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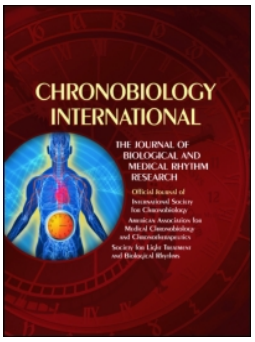

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EDITORIAL

The Full Moon as a Synchronizer of Circa-monthly Biological Rhythms: Chronobiologic Perspectives Based on Multidisciplinary Naturalistic Research

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ABSTRACT
Biological rhythmicity is presumed to be an advantageous genetic adaptation of fitness and survival value resulting from evolution of life forms in an environment that varies predictably-in-time during the 24 h, month, and year. The 24 h light/dark cycle is the prime synchronizer of circadian periodicities, and its modulation over the course of the year, in terms of daytime photoperiod length, is a prime synchronizer of circannual periodicities. Circadian and circannual rhythms have been the major research focus of most scientists. Circa-monthly rhythms triggered or synchronized by the 29.5 day lunar cycle of nighttime light intensity, or specifically the light of the full moon, although explored in waterborne and certain other species, have received far less study, perhaps because of associations with ancient mythology and/or an attitude naturalistic studies are of lesser merit than ones that entail molecular mechanisms. In this editorial, we cite our recent discovery through multidisciplinary naturalistic investigation of a highly integrated circadian, circa-monthly, and circannual time structure, synchronized by the natural ambient nyctohemeral, lunar, and annual light cycles, of the Peruvian apple cactus (*C. peruvianus*) flowering and reproductive processes that occur in close temporal coordination with like rhythms of the honey bee as its pollinator. This finding led us to explore the preservation of this integrated biological time structure, synchronized and/or triggered by environmental light cues and cycles, in the reproduction of other species, including *Homo sapiens*, and how the artificial light environment of today in which humans reside may be negatively affecting human reproduction efficiency.

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Introduction

The role of the 24 h light/dark cycle in the synchronization of circadian processes and their perturbation by artificial light at night is of great current interest as demonstrated, for example, by the large number of recent publications in this journal (Asher et al., 2015; Aubrecht et al., 2015; Cho et al., 2015; Harb et al., 2015; Heath et al., 2014; Hernández-Pérez et al., 2015; Kim et al., 2015; Martinez-Nicolas et al., 2014; Mata-Sotres et al., 2015; Obayashi et al., 2014a, b, c, 2015; Rea & Figueiro, 2014; Rybnikova et al., 2015; Sander et al., 2015; Smolensky et al., 2015; Stowie et al., 2015). In contrast, the role of the ~30-day lunar cycle, particularly the light of the full moon, in the synchronization of monthly rhythms, whether researched through laboratory or naturalist field study, seems to be of far less interest and much less investigated. The aim of this editorial is to call attention to the significance of the ~30-day (lunar) cycle of moonlight on the chronobiology of life forms, including humans, which seems to be underappreciated or dismissed because of ancient myths, poor research methods, or other reasons. Our goal is not to exhaustively review ~30-day biological rhythms, but rather to present relevant examples. Circa-monthly temporal variation of biological processes and reproduction has long been of interest to naturalists and other scientists; however, for a variety of reasons, e.g. many published reports either have been forgotten and thus rarely quoted, as in the case of the "old" papers of Fox (1923, 1924), or difficult to access because of improper categorization as the exogenous tidal cycle rather than moon-phase triggered or synchronized endogenous biological rhythm phenomena. Furthermore, we believe the extra-scientific as

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well as multidisciplinary perspectives of the discovery of such phenomena are also relevant, e.g. how Mossadok Ben-Attia (2016), an accomplished medical chronobiologist, fortuitously noticed when peering out the window of his academic office ~00:00h – between the sampling times of an around-the-clock research project exploring circadian rhythm-dependent effects of medications – the unexpected full blooming of the cactus plant of the university garden at the time of the full moon.

Serendipitous scientific discovery: Flower blooming at midnight only at full moon

We begin with a true story based on our research of the monthly flowering rhythm of *C. peruvianus* (Ben-Attia et al., 2016). Once upon a time, ~00:00 h, in a public garden far removed from artificial light Mossadok Ben Attia approached the tall thorny candle cactus to photograph its beautiful flowers in full bloom. Even though the full moon was brightly shining, the flashing camera light immediately drew the attention of two nighttime security guards. “What are you doing here? You know visiting the public garden at night is against the law”. “I just wanted to photograph this natural marvel” replied Mossadok. After a fast and thorough search of Mossadok and his possessions, it was evident he did not carry a weapon and that he was actually a Professor at the Université de Carthage. “Are you a Botanist? Were you trying to pick flowers? You know it’s against the law” “No” answered Mossadok. “I am just recording their image; check my camera”. “Why don’t you photograph the flower during the daytime when natural light conditions are best?” “Sorry, my flower opens only during nighttime” Mossadok retorted “Are you joking? “Not at all… and for your information, my flower blooms only at the time of the full moon as a 29.5 day rhythm; when the moon is dark, the cactus is almost totally flowerless, and when the full moon returns flower blooms are again abundant.” The guards were skeptical. “Are you willing to wager your money flowering will occur again at the next full moon? “Yes” asserted Mossadok. “I know the behavior of this cactus; for two years I have been tracking the time-of-month and time-of-day of its flowering.” The guards now intrigued by Mossadok’s story wanted to learn more about the magic wonder flower that they initially perceived as a fairy tale, like that of the legendary Arabic *One Thousand and One Nights*. We cannot warrant the discussion that took place around midnight in the public garden was exactly as worded here, but we can certify it is factually correct.

