Contents

Chapter One

Living in Earth's Geophysical Cycles

I grew up in the historic tourist town of Rotorua. It wasn't uncommon for jet-lagged 'foreigners' to have motor vehicle crashes because they were driving on the wrong side of the road (we drive on the left). My father, a policeman, was a shift worker. My mother was the second of 13 children and gardening, by necessity, was important for our extended family.

Looking back on it now, I see that my childhood gave me practical awareness of the challenges of flying across time zones and trying to work out of step with the day/night cycle. I can still visualise the seasonal changes in Mum's flowers and the family vegetable gardens. I recall the bitterly cold walk to school on some winter mornings and the summer joy of swimming in clean lakes. Perhaps this explains why, when I began studying chronobiology, it immediately seemed to make intuitive sense.

This chapter steps through some of the basic principles in chronobiology: how the day/night cycle, the lunar cycles, and the seasonal cycles arise, and some of the amazing adaptations that different species have developed to cope with these predictable changes in their environments.

A note on terminology. Throughout this book, the word 'cycles' is used to describe the regular fluctuations in the external environment (day/night cycles, tide cycles, lunar cycles, seasonal cycles). The word 'rhythm' always refers to an internally generated oscillation in some function of a living organism, which is an adaptation to a geophysical cycle. These internally generated rhythms typically do not have exactly the same periodicity as the geophysical cycles, so they have the prefix 'circa' (about). Circadian rhythms are about 24 hours; circatidal rhythms, about 12.4 hours; circalunar rhythms, about 28 days; and circannual rhythms, about a year. Time cues from the geophysical cycles lengthen or shorten these internal rhythms to keep them in step with the environmental cycles caused by Earth's rotation on its axis, its orbit around the sun, and the moon's orbit around Earth.

Daily (circadian) rhythms: legacy of Earth's rotation on its axis

As we go about our daily lives, the geophysical cycle we are most aware of is the 24-hour day/night cycle that results from Earth spinning on its axis. Daylight occurs while your part of Earth is facing towards the sun, which is about 150 million kilometres away, so sunlight takes about eight minutes to reach Earth. If you are at the equator, you are spinning at about 1667 kilometres per hour – fortunately we are not aware of this. The rotation speed decreases at higher latitudes, diminishing to zero at the poles. In fact, Earth's axis is slightly tilted with respect to the plane of its orbit around the sun. This tilt is what causes the seasons, as described later in this chapter.

Across the day/night cycle, there are marked changes in light, temperature, and humidity. The most favourable time of day for a given species to be active is influenced not only by the physical environment, but also by the rhythmicity of other species that are key to its survival, such as when its preferred food sources are available

Figure 1.1 The day/night cycle caused by Earth's rotation on its axis (not to scale) with the seasonal cycle caused by the axial tilt.

or when predators are active. Some species are nocturnal, some are diurnal, and some are active around dawn and dusk (crepuscular).

This raises a fundamental question at the heart of chronobiology: are these preferred times for activity simply a direct response to the day/night changes in the environment, or is there an internal timekeeping system that drives these preferences and is sensitive to the environmental changes? A key advantage of having an internal circadian clock is that it enables organisms to predict and prepare for regular daily changes in the physical environment and in important biological factors. As noted above, the main environmental time cue that synchronises the internal circadian clocks of most species is the changing light intensity across the day/night cycle.

One part of my PhD thesis research was designed to examine what controls the daily activity patterns of the Polynesian rat. This small rat is widely distributed throughout the Pacific and is thought to have been carried (intentionally or unintentionally) by the extraordinary Polynesian navigators who dispersed and settled in the different island groups. New Zealand is the southernmost landmass where Polynesian rats are found and are commonly known by their Māori name, kiore. During my research at the University of Auckland, I regularly spent time on beautiful Tititiri Matangi Island off the north-east coast, setting live traps at night to gather my nocturnal research participants. (On New Zealand's main

Figure 1.2 An adult female kiore sitting on my hand. Photo: C. R. Austin

islands, kiore did not manage to compete successfully with the larger Norwegian and ship rats that arrived later with European settlers.)

To see whether the nocturnal activity patterns of these kiore were driven by an internal circadian clock, we kept females in a controlled laboratory environment where all the time cues associated with the day/night cycle were carefully excluded. Figure 1.3 shows the activity patterns of one animal living in her own cage in the laboratory for a total of 87 days at a constant temperature of 21 degrees Celsius. When she moved through a dim red-light beam that crossed the cage, a pen resting on a scrolling paper strip was deflected. When she was moving around a lot, the pen moved back and forth frequently, producing the black 'activity' bars in the figure. Each horizontal line is a strip of paper that represents one day of recording. These pasted strips of paper from more than four decades ago seem a bit visually cluttered compared to the clean digital presentations we are now accustomed to, but they still tell a story.

