Using a Circadian Rhythms Model to Develop Optimal Shift Work Scheduling

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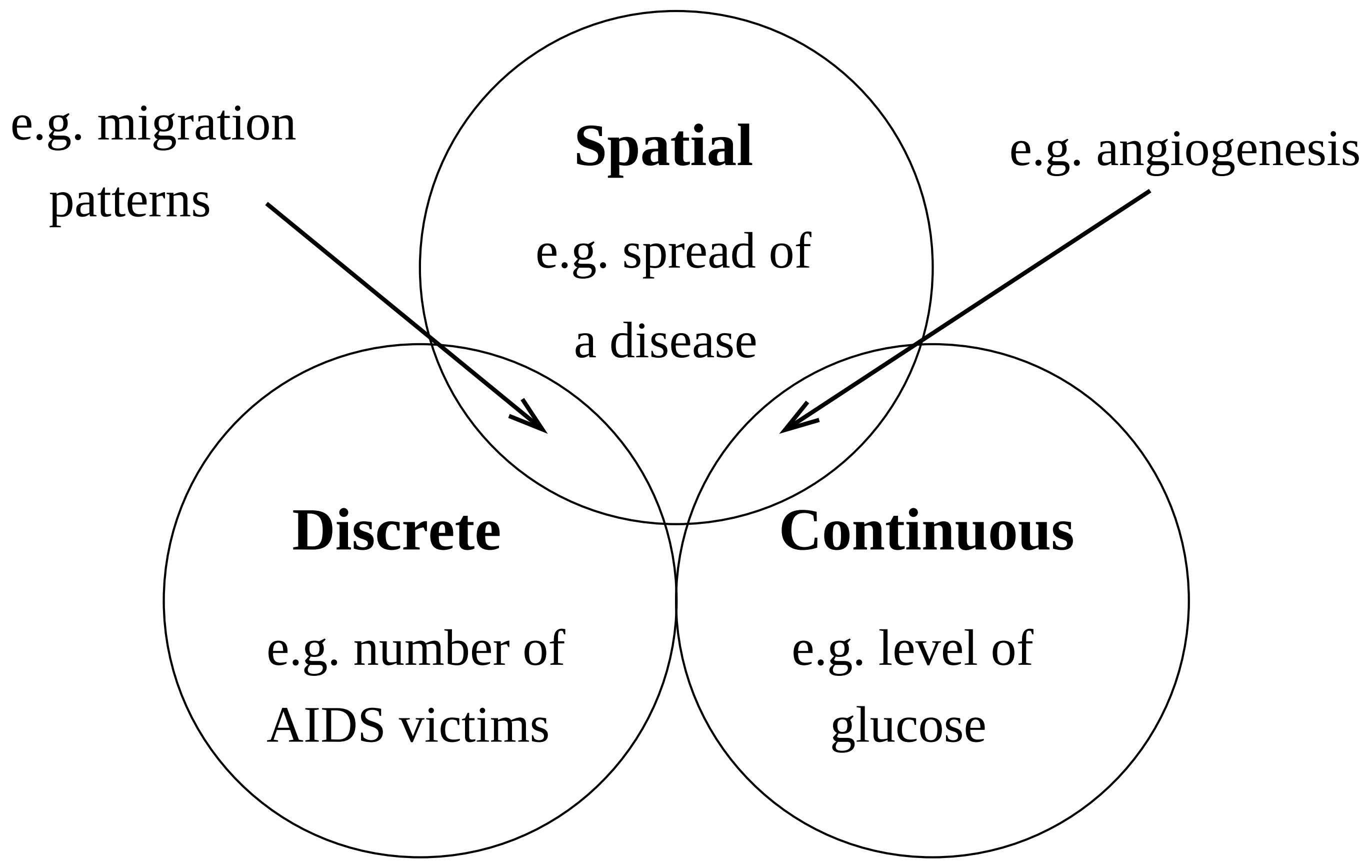
Erin McNelis
Department of Mathematics and Computer Science