Mossadok, an accomplished medical chronobiologist, along with other faculty colleagues and students frequent work late into the night at the university. One night while standing before the large bay window of his academic office that provided unrestricted view of the well planted Science Faculty Garden, Mossadok was surprised to see the *C. peruvianus* cactus, which had been completely devoid of flowers earlier in the daytime when he arrived to his office, was now majestically in full bloom. Why was the cactus blooming during the nighttime and not daytime, and why this night and not all other nights? Both for scientific reasons and fun, the flowering rhythm of *C. peruvianus* was carefully explored. In this and other public gardens in Tunisia the cactus with its characteristic candle shaped limbs grows to great height. Mossadok convinced Professor Neziha Ganhem Boughamni, a well-trained plant physiologist of the Université de Carthage, to collaborate and undertake photographic safaris at the time of every full moon to selected *C. peruvianus* plants growing in diverse and rather remote locations in the wild. Mossadok also invited one of us authors (AR) to join the group based on longstanding interest in monthly rhythms (Halberg & Reinberg, 1967; Reinberg, 1970, 1973) and various paradoxical effects attributed to our natural satellite (Reinberg, 1998). Mossadok collected a vast amount of data documenting the flowering rhythm of *C. peruvianus*, and we encouraged him to search for underlying mechanisms. The working hypothesis was the cactus photoreceptors of buds that induce flowering are sensitive to moonlight, even if its intensity is typically 600,000-fold less than sunlight (Baillaud, 2004). The goal was to test, rather than study in depth, the validity of the hypothesis that the nighttime light of the full moon is a putative triggering mechanism of flowering. Thus, the investigative approach was not to construct a sophisticated structure to totally shadow a given cactus, but instead to cover the flower buds of randomly selected branches of plants with black, red, or blue colored cotton sheets – cut with small holes to allow H_2O, CO_2, and O_2 gas exchange (Sweeney, 1987) – to filter suspected biologically active moonlight spectra when positioned exclusively during the nighttime. The buds ceased to grow and flowers ceased to open when the light of the full moon was essentially totally shielded by the black colored sheets, and these inhibitory effects were induced, although to a lesser extent, by the blue and red colored sheets (Ben-Attia et al., 2016).

At the completion of the 3 year investigation, the working group composed a manuscript detailing the profound integrated multi-period flowering rhythmicity of *C. peruvianus*. It was submitted to a high-impact scientific journal. The peer reviewers were less intellectually curious and impressed than the security guards encountered after closing time in the public garden. The reviewers concluded the research to be of low scientific interest, from both theoretical and applied perspectives; a double error in our opinion. The paper was rejected. The first reviewer wrote "A full moon effect; so what?" The second wrote "The naturalistic approach is obsolete, even if a rather unexpected phenomenon is reported". Unfortunately, these opinions concerning the relevance of naturalistic research are prevalent today among scientists of many disciplines. Rhythmic phenomena of plants highly sensitive to changes in ambient light and related mechanisms, including mediating photoreceptors, warrant scientific study and reporting, especially given the growing concern worldwide about light pollution, climatic warming, and desertification that favor in arid areas, for example, those of Tunisia and Israel, development of plants like the Peruvian apple cactus for fruit production (Nerd et al., 1990).

Chronobiology and its multidisciplinarity

A problem experienced by biological rhythm researchers of certain disciplines is scarcity of scientists that possess appropriate expertise to judge the scholarly merit of their work, especially when multidisciplinary. This is nothing new. In 1965, Jürgen Aschoff, a leading European chronobiologist, organized the Feldafing (Germany) international meeting on biological rhythms (Aschoff, 1965). Evenings were devoted to informal discussions; the specific focus of one was: (i) whether biological rhythm research is a new and independent field of investigation and (ii) if specialized journals are needed by chronobiologists to publish their research? Jürgen and Colin Pittendrigh, a prominent American chronobiologist, argued for the publication of biological rhythm papers in conventional journals of the authors' primary field of specialization. Franz Halberg, another leading American chronobiologist, and one of us (AR) vigorously disagreed. We campaigned for a multidisciplinary journal devoted solely to biological rhythm research, since in that era chronobiology constituted a new science with a distinct aim: time as a biological dimension that necessitates new methods of data gathering and statistical analyses. AR posited chronobiology as a field needs to spread the concept that rhythmicity is a fundamental property of all living matter and as such is transdisciplinary (Halberg & Reinberg, 1967; Reinberg & Ghata, 1964). He presented the example of time series data depicting the circadian rhythm of human skin reactivity to a standardized intra-dermal injection of histamine occurring in phase with the circadian rhythm of adrenocortical hormone concentration (Reinberg, 1965). He asked the delegates, "Should I submit my findings to an allergy, dermatology, endocrinology, pharmacology, or biological rhythm journal?" Time passes! Several journals dedicated to chronobiology were subsequently launched, and Aschoff and Pittendrigh published their papers in them.

