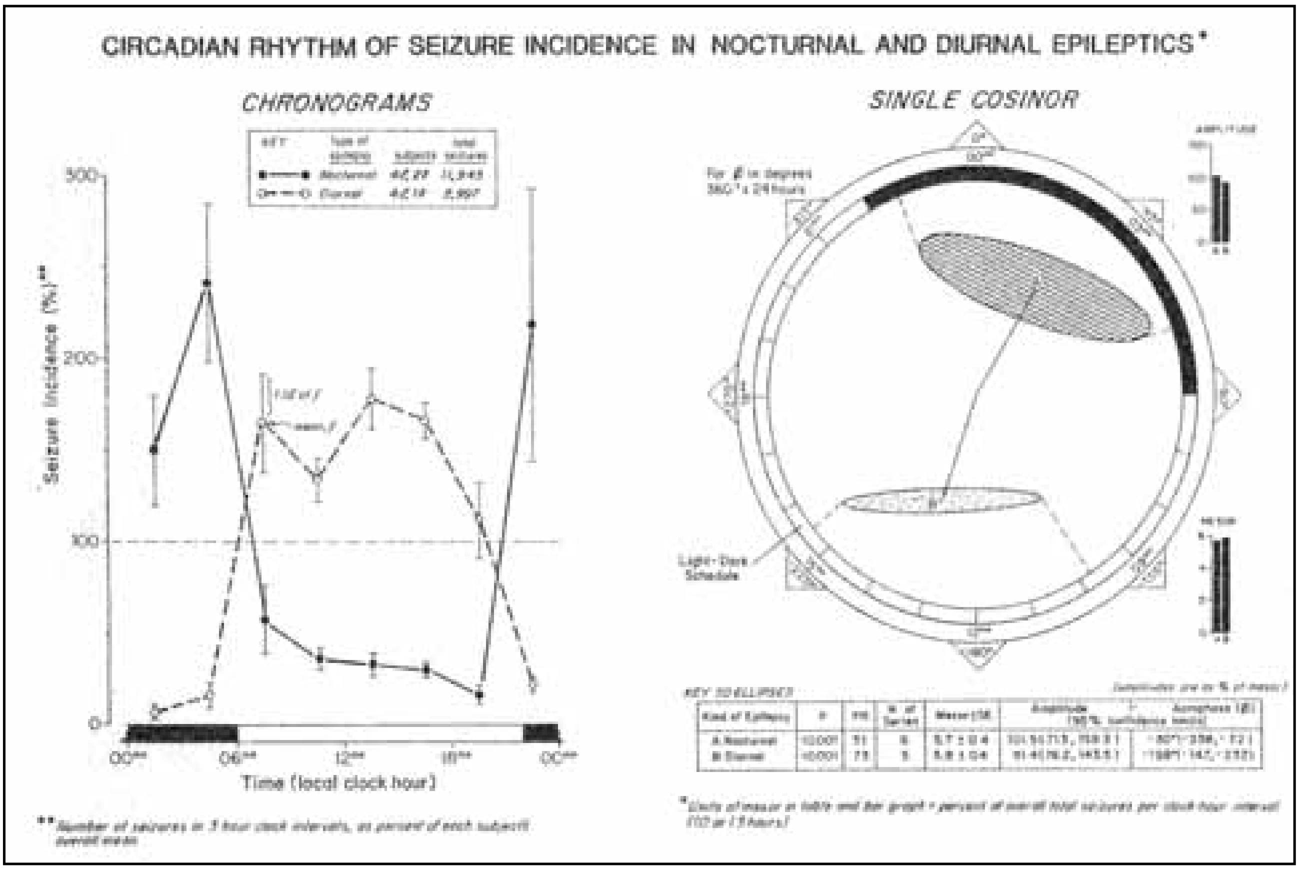


Figure 1. Circadian group rhythm of seizures in patients with convulsive disorder plotted time-macroscopically (left) and analyzed time-microscopically (by population-mean cosinor, right). The elliptical 95% confidence region that does not cover the pole (center) documents the rejection of the zero circadian amplitude assumption (in keeping with a rhythm with a frequency near that fitted). © Halberg.

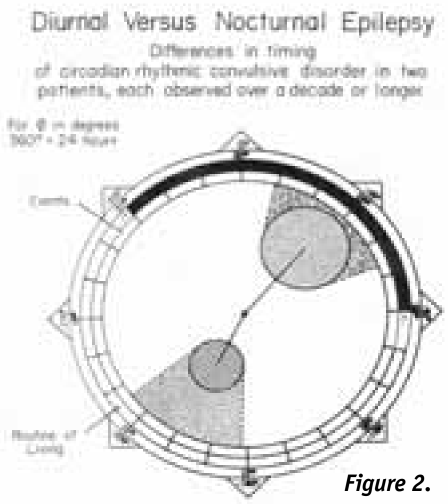


Figure 2.

Figure 2. Individualized single cosinor assessment of seizure incidence in two patients on the same hospital routine. Such information may serve for the timing of medication and for study of etiology. © Halberg.

Figure 3. Display only of phase from individualized single cosinor assessment, as shown in Figure 2. Point estimates of phase are given with their 95% confidence arcs, except for cases when the hypothesis of "no circadian rhythm" cannot be rejected. Then, only a point estimate is provided. © Halberg.

Figure 4. Time-macroscopic (left) and time-microscopic (right) display of individualized single cosinor assessment of circadian rhythm in seizure incidence of six patients. © Halberg.

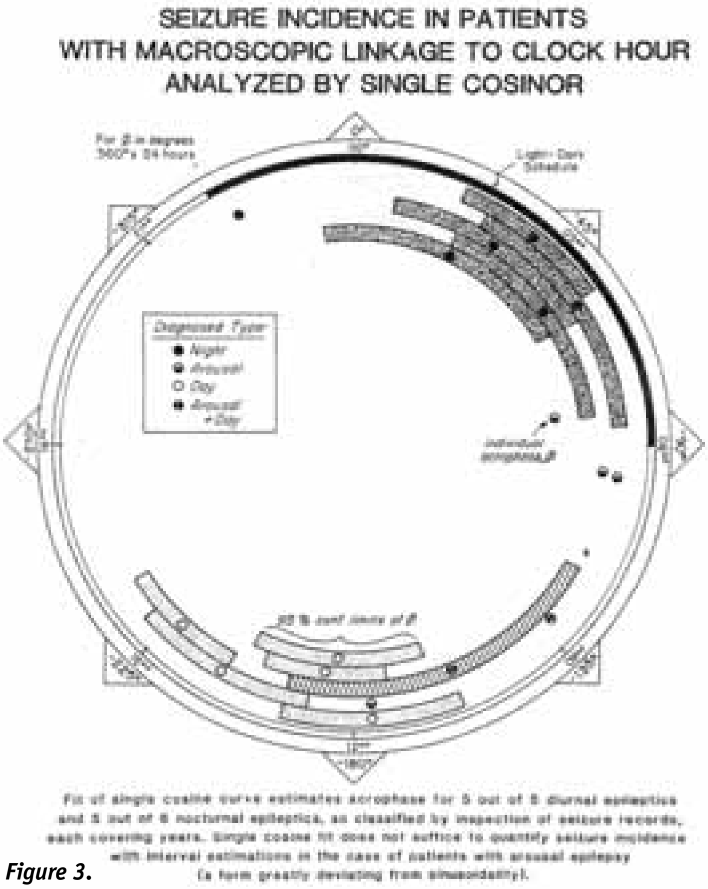


Figure 3.

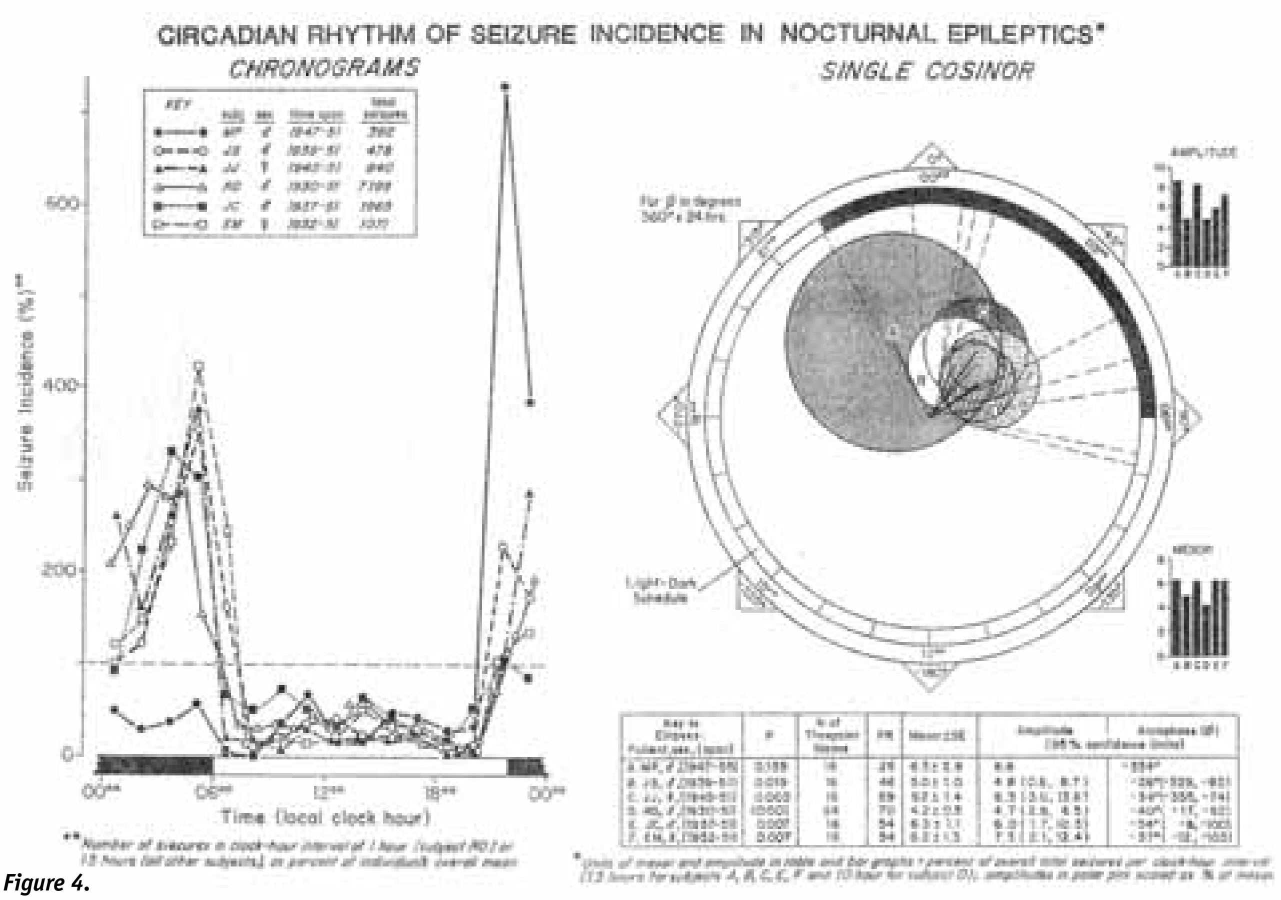
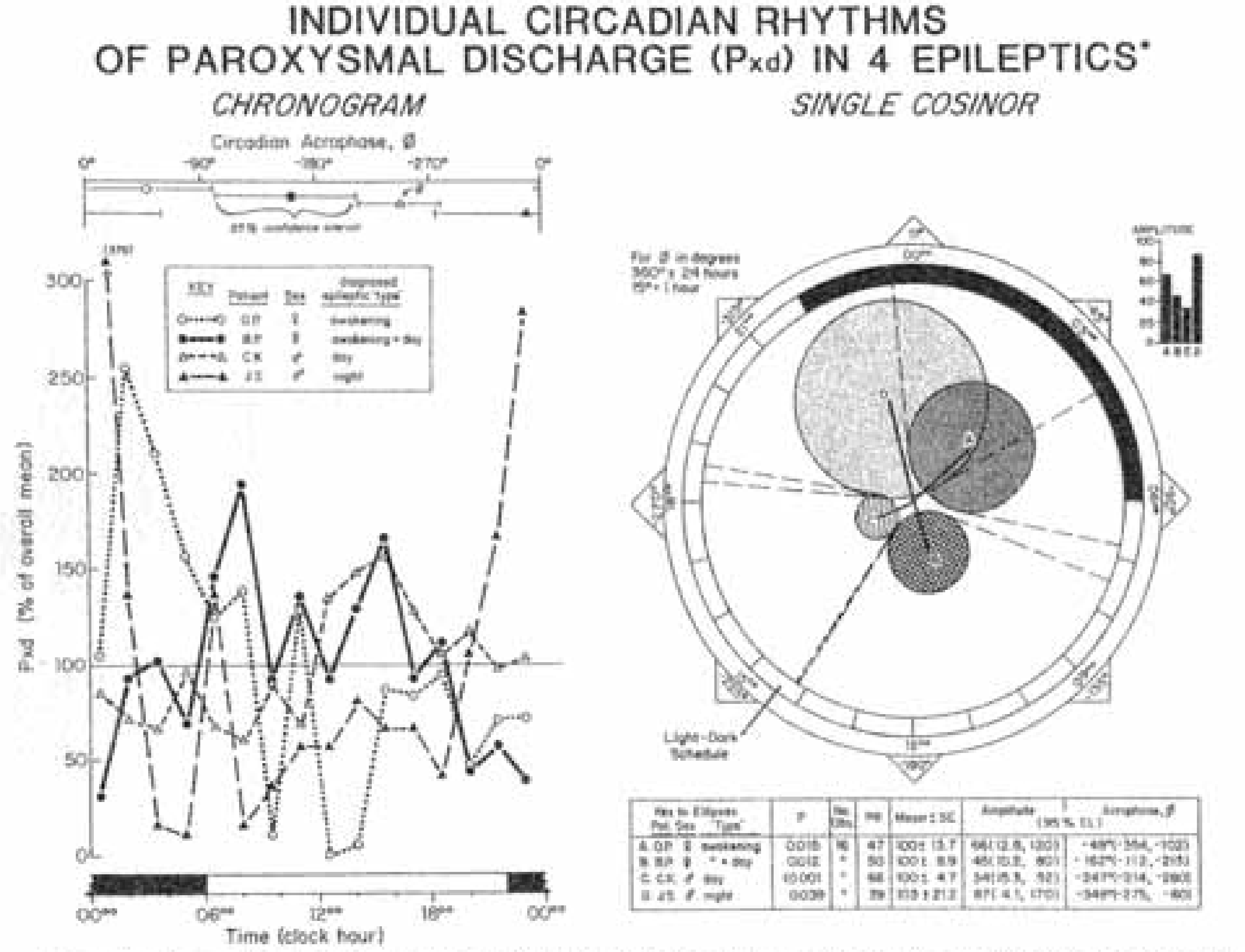


Figure 4.

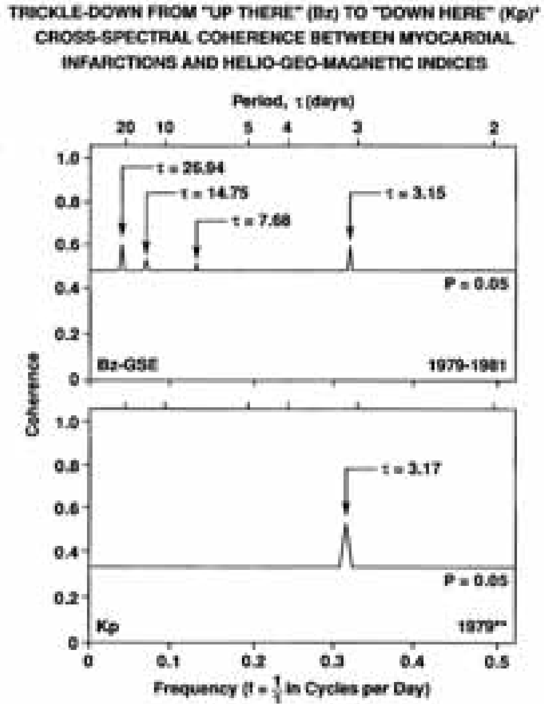


*Incidence of Pxd calculated from 5 minute EEG tracings obtained at 1.5 hourly intervals for 24 hours; subjects institutionalized for treatment (but not medicated at time of study)

Figure 5.

Figure 5. The time percent of paroxysmal discharge determined on hard copy EEGs in the 1950s undergoes a circadian rhythm, as was predicted for JS with an acrophase at -348˚ and a 95% confidence arc extending from -275˚ to -60˚, thus including the point estimate of -26˚ for JS in Figure 4. The excessively wide arc is a reason for caution in considerations of time lags between the average times of onset of EEG-revealed pathology and of seizure incidence, although the 95% confidence intervals for the two variables greatly overlap one another for JS. Not only seizure incidence, but the temporal placement of circadian rhythms in pathology shows circadians and the acrophase differences between EEG and overt pathology may provide clues about mechanisms and may be considered in timing medication. © Halberg.