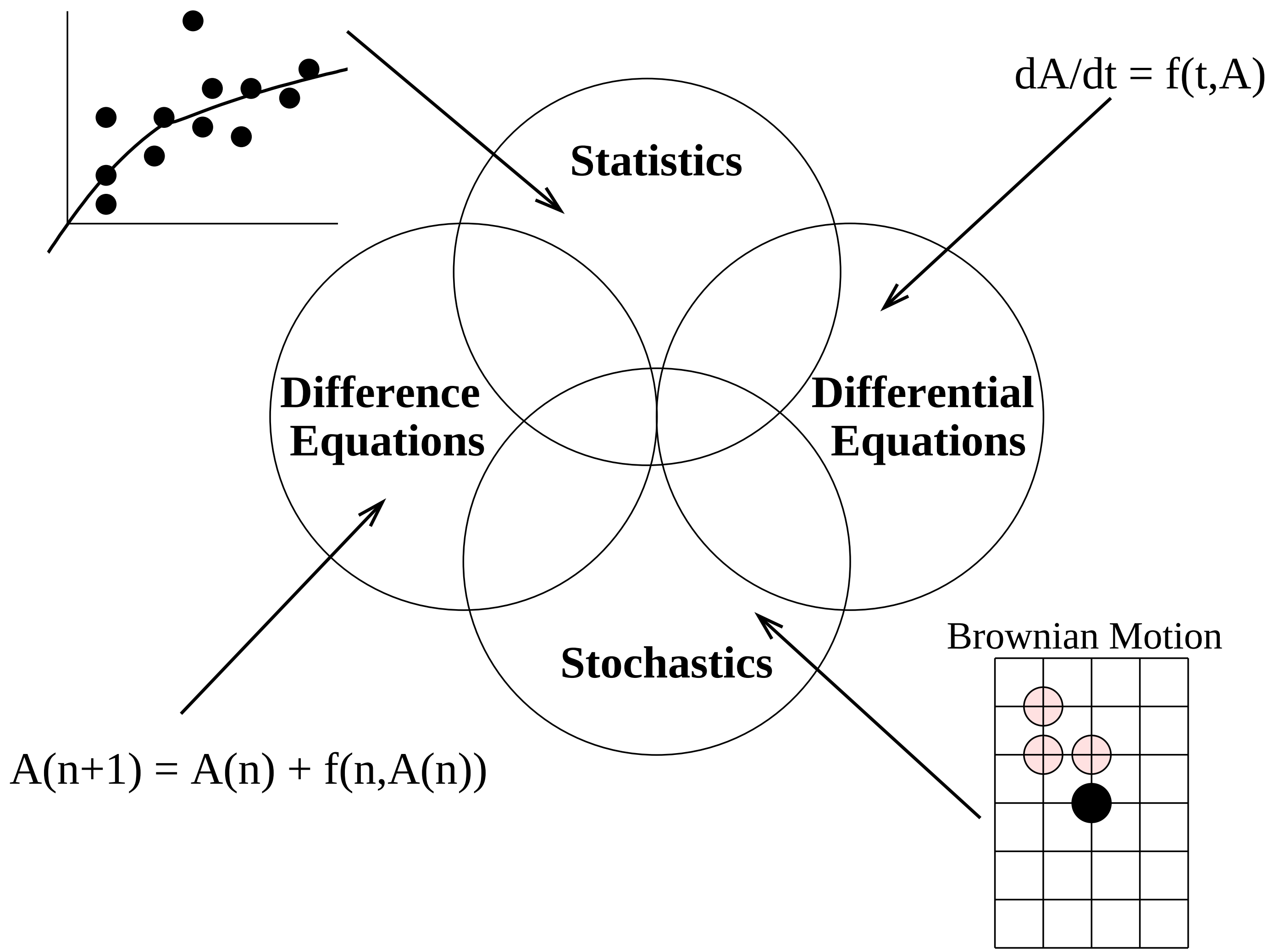
Samples of Mathematical Modeling in Biology

