THE SYNCHRONIZATION & SYNTONIZATION OF MOLECULAR (BIOLOGICAL) CLOCK ENSEMBLES

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ABSTRACT

The NASA/JPL Deep Space Network (DSN) operates four facilities on three continents 24 hours/day, everyday. The DSN Operations Control Center (NOCC), in Pasadena, California, continually monitors and reports the status and performance of all DSN spacecraft project operations. The author, as a DSN Operations Frequency & Timing Systems performance analyst-engineer, reviewing these Daily Status Reports, noted that equipment failure is not the only cause of discrepant performance. Operator errors are a major contributor. Discrepancies tend to occur more frequently on weekends and at local solar time off-hours (nights). Presented here are the result of the author's research into correlations between synchronization/desynchronization of human biological clocks and operator performance.

All biological organisms contain clocks. These clocks control the health, behavior and life cycle of the organism. To perform this function, they must be synchronized. For earthbound bio-clocks the synchronizing agents are solar radiation (the cyclic day/night pattern) and tidal modulation of the local gravitational field. The bio-clock is synchronized by lunar/solar tidal forces to form a lunar clock-calendar system. The time-of-day clock controls behavior patterns (depression levels), sleep/wake pattern, body temperature, etc. The clock-calendar regulates life phases (e.g. infancy, childhood, adolescence, adult, menopause, ageing).

Desynchronization can cause behavioral affects as minor as loss of concentration, or as serious as fits of deep depression. Desynchronization can be caused by: 1) A genetic defect; 2) The ingestion of mood modifying foods and chemicals; 3) Rapid travel across time zones; or 4) Sensory deprivization (extended periods of darkness or extended periods without sleep). Desynchronization is an occupational hazard for DSN Spacecraft Tracking Net Operators, air traffic controllers, international flight crews, etc.

Where there is a need for sonic communications amongst a common species, there is also a need for the syntonization of the bio-clocks (e.g., birdsongs, human speech, porpoise clicks and whistles, wolf calls, etc.) The encoding of information requires

an accurate and stable reference clock rate.

(This is also a prime requisite for a good time keeping system.) The basic accuracy and stability of this bio-oscillator is inherent to the human bio-organism and only varies slightly in level from one individual to another (e.g., persons with "absolute pitch" have a very stable bio-oscillator and therefore a bio-clock that is not easily desynchronized; At the other extreme is the "tone deaf" person whose bio-clock is easily desynchronized). Tone encoded languages, such as Chinese, place a greater dependence on the need for syntonization than do the western languages.

The overall efficiency of Operations Systems can be increased ana made more error free if bio-clock sync/descync criteria are considered in: 1) The overall system design; 2) The control of light and temperature in the work environment; and 3) The selection of operations personnel.

INTRODUCTION

The 9th Annual PTTI banquet featured a presentation on the subject of "Human Periodic Phenomena" presented by Professor Dr. Franz Halberg of the University of Minnesota Medical School. My presentation will consider how these "phenomena" are entrained to environmental factors (der Zeitgeber), and how the loss of entrainment affects performance in an operational work environment.

My motivation and interest in researching this subject stems from three facts: First, my daily professional pre-occupation is with the syntonization and synchronization of atomic clock ensembles. Second, I have a deep abiding interest in anthropology and archaeoastronomy. And finally, two spinal injuries have left me with a brain dysfunction that is periodic. A deeper understanding of biological clock physiology will allow me to develop effective work arounds.

The NASA-Jet Propulsion Laboratory operates a worldwide network of spacecraft data gathering facilities. These facilities operate 24 hours per day, year round. The status and performance is monitored from a central facility (Network Operations & Control Center) in Pasadena, California, U.S.A. The NOCC issues DAILY STATUS REPORTS, herein called Discrepancy Reports (DRs), noting significant events that have occurred throughout the Deep Space Network (DSN) over the most recent 24 hours. As the Frequency & Timing System (FTS) Cognizant Operations Engineer, one of my duties is to peruse these DAILY STATUS REPORTS to determine if the FTS is contributing to discrepant performance in the network. In the performance of this duty, I noticed that the number of DRs tended to increase on weekends.

A software package was generated to collect and perform statistical analysis upon the DRs. Figures 8, 9, 10 and 11 are bar graphs of these data results. The data were divided into two categories, hardware vs. non-hardware. The non-hardware category was further divided into "Operator" vs "Other" [Figure 8]. "Other" includes such causes as, power outages, inclement weather, RFI, intra and extra data communications outages and "cause unknown" failures. The resulting analysis indicates hardware caused less than 29% of the DRs. Further analysis of the non-hardware DRs [Figure 11] revealed that 55.6% of the DRs were on weekends. This is 27% higher than one would expect. Further analysis on a time-of-day (work shift) basis [Figure 10] shows less than 10% variance in the number of DRs on a per shift basis. One can arrive at the conclusions that: 1) Some operator errors are being reported as hardware failure; and 2) There is a significant difference in the weekend environment not present during weekdays.

The weekend environment differs in two ways: 1) Management, engineering and technical staff personnel are present 4 days av./week, daylight hours only; and 2) There is some periodic function, synchronous to time-of-week, that is affecting operator performance. If the former (1) was a major factor, then the DAY SHIFT DRs would have been significantly fewer. This treatise deals with the possible causes of the periodic changes in the operator performance.

What are biological clocks?