Being nocturnal, in dim light this kiore was able to see well enough to move around, feed, and groom when she was awake. Across the 45 days in constant dim light (left panel of the figure), she started becoming more active about 45 minutes later each day. In other words, the innate rhythm of her circadian clock in constant

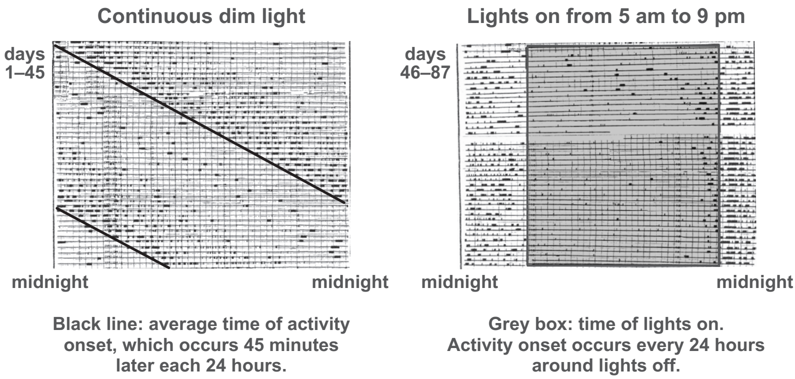

Figure 1.3 Activity rhythm of a female kiore living in a controlled laboratory environment.

dim light was 24 hours and 45 minutes. This is shown by the black activity bars moving progressively to the right (each horizontal strip in the figure represents 24 hours).

From day 46 to day 87, bright lights were turned on from 5 am to 9 pm every day and the rat changed her pattern of activity. Every day she started becoming more active just before the lights went out and then reduced her activity just before the lights came on again. In the right panel of the figure, the black activity bars line up vertically down the page. Her circadian clock was synchronised to exactly 24 hours by the artificial 24-hour light/dark cycle.

Here we see two essential features of circadian clocks: 1) without any 24-hour time cues from the environment, the innate rhythms of circadian clocks are typically not exactly 24 hours; but 2) they can be synchronised to exactly 24 hours by a 24-hour light/dark cycle.

The circadian clocks of kiore control many other aspects of their lives in addition to their daily patterns of activity. The estrous cycle of female rats is regulated by a daily hormonal signal driven by the circadian clock, but it only triggers ovulation every five to six days when the eggs in their ovaries are mature enough. I discovered that I could switch on the estrous cycles of young females that hadn't yet started ovulating by giving them 16 hours of light each day. This sensitivity to day length helps explain why the population on the island started breeding about the same time in November each year (give or take a week or so).

The story of this particular population of kiore gives me pause for reflection on our attitudes to the ecosystems in which we live. Māori, and presumably kiore, had inhabited Tiritiri Matangi from at least the fourteenth century.[1] In the 1850s, European farmers arrived and introduced livestock grazing, which had recently ceased when I started my research in 1977. In 1984, a community habitat restoration project was launched that included extensive planting of native flora and the extermination of introduced species including kiore (New Zealand has no native land mammals except bats). The island is now a wonderful predator-free native wildlife sanctuary that is also actively protected from environmental damage caused by humans.

In contrast to the nocturnal kiore, we humans are programmed by our internal circadian timekeeping system to sleep at night. Our night vision is not great and when we are asleep, our brain largely disengages from what is going on in the environment. This makes us vulnerable so we seek shelter at night, which would also have been a good way for our distant ancestors to avoid nocturnal predators.

The circadian timekeeping system in mammals like us is relatively well understood and is covered in more detail in Chapter Two. Briefly, we have a circadian master clock consisting of about 20,000 nerve cells clustered together in the hypothalamus area of the brain. This master clock coordinates our circadian rhythms from the cellular level through to our moods and behaviour. It has two major tasks: to keep all our rhythms synchronised internally, and to keep them in step with the day/night cycle. Its most important time cue from the environment is the intensity of blue light, which it tracks via specialised cells in the retina of the eye (these are not part of the visual system that enables us to see). Sunlight and artificial white light both contain mixtures of colours (light frequencies) including blue light. For most of the history of life on Earth, the blue component of sunlight would have been the dominant time cue for our circadian rhythms, but the last two centuries have seen an increasingly rapid expansion of artificial light sources with a strong blue light component (see Chapter 6).

Having a built-in circadian timekeeping system prepares us for the predictable environmental changes of the day/night cycle. For example, if we sleep according to our natural rhythms, in the few hours before we wake up in the morning the circadian timekeeping system starts preparing us for the demands of being awake. Our core body temperature begins to rise ahead of the increasing metabolic demands of wakefulness. The ability of our blood to clot increases, ahead of the increased likelihood of accidental cuts after we wake up and become active.

We are unique among species in our determination to try to override the pattern of living dictated by our circadian timekeeping system. Working night shifts, flying across time zones, or staying up late on the internet disrupts our exposure to the natural time cues provided by the 24-hour day/night cycle. The recent human habit of living in orbit around Earth creates a particularly bizarre environment for circadian clocks – for example, crew members on the International Space Station experience 16 sunrises in every 24 hours.[2] All these activities disrupt the intricate synchrony among circadian rhythms throughout the brain and body. A common analogy is that the result is like all the players in a symphony orchestra doing their own thing, or following different conductors, instead of keeping in time with each other. The result is not music, but cacophony. The adverse consequences of circadian desynchrony for our health, safety, and well-being are a central theme of this book.