Figure 6. A series of daily incidence of myocardial infarction (MI) in Moscow during 1979-1981 (years of high solar activity) (N=85,819) had been analyzed for associations with the local index of geomagnetic disturbance K. A statistically significant global cross-spectral coherence was found at a period of about 3.17 days (bottom). When the data were analyzed for each year separately (not shown), the same result was obtained during the first and third year, but reached statistical significance only in 1979; in 1980, a statistically significant coherence was again found at a shorter-than-3.5-day period. Similar cross-spectral coherences at almost the identical period (3.15 days) were also found with the B_z-GSE, the north-south component of the interplanetary magnetic field (B_z) (top). Statistically significant coherences between MI and B_z were also found for periods of about 26.9, 14.7, and 7.7 days, which correspond approximately to the major harmonic terms of the solar rotation around its axis. Original data of myocardial infarctions in Moscow from Tamara Breus. © Halberg.



* B_z-GSE = vertical component of the induction vector of the interplanetary magnetic field; K_p = geomagnetic index.

** In 1981, a spectral coherence peak (also at precisely 3.17 days) does not reach statistical significance. In none of the three years was there coherence at a societal (e.g., once weekly) frequency.

Figure 6.

frequency of humans or rodents differing among the time series examined (for free-running circadians see section ID of Figure 7 in [127]). Figure 10I in (127) shows the different frequencies of each menstrual cycle with the period lengths in these cases again being equated with 360°. We had also learned, what may again broaden the scope of electro- and magnetoencephalography alike, that the brain in health (128) exhibits circadians, among other rhythms with frequencies higher than 1 Hz, a point pertinent to Bärbel's prior work and to that of her many co-investigators! Apart from the brain, we had also learned that circadian phase is important for timing radio- and chemotherapy given to cancer patients (129, 130).

Inferential statistical considerations toward phase relations among time series, summarized by Christopher Bingham

A stationary time series $\{X_t\}$ and even one that is only locally stationary, can be decomposed as a superposition of many terms of the form $A_x(f)\cos(2\pi tf - \varphi_x(f))$ where f is a frequency in cycles per unit time, and $A_x(f)$ and $\varphi_x(f)$ are random amplitude and phase. Near frequencies where there is periodic or near periodic behavior, $E[A_x(f)^2]$ tends to be large. In fact, the spectrum $S_x(f)$ of X_t is proportional to $E[A_x(f)^2]$.

The stationarity of the series implies that $\varphi_x(f)$ should have the uniform distribution on the circle $0 \le \varphi_x \le 2\pi$. When $f_1 \ne f_2$, $A_x(f_1)$ and $A_x(f_2)$ should be uncorrelated, as should $\cos(2\pi\varphi_{x,k}(f_1))$, $\sin(2\pi\varphi_{x,k}(f_1))$, $\cos(2\pi\varphi_{x,k}(f_2))$ and $\sin(2\pi\varphi_{x,k}(f_2))$.

Similarly a parallel stationary time series Y_t can be decomposed as a superposition of terms of the form $A_y(f)\cos(2\pi tf - \varphi_y(f))$ where $A_y(f)$ and $\varphi_y(f)$ have similar properties, with the spectrum $S_y(f)$ proportional to $E[A_y(f)^2]$.

If the two series are jointly stationary then the cross spectrum $S_{xy}(f)$ at frequency f is proportional to the complex quantity $E[A_x(f)A_y(f)\exp(-i(\varphi_x(f) - \varphi_y(f))]$, where $i^2 = -1$. This can be viewed as a weighted expectation of $\exp(-i(\varphi_x(f) - \varphi_y(f))$, the weights being proportional to the product $A_x(f)A_y(f)$ of the random amplitudes.

The magnitude $|\rho(f)|$ of the complex coherence $\rho(f) = S_{xy}(f)/\sqrt{\{S_x(f)S_y(f)\}}$, the cross spectrum "adjusted" for the expected size of the random amplitudes, is 0 when the distribution of the phase difference $\varphi_x(f) - \varphi_y(f)$ is uniform on the circle so there is no synchronization of the two series at frequency f. The more concentrated is the distribution of $\varphi_x(f) - \varphi_y(f)$, the more synchronization there will be and the closer will $|\rho(f)|$ be to 1. $|\rho(f)| = 1$ corresponds to the case of complete phase synchronization when the phase difference $\varphi_x(f) - \varphi_y(f)$ is a fixed constant.

Thus the squared coherence $|\rho(f)|^2$ can be in part considered a measure of how closely linked are the random phases $\varphi_x(f)$ and $\varphi_y(f)$.

Another possible measure of the association between $\varphi_x(f)$ and $\varphi_y(f)$ is the magnitude of the unweighted expectation $|E[\exp(-i(\varphi_x(f) - \varphi_y(f)))]|$. Like $|\rho(f)|$, this runs from 0 to 1, with 1 occurring only in the case of perfect synchronization.

When you have K replicate time series pairs, say K non-overlapping segments of fixed length, and are able to find estimates $\hat{A}_{x,k}(f)$, $\hat{A}_{y,k}(f)$, $\hat{\varphi}_{x,k}(f)$, $\hat{\varphi}_{y,k}(f)$, $k=1,\dots,K$ of the amplitudes and phases, you can estimate $|\rho(f)|$ by

$$|\hat{\rho}(f)| = \frac{\left|\frac{1}{K}\sum_{k=1}^{K}\hat{A}_{x,k}(f)\hat{A}_{y,k}(f)e^{i(\hat{\varphi}_{x,k}(f)-\hat{\varphi}_{y,k}(f))}\right|}{\sqrt{\frac{1}{K}\sum_{k=1}^{K}\hat{A}_{x,k}(f)^2\,\frac{1}{K}\sum_{k=1}^{K}\hat{A}_{y,k}(f)^2}}$$

where the numerator is a weighted average of $\exp(i(\hat{\varphi}_{x,k}{}^{(f)} - \hat{\varphi}_{y,k}(f)))$.

Similarly you can estimate $|E[\exp(-i(\varphi_x(f) - \varphi_y(f)))]|$ by the unweighted average PLI =

$$\left|\frac{1}{K}\sum_{k=1}^{K}e^{i(\hat{\varphi}_{x,k}(f)-\hat{\varphi}_{y,k}(f))}\right|.$$

When there is no phase synchronization so that $\hat{\varphi}_{x,k}(f) - \hat{\varphi}_{y,k}(f)$ is uniform on the circle, for moderate K, $2K \times PLI^2$ has approximately a χ^2_2 distribution. The use of this statistic for testing uniformity is due to Rayleigh (Batschelet, E. 1981. Circular Statistics in Biology. Academic Press, p. 55).

A disadvantage of the use of PLI rather than $|\rho(f)|$ is that, when $\hat{A}_{x,k}(f)$, $\hat{A}_{y,k}(f)$ is small, the distribution of $\hat{\varphi}_{x,k}(f) - \hat{\varphi}_{y,k}(f)$ is close to uniform and provides little information about the phase synchronization at frequency f. This will tend to reduce the power of the Rayleigh test as compared to a test based on $|\rho(f)|$.

Cautionary note

In the case when replicated series are not available, the spectra and cross spectrum are usually estimated by weighted averages of periodograms and the cross-periodogram at frequencies near f. This works well when the true spectra and cross-spectrum change little in the neighborhood of f. The standard approximate tests and confidence intervals concerning coherence assume this near constancy of spectrum and cross-spectrum. When either X_t or Y_t has a very sharp spectral peak at frequency f which rises well above the spectrum at neighboring frequencies, the averages across frequency that make up the spectrum and cross spectrum estimates are dominated by the values of periodograms and cross periodograms at f and the stabilizing effect of averaging is defeated. This can gravely damage the accuracy of the standard tests and confidence intervals. In the extreme, when

$$X_t = A_x\cos(2\pi tf - \varphi_x) + \zeta_t \text{ and } Y_t = A_y\cos(2\pi tf - \varphi_y) + \eta_t$$

where (A_x, φ_x) is independent of (A_y, φ_y) and $\{\zeta_t\}$ and $\{\eta_t\}$ are independent with much smaller variances than A_x and A_y, the estimated coherence can be close to 1 although $\{X_t\}$ and $\{Y_t\}$ are independent of each other. When the coherence can be estimated by averaging across replicate series, this problem does not occur.

Lessons from Bärbel Schack

Bärbel complemented single (series) and population-mean cosinors and linear and nonlinear rhythmometry by the study of instantaneous relations among time series as these relations may change at many frequencies. We were in a position to validate the extreme sensitivity of Bärbel's methods for time-varying quantification of phase coupling (phase synchronization, as she called it) by anticipating at least some of her results by global coherence published 12 years earlier (131) and recently republished (Figure 6 in reference 132). We had found that myocardial infarctions (MIs) show global cross-spectral coherence at a trial period of 3.16 days (overall and during two of 3 years analyzed separately) with both the north-south component of the interplanetary magnetic field (B_z) and the local geomagnetic index (K) in Moscow during the years 1979–1981, Figure 6a. Independently, Bärbel detected time-variant coherence and phase synchronization at the same frequency between MIs and local K in the same data set. Moreover, she extended the finding to reveal dynamic coherence and phase synchronization most prominently at the same frequency and at other frequencies between MIs and sunspots in 29 years of MIs in Minnesota.

Bärbel found further phase-synchronization at many more frequencies, not only among MIs and interplanetary and terrestrial magnetics, but also among MIs and variables of the solar wind in added cases where no prior information was available. This circumstance leads again to the problem of multiple testing. She found very small differences, i.e., a very tight phase synchronization, as one would expect, among many or almost all frequencies between the original data on MIs in Minnesota and the same data after detrending. This finding constitutes a reference standard, since we might anticipate it when looking at nearly the same time series before and after detrending. The same anticipation is validated for phase-synchronization found by her among geomagnetic indices such as the antipodal index aa, the planetary index K_p or the equatorial index Dst themselves. These findings all serve to validate her technique by the equivalent of good reference standards.

Phase synchronization of solar variables at a half-yearly cycle?

Bärbel was very cautious when her method for detecting phase synchronization picked up a phase relation (she called it "phase synchronization") at the half-yearly trial period between Wolf's sunspot numbers and the coronal index of the sun, and thought of possible blurring. At this half-year period, there were peaks in neither of the spectra of these two variables. In other words, she found a relation in two time series in a location without spectral peaks and at a frequency that was not anticipated, and these results require rigorous checking and cannot be interpreted in themselves. As others, we had found the presence of sharp peaks in aa, K_p and Dst at a frequency of 1 cycle in half a year (133). Peaks at the half-year in geomagnetics can continue to be looked upon as terrestrial, not solar phenomena (133; cf. 131, 134–143). According to McPherron (personal communication), the Russell-McPherron effect depends on the tilt angle of the earth's axis toward or away from the sun; but the problem also noted by McPherron is that "the historical records are not long enough to define well the statistical significance of various periodicities and correlations".

The ~1.3 (trans-)year

Apart from the purely physical problems, it is interesting to find signatures of a half-year cycle (144) and of the ~1.3 (trans-)year of the solar wind in a number of biological variables. Again, these will have to be checked for whether they are current and/or past signatures of our cosmos in the biosphere (50, 73). On occasion in the human pulse or blood pressure, the amplitude of the trans-year can be greater than that of the 1-year component, i.e., the contribution of the mostly unseen solar wind can exceed that of changes from a hot summer to a cold Minnesotan midcontinental winter.

The helio-geophysical week

Abbott was the first to describe a near-week in rainfall (145). The sun's magnetism shows a near-week (146), reminiscent of another very wobbly near-week rhythm with a frequency of 1 cycle in ~6.75 days in geomagnetism (131) which is found usually on earth, in data of the past century and again now in the aa-index series accumulated since the nineteenth century to the new millennium. This is at apparent variance with an earlier report (147) of a precise 7-day week, found by a leading physicist in the data on a geomagnetic index when he happened to examine the series accumulated up to the early 1970s (147). His finding was fully confirmed by us for the span he happened to examine (148). We also found, however, that the spectral component of a precise week length was not reproducible in 22- or 21-year data sections of the geomagnetic index aa accumulated until 2001 (148).

Our finding of an overall near-but-not-precise week (131) in geomagnetics was confirmed by physicists (149, 150). Both the near-week and a precise 7-day human-made component gauging magnetic pollution were next found in Antarctica (151). It is anticipated that the relative prominence of the precise anthropogenic geomagnetic week will increase in amplitude further as a function of further increases in magnetic pollution. Accordingly, the difference between the amplitudes in spectra of aa, other complicating factors being what they are, is likely to disappear and eventually to change sign (148). If so, the way humans change their purely earthly environment can rest on clues from biology, by study of a periodicity believed to be purely social (by many) (152, 153). Bärbel, like us, found near-weekly components in her spectra.

The phase-synchronizations along with coherences among other relations Bärbel found earlier within the human brain along the time scales conventionally used by magneto- and electroencephalographers could be systematically extended along a scale of frequencies covering 10 orders of magnitude and along with the findings of relations of the human heart and the rest of the body to solar activity (131, 154–156). This could be an ambitious project for which chronomics provides maps for cost-effective sampling schemes covering the major cycles now known to be involved in just such long-term studies.

Some rhythms are genetically programmed (154–156), as are developmental trends in biological chronomics (157, 158), and the trends are subject to rhythms (159–161), as is chaos in biology (162, 163). We learned much from Bärbel, and the task at hand, for generations to come, is to continue an extension of phase synchronization by ascertaining the reproducibility and scope of what she did, preferably with amplitude weighting. Most important are computer routines, enabling time-varying phase-synchronization and coherence studies on unequidistant data that are very common in biology. Linear interpolation but not other methods used by Bärbel to bridge data gaps did introduce demonstrable artifacts in Germaine Cornélissen's checking. Illustrative examples of Bärbel's procedures are documented by her graphs in Appendix A, with information of A6 and A7 to be requested only from Herbert Witte.

Epilogue

To implement the wish that Bärbel's legacy will turn her contributions into an essential of future history, it is hoped that the authors of this eulogy will maintain contact. Certainly replications of work on rhythms with frequencies above 1 Hz should record stages of circadians and circaseptans, among other rhythms including circadecadals and, when possible, vice versa.

Cycles with different frequencies are the reproducible features offering themselves for scientific investigation. Cycles already found characterize the diseases of society such as crime and war (164), that have periods measured in decades, as does spirituality (165); they involve human brains with more specific primary cycles above 1 Hz. The modulation by circadians of pathological electroencephalographic discharge was mapped over 50 years ago (113–117). The different types of seizure incidence were recognized in the 19th century (166). By the 1960s, circadians were mapped in the power of the different regions of the Berger range of the EEG of clinically healthy neurology residents (128). Eventually, human mood was shown to undergo a circadecadal change (155) as well as circadian rhythmicity (167). Circadians and about 7-day changes differ for positive vs. negative affect (168).

It would be a surprise if cognition were to prove to be an exception and an even greater finding if this were so. The next step is to study rhythms both above and below 1 Hz by MEG, EEG and otherwise, in the search for mechanisms underlying diseases not only of individuals but also of populations. These are urgent tasks, second in importance to none, as we listen to each day's news. The endocrinologist's removal of a gland and replacement of its hormone has a parallel in a subtraction and addition approach, with the subtraction and replacement done by the solar wind of components with validatable periods measured in decades. This may be the indispensable safeguard, since as yet there is no invaluable "blank" equivalent, which Bärbel sought for the last 15 months.

Circadecadals influence almost certainly not only the human heart, as various methods suggest, but also the brain. EEGs, MEG and other imaging and physiological approaches may provide clues to conclusions both at frequencies above and below 1 Hz. Bärbel's methodology, as we see it in a chronomic perspective, brought us from global correlations and cross-spectral coherences to time-varying coherence and complementary time-varying phase-"synchronization", extending by far the scope of a synchronization reported about half a century ago at a single frequency (169). Concurrent relations among multiple rhythms with different frequencies remain to be explored.

Conclusion

A medieval painter sent a bill to a monastery, charging them "*x* ducats for enlarging the sky and adding a few stars". Bärbel in turn enlarged the study of galactic and/or solar influences upon human affairs by phase synchronizations, described at several frequencies. Thereby she enlarged the concept of phase in chronomics. Conceivably she opened the eye of those who, of necessity, first focus exclusively on rhythms within a limited range of more or less specific frequencies, but will greatly benefit immediately by consideration of rhythms with many more frequencies. In a letter to Hans-Georg Geissler, included in the title of this memorial, she alludes to rhythms beyond short ones *("Wenn man über kurze Rhythmen hinausgeht").* In any event, we are reminded of the artist's bill, since she added a star to the sky of science, second to none and priceless, namely herself. If she were to read this, she would say *"Oh jeh,* I am red-faced!" She need not have been; she deserved this eulogy by virtue of what Hellmuth Petsche called her *Lauterkeit,* which is the best description of a scientist who follows whatever goes through her head *(mir durch den Kopf geht),* as Bärbel put it. In Bärbel, scientists with many interests, and thus transdisciplinary science, had a *Kameradin* like no other *(wir hatten eine Kameradin),* who kept on asking questions (presumably Einstein's advice).

The region of Thuringen, that was home to the composers Johann Sebastian Bach and Franz Liszt, the painter Lucas Cranach, the writers Johann Wolfgang von Goethe, Johann Gottfried Herder and Friedrich Schiller, the poet Christoph Martin Wieland, the industrialist Karl Zeiss, and the physicist and mathematician Ernst Abbe, can now claim Bärbel Schack as a transdisciplinary scientist. Themes of her bibliography fit the diversity of her predecessors. Bärbel built bridges from her disciplines, engineering and mathematics, to endeavors in the letters, the broader humanities, related to language and cognition, all requiring the increasingly more complete mapping of our make-up in time and space, the topics of complementary genomics and chronomics.