Moon mythology

Study and appreciation of the biological significance of lunar rhythms by the scientific community at large are clouded by ancient myths. In ancient cultures, myths served to re-tell historical events enabling people to connect with ancestors, places, and past events and to explain natural and everyday phenomena – life, religion (including the origin and lives of deities), derivation of humanity, destination after death, pathway to happiness, and passage of time. Of interest to chronobiologists is astronomical time as conceived in Greece before the time of Christ was in large part based on mythology: Helios' seven herds of 350 cattle correlate closely to the number days of the year, Persephone's half-year descent to Hades and Selene's 50 daughters, respectively, the seasons and weeks of the year, and Helios' 12 daughters the hours of daylight.

The moon and sun in many civilizations are identified by gender, as male gods or female goddesses. Ancient Greeks bestowed more power to female than male deities, particularly sexuality and fecundity (Sissa & Destienne, 2000). Nonetheless, the ancient prototype Indo-European deities appear to have been male, and based on gender-specific language designations, male moon gods greatly outnumbered female moon goddesses. The latter were characteristic of Eastern Mediterranean civilizations. The female Greco-Latin lunar deities, Hecate and Artemis, were not initially linked to the moon (Dexter, 1984), and it was only later that the feminine image was attributed to the East-Mediterranean moon goddesses and associated with humidity, shape, and monthly rhythms. The monthly lunar cycle has long been associated in many cultures with the menstrual rhythm, as evidenced by the derivation of related terminology (See Hardling, 1971).

The moon god – or goddess – is usually viewed as the Master of Time and/or Lord of Wisdom. It was a popular pre-Islamic divinity, exemplified by the Babylonian Sin (also named Nanna) and the ibis or baboon-headed Thoth, the Egyptian god carrying a moon-like disk as a hat. It is of interest that the moon is exhibited as a crescent at the top of many mosques and depicted on the national flag of various Muslim countries. Although the rather widespread prominence of the crescent moon symbol since the fourteenth century does not connote specific religious meaning, it, nonetheless, conveys a link between the moon god and Allah. In Mecca during pre-Islamic times (before 622 CE), the moon god Al-Ilah and its three super-goddess daughters – al-Lat, al-Uzza, and Manat – were honored in the Ka'abh by pagan Arabs, as was Hubal the moon god and lord of 360 idols. The prophet Mohammad rejected these idols; however, the crescent moon symbol survived, for example, as the "Red Crescent" – the Muslim organization cooperating with the "Red Cross" humanitarian network (Morey, 1994; Walker, 1983). The moon god was also prominent in early Chinese, Indian, and South American cultures. Commencing with the Chinese Shang Dynasty ~2000 BC, Heng O was worshiped as a moon goddess and celebrated annually around the fall equinox. Heng O is integrated into Taoist philosophy and religion, symbolizing yin – feminine, negative, and dark – versus yang – masculine, positive, and bright. The Hindu too had specific moon Goddesses, Lakshmi and Parvarti. Moon gods and/or goddesses were incorporated into the culture of early populations worldwide, numbering, e.g. 6 to 7 in North America, 6 in Mesoamerica, 8 in South America, 11 to 12 in the Near East, 21 to 22 in Europe, 16 in Asia, 10 in Africa, and 9 in Oceania (Dexter, 1982; Hardling, 1971; Walker, 1983).

The repetitive and cyclic waxing and waning of moon phase were perceived both as a measure of time and symbol of predictable change, e.g. alternation of birth and death, creation and destruction, etc. Selene, also known as Phoebe, is the origin of the Greek moon goddess; she is typically depicted as driving a chariot drawn by two white horses across the night sky with moon in tow. She is a daughter of Hyperion and Theia from the Titans, a race of deities. The two siblings of Selene are Eos, the dawn goddess, and Helios, the sun god. Together, these three deities bridge day and night, sun and moon, and masculine and feminine. By the process termed syncretism, attributes of some deities were passed to succeeding ones with shift in culture or conquest of empire. Typically, deities were not discarded or rendered obsolete, but assimilated and honored with new names. During the time of the Olympians, Selene was replaced by Artemis, again linked with her twin brother Apollo the sun god, and worshiped as the virgin goddess of childbirth and wild animals. The moon goddesses in Greek mythology also included Hecate and Cynthia, with Selene being regarded as the personification of the moon, more precisely the full moon, associated with birth and creation, Artemis the crescent shaped moon representative of the hunting bow, and Hecate the new moon connected to death, hell, and destruction. The triggering effect of the moon on biological phenomenon might thus be viewed as Selenian (birth and creation). In Roman culture, the moon goddess was initially named Luna (Latin: moon) and later Diana. Just as Helios, from his identification with Apollo, was called Phoebus ("bright"), Selene, from her identification with Artemis, was commonly referred to as Phoebe (Latin feminine form of Phoebus), likely connected to the word selas (σέλας), meaning "light".