Lunar and tidal rhythms: legacy of the moon's rotation and orbit around Earth

From observing 'lunatics' to planting crops at specific phases of the moon and predicting the tides, humans have known for millennia that the cycles of the moon influence us and other living organisms. There are multiple geophysical cycles associated with the moon, and to add to the complexity we talk about them in terms of the 24-hour solar day. This section looks at the evidence for internal clocks in living organisms that are adaptations to the environmental cycles generated by the moon.

The moon orbits Earth every 27.3 days (roughly four weeks). It also rotates on its axis once every 27.3 days, so to an observer on Earth its face doesn't seem to change (this is known as synchronous rotation). The combined effect of the moon orbiting Earth every 27.3 days and Earth spinning on its axis every 24 hours means that the moon goes past any given point on Earth every 24.8 hours – the lunar day.

The moon's gravitational pull on the oceans causes simultaneous tidal bulges on opposite sides of Earth, resulting in two tide cycles every 24.8 hours (with about 12.4 hours between high tides). The sun also exerts a gravitational pull on the oceans. When the gravitational pulls of the sun and the moon are aligned, at the new moon and full moon, there are spring tides, with more extreme highs and lows. When their gravitational pulls are at right angles, seven days after the spring tides, there are neap tides, with more moderate highs and lows.

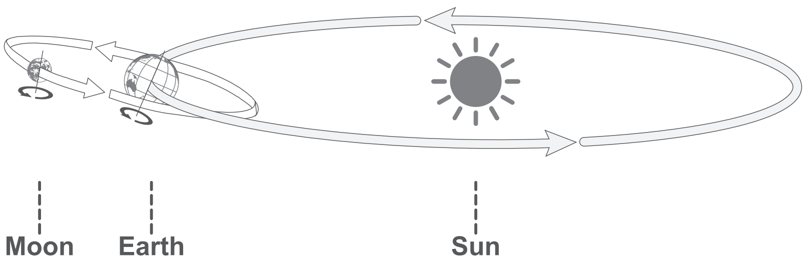

Figure 1.4 Orbits of the moon around Earth and Earth around the sun (not to scale). Both Earth and the moon also rotate on their axes.

The moon does not produce light – moonlight is reflected light from the sun. We see the lighted part of the moon getting larger (waxing) up to the full moon, and then smaller again (waning) down to the new moon. At new moon, the moon is directly between the sun and Earth, so the side facing us is away from the sun. The moon is directly overhead in the middle of the day and not visible at night. At full moon, Earth is between the moon and the sun. The moon is directly overhead in the middle of the night and reflects the sun's light back at us. The full cycle from one new moon to the next is about 29.5 days.

Light intensity is commonly measured in lux. One lux is equal to the illumination of a one-metre square surface that is one metre away from a single candle. Even at full moon, the intensity of moonlight as perceived by the human eye (under 1 lux) is much weaker than direct sunlight (up to 130,000 lux), office light (300–500 lux) or even your computer or phone screen (typically 30–50 lux). Nevertheless, behaviour patterns related to the cycles of the moon

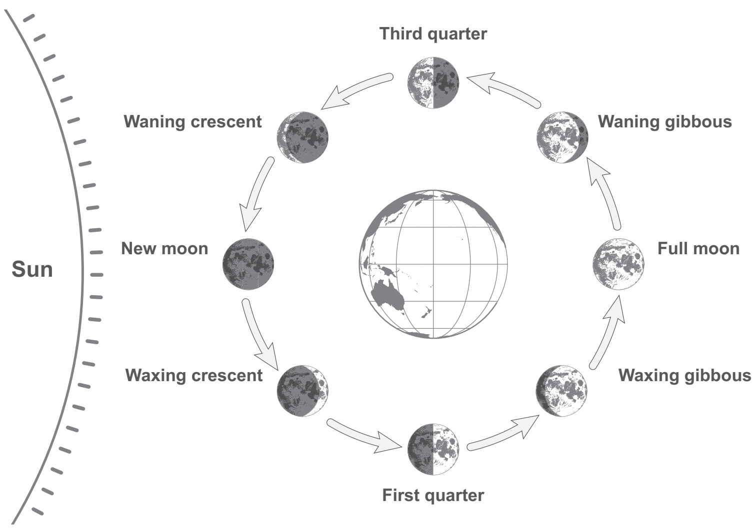

Figure 1.5 Phases of the moon as seen from Earth (not to scale).

have been documented in a wide range of organisms, particularly marine species. What causes them is often difficult to decipher. Some are apparently driven by internal clocks with cycle lengths close to the geophysical cycles (circatidal and circalunar clocks), while others seem to be a direct response to the environmental changes that accompany the tide cycles or the lunar month. In some species there is evidence to suggest that circadian and circalunar clocks interact.[3]

Ancient horseshoe crabs belonging to the genus *Limulus* provide an intriguing example of how complex rhythmicity can be in marine animals.[4] These unusual creatures have been around for about 450 million years. The circadian clock of horseshoe crabs greatly increases the sensitivity of their eyes to light at night, so they can probably see as well at full moon as they can during the day.