Footnote 1. Prof. Hans-Georg Geissler also points out that in his field, Prof. Werner Krause had much more extensive relations to Bärbel than he (Geissler) himself had to her, and that he had met Bärbel at a meeting organized by Krause. Bärbel's close cooperation is apparent from the many joint papers with Krause, to whom she provided most of the computer routines he used. Moreover, during her visit in Minnesota, Bärbel emphasized that she owed much to Werner Krause.

Appendix A of figures by Barbara Schack

Institute of Medical Statistics, Computer Science and Documentation, University of Jena, Germany, and honorary associate of the Halberg Chronobiology Center, University of Minnesota, Minneapolis, Minnesota, USA

Chronobiologic analyses of data on daily mortality from MI in Minnesota during 1968–1996 revealed the presence of about-yearly and about-weekly variations peaking in the winter and on Mondays, respectively, and further an about-10.5-year component similar in

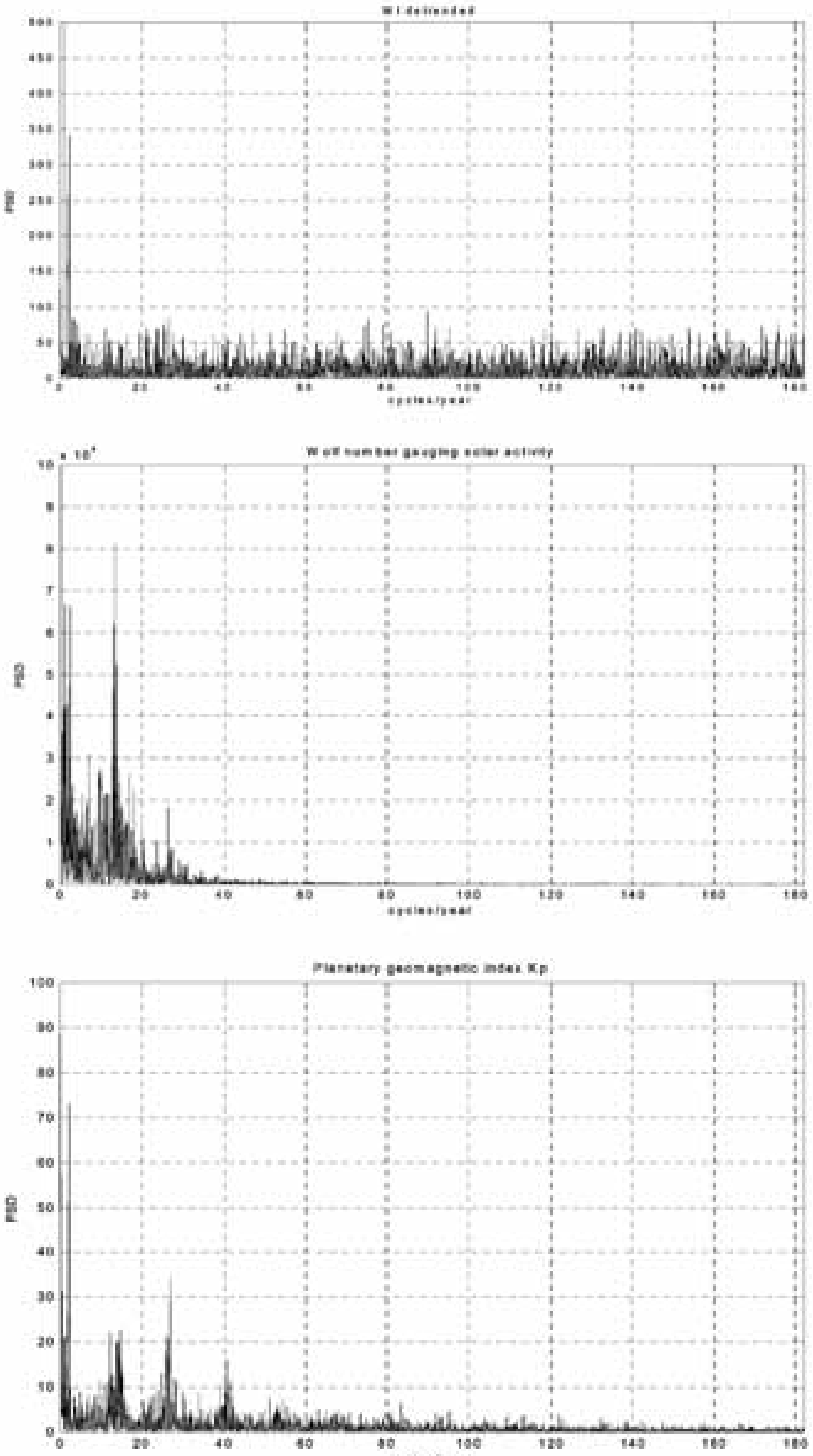


Figure A1.

Figure A1. Power spectral densities (PSD) of the daily incidence of mortality from myocardial infarction in Minnesota during 1968-1996 (29 years) (after removal of a linear decreasing trend) (top) and of Wolf numbers (reflecting solar activity) (middle) and of the planetary index of geomagnetic disturbance K_p (bottom) during the same 29-year span were obtained by averaging spectra from 29 consecutive years. Apart from prominent low-frequency components corresponding to the about 10.5-year solar activity cycle, common to all three variables, major spectral peaks are seen for Wolf numbers and K_p at frequencies of about 14 cycles per year (or about 27 days) and harmonics thereof, corresponding to the solar rotation period around its axis.

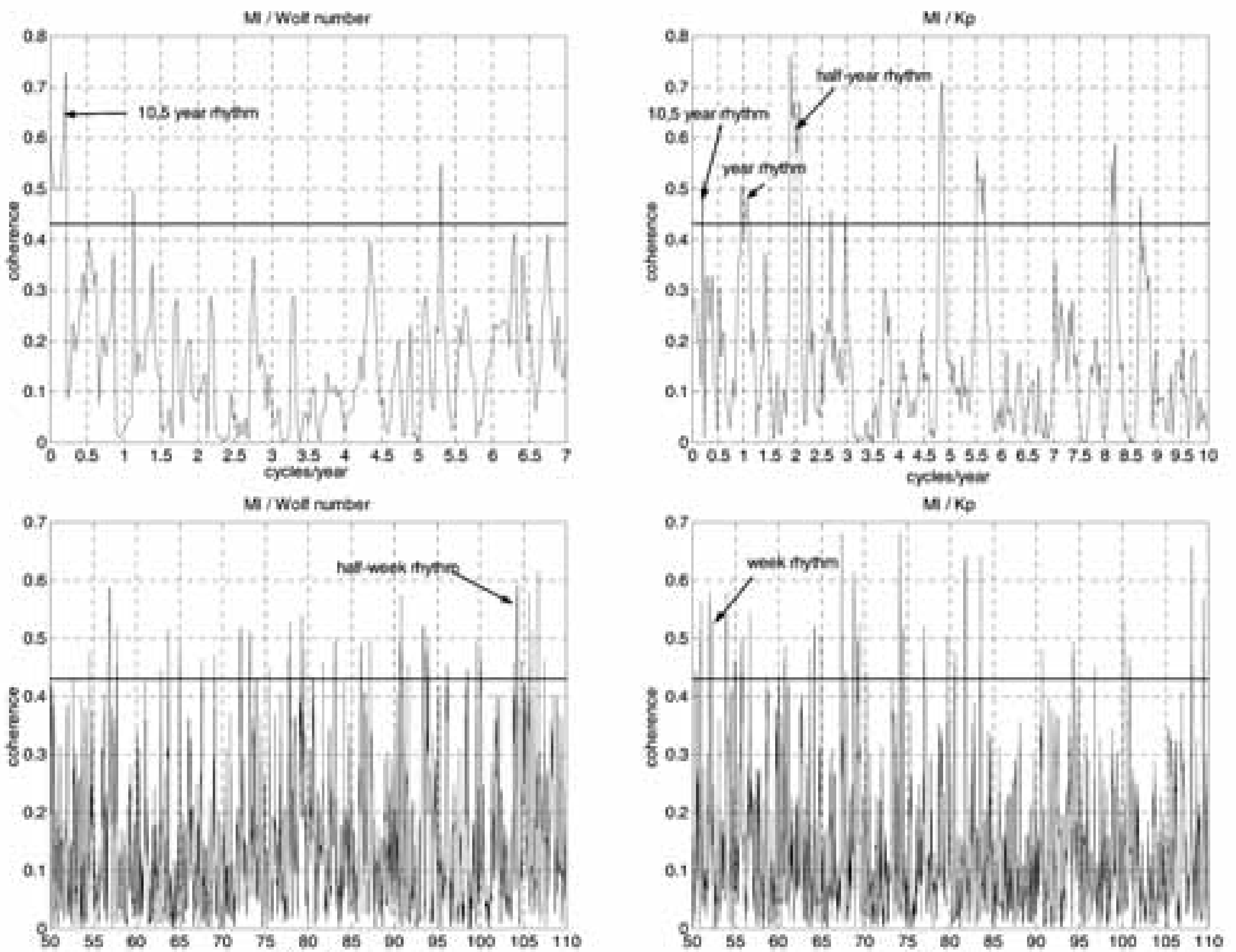


Figure A2.

Figure A2. Results from cross-spectral analyses between MI and Wolf numbers (reflecting solar activity) (left) or the planetary index of geomagnetic disturbance K_p (right) in two selected frequency ranges: the low-frequency region extending from 29 to about 4 years (top), and the about weekly/half-weekly or circaseptan/circasemiseptan region extending from about 7.3 to about 3.3 days (bottom). Cross-spectral coherence is found prominently between MI and Wolf numbers around 10.5 years and between MI and K_p around 1.0 and 0.5 year.

length to the solar activity cycle, that accounted for an about 5% difference in the number of deaths occurring during years of maximal versus years of minimal solar activity (154).

In order to further understand any putative influence of solar and/or geomagnetic effects on the incidence of MIs in Minnesota, associations were sought with a number of physical variables retrieved from the web (170), namely the coronal index (CI), the number of sunspots (Wolf numbers; WN) and indices of geomagnetic activity K_p, aa and Dst. Because the incidence of MIs decreased over the 29-year span investigated herein, the data on MI were linearly detrended.

To this effect, analytical techniques such as phase synchronization, originally developed mostly in the context of brain activity and cognition (1–103; notably 23, 26, 29, 31, 34), were applied to the data on MI mortality in Minnesota, and results were compared with those obtained with the classical approach by spectral analysis. Herein, we focus on relations between WN and MI and between K_p and MI in order to compare putative non-photic effects from the sun or from the earth.

Figure A1 compares the power spectral densities of the detrended MI (top), WN (middle) and K_p (bottom). Not surprisingly, spectral power around one cycle in 27 days is observed for WN and K_p, and is likely associated with the solar rotation period. Spectral power is also observed for these two variables as well as for MI around two cycles in 27 days. Whereas the spectral power rapidly decreases at higher frequencies for WN, additional peaks are visible for K_p, including one around one cycle in about a week. Some low-frequency components also appear to be common to all three variables.

Figure A2 displays the cross-spectral coherence between WN and MI (left) and between K_p and MI (right) in two selected frequency ranges focusing on the low-frequency region of the spectrum (top) and in the circaseptan/circasemiseptan region of the spectrum (bottom). Cross-spectral coherence is seen primarily around one cycle in 10.5 years, where it is

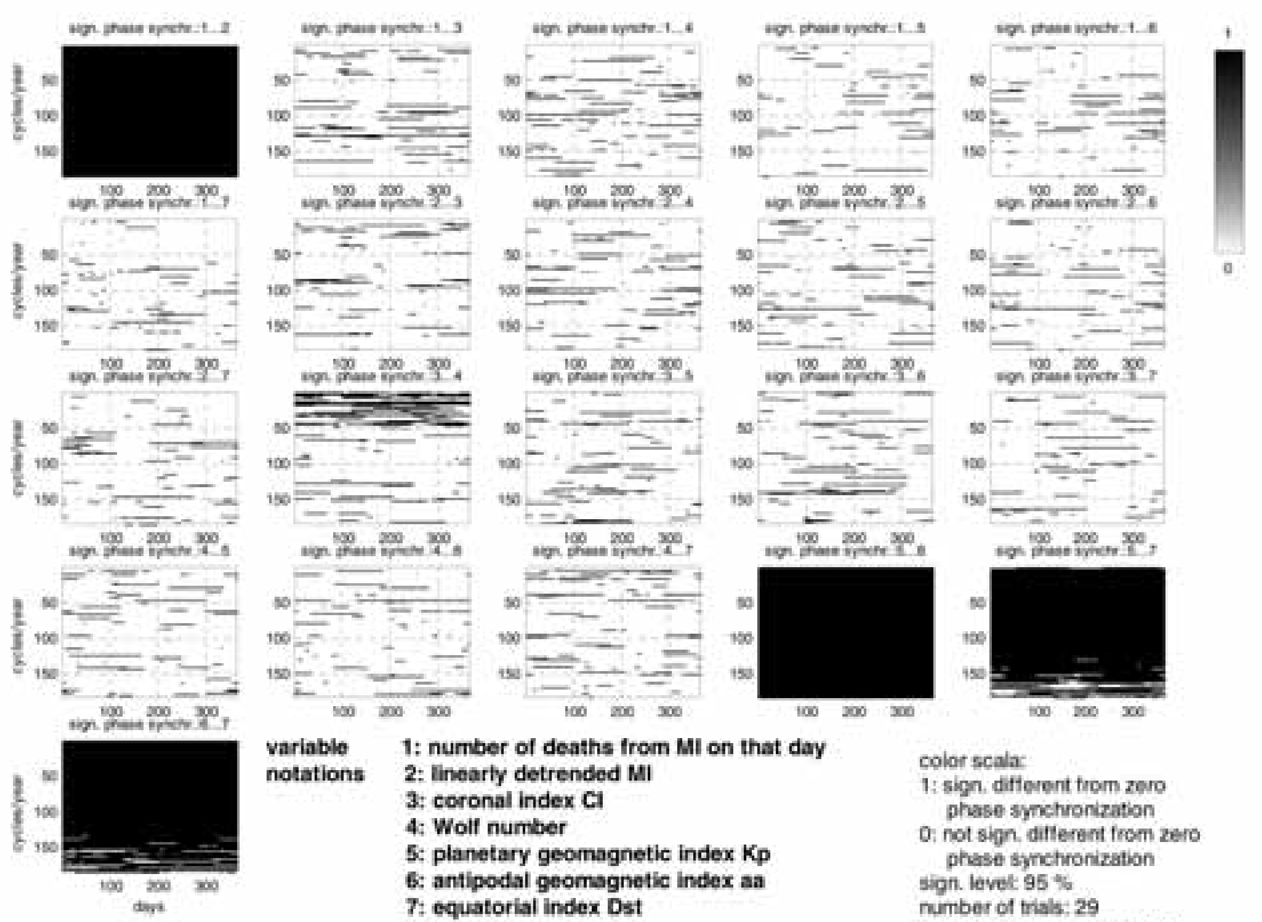


Figure A3a.

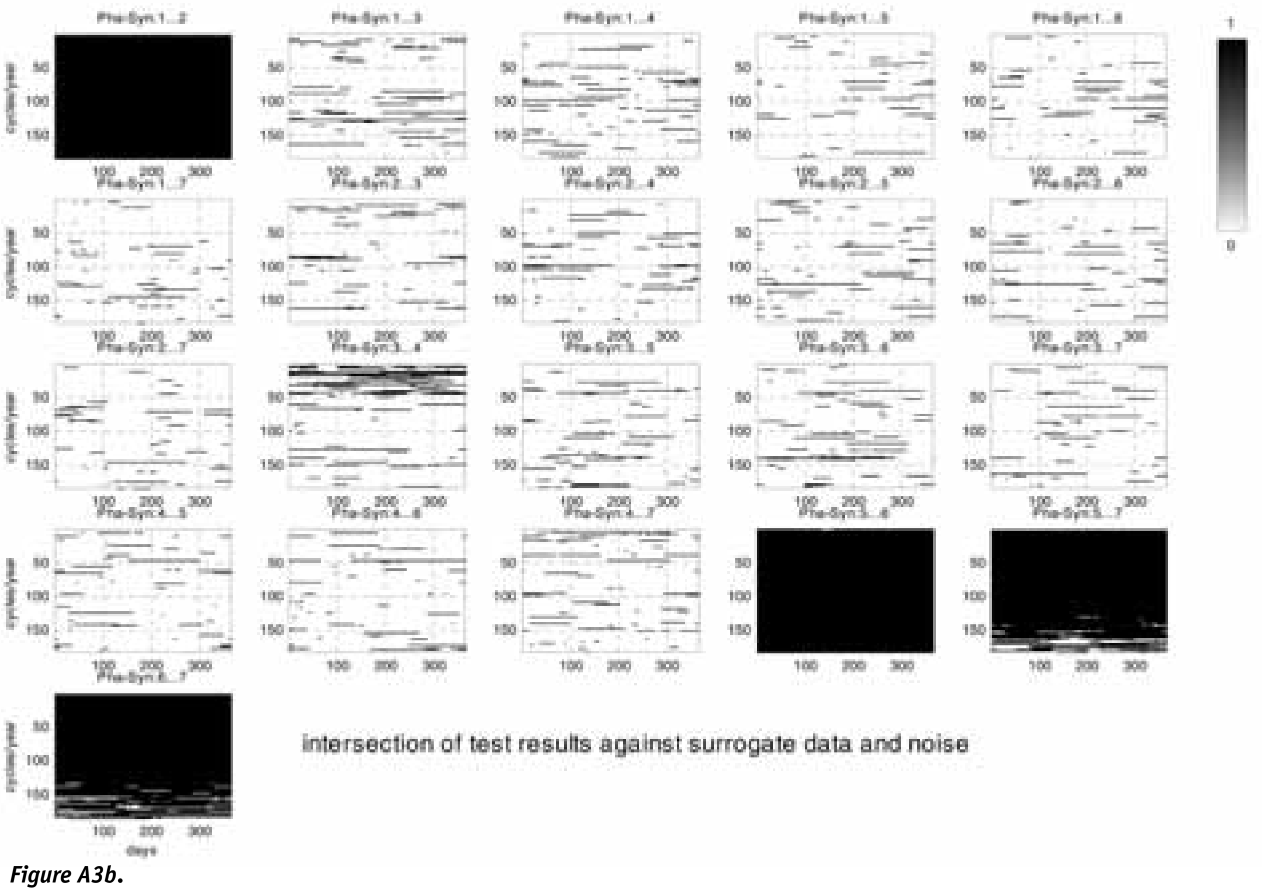


Figure A3b.