Different Types of Phenomena



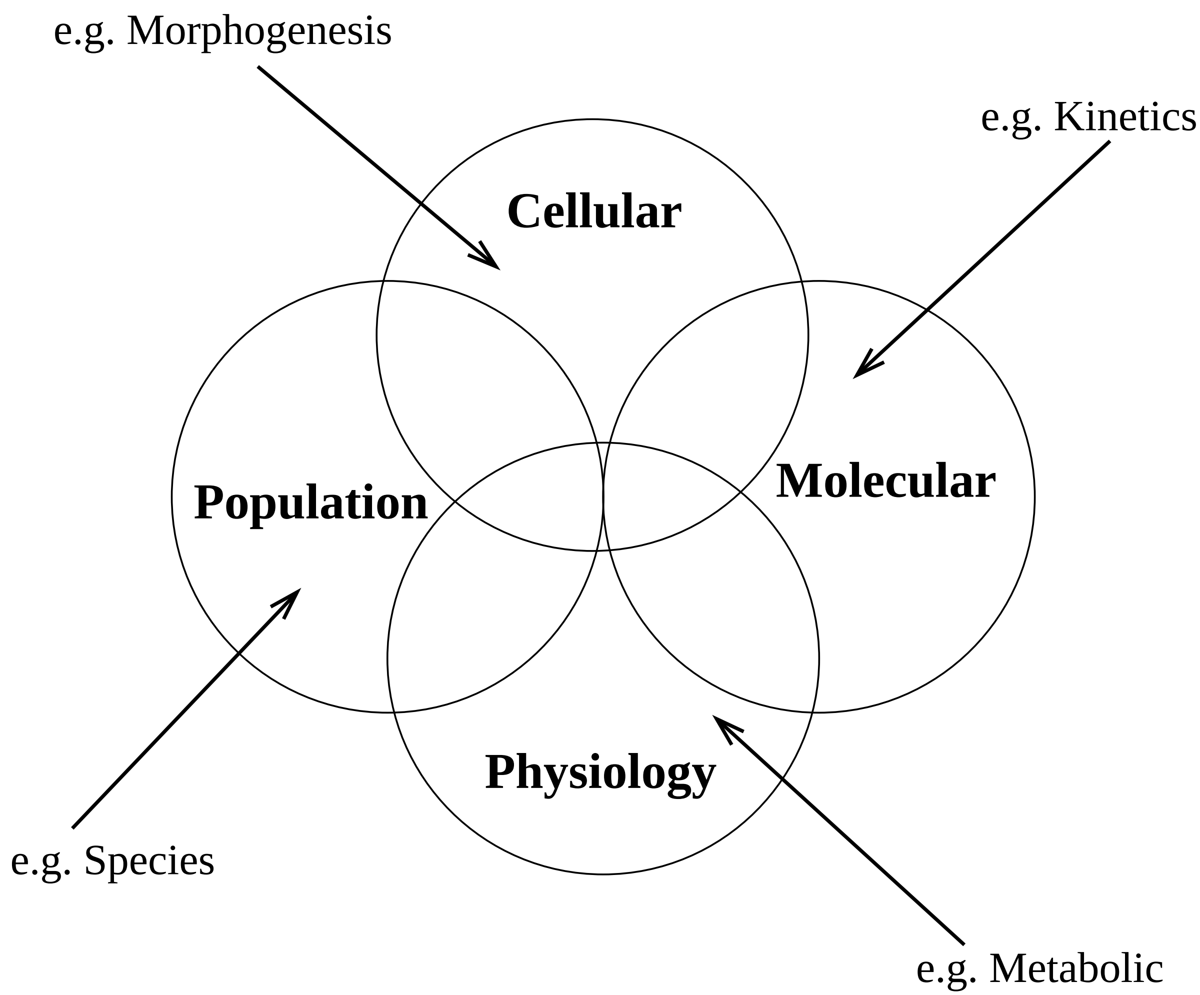
Discrete vs. Continuous vs. Spatial

Different Types of Mathematical Models



Difference Equations vs. Differential Equations vs. Statistics vs. Stochastics

Different Types of Biology Applications



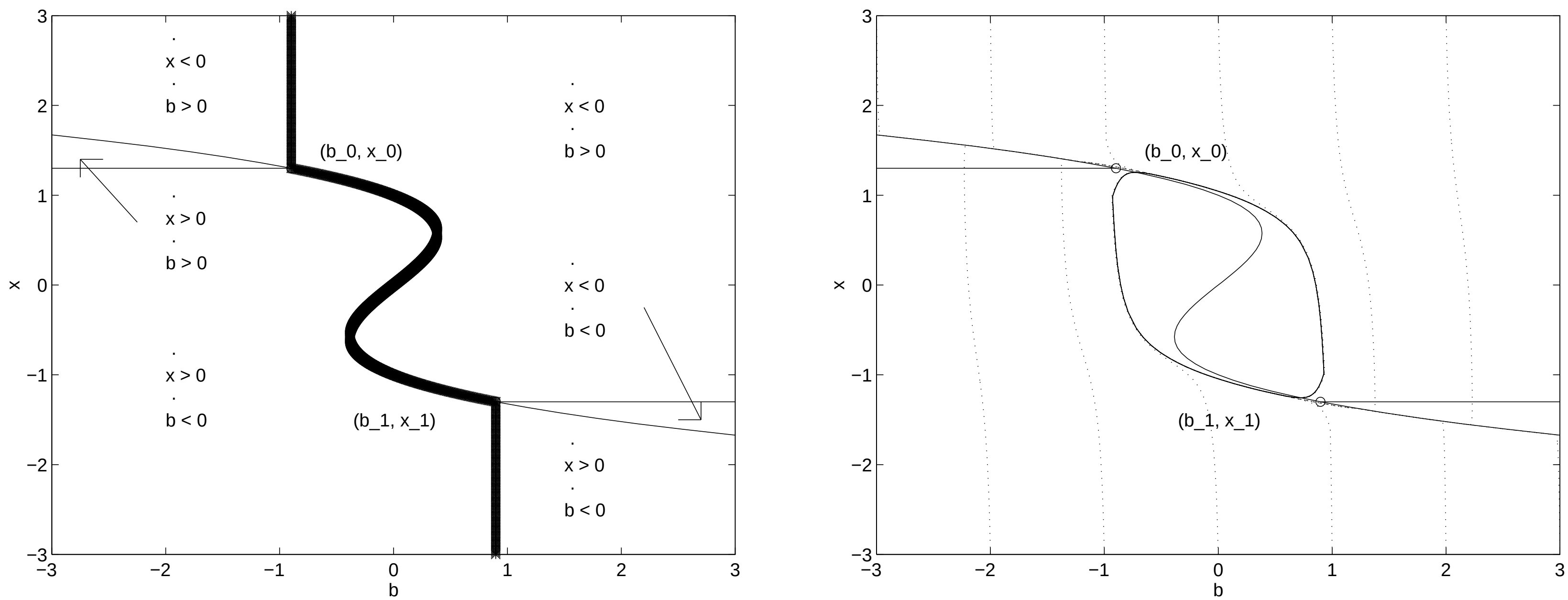
Molecular vs. Cellular vs. Physiology vs. Population