In many empires, faith in the moon as a deity was so powerful it perpetrated monotheistic religions. Selene (Σεληνη), Artemis (Αρτεμις), Hecate (Εκατη), and their Roman twin sisters, Luna and Diana, had privileged access to the Pantheon – a kind of "Club Med" resort for deities of the ancient Greek civilization (Sissa & Destienne, 2000). The mythological feminine image of the moon predominated in Greek, Roman, and many other ancient civilizations, as a triple-faced White Goddess, up until " … the male-dominant monotheistic god of Judaism and its successors were the cause of the White Goddess's downfall…" (Graves, 1961). Nonetheless, the ~30-day lunar cycle remained the means of charting the time (day of a numbered lunar month) of celebrating religious holy days and festivals. Although the times of major secular fixed-date events may be designated according to the sun calendar, those of major religious events of importance to believers are based on the moon calendar, for example, for Jews the holiday of Passover (Hebrew Pasech, celebrated between the 15th–22nd day of the Hebrew lunar month of Nissan, the month of Nisan being the 30-day period from the new moon in March to the new moon in April); for Christians the holiday of Easter (a moveable feast celebrated on the first Sunday after the first full moon of the spring); and for Muslims Aid el-Kebir (also called Eid al-Adha that begins on the 10th day of Dhu'l-Hijja, the last month of the Islamic lunar calendar). These time-honored traditions are presumably linked to the fact it was easier for the unschooled and unsophisticated common people of ancient times to tie religious holy days and festivals to specific days of observable and numbered moon cycles than specific days of perhaps a more difficult annual sun cycle calendar.

Interestingly, the moon and sun persist today in the time-referenced language of diverse cultures. The names given to days of the week originate from Teutonic and Roman deities. Saturday was the first day of the week for the early Romans; however, as worshipping of the Sun increased, the Sun's day (Sunday: Latin *dies solis*, meaning "sun's day", a pagan Roman holiday) advanced from the 2nd to 1st day of the week (and Saturday moved to the 7th day), giving rise to Sonntag and Zondag (sun day) in German and Dutch. However, in the modern Romance languages Sunday is tied to the Christian faith and called *Dominica* ("Day of God"), giving rise to Dimanche (god-day in French), Domenica (god-day in Italian). Monday, tied to the pagan worshipping of the moon, is derived from the Anglo-Saxon *monandaeg* and Latin *diēs lūnae* ("moon's day"); this 2nd day was sacred to the goddess of the moon and corresponds today to Lundi in French, Lunedi in Italian, Montag in German, and Maandag in Dutch (http://www.omniglot.com/language/time/days.htm).

Circa-monthly biological rhythms

There is a huge gap, on the one hand, between the almost 4000 year history of the above-discussed traditions and myths that attribute moon phases to various phenomena, and, on the other hand, scientific validation of biological, behavioral, and other rhythms of ~30 days triggered and/or synchronized by the lunar cycle. For example, in many regions every step of grape growing and wine maturation remains oriented to whether the moon is ascending or descending, without challenge to the "Mother of Months", the label given to the lunar cycle by the renowned British poet Percy Bysshe Shelley. An excellent early scientific paper devoted to filling this gap is the 1923 publication of Harold Munro Fox. Quoting ancient scholars in their native Greek and Latin languages, Fox reported the belief (that continues yet today to some extent) among the fishermen of the Mediterranean Sea that eatable gonads, ovary and testis, of sea species are "full" at full moon and "empty" at the new moon. *There is a time to be born and a time to die, a time to plant and a time to unearth what was planted* …." (Ecclesiastes: 2,32). This Hebrew biblical verse is taken into account almost automatically in agricultural and husbandry activities according to the annual cycle as well as fishing activities according to integrated 24 h, lunar, and annual cycles. Fox took an objective approach to investigating the odd biological phenomena of the moon-related gonadal cycle of a Red Sea urchin, considered at that time by some to be a mythical event. Scientists are expected to differentiate myths from facts; nonetheless, it is often difficult to publish valid findings in highly regarded scientific journals about unusual phenomena, particularly when entailing a chronobiological approach and quoting ancient philosophers/scientists like Aristotle and Pliny as done by Fox (1923). According to Fox (1923), many early authors like Aristotle, Pliny, Cicero, St. Augustine, and Bacon contributed to the over generalization of the idea that sea-water species are "full" at the full moon and "empty" in between. Nowadays, this widespread and long-held belief appears to be experimentally true only for a few species, one being the Red Sea urchin studied by Fox. The excellent research of Fox (1923, 1924) and Erwin Bünning (1963) illustrates the value of the "older" ***multidimensional*** naturalistic perspective to complement the currently popular ***unidimensional*** reductionist approach by which the understanding and interpretation of phenomena, including rhythmic ones, may be incomplete or even misleading (Reinberg & Ashkenazi, 2003).

