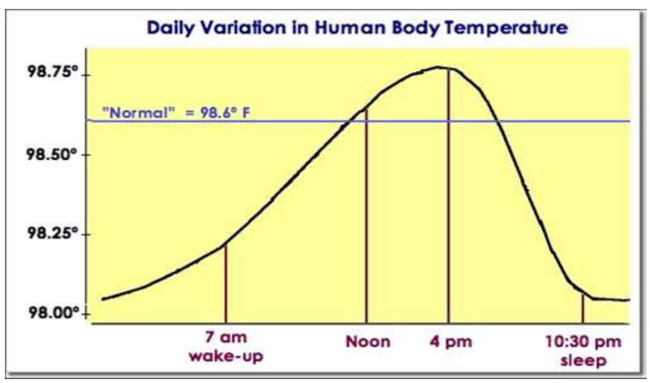
CIRCADIAN, INFRADIAN, AND ULTRADIAN RHYTHMS, INCLUDING THE ROLE OF ENDOGENOUS PACEMAKERS AND OF ENDOGENOUS ZEITGEBERS IN THE CONTROL OF CIRCADIAN RHYTHMS

A **biological rhythm** can be defined as *a cyclical variation over some period of time in physiological or psychological processes*. There are at least 5 types of biological rhythm. However, only three need concern us: **circadian**, **ultradian**, and **infradian rhythms**.

Circadian rhythms ('about a day' in length rhythms)

'Circa' means 'about and 'dies' means 'a day', so a circadian rhythm is one which is 'about a day' in length. Circadian rhythms are a feature of both human and non-human (including plants) physiology and behaviour. Lots of things show a circadian rhythm, but the one we will look at is the **sleep/waking cycle**.



Body temperature shows a circadian rhythm

The main debate with respect to the sleep/waking cycle is whether it is determined by **endogenous pacemakers** or by **exogenous zeitgebers**. In plain language, this is a debate over whether the rhythm is determined by a 'biological clock' or by environmental cues to the time of day, such as whether it is light or dark. This is an example of a **nature versus nurture debate**.

Research suggests that the sleep/waking cycle is clearly *linked* to the day/night cycle, since we tend to be active during the day when it is light, and inactive during the night when it is dark. However, research also suggests that exogenous zeitgebers *do not cause* the sleep/waking cycle, although they may influence it.

Instead, there are several findings which indicate that the sleep/waking cycle is determined by a 'biological clock':

- Everyone sleeps 7 to 8 hours a day irrespective of how much light there is in the environment

- Our biological rhythms persist for a while if our activity patterns change

- Both humans and non-humans maintain an approximately circadian rhythm even if all cues to the time of day are removed

Studies of humans which show that circadian rhythms persist even if all cues to the time of day are removed

Aschoff & Wever (1962): These researchers isolated participants in an underground Second World War bunker for three to four weeks. Although participants could turn the lights on and off when they wanted, there were no cues to tell them what time of day it was. All of the participants showed a circadian rhythm with a sleep/wake cycle of about **25 hours**. Experimental changes in room temperature had no effect on the cycle.

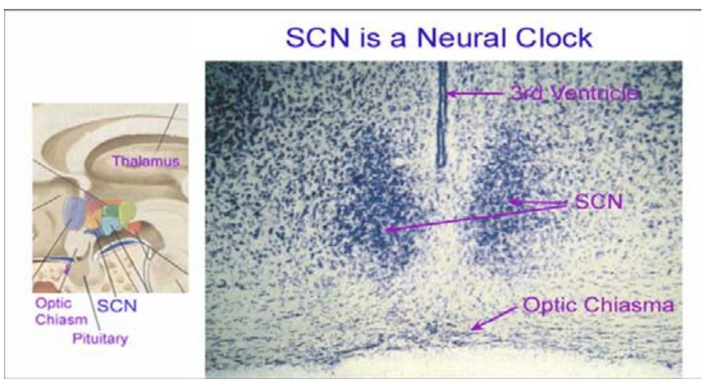
Siffre (1972): Siffre spent 179 days in 'Midnight Cave' in Texas. No natural sounds or light could reach him. He had adequate food and drink, and was able to exercise, but decisions about *when* to eat and sleep were left to him. Whilst he was in contact with the outside world via a permanently staffed telephone, he had no wrist watch or TV set, or any other cues as to the time of day. Various bodily functions and activity patterns were measured. At first, his sleep/waking cycle was erratic. Eventually, though, he settled into a cyclical pattern. However, his regular pattern had a periodicity of **25 hours** rather than 24. So, once every 12 days, Siffre ate breakfast when the world immediately above him ate an evening meal! When he emerged, he believed he had been underground for 151 days (rather than 179). Interestingly, his mood was correlated with how out of step his body was with the outside world: he reported being more depressed and pessimistic when his body was most out of step with the outside world.

Michel Siffre

Miles, et al. (1977) These researchers found a circadian rhythm of **24.9 hours** in a man that was blind from birth. Although there were environmental cues for him to use, he found it difficult to cope with the 24 hour day, and had to take stimulants and depressants in order to cope.

