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Fatigue Risk Management: Modeling the Sleep/Wake-Based Dynamics of Performance

Peter J. McCauley

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FATIGUE RISK MANAGEMENT: MODELING
THE SLEEP/WAKE-BASED DYNAMICS
OF PERFORMANCE

By

Peter J. McCauley

M.A. Mathematics, University of Montana, Missoula, Montana, 2005
B.A. Physics, University of Montana, Missoula, Montana, 2002
B.A. Mathematics, University of Montana, Missoula, Montana, 2002

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Approved by:
Dr. Perry Brown, Associate Provost for Graduate Education
Graduate School
Dr. Leonid V. Kalachev, Chair
Department of Mathematical Sciences, The University of Montana, Missoula, MT
Dr. Hans P.A. Van Dongen, Co-chair
Sleep and Performance Research Center, Washington State University, Spokane, WA
Dr. Alden Wright
Department of Computer Sciences, The University of Montana, Missoula, MT
Dr. Eijiro Uchimoto
Department of Physics and Astronomy, The University of Montana, Missoula, MT
Dr. Gregory Belenky
Sleep and Performance Research Center, Washington State University, Spokane, WA
Several biomathematical models have been developed to predict cognitive performance impairment due to sleep loss and/or circadian misalignment. In essence, these models are all based on the Two-Process Model (TPM) which contains a homeostatic process for the build-up and decline of sleep pressure across days, and a circadian process to keep track of time of day. The TPM has been used successfully to predict performance under conditions of total sleep deprivation. However, for conditions of chronic sleep restriction, the TPM predicts a rapid stabilization of performance impairment (within a day or two)—which is not in agreement with experimental observations. This discrepancy has led to the development of TPM variations with an additional process modulating the homeostatic process across days of sleep restriction. Yet, these models predict adaptation to chronic sleep restriction in the long run as well, regardless of how substantial the daily sleep reduction actually is.

We show in this thesis that the TPM, and the various models based on it and expanding it with a modulating process, can be written as a system of nonhomogeneous first-order ordinary differential equations with a much richer repertoire of predictions. We examine the dynamical properties of the model for states of equilibrium and stability, in the context of wake/sleep schedules with consolidated sleep episodes and schedules that repeat across days. We also extend the model framework to include multiple wake/sleep segments per day and explore the model behavior with scenarios that include napping.

We discovered that the model produces a bifurcation whereby daily wake durations extending up to a critical value lead to adaptation, whereas daily wake durations that extend beyond the critical value lead to escalating performance impairment over days. We found that the underlying model characteristics were unchanged for repeating schedules and scenarios with napping—the bifurcation was defined by the average duration of total daily wakefulness. Finally, we used our new modeling framework to develop a model formulation that exhibits realignment characteristics between the environment and the biological clock, which can be used to create a comprehensive dynamic model of the homeostatic and circadian regulation of cognitive performance.
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# Contents

Introduction 1

1 Formulation of the Generalized Model 3

1.1 The two-process model as a system of coupled nonhomogeneous first-order ordinary differential equations 4

1.1.1 Analogous system of compartments for the generalized Two-Process Model (gTPM) 9

1.1.2 Initial values at wake onset and sleep onset 9

1.1.3 Model dynamics 11

1.1.3.1 Dynamics across days 18

1.2 Laboratory performance data in sleep deprivation studies 21

1.2.1 Parameter estimates and predictions for the gTPM 22

1.2.1.1 Analytical solution within days 22

1.2.1.2 Initial performance level 24

1.2.1.3 Parameter estimates and model predictions 24

1.3 Generalized model as coupled first-order ordinary differential equations 30

1.3.1 Analogous system of compartments for the Modulating Two-Process Model (MTPM) 33

1.3.2 Initial values at wake onset and sleep onset 35

1.3.3 Model dynamics 35

1.3.3.1 Dynamics across days 38

1.3.4 Another look at the generalized ODE system for the ETPM 40

1.3.4.1 Model case dynamics 41

1.3.4.2 Dynamics across days 43

1.4 Model cases of the MTPM 46
1.4.1 A model case with a bifurcation ........................................ 47
1.4.1.1 Model case dynamics ........................................... 48
1.4.1.2 Dynamics across days ...................................... 51
1.4.2 A model case with feedback ......................................... 55
1.4.2.1 Model case dynamics ........................................... 56
1.4.2.2 Dynamics across days ...................................... 58
1.4.3 The full model .................................................. 59
1.4.3.1 Model case dynamics ........................................... 59
1.4.3.2 Dynamics across days ...................................... 61
1.5 Oscillatory behavior .................................................. 61
1.6 Parameter estimates and predictions for the MTPM ................. 62
1.6.1 Parameter estimates and predictions for the model case with a bi-
furcation ................................................................. 63
1.6.1.1 Analytical solution within days ........................... 64
1.6.1.2 Initial performance level .................................... 64
1.6.1.3 Parameter estimates and model predictions .............. 65
1.6.2 Parameter estimates and predictions for the model case with feedback 71
1.6.2.1 Analytical solution within days ........................... 71
1.6.2.2 Initial performance level .................................... 72
1.6.2.3 Parameter estimates and model predictions .............. 73

2 Modeling Repeating Wake/Sleep Schedules .......................... 79
2.1 Analysis of the MTPM for repeating wake/sleep schedules ....... 80
2.1.1 Initial values at wake onset and sleep onset .................. 80
2.1.2 Model dynamics .................................................. 81
2.2 A model case of the MTPM for repeating wake/sleep schedules and with a bifurcation ......................................................... 82
2.2.1 Model case dynamics ........................................... 83

3 Modeling Split Sleep Schedules .......................................... 87
3.1 Extending the MTPM for split sleep schedules .................... 87
3.1.1 Initial values at wake onset and sleep onset ................. 89
3.1.2 Model dynamics .................................................. 90
3.2 A model case of the MTPM for split sleep schedules and with a bifurcation
3.2.1 Model case dynamics

4 Modeling Shift Work Schedules
4.1 A modeling approach for realignment of the circadian pacemaker with the environment

Conclusion

A Proofs for the generalized Two-Process Model (gTPM)
A.1 Derivation of the difference equations for initial values at the onset of wakefulness and the onset of sleep in the gTPM
A.2 Periodic form of the nonhomogeneous part of the iterative equations for the initial values in the gTPM
A.3 Asymptotic stability of the equilibrium state in the gTPM
A.4 Asymptotic stability of the periodic fixed points in the gTPM
A.5 Analytical solutions for a gTPM model case
A.6 Analytical solution for initial value of performance at the onset of wakefulness and the onset of sleep

B Mathematical models that insure invariance to choice of time step in difference equations
B.1 The model by Johnson and colleagues (2004) as a system of coupled nonhomogeneous first-order differential equations

C Proofs for the Modulated Two-Process Model (MTPM)
C.1 Analytical solutions for the generalized model
C.2 Derivation of the difference equations for initial values in the generalized model
C.3 Closed form solution in total sleep deprivation for the ETPM
C.4 Analytical solutions for the MTPM within days
C.5 Proof that eigenvalues of shifted matrices are identical
C.6 Proof that determinants of shifted matrices are identical
C.7 Oscillatory condition for the generalized model
List of Figures

1.1 Plot showing an example of linking across days with the gTPM ............ 8
1.2 Analogous system of compartments for the gTPM .......................... 9
1.3 Equilibrium state for performance with the two-process model ............ 13
1.4 Performance predictions with the TPM ...................................... 15
1.5 Plot showing the level of the equilibrium state versus wakefulness duration 16
1.6 Plot showing the value of the eigenvalue versus wakefulness duration ...... 17
1.7 A periodic state of equilibrium for performance prediction with the two-
process model ................................................................. 18
1.8 Analogous system of compartments for the gTPM with specific nonhomoge-
neities .......................................................... 23
1.9 Projections of MCMC chains and estimated boundaries of reliability re-
geions for the parameters $\alpha$, $\kappa$ and $\phi$ in the gTPM ................. 25
1.10 Projections of MCMC chains and estimated boundaries of reliability re-
geions for the parameters $\alpha$, $\kappa$, $\sigma$ and $\mu$ in the gTPM ............. 25
1.11 Projections of MCMC chains and estimated boundaries of reliability re-
geions for the parameters $\phi$, $\sigma$ and $\mu$ in the gTPM ...................... 26
1.12 Model predictions from the gTPM for the four sleep deprivation conditions
in Van Dongen et al. (2003) ..................................................... 27
1.13 Model predictions from the gTPM for the four sleep deprivation protocols
in Belenky et al. (2003) ......................................................... 28
1.14 Plot showing performance predictions using the gTPM .................... 29
1.15 Analogous system of compartments for the Modulating Two-Process Model
(MTPM) ................................................................. 34
1.16 Analogous system of compartments for the ETPM case of the MTPM .... 42
1.17 Plot showing the performance level at the equilibrium state versus wakefulness duration for the ETPM ............................................. 44
1.18 Plot showing the values of the two eigenvalues versus wakefulness duration for the ETPM .................................................. 44
1.19 Plot showing performance predictions with the ETPM case of the MTPM . 46
1.20 Analogous system of compartments for the case of the MTPM with a bifurcation ................................................................. 48
1.21 Plot showing performance predictions with the case of the MTPM with a bifurcation ................................................................. 54
1.22 Analogous system of compartments for the case of the MTPM with feedback 56
1.23 Analogous system of compartments for the case of the MTPM with a bifurcation and with specific nonhomogeneities ........................ 63
1.24 Projections of MCMC chains and estimated boundaries of reliability regions for the $\alpha_{1,1}, \alpha_{1,2}$ and $\alpha_{2,2}$ parameters for the case of the MTPM with a bifurcation .................................................. 66
1.25 Projections of MCMC chains and estimated boundaries of reliability regions for the $\alpha_{1,1}, \alpha_{1,2}, \alpha_{2,2}$ and $\sigma_{2,2}$ parameters for the case of the MTPM with a bifurcation .................................................. 66
1.26 Projections of MCMC chains for the parameter pair $\sigma_{1,1}$ and $\sigma_{1,2}$ for the case of the MTPM with a bifurcation ............................ 67
1.27 Projections of MCMC chains and estimated boundaries of reliability regions for the $\kappa, \phi, \delta$, and $\mu$ parameters for the case of the MTPM with a bifurcation .................................................. 67
1.28 Model predictions for the case of the MTPM with a bifurcation for the four sleep deprivation conditions in Van Dongen et al. (2003) .... 68
1.29 Model predictions for the case of the MTPM with a bifurcation for the four sleep deprivation conditions in Belenky et al. (2003) ............. 69
1.30 Plot showing the performance level at the equilibrium state versus wakefulness duration for the case of the MTPM with a bifurcation ......... 70
1.31 Plot showing the values of the two eigenvalues versus wakefulness duration for the case of the MTPM with a bifurcation ...................... 70
1.32 Analogous system of compartments for the case of the MTPM with feedback and with specific nonhomogeneities ................................................. 71

