University of Toronto
Faculty of Applied Science and Engineering
MAT231 - Modelling with Differential and Difference Equations
Project Two - Team 19

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1. Introduction and Summary

This project focuses on the circadian sleep cycle in which we humans have a 24-hour rhythm that is based on the light/dark cycle. We are looking to develop a predictive sleep model that takes into account timing and duration. We are looking at sleep homeostasis which is describing the sleep drive or the amount of sleepiness. Initially, we are given a piecewise function that varies depending on if the subject is awake or asleep on a scale of 1 to 0 respectively. Our group will document this project in stages starting by defining the problem, listing assumptions that are relevant to constructing the model as well as determining key factors that affect the scenario we are analysing.

2. Defining the Problem

The most meaningful and effective representation of the phenomenological model of sleep regulation and homeostasis is via a two-process model involving the circadian rhythm. The propensity to sleep increases as one is awake and decreases during sleep. The change in this tendency is best modelled via a differential equation in which sleep pressure increases when awake and decreases when asleep. To achieve this, we require certain defining features and parameters to build the model and its restrictions. The most considerable factors include:

- ➢ A differential equation to govern the behaviour and changes in sleep homeostasis
- ➢ Parameters that vary the rate of sleep pressure to fit the subject in analysis
- ➢ Time-dependent functions for the circadian clock to catalyse sleep or wakefulness
- ➢ Constants that define the maximum and minimum thresholds for sleep drive
- ➢ A common period over which the sleep homeostasis and circadian clock operate

With a model that incorporates these factors, various applications regarding one's sleep cycle can be analysed. Such cases include polyphasic sleep, jetlag, effects of stimulants, optimising natural sleep timing, and impact on reaction times.

3. Constructing the Model

Given the change in homeostatic pressure follows a two-process model, it necessitates a piecewise form for the governing differential equation. Each state in homeostasis requires a different time constant given that the rate changes when asleep or awake. Thus, we arrive at a piecewise differential equation:

$$\frac{dH}{dt} = \begin{cases} (1-H)/\chi_{\mathrm{w}} & \text{if awake} \\ -H/\chi_{\mathrm{s}} & \text{if asleep}' \end{cases}$$

Where H is the sleep homeostasis, χ_w and χ_s are time constants that depend on neuronal firing rates, causing the rate for sleep drive to change in between states [1]. For the time-dependent thresholds, we require a cyclical circadian input with an offset to represent the maxima and minima for H. Using these criteria, we get the following functions:

$$H^+(t) = H_0^+ + aC(t) \quad \& \quad H^-(t) = H_0^- + aC(t),$$

Where H_0^+ and H_0^- are the mean thresholds, along with $C(t)$ as a sinusoid of the general form:

$$C(t) = \sin\left(\frac{2\pi}{T}(t - \alpha)\right),$$

With period amplitude a, period T, and phase α. Of these constants and parameters, all but the period T are likely to vary from person to person. This is due to the built-in biological clock of humans being tuned to the Earth's day and night cycle, thus we set the period based on the average human circadian rhythm as $T = 24$ hours [2]. Neuronal firing rates vary between individuals and have noise when measuring, thereby changing the constants χ_w and χ_s, having an effect on the rate of sleep homeostasis [1]. For the base model, we set the subject of analysis to an individual with a stable sleep cycle. For the time constants, we assume average values, thus we get $\chi_w = 18.2$ hours and $\chi_s = 4.2$ hours. Using similar reasoning for the mean thresholds, we arrive at $H_0^+ = 0.60$ and $H_0^- = 0.17$. Given the base case, we assume a synchronised circadian rhythm and as such, the phase $\alpha = 0$ hours [2]. With sleep pressure being bounded in [0, 1], we set the circadian amplitude $a = 0.1$ to confirm the restriction.

4. Analysing the Model and Key Results

We classify the differential equation for $H(t)$ as a linear first-order homogeneous ordinary differential equation and as such, the method of the integrating factor or separation of variables can be used to explicitly solve it. However, to provide more versatility in analysis, we will employ Euler's method to approximate the solution $H(t)$. To make the differential equation a continuous function of $H(t)$ rather than being piecewise, we introduce a sleep indicator variable *s(t)*, which has binary values of *1* and *0* during sleep and wakefulness respectively. Revising the differential equation to accommodate the sleep indicator, we get:

$$\frac{dH}{dt} = \frac{s - H}{\chi},$$

Where s is the indicator variable and χ is the time constant, which changes to χ_w or χ_s depending on whether asleep or awake. Arbitrarily setting the initial condition $H(0) = 0.265$, numerically solving via Euler's method through the Python programming language and using imported modules to plot the solution (see Appendix A), we get the following:

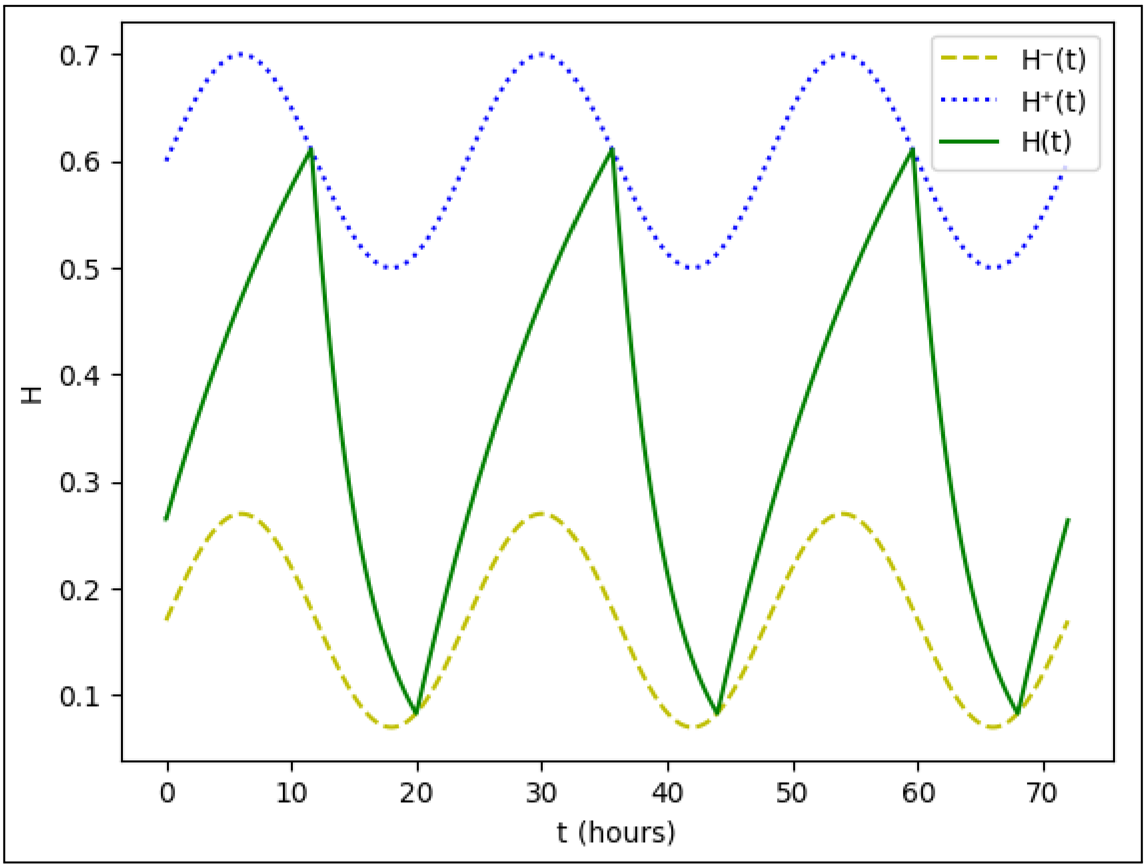


Figure 1. Python plot of the solution *H(t)*, upper threshold $H^+(t)$, and lower threshold $H^-(t)$.

As given in Figure 1, *H(t)* is cyclical in nature. So it would be useful to check whether the differential equation approaches a *T*-periodic solution. To proceed with this, we must confirm that an initial *H(0)* equals *H(T)* in the long run with the condition that *s(0)* equals *s(T)* as well. By running the algorithm until *30T* rather than the default *3T*, we can simulate long-term behaviour. Thus, proceeding with Euler step size $h = 0.001$ (see Appendix B), we get:

```
H(0)  = 0.265
H(T)  = 0.26518032191268465
```

Figure 2. Results in Python for *H(0)* and *H(T)* after being run for 30 periods.

As can be seen in Figure 2, $H(T)$ is not exactly equal to $H(0)$ but very close. This is expected given that it is a numerical approximation. Had it been an explicit solution, then they would have likely been equal. The question of stability in this solution is answered in Appendix C. With this, we can conclude that there always exists a T-periodic solution.

A meaningful analysis that can be done with this model is the case of sleep deprivation. With this, the upper sleep threshold $H^+(t)$ is ignored and falling asleep only occurs when the deprivation is removed and the condition of $H \geq H^+$. We model the sleep deprivation via a time constant representing the number of hours awake since $t = 0$ hours. Thus, we repeat the same Euler's method algorithm with the condition that the upper threshold $H^+(t)$ is ignored for the first period T (see Appendix D). We then arrive at the following plot:

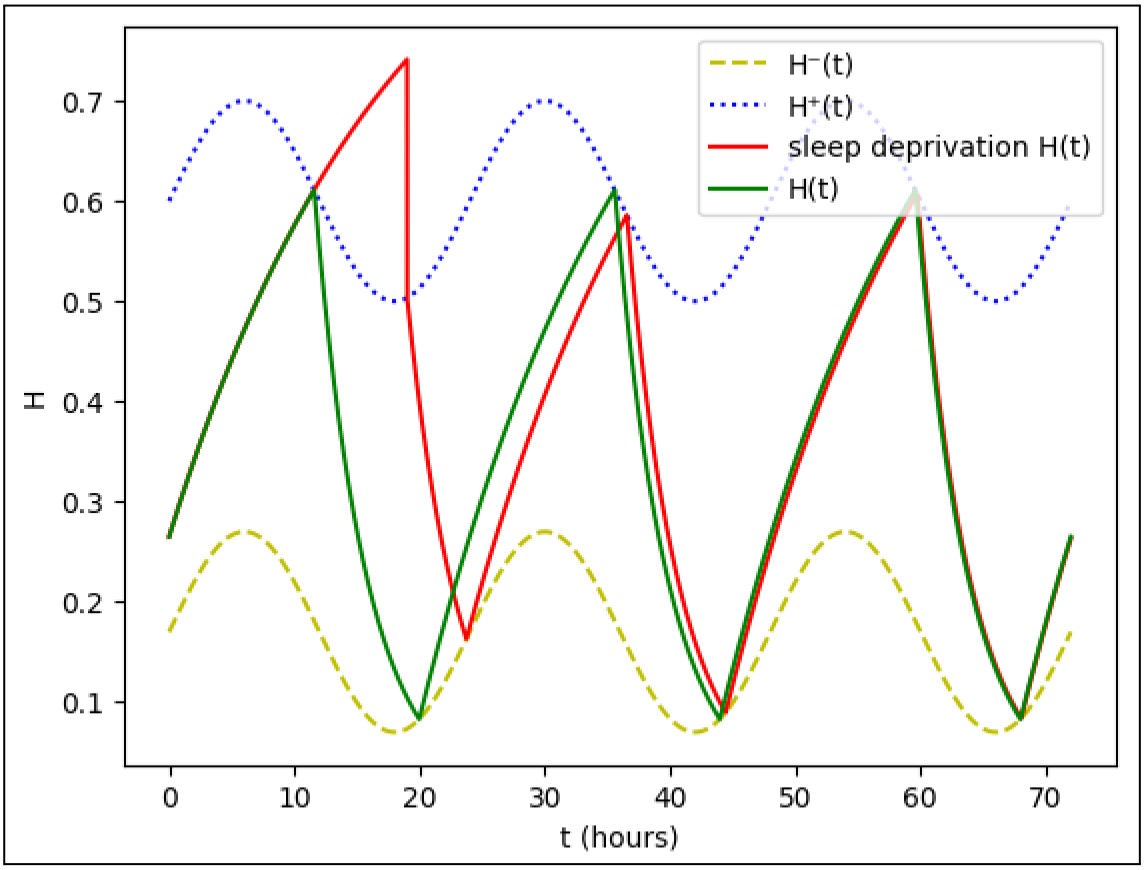


Figure 3. Plot of the sleep deprivation solution $H(t)$, crossing the upper threshold $H^+(t)$.

Via the approximated solution for sleep-deprived homeostasis, we can see in Figure 3 that it approaches the solution for regular sleep homeostasis after a few cycles, which is akin to what happens when one is deprived of sleep. That is, the circadian clock reconfigures and returns to its original cycle after becoming desynchronized. Through rough estimation from the plot, we can see that the sleep duration is relatively the same regardless of whether there has been sleep deprivation or not.

Another relevant analysis that can be conducted is that of polyphasic sleep. That is, having multiple sleep bouts per day, which is a behaviour that infants and many animals exhibit. To model this, we decrease the difference between the mean thresholds H_0^+ and H_0^-. In a sense, this would cause $H(t)$ to ricochet more frequently, thereby being indicative of polyphasic sleep. We alter the upper threshold and set $H_0^+ = 0.40$. Thus we arrive at the following:

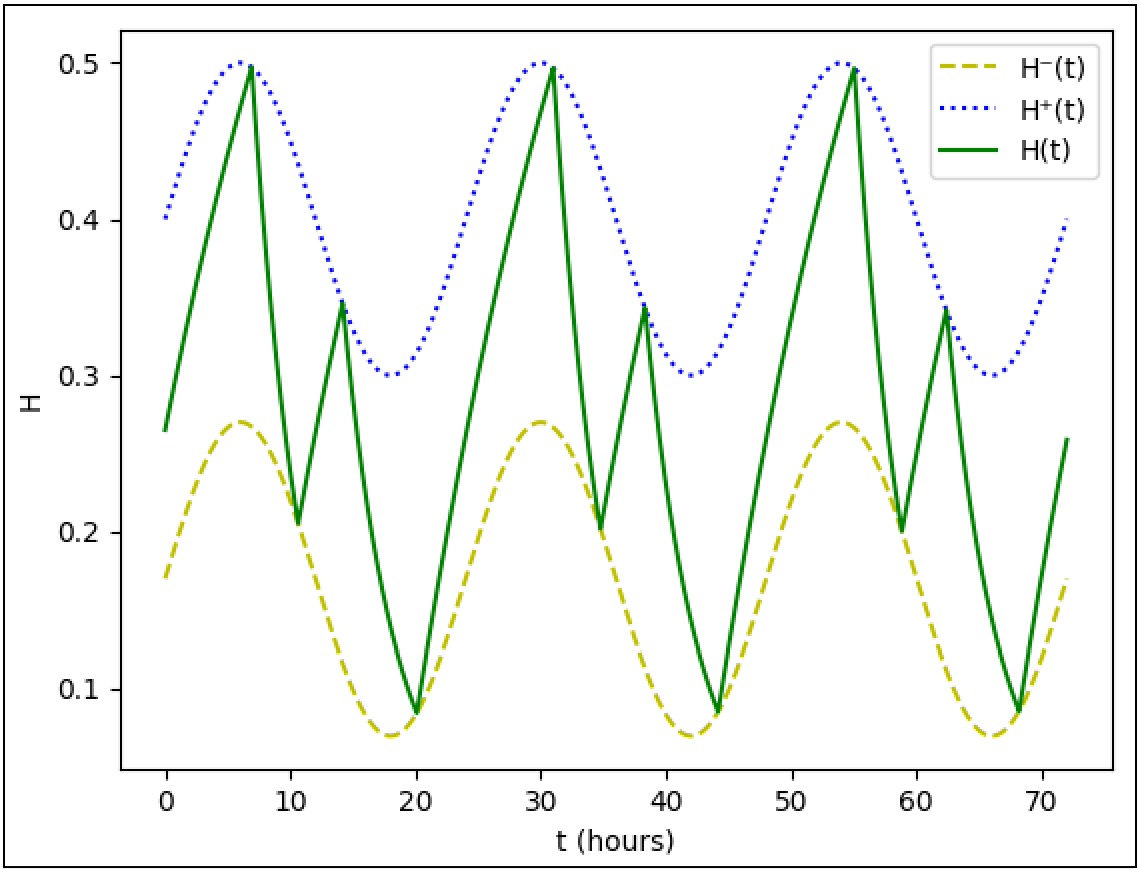


Figure 4. Plot of the solution $H(t)$ with a reduced upper threshold to show polyphasic sleep.

Via the graph displayed in Figure 4, there are more sleep sessions per period T, two to be exact. To determine whether the total amount of sleep changes with multiple sleep bouts per day, we perform analytic measurements for the sleep duration in the first period for regular sleep homeostasis and polyphasic sleep (see Appendix E). We find that the total duration for polyphasic sleep results in about one or two hours higher than regular sleep. For more analysis of applications, see the further research section.

For a final analysis of the properties of this two-process model, we will examine the amplitude a for the circadian input $C(t)$. This model possesses what is known as a glancing bifurcation. That is, a small change in the amplitude a, can result in a large delay in the onset of sleep. We show this by setting the amplitude as $a = 0.05$ and $a = 0.15$ as such:

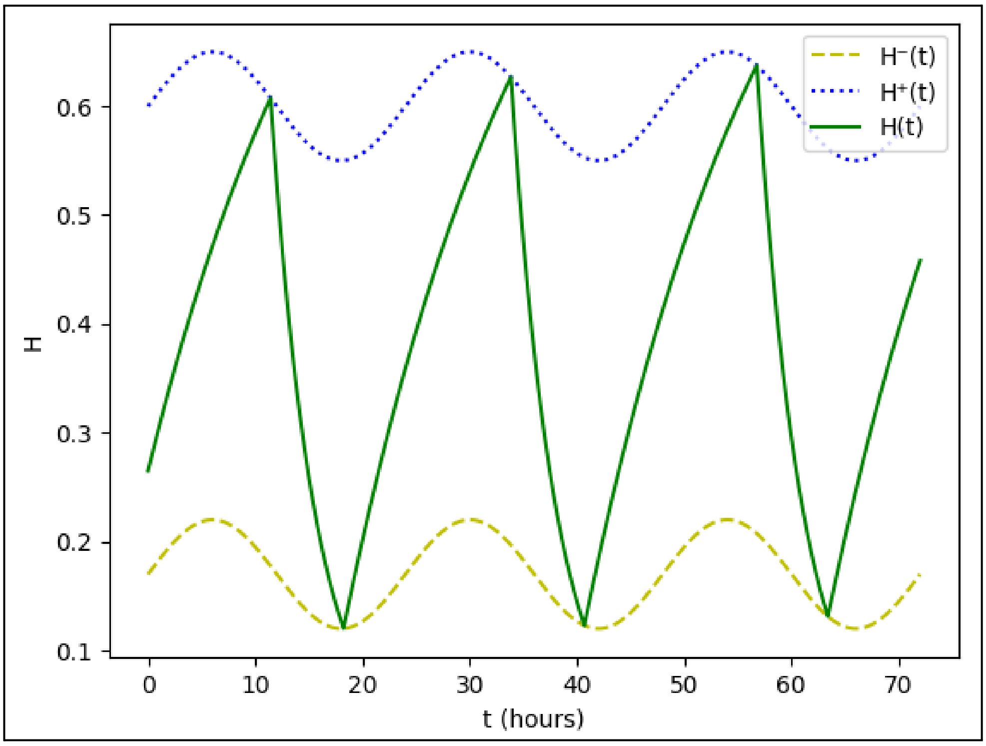


Figure 5. Plot of the regular sleep solution $H(t)$ with circadian input amplitude as $a = 0.05$.