Cells and groups of cells that give an organism the capability to measure the passage of time. These clocks may be manifested in any of three forms: Subcellular (as in single cell organisms), or multicellular neurodendric groups (as in the brain), or multicellular neuromyopathic groups (as in the heart pacemakers). [1] [6] [26] [11]

Der Zeitgeber

Zeitgeber (1) is the entrainment of biological clock rhythms to exogenic environmental periodic forces,among them being electro magnetic radiation (VLF to Gamma), gravitational (tidal), pressure (barometric to sonic), and energetic particles (atomic or nuclear). It is this entrainment (synchronization) that permits an endogenous free running clock to be used as a clock-calendar system. [2] [20]

NOTES: 1.n[G,fr. zeit time (fr. OGH zit) + geber, lit., giver, donor, fr. OHG geban; akin to OE giefant to give - more at TIDE TIVE] (1968): an environmental agent or event (as the occurrence of light or dark) that provides the stimulus setting or resetting a biological clock of an organism. WEBSTER'S Ninth New Collegiate Dictionary.

Environmental Factors

The environmental factors under consideration are those discussed in "der Zeitgeber", and how they vary as a function of altitude, latitude, sea depth and epochal time. The effect of sea depth is beyond the scope of this treatise. This discussion considers the effect of altitude, latitude and time only.

Figure 1: depicts the change in the magnitude of the gravitational force as the geographic latitude changes. Again the lack of linearity is due to the earth's oblateness. [3] [19]

Not shown are: Cosmic and ionized particle bombardment effects which generally increase with an increase in altitude (above 10K ft) and/or latitude (above 60 degrees). They also vary with time (roughly 10 yr and 26K yr cycles). [8]

Figure 2: shows how the earth's oblateness affects the local gravitational force, as a function of altitude above the center of mass. The gravitational force will decrease as the square of the increase in altitude.

Figure 3: illustrates how the earth's rotational period and the moon's orbital period modulate the received solar radiation (sunlight) and gravitational force (tidal) as a function of time. The exact phase relationship illustrated is repeated every 18.6 solar years. However, for the approximate case, it repeats every 29.5 days. Not shown is the solar tidal force which has a fixed phase offset (delay) from the phase of the received sunlight, and which does not vary with latitude. It does have a seasonal periodicity (highest in winter).

Figure 4: illustrates that the level of received solar radiation and the gravitational force varies with time and latitude. The values presented are relative. It is not to be construed that lunar tidal forces disappear beyond 62 degrees latitude or at the equator. The figure does not show the periodic solar tidal force. [3]

Other elements considered but not detailed here are climate and the social environment. [5] Seasonal change of the climate is a major factor as to why the organism requires a clock/calendar. But periodic climate changes have no effect on clock rate or rhythm. However, pheromones do synchronize clocks within a social group to enhance fertility. [5] The detectors are located in the roof-of-mouth/nasal area (Fig. 5) and probably connect to the pineal body (Fig. 6).

Genetic Evolution

Genetic materials (DNA) are biologic ROMs (read only memory) that carry the information that determines species, variations within a species and variations of traits within a sub-species. Random genetic transmutations induced by endogenous noise, bombardment by energetic particles, high level electro-magnetic radiation and/or oncogenic chemicals can cause variations in the traits within a subspecies. [16] [25]. Genetic evolution results when these randomly induced changes go in a direction that gives the organism a survival advantage, a competitive edge and/or greater efficiency in the use of the available energy pool. [18] [25] As a result, all earth-borne biologic organisms have evolved clocks. These clocks, when synchronized, permit the organism to develop a sense of time (past-present-future), to plan for and respond to periodic changes (diurnal, seasonal, yearly, etc.) in its local environment (e.g., sunlight-darkness cycles, diurnal and seasonal temperature cycles, tides, etc.). [6] [26]

Most multicell organisms rather than depend upon a single clock in a single location, contain an ensemble of clocks distributed to centers, usually within the brain. [1] [28] [14] [4] Because of this, there is strong pressure to evolve the communications necessary to maintain synchronizm between the clocks. These clock ensembles can take two forms. One, where there is an endogenous master clock along a one-way communication path to maintain synchronization with the other members of the ensemble (the human clock ensemble is probably this type). [16] [18] The other is where there is an ensemble of more or less independent endogenous clocks with two-way communication paths to maintain synchronization. (The earthworm is an example of an organism containing multiple endogenous clocks. Cut it into sections. If each section contains a clock, it will develop new clocks and become a complete worm.) In order that these endogenous clocks become clock-calendars, they must evolve the means to sense and become entrained to exogenous (nonendogenous) periodic variations in the environment (Zeitgeber), [10] [14] [16] [20] forming a transducer/encoder-decoder/ transducer communication system. Three communications media have evolved:

1) A light sensitive one, the eyes using sunlight to synchronize the clocks to the period of the earth's rotation about its axis.
2) A tidal sensor (graviceptor) to synchronize the clocks to the period of the moon's rotation about the earth. [23] [30] [31]
3) An odor transceiver (pheromones) system for enhancing the synchronizm of reproductive functions. [5]
4) A bilateral sound generator-detector system to syntonize communications between members of a common sub-species. [1] [2] [20] For this case, the message (mating/distress/danger warning/ etc.) to be communicated is encoded in the pitch (frequency offset from a reference frequency). It is this communication requirement that imposes accuracy on the

biological clock. The stability of this clock reference oscillator has been measured (1) (Aschoff and others) as no worse than $\pm 0.136\%$. [1] [6] [27] [26]

Figure 5 is a graphic model of how a sound transmitter (the vocal cords) and sound receiver (the ear) are syntonized to a hypothetical masterclock reference frequency generator.
This syntonized model system serves multiple functions, among them being:

1) A frequency offset measurement system for the coding and decoding of aural communications, e.g., all sing-song languages such as, Chinese, East Indian, Amerindian (west of Rockies), etc.
2) A reference for time interval coded aural communications, e.g., languages that evolved from signal drums, such as modern Japanese, Greek, Italian, Russian, Swahili, etc.
3) A sonic source spatial position measurement system.
4) A body attitude and graviceptor detector (an otolithic organ). [30] [31]

Figure 6: A functional block diagram of a homo sapien biological clock-calendar system. The terminology "Zeitgeber", "ultradian", "circadian" and "infradian," was adopted at the Cold Spring Harbor Conference on Biological Clocks 1967. They take on a unique definition when applied to biological clocks: (i.e. ultradian period is shorter than 24 hours, infradian periods are longer than 24 hours and Zeitgeber is the entrainmenter of a biological clock to a stable periodic force exogenic to the clock. The word "synchronize" infers that the clocks affect one another. It would be ridiculous to infer that a bio-clock has an effect upon the rotation rate of the earth, therefore the word "entrainment" is used).