1.33 Projections of MCMC chains and estimated boundaries of reliability regions for the parameters $\alpha_{1,1} < 0$, $\alpha_{1,2}$ and $\alpha_{2,2}$ for the case of the MTPM with feedback .......................................................... 73

1.34 Projections of MCMC chains and estimated boundaries of reliability regions for the parameters $\alpha_{1,1} < 0$, $\alpha_{1,2}$, $\alpha_{2,1}$, and $\sigma_{2,2}$ for the case of the MTPM with feedback .......................................................... 74

1.35 Projections of MCMC chains and estimated boundaries of reliability regions for the parameters $\alpha_{2,1}$, $\alpha_{2,2}$ and $\sigma_{2,2}$ for the case of the MTPM with feedback .......................................................... 74

1.36 Projections of MCMC chains for the parameter pair $\sigma_{1,1}$ and $\sigma_{1,2}$ for the case of the MTPM with a bifurcation .................................................. 75

1.37 Projections of MCMC chains and estimated boundaries of reliability regions for the $\kappa$, $\phi$, $\delta$, and $\mu$ parameters for the case of the MTPM with feedback .................................................. 75

1.38 Model predictions for the case of the MTPM with feedback for the four sleep deprivation conditions in Van Dongen et al. (2003) .............................. 76

1.39 Model predictions for the case of the MTPM with feedback for the four sleep deprivation conditions in Belenky et al. (2003) ...................................... 77

1.40 Plot showing the performance level at the equilibrium state versus wakefulness duration for the case of the MTPM with feedback ..................................... 78

1.41 Plot showing the values of the two eigenvalues versus wakefulness duration for the case of the MTPM with feedback .......................................................... 78

2.1 Plot showing performance predictions for a repeating schedule using the case of the MTPM with a bifurcation .................................................. 86

3.1 Plot showing an example of linking multiple daily wake/sleep episodes .................................................. 88

3.2 Plot showing performance predictions for three wake/sleep schedules using the case of the MTPM with a bifurcation and with extended notation for multiple sleep episodes .................................................. 95
3.3 Expanded view showing performance predictions for a wake/sleep schedule using the case of the MTPM with a bifurcation and with extended notation for multiple sleep episodes ................................. 96

4.1 Resynchronization examples of the circadian rhythm with the environment for constant shift timing ............................................................ 100

4.2 Resynchronization example of the circadian rhythm with the environment across a range of desynchronization timing ........................................ 101
List of Tables

1.1 Parameter estimates: means and standard errors for the gTPM . . . . . . . . . 26
1.2 Published parameter estimates for the $\alpha$ and $\sigma$ matrices from McCauley et al. (2009a) . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 53
1.3 Parameter estimates: means and standard errors for the case of the MTPM with a bifurcation . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 65
1.4 Parameter estimates: means and standard errors for the case of the MTPM with feedback . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 73
Introduction

Fatigue from sleep loss or night work impairs cognitive performance, causing loss of efficiency and jeopardizing safety in many operational settings. Even moderate levels of sleep loss produce impaired performance (Carskadon and Dement, 1981; Dinges et al., 1997; Belenky et al., 2003; Van Dongen et al., 2003). Fatigue caused by inadequate sleep can reduce memory, vigilance, capacity for effective decision-making, attention and reaction time (Dinges and Kribbs, 1991; Banks and Dinges, 2007), increasing the likelihood of human error and accidents. In industries where individuals hold crucial safety roles, such as transportation, health care, space flight, resource extraction, and manufacturing, it is therefore critically important to understand and manage fatigue risk.

The emerging science of fatigue risk management brings together many disciplines, including occupational medicine, resource management, biology, cognitive psychology, mathematics, and computer science. Though the neurobiology underlying the effect of sleep loss is not completely understood, there has been significant progress over the last decade (Porkka-Heiskanen et al., 2000; Saper et al., 2001; Krueger and Obál Jr., 2003; Tononi and Cirelli, 2006). Mathematical models have been developed which can be used to help manage the risks associated with human fatigue (see Borbély and Achermann, 1999; Van Dongen, 2004; McCauley et al., 2009a). These models can be employed to predict the risk of fatigue in various work schedules and to plan schedules that reduce fatigue, minimizing human error and improving productivity and safety.

Models for the prediction of cognitive performance impairment due to sleep loss often involve two primary processes of sleep/wake regulation (Achermann, 2004): a homeostatic process which models the dynamics of sleep pressure across time awake and time asleep, and a circadian process (i.e., the internal biological pacemaker) which keeps track of time of day. Sleep homeostasis is the mechanism that balances the build-up of pressure for sleep during wakefulness with the dissipation of deficits during sleep. Using this concept
as a modeling criterion, Borbély (1982) and Daan et al. (1984) introduced a mathematical model for sleep homeostasis that included an increasing saturating exponential function during wakefulness, and a decreasing exponential function during sleep. However, this formulation of the homeostatic process proved unsatisfactory for the prediction of performance impairment due to chronic sleep restriction (Van Dongen et al., 2003).

Another component of fatigue prediction models is the circadian rhythm. The internal circadian pacemaker (or "biological clock") affects fatigue levels and performance capability. Desynchronization occurs when the internal circadian rhythm becomes misaligned relative to the environment, such as happens when a diurnal worker reschedules to nocturnal work or vice versa. Resynchronization of the circadian rhythm takes place in response to light exposure, as governed by a dose response curve (Boivin et al., 1994), and according to a phase response curve (Minor et al., 1991).

In this thesis we develop and analyze in Chapter 1 a new biomathematical model for predicting the level of performance as it responds to total sleep deprivations and chronic sleep restriction across days of consolidated sleep. In Chapters 2 and 3 we extend the model analysis for a variety of wake/sleep situations to include repeated and split sleep schedules. Chapter 4 introduces a related modeling approach which may be employed for predicting changes due to misalignment and resynchronization of the internal biological clock with the environment. The remainder of the thesis consists of concluding remarks, appendices with mathematical proofs, and references.
Chapter 1

Formulation of the Generalized Model

A variety of biomathematical models have been developed to predict cognitive performance impairment due to sleep loss and/or circadian misalignment (Mallis et al., 2004). In essence, these models are all based on the Two-Process Model (TPM) (Borbély, 1982), which posits the involvement of two primary processes of sleep/wake regulation (Achermann, 2004): a homeostatic process representing the progressive build-up of sleep pressure across time awake and the progressive decline across time asleep; and a circadian process representing the waxing and waning of sleep pressure between night and day.

The TPM has been used successfully in predicting performance under conditions of total sleep deprivation (Daan et al., 1984), as have other biomathematical models based on the TPM (see Van Dongen, 2004). However, for conditions of chronic sleep restriction (i.e., a reduced ration of sleep each day), the TPM predicts a rapid stabilization of performance impairment (within a day or two)—which is not in agreement with experimental observations (Van Dongen et al., 2003). This discrepancy has led to the development of TPM variations with an additional process modulating the homeostatic process across days of sleep restriction (Hursth et al., 2004; Johnson et al., 2004; Avinash et al., 2005; Åkerstedt et al., 2008). Still, these models predict adaptation to chronic sleep restriction in the long run as well, regardless of how substantial the daily sleep reduction actually is. The validity of such a prediction when sleep is restricted to less than approximately 4 hours per day is questionable (Belenky et al., 2003; Van Dongen and Dinges, 2003b).

Here we show\(^a\) that the homeostatic process of the TPM, and the various models based on it and expanding it with a modulating process, belong to a class of differential equations with a much richer repertoire of predictions. In fact, the essence of the currently

\(^{a}\)Published as McCauley et al. (2009a).
available biomathematical models of performance, and beyond, can be captured by a system of coupled nonhomogeneous first-order ordinary differential equations (ODEs). We will introduce and analyze the dynamic properties of this new generalized class of models. We will produce computer simulations of the new model and consider an extension of the model framework that guides us to the development of an improved biomathematical model of human cognitive performance.

1.1 The two-process model as a system of coupled nonhomogeneous first-order ordinary differential equations

The homeostatic process of the two-process model (TPM) has historically been formulated as a set of iterative equations (Borbély and Achermann, 1999), which can be written as follows:

\[ w_n(t + \Delta t) = 1 - e^{-\Delta t/\tau_r}(1 - w_n(t)), \quad \text{for} \quad t \in [t_n, t_n + W_n], \quad (1.1.1) \]

\[ s_n(t + \Delta t) = e^{-\Delta t/\tau_d}s_n(t), \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}]. \quad (1.1.2) \]

In these equations, \( w_n \) and \( s_n \) are the homeostatic pressure for sleep during wakefulness and sleep, respectively, on day \( n \), where \( n = 0, 1, 2, \ldots \). Each day has a duration \( T_n \) (e.g., 24 hours) consisting of a waking period of duration \( W_n \) and a sleep period of duration \( T_n - W_n \). Time \( t_n \) is the time of awakening on day \( n \): \( t_{n+1} = t_n + T_n \), where \( t_0 \) is the initial time of awakening. The parameters \( \tau_r > 0 \) and \( \tau_d > 0 \) are time constants, respectively, for the exponential rise of homeostatic sleep pressure during wakefulness and the exponential decay thereof during sleep; and \( \Delta t \) is a time step (typically set to 0.5 hours) by which the equations are evaluated iteratively. Note that the formulation of the homeostat, Eqs. (1.1.1) and (1.1.2), is such that the homeostatic pressure increases exponentially to an upper asymptote of 1 during (prolonged) wakefulness, and decreases exponentially to a lower asymptote of zero during sleep. The equations for wake and sleep are coupled by:

\[ s_n(t_n + W_n) = w_n(t_n + W_n), \quad (1.1.3) \]

\[ w_{n+1}(t_{n+1}) = s_n(t_{n+1}). \quad (1.1.4) \]

The circadian process of the TPM has historically been formulated in closed form, and can be written as follows (Borbély and Achermann, 1999):

\[ c(t) = \sum_{k=1}^{s} a_k \sin\left(\frac{2k\pi}{\tau}(t - \phi)\right), \quad (1.1.5) \]
where \( c(t) \) can be seen as a circadian pressure for wakefulness (Czeisler and Dijk, 1995). Eq. (1.1.5) represents a sinusoidal curve containing five harmonics with progressively decreasing amplitudes \( a_k \), a fundamental period \( \tau \) (typically assumed to be 24 hours), and an alignment in time determined by circadian phase parameter \( \phi \). Other versions of the circadian process have been used (Achermann and Borbély, 1994), including a version in which \( c(t) \) is based on differential equations (Kronauer, 1990).