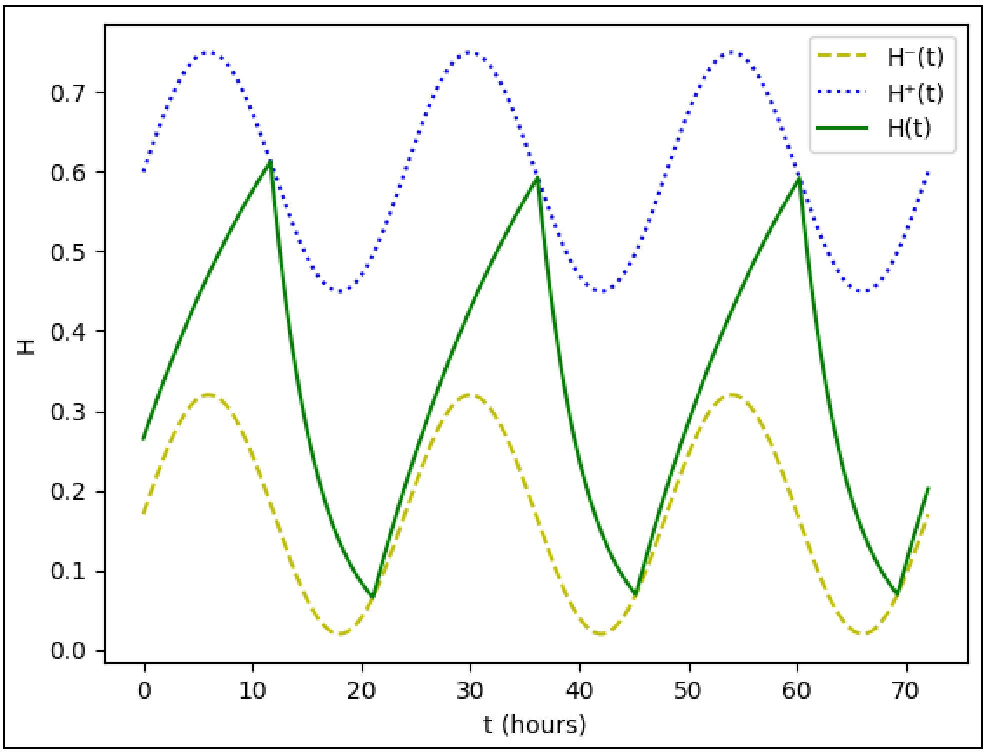


Figure 6. Plot of the regular sleep solution $H(t)$ with circadian input amplitude as $a = 0.15$.

As can be seen in Figures 5 and 6, we have adjusted the parameters of a to a small effect. In plotting these respective values of a, we discover that $H(t)$ reaches its upper threshold in a delayed period. We can conclude that as values of a increase, it takes longer for the green curve to intersect the dotted blue and yellow curves. Using this bifurcation model can allow us to account for circadian oscillations in variating conditions. For example, accounting for different amounts of light and darkness. This parameter can change when travelling to a new region where your body has not adjusted to the 'new' light/dark cycle. In this scenario, there may be a delayed onset of sleep which explains why some people struggle to stay awake during parts of the day when they travel to another time zone.

5. Strengths and Limitations of the Model

Strengths:

- Logic of model is accurate for situations relating to jet lag or daylight saving
- Successful at predicting human alertness in different sleep patterns [5]
- Accounts for deprivation of sleep
- Model is intuitive and simple to understand. Accounts for human behaviour such as napping to readjust sleep cycle.
- The model links the circadian sleep cycle to the light/dark cycle which is logical and conforms to most people's sleep cycle.

Weaknesses:

- Does not take into account chronic cases of insomnia
- Model might only work for a small age range. It could be of benefit to increase sample size that includes various age groups to accommodate different sleep patterns
- In the case where there is a person who works night shifts, the model is limited as it is based on the light/dark cycle.
- If a person's nap patterns are uneven, the model won't be able to account for sleep times as this may change on a day-to-day basis

6. Further Research

Natural sleep time configuration:

This question is extremely dependent on the initial time the subject is currently falling asleep. We will make an assumption that the subject is currently falling asleep naturally later than their preference. Logically, this would mean that they would have to shift their wake-up time earlier each day to achieve this sleep time. Forcing the subject to try and fall asleep at their preferred sleep time would be detrimental to them and may even cause insomnia [6]. According to Dianne M. Augelli, M.D., a person should not shift their wake-up time in big time intervals like 2-3 hours. A more achievable period would be 15-30 min each weak [6], as to allow the body to gradually adapt. However, the question states that the person wants to start this new sleep cycle a few days from now. In this case, the subject should figure out the difference between their current sleep time and their preferred sleep time and calculate the minimum time intervals to decrease wake-up time over a 'few days' from now to set corresponding alarm times each day until they naturally fall asleep at their targeted time.

Prediction after sleep deprivation:

According to the previous analysis, it is obvious to see a daily trend in the fluctuating sleep deprivation from Figure 3. It usually reaches its peak after 20 hours and comes back down after around 5 hours of rest. The model is consistent with the common experience of difficulty falling asleep after sunrise, due to the significant increase in sleep deprivation value starting around morning to midday. Additionally, the difference between staying awake for 4 hours and waking up 4 hours early is based on each individual's sleep cycle. As people are most likely to be sleepiest between 1 to 3 p.m. and 2 to 4 a.m., proven by studies [7], hours of deep sleep decide the amount of rest human bodies can get. According to the model, getting up 4 hours early seems more reasonable since it is able to lower the sleep deprivation value instead of accumulating the lack of sleep if staying up extra 4 hours.