Elements of the homo sapien biological clock-calendar system are in several locations in the brain, among them being the amygdala, the hypocampus, the suprachiasmic bundle, the pineal body, etc. It is known which centers are involved, but their specific functions are not clear. [2] [7] [14] [16] [20] [25] However, the role of "entrainer" (synchronizer) played by the pineal body is quite clear. [7] The optic nerve takes a direct path from eyes to pineal body by way of the suprachiasmic bundle.

NOTES: 1. Test conducted under constant light level conditions, gravity free (space) environments and following electro therapy had no significant affect upon the frequency.

If you will accept the hypothesis that the reference frequency standard for the intra species communications is also the master clock reference oscillator, and that the human ear contains both the sonic communications detector and the otolith (tidal sensor) (the viscera also serves a dual role as an otolithic organ and low frequency (long wave) sonic detector), and that the eyes, a photoperiod detector, provide the means to measure the period of revolution of a stable body, the earth, then one has all the components required for an accurate clock and calendar (Fig. 7).

Careful perusal of the literature gave no support for a digital divider chain type clock. There was, however, support for a hypothetic chemical integrator/divider chain type clock (an integrate and dump-reset routine). [11] [14] [17] [23] Many researchers have measured the free running period of the master clock as 27 hours $\pm$ 0.136%. [1] This being the case, one or both the photoperiod or tidal detectors will trigger a dump-reset (23 to 26 hours) prior to the 27 hour self reset. In the absence of output from the photo and/or tidal detectors (Fig. 7) (as when on a westward inter continental flight or in space), the master clock will self reset at 27 hours.

TABLE I: Is a listing of some of the human health and behavior factors that are controlled by ultradian clocks (time-of-day clocks). "Time-of-Day Regulators" do not regulate the time, but regulate some function to occur at a particular time, and for a particular period. For example, sleep should occur at night and should last throughout the night. Bodily excretion should occur during the day. (Not because there is a best time of day for the function but, because it would not be convenient for the excretory functions to occur during sleep.) Further, the level of alertness, concentration or mood should be timed to occur during the awake period for the same reasons that excretion should not occur during sleep. So it is apparent why a Time-of-day clock is needed, and why it needs to be entrained to and kept in phase with the earth's rotation. [12] [19] [27]

When, for any reason, the Time-of-day clock is out of phase (desynchronized) with the earth phase, the regulatory functions are degraded, and, in extreme cases, are lost. For instance, it is very difficult to sleep in step with the local night when your internal clock keeps your alert level in step with day at another place (90 degrees (6 hours) away). Desynchronization can stem from several causes:

1) Rapid travel over global distances (greater than 45 deg. or 3 hours).
2) A genetic defect in the clocks or the communication pathways,
3) A medical accident (mechanical, electrical or chemical) that involves parts of the brain involved in clock or clock sync activities.

TABLE 1: TIME-OF-DAY REGULATORS

REGULATES			
SYNCHRONIZED		DESYNCHRONIZED	
HEALTH	TEMPERAMENT	HEALTH	TEMPERAMENT
body temperature/ blood pressure/ heart rate/sleep-wake/endocrine glands/endorfin production/ digestion/ excretion/metabolism/sex hormon release	alert/concentration/sexuality/ mood (euphoria-depression)/ oriented to the environment/	hypertension/hypotension/heart arrythmia/sleep apnea/indigestion/ sexual dysfunction/ hyperglycemia/hypoglycemia/	manic depression confused/disoriented/ abbreviated attention span/

TABLE 2: CIRCADIAN REGULATORS

REGULATES			
SYNCHRONIZED		DESYNCHRONIZED	
HEALTH	TEMPERAMENT	HEALTH	TEMPERAMENT
blood pressure/ kidney function/ sex hormon production/bone cell growth/ neuron cell growth/tissue cell growth	oriented to the environment/	chronic hypertension/chronic hypotension/ diabetes/	schizophrenia/ manic depression/ chronic depression/disoriented/ distracted/

TABLE 3: STAGE-OF-LIFE REGULATORS

STAGE #	REGULATES			
	SYNCHRONIZED		DESYNCHRONIZED	
	HEALTH	TEMPERAMENT	HEALTH	TEMPERAMENT
Stage 1 PREADULT Av Age 9.3 yr (conception to 18.6)	bone cell growth/muscle & brain cell growth/ blood cell maintenance/ sex hormons/ reproduction/ pancreas function/ induce menstruation/	mood elevators/ depression inhibitors/ elevated mood/ exhuberant	stunted growth/epileptic seizures/ excessive growth/ leukemia/ osteogenesis/ diabetes insipitus/	disoriented/ poor concentration/ manic/ schizophrenic/
Stage 2 ADULT Av Age 28 yr (18.6 to 37.2)	bone cell growth/ inhibited/ bone cell maintenance only/ brain cell production inhibited/ sex hormons/ reproduction/ pituitary function/	DNA	DNA	DNA
Stage 3 MIDDLE AGE Av Age 46.6 yr (37.2 to 55.8)	bone cell maintenance/ inhibit sex hormons/ induce menopause/	DNA	female osteoporosis/ Parkinson's/ Alzheimers/ diabetes melitus/	DNA
Stage 4 DECLINING YRS Av Age 65.2 yr (55.8 to ?)	bone cell maintenance/ blood cell maintenance/ diminished neurochemical production/	DNA	male&female osteoporosis/ Parkinson's senility/	DNA

However, jet travel is the largest single cause of desynchronization.