In spite of several reviews having been published during the past decade (e.g. Baillaud, 2004; Cajochen et al., 2013; Kronfeld-Shor et al., 2013) that document moonlight exerts effects on various plant and animal species, many biologists and chronobiologists seem to be unaware of the existence of such phenomena. In fact, there was low probability of discovering the ~30-day rhythm of cactus blooming, because in Tunisia and most other countries visiting city gardens is forbidden at the "witchy hours of night" (Shakespeare: Hamlet). "Aladdin and the enchanted lamp" is an old fairy tale, but the story of "Mossadok and the wonder-flower that blooms at full moon" is real, and as such deserves to be known, even if perceived by some to be strange and trivial. How can it be that when blooming at 00:00h at the time of the full moon the cactus flower is larger than a regular dish plate but during the daytime is closed and concealed? Moreover, how is the nighttime flowering *C. peruvianus* pollinated to ensure its survival? The role of bees was considered, but they are assumed to be diurnally not nocturnally active! We searched the scientific literature for papers devoted to honey bee circadian activity-rest rhythmicity and its flexibility (Eban-Rothschild & Block, 2012; Moore, 2001; Moore et al., 1998; Shemesh et al., 2007) plus publications relating to ~30 day rhythms (Oehmke, 1973). Research spanning the rhythms of *C. peruvianus* flowering and bees constitutes an excellent illustrative example of the transdisciplinary nature of chronobiology, and Mossadok deserves recognition not only for discovering the 29.5 day cycle of flower blooming but uncovering the fact that bees forage its blooming flowers with identical periodicity; they are abundantly present on the blooming flowers during the night and early morning at the time of the full moon as documented by time series photographs taken by Mossadok (Ben-Attia et al., 2016). Substantiation of this periodicity motivated further research to understand its mechanisms, which is reminiscent of the birth of experimental plant chronobiology some 300 years ago through research conducted by de Mairan (1729), who demonstrated in the light-sensitive heliotrope persistence of 24 h rhythmicity of leaf movement in an environment of constant darkness.

Review of the literature suggests preservation across diverse life forms of an integrated circadian, circa-monthly, and circannual time structure of reproduction to ensure survival of species. Space does not enable us to make a comprehensive presentation of all the published findings herein; thus, we focus on a few interesting illustrative examples. Scientific evidence of the importance of the lunar cycle of moonlight intensity mainly comes from study of reproductive phenomena of waterborne species, e.g. the palolo worm (*Eunice viridis*), marine midge (*Clunio marinus*), and grunion

(*Leuresthes tenuis*), besides the previously discussed Red Sea urchin (*Centrechinus (Diadema) setosus*) investigated by Fox (1923), and it likely involves endogenous melatonin/melatonin receptor system and Cryptochrome (*Cry1 and Cry3*) and Period (*Per2*) clock gene neural tissue expression patterns (Ikegami et al., 2014; Takemura et al., 2010). Reproduction of these and other life forms is highly ordered in time, involving not only ~30-day but also circadian and circannual rhythms, presumably indicative of an adaptive trait entailing a well-organized biological time structure established during evolution that took place in a periodic environment with prominent time cues, e.g. light and darkness linked to rotation of the moon around the earth every 29.5 days and rotation of earth around its axis every 24 h and around the sun every 365.25 days (Halberg & Reinberg, 1967; Reinberg, 1970, 1973, 1974, 1996; Reinberg & Ghata 1964; Reinberg & Smolensky, 1983a; Smolensky & Reinberg, 1985).

Palolo worm

Eunice viridis is a polychaete (multiple bristles) worm that dwells among the coral reefs of the South Pacific Samoan Islands. During spawning, sperm and eggs produced in the posterior segment termed the epitoke are shed only for few hours ~00:00 h, generally for three consecutive nights of the waning phase of the 3rd quarter of the lunar cycle during spring – months of October and November in the Southern Hemisphere (Caspers, 1984). The anterior segment of the worm sinks into the sea, while the enormous mass of gonads accumulates at its surface, appearing as a milky mucous as thick as vermicelli soup. Native fishermen closely monitor moon phase to know in advance when to harvest the fatty gonads and schedule palolo feast parties. What is (are) the signal(s) provided by the moon that triggers such events? Moonlight, itself, seems to be the major one; although, the phenomenon is not obliterated when obscured by clouds. Survival of this species relates strictly to the time points of three coinciding periodicities: ~00:00 h (24 h rhythm), ~full moon (~30 day rhythm), and spring (~365 day rhythm), essentially the exact same ones, with almost identical temporal staging, that characterize the reproductive, i.e. flowering (in synchrony with bee pollination), process of *C. peruvianus* (Ben-Attia et al., 2016)