Changes in time zone:

As a person moves from one time zone to another, their body needs to adjust to this change. Several factors affect how quickly our bodies can make this adjustment including how fast we move from one time zone to another as well as direction. There have been many claims that travelling west is easier to adjust to than travelling east for example [8]. Relating it back to our mathematical model, when a person moves to a different time zone, alpha, which is the phase shift, changes slowly for a period T. The parameter alpha needs to change slowly because our body's clock needs to gather signals that are recurring over a period of T days for it to adjust biologically. To answer the question, our sleep times when moving to a new time zone would initially stay similar to the body clock at the place of origin. However, our body's circadian cycle will slowly tend to match the solar light/dark cycle. Typically, this change is expected to take one day for every hour our body's clock has shifted [9]. We can apply the time zone change to the model by changing the phase shift α. We represent a 6-hour and 12-hour jet lag with a phase shift of the same value as such:

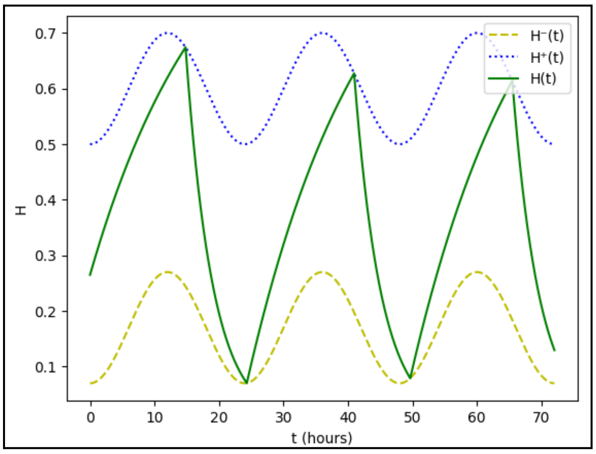


Figure 7. Plot with phase shift α = *6* hours

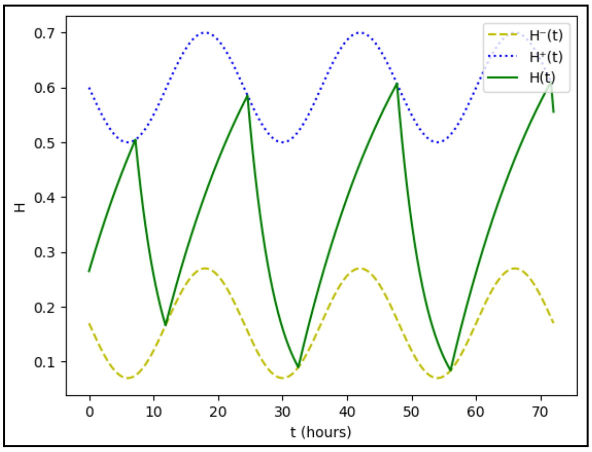


Figure 8. Plot with phase shift α = *12* hours

Thus, we see that the sleeping times have more of a drastic change with the 12-hour jet lag and the circadian rhythm requires more time to synchronize afterwards rather than with the 6-hour jet lag.

7. Appendix

Appendix A:

For use in Python, three libraries are imported to implement the required functionalities:

```
# header files
import math as m
import numpy as np
import matplotlib.pyplot as plt
```

We declare the assumed parameters and initial conditions as their own respective variables:

```
# assumed parameters
Xw = 18.2
Xs = 4.2
a = 0.1
alpha = 0
T = 24
H0p = 0.6
H0n = 0.17

# initial conditions
t0 = 0
H0 = 0.265
s = 0
h = 0.001
tMax = 3*T
```

We define a function taking the initial conditions as input parameters. representing the differential equation with the indicator variable for both cases when awake or asleep:

```
# differential equation
def L(H,t):

    # awake
    if s == 0:
        dHdt = (1 - H) / Xw
        return dHdt

    # asleep
    else:
        dHdt = -H / Xs
        return dHdt
```

We define another function to represent the circadian input as part of the threshold functions:

```
# time varying circadian input
def C(t,T,a):
    return np.sin(((2 * m.pi)/T)*(t - a))
```

We set up the final requirements for the algorithm and create the threshold functions:

```
# time points
t = np.arange(t0,tMax,h)

# initial function setup
H = []
H.append(H0)

# threshold functions
Hp = H0p + (a * C(t,T,alpha))
Hn = H0n + (a * C(t,T,alpha))
```

We iterate and collect numerically approximated points for the solution via Euler’s method:

```
# loop for regular sleep homeostasis
for i in range(len(t)-1):

    # approximated sleep pressure
    H.append(H0)

    # awake
    if s == 0:
        H0 += L(H0,t[i])*h

        # crossed upper threshold
        if H0 >= Hp[i]:
            H0 = Hp[i]
            s = 1

    # asleep
    else:
        H0 += L(H0,t[i])*h

        # crossed lower threshold
        if H0 <= Hn[i]:
            H0 = Hn[i]
            s = 0
```

With the data collected, we plot the solution and thresholds, labelling them with a legend:

```
# plot results
plt.plot(t,Hn,"y--",label = "H⁻(t)")
plt.plot(t,Hp,"b:",label = "H⁺(t)")
plt.plot(t,H,"g",label = "H(t)")
plt.xlabel('t (hours)')
plt.ylabel('H')
plt.legend(loc = "upper right")
plt.show()
```