TABLE 2 lists some of the bodily functions that are controlled by circadian regulators.

TABLE 3 lists some of the biological functions that are controlled by "stage-of-Life" (infradian clocks) regulators.

SUMMARY

The dynamics in periodic environmental factors do affect human health and performance. When Zeitgebers are at high levels, the health is good and performance is high. Obversely, under conditions of low Zeitgeber (desynchronization) both health and performance suffer. (e.g. both 3 Mile Island and Chenobyle accidents (1) occurred on the 3rd shift). In an operational work environment there are some factors that can be controlled to enhance performance.

Some of these controllable factors one should consider are:

1) The color temperature of the lighting. "The amplitude swings of body temperature are directly proportionate to the level of light," Aschoff. [1]
2) The optimal length of the work shift (7 to 10 hours). "Circadian variability in vigilance performance," Frazier. [9]
3) The interval between scheduled shift rotation (optimally 30 days). i.e. The period of desynchronization following a shift change can be as short as 3 days and as long as 2 weeks. Halberg [12], Quadens [23].
4) The history of operator performance in a rotating shift environment when making task assignments. Lacking historical data, submit the candidate to psychological profile tests to measure the relative susceptibility to desynchronization. (e.g. Does the candidate have a regular and stable sleep pattern and/or menstruation? How much does jet lag disturb him or her? How long is the recovery period?)

ACKNOWLEDGEMENTS

My thanks to J. Streit, Allied-Bendix Corp., who developed the DRs statistical analysis program and graphics.

NOTES: 1. The genesis of biological clock evolution at the high latitudes (>55 deg.) includes relatively high levels of cosmic radiation. Can it therefore be assumed that Lapplanders and Eskimos will be relatively immune to Chernobyl fallout?

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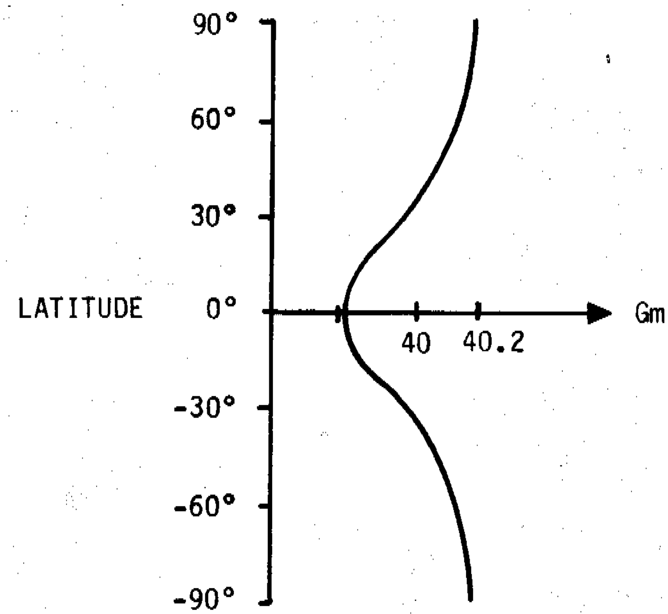

Figure 1: STATIC EARTH GRAVITATIONAL FORCE AS A FUNCTION OF LATITUDE.

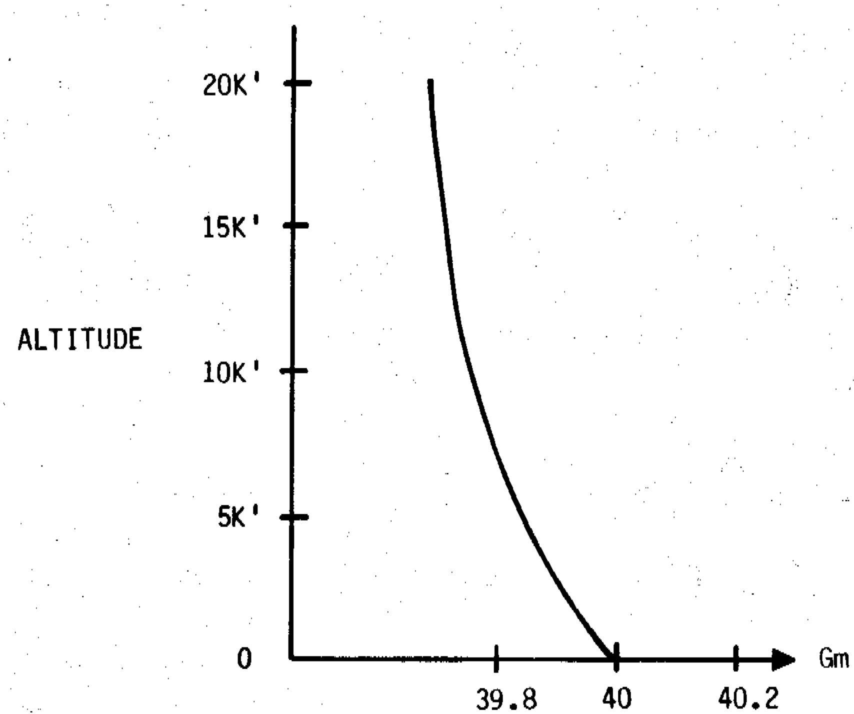

Figure 2: STATIC EARTH GRAVITATIONAL FORCE AS A FUNCTION OF ALTITUDE.

