Understanding Sleep-Wake Dynamics with Two Process Model and BDB Model

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Abstract

In this paper, we study the 24 hour sleep-wake cycle as a nonlinear system and explore the dynamics of this system as it is influenced by processes such as Homeostatic sleep pressure and Circadian rhythm. To fully understand the dynamics these systems, we first look at the simple Two Process Model and construct one dimensional maps that predict the sleep onset of day $n+1$ based on a given sleep onset of day n. However, in constructing these maps, we notice various discontinuities at certain time points. After careful analysis of these particular areas with discontinuities, it was found that there are grazing bifurcations present that attribute to the jumps in these maps. In plotting these sleep curves at these time points, it found that these curves skirt along the modulating circadian thresholds until reaching a trough where there is an abrupt change in sleep onset. In addition to studying a simple model, we augment our model to the BDB model to incorporate various biological factors such as firing rates of certain neuronal populations. In creating maps of this model, we see similar discontinuities which are also found to be caused by these grazing bifurcations. Therefore it can be concluded that in both models, a small adjustment in initial sleep onset at these particular times can result in a drastic difference in the next sleep onset due to the combination of both Homeostatic Sleep Pressure as well as Circadian Rhythm.

Introduction

The dynamics of sleep are greatly influenced by processes such as sleep need and circadian rhythm[4]. However, the interactions between these processes and our sleep-wake cycle are somewhat nebulous. We look at various models such as the Two Process Model and BDB model to explore these interactions in depth. Our circadian rhythm rises and falls throughout the day and dictates the hours at which we are most alert and inclined to sleep[4]. However, this rhythm is not the sole factor in whether or not we stay awake. Sleep need, or homeostatic sleep pressure, plays a large role in the dynamics of our sleep-wake cycle. As we stay awake, our sleep pressure continues to rise until it reaches a certain threshold. Following this threshold, we feel an inclination towards sleep. Once we finally sleep, this pressure decreases exponentially until we reach a lower threshold at which we are inclined to wake up.

In the BDB model, we start to incorporate factors such as the firing rates of certain populations of neurons like the locus coeruleus (LC) and the ventrolateral preoptic nucleus (VLPO)[1]. Our LC neurons are wake promoting and our VLPO neurons are sleep promoting[2]. These populations are mutually inhibitory[4]. Therefore, when LC neurons are firing, VLPO neurons are not active and vice versa.

Nonlinear equations are particularly useful in modeling various biological systems. For example, we can use the equation $N_{t+1} = RN_t - b{N_t}^2$ to model the growth and decay of a fly population, where R is the number of offspring per generation and b is responsible for the growth rate decrease[6]. By substitution ($x_t = \frac{bN_t}{R}$), we can reduce this nonlinear equation to make $x_{t+1} = Rx_t(1-x_t)$ The behavior of these graphs can vary depending on the R value and can change from a steady state value to periodic to aperiodic. We can generate bifurcation diagrams plotting the behaviors of each of the R values. From these diagrams, we can see the R values at which the periodicity changes. In Figure 1 at R = 2.25, the map changes from steady state to a map of period 2. At R = 2.9, the map changes from period 2 to 4. Following R = 3.1, we start to see aperiodic maps of chaotic nature.

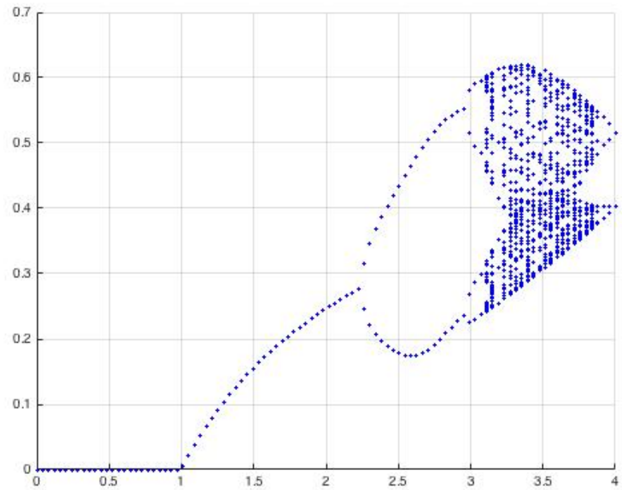

Figure 1: Bifurcation diagram with starting value, 0.5

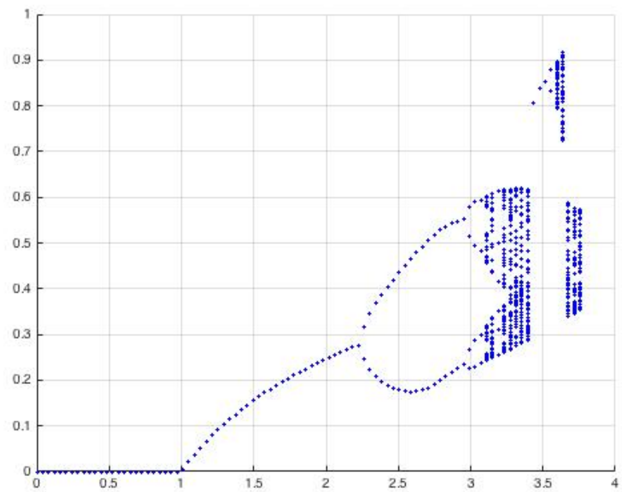

Figure 2: Bifurcation diagram with starting value, 0.8

However, if we try different starting values, it is found that the bifurcation diagrams vary. In Figure 2, we see similar behavior to that of Figure 1, but there appears to be a break in the diagram around R values of 3.4 to 3.6, which the discrete maps temporarily change from aperiodic behavior to periodic behavior. Therefore, it is important to note that different starting values can greatly affect the resulting bifurcation diagrams and the behavior of the discrete maps.