In the context of the TPM, cognitive performance capability \( p_n(t) \) during wakefulness is modeled by the interaction of the homeostatic process \( w_n(t) \) and the circadian process \( c(t) \). Likewise, cognitive performance capability \( q_n(t) \) during sleep—which is not measurable but would correspond to performance immediately after awakening from sleep—\( ^b \)—is predicted by the interaction of the sleep equation for the homeostatic process \( s_n(t) \) and the circadian process \( c(t) \). Although there is evidence that the interaction between the homeostatic process and the circadian process is nonlinear (Van Dongen and Dinges, 2003a), a linear form has been successful in predicting performance observations under a variety of experimental circumstances (Achermann, 2004). Achermann and Borbély observed that the arithmetic difference between the homeostat and the circadian rhythm accurately captured performance impairment during total sleep deprivation experiments. Assuming the linearity holds during sleep, we can write:

\[
p_n(t) = w_n(t) - c(t), \quad \text{for} \quad t \in [t_n, t_n + W_n], \quad (1.1.6)
\]

\[
q_n(t) = s_n(t) - c(t), \quad \text{for} \quad t \in [t_n + W_n, t_n + 1]. \quad (1.1.7)
\]

In this formulation greater values of \( p_n \) and \( q_n \) reflect reduced performance capability.

The homeostatic process of the TPM, Eqs. (1.1.1) and (1.1.2), can be written in the form of a system of nonhomogeneous first-order ODEs (see Lemma 1.1.1).

**Lemma 1.1.1.** Let

\[
s_n(t + \Delta t) = e^{bt} s_n(t), \quad (1.1.8)
\]

be an iterative equation with time step \( \Delta t \) and \( b \) is constant. The initial value (e.g., at \( t = 0 \)) \( s_n(0) \) is assumed given. The equivalent representation as a first-order ordinary differential

\(^b\)The short-term effects of sleep inertia (Dinges, 1990) on performance immediately upon awakening are not of interest for the dynamic properties of performance predictions across wake/sleep cycles, and are therefore ignored throughout this thesis and will be addressed in future research.
equation (ODE) is:

\[
\frac{d s_n(t)}{dt} = b \ s_n(t),
\]

where the initial condition \( s_n(0) \) is assumed given.

**Proof.** We begin by subtracting \( s_n(t) \) from both sides of Eq. (1.1.8) and dividing by \( \Delta t \):

\[
\frac{s_n(t + \Delta t) - s_n(t)}{\Delta t} = \frac{e^{b \Delta t} s_n(t) - s_n(t)}{\Delta t}.
\]

Let us now take the limit as \( \Delta t \to 0 \):

\[
\lim_{\Delta t \to 0} \frac{s_n(t + \Delta t) - s_n(t)}{\Delta t} = \lim_{\Delta t \to 0} \frac{e^{b \Delta t} s_n(t) - s_n(t)}{\Delta t}.
\]

The left-hand side of Eq. (1.1.10) represents the definition of \( d s_n(t)/dt \). Since the right-hand side has as its limit 0/0, we can enlist l’Hôpital’s rule and take the derivative of the numerator and denominator with respect to \( \Delta t \):

\[
\frac{d s_n(t)}{dt} = \lim_{\Delta t \to 0} \frac{b \ e^{b \Delta t} s_n(t)}{1} = b \ s_n(t).
\]

The analytical solution to this ODE is:

\[
s_n(t) = e^{b t} s_n(0).
\]

We obtain the system of ODEs:

\[
\frac{d w_n}{dt} = -\frac{1}{\tau_r} (w_n - 1), \quad \text{for} \quad t \in [t_n, t_n + W_n],
\]

\[
\frac{d s_n}{dt} = -\frac{1}{\tau_d} s_n, \quad \text{for} \quad t \in [t_n + W_n, t_n + 1],
\]

where the initial condition for the first cycle, \( w_0(t_0) \) is assumed to be given, and \( w_n \) and \( s_n \) are again coupled as described by Eqs. (1.1.3) and (1.1.4). Note that in Eqs. (1.1.11) and (1.1.12), \( w_n(t) \) and \( s_n(t) \) are still functions of time, but to limit clutter we will use the shorthand \( w_n \) and \( s_n \) notation in the differential equations. Using Eqs. (1.1.6) and (1.1.7), the equations for performance for the TPM can now be written as:

\[
\frac{d p_n}{dt} = -\frac{1}{\tau_f} p_n + \beta(t), \quad \text{for} \quad t \in [t_n, t_n + W_n],
\]

\[
\frac{d q_n}{dt} = -\frac{1}{\tau_d} q_n + \gamma(t), \quad \text{for} \quad t \in [t_n + W_n, t_n + 1],
\]
where the level of performance at the beginning of the first cycle is $p_0(t_0) = w_0(t_0) - c(t_0)$, and $p_n$ and $q_n$ are coupled (using Eqs. (1.1.3) and (1.1.4)) by:

\[ q_n(t_n + W_n) = p_n(t_n + W_n), \]  
\[ p_{n+1}(t_{n+1}) = q_n(t_{n+1}). \]  

For the TPM, the nonhomogeneities $\beta(t)$ and $\gamma(t)$ are given by:

\[ \beta(t) = -\frac{1}{\tau_r} (c(t) - 1) - \frac{dc(t)}{dt}, \]  
\[ \gamma(t) = -\frac{1}{\tau_d} (c(t) - LA) - \frac{dc(t)}{dt}. \]  

where the asymptote of 1 for Eq. (1.1.1) is in the nonhomogeneity of Eqs. (1.1.17). The ODE system of Eqs. (1.1.13) and (1.1.14) represents the exact same model as the performance model of the original TPM in Eqs. (1.1.6) and (1.1.7). Another representation of the two-process model which is often seen in the literature is written as follows:

\[ w_n(t + \Delta t) = UA - e^{-\Delta t/\tau_r}(UA - w_n(t)), \text{ for } t \in [t_n, t_n + W_n], \]  
\[ s_n(t + \Delta t) = LA - e^{-\Delta t/\tau_d}(LA - s_n(t)), \text{ for } t \in [t_n + W_n, t_{n+1}], \]  

where UA and LA are the upper and lower asymptotes, respectively, which are now estimated from the data. In this model the equivalent ODE representation for performance is written exactly as Eqs. (1.1.13) and (1.1.14) except for a different nonhomogeneity:

\[ \beta(t) = -\frac{1}{\tau_r} (c(t) - UA) - \frac{dc(t)}{dt}, \]  
\[ \gamma(t) = -\frac{1}{\tau_d} (c(t) - LA) - \frac{dc(t)}{dt}. \]  

We can generalize the performance equations to both of these to the following linear\(^a\) nonhomogeneous first-order differential equations (ODEs):

\[ \frac{dp_n}{dt} = \alpha p_n + \beta(t), \text{ for } t \in [t_n, t_n + W_n], \]  
\[ \frac{dq_n}{dt} = \sigma q_n + \gamma(t), \text{ for } t \in [t_n + W_n, t_{n+1}], \]  

where the initial level of performance $p_0(t_0)$ is assumed to be given and coupling is achieved by Eqs. (1.1.15) and (1.1.16) (see Fig. 1.1).

\(^a\)Linear means that the right-hand side of Eqs. (1.1.23) and (1.1.24) are linear in the dependent variables $p$ and $q$, respectively.
This generalized form encompasses the interplay between two processes for predicting neurobehavioral performance; process $p_n$ with the time-dependent nonhomogeneity $\beta(t)$ during wakefulness, and process $q_n$ with the time-dependent nonhomogeneity $\gamma(t)$ during sleep. We will refer to the generalized model of Eqs. (1.1.23) and (1.1.24) as the gTPM. In this general form $\alpha$ and $\sigma$ are (possibly time-dependent) rate parameters with no restriction.
Figure 1.2: Analogous system for the gTPM. We show two separate compartments which describe performance, \( p_n(t) \), during wakefulness (panel a) and nominal performance, \( q_n(t) \), during sleep (panel b). In general the contents of these compartments grow or decay depending on the value and sign of their respective rate constants: \( \alpha \) for performance during wakefulness and \( \sigma \) for nominal performance during sleep. The two time-dependent inputs \( \beta(t) \) and \( \gamma(t) \) are assumed to be bounded, oscillatory functions.

on sign, where in the TPM \( \alpha = -1/\tau_r \) and \( \sigma = -1/\tau_d \). The continuous, bounded functions \( \beta(t) \) and \( \gamma(t) \) are time-dependent “external” forces on performance during wakefulness and sleep, respectively. These include the effect of the endogenous circadian pacemaker but may also include other effects, e.g., from the exogenous environment.

1.1.1 Analogous system of compartments for the generalized Two-Process Model (gTPM)

In understanding the physiological meaning of a biomathematical model it is often helpful to visualize the system as interconnected compartments (see Fig. 1.2). As such, the linear system of Eqs. (1.1.23) and (1.1.24) can each be described as a single chamber which contains a time-dependent agent that is assumed to be proportional to the level of performance during wakefulness, \( p_n(t) \), and to nominal performance during sleep, \( q_n(t) \). The concentrations of these agents are governed by the rate constants \( \alpha \) and \( \sigma \), respectively. Each compartment has an external time-dependent input, which may be linked to the endogenous effects of the biological pacemaker on cognitive performance during wakefulness or may originate from exogenous effects such as by the environment in the form of light or ambient temperature. These inputs are the nonhomogeneities \( \beta(t) \) in Eqs. (1.1.23) during wakefulness and \( \gamma(t) \) in Eqs. (1.1.24) during sleep.