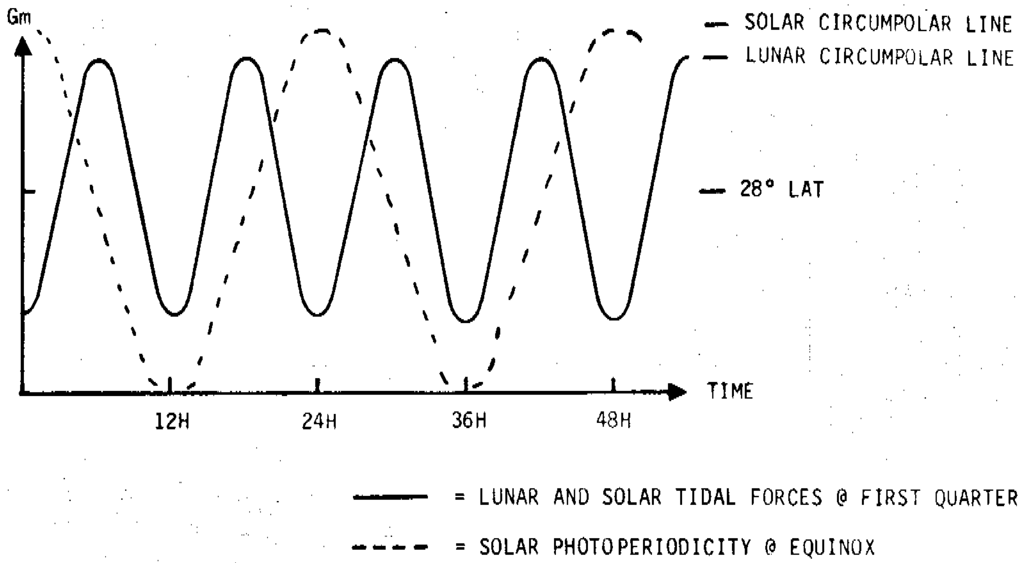

Figure 3: EARTH'S STATIC GRAVITY MODULATED BY LUNAR/SOLAR TIDAL FORCES VS TIME.

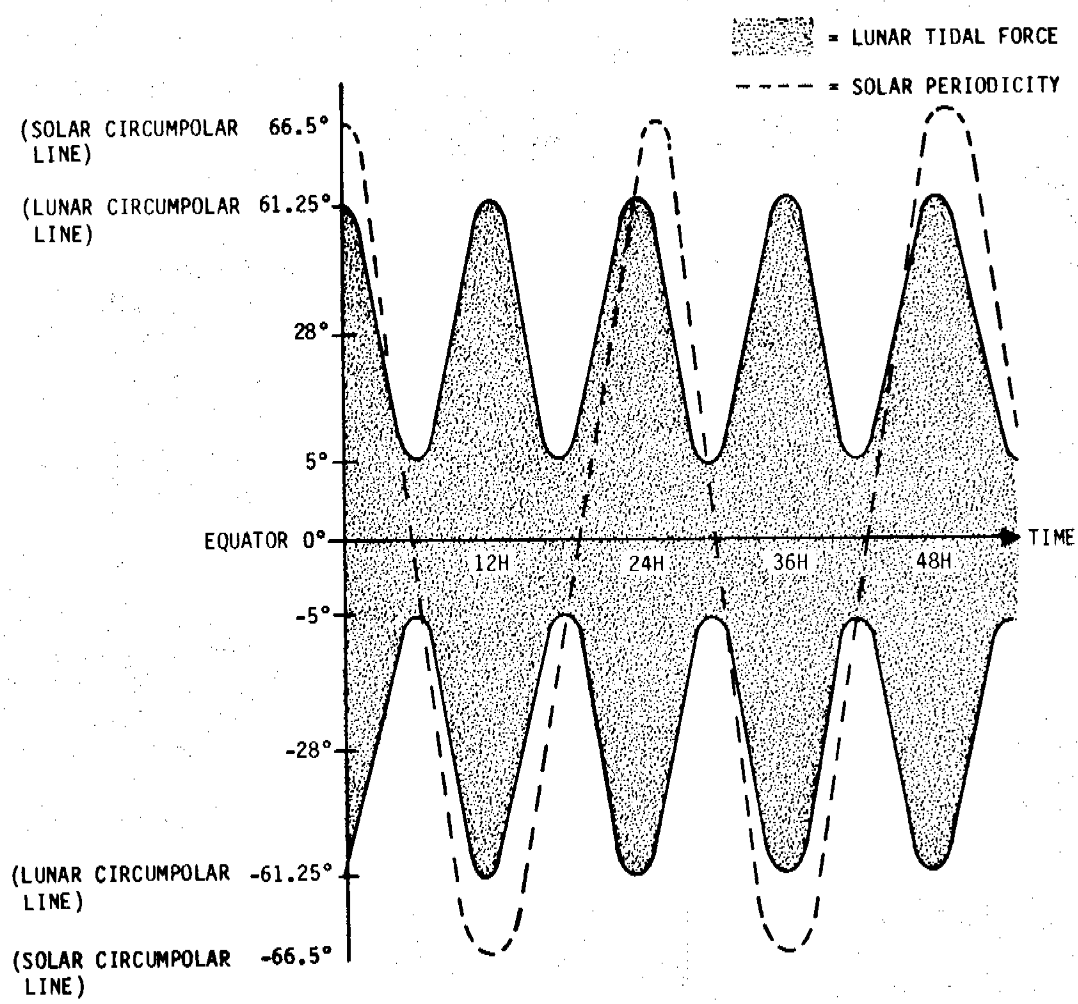

Figure 4: AVAILABILITY OF PERIODIC GRAVITATIONAL AND PHOTOPERIODIC FORCES TO PROVIDE BIOLOGICAL CLOCK SYNCHRONIZATION AS A FUNCTION OF LATITUDE.