Folkhard, et al. (1996): In this study six students at Swansea University spent one month in a laboratory that had no cues as to the time of day. As in other studies, the students' 'day' lengthened to **25-26 hours**. Additionally, they also showed cyclical variations in memory – STM was better in the morning than in the evening, whilst the reverse was true for LTM.

The biological clock that controls the sleep/waking cycle is called the **Group 2 oscillator**, and it is and it is located in the **suprachiasmatic nucleus (SCN)**, which is part of the hypothalamus. Research with non-humans shows that if the SCN is damaged, the sleep/waking cycle goes haywire. Research also shows that when SCN cells are transplanted in non-humans, the recipient shows the same rhythmic activity as the donor animal.



Note, though, that studies using surgical procedures with non-humans raise questions about ethics, and also about the extent to which the findings can be generalised to humans. However, because case studies of humans with tumours in the SCN show that they suffer disrupted sleep/waking cycles, we can be confident that the SCN is a clock governing sleep and waking.

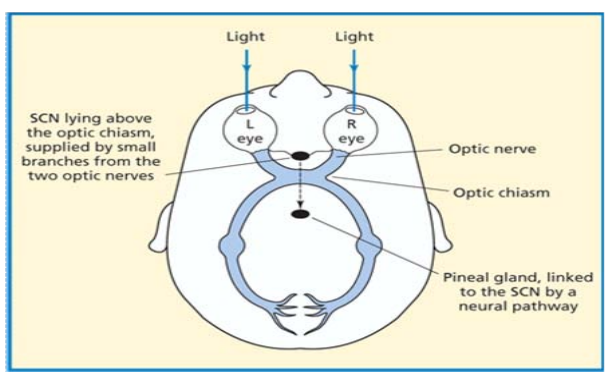
Additionally, the Group 2 oscillator is almost certainly an inherited genetic mechanism. We know this because research shows that this rhythm occurs in developing embryos. Although we can't be certain, the sleep/waking cycle probably evolved to help us anticipate the coming of the sun's rays, and change our metabolism accordingly.

As the studies described above show, without cues as to the time of day, the Group 2 oscillator seems to prefer to operate on a 25-30 hour cycle. We do not know why. However, because the day is only 24 hours long, the clock must be continually 'reset' each day so that the rhythm is co-ordinated with the world we live in. This has important implications when our biological rhythms are disrupted in some way (e.g. by crossing time zones very quickly).

If we accept the research findings from studies such as Siffre's, then the sleep-waking cycle endogenous pacemaker is not perfect, and needs some kind of *environmental input* to correct it each day. When external events play a role in rhythmic activities they are called **exogenous zeitgebers**. In the case of sleep, one of the most influential zeitgebers is light, and we will look at its role in the sleep-waking cycle shortly.

Before that, we will look at the structures that are involved in sleep and waking. **Michel Jouvet** was the psychologist who identified how these structures interact in humans and mammals to cause sleep. The four structures are the **SCN**, the **pineal gland**, the **raphe nuclei**, and the **reticular activating system**.

Specialised photoreceptors in the retina send information about light to the SCN using fibres from the optic nerve. The SCN then passes this information to the pineal gland.



The pineal gland converts serotonin to **melatonin**, which acts on the raphe nuclei. The raphe nuclei uses **serotonin** to send information to the reticular activating system which induces sleep.

What is the evidence supporting Jouvet's theory?

As we have seen, many non-human studies show that if the **SCN** is damaged, light can't reset the clock and the sleep/waking cycle is abolished.

Even when light cues are absent, **melatonin** is still released cyclically by the **pineal gland**, and injections/tablets of melatonin can induce sleep

Substances which inhibit **serotonin** synthesis in the **raphe nuclei** prevent sleep. Sleep is restored if these substances are deactivated

Damage to the **reticular activating system** induces a coma or insomnia, depending on the location of the damage

As noted previously, if we accept the research findings from studies such as Siffre's, then the sleep-waking cycle endogenous pacemaker is not perfect, and needs some kind of environmental input to correct it each day. **Light** is the most obvious zeitgeber, and is necessary if our circadian rhythms are to be co-ordinated with the external world.

Because we normally spend time in natural light, our circadian rhythms can become aligned to changes in light conditions (a process called '*entrainment*'). For example, if you cross time zones quickly, a new set of environmental cues operates. Although some people find adjusting to this more difficult than other people, most of us eventually do adjust to these new cues.

One interesting finding about light as an exogenous zeitgeber was reported by **Campbell & Murphy (1998)**. These researchers monitored the body temperatures of 15 volunteers who slept in a laboratory. The male and female participants were woken at different times and a light pad was shone on the back of their *knees*. The participants' circadian rhythms fluctuated by as much as three hours away from their normal cycle, depending on the time the light was given.

The back of the knee was chosen since light applied here would not reach the participants' eyes and the blood vessels here are very near the surface.

The results suggested that humans do not rely solely on the light that enters the eyes, and that blood may be the messenger that carries the light signal from the skin to the brain.