1.1.2 Initial values at wake onset and sleep onset

In order to investigate model dynamics across days, it is useful to focus only on the predicted initial values at wake onset \( (t = t_n) \) and sleep onset \( (t = t_n + W_n) \). For the case
when α and σ are constant, we note that Eqs. (1.1.23) and (1.1.24) can be integrated to obtain the general solution for time \( t \in [t_n, t_{n+1}] \), for any particular day \( n \):

\[
p_n(t) = \Psi_n(t)p_n(t_n) + \int_{t_n}^t \psi_n(t)\psi_n^{-1}(s)\beta(s)ds, \quad \text{for} \quad t \in [t_n, t_n + W_n], \tag{1.1.25}
\]

\[
q_n(t) = \Phi_n(t)q_n(t_n + W_n) + \int_{t_n + W_n}^t \phi_n(t)\phi_n^{-1}(s)\gamma(s)ds, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}], \tag{1.1.26}
\]
during wake and sleep, respectively, and where:

\[
\Psi_n(t) = \psi_n(t)\psi_n^{-1}(t_n), \tag{1.1.27}
\]

\[
\Phi_n(t) = \phi_n(t)\phi_n^{-1}(t_n + W_n), \tag{1.1.28}
\]

and

\[
\psi_n(t) = e^{\alpha t}, \tag{1.1.29}
\]

\[
\phi_n(t) = e^{\sigma t}. \tag{1.1.30}
\]

Using equations (1.1.15), (1.1.16), (1.1.25) and (1.1.26) and introducing simplified notation:

\[
\Omega_n(t) = \int_{t_n}^t \psi_n(t)\psi_n^{-1}(s)\beta(s)ds, \tag{1.1.31}
\]

\[
\Theta_n(t) = \int_{t_n + W_n}^t \phi_n(t)\phi_n^{-1}(s)\gamma(s)ds, \tag{1.1.32}
\]

we obtain the difference equations for the level of performance at both the onset of wakefulness and the onset of sleep for each day \( n \) given \( p_0(t_0) \) (see Appendix A.1):

\[
p_{n+1}(t_{n+1}) = \Phi_n(t_{n+1})\Psi_n(t_n + W_n)p_n(t_n) + F_n, \tag{1.1.33}
\]

where \( F_n = \Phi_n(t_{n+1})\Omega_n(t_n + W_n) + \Theta_n(t_{n+1}) \), and

\[
q_{n+1}(t_{n+1} + W_n) = \Psi_{n+1}(t_{n+1} + W_n)\Phi_n(t_{n+1})q_n(t_n + W_n) + G_n, \tag{1.1.34}
\]

where \( G_n = \Psi_{n+1}(t_{n+1} + W_n)\Theta_n(t_{n+1}) + \Omega_{n+1}(t_{n+1} + W_{n+1}) \), for all \( T_n, W_n : 0 < W_n \leq T_n \) and \( n = 0, 1, 2, \ldots \). Note that \( q_0(t_0 + W_0) \) can be determined from Eqs. (1.1.15) and (1.1.25) in terms of the initial value \( p_0(t_0) \):

\[
q_0(t_0 + W_0) = p_0(t_0 + W_0)
\]

\[
= \Psi_0(t_0 + W_0)p_0(t_0) + \Omega_0(t_0 + W_0). \tag{1.1.35}
\]

\( ^d \)The simple case of constant parameters was chosen to reduce complexity, though solutions for time-dependent parameters may be derived for this linear system.
1.1.3 Model dynamics

An important feature of models that are developed to predict cognitive performance is whether, and under what conditions, the solution of the model reaches a state of equilibrium under (near-)constant wake/sleep schedules. For instance, under a constant wake/sleep schedule, the model may reach a state in which the predictions for one wake/sleep cycle are exactly the same as those for the next wake/sleep cycle. In terms of the initial values, this condition is described by:

\[ p_{n+1}(t_{n+1}) = p_n(t_n), \]
\[ q_{n+1}(t_{n+1} + W_n) = q_n(t_n + W_n). \]

(1.1.36)

(1.1.37)

More generally, the model may reach a state in which the predictions for one wake/sleep cycle are exactly the same as those occurring \( m \) wake/sleep cycles later, in a periodic manner:

\[ p_{n+m}(t_{n+m}) = p_n(t_n), \]
\[ q_{n+m}(t_{n+m} + W_n) = q_n(t_n + W_n), \]

(1.1.38)

(1.1.39)

where \( m \in \{1, 2, \ldots\} \). We call this situation an equilibrium state of the model.

If a state of equilibrium exists given a (near-)constant wake/sleep schedule, it is of interest whether the model converges to this point even if its current state is different. We say that the model is asymptotically stable \((m = 1)\) or asymptotically periodic (Verhulst, 2006) \((m > 1)\) if:

\[ \lim_{n \to \infty} p_{n+m}(t_{n+m}) = p_n(t_n), \]
\[ \lim_{n \to \infty} q_{n+m}(t_{n+m} + W_n) = q_n(t_n + W_n), \]

(1.1.40)

(1.1.41)

regardless of starting values \( p_0(t_0) \) and \( q_0(t_0 + W_0) \). In general, such as in nonlinear models (see Verhulst, 2006), it is possible that Eqs. (1.1.40) and (1.1.41) only hold if \( p_0(t_0) \) and \( q_0(t_0 + W_0) \) are reasonably close to the \( \lim_{n \to \infty} p_n(t_n) \) and to the \( \lim_{n \to \infty} q_n(t_n + W_n) \), respectively. The values of \( p_0(t_0) \) and \( q_0(t_0 + W_0) \) for which the model is attracted to the state of equilibrium or to the periodic state of equilibrium constitute the domain of attraction.

To investigate the existence of equilibrium states for the gTPM, let’s consider wake/sleep schedules in which \( T_n = T \) and \( W_n = W \) are constant. In this case \( \Psi_n(t_n + W_n) = \Psi(t_n + W) \) and \( \Phi_n(t_{n+1}) = \Phi(t_n + T) \) are also constant. Let us also assume that \( \beta(t) \) and \( \gamma(t) \) are
bounded, oscillatory functions capturing the circadian rhythm, and that the circadian period \( \tau = T \) (as is typical when the circadian rhythm is entrained). Under these conditions, \( \Omega_n = \Omega \) and \( \Theta_n = \Theta \) are constant as well (see Eqs. (1.1.31) and (1.1.32)), which means \( F_n = F \) and \( G_n = G \) are constant (see Appendix A.2 for \( m = 1 \)). States of equilibrium may now be derived by solving Eqs. (1.1.33) and (1.1.34) for \( p(t_n) \) and \( q(t_n + W) \) by setting 

\[
\begin{align*}
\frac{p_{n+1}}{p_n} &= \frac{p_n}{p(t_n)} = \frac{F}{1-\Phi(t_n + T)\Psi(t_n + W)}, \\
\frac{q_{n+1}}{q_n} &= \frac{q_n}{q(t_n + W)} = \frac{G}{1-\Psi(t_n + W)\Phi(t_n + T)}.
\end{align*}
\]

Here, \( p(t_n) \) is the state of equilibrium for the onset of wakefulness and \( q(t_n + W) \) is the state of equilibrium for the onset of sleep. This is illustrated in Fig. 1.3.

Examination of Eqs. (1.1.42) and (1.1.43) reveals that equilibrium states exist when the denominators do not equal zero, i.e., \( \Phi(t_n + T)\Psi(t_n + W) \neq 1 \). By virtue of Eqs. (1.1.29) and (1.1.30) it follows that for the TPM (e.g., the case of the gTPM where both parameters \( \alpha \) and \( \sigma \) are negative) we have:

\[
0 < e^{\sigma(W)}e^{\alpha(W)} < 1,
\]

for all \( T, W: 0 < W \leq T \). We see that for the TPM case a state of equilibrium is reached under all possible (near-)constant wake/sleep scenarios. However, in general for the gTPM (e.g., no restrictions on the signs of \( \alpha \) or \( \sigma \)) this is not the case, as we shall see.

Asymptotic stability of the equilibrium states when they do exist can be determined by a process called linearization (Verhulst, 2006). In the case of the gTPM, this is accomplished by evaluating the first derivative of \( p_{n+1} \) in Eq. (1.1.33) with respect to \( p_n \) at the state of equilibrium \( p(t_n) \), and the first derivative of \( q_{n+1} \) in Eq. (1.1.34) with respect to \( q_n \) at the state of equilibrium \( q(t_n + W) \). Specifically, the equilibrium states are asymptotically stable if the difference between \( p_{n+1}(t_n + 1) \) and \( p_n(t_n) \) tends to decrease, and likewise for \( q_{n+1}(t_n + 1) \) and \( q_n(t_n) \), which is the case when:

\[
\frac{dp_{n+1}}{dp_n} < 1, \quad \frac{dq_{n+1}}{dq_n} < 1.
\]

\( ^e \)We recognize that this model is linear and thus derivatives are trivial. In general, linearizing nonlinear models allows for stability analysis near the equilibrium state (Verhulst, 2006).
Figure 1.3: This plots shows an equilibrium state for performance prediction with the TPM case (see Eqs. (1.1.13) through (1.1.18)) of the gTPM. The figure shows 4 wake/sleep cycles ($n = 0, 1, 2, 3$), each with constant day length $T = 24$ h and sleep duration $T - W = 4$ h. In this example the circadian process is assumed to have the same period as the length of day, $\tau = 24$ h. The lower horizontal dash-dotted line connects points (lower black squares) for the equilibrium state at onset of wakefulness $p(t_n)$, predicted by Eq. (1.1.42). The upper horizontal dotted line connects points (upper black squares) for the equilibrium state at onset of sleep $q(t_n + W)$, Eq. (1.1.43). Under this constant wake/sleep schedule the initial values for wake onset (triangles) and sleep onset (circles) converge to their respective equilibrium states and stabilize there.