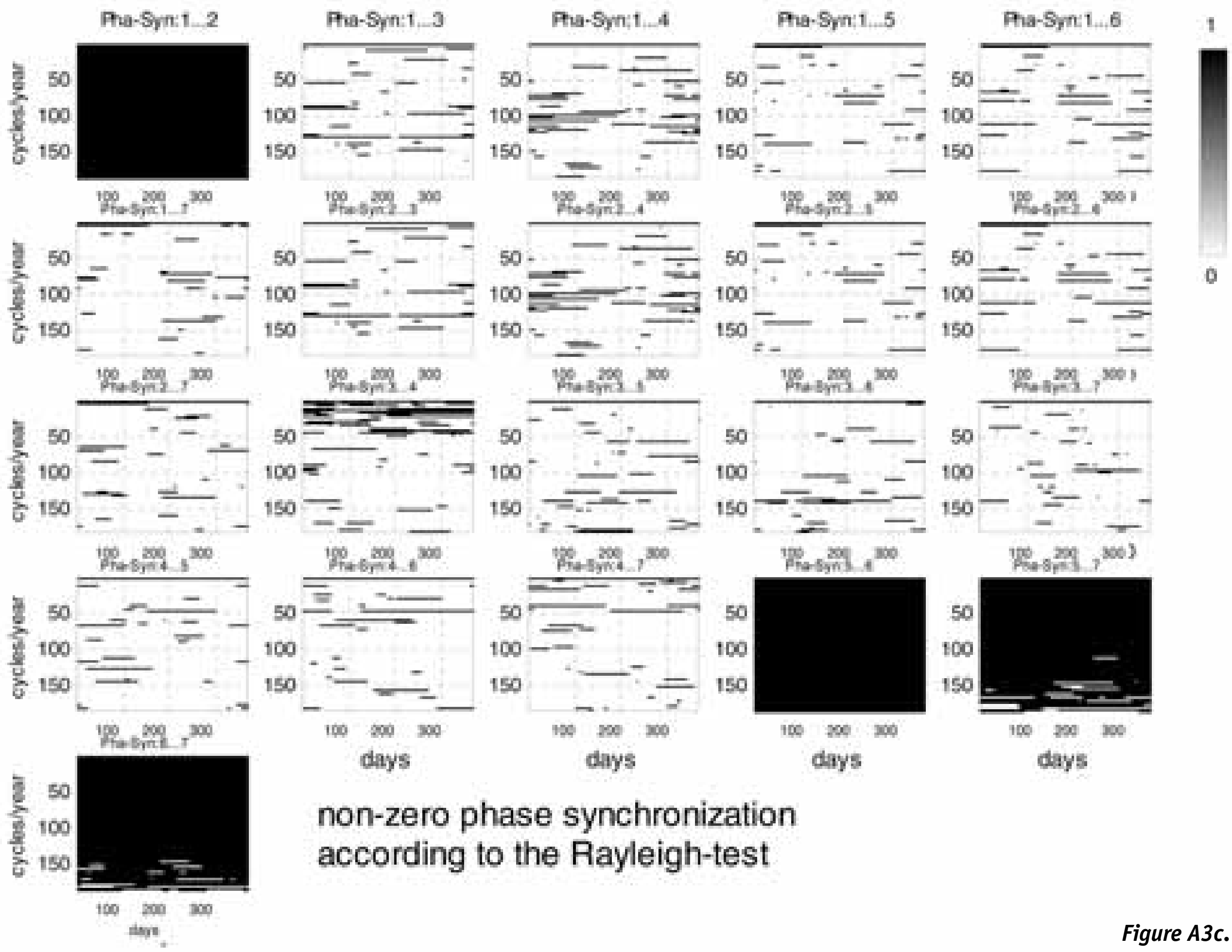


Figure A3c.

Figure A3. Illustration of three different approaches to determine non-zero phase synchronization between pairs of variables. The data set consists of the daily incidence of mortality from myocardial infarction (MI) in Minnesota during 1968-1996 (29 years) (variable 1), the same data after removal of a linear decreasing trend (variable 2), and different physical environmental variables reflecting the influence of the sun (coronal index and Wolf numbers, variables 3 and 4, respectively) or that of geomagnetism (the planetary index of geomagnetic disturbance K_p, the antipodal index of geomagnetic disturbance aa, and the equatorial index of geomagnetic activity Dst, variables 5, 6, and 7, respectively). Thresholds for the phase synchronization index computed at each time-frequency for each pair of variables were computed either by random permutation of trials, here represented by 29 1-year spans, used as replications (*Figure A3a*), by simulation of noise series (*Figure A3b*), or theoretically, according to the Raleigh distribution (*Figure A3c*). Anticipated results are obtained, such as the identical time-frequency structure of MI and detrended MI, and the very close – but not identical – time-frequency structure of K_p, aa, and Dst, K_p and aa being very similar to each other but both showing some slight differences, mostly at higher frequencies, with Dst, and the similarity in the low-frequency region between the two solar variables. Results are also very similar irrespective of the approach selected to determine the thresholds of statistical significance, giving added credence to the results, the unresolved problem of multiple testing notwithstanding.

most prominent with respect to WN. Cross-spectral coherence is also found around one and two cycles per year, primarily in relation to K_p. At higher frequencies, cross-spectral coherence around two cycles per week with WN and around one cycle per week with K_p are noteworthy.

Because phase is often a more sensitive parameter than amplitude, a method of phase synchronization was used to investigate any associations of MI with respect to WN and K_p. In order to apply this technique, several trials of the same process are needed. Since in this context there is no specific ‘event’ (such as the presentation of a stimulus or a test routine) to which trials can be referred as phase zero, the original time series were arbitrarily subdivided into 29 yearly subspans, considered as replications or ‘trials’. The phase synchronization index quantifies the variation of phases among the different ‘trials’ (years) for each time-frequency pair. The phase synchronization index ranges between zero (no synchronization) and one (total synchronization). To test for non-zero phase synchronization, several approaches were followed. First, the method proposed by Rodriguez *et al.* (171) was performed, which consists of calculating the phase differences for each of 100 randomly chosen trial pairs (the data of one variable during one year being matched

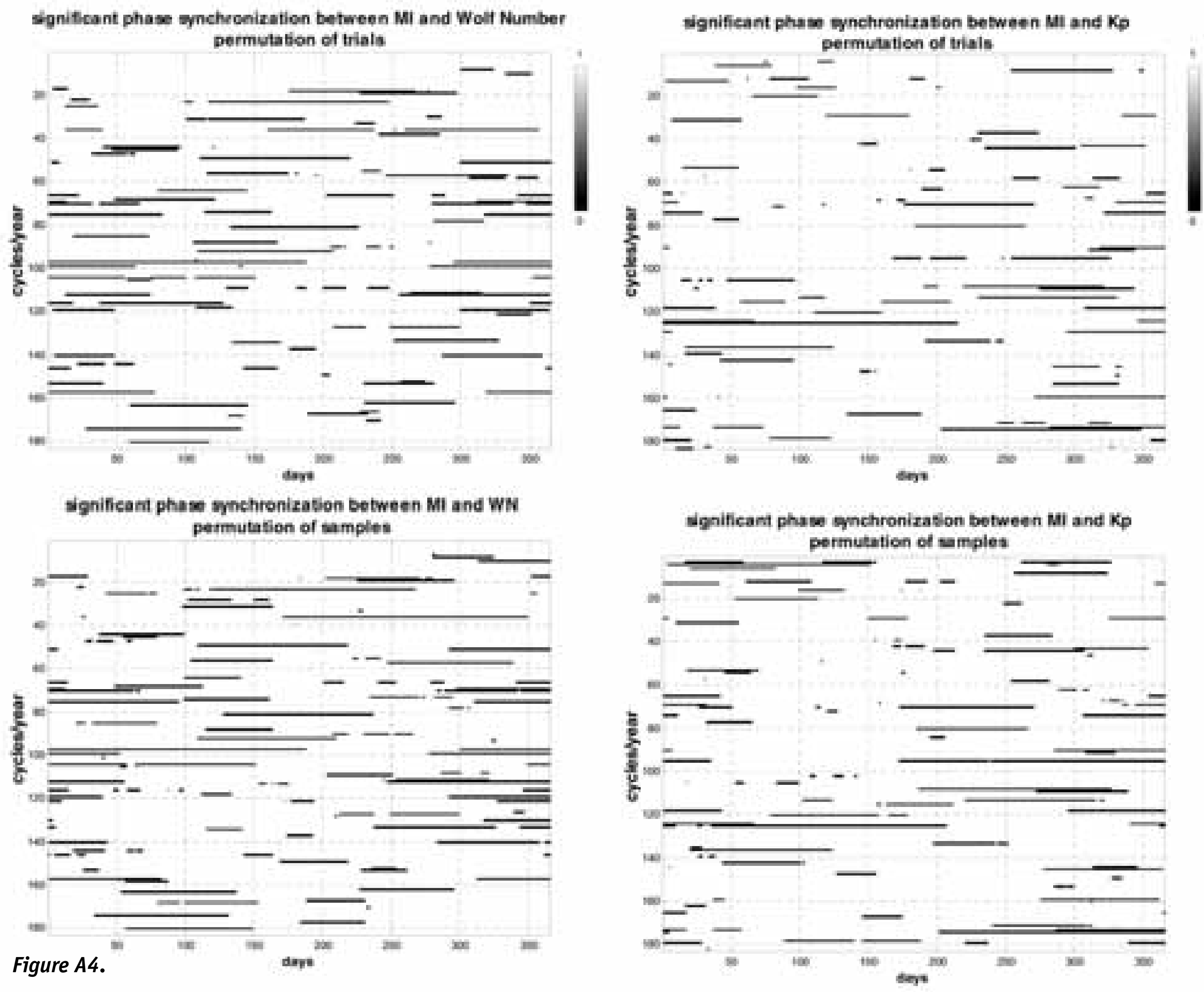


Figure A4.

Figure A4. Further comparison of non-zero phase synchronization resulting from a random permutation of trials (top) or from a random permutation of samples (bottom). MI appears to show a closer association with solar activity, gauged by Wolf numbers (left), than with geomagnetism, gauged by K_p (right). For a description of the data set, see *Figure A3*.

with the data of the other variable during another year picked at random and not necessarily corresponding to the same year as the first variable). The phase synchronization index was determined for each set of phase differences (at all times and frequencies considered). For each time-frequency pair, a threshold was defined as the 95% quantile from the 100 combinations. Phase synchronization indices of the actual data above these thresholds were considered to have a less than 5% probability of occurring by chance alone. Second, instead of random permutations of trials (years), noise series were used to establish the threshold values. Third, non-zero phase synchronization was determined theoretically, according to the Raleigh test (118).

Figures A3a-c illustrate non-zero phase synchronizations between pairs of variables, computed according to each of the 3 approaches described above. It can be seen that results are very similar irrespective of the approach used. As expected, there is practically no time-spectral difference between MI and detrended MI (except for the lowest frequency corresponding to the removal of the linear trend). Results of non-zero phase synchronization between MI or detrended MI and each of the physical variables are very similar and are identical when relying on the Raleigh test (Figure A3c) (118). CI and WN are very similar at low frequencies. K_p and aa have a phase synchronization index above threshold for almost all time-frequency pairs, suggesting that these two variables are very similar but not necessarily identical. Great similarity is also observed between either K_p or aa and Dst, differences occurring primarily at high frequencies, a finding making good geophysical sense. In addition, there is non-zero phase synchronization found consistently at some specific frequencies between MI (or detrended MI) and each of the physical variables.

Figure A4 compares results obtained by random permutation of trials (years) (top) or by random permutation of samples (data) (bottom) for the case of MI versus WN (left) or K_p (right). Results appear similar whether the random permutations are performed on trials or on samples. MI also seems to exhibit more phase synchronization with respect to WN than with respect to K_p.

Using the approach by random permutation of trials, Figure A5 compares nonzero phase synchronizations between MI and WN (left) or K_p (right) using the upper 95% (top) or 99% (bottom) quantile from the distributions to reflect associations statistically significant at the nominal 5% or 1% probability level (without correction for multiple testing).

The conclusion that MI is more closely associated with solar activity (WN) than with geomagnetic disturbance (K_p) is also reached from the instantaneous cross-spectral coherence results around one cycle per 10.5 years, shown in Figure A6. An association between mortality from MI and WN (top) or K_p (bottom) at a frequency of one cycle in about 10.5 years (solar activity cycle) is documented by dynamic power, coherence and cross-phase analyses of detrended data filtered with a narrow band (0.04 to 0.16 cycle/year or 6.25 to 25 years) filter. Figure A6 shows the dynamic power and coherence of the two pairs of variables analyzed as bivariate processes. The results indicate a much stronger association of MI with solar activity than with geomagnetic activity, occurring only intermittently.

Coherence of MI with the different physical variables is displayed again in Figure A7 (top). It can be seen that the strong association of MI with WN is very similar to that observed between MI and CI, another index of solar activity. By contrast, the weak or absence of coherence between MI and K_p is similar to results between MI and aa or Dst, two other indices of geomagnetic activity. Figure A7 (bottom) also shows results from cross phase analyses, which are slightly positive, indicating that at the frequency tested of one cycle in 10.5 years, mortality from MI in Minnesota follows tightly Wolf (sunspot) numbers. In the second half of the 29-year record, MI is practically in

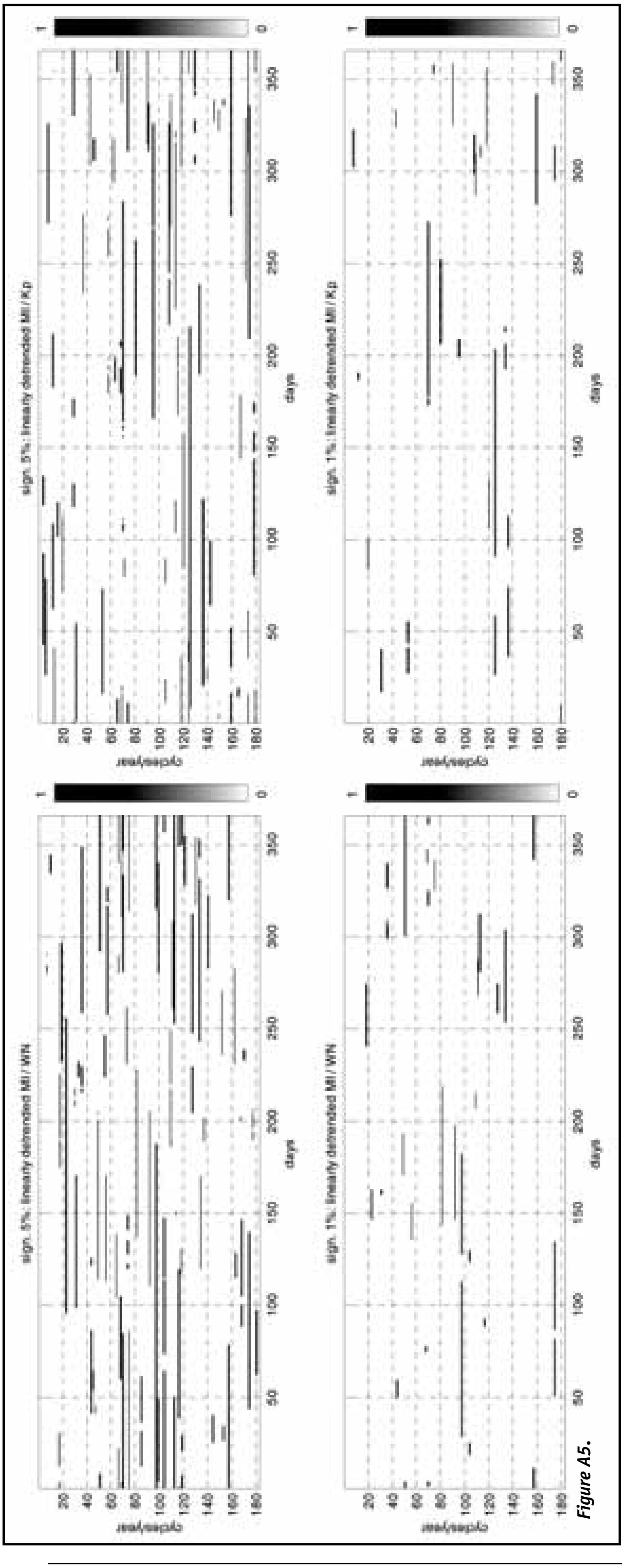


Figure A5.