Marine midge

Clunio marinus is a small bizarre insect (Diptera) ~1 mm in length that nonetheless is unable to fly. It spends its entire life in the sea, and its survival as a species is strictly full-moon -dependent. The life span of adult males is only 1–3 h and that of adult females even shorter. *C. marinus* is characterized by a striking sexual dimorphism with very peculiar mating behavior. Mature females are wingless without eyes, antennae, and legs, and although the male body is more fly-like than that of females it lacks mouthparts. In Europe, these animals occupy the intertidal zone of rocky shores along the coast of the Atlantic Ocean. Larvae require the lower fringe of the eulittoral habitat for survival, while adults require substrates outside the water environment for oviposition. The evolutionary solution to the this conflict and survival as a species is a very short adult life-span of a few hours only and precisely coordinated timed emergence of adults of both sexes from the sea to mate, i.e. when water level is lowest during spring tides, around the new and full moon phases. Upon emergence, midges immediately mate, oviposit, and then die in the rising tide. Males, which emerge from the sea 30 to 60 min before females, search for female pupae; when locating a partner, he helps sheds the pupal skin, mates, and then carries the substrates to a larval habitat for oviposition. *C. marinus* can lay eggs only when the sea bottom is exposed, i.e. only for a few hours at lowest tide. Fertilized eggs are positioned on red algae exposed to open air when the sea is at its lowest level, around the full and new moon phases, during spring. Days of spring tide and corresponding lunar emergence temporal patterns of different *C. marinus* populations are similar for all locations along the European Atlantic coast (Kaiser & Heckel, 2012; Kaiser et al., 2010, 2011; Neumann, 1966). However, the time of low tide on spring tide days varies among different localities, with emergence times of the different populations being locally adapted (Neumann, 1966; Neumann & Heimbach, 1979). Both (semi) lunar and 24 h patterns in emergence are controlled by biological clocks; the daytime light/nighttime dark cycle cues the circadian rhythm and moonlight and tidal fluctuation in water turbulence and temperature are proposed synchronizers of the circa(semi)lunar rhythm (Neumann, 1966; Neumann & Heimbach, 1979, 1984). As discussed by Kaiser & Heckel (2012), *ciliary opsin 2* (cOps2) is the candidate photoreceptor mediating both lunar and circadian time cues, with the *cryptochrome 1* (*Cry 1*) clock gene likely mediating lunar timing and two *timeless* genes – *tim2 and tim3* – diurnal timing. Precise coordination with respective to the 24 h, ~30 day, and annual time scales of reproduction-associated activities is required for successful mating of *C. marinus*. The adaptive value of the ~30-day endogenous rhythm triggered by the full moon is obvious. Such a biological rhythm ("circatrigintan" for those who like Halberg et al. [1977] neologisms) is a *sine qua non* for survival of *C. marinus* as a species.

Amazing grunion

Reproduction of the amazing grunion, *Leuresthes tenuis* – small slender relative of the smelt with bluish green back and silvery colored sides and belly – is another full moon-related event (California Department of Fish and Wildlife: https://www.wildlife.ca.gov/Fishing/Ocean/Grunion#28352307-grunion-facts-and-faqs; Reinberg, 1998; Woodling, 1968). At full moon and highest tide along the southern California sandy beach, between early March and early September, the grunion comes ashore to spawn in the middle of the night. A spawning "run" typically commences with a single male fish beaching by wave movement. Successive waves deliver increasingly greater numbers of fish to the upper shore area wetted by the high tide of the full moon, resulting in the beach becoming densely blanketed by grunion. Fertilized eggs are deposited some 20 to 40 cm deep into the moist sand before exhausted male and female grunions are passively returned to sea. A run lasts from 1 to 3 h and terminates as suddenly as it commences, when the tide declines ≥30 cm. Daytime elevated temperature induced by solar irradiation matures the eggs, with young grunion hatching in ~10 days and moved into the sea at the time of the next high tide. Why is the nighttime overcrowded grunion get-together-party, which occurs exclusively under the light of the full moon, almost never cited in review papers devoted to moonlight effects? Perhaps, it is because of the bias of authors to emphasis high tide, i.e. tidal influence, as the determining factor. The fact that spawning grunion runs always commence ~00:00 h indicates involvement of endogenous circadian rhythms. The gravitational pull of highest tide plus bright light of the full moon at the right time during the 24 h (night) and year (spring) in combination most likely constitute synchronizing time cues that signal reproductive activities of grunion to ensure their survival as a species.

The question of what is (are) the advantage(s) for a given individual and/or a given species to possess an endogenous ~30 day biological time structure synchronized by the lunar cycle is not easy to answer (Reinberg & Ashkenazi, 2003). In the case of the marine midget, there is no doubt its survival as species is directly related to the full moon acting as a synchronizing signal at the molecular level mediated by specific clock genes. The same explanation applies to the grunion, for which the effect of the highest tide at full moon ~00:00 h is critical, since it ensures survival of it as species. However, is it advantageous for the palolo worm to have its eggs fertilized at full moon? Obviously, the mass production of gonads increases the probability the next generation will survive, despite the voracious harvesting behavior of its major predator – the fishermen of the Samoan Islands. Why this activity is programmed at full moon, nonetheless, remains unanswered. Also, why is one species of the Red Sea urchin "full" at the full moon but not the other species of urchins dwelling in the same and other bodies of water, such as the Mediterranean Sea and Channel of the North Atlantic Ocean (Fox, 1923, 1924)? This kind of exception, perhaps, contributes to the myth of certain marine animals with a mating behavior triggered by a given lunar phase.