During the spring and summer months, females and males come ashore at high tide to breed. In the laboratory, where there are no tidal or lunar time cues, most horseshoe crabs continue to show increased physical activity roughly every 12.4 hours, mimicking their pattern of coming ashore at high tide on their home beach.

This suggests that horseshoe crabs have an internal circatidal timekeeping system that enables them to anticipate and synchronise their activity to the natural tidal cycles. When artificial tides are produced in the laboratory, the peaks in activity synchronise to them. This is the same principle as was shown earlier for the non-24-hour circadian clock of the kiore, which could be synchronised to an artificial 24-hour light/dark cycle.

In nature, the tide-related pattern of activity of horseshoe crabs is most obvious during the breeding season. It may help synchronise the behaviour of males and females to the local tides, thus enhancing the probability of finding a mate and of the female depositing eggs in an optimal location around the high-water line. Outside the breeding season, horseshoe crabs become much less physically active overall, but they have also been observed to move onto the tidal flats during high tides, when they are probably actively foraging, and then move off again during low tides.

Interestingly, in the laboratory horseshoe crabs are more active in warm water (17 degrees Celsius), regardless of whether the experimental light cycle is mimicking long summer days or short winter days. On the other hand, in cold water (4 degrees Celsius) the circatidal activity pattern (becoming more active about every 12.4 hours) disappears. It is possible that horseshoe crabs also have an internal annual timekeeping system (a circannual clock) that regulates the timing of the breeding system, but more research is needed to confirm this.

Do humans have internal clocks to predict and prepare for the cycles of the moon? Opinions vary. The 28-day menstrual cycle approximates the 27.3-day orbit of the moon around Earth so closely that we often assume that the two are related. However, this has not yet been scientifically confirmed. It could be a chance coincidence (badgers also have a 28-day menstrual cycle). In humans, the timing of births has also been thought to relate to lunar cycles. A study in New York City in the 1940s and 1950s found that birth rates were 2–3 per cent higher than average around the full moon, and 2–3 per cent lower than average around the new moon. More recent studies have not always replicated these findings. This could be due to changes we have made since the 1950s, such as increasing use of techniques to induce labour, elective caesarean birth, private clinics having fewer births on weekends, and changes in our use of artificial light.[5]

Intriguing evidence that men may have internally generated circalunar (monthly) rhythms was found in the Mars105 and Mars520 space flight simulation studies.[6] In these studies, 12 healthy young male volunteers spent 105 and 520 days, respectively, in an enclosed habitat designed to mimic living conditions during a round trip to Mars. This consisted of hermetically sealed interconnecting modules with constant environmental conditions, and the crews lived and worked like crews on the International Space Station (but not in microgravity). Although there were no monthly time cues, during the missions they had monthly rhythms in the total amount of sodium in their bodies, even though they had a constant daily intake of sodium and their body weight and total extracellular water content remained unchanged. Monthly rhythms were also detected in the levels in their urine of two hormones made by the adrenal glands, aldosterone and cortisol, which could have contributed to the monthly changes in total-body sodium.

There is a long-standing belief in a connection between lunar cycles and mental illness. According to Shakespeare,

> It is the very error of the moon. She comes more nearer Earth than she was wont. And makes men mad. (*Othello*, 5.2.135)

Indeed, a link between the moon and mental health is implicit in the word 'lunatic'.

How did this belief arise?[7] Some argue that before artificial light became readily available, people were more likely to go out and about on nights around the time of the full moon to work, hunt, travel, etc. This periodic sleep deprivation could switch people with bipolar disorder into mania or increase the rate of epileptic seizures. Lunar cycles could potentially also affect our mental health if they have a direct effect on sleep duration or quality, thereby changing waking mental function. There is some evidence to support this, with indications that there may be differences in how much the lunar cycles affect the sleep of men versus women and across the lifespan.

There is still a widespread belief that mental health crises are more common around the full moon, although recent studies of patterns of patient admissions do not support this.[8] There may be a methodological problem here. If we do have internal clocks changing how we function across the phases of the moon, they would need consistent exposure to the phases of the moon to stay synchronised to them. Society still works predominantly on the 24-hour solar day and most of us have variable exposures to artificial light at night, not regular exposure to moonlight. If some people have internal monthly clocks that affect their mental health, those internal clocks are unlikely to be running in step with the phases of the moon or synchronised among individuals. This makes it highly unlikely that studies focusing on populations of people would find consistent monthly patterns in sleep or any aspect of waking mental health, particularly among urban dwellers in industrialised countries.