Figure A5. Results from non-zero phase synchronization between MI and Wolf numbers (left) or the planetary geomagnetic disturbance index K_p (right) at the 5% (top) or 1% (bottom) nominal or, rather, ordering probability level. For a description of the data set, see *Figure A3*.

phase also with the three geomagnetic indices, the phases being almost zero with respect to K_p and aa, and almost in antiphase (5.22 years) with respect to Dst, as anticipated since magnetic storms are associated with large positive values of K_p and aa but large negative values of Dst.

Results from global analyses shown in Figure A2 suggest that at a frequency of about one cycle per week, the association is stronger between MI and geomagnetics than between MI and solar activity. We may resonate with different environmental drummers to a different extent at different frequencies, but the resonance as such is beyond a reasonable doubt.

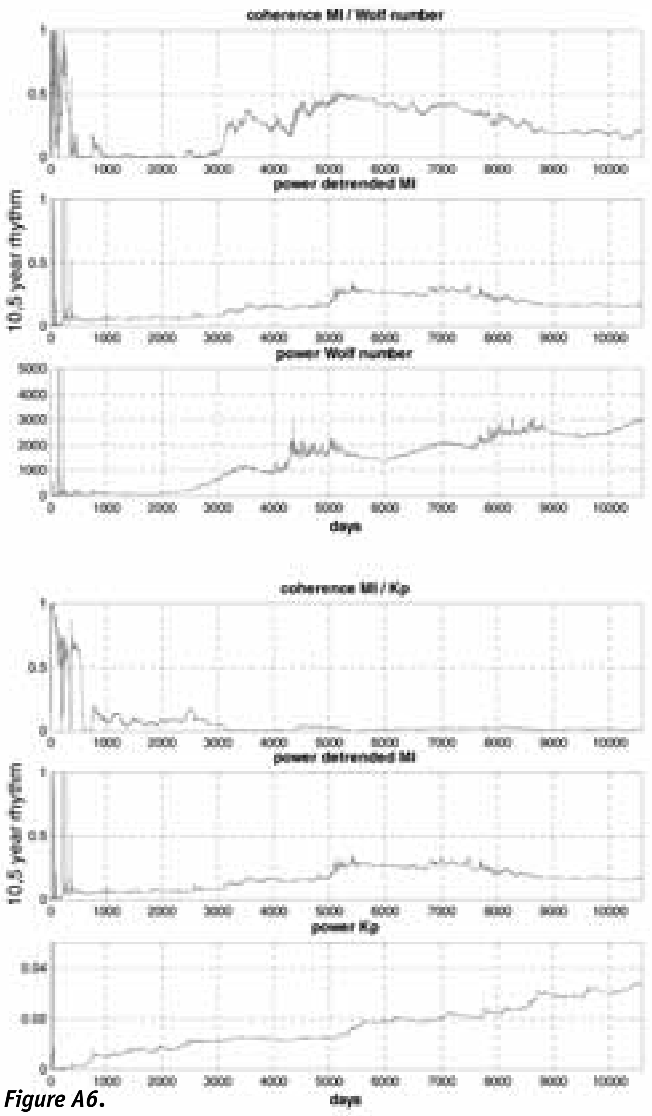


Figure A6.

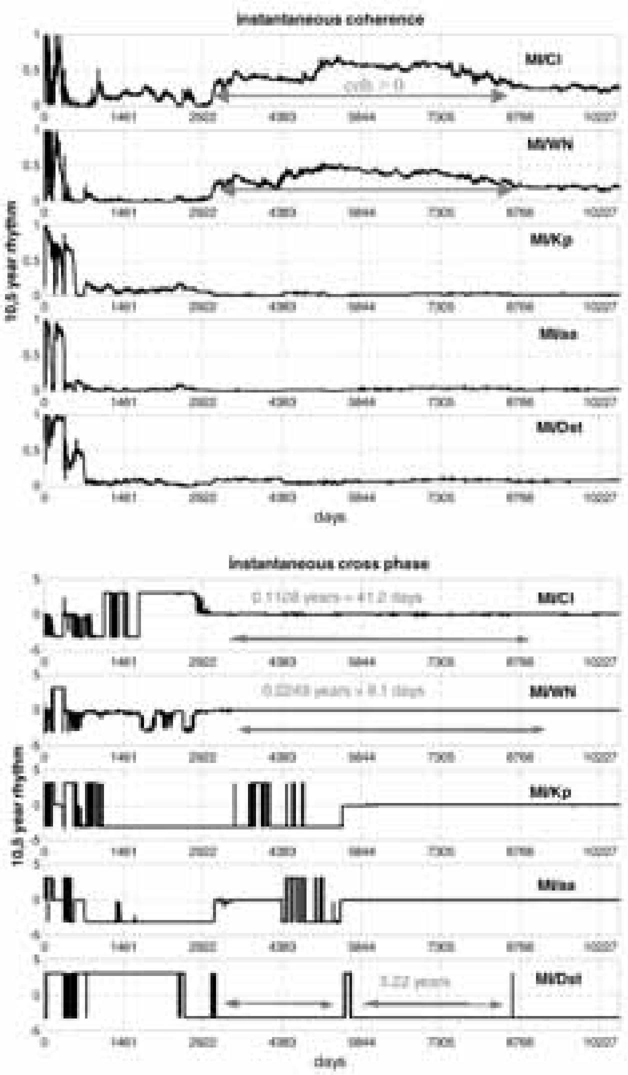


Figure A7.

Figure A6. Results from dynamic coherence between MI and Wolf numbers (top) or geomagnetic activity (bottom) at a frequency of about one cycle in 10.5 years (solar activity cycle). Mortality from MI in Minnesota (1968-1996) appears to be more closely associated with solar activity than with geomagnetic disturbance at this relatively low frequency, since the coherence with Wolf numbers reaches 0.5 during most of the middle part of the 29-year record, but remains close to zero in relation to K_p.

Figure A7. Results shown in *Figure A6* are further corroborated by the similarity around one cycle in 10.5 years of instantaneous coherences with respect to both the coronal index and Wolf numbers on the one hand, and among the three indices of geomagnetic activity K_p, aa, and Dst on the other hand (top). Moreover, instantaneous cross phases are invariably close to zero and slightly positive (bottom), indicating that the dynamics of MI follow tightly those of the physical environmental variables. The near-antiphase seen with respect to Dst stems from the fact that magnetic storms are associated with large positive values of K_p and aa, but large negative values of Dst.

Appendix B

Temporal mapping, chronomics, of environmental associations with human cerebral and related physiology and pathology

B. Schack[1], G. Cornélissen[2], Y. Watanabe[2], O. Schwartzkopff[2], E. Bakken[2], F. Halberg[2] and the BIOCOS participants

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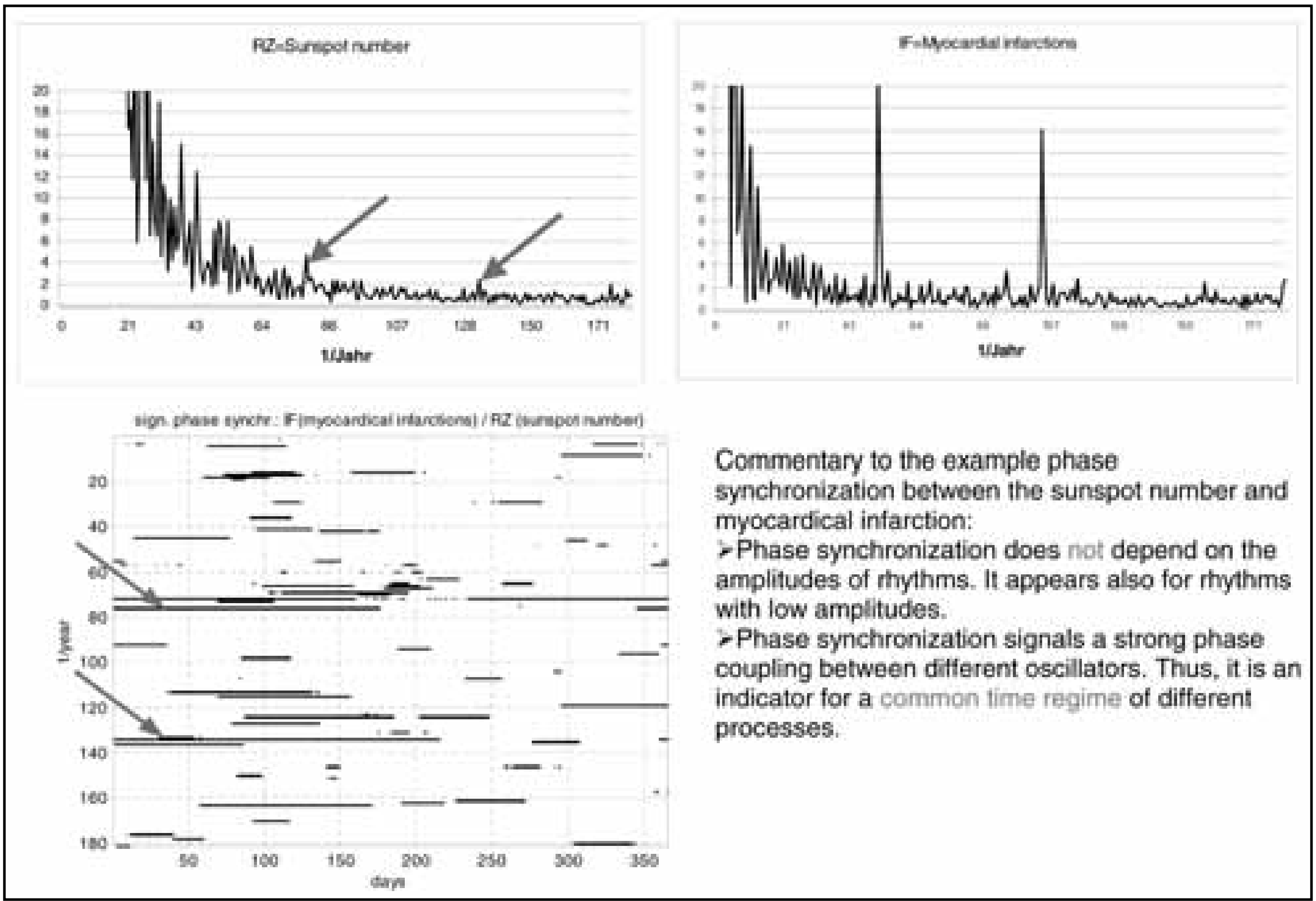
AIM. To explore amplitude and phase relations of putative cyclic associations among environmental and biospheric variables, many involving the human brain, heart and circulation, with individual and societal health-related consequences.

BACKGROUND. An international transdisciplinary project on the biosphere and the cosmos (BIOCOS) aims at producing an atlas of inferentially statistically documented time structures (chronomes), consisting of 1. a broad spectrum of cycles, with frequencies covering over 10 orders of magnitude, from those of many hertz in the brain to decade-long cycles of the human circulation and motivation, criminality and international battles, 2. deterministic chaos, gauged by indices such as the correlation dimension and approximate entropy, and 3. trends in cyclic and/or chaotic endpoints as a function of age, disease risk or pathology.

MATERIALS AND METHODS. Archives and accumulating databases of physiological and pathological variables were analyzed by spectral, cross-spectral and phase synchronization methods combined with superposed epochs and other addition and subtraction methods. The latter extend the endocrinological removal and hormone replacement by manipulating or exploiting the presence (addition) or absence (subtraction) of socio-eco-cosmologic variables, such as series of the satellite-recorded acceleration changes in the solar wind or changes in the north-south vectorial component of the interplanetary magnetic field, that may be of interest in themselves in physics and by their association in the biosphere of interest also to disciplines as varied as physiology and sociology or pathology and criminality.



Commentary to the example phase synchronization between the sunspot number and myocardical infarction:

- ➢Phase synchronization does not depend on the amplitudes of rhythms. It appears also for rhythms with low amplitudes.
- ➢Phase synchronization signals a strong phase coupling between different oscillators. Thus, it is an indicator for a common time regime of different processes.

Figure B1. Spectra of Wolf numbers (reflecting solar activity) (top left) and the daily incidence of myocardial infarction (MI) in Moscow during 1979-1981 (top right) reveal prominent low-frequency changes in both variables and a prominent weekly and half-weekly variation in MI. Despite the relatively small amplitudes of components with periods of about 4.7 and 2.7 days (arrows), a phase synchronization method developed by Bärbel Schack who prepared this graph suggests that MI and solar activity share a common time regime at these two frequencies.

RESULTS. Already available items of future atlases are mapped: ultra- as well as infra-annual spectral components, the latter with circadecadal, circadidecadal and circaquindecadal phenomena, displayed in both the frequency or period and the phase domains, complement about 24-hour (circadian), about-weekly (circaseptan), about-monthly (circatrigintan), about-half-yearly (circasemiannual), about-yearly (circannual) and separate, trans- (somewhat longer than) annual changes, among others. The lower half of Figure B1 shows an example of time-varying phase synchronization between two variables on the abscissa; spectra of these variables are seen on top, with cycles per year on the abscissa on top. Relations of amplitudes and phases were resolved elsewhere, with emphasis on diverse functions, some involving the human brain, others the electrical activity of a single eukaryotic cell or the behavior of bacteria, among a host of other morphological and physiological variables in the biosphere. The relative importance of competing photic and non-photic synchronizers is illustrated elsewhere (50, 73, 154; cf. 131, 148, 154, 164).

DISCUSSION. Long-standing controversies that led to the universal acceptance of a heliobiology in the then-Soviet Union, persisting unchanged in current Russian science, on the one hand, and often unwarranted western bias on the other hand, can be resolved by inferential statistical chronomics, yielding the recognition of the putative roles of temporo-spatial factors, including geography and ethnicity as well as solar cycle stage and number. The chronomes of the human brain involve phenomena relating to problems of our day. The resolution of identifiable cyclic mechanisms allows focus upon human motivation for religious activity and upon major diseases of our society, whose cycles are now documented not only upon the crimes committed by individuals, such as homicides, but by the chronomics of a series of international battles covering 2,556 years.

Appendix C by Herbert Witte

Methodological amplification in a physical-engineering perspective: Comments on the mathematics underlying Barbara Schack's methodology

For a sinusoidal signal

$$x(t) = c \cdot cos(2\pi ft + \theta) = a \cdot cos(2\pi ft) + b \cdot sin(2\pi ft)$$

with $c = \sqrt{a^2 + b^2}$ and $\theta = arctan\left(\frac{-b}{a}\right)$,

the instantaneous phase is $\Phi(f,t) = 2\pi ft + \theta$, where f is the frequency and θ is the zero phase (phase $\Phi(f,t)$ at $t=0$). Note that $\Phi(f,t) = 2\pi ft + \theta$ is a linear time function with slope $2\pi f$. *n:m* phase coupling between two oscillations can be defined by

$$\left| n\Phi_1(f_m,t) - m\Phi_2(f_n,t) \right| < \sigma \tag{1}$$

with $\Phi_1(f_m,t) = 2\pi f_m t + \theta_m$, $\Phi_2(f_n,t) = 2\pi f_n t + \theta_n$ and $f_m / f_n \approx m/n$, where (for coupled oscillators) n and m are integers that describe the ratio of the frequencies and σ is a small positive constant.

Multiples of the instantaneous phases, which are linear time functions with slopes $2\pi f_m$ and $2\pi f_n$ for sinusoidal signals, lead to identical slopes and comparable zero phases.

For identical frequencies $m/n=1$ (*1:1* phase coupling), the phase difference (shift) can be given by

$$\Delta\Phi(f,t)\Big|_{f_m=f_n=f} = \Phi_1(f,t) - \Phi_2(f,t) = \theta_1 - \theta_2 \tag{2}$$

Synchronization effects can be observed in coupled oscillating systems and phase shifts result from signal propagation (signal transfer through a system), i.e. if two oscillations show a stable 1:1 phase coupling, then they can be synchronized with $\left|\Delta\Phi(f,t)\right| < \sigma$ or phase shifted $\left|\Delta\Phi(f,t)\right| >> 0$ with the constraint $VAR[\Delta\Phi(f,t)] < \lambda$, where σ and λ are small positive constants. Synchronization in a dual oscillator system means the existence of certain relations between their phases and frequencies, i.e. equ. (1) is often used for the definition of synchronization. Therefore, n:m phase coupling, n:m synchronization and n:m phase synchronization (used by Bärbel Schack) are used as synonyms in this field.