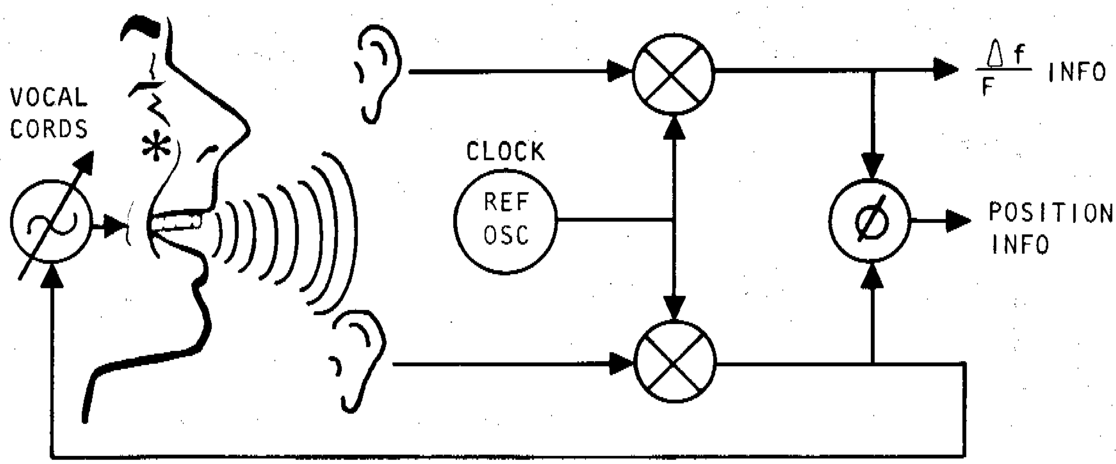

Figure 5: A SYNTONIC BIOLOGICAL CLOCK

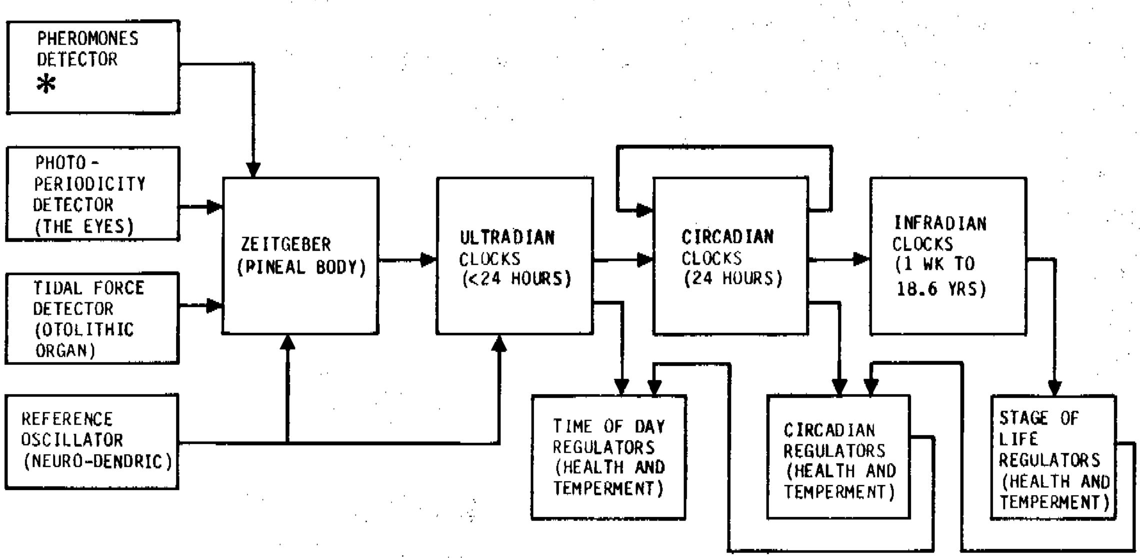

Figure 6. A FUNCTIONAL BLOCK DIAGRAM OF A HOMO SAPIEN BIOLOGICAL CLOCK-CALENDAR SYSTEM.