Be aware, though that this study has *not* been replicated in humans, even by Campbell and Murphy themselves. Other exogenous zeitgebers that affect circadian rhythms include *temperature, humidity, exercise, noise,* and the *availability of food.* However, the relative importance of these is not clear.

Is the sleep/waking cycle really longer than 24 hours?

Although many studies show that our natural cycle is about 25-26 hours in length, there are wide variations around this. **Czeisler, et al. (1999)** have pointed out that it doesn't make sense for us to have evolved an endogenous pacemaker that isn't the same as the solar day. They point out that studies of non-humans show that if kept under constant light conditions, they still maintain a roughly 24 hour cycle.

Czeisler and his colleagues have also conducted their own research using human participants which shows that when kept in very low subdued light, with no cues as to the passage of time, the human sleep/waking cycle operates on a schedule of 24 hours and 11 minutes, rather than the 25 hours reported in other studies.

A further evaluation point could be that in many studies a single individual is the focus of research (i.e. the research method is a **case study**). It could be argued that there is something different about people who volunteer to spend six months underground with no cues as to the time of day, and therefore that data obtained from them do not ***generalise*** to the rest of the population. The same issue applies to research with brain-damaged humans.

All of the research described above suggests that circadian rhythms are biological, which supports the 'nature' side of the nature versus nurture debate. However, these biological rhythms can be influenced by environmental factors. Therefore, circadian rhythms are an **interaction** between nature and nurture.

Ultradian rhythms ('shorter than a day' in length rhythms)

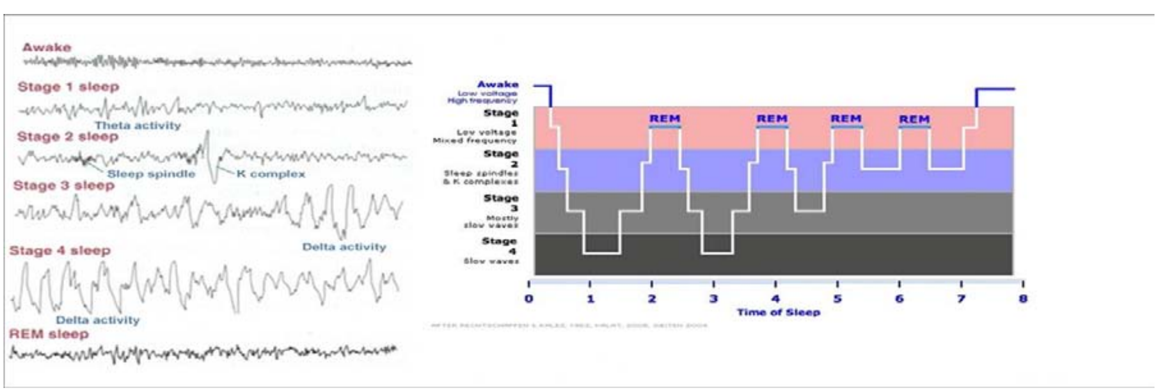
The most well-researched ultradian rhythms are those that occur whilst we are ***asleep***. The finding that the brain is an organ which is electrically active was originally made by a German scientist called **Hans Berger (1929)**.

However, Berger's findings were largely ignored until **1934**, when **Adrian & Matthews** developed a new apparatus for recording brain activity. They called this apparatus the **electroencephalogram (EEG)** and it led to the discovery of different types of 'brain wave'.

Before the EEG's invention, studying what went on in sleep was impossible. However, researchers quickly realised that the EEG was an invaluable tool for studying sleep.

Loomis and Harvey using an EEG machine.
Hobert took the picture. Probably.

The first researchers to measure changes in brain activity during sleep were **Loomis, Harvey & Hobert (1937)**. They found that contrary to popular belief, the brain is not uniformly active/inactive over the course of a night's sleep. Instead, there are times when electrical activity is high, and other times when it is low.



We will return to the stages of sleep in the next topic.

Infradian rhythms ('longer than a day' in length rhythms)

Some infradian rhythms occur on a *seasonal basis*, and are also known as **circannual rhythms**. Circannual rhythms occur on a *yearly* basis. Examples include *migration* in birds, *hibernation* in squirrels, bears and hedgehogs, and *reproduction* in many non-human species. An example of an infradian rhythm in humans is the *menstrual cycle*.

Hibernation is an infradian rhythm

As we have seen with both circadian and ultradian rhythms, there are endogenous pacemakers which govern various behaviours, although these can be influenced by external zeitgebers. The same is true with infradian rhythms. For example, male hamsters show annual rhythms of testosterone secretion that appear to be based on the *amount of light* that occurs each day. The hamsters' breeding season begins as the days lengthen and ends when they get shorter again.

Damage to the suprachiasmatic nucleus destroys these annual breeding cycles, and male hamsters secrete testosterone all year. Presumably, damage disrupts the cycle because it destroys the 24-hour clock against which daily light levels are measured to determine the season. If the period of light is less than 12 hours, it must be winter; if it is more than 12 hours, it must be summer.