See Appendix A.3 for a proof. From Eqs. (1.1.33) and (1.1.34) and using Eqs. (1.1.29) and (1.1.30) we find:

$$\left| \frac{d p_{n+1}^p}{d p_n^p} \right| = \Phi(t_n + T)\Psi(t_n + W)$$

$$= e^{\sigma(T-W)} e^{\alpha W},$$

(1.1.47)
and

\[
\left| \frac{dq_{n+1}}{dq_n} \right|_q = \Psi(t_n + W)\Phi(t_n + T) = e^{\alpha W}e^{\sigma(T - W)}.
\]

(1.1.48)

When both \(\alpha\) and \(\sigma\) are negative (e.g., as in the TPM), inequalities (1.1.45) and (1.1.46) are held for all \(T, W: 0 < W \leq T\). Hence, the equilibrium state \(p(t_n)\) and \(q(t_n + W)\) of the TPM case of the gTPM are all asymptotically stable.

Notice that Eqs. (1.1.47) and (1.1.48) do not depend on \(p(t_n)\) and \(q(t_n + W)\) (as is the case for linear ODE systems). Therefore, under (near-)constant wake/sleep schedules and the negativity assumptions on \(\alpha\) and \(\sigma\), a state of equilibrium is always reached in the TPM regardless of what the initial values \(p_0(t_0)\) and \(q_0(t_0 + W)\) are (see Fig. 1.4). In other words, the TPM is \textit{globally} asymptotically stable. Physiologically, this means that the TPM predicts that any amount of daily sleep restriction, including total sleep deprivation, eventually results in adaptation.\(^4\) From the compartment perspective, equilibrium is achieved when the \(p_n\) compartment fills the same amount during wakefulness as the \(q_n\) compartment empties during sleep (see Fig. 1.2). The rate constants \(\Phi(t_n + T)\Psi(t_n + W)\) in Eq. (1.1.33) and \(\Psi(t_{n+1} + W)\Phi(t_{n+1})\) in Eq. (1.1.34) determine how quickly the adaptation process occurs (see Fig. 1.4).

However, by relaxing the condition that both \(\alpha\) and \(\sigma\) are negative, we may have a situation where Eq. (1.1.44) is no longer held. To examine this, let us assume parameter \(\sigma\) is negative, but parameter \(\alpha\) is positive. For this case, the denominator in Eq. (1.1.42) or equivalently the denominator in Eq. (1.1.43) could be zero. This can be seen by examination of the product \(e^{\sigma(T - W)}e^{\alpha W}\) in Eq. (1.1.44). Here, \(e^{\sigma(T - W)} < 1\), while \(e^{\alpha W} > 1\). For a particular combination of \(\sigma\) and \(\alpha\), and by varying the amount of wakefulness \(W\), this product may change from \(e^{\sigma(T - W)}e^{\alpha W} < 1\) to \(e^{\sigma(T - W)}e^{\alpha W} > 1\), where at unity the equilibrium state does not exist.

In the case when \(\alpha\) is positive, there are three possibilities for the product \(e^{\sigma(T - W)}e^{\alpha W}\). For \(e^{\sigma(T - W)}e^{\alpha W} < 1\), the system has a stable state of equilibrium. For \(e^{\sigma(T - W)}e^{\alpha W} > 1\) there is also a state of equilibrium, but it is unstable. For \(e^{\sigma(T - W)}e^{\alpha W} = 1\), the equilibrium state disappears altogether. We see that by changing the amount of sleep, \(T - W\), a qualitative change—a bifurcation—in the model dynamics can occur: from stable (performance

\(^4\)Adaptation is used here as another word for state of equilibrium, indicating that no further performance deficits are accumulated. Adaptation is not used to mean a return to baseline levels in this thesis.
level tends exponentially toward the equilibrium state), to a condition with no equilibrium state, to unstable (performance level tends exponentially away from the equilibrium state).

We can determine the relationship between $W, T, \alpha$ and $\sigma$ at the bifurcation by setting the product $e^{\sigma(T-W)}e^{\alpha W}$ to unity in Eq. (1.1.44), and derive a formula for the critical amount of daily wakefulness $W_c$ beyond which asymptotic stability is no longer achieved:

$$W_c = \frac{\sigma}{\sigma - \alpha} T. \quad (1.1.49)$$

If wakefulness falls below the critical amount defined by Eq. (1.1.49) ($W < W_c$), then this model predicts exponential convergence to the state of equilibrium. If wakefulness exceeds
Figure 1.5: The plot shows the dynamics of the states of equilibrium for a continuous range of wakefulness durations (solid lines). The vertical dashed line represents the critical amount of wakefulness defined by Eq. (1.1.49) where the equilibrium state vanishes. As can be seen from Eq. (1.1.49), the critical value $W_c$, depends on the estimates for the parameters $\sigma$ and $\alpha$. However, we can see as wakefulness approaches $W_c$ from the left the equilibrium state increases hyperbolically toward infinity. As wakefulness approaches $W_c$ from the right side the equilibrium state decreases hyperbolically toward negative infinity.

Notice that the equilibrium state remains negative as wakefulness increases from the bifurcation point upwards toward the duration of day, $T$. When wakefulness duration is greater than the bifurcation predictions across days (e.g., at the onset of wakefulness or at the onset of sleep) the trajectory will continually and smoothly diverge away from the negative and now unstable (see Fig. 1.6) equilibrium state. We will see for a new model formulated in Chapter 1.3 that this is not always the case. That is, the equilibrium state may become positive for wake durations

\[\text{though the negative equilibrium may not be physically meaningful (e.g., when performance is expressed as PVT lapses) it does provide an asymptote for the unstable trajectory to diverge from.}\]
Figure 1.6: Plot showing the magnitude of the product $e^{\sigma(T-W)}e^{\alpha W}$ in Eq. (1.1.44) (i.e., the single eigenvalue of the coefficient in Eq. (1.1.25)) versus duration of wakefulness. The vertical dashed line represents the critical amount of wakefulness defined by Eq. (1.1.49) where the equilibrium state vanishes. From Eq. (1.1.49), the critical value $W_c$, depends on the estimates for the parameters $\sigma$ and $\alpha$. However, we can see that the eigenvalue crosses unity exactly at the bifurcation point, showing the qualitative change in model behavior from stable to unstable.

near length of day. This characteristic provides an interesting and useful model behavior.

Let us now consider the case where $T \neq \tau$. With both $T$ and $\tau$ still held constant, we will assume they are related such that the temporal alignment of the circadian cycle relative to the wake/sleep cycle is periodically the same. In mathematical terms we assume that $T/\tau = d/m$, where $d/m \in \mathbb{Q}$ is reduced to the lowest terms. Since the integrals $\Omega_n$ and $\Theta_n$ in Eqs. (1.1.31) and (1.1.32) are formulated by integration over a domain now different than the period of the nonhomogeneities $\beta(t)$ and $\gamma(t)$, the system of Eqs. (1.1.33) and (1.1.34) becomes periodic (see Appendix A.2), with period $mT$. Starting with values $p(t_n)$ and $q(t_n + W)$ in an arbitrary day $n$, and applying Eqs. (1.1.33) and (1.1.34) $m$ times, one returns to the same values $p(t_n)$ and $q(t_n + W)$. This equilibrium state is different for each of the starting days $n, n+1, \ldots, n+m-1$; effectively, therefore, the gTPM cycles through $m$ different equilibrium states. For the TPM each of these equilibrium states are globally asymptotically stable (see Appendix A.4). Thus, the dynamical system is always attracted to an asymptotically stable periodic equilibrium state modulated by the oscillations of $\Omega_n$ and $\Theta_n$ (see Fig. 1.7).
Figure 1.7: The plot shows a periodic state of equilibrium for performance prediction with the TPM. The figure shows 14 wake/sleep cycles ($n = 0, 1, \ldots, 13$), with each cycle of constant length $T = 28$ h, and sleep duration $T - W = 4$ h. The circadian process is assumed to have a constant period $\tau = 24$ h for the purpose of this example, although this may be only approximately true in reality (Czeisler et al., 1999). The initial values for wake onset (triangles) and sleep onset (circles) rapidly converge to the sequence of $m$ periodic fixed points producing an oscillatory pattern that repeats every $m$ wake/sleep cycles. In this case $T / \tau = 28 / 24 = 7 / 6; \text{ thus, } m = 6$.

1.1.3.1 Dynamics across days

The model behavior across days can further be studied by deriving the closed form of Eq. (1.1.33) for the level of performance at the onset of wakefulness and Eq. (1.1.34) for the onset of sleep. These solutions can be derived based on the following two proofs.

**Lemma 1.1.2.** Let $a$ be a real valued number. Consider $\sum_{i=0}^{n} a^i : i \in \mathbb{N}$. The closed form is:

$$\sum_{i=0}^{n} a^i = \frac{1 - a^{n+1}}{1 - a}.$$
Proof.

\[
\sum_{i=0}^{n+1} a^i = \sum_{i=0}^{n} a^i + a^{n+1} \\
= 1 + a + a^2 + \ldots + a^{n-1} + a^n + a^{n+1} \\
= 1 + a \left( 1 + a + \ldots + a^{n-1} + a^n \right) \\
= 1 + a \sum_{i=0}^{n} a^i.
\]

Therefore

\[
\sum_{i=0}^{n} a^i + a^{n+1} = 1 + a \sum_{i=0}^{n} a^i,
\]

and

\[
\sum_{i=0}^{n} a^i = \frac{1 - a^{n+1}}{1 - a}.
\]

\[\square\]

Lemma 1.1.3. Let

\[p_{n+1}(t_{n+1}) = a p_n(t_n) + F,\]

where the coefficient \(a\) and \(F\) are constant, be a linear nonhomogeneous difference equation (DE). The closed form solution is then:

\[p_n(t_n) = a^n p_0(t_0) + (1 - a^n) (1 - a)^{-1} F, \quad (1.1.50)\]

where \(n \in \mathbb{N}\).

Proof. For \(n = 1\) we have:

\[p_1(t_1) = a p_0(t_0) + F \]

\[= a p_0(t_0) + (1 - a)(1 - a)^{-1} F.\]

Assume

\[p_k(t_k) = a^k p_0(t_0) + (1 - a^k)(1 - a)^{-1} F.\]
Now consider:

\[
p_{k+1}(t_{k+1}) = ap_k(t_k) + F
\]

\[
= a \left( a^k p_0(t_0) + (1 - a^k)(1 - a)^{-1}F \right) + F
\]

\[
= a^{k+1} p_0(t_0) + a(a^{k-1} + a^{k-2} + \ldots + 1)F + F
\]

\[
= a^{k+1} p_0(t_0) + (a^k + a^{k-1} + \ldots + a)F + 1F
\]

\[
= a^{k+1} p_0(t_0) + (a^k + a^{k-1} + \ldots + a + 1)F
\]

\[
= a^{k+1} p_0(t_0) + (1 - a^{k+1})(1 - a)^{-1}F,
\]

where we have used Lemma (1.1.2).