Two Process Model

We now examine the two process model, which maps the increase and decrease of sleep pressure as one sleeps and wakes using the following equations:

$$S(t) = \begin{cases} 1 + (S_{wo} - 1)e^{(t_{wo}-t)/\tau_w}, & \text{if awake} \\ S_{so}e^{(t_{so}-t)/\tau_s}, & \text{if asleep} \end{cases}$$

These curves are plotted with the thresholds of circadian rhythm, portrayed by the following upper and lower thresholds, respectively:

$$C_w(t) = H + c(t), \tag{1}$$

$$C_s(t) = L + c(t), \tag{2}$$

where

$$c(t) = A[0.97sin(2\pi(t-t_0)/p)+0.22sin(4\pi(t-t_0)/p)+0.07sin(6\pi(t-t_0)/p)+0.03sin(8\pi(t-t_0)/p)+0.001sin(10\pi(t-t_0)/p)]$$

and H = .67 and L = .17 for the following iterations.

As seen in the graphs, the blue line is the higher threshold of circadian rhythm and the red line is the lower threshold of circadian rhythm. Between these curves we see the mapping of sleep pressure. As seen by the green lines, as the sleep pressure decreases as one is asleep. When this green line intersects the lower threshold of circadian rhythm, it is the optimal time for one to wake up. This intersection is termed, wake onset. In contrast, when the subject is awake, the sleep pressure builds until the curve reaches and intersects the higher threshold of circadian rhythm. This point in time is where sleep is optimal for the subject and is termed sleep onset. We are interested in how the following sleep onset changes as we alter the time the subject sleep initially. Below, we create discrete maps that essentially map the time in which the subject is expected to sleep the next day.

However, if we examine these maps closely, we notice that there are some unique and characteristic attributes of these maps. Contrary to the general maps studied previously, there appears to be some jumps, or discontinuities, at certain points, where the next sleep onset changes drastically. To understand what contributes to these striking discontinuities, we look at the sleep-wake curves. If we look further at these sleep pressures, we notice that during some iterations, the sleep pressure curves do not quite hit the trough of the higher thresholds. Instead, it seems to graze off the surface and does not actually make full contact with the curve until much later. As a result, we see a spike in sleep onset on our discrete map. However, these grazing bifurcations do not just occur along the higher threshold. In some cases, it occurs along the lower threshold as well. If we look after this first grazing bifurcation in the following graphs, we see that another one occurs along the red curve. The green line portraying sleep pressure seems to graze along the surface of the red curve for quite some time before making contact. It is the grazing seen here that attributes to these discontinuities found on our discrete map.

Now, we look at the following discrete maps and curves for the following age groups: Child, teen, and adult. These parameters for these ages are all the same except for the time constants for sleep and wake. In Figure 3 ($\tau_w = 12.91, \tau_s = 2.95$), we examine the model for the initial time onset values of 7 to 9 hours. We can see that the first grazing bifurcation occurs along the blue curve when the time onset is 3 pm on Day 2. The blue line grazes along the trough and instead hits intersects the higher threshold at 4 pm on Day 3. We see the second grazing bifurcation around the time onset of 4 pm. The green curve skirts the red curve until it intersects the trough of the graph and intersects the blue curve much later, resulting in a jump in the next time set. As a result, the time onset for the following day is 6 pm. These bifurcations account for the two discontinuities in the discrete maps, seen in Figure 4.

Similarly, if we look at the discrete maps and curves for the average teen ($\tau_w = 21.45, \tau_s = 4.96$), we find various discontinuities in the discrete maps. In Figure 5, we find that at time points, 11am and 12 pm of Day 2, there are two major jumps in time onset values. We can see this is consistent with the behavior of the graph generated in Figure 6. The graph once again grazes the trough of the blue curve during the iteration of initial time 3.3 hours and then grazes the surface of the red curve during the iteration of initial time, 4 hours.