*Fascinating human (*Homo sapiens*)*

Reports of lunar periodicity in the biology and/or behavior of human beings, in particular, are often met with skepticism. Poor research methods, incomplete and biased databases, inappropriate statistical techniques, faulty and/or over-generalized conclusions, and non-reproducible findings strengthen mythological beliefs about the moon. Moreover, too many investigators mistakenly interpret statistically significant correlation in time between moon phase and change in one or more study variables as evidence of causality, which need not be the case, particularly when the full complement of germane variables is not simultaneous explored and research methods insufficient. Thus, over the years publications report, for example, evidence of lunar periodicity in human labor and birth, mental health crises and hospitalizations, acute coronary syndrome, myocardial infarct, cardiac arrest, intracranial aneurysm rupture, stroke, accidents/trauma, and medical procedure outcomes (e.g. Ahmad et al., 2008; Ali et al., 2008; Ghiandoni et al., 1998; Gupta et al., 2015; Mao et al., 2015; May et al., 2007; Oomman et al., 2003; Schuld et al., 2011; Templer et al., 1982; Wake et al., 2008), while essentially an equal or greater number of publications pertaining to these very same topics do not (e.g. Arliss et al., 2005; Biermann et al. 2005; Byrnes & Kelly, 1992; Coates et al., 1989; Eisenburger et al., 2003; Kelly & Rotton, 1983; Lahner et al., 2009; Laverty & Kelly, 1998; Martin et al., 1992; Nadeem et al., 2014; Wende et al., 2013; Wilson & Tobacyk, 1990).

Nonetheless, findings of several well-conducted investigations suggest evidence of a circa-monthly time structure of women of reproductive age. Several decades ago, one of us (Reinberg, 1970; Reinberg et al., 1966) conducted studies to determine if ~30 day rhythms of young women (i.e. body temperature and menstruation) are endogenous or exogenous in origin. Isolation experiments were performed in constant environmental conditions of an underground cave, essentially without temporal change in temperature and relative humidity, and in the absence of natural or artificial (clocks) time clues and cues. In one study, a 28 year old healthy woman with normal and regular menstrual cycles, without medical history of oral contraceptive use, volunteered to self-assess a set of biological rhythms before (296 days), during (88 days), and after (87 days) such isolation. Dim light provided by a forehead-worn lamp (<50 lux at 1 m) was allowed as desired when awake. The period (τ) of the menstrual cycle ($\overline{x}$ ± S.E.M.) was 29.1 ± 0.4 days before, 25.7 ± 0.6 days during, and 29.4 ± 0.8 days after isolation. Spectral analysis of the body temperature time series data revealed the circadian τ was 24.0 h before and after isolation but longer, 24.5 h, during it, while the body temperature circatrigintan τ was, respectively, 29.4 and 29.3 days before and after isolation, but shorter, 25.9 days, during isolation (Reinberg & Smolensky, 1983b; Reinberg et al., 1966). Thus, the direction and amount of change in the menstrual cycle τ was essentially identical to those of the body temperature circatrigintan rhythm, thereby indicating both the circatrigintan and circadian body temperature rhythms are endogenous.

The words “menstruation” and “menses” are derived from the Latin *mensis* (month), which relates to the Greek *mene* (moon) – root of *month* and *moon*; however, does the ~30-day lunar cycle and/or full moon synchronize the menstrual cycle and/or reproductive activities of human beings? Results of most recent studies conducted on young women residing in today’s man-made 24 h environment of controlled temperature and artificial light fail to support the ancient myth the moon affects human reproduction and fertility. On the other hand, what to do the findings of naturalistic field studies tell us? In the wild, mature female Rhesus monkeys (*Macaca mulatta*) – a distant biological relative of the human from an evolutionary perspective – display regular menstrual cycles, but only during specific months of the year “gated” by the annual cycle in daytime photoperiod duration (Smolensky et al., 1972). Most intriguing is the field study observation in 1842 by Hille (cited by Dewan, 1967; Dewan et al., 1978; Smolensky & Lamberg, 2000) that female Rhesus monkeys menstruate at the time of the new moon indicating, based on knowledge the luteal phase is of 14 days duration, that ovulation and the most fertile time of the month is at full moon.