Zeeman's Model for the Heartbeat: The Control Model

The System of Differential Equations:

$$\epsilon \dot{x} = -(x^3 - Tx + b) \quad (1)$$
$$\dot{b} = (x - x_0) + u(x_0 - x_1) \quad (2)$$

where x is the length of a cardiac fiber (minus some constant), b represents the amount of electrochemical activity in the fiber, and u is the control for the pacemaker.



Phase Plane Analysis

The Fitzhugh-Nagumo Model of Conduction a Neuron

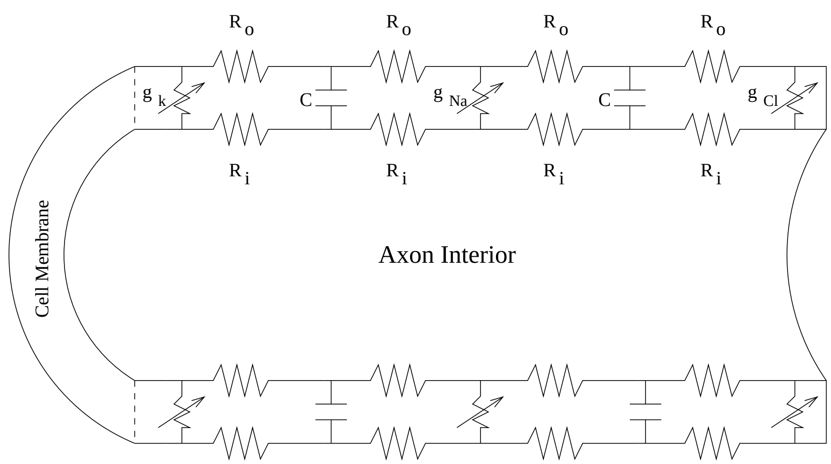
$$\frac{dx}{dt} = c[y + x - \frac{x^3}{3} + z(t)] \quad (3)$$

$$\frac{dy}{dt} = -\frac{x - a + by}{c} \quad (4)$$

x = the excitability of the system (identified with V and m of Hodgkin–Huxley equations),

y = the recovery variable, represents combined forces that tend to return the state of the axonal membrane to rest (identified with n and h of Hodgkin–Huxley equations),

$z(t)$ = the applied stimulus that leads to excitation, such as the input current.



Electrical Wiring Diagram Model for Axonal Membrane

Circadian Rhythms

What are circadian rhythms?

- Biological rhythms that repeat approximately every 24 hours.
- Examples:
  Hormone levels (cortisol, melotonin, thyroid-stimulating hormone), Body temperature, Sleep/wake patterns, Alertness

Why are circadian rhythms studied?

- Natural tie to alertness levels
- Uses of chronobiological research:
  Treating sleep disorders, Adaption to jet-lag, Adaption of astronauts to 'round-the-clock work, Design of rotating shift work schedules

Shift Work

What constitutes shift work?

- Any work not occurring between the hours of 6 a.m. and 6 p.m.
- Characterizing features of shift work:
  - Permanent or rotating shifts
  - Length of a single shift
  - Number/Pattern of days worked in a week
  - Time of day the shift occurs
  - Rotation pattern of non-permanent shifts

What are some of the problems associated with shift work?

- Gastrointestinal and cardiovascular disorders
- Disturbed sleep and fatigue
- Low-productivity and on-the-job accidents

Tying Circadian Rhythms to Shift Work

Why is the study of circadian rhythms relevant to shift work?

- Some of these problems can be traced back to physiological disturbances in circadian rhythms.
- Recommendations for designing shift schedules that minimize adverse effects of shift work on human health and performance.

Objectives

- To develop a model for circadian rhythms of a laborer working specified shift schedules,
- To develop a method for quantifying the degree to which a given shift schedule disrupts circadian rhythms by comparing work-related rhythms to natural benchmark rhythms
- To use this method to:
  - Evaluate the circadian compatibility of a given shift schedule
  - Develop general shift work schedules that least disturb the shift worker's natural circadian rhythms

Kronauer's Circadian Rhythms Model [1]

$$\left(\frac{24}{2\pi}\right)^2 \ddot{x} + \mu(-1+4x^2)\left(\frac{24}{2\pi}\right)\dot{x} + \left(\frac{24}{\tau_x}\right)^2 x \;=\; \left(\frac{24}{2\pi}\right)\dot{B} \qquad (5)$$

where

$$B = (1 - mx)CI^{1/3} \qquad (6)$$

x represents the temperature oscillator,

B represents the "perceived" brightness,

I represents the physical intensity of light,

μ represents the internal "stiffness" of the x oscillator,

τ_x represents the intrinsic period of the x oscillator,

m is a modulation index,

C is a constant of proportionality, and

$\frac{24}{2\Pi}$ is the time parameter converting one unit of time to one hour.