The discrete maps for the average adults ($\tau_w = 18.2, \tau_s = 4.2$) also looks quite similar to those of the average child and teen. However, the discontinuities occur at different time points. In Figure 7, we see that at the time points, 1pm and 2pm, the graph displays discontinuities. These jumps, once again, are consistent with those of the graph illustrating sleep pressure along with circadian rhythm thresholds (Figure 8). For the iteration of time onset 1pm, the sleep pressure curve grazes along the higher threshold and intersects the

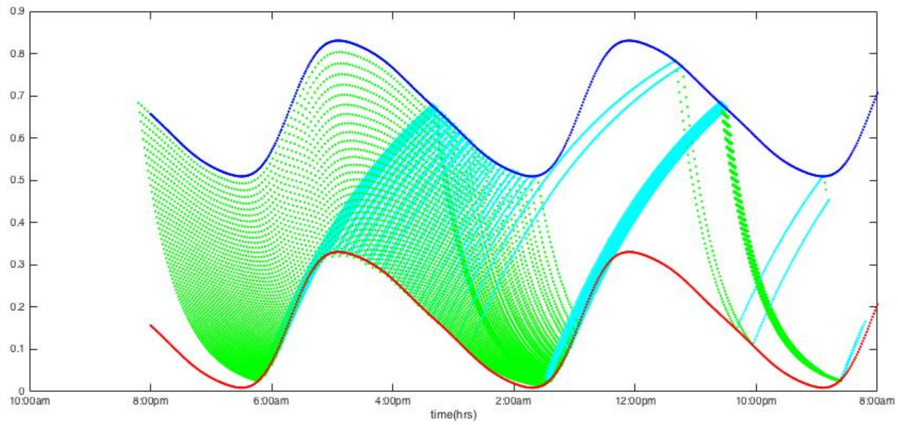

Figure 3: Two process model of average child

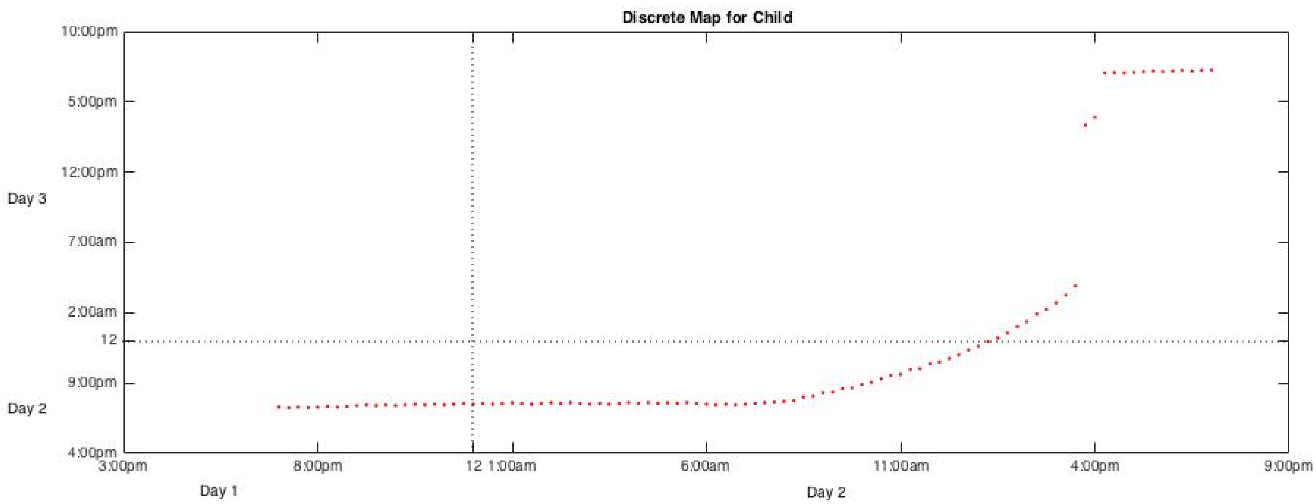

Figure 4: Discrete map for average Child

curve at 4 pm on Day 3. Similarly, for the iteration of time onset 5 pm, the green curve grazes the lower threshold curve until it intersects it at 10pm on Day 3.

All in all, when looking at these discrete maps, we find peculiar jumps at certain time points. We can explain this behavior by looking at the corresponding curves of the model. It is found that at these particular time points, the sleep pressure graph seems to graze along the surface of these thresholds of circadian rhythm, resulting in grazing bifurcations. Therefore, a small adjustment in initial sleep onset at these particular times can result in a drastic difference in the next sleep onset.

Physiological Meaning Behind Two Process Model Findings

Behind each of these discrete maps and plots of the two process model, there is a physiological meaning. In reading these discrete maps, we look at a particular value on the x axis. This value tells us the time at which the subject fell asleep. The corresponding y value represents the time at which the subject will fall asleep the following day.

However, as mentioned in the mathematical component, there are various discontinuities throughout these discrete maps. These discontinuities were due to these grazing bifurcations where the sleep pressure will increase, but not touch the trough of the curve, but rather much later. Physiologically, these means that if the subject had waited a short period of time before actually going to sleep, the following day's time