Does moonlight have the potential to synchronize and "gate" biological events of the human menstrual cycle? Perhaps; that is, results of some studies do not, while others do support such a conclusion. Findings published by Law (1986) are somewhat supportive. He reported a statistically significant synchronous relationship between the menstrual rhythm stage and the lunar cycle phase among 826 young women 16 to 25 years of age not reliant on medical intervention for birth control and having a normal menstrual cycle length; however, only 28.3% experienced menstruation around new moon, suggesting ovulation occurred around full moon, in comparison to the 8.5 to 12.6% of young women who experienced menstruation and presumably ovulation at other times during the lunar month. Moreover, Cutler (1980), who analyzed the menstrual cycle calendars of 312 young women, also not reliant on medical intervention for birth control, did not find ovulation locked in phase with the full moon. In women whose menstrual cycle duration approximated the lunar cycle (29.5 days), ovulation tended to occur between the last through first quarter of the lunar cycle, and this was also the case for women who had an irregular menstrual cycle length. On the other hand, a small number of cleaver studies entailing women with abnormally long menstrual cycles (>>30 days) show exposure during sleep to relatively low-intensity artificial light from a 100 watt bulb of a bedside lamp, so as to simulate moonlight, only on the menstrual cycle nights 14 through 17 (menstrual day 1 corresponding to day 1 of menses) for 2–3 consecutive menstrual cycles normalizes the menstrual cycle to ~30 days (Dewan, 1967; Dewan et al., 1978; Lin et al., 1990). Based on compelling evidence from study of 16 women, Edmond Dewan was granted a patent in 2002 by the US Government (US 6497718 B1: http://www.google.com/patents/US6497718) for use of such light as a "process of phase-locking human ovulation/menstrual cycles". Dewan's findings, along with observations of cycles of reproductive behavior and conception of a wide range of species in the wild linked to the lunar phase, specifically the light of the full moon, spurred the populist movement of "lunaception" – a non-medication means of controlling, i.e. enhancing or suppressing, conception (Lacey, 1975). In addition, epidemiologic and other types of investigations suggest rather prominent innate and/or environmentally triggered or synchronized annual rhythms in human reproductive biology, behavior, and conception (Bronson, 1995; Cummings, 2010; Roenneberg & Aschoff, 1990a, 1990b; Smolensky & Lamberg, 2000; Smolensky et al., 1972, 1981; Tjoa et al., 1982). Too, there is abundant evidence of profound circadian organization at the molecular level of the hypothalamo-pituitary-ovarian-oviduct-uterine axis (see Boden & Kennaway, 2006; Kennaway, 2005; Sellix, 2013, 2015; Sellix & Menaker, 2010) of mammals, including humans. The LH surge in diurnally active women is estimated to take place during or at the end of nighttime sleep (Cahill et al., 1998; Kerdelhué et al., 2002), with ovulation 24 (Vermesh, 1987) or 36–48 h thereafter (Khattab et al., 2005; Wilcox et al., 1995), although its usual circadian time is not yet known. Interestingly, the LH surge of the diurnally active rodent *Arvicanthus niloticus*, sometimes utilized as a laboratory model for the time structure of diurnally active humans, typically occurs near the end of the dark (rest) span, with mating and likely ovulation before dawn (McElhinny et al., 1999).

Taken together, the majority of research findings is consistent with the hypothesis that reproduction of humans, like that of various plant and marine species, some of which were reviewed herein, is organized with respect to the 365.25 day, 29.5 day, and 24 h time scales as biological rhythms that under *natural* environmental conditions are synchronized by corresponding annual, lunar, and nyctohemeral photoperiodicities. In other words, emerging findings suggest the same biological cycles of reproduction observed in certain plants and waterborne animals may be preserved across diverse species, including *Homo sapiens*. A proposed possible underlying mechanism of circamonthly rhythmicity in humans could involve the intrinsically photosensitive retinal ganglion cells (ipRGC) that sense specific (blue spectrum) wavelengths of both daytime and nighttime natural ambient illumination, with this biologically meaningful information conveyed via the retinohypothalamic neural pathway first to the SCN to regulate transcription of clock genes – including the preserved protein-coding cryptochrome genes, *Cry1* and *Cry2* – and thereafter paraventricular nucleus, hindbrain, spinal cord, and superior cervical ganglion pathways to β- and α-receptors of the pineal gland to regulate melatonin synthesis nocturnally (Arendt, 1997; Reiter, 1998). The inability to detect a consistent and robust moonlight effect on menstrual cycle staging could be the unintended consequence of life today in a man-made artificial environment that almost completely shields humans from natural light of the sun, moon, and stars, with exposures instead to biologically active blue spectrum-rich synthetic light both during night and day. The expected outcome effect could thus be disturbed, masked, or obliterated innate human reproductive rhythms – as demonstrated in experiments entailing *C. peruvianus* when buds were shielded from moonlight by cotton sheets of various colors (Ben-Attia et al., 2016) – and additionally risk of disturbed well-being, pathology (Cho et al., 2015; Haus & Smolensky, 2013; Kim et al., 2015; Smolensky et al., 2015), and perhaps altered fertility through disruption of the time structure of the biology of reproduction (Boden & Kennaway, 2006; Cahill et al., 1998; Kennaway, 2005; Kerdelhué et al., 2002; Sellix, 2013, 2015; Sellix & Menaker, 2010), as suspected in the blind (Bellastella et al., 2014). Finally, it is noteworthy that in the absence of fundamental natural field observations and investigations, as highlighted herein, knowledge and understanding of the potential role and mechanisms of integrated 24 h, lunar, and annual biological rhythms and their synchronization by environmental light cues of corresponding period on the reproduction and survival of plant, fish, and other animal species – even human beings – surely would have been slowed and compromised.

Conclusion

The aim of this editorial is to bring to the fore the importance of the often disregarded ~30 day temporal patterns, especially apparent in natural settings, of various life forms, as exemplified herein by the Peruvian apple cactus, Red Sea urchin, palolo worm, marine midge, grunion, and perhaps human being, triggered and/or synchronized by the light of the full moon. However, admittedly indisputable evidence of an exact causal relationship is yet to be established in many cases. No doubt this is a weakness. In part, this is compensated by the predictability of biological events, i.e. that they do and *will* in the future occur at the same time of the lunar cycle, such as the full moon. Both palolo and grunion fishermen can fully rely upon the full moon to trigger the precise time of spawning, as did Fox (1923) with his Red Sea urchin. The probability of missing this expected full moon-related event is essential zero. Thus, even though the specific nature of the triggering signal(s) may remain unclear, involvement of the lunar cycle can be tested and verified as a causal factor.

Conflict of interest

The content of this article represents the collective contributions of the listed authors. No one has commercial interests of any kind to declare that are of relevance to the contents of this article.

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