Using Eq. (1.1.50) we can explicitly write the closed form solution of Eq. (1.1.33) for the onset of wakefulness:

\[
p_n(t_n) = \left( e^{\alpha W} e^{\sigma(T - W)} \right)^n p_0(t_0) + \left( 1 - \left( e^{\alpha W} e^{\sigma(T - W)} \right)^n \right) \left( 1 - e^{\alpha W} e^{\sigma(T - W)} \right)^{-1} F,
\]

(1.1.51)

and Eq. (1.1.34) for the onset of sleep:

\[
q_n(t_n + W) = \left( e^{\sigma(T - W)} e^{\alpha W} \right)^n q_0(t_0 + W)
\]

\[
+ \left( 1 - \left( e^{\sigma(T - W)} e^{\alpha W} \right)^n \right) \left( 1 - e^{\sigma(T - W)} e^{\alpha W} \right)^{-1} G.
\]

(1.1.52)

Notice that Eqs. (1.1.51) and (1.1.52) are invariant with respect to time \( t_n \), and that when \( 0 < e^{\alpha W} e^{\sigma(T - W)} < 1 \), as in the TPM, both equations tend to their equilibrium points defined by Eqs. (1.1.42) and (1.1.43), respectively. We can also see that these two closed form equations do not apply exactly at the bifurcation since the denominators in their right-hand sides (e.g., \( 1 - e^{\alpha W} e^{\sigma(T - W)} \)) vanish. Exactly at the bifurcation point \( W = W_c \), where \( e^{\alpha W_c} e^{\sigma(T - W_c)} = 1 \), the iterative Eqs. (1.1.33) and (1.1.34) take on the form:

\[
p_{n+1}(t_{n+1}) = p_n(t_n) + F(W = W_c), \tag{1.1.53}
\]

\[
q_{n+1}(t_{n+1} + W_c) = q_n(t_n + W_c) + G(W = W_c). \tag{1.1.54}
\]

It can be shown that the closed form solutions of these equations are:

\[
p_n(t_n) = nF(W = W_c) + p_0(t_0), \tag{1.1.55}
\]

\[
q_n(t_n + W_c) = nG(W = W_c) + u_0(t_0 + W_c). \tag{1.1.56}
\]
Here we see that at the bifurcation the gTPM model predicts that the rate of change in the level of performance at the onset of wake and the onset of sleep across days will be constant with slopes $F(W = W_c)$ and $G(W = W_c)$, respectively.

1.2 Laboratory performance data in sleep deprivation studies

The gTPM biomathematical model of Eqs. (1.1.23) and (1.1.24) was fit to data acquired from two separate sleep studies (Belenky et al., 2003; Van Dongen et al., 2003). Each of these laboratory studies consisted of four different sleep deprivation schedules.

In one study a total of 48 healthy young adults were subjected to one of four laboratory sleep deprivation protocols (Van Dongen et al., 2003). Each protocol began with several baseline days involving 8 h time in bed (TIB). Subsequently, 13 subjects were kept awake for three additional days, for a total of 88 h awake. The remaining subjects underwent sleep restriction schedules for 14 days involving one of three possible TIB conditions: 4 h TIB per day for 13 subjects; 6 h TIB per day for 13 subjects; and 8 h TIB per day for the remaining nine subjects. The study concluded with two days of recovery with 8 h TIB for all subjects. Awakening was scheduled at 07:30 each day with the exception of the total sleep deprivation schedule, where awakening was at 07:00. Neurobehavioral performance was tested every 2 h during scheduled wakefulness using the PVT (psychomotor vigilance task) (Dinges and Powell, 1985b), for which the number of lapses (reaction times greater than 500 ms) was recorded. Since the model does not account for sleep inertia, the first test bout was removed.

In the other study a total of 66 healthy young adults were subjected to one of four laboratory sleep deprivation protocols (Belenky et al., 2003). Each protocol began with several baseline days involving 8 h TIB. The subjects subsequently underwent various doses of sleep restriction for seven consecutive days and followed by three recovery days with 8 h TIB. The sleep restriction schedule involved 3 h TIB per day for 13 subjects; 5 h TIB per day for 13 subjects; 7 h TIB per day for 14 subjects; and 9 h TIB per day for 16 subjects. Awakening was scheduled at 07:00 each day. Neurobehavioral performance was tested daily at 09:00, 12:00, 15:00 and 21:00 using the PVT. In the 5 h TIB condition an additional test bout occurred at midnight, and in the 3 h TIB condition yet another one took place 2 h after midnight. As in the previous experiment, the first test bout was removed to
account for sleep inertia.

These data sets were combined with a total of 676 data points (the first data point after awakening was removed to account for sleep inertia) to identify model parameter estimates for the gTPM. To find parameter estimates we first utilized the simplex search method (Lagarias et al., 1998), provided by the Matlab parameter estimation tool fminsearch, to obtain an initial parameter estimation. This initial guess was subsequently used as a starting point for the Markov Chain Monte Carlo (MCMC) algorithm (Haario et al., 2005) to obtain a distribution for each of the parameters.

1.2.1 Parameter estimates and predictions for the gTPM

To obtain parameter estimates and predictions from the model described by Eqs. (1.1.23) and (1.1.24), first, one must either numerically solve (see Appendix D) the system of ODEs (e.g., using a Matlab solver) or derive an exact analytical solution to the system of ODEs. The later is preferred, as it uses less computational resources and has no numerical error. However, deriving an analytical solution depends greatly on the specific form of the nonhomogeneities $\beta(t)$ and $\gamma(t)$.

1.2.1.1 Analytical solution within days

Let us consider simple constructions for both of the nonhomogeneities that are oscillatory and bounded:

$$\beta(t) = \kappa c(t) + \mu, \quad (1.2.1)$$
$$\gamma(t) = \kappa c(t) + \mu. \quad (1.2.2)$$

Here the circadian rhythm $c(t)$ is explicitly described by Eq. (1.1.5), $\kappa$ is the amplitude, and the parameter $\mu$ is a constant forcing term on the performance level (as depicted in Fig. 1.8). Using the functions described in Eqs. (1.2.1) and (1.2.2) we can explicitly write this gTPM model case:

$$\frac{dp_n}{dt} = \alpha p_n + \kappa \sum_{k=1}^{5} a_k \sin\left(2k\pi(t - \phi)/\tau\right) + \mu, \quad \text{for} \quad t \in [t_n, t_n + W_n], \quad (1.2.3)$$
$$\frac{dq_n}{dt} = \sigma q_n + \kappa \sum_{k=1}^{5} a_k \sin\left(2k\pi(t - \phi)/\tau\right) + \mu, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}], \quad (1.2.4)$$

where we use published parameters values for the $a_k$’s and $\tau = 24$ (Borbély and Achermann, 1999).
We can now derive an analytical solution to Eqs. (1.1.23) and (1.1.24) (see Appendix A.5), where we find during wakefulness:

\[ p_n(t) = e^{\alpha(t-t_n)} p_n(t_n) + \Omega_n(t), \]  

with

\[ \Omega_n(t) = \kappa \sum_{k=1}^{5} \frac{2k\pi \tau \left( e^{\alpha(t-t_n)} \cos \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - \cos \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)}{4k^2 \pi^2 + \alpha^2 \tau^2} \]
\[ + \kappa \sum_{k=1}^{5} \frac{\alpha \tau^2 \left( e^{\alpha(t-t_n)} \sin \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - \sin \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)}{4k^2 \pi^2 + \alpha^2 \tau^2} \]
\[ + \frac{\mu}{\alpha} \left( e^{\alpha(t-t_n)} - 1 \right), \]  

and during sleep:

\[ q_n(t) = e^{\sigma(t-(t_n+W_n))} q_n(t_n + W_n) + \Theta_n(t), \]  

where

\[ \Theta_n(t) = \kappa \sum_{k=1}^{5} \frac{2k\pi \tau \left( e^{\sigma(t-(t_n+W_n))} \cos \left( \frac{2k\pi}{\tau} (t_n + W_n - \phi) \right) - \cos \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)}{4k^2 \pi^2 + \sigma^2 \tau^2} \]
\[ + \kappa \sum_{k=1}^{5} \frac{\sigma \tau^2 \left( e^{\sigma(t-(t_n+W_n))} \sin \left( \frac{2k\pi}{\tau} (t_n + W_n - \phi) \right) - \sin \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)}{4k^2 \pi^2 + \sigma^2 \tau^2} \]
\[ + \frac{\mu}{\sigma} \left( e^{\sigma(t-(t_n+W_n))} - 1 \right). \]  

These solutions are coupled across days by Eqs. (1.2.5) and (1.2.7) to form a continuous prediction for performance level during wake and a nominal prediction for performance level during sleep. However, to initialize Eq. (1.2.5) we need a value for \( p_0(t_0) \); likewise we need a value for \( q_0(t_0 + W) \) to initialize Eq. (1.2.7).
1.2.1.2 Initial performance level

Eqs. (1.2.5) or (1.2.7) can be used given the initial value \( p_0(t_0) \) (i.e., when initiating model predictions at the onset of wakefulness) or \( q_0(t_0 + W_0) \) (i.e., when initiating model predictions at the onset of sleep), respectively. At baseline it is assumed that cognitive performance level at the onset of wakefulness and at the onset of sleep across days is constant for a particular duration of daily sleep, \( T - W \). In laboratory experiments on the effects of sleep restriction on human performance it is common that participants begin the study in a well rested state. As such, given the baseline sleep duration (i.e., 8 h TIB in the sleep study of Van Dongen et al. (2003)), we can derive the initial values which would maintain a constant level of performance at the onset of wakefulness and the onset of sleep, across days, as a state of equilibrium for any set of parameters (see 8 h TIB predictions in Fig. 1.4).