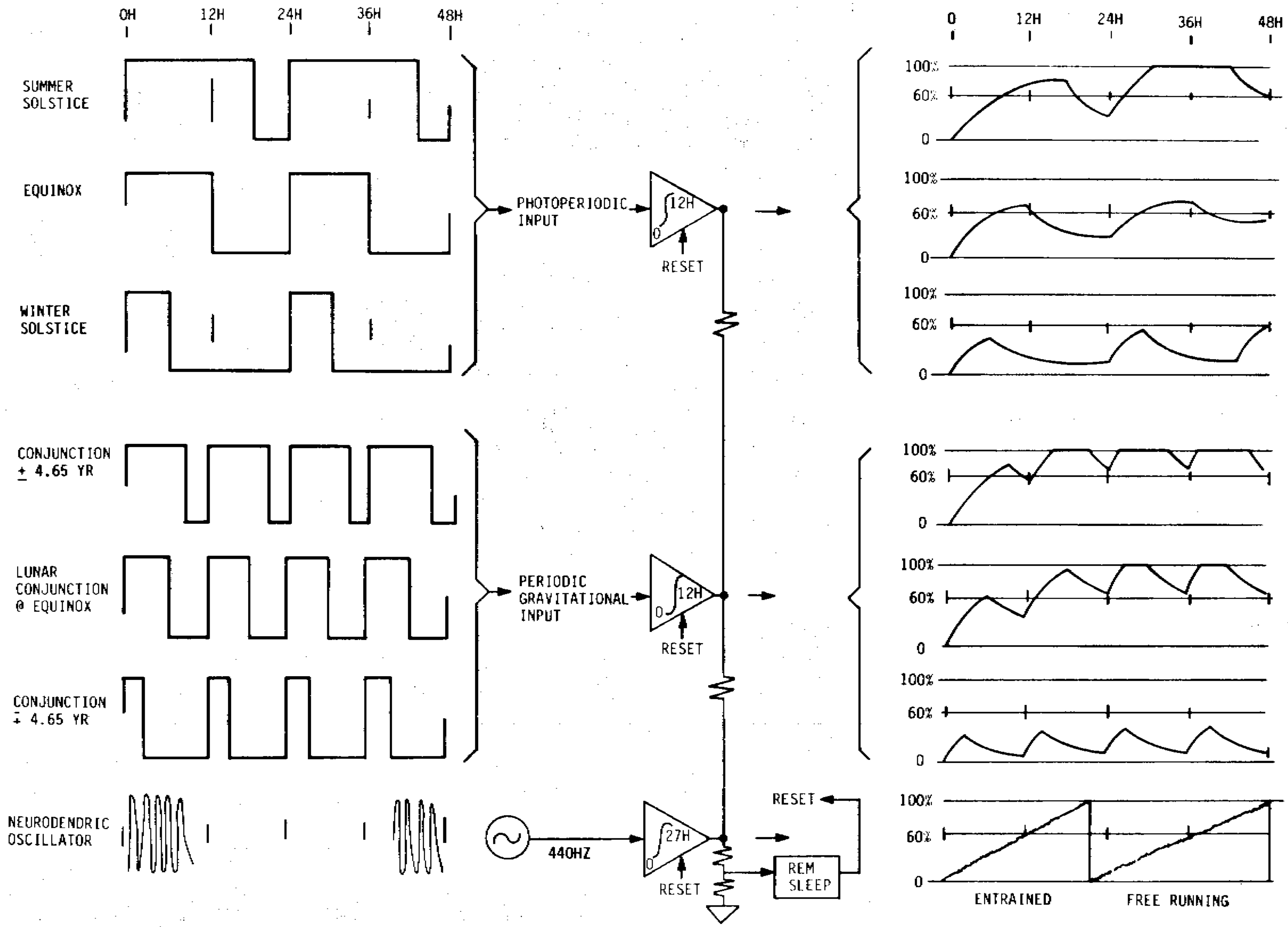

Figure 7. ZEITGEBER AND A MODELED HUMAN BIOLOGICAL CLOCK ENSEMBLE

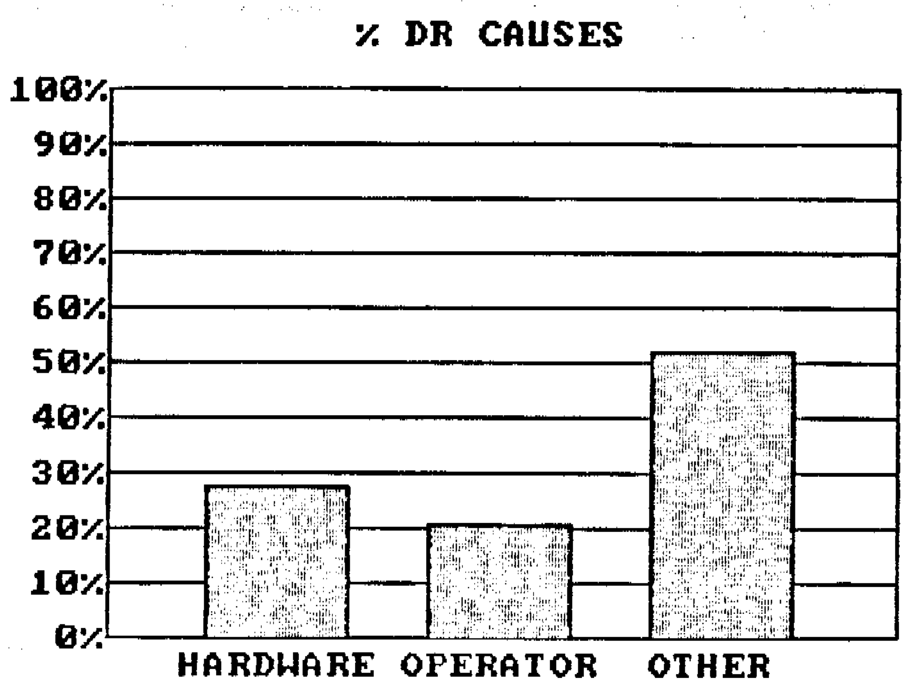

Fig. 8 DSN Operations discrepancies summary from all causes.

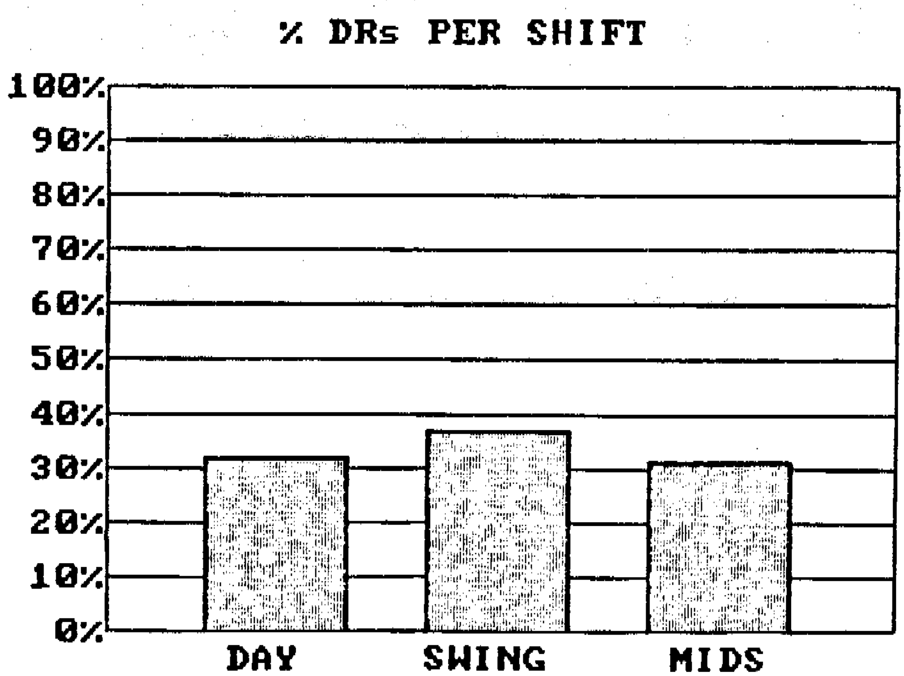

Fig. 9 DSN Operations discrepancies summary from all causes on a per shift basis.