Both models are important for the interpretation of results but the observed data can be analyzed by the same methods. In contrast to our definition of a signal given above, in statistical time series analysis, signals are often defined as zero mean valued stationary random signals, i.e. amplitude and phase are random variables. For non-stationary signals, time-varying analysis methods can be seen as efficient tools. Therefore, time-varying spectral analysis methods have been developed and applied by Bärbel Schack.

Time-varying coherence and cross-phase spectrum

Time-varying methods have been introduced by Schack *et al.* (13–15) for estimating time-varying spectra and spectral parameters, i.e. non-stationarity can be assumed for two signals investigated. Accordingly, the time-varying (instantaneous) cross-spectral coherence and cross-phase spectrum can be given in general by

$$\hat{\gamma}^2_{12}(f,t) = \frac{\left|\hat{S}_{12}(f,t)\right|^2}{\hat{S}_{11}(f,t) \cdot \hat{S}_{22}(f,t)} \qquad 0 \le \gamma^2_{12}(f,t) \le 1 \tag{3}$$

$$\hat{\Phi}_{12}(f,t) = arctan\frac{Im\{\hat{S}_{12}(f,t)\}}{Re\{\hat{S}_{12}(f,t)\}}, \tag{4}$$

where $Re\{.\}$ and $Im\{.\}$ denote the real and the imaginary parts of a complex spectrum, $\hat{S}_{11}(f,t)$ and $\hat{S}_{22}(f,t)$ are the estimated time-varying autospectra and $\hat{S}_{12}(f,t)$ is the estimated time-varying cross-spectrum, as functions of discrete frequencies and time.

The time-varying cross-phase spectrum can be expressed (according to equ.(2)) as the instantaneous phase differences for each frequency as a function of time. According to equ. (1) and (2), a *1:1* synchronization of two signals (common frequency components $f_m=f_n=f$) can be stated, if the conditions $|\Delta\Phi(f,t)| < \sigma$ and $\gamma_{12}^2(f,t) > \xi$ are fulfilled· The threshold value ξ designates statistically significant coherence values (e.g. significance level at 5%) and depends on the estimation method and signal properties, i.e. by means of the cross-spectral coherence values, the estimation accuracy of the cross-phase can be obtained. Two signals (signal components) are shifted $|\Delta\Phi(f,t)| << \sigma$ with the constraint $VAR[\Delta\Phi(f,t)] < \lambda$, where σ and λ are small positive constants.

The cross-spectral coherence values depend on the noise content (signal-to-noise-ratio) of both investigated signals. Therefore, the deviation of the cross-spectral coherence values from 1 is a quantitative measure for external noise. The following interpretations of the cross-spectral coherence spectra (coherence values) are possible. The cross-spectral coherence is

- a measure of the accuracy of the cross-phase estimation,
- the squared linear correlation coefficient for each frequency component,
- a measure of phase stability or stability of phase coupling

and/or gives

- the fraction at a system's response that is due to the input and
- the amount of common information with regard of oscillations within certain frequency bands.

A mean time-varying cross-spectral coherence can be obtained by

$$\bar{\gamma}_{12}^2(f,t) = \left\langle \hat{\gamma}_{12}^2(f,t)^{(k)} \right\rangle \tag{5}$$

where $\langle\cdot\rangle$ denotes averaging (for each time point) and $\hat{\gamma}_{12}^2(f,t)^{(k)}$ is the time-varying cross-spectral coherence estimation of the k-th trial. The cross-phase is defined in the interval [-π, π]. Therefore, an averaging may result in erroneous low mean values if the single trial phases accumulate in the neighbourhood of the saltus ±π. Thus, the coordinates on the unit circle ($Re=cos$, $Im=j \cdot sin$) are averaged and the mean time-varying cross-phase spectrum $\overline{\Phi}_{12}(f,t)$ is calculated by

$$\overline{\Phi}_{12}(f,t) = arctan \frac{\left\langle sin\left[\hat{\Phi}_{12}(f,t)^{(k)}\right]\right\rangle}{\left\langle cos\left[\hat{\Phi}_{12}(f,t)^{(k)}\right]\right\rangle} \tag{6}$$

where $\hat{\Phi}_{12}(f,t)^{(k)}$ is the time-varying cross-phase spectrum estimation of the k-th trial. From the mean coordinates of the phase on the unit circle the so-called time-variant phase coherence spectrum [2] can be derived

$$\hat{\kappa}(f,t) = \sqrt{\left(\left\langle cos\left[\hat{\Phi}_{12}(f,t)^{(k)}\right]\right\rangle\right)^2 + \left(\left\langle sin\left[\hat{\Phi}_{12}(f,t)^{(k)}\right]\right\rangle\right)^2} \tag{7}$$

This time variant parameter can be used for the quantification of the stability of time-variant cross-phase at a frequency ω.

Phase coupling and synchronization indices

From now on, a shortened text of Bärbel Schack (in preparation) is used to explain the synchronization parameters introduced by Bärbel (our comments are cursive).

The evaluation of phase synchronization presumes the calculation of instantaneous phases. Widespread approaches are (a) the Hilbert transform and (b) the convolution with a complex wavelet (*she used another method, the Gabor expansion described in* (38)). In contrast to the Hilbert transform approach, which requires narrow band pass filtering for each frequency of interest, Gabor expansion allows to calculate instantaneous phases for the whole frequency range at once.

Phase locking index

The circular statistics for phases at a fixed time point after a stimulus onset evaluates phase locking with regard to an event. Therefore, in order to quantify the phase variation with respect to a stimulus onset, the phases $\Phi(f_m,t)^{(k)}$, $k=1,\ldots,K$ *were calculated for each single trial* k. *The so-called phase locking index (*PLI*) is defined by*

$$PLI(f_m,t) = \left|\left\langle e^{j\Phi(f_m,t)^{(k)}}\right\rangle\right| \ , \ j=\sqrt{-1} \ . \tag{8}$$

The *PLI* represents the circular statistics for instantaneous phases of the signal for the set of trials and ranges between zero and one. An increased $PLI(f_m,t)$ indicates stronger phase locking to the onset for a certain frequency f_m at time point t.

Phase synchronization index

A stable relationship between phases of two oscillations with the same frequency may be evaluated by the *1:1* phase synchronization index. Let $\Phi_1(f_m,t)^{(k)}, \Phi_2(f_m,t)^{(k)}$ be the instantaneous phases of two signal components for the frequency f_m at time point t of the *k-th* trial. From phase differences (according to equ. 2) of each trial k

$$\Delta\Phi(f_m,t)^{(k)} \cong \Phi_1(f_m,t)^{(k)} - \Phi_2(f_m,t)^{(k)} \ \ mod \ 2\pi \tag{9}$$

the 1:1 phase synchronization index is calculated according to

$$\hat{\Gamma}_\Phi(f_m,t) = \left|\left\langle e^{j \cdot \Delta\Phi \ (f_m,t)^{(k)}}\right\rangle\right| \ , \ j=\sqrt{-1} \ . \tag{10}$$

Equivalently to the *PLI*, the *1:1* phase synchronization index ranges between zero and one. An increased *1:1* phase synchronization index hints to a strong phase relationship between oscillations of frequency f_m measured at two different sites. In contrast to the phase locking index, *1:1* phase synchronization may appear for both evoked (stimulus-locked) and induced (stimulus-unlocked) oscillations.

n:m phase synchronization index

Phase synchronization described above may be seen as a special case of synchronization of two oscillators with arbitrary frequencies. The synchronization between two oscillations with different frequencies may be described as follows. Let $\Phi_1(f_m,t)^{(k)},\Phi_2(f_n,t)^{(k)}$ be the instantaneous phases of two oscillators with frequencies f_m and f_n of one or two signal components of the *k*-th trial with the *n:m* frequency relationship. The generalized phase difference is calculated according to equ. (1)

$$n\cdot f_m = m\cdot f_n$$

$$\Delta\Phi(f_m,f_n,t)^{(k)} \cong n\cdot\Phi_1(f_m,t)^{(k)} - m\cdot\Phi_2(f_n,t)^{(k)} \quad mod\, 2\pi \, . \tag{11}$$

The *n:m* phase synchronization index is defined by

$$\hat{\Gamma}_\Phi(f_m,f_n,t) = \left|\left\langle e^{j\cdot\Delta\Phi(f_m,f_n,t)^{(k)}}\right\rangle\right| \quad , \; j=\sqrt{-1}\, . \tag{12}$$

The *n:m* phase synchronization index may be calculated for the arbitrary frequency pair $(\mathrm{f_m},\mathrm{f_n})$, $\mathrm{m}\neq\mathrm{n}$ of one or two signal components.

REFERENCES,
including full bibliography of PD Dr. Bärbel Schack

A Journals cited in SCI and/or with peer review process

1 Thiele (Schack) B. Eine Umkehrformel für einfache stationäre Punktprozesse endlicher Intensität im R^2 , Math.Nachr. 1979; **91**: 171–179.
2 Schack B., Zufällige Felder als Fixpunkte stochastischer Operatoren, Math.Nachr. 1980, **96**:125–149 .
3 Fichtner K.-H, Schack B., Zustand und Ortsmessung quantenmechanischer Teilchen, Serdica 1986; (12):279–282.
4 Witte H, Rother M, Schack B, Hoyer D. Rechentechnische Möglichkeiten der Verstärkerkalibrierung bei der automatischen EEG - Analyse, *Medizintechnik*,1988; **28**:65–68.
5 Hoyer D, Grießbach G, Witte H, Schack B. Adaptive Verfahren zur Vorverarbeitung evozierter Potentiale, Biomed. Technik 1990; **35**(11):263–270.
6 Witte H, Grießbach G, Schack B, Stallknecht K, Krajca V, Patakova I. Nutzung der Fouriertransformation als Basisalgorithmus für die Datenvorverarbeitung in der automatischen EEG- Analyse, *Medizintechnik*,1990; **30**:65–71.
7 Bareshova E, Hoyer D, Schack B, Hoyer H. Ein Filterverfahren zur Hervorhebung wesentlicher Anteile evozierter Potentiale am Beispiel der P100 Visuell Evozierter Potentiale, Medizintechnik 31 (1992) H.1, 7–9.
8 Schack B, Wagner H, Witte H. Statistical comparison of band spectral power: an aid in stochastical analysis of brain electrical activity Part 1: Approximation of the distribution of broad band power by a χ^2–distribution, Biom. J. 1992, **34**(2):179–192 .
9 Schack B, Wagner,H Grießbach, G Witte, H. Statistical comparison of band spectral power: an aid in stochastical analysis of brain electrical activity Part 2: Construction of confidence intervals of spectral band power and its application to EEG- analysis, Biom. J. 1992, **34**(7):827–841 .
10 Grießbach G, Schack B., Adaptive Quantile Estimation and its Application in Analysis of Biological Signals, Biom.J. 1993, **35**(2):165–179 .
11 Grießbach G, Schack B, Putsche P, Bareshova E, Bolten J. The Dynamic Description of a Stochastic Signal by its Adaptive Momentary Power and Momentary Frequency Estimation and its Application to Biological Signals, Med. & Biol. Eng. & Computing 1994; **32**(6): 632–637.
12 Schack B, Grießbach G. Adaptive Methods of Trend Detection and its Application in Analysis of Biosignals, Biom. J. 1994; **36**(4): 429–452 .
13 Schack B, Bareshova E, Grieszbach G, Witte H. Methods of Dynamic Spectral Analysis by Self-exciting ARMA Models and their Application to Analysing Biosignals, Med. Biol. Eng. Comput. 1995; **33**(3):492–498.
14 Schack B, Grießbach G, Arnold M, Bolten J. Dynamic Cross Spectral Analysis of Biological Signals by means of Bivariate ARMA Processes with Time- Dependent Coefficients, Med. Biol. Eng. Computing 1995, **33**(4): 605–610.
15 Schack B, Krause W. Dynamic Power and Coherence Analysis of Ultra Short-Term Cognitive Processes - A Methodical Study. Brain Topography 1995, **8**(2):127–136.
16 Vilser W, Schack B, Bareshova E, Senff I, Bräuer-Burchardt Ch, Münch K, Strobel J. Adaptive Verfahren zur Messung arterieller Blutgeschwindigkeiten in Netzhautgefäßen mittels Indikatortechnik, Ophtalmologie 1995 **92**(5): 728–734.
17 Schack B, Vilser W, Putsche P, Bräuer-Burchardt Ch, Bareshova E, Witte H. A New Approach for Detecting the Position of Retinal Vessels and Calculating Their Diameter on the Basis of Dynamic Spectral Analysis, Medinfo 1995, **8**: 701–705.
18 Bareshova E, Grieszbach G, Schack W, Vilser W, Bräuer-Burchardt Ch, Senff I. Filtering Properties of Adaptive Operators for the Mean Value and for the Linear Trend of Instationary Signals and their Application to Determining the Arterial Blood Velocity in Retinal Vessels, Medical Progress through Technology 1995–96, **21**(3):123–134.
19 Krause W, Schack B, Gibbons H, Kriese B. Über die Unterscheidbarkeit begrifflicher und bildhaft-anschaulicher Repräsentationen bei elementaren Denkanforderungen. Z. Psych. 1997, **205**:169–203.
20 Witte H, Putsche P, Eiselt M, Hoffmann K, Schack B, Arnold M, Jäger H. Analysis of the interrelations between a low-frequency and a high-frequency signal component in human neonatal EEG during quiet sleep. Neuroscience Letters 1997; **236**(3):1–5.
21 Witte H, Arnold M, Schack B. (1997) Time-variant spectral analysis of {LDF} signals on the basis of autoregressive modelling. In: *Lecture Notes of the ICB Seminars*, 27 (1997), Biomeasurements, Optoelectronics in Medical Diagnosis, 48–57.
22 Krause W, Gibbons H, Schack B. Concept activation and coordination of activation procedure require two different networks. NeuroReport 1998, **9**(7):1649–1653.
23 Schack B, Grießbach G, Krause W. The Sensitivity of Instantaneous Coherence for Considering Human Information Processing. Part I: The Relationship between Mental Activities and Instantaneous EEG Coherence. Int. J. Psychophys. 1999; **31**(3): 219–240.
24 Schack B, Grießbach G, Nowak H, Krause W. The Sensitivity of Instantaneous Coherence for Considering Human Information Processing. Part II: Similarities and Differences between EEG and MEG Coherences. Int. J. Psychophys. 1999, **31**(3):241–259 .
25 Schack B, Chen A.C.N, Mescha S, Witte H. Instantaneous EEG Coherence Analysis during the Stroop Task. Clin. Neurophysiol. 1999, **110** (8):1410–1426.
26 Schack B, Rappelsberger P, Weiss S, Möller E. Adaptive phase estimation and its application in EEG analysis of word processing. Journal of Neuroscience Methods 1999, **93**(1): 49–59.
27 Sommerfeld E, Krause W, Schack B, Markert Ch, Pies R, Tietze H. Zur Messung von Übungs- und Trainingserfolg auf der Grundlage von EEG-Parametern. Zeitschrift für Pädagogische Psychologie 1999, **13**:60–73.
28 Zwiener U, Eiselt M, Flemming L, Wagner H, Schack B. Early magnetic field changes preceding the intracortical penicilin induced spikes. Epilepsy Research 2000, **38**(2–3):217–229.

29 Schack B, Rappelsberger P, Anders Ch, Weiss S, Möller E. Quantification of synchronisation processes by coherence and phase and its application in analysis of electrophysiological signals. Bifurcation and Chaos 2000, **10**(11):2565–2586 .

30 Möller E, Grießbach G, Schack B, Witte H. Statistical properties and control algorithms of recursive quantile estimators, Biometrical Journal 2000, **42**:139–156 .

31 Rappelsberger P, Schack B, Weiss S, Möller E. (2000) Instantaneous EEG coherence and phase analysis during word processing. ÖGAI Journal 19, 16–21.

32 Witte H, Schack B. Helbig, M Putsche, P. Schelenz Ch, Schmidt K, Specht M. Quantification of transient quadratic phase couplings within EEG burst patterns in sedated patients during electroencephalic burst-suppression. Journal of Physiology (Paris) 2000; **94**(5–6):427–434 .

33 Witte H, Putsche P, Eiselt M, Arnold M, Schmidt K, Schack B. Technique for the quantification of transient quadratic phase couplings between heart rate components. (Verfahren zur Quantifizierung transienter quadratischer Phasenkopplungen zwischen Herzfrequenzkomponenten) Biomedizinische Technik 2001; **46**(3):42–49.

34 Schack B, Rappelsberger P, Vath N, Weiss S, Möller E, Grießbach G, Witte H. EEG frequency and phase coupling during human information processing. Methods of Information in Medicine 2001; **40**(2):106–111.

35 Möller E, Schack B, Arnold M, Witte H. Instantaneous EEG coherence analysis by means of adaptive high-dimensional autoregressive models. Journal of Neuroscience Methods 2001; **105** (2):143–158.

36 Witte K, Edelmann-Nusser J, Schack B. Auswertung von EMG-Daten mit Verfahren der zeitvarianten Spektralanalyse – dargestellt am Beispiel des Bogenschießens. Spectrum der Sportwissenschaften, Jahrgang 2001; **13**(2):27–43.