Without loss of generality, let us assume we begin with performance predictions at the onset of wakefulness. Using the equilibrium state for the onset of wakefulness defined in Eq. (1.1.42), the initial value \( p_0(t_0) \) in terms of parameters for the gTPM is:

\[
p_0(t_0) = \left( 1 - e^{\sigma(T - W_b)} e^{\alpha W_b} \right)^{-1} \left( e^{\sigma(T - W_b)} \Omega(t_0 + W_b) + \Theta(t_0 + T) \right),
\]

(1.2.9)

where \( T \) is constant (typically 24 h), \( W_b \) is the duration of wakefulness (or likewise \( T - W_b \) is the duration of baseline sleep) which provides a constant, baseline performance level across days, and \( \Omega_n(t_n + W_b) \) and \( \Theta_n(t_n + T) \) can be obtained from Eqs. (1.2.6) and (1.2.8), respectively. Using Eq. (1.2.9) to derive the initial performance value at the onset of wakefulness during baseline, the analytical solutions within days, Eqs. (1.2.5) and (1.2.7), coupled by Eqs. (1.1.15) and (1.1.16), can now be used to build a continuous trajectory for performance level within and across days or weeks in the laboratory experiments.

1.2.1.3 Parameter estimates and model predictions

In the following section we present the parameter estimates using the MCMC algorithm (Haario et al., 2005) and the model predictions for the general gTPM defined by Eqs. (1.1.23) and (1.1.24) (see Figs. 1.9 through 1.14 and Table 1.1). These results were obtained using the analytical solutions of Eqs. (1.2.5) and (1.2.7). To establish initial values for Eq. (1.2.5), and per study conditions, the baseline wakefulness is \( W_b = 16 \) h per day.

This means that the predictions at wake and sleep onset for an 8 h TIB schedule (such
Figure 1.9: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the parameters $\alpha$, $\kappa$ and $\phi$ in Eqs. (1.2.3) and (1.2.4). Contour curves represent the 50% and 90% probability levels. As can be seen the parameters are well defined by the data and have near-Gaussian distributions.

Figure 1.10: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the parameters $\alpha$, $\kappa$, $\sigma$ and $\mu$ in Eqs. (1.2.3) and (1.2.4). Contour curves represent the 50% and 90% probability levels. As can be seen the parameters are well defined by the data and have near-Gaussian distributions.
Figure 1.11: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the parameters $\phi$, $\sigma$ and $\mu$ in Eqs. (1.2.3) and (1.2.4). Contour curves represent the 50% and 90% probability levels. As can be seen the parameters are well defined by the data and have near-Gaussian distributions.

as shown in the wake/sleep schedule in the upper left panel of Fig. 1.12) will be constant across days.

<table>
<thead>
<tr>
<th>parameter</th>
<th>mean</th>
<th>standard error</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$</td>
<td>0.011</td>
<td>0.0009</td>
</tr>
<tr>
<td>$\kappa$</td>
<td>0.34</td>
<td>0.06</td>
</tr>
<tr>
<td>$\phi$</td>
<td>21</td>
<td>0.6</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>$-0.087$</td>
<td>0.005</td>
</tr>
<tr>
<td>$\mu$</td>
<td>0.11</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Table 1.1: Parameter estimates and standard errors for the model described by Eqs. (1.2.3) and (1.2.4) using 676 data points from two laboratory sleep deprivation experiments (Belenky et al., 2003; Van Dongen et al., 2003). Notice the parameter $\alpha$ is predicted positive, contrary to the published parameters for the original two-process model (Borbély and Achermann, 1999).

In Fig. 1.13 we can see for the schedule in the upper-left panel that predicted PVT lapses slowly decrease during the 7 days of sleep restriction. Since baseline is assumed to be 16 h of wakefulness per day (i.e., 8 h of sleep), the 9 h TIB condition actually involves sleep extension relative to baseline. Thus, the model predicts an improvement in performance. However, because the recovery days 8 through 10 have sleep durations of 8 h TIB per day, the predictive trajectory returns to the baseline. Both Figs. 1.12 and 1.13 predict that, after
Figure 1.12: Model predictions for four laboratory sleep deprivation conditions (Van Dongen et al., 2003). The upper-left panel shows 16 days with 8 h TIB per day; the upper-right panel shows 14 days with 6 h TIB per day followed by 2 days with 8 h TIB per day; the lower-left panel shows 14 days with 4 h TIB per day followed by 2 days with 8 h TIB per day; and the lower-right panel shows total sleep deprivation for 88 h. Grey regions represent 90% confidence bands for the predicted means. Dots are grouped average PVT lapses data (Van Dongen et al., 2003).

extended chronic sleep restriction, performance level restores quicker for more severely reduced sleep scenarios. Also notice that the first part of the sleep episode is predicted to have the greatest restorative impact on performance.

Using Table 1.1 and Eq. (1.1.49), we determine that the mean value of the bifurcation point $W_c$ is 21.3 h of wakefulness (i.e., 2.7 h of sleep). For this reason, all of the wake/sleep schedules and coinciding performance level predictions at the onset of wake and at the onset of sleep across days shown in Figs. 1.12 and 1.13 converge to a state of equilibrium, except for total sleep deprivation (see the lower right panel in Fig. 1.12). The magnitude of $\sigma$ is approximately 8 times larger than the magnitude of $\alpha$. Therefore, the gTPM predicts
that recovery from performance deficits occurs much faster during sleep than performance degrades during wakefulness. Since recovery in the model is exponential, the beginning of sleep is predicted to be the most beneficial.

Notice, in the parameter estimates shown in Table 1.1, that the parameter $\alpha$ was estimated as a positive number and $\sigma$ as negative. This is contrary to the published parameters for the original TPM (Borbély and Achermann, 1999) where both parameter were predicted to be negative. Because of the predicted change in sign in $\alpha$, the characteristic behavior of the gTPM model is significantly different than that of the TPM. Now a bifurcation is present, which defines the minimum daily amount of sleep needed in order to maintain a
Figure 1.14: Plot showing performance predictions using the gTPM, Eqs. (1.2.3) and (1.2.4). The figure shows 14 wake/sleep cycles ($n = 0, 1, \ldots, 13$), each with constant day length $T = 24$ h. There are five wake/sleep schedules shown with different amounts of daily nocturnal sleep: 0 h (triangles), 2 h TIB (stars), 4 h TIB (circles), 6 h TIB (squares) and 8 h TIB (diamonds), with sleep ending at 07:30 (symbols mark 07:30 each day). Light grey vertical bars depict time in bed. Parameters used are given in Table 1.1. The circadian process is assumed to have the same period as the length of day, $\tau = 24$ h. Heavy dashed lines connect points at the onset of wakefulness $p_n(t_n)$, predicted by Eq. (1.1.33). Notice that since the bifurcation is predicted to be at 2.7 h TIB (see Table 1.1), the 2 h TIB schedule and total sleep deprivation condition are diverging away from their corresponding (negative) unstable states of equilibrium (cf. Fig. 1.5).

When sleep duration is reduced to below the critical amount, performance impairment is predicted to increase exponentially (see Fig. 1.14). The gTPM correctly predicts the escalating performance impairment across extended days seen in experimental observations for severely restricted sleep (e.g., in the 3 and 4 h TIB scenarios shown in Figs. 1.12 and 1.13). However, the model predictions no longer correctly show the rapid degradation in performance impairment for total sleep deprivation (see lower-right panel Fig. 1.12).
1.3 Generalized model as coupled first-order ordinary differential equations

As shown previously, the TPM is a particular case of the gTPM. The TPM predicts rapid stabilization of performance impairment, within a few days, under conditions of chronic sleep restriction. This is not in agreement with experimental observations (Belenky et al., 2003; Van Dongen et al., 2003), which show that performance continues to decline for more than a few days when sleep is chronically reduced. In the gTPM, by relaxing the negativity assumption on the parameters $\alpha$ and $\sigma$ and finding a new set of parameter estimates using data from two separate sleep studies (Belenky et al., 2003; Van Dongen et al., 2003), we found that the gTPM predicts that a bifurcation occurs at approximately 2.7 h TIB per day (see Table 1.1). The corresponding predictive plots in Figs. 1.12 and 1.13 show that performance level approaches a stable state of equilibrium in all cases examined except for total sleep deprivation (lower right panel, Fig. 1.12). For total sleep deprivation, the gTPM predictions diverge away from an unstable equilibrium state. However, we see that the observations for total sleep restriction are significantly underpredicted, whereas the original TPM does correctly predict the rapid performance impairment seen in total sleep deprivation (see McCauley et al., 2009a).

Based originally on an idea proposed by Johnson and colleagues (Johnson et al., 2004) Van Dongen and colleagues introduced a modification of the TPM (referred to as the Extended Two-Process Model (ETPM)) involving the modulation of the lower and upper asymptotes over extended time periods (days and weeks) (Avinash et al., 2005). This modification, which involved the inclusion of an additional process, expanded the behavior of the model to include progressive performance impairment across days of sleep restriction, as follows.