In contrast, when US psychiatrist and sleep researcher Tom Wehr looked back at the switches in mood of 18 individual patients with bipolar disorder, he observed that the switches tend to be clustered in patterns lasting one, two, or three semilunar cycles (semilunar – about 14 days, the pattern of the spring and neap tides). This might suggest a possible influence of the moon's gravitational field.[9] Analysis of one patient's sleep/wake cycles suggested that both the 24-hour solar day and the 24.8-hour lunar day were influencing his sleep/wake cycle. When the 24.8-hour lunar cycle dominated, he switched from depression into mania with the new moon, and from mania into depression with the full moon. When he adhered to a rigid 24-hour schedule of rest and sleep during long periods of darkness every night, the lunar component in his sleep/wake cycle disappeared and his mood cycling stopped.

Clearly, there is a lot more to learn about how the cycles associated with the moon affect us and the rest of life on our planet.

Seasonal rhythms: legacy of Earth's rotation around the sun

In many cultures through the ages, the seasons have been celebrated as the repeating cycle of life: from birth in spring, through flourishing in summer, aging in autumn, and death in winter, followed by rebirth in spring.

Figure 1.6 The Green Man, a widespread traditional symbol of the regeneration of nature in spring. Artwork and photo: Philippa Gander

In chronobiology the perennial question arises: are the seasonal changes seen in many living organisms simply a direct response to the changing environmental conditions as Earth orbits around the sun, or is there an internal timekeeping system in those organisms that drives their seasonal changes and is sensitive to the environ-

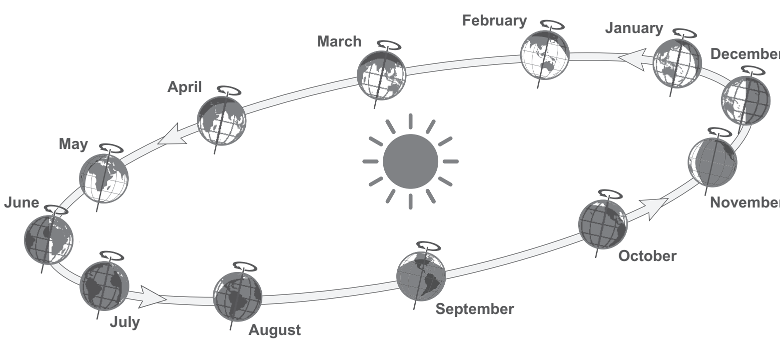

Figure 1.7 Annual orbit of Earth around the sun (not to scale).

Table 1.1 Seasonal Patterns Resulting from Earth's Tilt on its Axis

	Southern hemisphere	**Northern hemisphere**
December–February Southern hemisphere tilted towards the sun	Summer solstice and longest days in December	Winter solstice and shortest days in December
March–May Sun shines equally on both hemispheres	Autumn equinox in March	Spring equinox in March
June–August Northern hemisphere tilted towards the sun	Winter solstice and shortest days in June	Summer solstice and longest days in June
September–November Sun shines equally on both hemispheres	Spring equinox in September	Autumn equinox in September

mental changes? This section looks at the evidence for internal circannual clocks.

Earth takes 365.25 days to complete one orbit around the sun. To keep the calendar in step with this, we have three years of 365 days followed by a leap year with 366 days (by adding February 29).

Earth has seasons because its axis is tilted with respect to the plane of its orbit around the sun, which also means that the seasons in the northern and southern hemispheres are always opposite to each other, as summarised in the table above.

The full story is actually a bit more complex than this table suggests because changes in daylight hours across the year vary by latitude. At the equator (latitude 0 degrees), daylight lasts about 12 hours all year round. At the poles (latitudes 90 degrees north and south) there are almost six months of total darkness and six months of continuous sunlight per year. People living above 66.5 degrees (north or south) experience 24 hours of continuous daylight around the summer solstice and 24 hours of continuous darkness around the winter solstice. In Wellington, New Zealand, where I live (latitude 41.3 degrees south), seasonal daylength varies from just over nine hours to just over 15 hours. In temperate latitudes like Wellington,

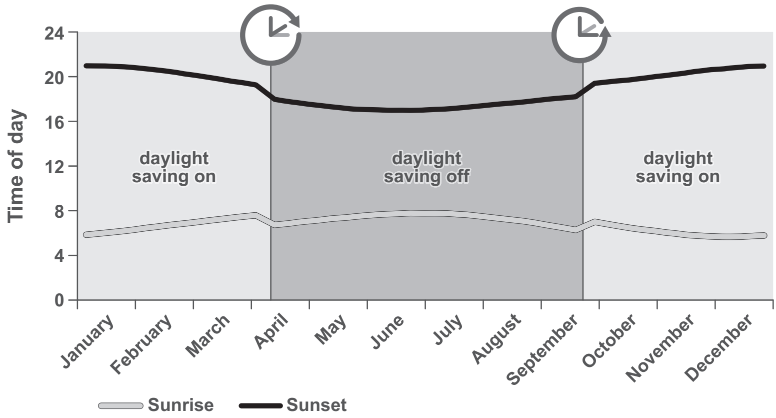

Figure 1.8 2020 times of sunrise and sunset in Wellington, New Zealand. In contrast, daylight saving in the northern hemisphere is typically between March and October - see Table 1.1.