37 Haueisen J, Schack B, Meier T, Curio G, Okada Y. Multiplicity in the high-frequency signals during the short-latency somatosensory evoked cortical activity in humans. Clin. Neurophysiol. 2001; **112**(7):1316–1325.

38 Schack B, Witte H, Helbig M, Schelenz Ch, Specht M. Time-variant non-linear phase-coupling analysis of EEG burst patterns in sedated patients during electroencephalic burst-suppression period. Clinical Neurophysiology 2001, 112 (8): 1388–1399.

39 Krause W, Seidel G, Schack B. Ordnungsbildung. Zeitschrift für Psychologie 2001; **209**:376–401.

40 Schack B, Vath N, Petsche H, Geissler H.-G, Möller E. Phase-coupling of theta-gamma EEG rhythms during short-term memory processing. Int. J. Psychophys. 2002; **44**(2):143–163.

41 Schack B, Klimesch W. Frequency characteristics of evoked and oscillatory electroencephalic activity in a human memory scanning task. Neuroscience Letters 2002; 107–110.

42 Terborg Ch, Birkner T, Schack B, Witte O. Acute effects of cigarette smoking on cerebral oxygenation and hemodynamics: a combined study with near-infrared spectroscopy and transcranial Doppler sonography. J Neurol Sci 2002; **205**:71–75.

43 Hesse W Moller E, Arnold M Witte H , Schack B. [Brief causal relations in EEG based on adaptive Granger causality.] Biomed Tech (Berlin) 2002; **47**(Suppl 1 Pt 2): 510–513.

44 Helbig M Griessbach G, Witte H Schack B. [Time variant bispectral analysis based on adaptive recursive Fourier transformation.] Biomed Tech (Berlin) 2002; 47 (Suppl 1 Pt 2): 585–587.

45 Steuer D, Griessbach G Krause W, Schack B. Single-trial classification of elementary comparison processes on the basis of instantaneous EEG and MEG coherences. Brain Topogr 2002; **15**: 125–137.

46 Hesse W Moller E, Arnold M Schack B. The use of time-variant EEG Granger causality for inspecting directed interdependencies of neural assemblies. J Neurosci Methods 2003; **124**:27–44.

47 Schack B, Weiss S, Rappelsberger P. Cerebral information transfer during word processing: Where and when does it occur and how fast is it? Human Brain Mapping 2003; **19**:18–36.

48 Terborg Ch, Birkner T, Schack B, Weiller C, Rother J. Noninvasive monitoring of cerebral oxygenation during vasomotor reactivity tests by a new near-infrared spectroscopy device. Cerebrovasc Dis 2003; **16**:36–41.

49 Schack, B. How to construct a microstate-based alphabet for evaluating information processing in time. Int. Journal of Bifurcation and Chaos 2002, in press.

50 Halberg F, Cornélissen G, Schack B, Wendt HW, Minne H, Sothern RB, Watanabe Y, Katinas G, Otsuka K, Bakken EE. Blood pressure self-surveillance for health also reflects 1.3-year Richardson solar wind variation: spin-off from chronomics. Biomed Pharmacol, in press.

B Short communications in SCI journals

51 Schack B, Witte H, Grieszbach G, Parametrische Methoden der dynamischen Spektralanalyse und ihre Anwendung in der Biosignalanalyse, Biomedizinische Technik 38, 1993; 79–80.

52 Grieszbach G, Witte H, Schack B, Möglichkeiten des Einsatzes von adaptiven dynamischen Spektralkenngrößen in der Biosignalanalyse, Biomedizinische Technik 38, 1993; 81–82.

53 Bareshova E, Grießbach G, Schack B, Vilser W, Bräuer-Burchardt Ch. (1994) Untersuchungen von Filtereigenschaften adaptiver Trendschätzungen und ihre Anwendung bei der Analyse von Indikatorlösungskurven in der Augenheilkunde, Biomedizinische Technik 39, Ergänzungsband, 246–247 .

54 Schack B, Weiss S, Rappelsberger P, Dynamic Topographic Methods of Coherence Analysis of Cognitive Processes. Med.&Biol. Eng.&Comput. **34***: Suppl. 1*, 1996; 207–208.

55 Schack B, Krause W, Huonker R, Nowak H, Witte H, EEG- und MEG-Analyse schnell ablaufender kognitiver Prozesse. *Biomedizinische Technik* 41, Ergänzungsband 1, 1996; 248–249.

56 Grießbach G, Bareshova E, Schack B, Witte H, Adaptive Detektion der Veränderungen von Verteilungseigenschaften in biologischen Signalen. Biomedizinische Technik 1996; **41** Suppl: 320–321.

57 Steuer D, Grießbach G, Schack B, Anwendung Neuronaler Netze zur Klassifikation kognitiver Prozesse auf der Basis hochauflösender Spektralparameter. Biomedizinische Technik 1996; **41**, Suppl: 578–579.

58 Putsche P, Witte H, Eiselt M, Schack B, Bispektralanalyse neonataler EEG-Muster. Biomedizinische Technik 1997; **42** Suppl: 413–414 .

59 Schack B, Chen A, Mescha S, Witte H. Instantaneous EEG Coherence Mapping of Cortical Activation during the Stroop Task. NeuroImage 1999; **9**; (6):761.

60 Krause W, Kotkamp N, Tietze H, Möller E, Schack B. Classifying words: activation of category concepts. Neuroimage 1999; **9**; (6):1083.

61 Sommerfeld E, Krause W, Schack B, Markert Ch, Pies R. The effect of practice in comparison tasks on synchronization of specific brain areas. NeuroImage 1999; **9**; (6):898.

62 Zwiener U, Eiselt M, Gießler F, Nowak H, Schack B. Relations Between Very Early Events, Spike Configuration, and Late Activity of the Interictal Penicillin Discharge. NeuroImage 1999; **10**; (3): 80.

63 Helbig M, Grießbach G, Schack B, Witte H. Methods for the Investigation of Time-variant Phase Couplings. NeuroImage 1999; **10**; (3):86.

64 Anders C, Schack B, Stegeman D.F. Coherence and Phase Analysis of Surface EMG – A Methodological Approach. NeuroImage 1999; **10**; (3):89.

65 Möller E, Schack B, Grießbach G, Witte H. (1999) Mean, parametric, time dependent spectral analysis of event related potentials. Med. & Biol. Eng. & Computing, 37, Supplement 2, 420–421.

66 Steuer D, Schack B, Grieszbach G, Krause W. (1999) Single-trial classification of elementary cognitive processes by neural networks. Med. & Biol. Eng. & Computing, **37**, Supplement 2, 422–423.

67 Helbig M, Grieszbach G, Schack B, Witte H. (1999) Application of time-variant bispectrum in biosignal analysis. Med. & Biol. Eng. & Computing, **37**, Supplement 2, 392–393.

68 Krause W, Schack B, Krause U, Kotkamp N, Tietze H, Möller, E. Classifying words. Neuroimage 11:**5** (2000); 410.

69 Krause W, Schack B, Seidel G, Heinrich F, Krause U. Entropy reduction in human mathematical thinking: A microstate study of EEG oscillations. NeuroImage (2001); 13: 6, 473.

70 Seidel G, Krause W, Schack B, Heinrich F, Krause U, Wüstenberg T, Jordan K, Lehmann W, Lutz K, Heinze H–J, Jäncke L. Entropy reduction and mathematical giftedness: A microstate study of EEG oscillation. NeuroImage (2001); 13: 6, 474.

71 Hesse W, Möller E, Arnold M, Witte H, Schack B. (2002) Untersuchung kurzzeitiger kausaler Beziehungen im EEG auf der Basis der adaptiven Granger Kausalität. Med. & Biol. Eng. & Computing 2002; **47** (Suppl 1 Pt 2):510–513.

72 Helbig M, Grieszbach G, Witte H, Schack B. (2002) Zeitvariante Bispektralanalyse auf der Basis einer adaptiv rekursiven Fouriertransformation. Med. & Biol. Eng. & Computing 2002; **47** (Suppl 1 Pt 2):585–587.

73 Halberg F, Cornélissen G, Schack B. Self-experimentation on chronomes, time structures; chronomics for health surveillance and science: also transdisciplinary civic duty? Behavioral and Brain Sciences, http://www.bbsonline.org/Preprints/Roberts/Commentators/Halberg.html.

C Citeable articles in proceedings etc.

74 Schack, B, Wagner, H. (1993) New approaches in statistics of EEG maps. In: M. Rother U. Zwiener (Hrg.): Quantitative EEG Analysis- Clinical Utility and New Methods. Universitätsverlag Jena, 133–137.

75 Schack B, Grieszbach G, Bareshova E. (1995) The Dynamic Description of Nonstationary EEG on the Basis of Adaptive Methods and Models. In: M. Eiselt U. Zwiener H. Witte (Hrg.): Quantitative and Topological EEG and MEG Analysis, Universitätsverlag Jena, 249–254.

76 Krause W, Schleußner Ch, Schack B, Bolten J. (1995) Categorization in Human Thinking and EEG-Mapping. In: M. Eiselt U. Zwiener H. Witte (Hrg.): Quantitative and Topological EEG and MEG Analysis, Universitätsverlag Jena 177–180.

77 Zwiener U, Funke M, Schack B, Plewe A, Struppert J, Heinz P. (1995) Estimation of spatial frequencies of maxima within spectral EEG band power of physiological and pathological activity. In: M. Eiselt U. Zwiener, H. Witte (Hrg.): Quantitative and Topological EEG and MEG Analysis Universitätsverlag Jena, 215–220.

78 Bolten J, Grießbach G, Schack B. (1994) Visuelle Programmierung durch Verkettung von Objekten der adaptiven Zeitreihenanalyse im Anwendungsgebiet der Biosignalanalyse. In: E. Köhler (Hrg.): 39. Internationales wissenschaftliches Kolloquium der Technischen Universität Ilmenau, 361–365.

79 Schack B, Grießbach G, Witte H, Krause W. (1994) Parametrische Methoden der multivariaten Zeit- Frequenz- Analyse und ihre Anwendung in der Biosignalanalyse. In: E. Köhler (Hrg.): 39. Internationales wissenschaftliches Kolloquium der Technischen Universität Ilmenau, 286–292.

80 Steuer D, Schack B, Bolten J, Grießbach G, Krause W. (1994) Klassifikation von Ergebnissen der multivariaten Zeitfrequenzanalyse bei menschlichen Denkprozessen mittels Neuronaler Netze. In: E. Köhler (Hrg.): 39. Internationales wissenschaftliches Kolloquium der Technischen Universität Ilmenau, 366–371.

81 Schack B, Vilser W, Bareshova E, Bräuer-Burchardt Ch, Grießbach G, Witte H, Arnold M, Putsche P. (1994) Anwendung adaptiver Verfahren zur Erfassung der Position und des Durchmessers von Blutgefäßen am Augenhintergrund. In: Kropatsch W.G, Bischof H. (Hrg.): Tagungsband Mustererkennung 1994, Springer-Verlag, 474–481.

82 Schack B, Vilser W, Putsche P, Bräuer-Burchardt Ch, Bareshova E, Witte H. (1995) A New Approach for Detecting the Position of Retinal Vessels and Calculating Their Diameter on the Basis of Dynamic Spectral Analysis, MEDINFO 95 Proceedings. R. A. Greenes et al. (editors), 1995 IMIA, 701–705.

83 Schack B, Arnold M, Witte H. (1995) Parametrische Methoden multivariater hochauflösender Spektralanalyse in der Biosignalanalyse. In H.J.Trampisch, S. Lange: Medizinische Forschung. Ärztliches Handeln. 493–499.

84 Grießbach G, Bolten J, Schack B. (1995) Objektorientiertes Design adaptiver Verfahren der Biosignalanalyse. In H.J.Trampisch, S. Lange: Medizinische Forschung. Ärztliches Handeln. 500–503.

85 Schack B, Grießbach G, Bareshova E, Anders Ch, Schumann N.-P, Florian G. (1996) Parametric methods of dynamic spectral analysis of non-stationary biological signals. Medical Informatics Europe '96, J. Brender et al. (Eds.), IOS Press, 1996, 744–748.

86 Schack B, Krause W. (1996) Instantaneous Coherence as a Sensible Parameter for Considering Human Information Processing. Proceedings of ICPR '96, Vol. II, IEEE Computer Society Press, 45–49.

87 Schack B, Haueisen J, Krause W, Grießbach G, Nowak H, Witte H. (1998) Simultaneous EEG and MEG Analysis of Short-Term Cognitive Processes. In: Witte H, Zwiener U, Schack B, Doering A. (eds.) Quantitative and Topological EEG and MEG analysis. Druckhaus Mayer Verlag GmbH, Jena-Erlangen, 399–402.

88 Möller E, Grießbach G, Schack B, Witte H. (1998) An Adaptive Relative Histogramm and ist Application for Detecting Typical States in Non-Stationary EEG-Signals. In: Witte H, Zwiener U, Schack B, Doering A. (eds.) Quantitative and Topological EEG and MEG analysis. Druckhaus Mayer Verlag GmbH, Jena-Erlangen, 272–27.

89 Schack B, Grießbach G. (1997) Momentane EEG-Kohärenzen und kognitive Prozesse. In: 42. Internationales Wissenschaftliches Kolloquium 22.–25.9.1997, TU Ilmenau, Band 2, 127–132.

90 Schlögl A, Schack B, Florian G, Lugger K, Pregenzer M, Pfurtscheller G. (1998) Classification of Single Trial EEG: A Comparison of Different Parameters. In: Witte H, Zwiener U, Schack B, Doering A. (eds.) Quantitative and Topological EEG and MEG analysis. Druckhaus Mayer Verlag GmbH, Jena-Erlangen, 266–268.

91 Steuer D, Grießbach G, Schack B. (1998) Classification of Elementary Cognitive Processes with Neural Networks by the Use of High-Resolution Signal Processing Methods. In: Witte H, Zwiener U, Schack B, Doering A. (eds.) Quantitative and Topological EEG and MEG analysis. Druckhaus Mayer Verlag GmbH, Jena-Erlangen, 251–253.

92 Weiss S, Schack B, Rappelsberger P. (1998) Lexical Processing within the Brain: Evidence from EEG Spectral Analysis and Topographic Coherence Analysis. (1998) In: Witte H, Zwiener U, Schack B, Doering A. (eds.) Quantitative and Topological EEG and MEG analysis. Druckhaus Mayer Verlag GmbH, Jena-Erlangen, 403–405.

93 Möller E, Grießbach G, Steuer D, Schack B, Witte H. (1997) Object oriented design of adaptive recursive algorithms and its application for estimators of distribution of signal values, In: Procházka A, Uhlír J, Sovka P. (ed.) Signal analysis and prediction 1 (Proceedings of ECSAP-97) ICT Press Prag S. 419–422.

94 Möller E, Schack B, Grießbach G, Witte H. (1998) Eine effiziente Schätzung der mittleren zeitabhängigen spektralen Kenngrößen von ereignisbezogenen EEG-Signalen. In: Greiser E, Wischnewsky M. (Hrsg.) Methoden der Medizinischen Informatik, Biometrie und Epidemiologie in der modernen Informationsgesellschaft. 43. Jahrestagung der GMDS.

95 Schack B, Möller E, Grießbach G, Witte H. (1999) EEG frequency and phase coupling during human information processing. In: N. Victor, M. Blettner, L. Edler, R. Haux, P. Knaup-Gregori, M. Pritsch, J. Wahrendorf, J. Windeler, S. Ziegler (Hrsg.) Medical Informatics, Biostatistics and Epidemiology for Efficient Health Care and Medical research, 198–201.

96 Grießbach G, Steuer D, Schack B, Witte H. (1999) Adaptiv rekursive Schätzung der korrelationsfunktion und ihre Anwendung in der Biosignalanalyse. In: N. Victor, M. Blettner, L. Edler, R. Haux, P. Knaup-Gregori, M. Pritsch, J. Wahrendorf, J. Windeler, S. Ziegler (Hrsg.) Medical Informatics, Biostatistics and Epidemiology for Efficient Health Care and Medical research, 208–211.

97 Helbig M, Grießbach G, Schack B, Witte H. (1999) Zeitvariante Bispektralanalyse in der Biosignalanalyse. In: N. Victor, M. Blettner, L. Edler, R. Haux, P. Knaup-Gregori, M. Pritsch, J. Wahrendorf, J. Windeler, S. Ziegler (Hrsg.) Medical Informatics, Biostatistics and Epidemiology for Efficient Health Care and Medical research, 212–215.

98 Schack B, Seidel G, Krause W, Heinrich F. Coherence Analysis of the Ongoing EEG by Means of Microstates of Synchronous Oscil-

lations. Proceedings-23rd Annual Conference-IEEE/EMBS Oct 25–28, 2001, Istanbul, Türkey.

D Book articles

99 Schack B. (1999) Dynamic Topographic Spectral Analysis of Cognitive Processes. In: Ch. Uhl (ed.) Model-based Analysis of Neurophysiological Brain Functioning. Lecture Notes of Synergetics, Springer-Verlag, 230–251, ISBN 3-540-65065-2.