Adapting the Model to Shift Work

- Through Consequential Changes to Light Intensity Function, $I(t)$
- Through Incorporation of a Shift Work Zeitgeber Function, $z(t)$

$$z(t) = \begin{cases} k & t^* \leq t \leq t^* + 8 \\ 0 & otherwise \end{cases} \tag{7}$$

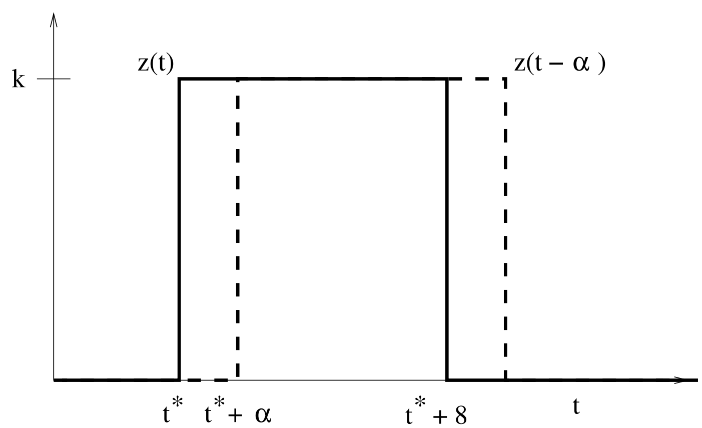
where k is a constant and t^* is the starting time of the shift to be worked. Then the model for shift work modified circadian rhythms is taken to be

$$\left(\frac{24}{2\pi}\right)^2 \ddot{x} + \mu(-1 + 4x^2)\left(\frac{24}{2\pi}\right)\dot{x} + \left(\frac{24}{\tau_x}\right)^2 x \;=\; \left(\frac{24}{2\pi}\right)\dot{B} + z(t) \tag{8}$$

Parameterization of the Problem

Adjusting the Shift Work Sleep-Wake Equation and Zeitgeber

$$\left(\frac{24}{2\pi}\right)^2 \ddot{x} + \mu(-1 + 4x^2)\left(\frac{24}{2\pi}\right)\dot{x} + \left(\frac{24}{\tau_x}\right)^2 x \;=\; \left(\frac{24}{2\pi}\right)\dot{B} + z(t-\alpha) \quad (9)$$



The Parameterized Shift Work Function $z(t-\alpha)$

Determining an Optimal Shift Schedule

Objective:

Given a set schedule of days to work, determine the optimal time of the day, α^*, in which to start that work schedule. In other words, find the value of α that minimizes the error associated with such a shift schedules sleep-wake rhythms, i.e.

$$\min_{0 \leq \alpha \leq 24} \sqrt{\sum_{i=1}^{n} (x_f(t_i) - x_{w(\alpha)}(t_i))^2}$$

Assumptions:

- The shift schedule consists of five days of work and two days off of work.
- Each shift lasts exactly 8 hours.
- Time $t = 0$ corresponds to 12 a.m. Monday morning.
- A shift can start at *any* time during the day.

Numerical Methods and Solution Procedure

- Define $F(\alpha) = \sqrt{\sum_{i=1}^{n} (x_f(t_i) - x_{w(\alpha)}(t_i))^2}$.

- Evaluate F for the values $\alpha = 1, 2, \cdots, 24$.
  Note, each evaluation of F requires solving the system of differential equations with MATLAB's ode solver.

- Determine an interval $[a, b]$ over which $F(\alpha)$ is unimodal and attains its minimum.

- Use Golden Section routine to find the value of α that minimizes F.