Data from the Royal Astronomical Society of New Zealand, https://rasnz.org.nz/in-the-sky/sun-rise-and-set

changes in daylength (photoperiod) provide a highly predictive signal of seasonal changes in the environment.

Do living organisms have internal circannual clocks that enable them to predict and prepare for the seasons? To demonstrate that this is so, you have to be very patient (and have long-term research funding). You need to keep an organism for years in an environment without seasonal time cues – constant lighting, temperature, and humidity. Nevertheless, a wide variety of species have been shown to have circannual clocks.

For example, in most breeds of sheep, ewes living in natural seasonal cycles come into breeding condition as the days begin to shorten in late summer–autumn.[10] Under these conditions, all the ewes in a flock begin ovulating at around the same time and the lambs are born the following spring. However, in an experiment where ewes were kept for four years in artificial short days (eight hours of light per 24 hours), they continued to show a rhythm of coming back into breeding condition, but this occurred on average every nine months, with some variability among the individual animals. Together with a variety of other evidence, this suggests that ewes have an internal circannual clock with an innate rhythm of about nine months that is synchronised by the 12-month cycle of the seasons. This is once again the same principle shown earlier for the non-24-hour circadian clock of the kiore, which could be synchronised by an artificial 24-hour light/dark cycle.

The idea that a single cell could contain a molecular mechanism that produces a cycle as long as a year initially seemed far-fetched. But fact can be stranger than fiction. The marine algae *Alexandrium* has been doing this for about 200 million years.[11] In summer, it grows as individual cells that self-replicate (by splitting into two identical cells) and can produce the massive toxic algal blooms known as red tides, which cause paralytic shellfish poisoning.

In autumn, pairs of cells join together to form a dense, resistant cyst that sinks to the cold darkness of the deep ocean floor for the winter, where there are no seasonal time cues. As spring approaches on the surface, the cysts germinate and split into two single cells that go back up and start the cycle again. Cysts collected in sea-floor sediment can survive in the laboratory for years in cold, dark conditions. When they are warmed up and placed in constant light, they show an 11-month cycle of reactivation, without any annual time cues from the environment.

Given that ancient single-celled organisms like *Alexandrium* have internal circannual clocks, it has been suggested that this might be an ancestral trait that was passed on to other organisms that arose later in evolutionary history.[12] Consistent with this idea is the evidence that a wide diversity of organisms have internal circannual clocks, including mosses, flowering plants, insects, molluscs, fish, reptiles, birds, and mammals, as well as algae.

One adaptive advantage of a circannual clock is that it provides an internalised sense of annual time where seasonal environmental cues are absent or ambiguous – for example, during hibernation when mammals hide away from the environment to escape the extreme conditions of winter, or when birds migrate seasonally, covering vast distances to change hemispheres and go from winter to summer. Another advantage is that many of the seasonal changes that different species must undergo to survive and reproduce require major physiological changes. It can take weeks to activate the reproductive system, grow or moult a winter coat, or gain weight ahead of migration or hibernation.

Compared to circadian timekeeping, we don't yet understand as much about how circannual timekeeping works in different organisms. For mammals, it has been proposed that there is a hierarchical circannual timekeeping system rather like the circadian timekeeping system for rhythms synchronised by the day/night cycle.[13] The circannual master clock probably resides in pacemaker cells in the pituitary gland and in the adjacent lining of the third ventricle (a fluid-filled space in the middle of the brain).

At the cellular level it is possible that the circannual clock genes may get switched on and off, which leads to marked differences in physiology and behaviour between summer and winter. For example, when mammals hibernate, they go through long periods of torpor, when their core body temperature can go as low as 0 degrees Celsius and their metabolism drops to between 1 and 5 per cent of normal. These are very radical changes compared to how they function when they are not hibernating. A possible mechanism for this has been found in adult thirteen-lined ground squirrels.[14] Not all genes are active all the time in all cells of the body. It has been shown that when these ground squirrels are in torpor, there is a shutdown in certain genes in the liver and skeletal muscles and in the production of the proteins that they code for. At the same time, other genes are activated, along with the production of their corresponding proteins. All this has to be switched back again for the ground squirrels to emerge from hibernation in spring. Clearly more research is needed on how the brain generates circannual rhythms – this research is fascinating, but it cannot be fast.

The primary environmental time cue that synchronises circannual clocks is the seasonal change in daylength.[15] Sensitivity to changing daylengths, known as photoperiodism, is found in many animals, plants and other types of organisms, although the underlying mechanisms vary.

In mammals, for instance, the critical translator of changing daylength to the body is the hormone melatonin. To understand how this might work we need to look more closely at some of what melatonin does in the body. Melatonin is one of two main 'messenger' hormones (the other is cortisol) that enable the circadian master clock to coordinate rhythms throughout the body. In the late evening, the circadian master clock switches on synthesis of melatonin in the pineal gland and then switches it off again in the early morning. This pattern of melatonin secretion is the same in species like humans who sleep at night and species like rats that are active at night, so melatonin is not always 'the sleep hormone', as is sometimes claimed. The circadian master clock not only switches melatonin synthesis on and off, but also has melatonin receptors, so it receives feedback about circulating melatonin levels.