Appendix B:

We change the maximum iterations for the algorithm such that 30 periods are cycled through:

```
# initial conditions
t0 = 0
H0 = 0.265
s = 0
h = 0.001
tMax = 30*T
```

Thus, to check for *T*-periodic solutions, we print the initial and the final values in the list of approximated solution points as such:

```
# check for T-periodic solution
print("H(0) =",H[0])
print("H(T) = ",H[len(H)-1])
```

Should these values be equal, or relatively close given the approximation, then it can be deduced that there exists a *T*-periodic solution. We find that this is precisely the case:

```
H(0) = 0.265
H(T) = 0.26518032191268465
```

Appendix C:

To check stability, we test initial values close to *H(T)*. If they approach *H(T)* in the long run, then we can conclude that the *T*-periodic *H(T)* is stable. We attempt a higher value first:

```
H(0) = 0.28
H(T) =  0.26527050050389295
```

Seeing how a relatively similar value is approached in the long run, we try a lower value:

```
H(0) = 0.24
H(T) =  0.26509017659322726
```

With relatively similar results again, we find that nearby solutions in fact have the long-term behaviour of approaching the *T*-periodic solution, thereby showing that stability exists.

Appendix D:

For modelling sleep deprivation in Python, we essentially repeat the same procedure that was done with regular sleep homeostasis but with the condition that the upper threshold $H^+(t)$ is ignored for the first period *T*. We, therefore, add the time constant to the initial conditions:

```
# initial conditions
t0 = 0
H0 = 0.265
s = 0
h = 0.001
tMax = 3*T
td = 19
```

We also update the initial setup to accommodate the loop for sleep-deprived homeostasis:

```
# initial function setup
H = []
Hd = []
H.append(H0)
Hd.append(H0)
```

With the initial setup done, we perform Euler's method for sleep-deprived homeostasis:

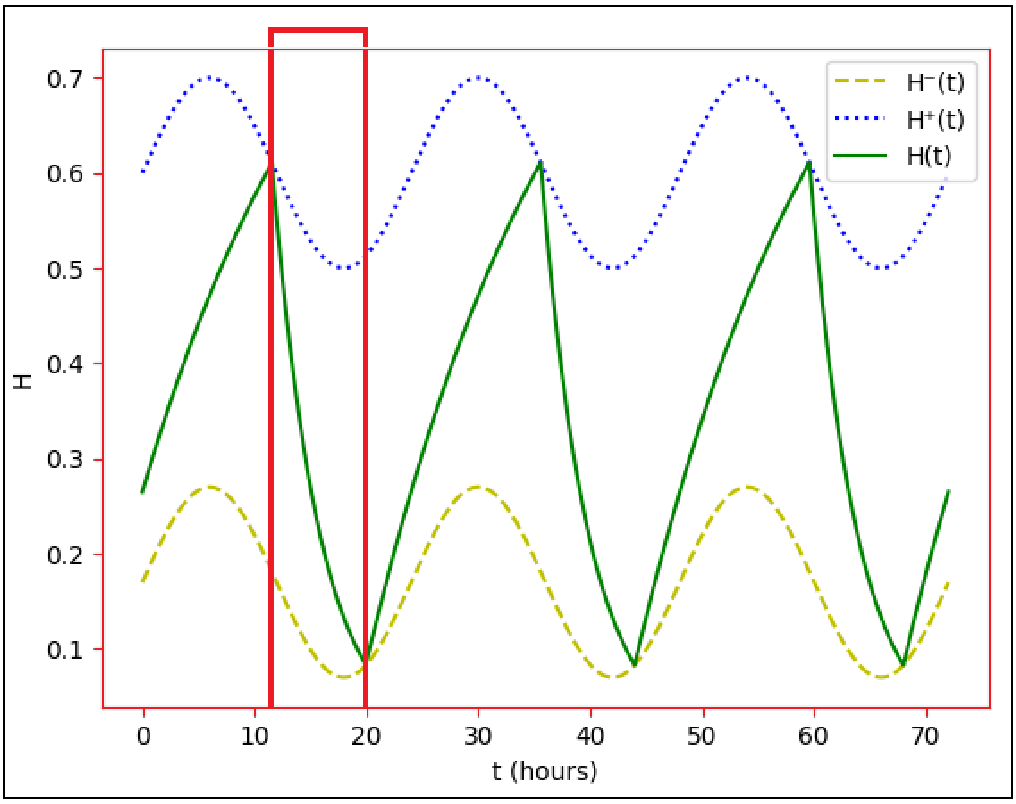
```
# loop for sleep-deprived homeostasis
for i in range(len(t)-1):

    # approximated sleep pressure
    Hd.append(H0)

    # awake beyond upper threshold
    if t[i] <= td:
        H0 += L(H0,t[i])*h

    else:
        # awake
        if s == 0:
            H0 += L(H0,t[i])*h

            # crossed upper threshold
            if H0 >= Hp[i]:
                H0 = Hp[i]
                s = 1

        # asleep
        else:
            H0 += L(H0,t[i])*h

            # crossed lower threshold
            if H0 <= Hn[i]:
                H0 = Hn[i]
                s = 0
```