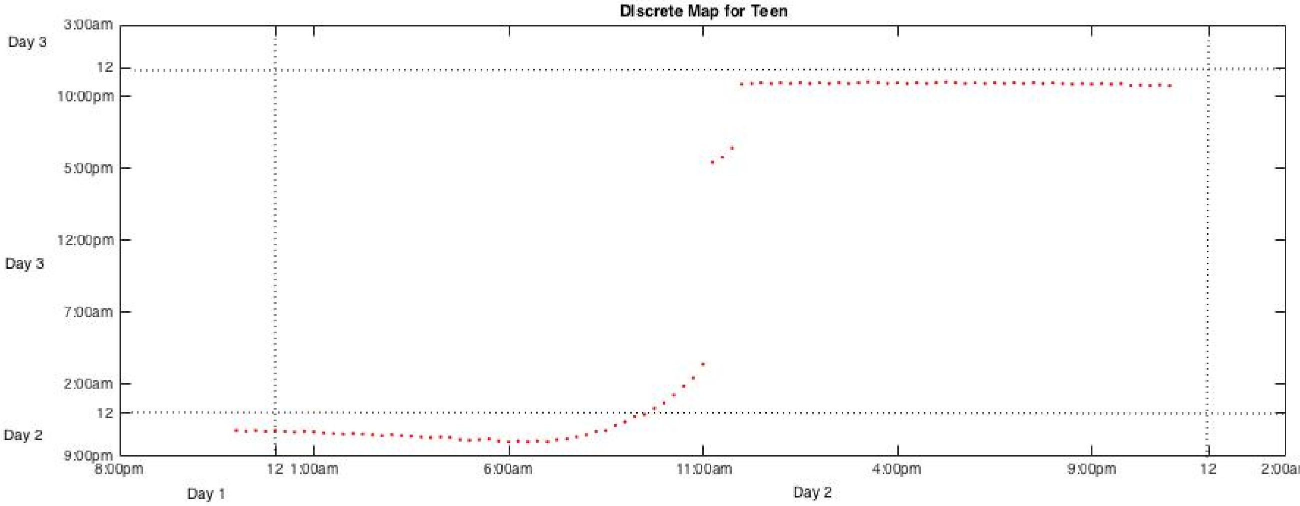

Figure 5: Discrete map for average Teen

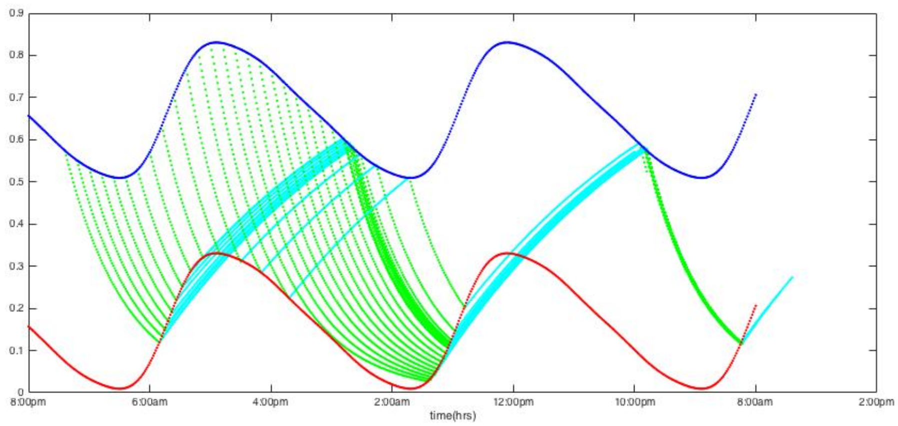

Figure 6: Two process model of average teen

onset will have changed drastically. Therefore, instead of falling asleep early, the subject will have more sleep drive to stay awake and will thus sleep much later the next day.

In looking at the plots of the two process model, it is important to understand what each of these curves actually mean. The top threshold of the circadian rhythm represents the subject's inclination towards sleep. At a trough, the subject could have a higher inclination to sleep. However, at a crest, the subject will have a higher sleep drive and will thus be more inclined to stay awake. In contrast, the lower threshold of the circadian rhythm represents the subject's inclination to wake. At a trough, the subject more inclined to wake up;however, at a crest, the subject is less inclined to wake up.

Reduced BDB Model

The two process model, while quite accurate, fails to include many biological aspects such as the firing rates of the various populations of neurons involved in sleep-wake cycles. We now upgrade our model incorporate these factors by using a reduced version of the BDB model. Using XPP AUTO, we find that we can create these 'Z-shaped' graphs for a fixed value of c. These Z-shaped graphs represent the stable equilibrium of each value of h, as h increases by a set step size. We can find this stable state by running the particular value of h in the model and continuing to the run the last value of h until the model reaches the same initial conditions.