The circadian master clock is not the only thing that switches melatonin synthesis on and off in mammals. Laboratory studies have shown that light above about 350 lux also stops us making melatonin. A recent Australian study with 62 healthy adults found that nearly half of their homes had light in the three hours before bedtime that was bright enough to suppress melatonin synthesis.[16] The study also confirmed that there are marked differences between individuals in the amount of suppression caused by light. Nevertheless, in this study the light levels in the average home would suppress melatonin by nearly 50 per cent in the average person. Greater exposure to light in the evening was associated with increased wakefulness after bedtime.

There are complex feedback loops in action here:

- The circadian master clock controls activity patterns and so influences the patterns of exposure to natural light, which in turn can reset the rhythm of the circadian master clock.

- The circadian master clock regulates the synthesis of melatonin, and the amount of circulating melatonin can in turn reset the rhythm of the circadian master clock.
- Bright light also directly blocks the synthesis of melatonin.

As a result of all this, under natural lighting conditions at temperate latitudes, more melatonin is secreted in the brains of mammals during long winter nights than during short summer nights. This can have different effects, depending on the species. For example, some mammals breed during short days while others breed during long days, depending on the optimum times for pregnancy, giving birth, and the survival of offspring.

Based on current evidence, synchronisation of the mammalian circannual master clock by the seasonal changes in daylength appears to be a two-step process. First, the changes in daylength alter the amount of circulating melatonin via two mechanisms: 1) daylight directly suppresses melatonin synthesis; and 2) daylight synchronises the circadian master clock, which switches melatonin synthesis on and off. Second, seasonal changes in circulating melatonin levels synchronise the circannual master clock. The proposed circannual master clock cells in the pituitary gland are sensitive to melatonin and they control the release of a thyroid-stimulating hormone, which is critical for seasonal rhythms in many species.

So what happens to the circannual rhythms of mammals living at high latitudes, where the sun stays below the horizon continuously for many weeks in midwinter and continuously above the horizon for many weeks in midsummer? Do they have to rely on the changes in daylength around the spring and autumn equinoxes to keep their internal circannual clocks synchronised to a yearly cycle?

Reindeer living in Tromsø, Norway at 70 degrees north don't hibernate to avoid winter. Interestingly, they also don't have circadian rhythms in melatonin levels for about two months around the winter solstice and again for about two months around the summer solstice.[17]

One set of experiments looked at what happened to their circannual rhythms when they were transferred from natural day/night cycles into indoor environments where the temperature was held constant. From midwinter onwards, one group lived in continuous darkness and a second group lived in continuous light. Both groups showed an accelerated onset of the typical springtime increase in food intake, antler growth, and moulting of their winter coats.

The researchers concluded that this happened because in both protocols, the reindeer missed out on the increasing daylengths that they would have experienced outdoors in springtime. They interpret this as evidence that the internal circannual clock in these reindeer had a natural rhythm shorter than a year and that the increasing daylengths in spring somehow stretched it out to 12 months. One possibility is that when the circadian melatonin rhythm first returns, the days are still short and the nights are long, so relatively large amounts of melatonin are produced, which acts as a brake on the usual springtime changes driven by the circannual clock. As the days get longer, the nights get shorter, and the amount of melatonin produced decreases to a level where the springtime changes can begin.

Seasonal changes in daylength are not the only important time cue for circannual rhythms. For example, a great deal of energy can be required for migration, staying warm in cold winter temperatures, and breeding and rearing of the young. For some species, seasonal food availability can affect the timing of circannual rhythms.[18] Interestingly, the proposed circannual master clock cells lining the third ventricle of the brain are sensitive to the nutritional status of mammals.

We have the same basic biology as other mammals. Does this mean that we have retained similar adaptations to Earth's orbit around the sun, including a circannual clock that is sensitive to seasonal changes in day length? One key difference is that we have an additional strategy for managing seasonal changes – we modify our environment.

Historical and experimental evidence suggests that our modification of the physical environment since the industrial revolution has suppressed our seasonal responses. Our increasing use of artificial light has clearly changed our exposure to seasonal changes in photoperiod. Minimising seasonal changes in temperature (through heating and air conditioning) and food availability (through global food distribution and supermarkets) may also have played a role. Facilitated by the internet, our recent headlong rush into 24/7 living is also likely to be having an impact not only on our exposure to the seasonal changes in photoperiod, but also on the day/night changes in light intensity that are the main environmental time cue for the internal circadian clock.