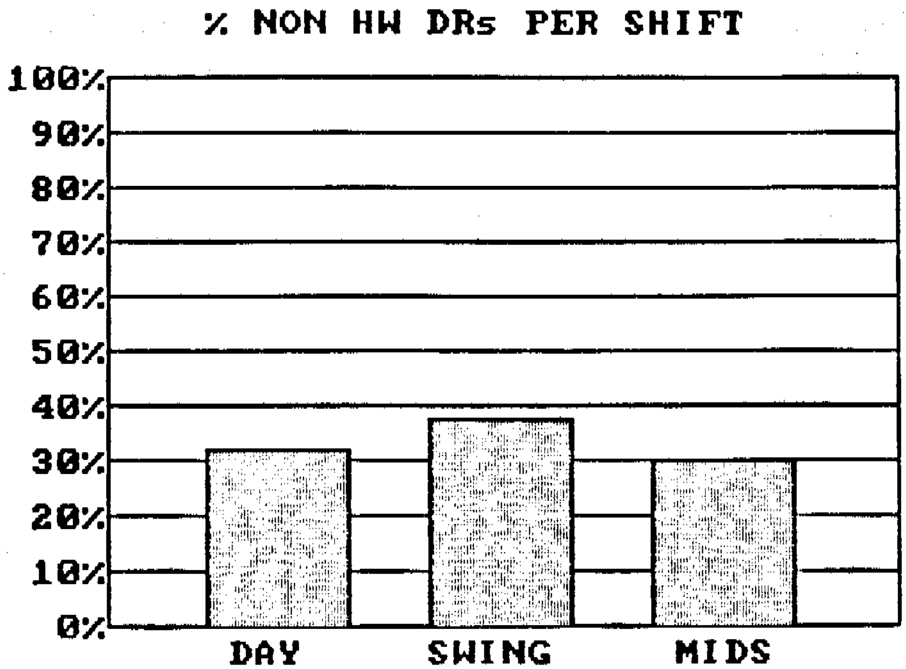

Fig. 10 DSN Operations discrepancies summary from non hardware causes on a per shift basis.

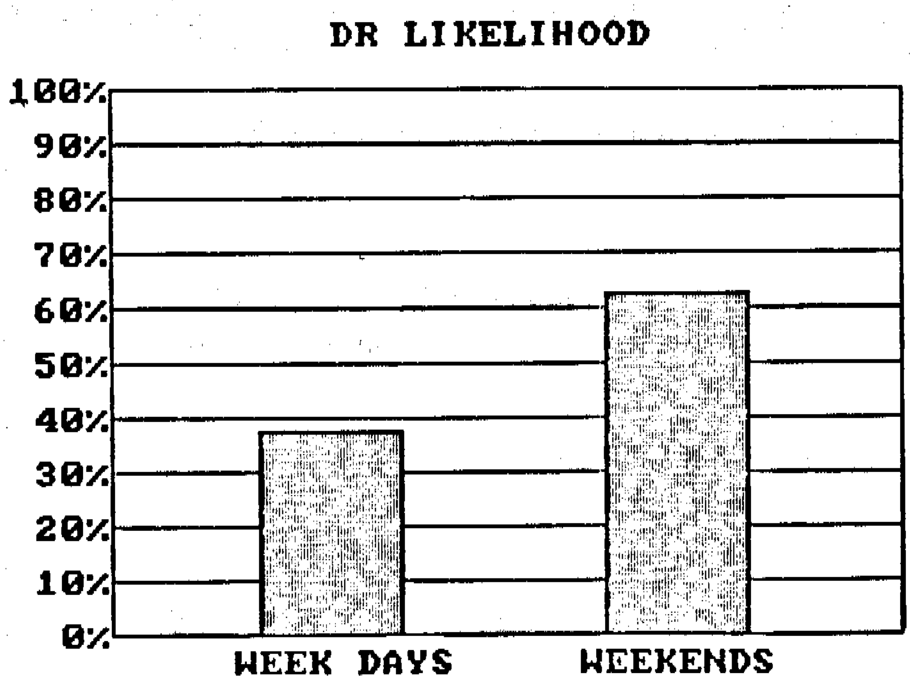

Fig. 11 DSN Operations discrepancies summary from non hardware causes on a day-of-week basis.

QUESTIONS AND ANSWERS

RICHARD NORTH, PORTLAND, OREGON: When I first received the copy of the Advance Program, I read through all the descriptions of the papers of interest, in particular yours. I showed it to a number of colleagues in the office and they thought "I wonder what that means?". After thinking for a while and realizing that some of us are tone deaf and some are not, I held a quick informal survey which tended to indicate that the people that knew that they were tone deaf were not affected very much by the weather and they never really knew what time it was, either. Some of us are more fortunate, though. I do enjoy music and I always know when it is time to go home.

MR. WARD: On the other hand, those who have absolute pitch are very seldom affected by jet lag and things like that. A very stable clock doesn't need to be synchronized frequently.