Twenty-One Possible Single-Week Schedules

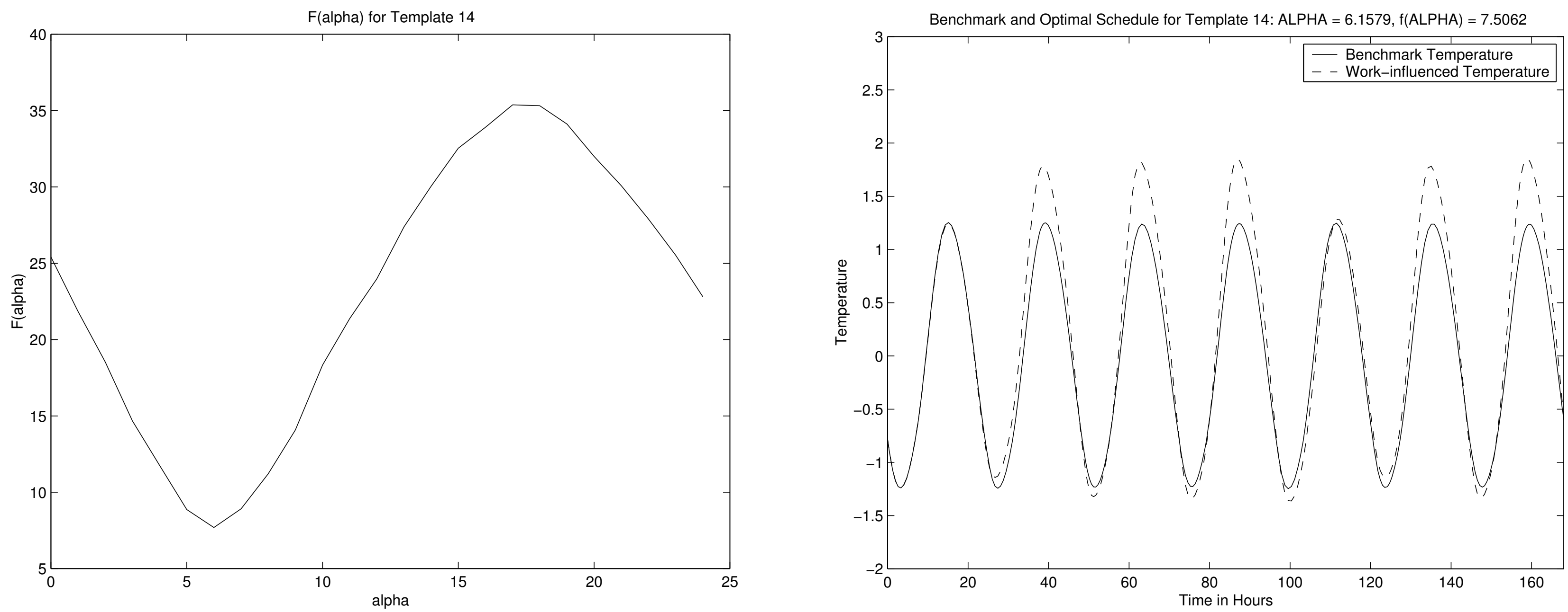
Schedule #			Days	Worked			
1	M	Tu	W	Th	F		
2	M	Tu	W	Th		Sa	
3	M	Tu	W	Th			Su
4	M	Tu	W		F	Sa	
5	M	Tu	W			Sa	Su
6	M	Tu		Th	F	Sa	
7	M	Tu			F	Sa	Su
8	M		W	Th	F	Sa	
9	M			Th	F	Sa	Su
10		Tu	W	Th	F	Sa	
11			W	Th	F	Sa	Su
12		Tu		Th	F	Sa	Su
13		Tu	W		F	Sa	Su
14		Tu	W	Th		Sa	Su
15		Tu	W	Th	F		Su
16	M		W		F	Sa	Su
17	M		W	Th		Sa	Su
18	M		W	Th	F		Su
19	M	Tu		Th		Sa	Su
20	M	Tu		Th	F		Su
21	M	Tu	W		F		Su

First Week Investigations: Sample Results

Smallest Optimal $F(\alpha)$ Value:

Schedule 14 with $F(\alpha) = 7.50618$

M	Tu	W	Th	F	Sa	Su

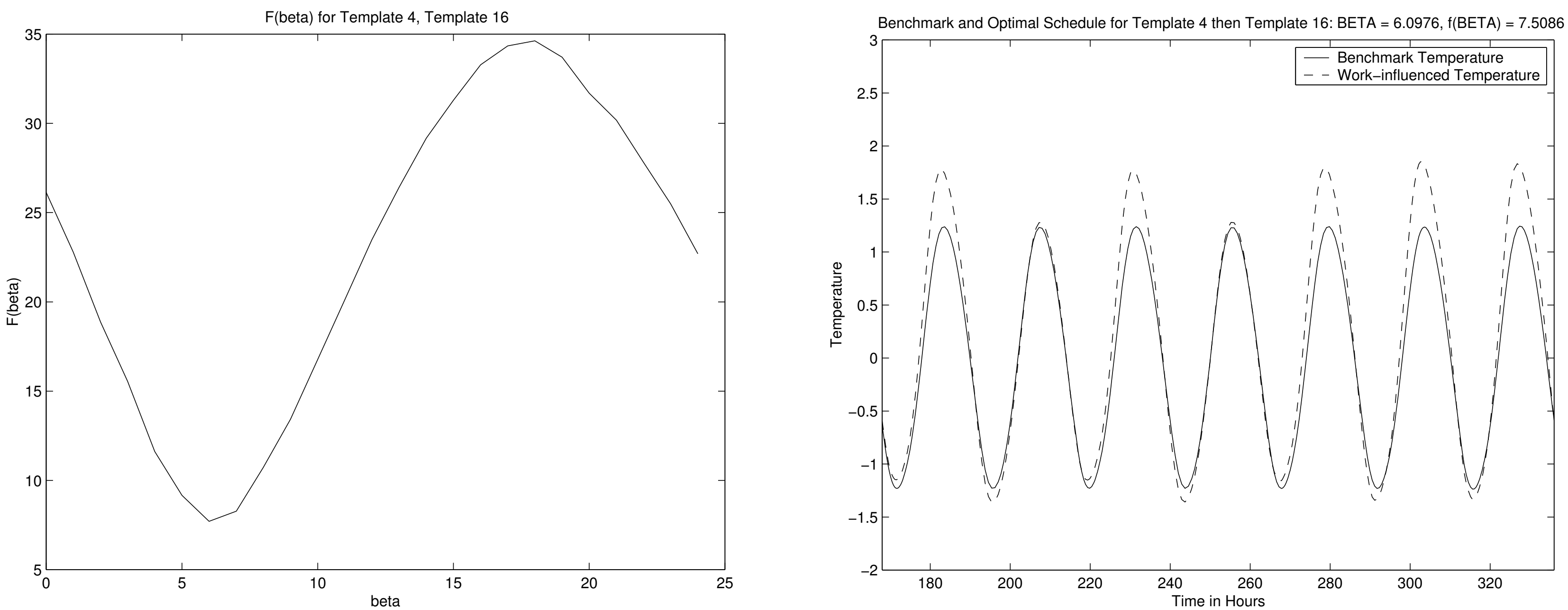


$F(\alpha)$ Graph and Optimal $x_w(t)$ Rhythm for Schedule 14

Second Week Investigations: Sample Results

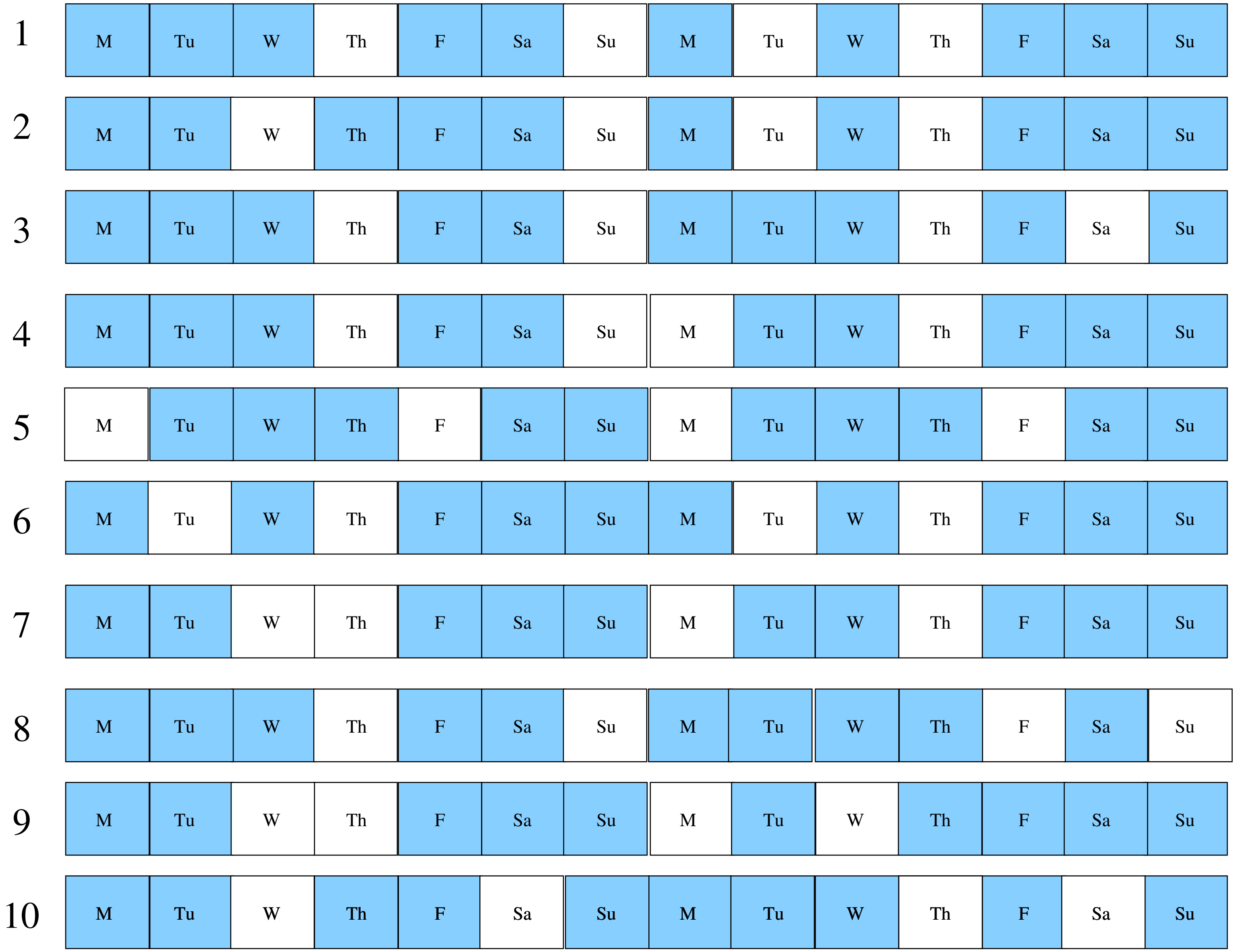
Smallest Optimal $F(\alpha) + F(\beta)$ Value:
Schedule 4 to Schedule 16 with $F(\alpha) + F(\beta) = 15.053$