Given strong evidence that breeding cycles in many mammals are controlled by an internal circannual clock, researchers have looked for evidence of this in human populations. Changes in conception cycles around the world are often cited as an example of how we may have altered our seasonal responses. There used to be spring and winter peaks in conception rates in temperate latitudes. With increasing industrialisation in different countries, the amplitude of the annual cycle in conception rates has declined and the autumn/winter peak has become increasingly dominant.[19] For example, in the USA the spring peak was larger until the 1930s, when it was overtaken by the winter peak. Looking at how these two peaks have changed over time, German chronobiologist Till Roenneberg has proposed that industrialisation results in many more people working indoors, thus reducing their exposure to seasonal changes in daylength and temperature. As with the breeding cycles of ewes kept for four years in short daylengths, if many people have circannual clocks that are no longer synchronised by the seasonal time cues and each individual is running on their own internal circannual rhythms, then they don't stay synchronised with each other and the seasonal pattern across the population diminishes.

There is also evidence, particularly in remaining pre-industrial populations, that the seasonal peaks in conception can be influenced by temperature, food availability, and/or cultural practices.[20] For example, the seasonal activities of Copper Inuit people living in Holman, 480 kilometres north of the Artic Circle, were documented in field studies in 1978–80.[21] During winter, people lived together in the settlement. Trapping and hunting activities, which involved men being out of the settlement for several days at a time, declined. Socialising increased with more visiting and shared festivities for Christmas and New Year. In contrast, during spring and summer, nuclear families and young couples spent greater periods of time outside the settlement in ice-fishing or seal-hunting camps, where they also had more privacy and opportunity for intimacy. Most conceptions occurred in spring and summer, and most births in the first half of the year.

Many other aspects of human physiology, behaviour and health also show seasonal patterns. For example, the brain functioning of healthy young people has recently been shown to vary seasonally.[22] The study had 28 participants and used functional magnetic resonance imaging (fMRI) to monitor the activity in different parts of their brains while they did a variety of tasks at different times of year. The patterns of seasonal variation were different for different brain functions. In regard to mental health, in both the northern and southern hemispheres there are winter peaks in attention deficit hyperactivity disorder, anxiety, mania in bipolar disorder, depression, eating disorders, obsessive compulsive disorder, schizophrenia, and suicide.[23]

Seasonal patterns in gene expression relating the the production of more than 4000 proteins have been demonstrated in white blood cells and adipose (fat) tissue. These patterns are reversed in the northern versus the southern hemisphere, matching the seasons occurring at opposite times in the calendar year.[24] The cellular composition of blood also varies seasonally, with reversed patterns in the northern and southern hemispheres. In the immune system, risk biomarkers for cardiovascular, psychiatric, and autoimmune diseases have been shown to peak in Europe in winter.

Once again, the fundamental chronobiological question is what causes all these seasonal patterns in our health and functioning. Multiple factors could be contributing to each pattern. Evidence for the importance of photoperiod is increasingly compelling. At the population level, the large British Biobank study of middle-aged adults controlled for many potential confounding factors and still found a significant association between daylength and cardiovascular mortality and risk factors (blood pressure, markers of inflammation, and body mass index), which all peaked in winter.[25] Longer winter nights were also associated with later and longer sleep, as well as higher rates of reporting insomnia and feelings of low mood and anhedonia (having little interest or pleasure in doing things). For many people with seasonal affective disorder, supplementing their winter light exposure using bright artificial light is an effective way to reduce their depressive symptoms.[26]

Does nightly melatonin production still vary seasonally in humans? Small experimental studies have found that people living in natural light/dark cycles (while camping at about 40 degrees north) produced melatonin for longer on long winter nights than on short summer nights.[27] This suggests that seasonal changes in melatonin might provide a synchronising cue to an internal circannual clock, if we have one.

Clearly, we still have a great deal to learn about circannual rhythms.

This chapter provides just a tiny glimpse into the intricacy and diversity of biological adaptations to the geophysical cycles on our planet that are found in all cell-based organisms. For me, 40-plus years of research in chronobiology has highlighted two vital themes. First, the more we learn, the more there is to know. Second, knowing more about the complex temporal adaptations of life on Earth has become increasingly urgent for our future as a species and for the future of the complex ecosystems that sustain us.

We have also forgotten much that our ancestors understood from careful direct observation of the cyclical changes in their physical and biological environments. This knowledge was often central to their spiritual beliefs and essential for their survival. For example, the ruins of the ancient Mayan city of Chichén Itzá in the northern Yucatán jungle are more than a thousand years old. In the middle of the site stands the 30-metre-high Pyramid of Kukulcán, the Feathered Serpent God. Around the spring and autumn equinoxes, the setting sun falls on the edges of the pyramid's stepped terraces, casting a series of interlocking, triangular shadows that create a beam of light slithering down the pyramid's sacred staircase like a giant snake. As the sun sets, the light beam connects with a stone serpent head at the base of the sacred staircase.[28] The Mayans clearly had detailed knowledge of seasonal changes in photoperiod as well as remarkable architectural and engineering skills.

Figure 1.9 The Pyramid of Kukulcán, Chichén Itzá, at the spring equinox.
Photo: Shawn Christie

Index

Entries in **bold** refer to image captions