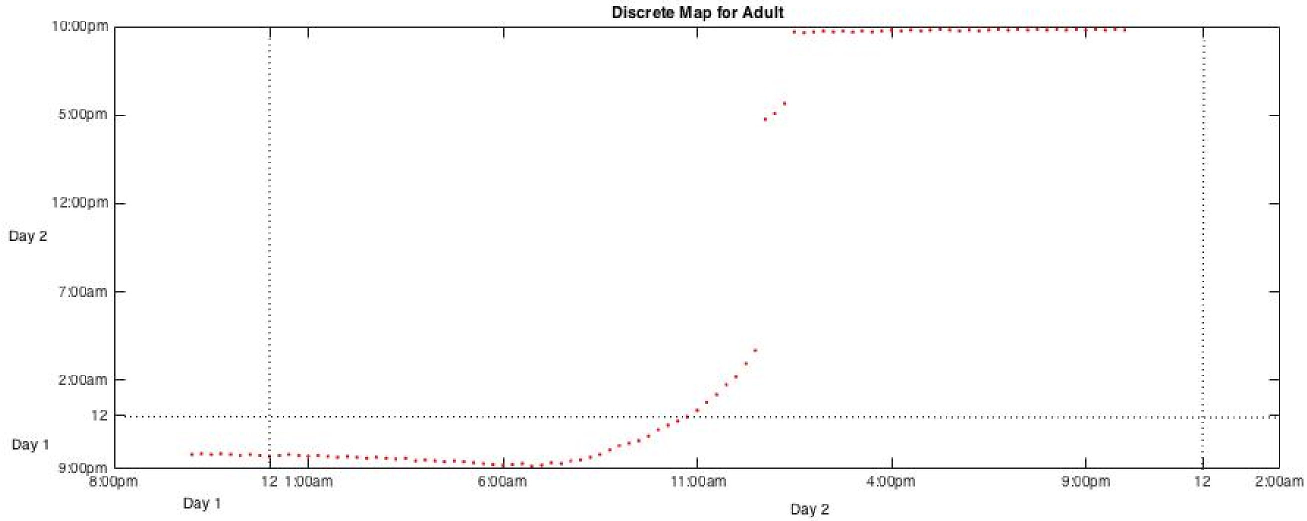

Figure 7: Discrete map for average Adult

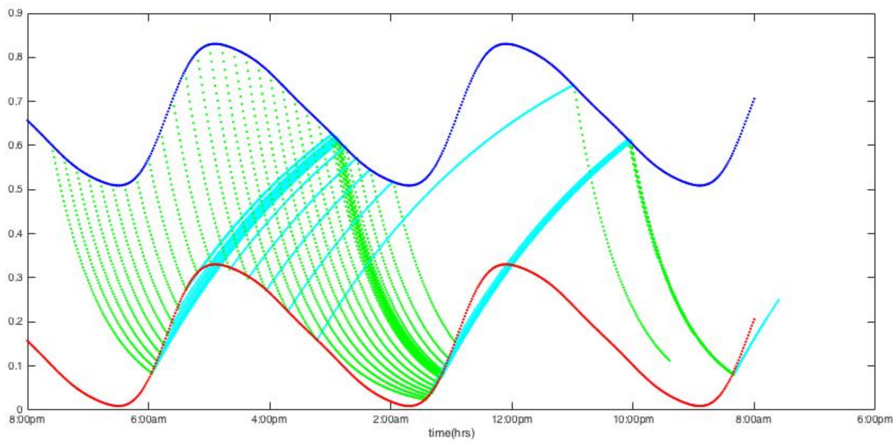

Figure 8: Two process model of average Adult

For each value of h, the steady state value is plotted on the Z-shaped graph and even has a corresponding color. A red point on the plot denotes that the point at that value of h is a stable point. However, a black point denotes instability. When we plot null clines, we see that there are two curves plotted. These curves intersect at junctions called fixed points. We can further verify the stability of each of these points by using the singularity points function of AUTO. By clicking on a point in the plot, we can truly understand the stability of a certain point. A stable point tends to have all clicks in the vicinity lead to it. However, an unstable point will try and repel any sort of iteration towards it and propel it in the direction of the nearest stable point. We see that as we reach intermediate levels of h, we find that there are three fixed points: two stable and one unstable. We will call this unstable point, the saddle point. The existence of this saddle point directly corresponds to the instability of the points in the Z-shaped graph.

If we look at the Z-shaped graph again, we find that there are these bends, or saddle nodes, in the graph where the stability changes. If we look closely at the null clines graph, we see that the distance between the first and second fixed points tends to decrease as we use values of h near that bend. As seen in Figure 12, these first and second fixed points start to 'coalesce' and become one if we use the value of h at that bend, hence the name, saddle node. Also, if we look at singularity points, we find that eigenvalues with a negative real component correspond to stable fixed points, whereas those with positive components are saddle points, or unstable.