With new data collected, we plot the results with the solution for regular sleep homeostasis:

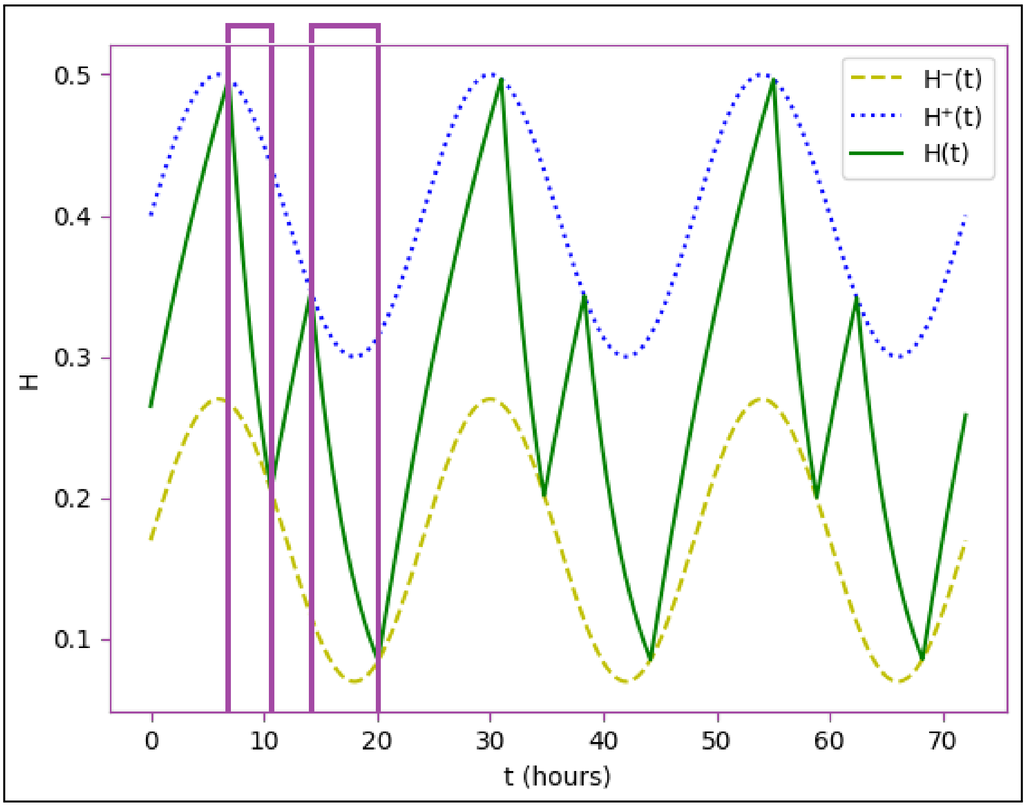
```
# plot results
plt.plot(t,Hn,"y--",label = "H⁻(t)")
plt.plot(t,Hp,"b:",label = "H⁺(t)")
plt.plot(t,Hd,"r",label = "sleep deprivation H(t)")
plt.plot(t,H,"g",label = "H(t)")
plt.xlabel('t (hours)')
plt.ylabel('H')
plt.legend(loc = "upper right")
plt.show()
```

Appendix E:

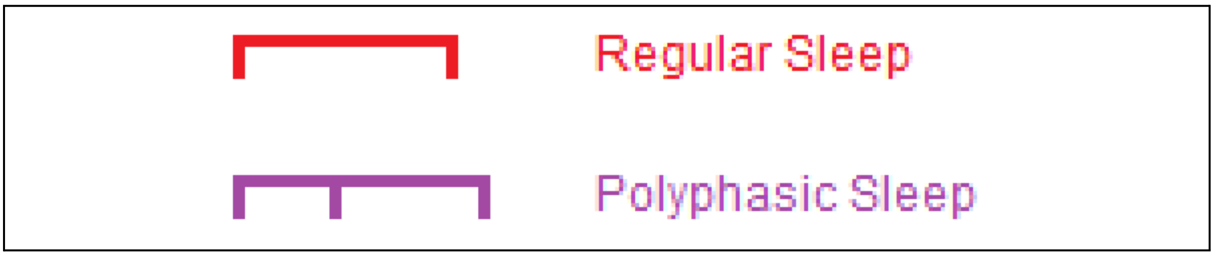
To compare the duration of sleep for regular sleep homeostasis, we measure the sleep time:



Repeating the same process of measurement for the case with polyphasic sleep, we get:



With the measured time durations from the plots, we can form their comparison as such:



We can see that the combined duration of the polyphasic sleep solution is slightly higher than that of the regular sleep, perhaps by the order of one or two hours. Thus with this, we conclude that the total amount of sleep does change with multiple sleep bouts per day.

References

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[2] W. O. J. C. A. F. DB; "A global quantification of 'normal' sleep schedules using smartphone data," *Science advances*. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/27386531/. [Accessed: 07-Dec-2022].

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[9] “Jet lag: Why the body clock is slow to adjust to time changes,” *ScienceDaily*, 29-Aug-2013. [Online]. Available: https://www.sciencedaily.com/releases/2013/08/130829124013.htm. [Accessed: 07-Dec-2022].