100 Krause W, Kotkamp N, Tietze H, Metzger U, Möller E, Schack B. (1999) Kann man Klassifizierungsprozesse sichtbar machen? Abruf von Kategoriebegriffen aus dem Gedächtnis und EEG-Kohärenzanalyse. In: Witruk E. und Lander H.-J. (Hg.) Informationsverarbeitungsanalysen. Kognitionspsycholigische und meßmethodische Beiträge. Leipziger Universitätsverlag, 67–82, ISBN 3-933240-92-1.

101 Rappelsberger P, Weiss S, Schack B. (2000) Coherence and phase relations between EEG traces from different locations. In: Miller R. (ed.) Time and the Brain. Harwood Academic Publishers, Conceptual Advances in Brain Research, Vol. 3; 297–330; ISBN 90-5702-060-0.

102 Weiss S, Rappelsberger P, Schack B, Müller H.M. (2002) Kohärenz- und Phasenuntersuchungen und ihre Bedeutung für die Untersuchung von Sprachprozessen. In: H.M. Müller und G. Rickheit (Hrsg.) Neurokognition der Sprache. Tübingen: Stauffenburg (in press).

103 Witte H, Schack B. Quantification of phase coupling and information transfer between electroencephalographic (EEG) signals: Analysis strategies, models and simulations. Theory in Biosciences, in press.

Other articles cited

104 Ribary U, Ioannides AA, Singh KD, Hasson R, Bolton JPR, Lado F, Mogilner A, Llinas R. Magnetic Field Tomography (MFT) of coherent thalamo-cortical 40-Hz oscillations in humans. Proc Nat Acad Sci USA 1991; **88**:11037–11041.

105 Llinas R, Ribary U. Coherent 40-Hz oscillation characterizes dream state in humans. Proc Nat Acad Sci USA 1993; **90**: 2078–2081.

106 Llinas R, Ribary U. Temporal conjunction in thalamocortical transactions. In: Jasper HH, Descarries L, Castellucci VF, Rossignol S, editors. Consciousness: At the Frontiers of Neuroscience. Advances in Neurology 1998; **77**:95–103.

107 Ribary U, Cappell J, Mogilner A, Hund M, Kronberg E, Llinas R. Functional imaging of plastic changes in the human brain. Advances in Neurology 1999; 81: 49–56.

108 Llinas R, Ribary U. Consciousness and the brain: The thalamocortical dialogue in health and disease. Ann NY Acad Sci 2001; **929**:166–175.

109 Rilke RM. “Klage”. In: Rainer Maria Rilke, Sämtliche Werke. Verstreute und nachgelassene Gedichte aus den Jahren 1906–1926. Frankfurt am Main: Inselverlag; 1992. p. 84. English translation “Complaint” by Crego C, http://www.cs-music.com/features/salbit.html, © 1999–2001.

110 Halberg F, Carandente F, Cornélissen G, Katinas GS. Glossary of chronobiology. Chronobiologia 1977; **4** (Suppl. 1):189 pp.

111 Halberg F. Physiologic 24-hour periodicity; general and procedural considerations with reference to the adrenal cycle. Z. Vitamin-, Hormon-u Fermentforsch 1959; **10**:225–296.

112 Halberg F. Some physiological and clinical aspects of 24-hour periodicity. Journal-Lancet (Minneapolis) 1953; **73**:20–32.

113 Halberg F, Engel R, Halberg E, Gully RJ. Diurnal variations in amount of electroencephalographic paroxysmal discharge and diurnal eosinophil rhythm of epileptics on days with clinical seizures. Fed Proc 1952; **11**: 62.

114 Engel R, Halberg F, Ziegler M, McQuarrie I. Observations on two children with diabetes mellitus and epilepsy. Journal-Lancet (Minneapolis) 1952; **72**:242–248.

115 Halberg F, Gully RJ, Engel R, Ziegler MR. Further studies on coexisting diabetes and epilepsy. In: Good RA, Platou ES, editors. Essays on pediatrics in honor of Dr. Irvine McQuarrie. Minneapolis, Minnesota: Lancet Publications, Inc.; 1955. p. 130–135.

116 Halberg F. The chronobiology of convulsive disorders. Totus Homo 1978; **10**:20–30.

117 Halberg F, Schwartzkopff O, Cornélissen G. Rudolf Engels Zeitstrukturen, Chronome, erwarten Werner Düchtings Modellieren zu einem chronobiomimetischen Ingenieurwesen. Festschrift zur Würdigung der 27-jährigen wissenschaftlichen Arbeit v. Univ.-Prof. Dr.-Ing. Werner Düchting am Institut für Regelungs- und Steuerungstechnik der Universität-GH Siegen. aus Anlaß seiner Emeritierung zum 28.02.1999. p. 165–186.

118 Batschelet E. Statistical methods for the analysis of problems in animal orientation and certain biological rhythms. Washington DC: American Institute of Biological Sciences; 1965. 57 pp; cf. also Batschelet E. Circular Statistics in Biology. New York: Academic Press; 1981. p. 55.

119 Halberg F, Tong YL, Johnson EA. Circadian system phase—an aspect of temporal morphology; procedures and illustrative examples. Proc. International Congress of Anatomists. In: Mayersbach H v, ed. The Cellular Aspects of Biorhythms, Symposium on Biorhythms. New York: Springer-Verlag; 1967. p. 20–48.

120 Halberg F, Johnson EA, Nelson W, Runge W, Sothern R. Autorhythmometry—procedures for physiologic self-measurements and their analysis. Physiol Tchr 1972; **1**: 1–11.

121 Halberg F. Chronobiology. Annu Rev Physiol 1969; 31: 675–725.

122 Halberg F. Chronobiology: methodological problems. Acta med rom 1980; 18: 399–440.

123 Rummel JA, Lee JK, Halberg F. Combined linear-nonlinear chronobiologic windows by least-squares resolve neighboring components in a physiologic rhythm spectrum. In: Ferin M, Halberg F, Richart RM, Vande Wiele R, eds. Biorhythms and Human Reproduction, Int. Inst. for the Study of Human Reproduction Conf. Proc. New York: John Wiley & Sons; 1974. p. 53–82.

124 Cornélissen G, Halberg F. Chronomedicine. In: Armitage P, Colton T. (editors-in-chief). Encyclopedia of Biostatistics, v. 1. Chichester, UK: John Wiley & Sons Ltd, 1998: 642–649.

125 Nintcheu-Fata S, Cornélissen G, Katinas G, Halberg F, Fiser B, Siegelova J, Masek M, Dusek J. Software for contour maps of moving least squares spectra. Abstract 15, MEFA 9th International Fair of Medical Technology and Pharmacy, Brno, November 6–11, 2001.

126 Bingham C, Arbogast B, Cornélissen Guillaume G, Lee JK, Halberg F. Inferential statistical methods for estimating and comparing cosinor parameters. Chronobiologia 1982; **9**:397–439.

127 Cornélissen G, Halberg F. Introduction to Chronobiology. Medtronic Chronobiology Seminar #7, April 1994, 52 pp. (Library of Congress Catalog Card #94–060580; URL [accessed 1994] http://www.msi.umn.edu/~halberg/)

128 Frank G, Halberg F, Harner R, Matthews J, Johnson E, Gravem H, Andrus V. Circadian periodicity, adrenal corticosteroids, and the EEG of normal man. J psychiatr Res 1966; **4**:73–86.

129 Halberg F, Gupta BD, Haus E, Halberg E, Deka AC, Nelson W, Sothern RB, Cornélissen G, Lee JK, Lakatua DJ, Scheving LE, Burns ER. Steps toward a cancer chronopolytherapy. In: Proc. XIV International Congress of Therapeutics. Montpellier, France: L'Expansion Scientifique Française; 1977. p. 151–196.

130 Halberg Francine, Halberg J, Halberg E, Halberg Franz. Chronobiology, radiobiology and steps toward the timing of cancer radiotherapy. In: Goldson AL, volume editor. Cancer Growth and Progression, vol. 9, ch. 19, Kaiser H, series editor. Dordrecht: Kluwer Academic Publ.; 1989. p. 227–253.

131 Halberg F, Breus TK, Cornélissen G, Bingham C, Hillman DC, Rigatuso J, Delmore P, Bakken E, International Womb-to-Tomb Chronome Initiative Group: Chronobiology in space. Keynote, 37th Ann. Mtg. Japan Soc. for Aerospace and Environmental Medicine, Nagoya, Japan, November 8–9, 1991. University of Minnesota/Medtronic Chronobiology Seminar Series, #1, December 1991, 21 pp. of text, 70 figures.

132 Breus TK, Pimenov KYu, Cornélissen G, Halberg F, Syutkina EV, Baevsky RM, Petrov VM, Orth-Gomer K, Åkerstedt T, Otsuka K, Watanabe Y, Chibisov SM. The biological effects of solar activity. Biomed Pharmacother 2002; **56** (Suppl. 2): 273s–283s.

133 Cornélissen G, Hillman D, Katinas GS, Rapoport S, Breus TK, Otsuka K, Bakken EE, Halberg F. Geomagnetics and society interact in weekly and broader multiseptans underlying health and environmental integrity. Biomed Pharmacother 2002; **56** (Suppl

2):319s–326s.

134 Cortie AL. Sunspots and terrestrial magnetic phenomena, 1898–1911. Mon Notic Roy Astron Soc 1912; **73**:52–60.

135 Chapman S, Bartels J. Geomagnetism. 3rd ed. Oxford: Clarendon Press; 1962. 1049 pp.

136 Grafe A. Einige charakterische Besonderheiten des geomagnetischen Sonneneruptionseffektes. Geofisica Pura e Applicata 1958; **40**:172–179.

137 Russell CT, McPherron RL. Semiannual variation of geomagnetic activity. J Geophys Res 1973; **78**:92–108.

138 McPherron RL. The semiannual variation in the rate of particle injection in the ring current as measured by Dst. Seminar, presented at Space Environment Center, Boulder, Colorado, October 26, 2000.

139 McPherron RL. Diurnal and seasonal effects observed in the Dst index. Abstract #S1-09, 1st S-Ramp Conference, Book of Abstracts, p. 13, SCOSTEP, Sapporo, Japan, 2000.

140 O'Brien TP, McPherron RL. The apparent dependence of ring current dynamics on the dipole-Sun angle. Abstract Tail/Substorm #11, NSF GEM 1999 Workshop, contributed talk, presented at Snowmass, Colorado, June 21–25, 1999.

141 McPherron RL. Solar cycle and universal time variations in geomagnetic activity. Seminar to IGPP, Los Angeles, 1999.

142 McPherron RL. Solar cycle changes in the statistical properties of magnetic indices. Abstract GA5.06/W/03-A3, contributed talk presented at 22nd General Assembly, International Union of Geodesy and Geophysics, Birmingham, England, July 19–30, 1999, p. A.385.

143 McPherron RL, O'Brien TP. Solar wind coupling to the ring current as a function of season and solar cycle (abstract #SM21D-03). Eos, Transactions of the American Geophysical Union 1999; **80** (17):S274.

144 Cornélissen G, Halberg F, Katinas GS, Minne H, Breus T, Sothern RB, Watanabe Y, Tarquini R, Perfetto F, Maggioni C, Wilson D, Gubin D, Otsuka K, Bakken EE. Circasemiannual chronomics: half-yearly biospheric changes in their own right and as a circannual waveform. Biomed Pharmacol, in press.

145 Abbot CG. Solar variation and weather, a summary of the evidence, completely illustrated and documented. Washington DC: Smithsonian Miscellaneous Collections 146, No. 3 (Publ. 4545); 1963. 67 pp. + 4 plates.

146 Katinas G, Cornélissen G, Engebretson M, Breus T, Halberg F. A near-week in solar magnetism? Abstract 12, Proceedings, 3rd International Symposium: Workshop on Chronoastrobiology and Chronotherapy, Eriguchi M, ed, Research Center for Advanced Science and Technology, University of Tokyo, Nov. 9, 2002.

147 Fraser-Smith AC. Spectrum of the geomagnetic activity index Ap. J Geophys Res 1972; **77**:4209–4220.

148 Halberg F, Cornélissen G, Bingham C, Hillman D, Katinas G, Sampson M, Revilla M, Prikryl P Sr, Prikryl P Jr, Sanchez de la Pena S, Gonzalez C, Amory-Mazaudier C, Bouvet J, Barnwell F, Maggioni C, Sothern RB, Wang ZR, Schwartzkopff O, Bakken E. Season's Appreciations 2001. Neuroendocrinol Lett 2002; **23**: 170–187.

149 Roederer JG. Are magnetic storms hazardous to your health? Eos, Transactions, American Geophysical Union 1995; **76**:441, 444–445.

150 Vladimirskii BM, Narmanskii VYa, Temuriantz NA. Global rhythmics of the solar system in the terrestrial habitat. Biophysics 1995; **40**:731–736.

151 Cornélissen G, Engebretson M, Johnson D, Otsuka K, Burioka N, Posch J, Halberg F. The week, inherited in neonatal human twins, found also in geomagnetic pulsations in isolated Antarctica. Biomedicine and Pharmacotherapy 2001; 55 (Suppl 1): 32–50.

152 Zerubavel E. The Seven Day Circle: The history and meaning of the week. New York: Free Press; 1985. 206 pp.

153 Young M. The Metronomic Society: Natural rhythms and human timetables. Cambridge, Massachusetts: Harvard University Press; 1988. 301 pp.

154 Cornélissen G, Halberg F, Schwartzkopff O, Delmore P, Katinas G, Hunter D, Tarquini B, Tarquini R, Perfetto F, Watanabe Y, Otsuka K. Chronomes, time structures, for chronobioengineering for "a full life". Biomed Instrum Technol 1999; **33**:152–187.

155 Halberg F, Cornélissen G, Otsuka K, Watanabe Y, Katinas GS, Burioka N, Delyukov A, Gorgo Y, Zhao ZY, Weydahl A, Sothern RB, Siegelova J, Fiser B, Dusek J, Syutkina EV, Perfetto F, Tarquini R, Singh RB, Rhees B, Lofstrom D, Lofstrom P, Johnson PWC, Schwartzkopff O, International BIOCOS Study Group. Cross-spectrally coherent ~10.5- and 21-year biological and physical cycles, magnetic storms and myocardial infarctions. Neuroendocrinol Lett 2000; **21**:233–258.

156 Halberg F, Cornélissen G, Otsuka K, Schwartzkopff O, Halberg J, Bakken EE. Chronomics. Biomedicine and Pharmacotherapy 2001; **55**(Suppl 1):153–190.

157 Duboule D. Time for chronomics? [editorial]. Science 2003; **301**:277.

158 Kmita M, Duboule D. Organizing axes in time and space; 25 years of colinear tinkering. Science 2003; **301**:331–333.

159 Schwartzkopff O, Cornélissen G, Johnson D, Halberg F. Chronome stage-dependent teratogenesis in meta-analyzed murine data on cortisone and hydroxyurea effects. Proc. XXXIII Int. Cong. International Union of Physiological Sciences, St. Petersburg, Russia, June 30–July 5, 1997, abstract P007.13.

160 Clayton DL, McMullen AW, Barnett CC. Circadian modification of drug-induced teratogenesis in rat fetuses. Chronobiologia 1975; **2**:210–217.

161 Sauerbier I. Recent findings relative to teratology and chronobiology. In: Scheving LE, Halberg F, editors. Chronobiology: Principles and Applications to Shifts in Schedules. Alphen aan den Rijn, The Netherlands: Sijthoff and Noordhoff; 1980. p. 535–540.

162 Otsuka K, Cornélissen G, Halberg F. Circadian rhythmic fractal scaling of heart rate variability in health and coronary artery disease. Clinical Cardiology 1997; **20**:631–638.

163 Burioka N, Cornélissen G, Halberg F, Kaplan DT. Relationship between correlation dimension and indices of linear analysis in both respiratory movement and electroencephalogram. Clin Neurophysiol 2001; **112**:1147–1153.

164 Halberg F, Cornélissen G, Otsuka K, Katinas G, Schwartzkopff O. Essays on chronomics spawned by transdisciplinary chronobiology: Witness in time: Earl Elmer Bakken. Neuroendocrinol Lett 2001; **22**:359–384.

165 Starbuck S, Cornélissen G, Halberg F. Is motivation influenced by geomagnetic activity? Biomed Pharmacother 2002; 56 (Suppl 2): 289s–297s.

166 Féré MCh. De la fréquence des accès d'épilepsie suivant les heures. Compt rend soc de biol 1888; **40**:740.

167 Günther R, Knapp E, Halberg F. Referenznormen der Rhythmometrie: Circadiane Acrophasen von zwanzig Körperfunktionen. Z angew Bäder- u. Klimaheilk 1969; **16**:123–153.

168 Cornélissen G, Watson D, Mitsutake G, Fiser B, Siegelova J, Halberg F. Circaseptan and circasemiseptan prominence in students' negative affect complements circadian prominence in positive affect. Abstract 13, Kongres MEFA, Brno, Czech Rep., 5–8 Nov. 2002.

169 Halberg F, Visscher MB, Bittner JJ. Relation of visual factors to eosinophil rhythm in mice. Amer J Physiol 1954; **179**: 229–235.

170 http://www.sec.noaa.gov/Data/Geomag.html

171 Rodriguez E, George N, Lachaux JP, Martinerie J, Renault B, Varela FJ. Perception's shadow: long-distance synchronization of human brain activity. Nature 1999; **397**:430–433.