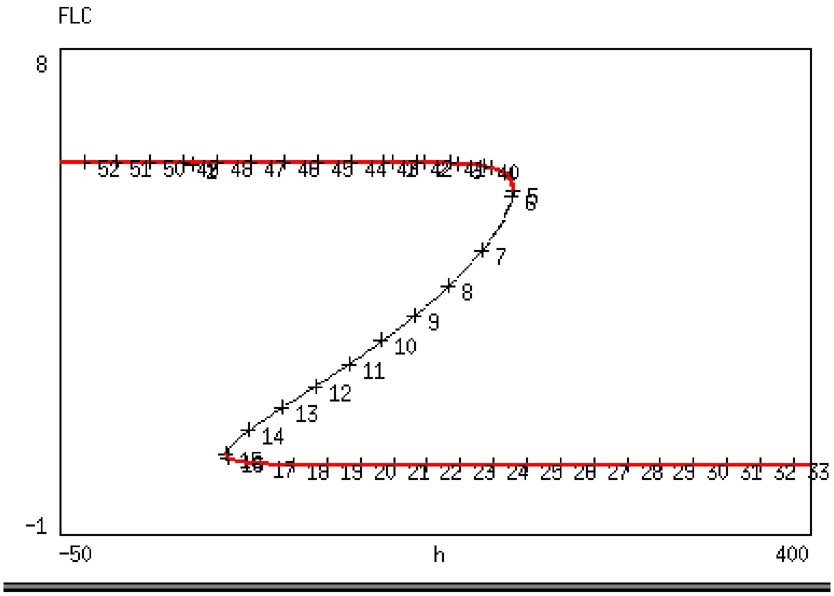

Figure 9: C=.5

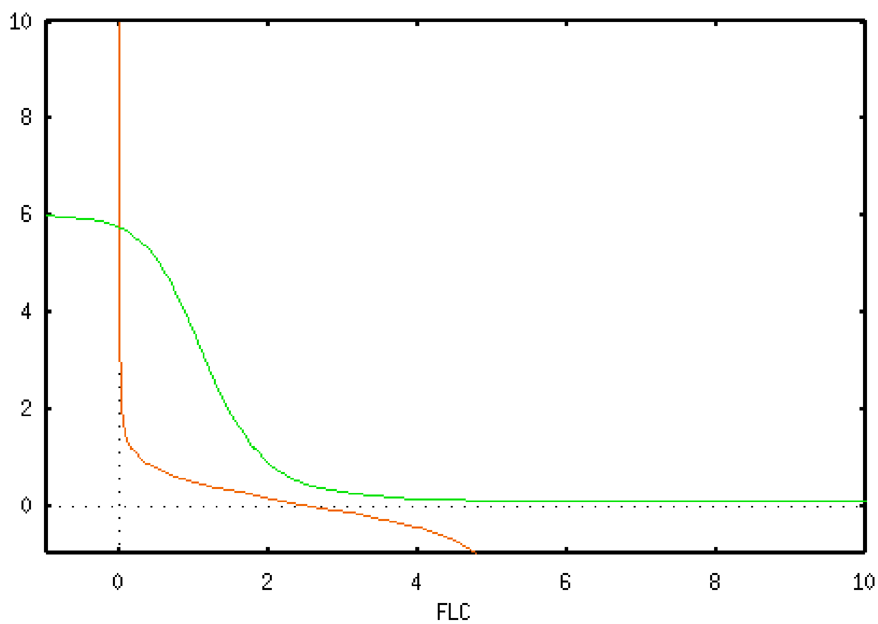

Figure 10: nullclines for h = -10

Now, let's look at how this graph changes if we change values of c. When looking at the graph below(c = 0), we see that the Z-shaped graph tends to shift to the left as the c values decrease. So, what does this mean physiologically? The saddle nodes as seen in each bend of Z represents the threshold at which one is able to overcome sleep and wake up or overcome wake and go to sleep, depending on the h value. When h values are sufficiently high, the subject will certainly be asleep as it will be the only stable point. Also, when h values are sufficiently low, the subject will certainly be awake. However, within intermediate values of h, where we have patches of instability, the outcome really depends on initial conditions. For the same exact h value, some initial conditions may be conducive for sleep, while others may be more conducive for wake. When we see these graph shifts, this means that the threshold for sleep or wake drive has shifted.