M	Tu	W	Th	F	Sa	Su	M	Tu	W	Th	F	Sa	Su



$F(\beta)$ Graph and Optimal $x_w(t)$ Rhythm for Schedule 16

Top Ten Schedules



Top Twenty-One Two-Week Schedules

M	**Tu**	**W**	Th	**F**	**Sa**	Su	**M**	Tu	**W**	Th	**F**	**Sa**	**Su**
M	**Tu**	W	**Th**	**F**	**Sa**	Su	**M**	Tu	**W**	Th	**F**	**Sa**	**Su**
M	**Tu**	**W**	Th	**F**	**Sa**	Su	**M**	**Tu**	**W**	Th	**F**	Sa	**Su**
M	**Tu**	**W**	Th	**F**	**Sa**	Su	M	**Tu**	**W**	Th	**F**	**Sa**	**Su**
M	**Tu**	**W**	**Th**	F	**Sa**	**Su**	M	**Tu**	**W**	**Th**	F	**Sa**	**Su**
M	Tu	**W**	Th	**F**	**Sa**	**Su**	**M**	Tu	**W**	Th	**F**	**Sa**	**Su**
M	**Tu**	W	Th	**F**	**Sa**	**Su**	M	**Tu**	**W**	Th	**F**	**Sa**	**Su**
M	**Tu**	**W**	Th	**F**	**Sa**	Su	**M**	**Tu**	**W**	**Th**	F	**Sa**	Su
M	**Tu**	W	Th	**F**	**Sa**	**Su**	M	**Tu**	W	**Th**	**F**	**Sa**	**Su**
M	**Tu**	W	**Th**	**F**	Sa	**Su**	**M**	**Tu**	**W**	Th	**F**	Sa	**Su**
M	**Tu**	**W**	Th	F	**Sa**	**Su**	**M**	**Tu**	**W**	Th	**F**	Sa	**Su**
M	**Tu**	**W**	**Th**	F	**Sa**	**Su**	M	**Tu**	**W**	Th	**F**	**Sa**	**Su**
M	**Tu**	**W**	**Th**	F	**Sa**	**Su**	M	**Tu**	W	**Th**	**F**	**Sa**	**Su**
M	**Tu**	W	**Th**	**F**	**Sa**	Su	**M**	**Tu**	W	**Th**	F	**Sa**	**Su**
M	**Tu**	W	**Th**	**F**	**Sa**	Su	**M**	**Tu**	**W**	Th	**F**	Sa	**Su**
M	**Tu**	**W**	Th	**F**	**Sa**	**Su**	M	**Tu**	**W**	Th	**F**	**Sa**	**Su**
M	**Tu**	**W**	**Th**	F	Sa	**Su**	**M**	Tu	W	**Th**	**F**	**Sa**	**Su**
M	**Tu**	**W**	**Th**	**F**	Sa	Su	M	**Tu**	**W**	**Th**	F	**Sa**	**Su**
M	**Tu**	**W**	Th	**F**	**Sa**	Su	**M**	Tu	**W**	**Th**	F	**Sa**	**Su**
M	**Tu**	**W**	**Th**	F	**Sa**	**Su**	**M**	Tu	**W**	**Th**	F	**Sa**	**Su**
M	**Tu**	**W**	Th	**F**	**Sa**	**Su**	M	**Tu**	**W**	**Th**	**F**	Sa	**Su**

Observations and Conclusions

In terms of observations regarding optimal two week shift work schedules:

- Better schedules have:
  - Fewer days off in a row
  - Fewer days worked in a row
  - One or two Thursdays off
- The best shift schedules involve work that starts between the hours of 5:45 a.m. and 6:30 a.m.
- There is no consistently good or poor choice of weekly schedules, it all depends on their combinations.
- The typical Monday through Friday two week schedule is one of the lower caliber performers (ranked 355 out of 441 schedules).

Observations and Conclusions

In terms of statistical analysis of data generated from these simulations:

- Later starting times for the first week of work correspond to decreases in the difference between weekly starting times.

- If the first week of work starts before 6 a.m., the second week of work tends to start later, where as if the first week of work starts after 6 a.m., the second week of work tends to start earlier.

- As the maximum span of consecutive days worked increases, the objective function increases, making these schedules less desirable.

References

[1] Kronauer, R.E., "A quantitative model for the effects of light on the amplitude and phase of the deep circadian pacemaker, base on human data." In *Sleep '90, Proceedings of the Tenth European Congress on Sleep Research*, edited by J. Horne. Dusseldorf, Germany: Pontenagel, 1990.