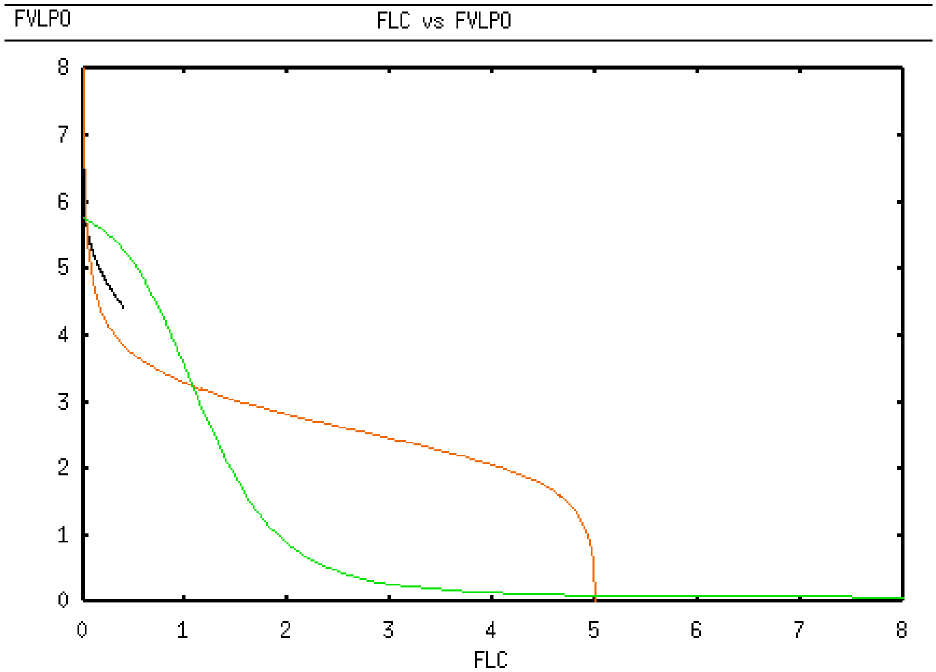

Figure 11: nullclines for h = 150

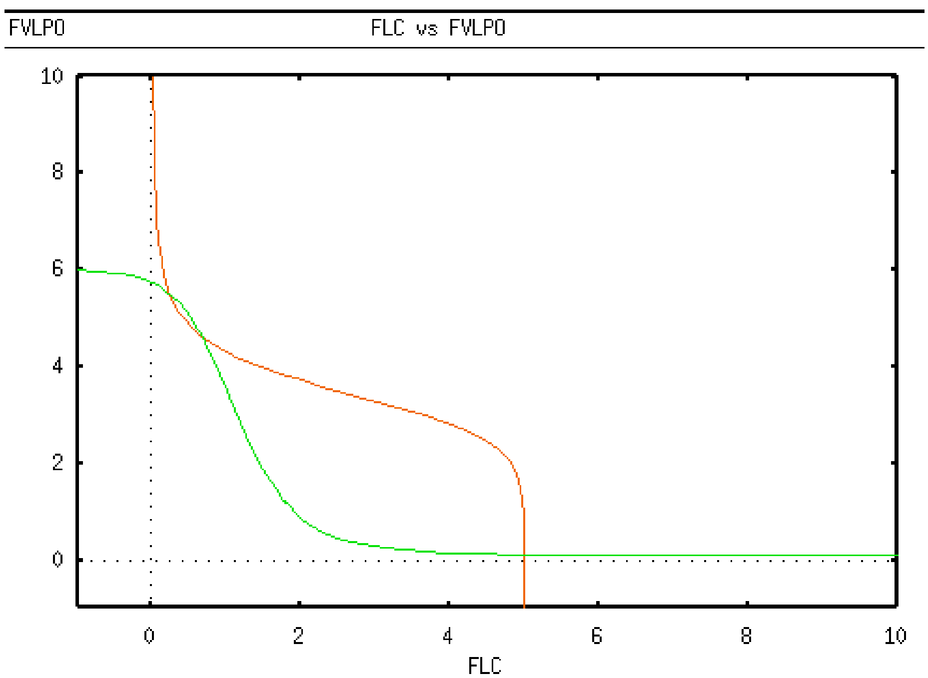

Figure 12: nullclines for h = 190

Extended BDB Model

In the Z-shaped graphs, we reduce the model by fixing the parameters, H and C. However, we can generate a three dimensional map illustrating the sleep phases as H and C changes over time. As seen in the figure below, we can Z shaped curves shift right as the values of c increase. In addition to the Z shaped curves, we can plot the steady state trajectories as well.

However, in applying various initial conditions, we can see that at some conditions, we can see the

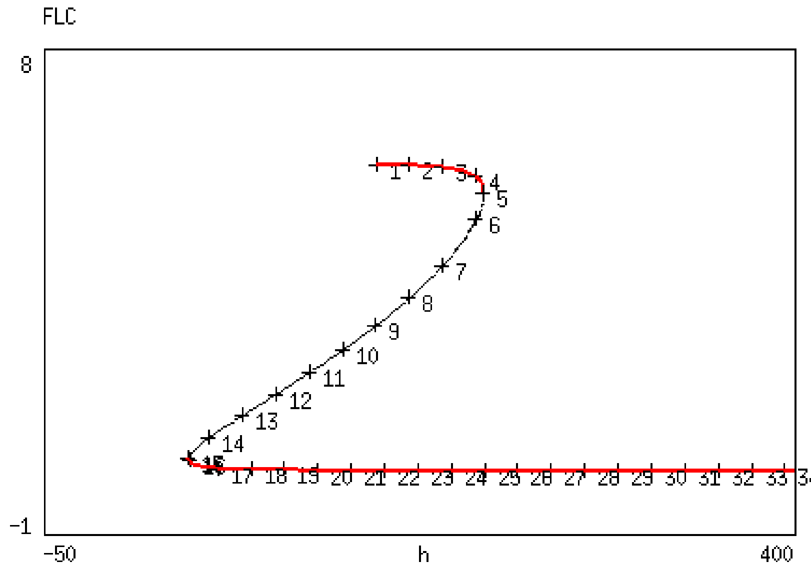

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Figure 13: C= 0

same grazing bifurcations that occurred in the two process model. In these instances, we can see that the trajectories in two consecutive conditions essentially diverge. These grazing bifurcations actually occur at multiple instances, at both the lower curve as well as the top curve of the Z shaped graph. In Figure 14, appears to graze along the surface until finally falling off the curve at a higher C value while the other simply falls off the surface at a significantly lower h value. In Figure 16, the red trajectory falls off the bottom curve at a higher C value while the yellow trajectory appears to graze along the bottom curve for quite some time before finally falling off the curve.

We can examine this behavior in even more depth by comparing time traces of these initial conditions. In Figure 15, we see that there appears a small dip in the blue curve of the bottom trace before it resurfaces. This dip demonstrates the grazing bifurcation in which the cyan curve grazes along the top curve before finally falling off. However, in Figure 17, the bottom curve grazing bifurcation can be represented by the small dip and resurfacing found in the red curve of the bottom graph.

We are able to see the same behavior in this more complex model as that of the two process model. Therefore, a small change in initial conditions and sleep onset can greatly affect the dynamics of one's sleep-wake cycle due to the combined influences of Circadian rhythm and Homeostatic sleep pressure.

Conclusion

In conclusion, it is found that nonlinear equations can be quite useful in modeling biological systems, and we can use discrete maps to fully understand the dynamics of a system. In models like the Two process model, we find that there are grazing bifurcations in which the sleep pressure curve grazes along the circadian curve before making contact much later. As a result, a small change in sleep onset at certain times can greatly affect the subject's sleep onset the following day. As we incorporate more biological factors like firing rates of certain neuron populations, we find that we can make 'Z-shaped curves' that have varying sleep pressure thresholds depending on the circadian value. As a result, we see that these curves shift to the right as the circadian value increases. As we run trajectories for various initial conditions, we start to see the grazing bifurcations found in the Two Process Model. Once again, we can say that small changes in initial conditions can greatly affect the outcome of the resulting sleep trajectories due to the combination of Circadian rhythm and Homeostatic Sleep Pressure.

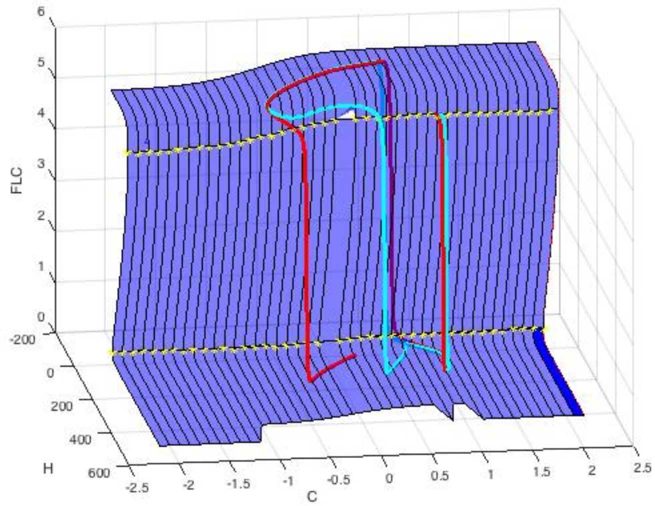

Figure 14: Grazing bifurcation along top curve

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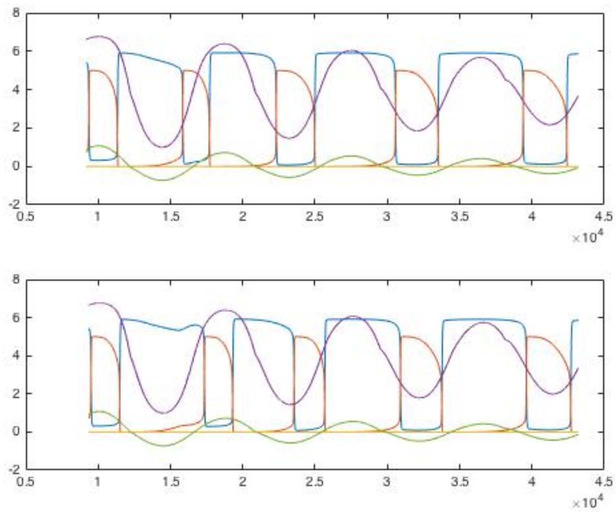

Figure 15: Time trace for top curve

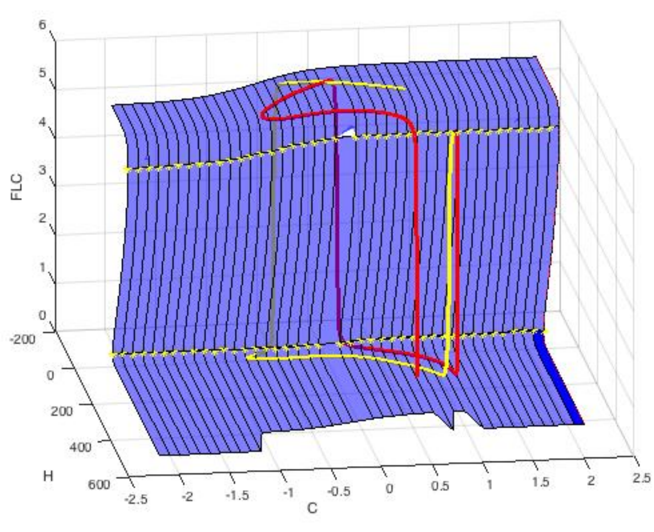

Figure 16: Grazing bifurcation along bottom curve

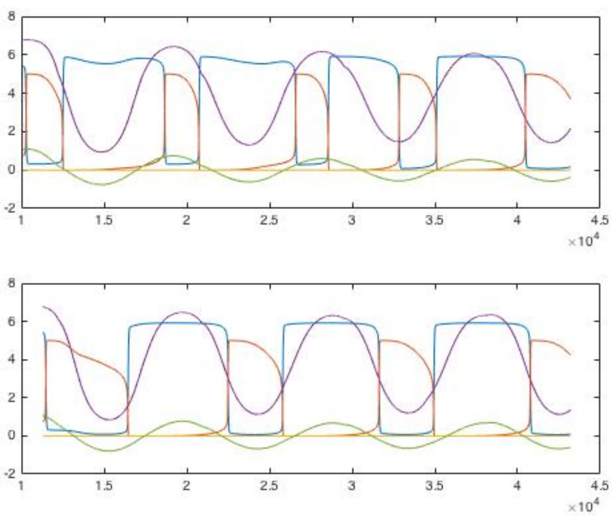

Figure 17: Time trace for bottom curve