We begin with the iterative form of the homeostatic process of the TPM, Eqs. (1.1.1) and (1.1.2):

\[
\begin{align*}
  w_n(t + \Delta t) &= 1 + (w_n(t) - 1)e^{-\Delta t/\tau_r}, \quad \text{for} \quad t \in [t_n, t_n + W_n], \\
  s_n(t + \Delta t) &= 0 + (s_n(t) - 0)e^{-\Delta t/\tau_d}, \quad \text{for} \quad t \in [t_n + W_n, t_n + 1],
\end{align*}
\]

(1.3.1, 1.3.2)

where we have recast the equations to make the asymptotes (0 and 1) explicit. Replacing the asymptote constants by variables $u_n$ and $v_n$ for the upper and lower asymptotes,
respectively, we get:

\[ w_n(t + \Delta t) = u_n(t + \Delta t) + (w_n(t) - u_n(t))e^{-\Delta t/\tau_r}, \quad (1.3.3) \]

\[ u_n(t + \Delta t) = 1, \quad (1.3.4) \]

for \( t \in [t_n, t_n + W_n] \), and

\[ s_n(t + \Delta t) = v_n(t + \Delta t) + (s_n(t) - v_n(t))e^{-\Delta t/\tau_d}, \quad (1.3.5) \]

\[ v_n(t + \Delta t) = 0, \quad (1.3.6) \]

for \( t \in [t_n + W_n, t_n + 1] \), where \( w_0(t_0) \) and \( s_0(t_0) \) are presumed given. The system is coupled by Eqs. (1.1.3) and (1.1.4) with the addition of \( u_n \) and \( v_n \):

\[ s_n(t + W_n) = w_n(t_n + W_n), \quad (1.3.7) \]

\[ v_n(t + W_n) = u_n(t_n + W_n) - \delta, \quad (1.3.8) \]

\[ w_{n+1}(t_{n+1}) = s_n(t_{n+1}), \quad (1.3.9) \]

\[ u_{n+1}(t_{n+1}) = v_n(t_{n+1}) + \delta, \quad (1.3.10) \]

where \( \delta \), the distance between the two asymptotes, is fixed at \( \delta = 1 \). Eqs. (1.3.3) through (1.3.10) still represent the original TPM. However, by replacing Eqs. (1.3.4) and (1.3.6), the two asymptotes can now be modified:

\[ u_n(t + \Delta t) = u_n(t) + \mu_r \Delta t, \quad \text{for} \quad t \in [t_n, t_n + W_n], \quad (1.3.11) \]

\[ v_n(t + \Delta t) = v_n(t)e^{-\Delta t/\mu_d}, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}], \quad (1.3.12) \]

where the slope \( \mu_r > 0 \) and time constant \( \mu_d > 0 \) are parameters for a linear rise of the upper asymptote during wakefulness and an exponential decay of the lower asymptote during sleep, respectively. The set of Eqs. (1.3.3) with (1.3.11) and (1.3.5) with (1.3.12) can be also written as a system of nonhomogeneous first-order ODEs:

\[
\begin{bmatrix}
\dot{w}_n \\
\dot{u}_n
\end{bmatrix} = \begin{bmatrix}
-\frac{1}{\tau_r} & \frac{1}{\tau_r} \\
0 & 0
\end{bmatrix}
\begin{bmatrix}
w_n \\
u_n
\end{bmatrix} + \begin{bmatrix}
\mu_r \\
\mu_t
\end{bmatrix}, \quad \text{for} \quad t \in [t_n, t_n + W_n],
\]

\[
\begin{bmatrix}
\dot{s}_n \\
\dot{v}_n
\end{bmatrix} = \begin{bmatrix}
-\frac{1}{\tau_d} & \left(\frac{1}{\tau_d} - \frac{1}{\mu_d}\right) \\
0 & -\frac{1}{\mu_d}
\end{bmatrix}
\begin{bmatrix}
s_n \\
v_n
\end{bmatrix}, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}],
\]

31
where the initial conditions for the first cycle, \( w_0(t_0) \) and \( u_0(t_0) \), are assumed to be given, and coupling is again described by Eqs. (1.3.7) through (1.3.10). With the linear interaction between the homeostatic process and the circadian process given by Eqs. (1.1.6) and (1.1.7), the model equations for performance become:

\[
\begin{bmatrix}
\dot{p}_n \\
\dot{u}_n
\end{bmatrix} = \begin{bmatrix}
\frac{1}{\tau_u} & \frac{1}{\tau_u} \\
0 & 0
\end{bmatrix} \begin{bmatrix}
p_n \\
u_n
\end{bmatrix} + \begin{bmatrix}
\beta_1(t) \\
\beta_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n, t_n + W_n], \tag{1.3.15}
\]

\[
\begin{bmatrix}
\dot{q}_n \\
\dot{v}_n
\end{bmatrix} = \begin{bmatrix}
\frac{1}{\tau_d} & \left( \frac{1}{\tau_d} - \frac{1}{\tau_u} \right) \\
0 & -\frac{1}{\tau_d}
\end{bmatrix} \begin{bmatrix}
q_n \\
v_n
\end{bmatrix} + \begin{bmatrix}
\gamma_1(t) \\
\gamma_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}], \tag{1.3.16}
\]

where \( p_0(t_0) \) and \( u_0(t_0) \) are assumed to be given. Coupling of \( p_n(t) \), \( u_n(t) \), \( q_n(t) \) and \( v_n(t) \) (using Eqs. (1.3.7) through (1.3.10)) is given by:

\[
\begin{bmatrix}
q_n(t_n + W_n) \\
v_n(t_n + W_n)
\end{bmatrix} = \begin{bmatrix}
p_n(t_n + W_n) \\
u_n(t_n + W_n) - \delta
\end{bmatrix}, \tag{1.3.17}
\]

\[
\begin{bmatrix}
p_n(t_{n+1}) \\
u_n(t_{n+1})
\end{bmatrix} = \begin{bmatrix}
q_n(t_{n+1}) \\
v_n(t_{n+1}) + \delta
\end{bmatrix}. \tag{1.3.18}
\]

The nonhomogeneities \( \beta(t) \) and \( \gamma(t) \) are given by:

\[
\begin{bmatrix}
\beta_1(t) \\
\beta_2(t)
\end{bmatrix} = \begin{bmatrix}
-\frac{1}{\tau_u} c(t) + \mu_t - \frac{dc(t)}{dt} \\
\mu_t
\end{bmatrix}, \tag{1.3.19}
\]

\[
\begin{bmatrix}
\gamma_1(t) \\
\gamma_2(t)
\end{bmatrix} = \begin{bmatrix}
-\frac{1}{\tau_d} c(t) - \frac{dc(t)}{dt} \\
0
\end{bmatrix}. \tag{1.3.20}
\]

We can now introduce a more generalized ODE system for the ETPM:

\[
\begin{bmatrix}
\dot{p}_n \\
\dot{u}_n
\end{bmatrix} = \begin{bmatrix}
\alpha_{1,1} & \alpha_{1,2} \\
0 & 0
\end{bmatrix} \begin{bmatrix}
p_n \\
u_n
\end{bmatrix} + \begin{bmatrix}
\beta_1(t) \\
\beta_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n, t_n + W_n], \tag{1.3.21}
\]

\[
\begin{bmatrix}
\dot{q}_n \\
\dot{v}_n
\end{bmatrix} = \begin{bmatrix}
\sigma_{1,1} & \sigma_{1,2} \\
0 & \sigma_{2,2}
\end{bmatrix} \begin{bmatrix}
q_n \\
v_n
\end{bmatrix} + \begin{bmatrix}
\gamma_1(t) \\
\gamma_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}]. \tag{1.3.22}
\]

We will discuss in Section 1.3.4 the dynamical behavior of the model of Eqs. (1.3.21) and (1.3.22) that will identify limitations to the predictions for neurobehavioral performance from the ETPM. Note that, similar to the transformation of the ETPM, the model of Johnson et al. (2004) can also be represented by a system of coupled nonhomogeneous first-order ODEs (see Appendix B.1).

These expansions of the TPM belong to a larger, more general class of linear, nonhomogeneous first-order ODEs:

\[
\begin{bmatrix}
\dot{p}_n \\
\dot{u}_n
\end{bmatrix} = \begin{bmatrix}
\alpha_{1,1} & \alpha_{1,2} \\
\alpha_{2,1} & \alpha_{2,2}
\end{bmatrix} \begin{bmatrix}
p_n \\
u_n
\end{bmatrix} + \begin{bmatrix}
\beta_1(t) \\
\beta_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n, t_n + W_n], \tag{1.3.23}
\]

\[
\begin{bmatrix}
\dot{q}_n \\
\dot{v}_n
\end{bmatrix} = \begin{bmatrix}
\sigma_{1,1} & \sigma_{1,2} \\
\sigma_{2,1} & \sigma_{2,2}
\end{bmatrix} \begin{bmatrix}
q_n \\
v_n
\end{bmatrix} + \begin{bmatrix}
\gamma_1(t) \\
\gamma_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}]. \tag{1.3.24}
\]
where $\alpha_{i,j}$ and $\sigma_{i,j}$ are (possibly time-dependent) parameters, $\beta_i(t)$, and $\gamma_i(t)$ are time-dependent nonhomogeneities, and the initial conditions, $p_0(t_0)$ and $u_0(t_0)$, are assumed to be given. We will refer to this generalized linear\(^b\) model as the Modulating Two-Process Model (MTPM).

Instead of two processes (the homeostatic process and the circadian process) affecting performance across days as in the gTPM, we now consider an additional, modulating process; defined by $u_n$ during wakefulness and $v_n$ during sleep. The functions $\beta_i(t)$ and $\gamma_i(t)$ are typically referred to as forcing functions and may be linked to the endogenous effects of the biological pacemaker or may originate from exogenous effects, such as by the environment in the form of light or ambient temperature.

As before, $p_n(t)$ and $u_n(t)$, and $q_n(t)$ and $v_n(t)$ are coupled by Eqs. (1.3.17) and (1.3.18), where the parameter $\delta$, originally set to unity in the TPM, may become a free parameter. The $\beta_i(t)$ and $\gamma_i(t)$ functions again capture the dynamics of performance within days; their specific form needs to be determined depending on how the parameters $\alpha_{i,j}$ and $\sigma_{i,j}$ are specified (see Eqs. (1.1.17) and (1.1.18)). The rate parameters $\alpha_{i,j}$ and $\sigma_{i,j}$ in the model of Eqs. (1.3.23) and (1.3.24) determine the interactions between $p$ and $u$, and between $q$ and $v$, respectively. Positive values of $\alpha_{i,j}$ and $\sigma_{i,j}$ correspond to exponential growth, while negative values correspond to exponential decay. For example, the parameter $\alpha_{2,1}$ determines the effect of $p$ on $u$: if $\alpha_{2,1} > 0$ then higher values of $p$ (greater performance impairment) lead to proportionately faster increases in $u$.

### 1.3.1 Analogous system of compartments for the Modulating Two-Process Model (MTPM)

Similar to the gTPM, the MTPM of Eqs. (1.3.23) and (1.3.24) can be visualized using compartments. However, each system is now described by two compartments which contain time-dependent volumes or concentrations of some compound in a medium. One compartment is assumed to be proportional to performance during wakefulness, $p_n(t)$, and proportional to nominal performance during sleep, $q_n(t)$. The second compartment contains a compound which interacts with the $p_n(t)$ container during wake, either as an input into $p_n(t)$ or a feedback from $p_n(t)$ (similarly for the $v_n(t)$ container during sleep). The concentrations are governed by the rate constants $\alpha_{i,j}$ during wake, and $\sigma_{i,j}$ during sleep.

\(^b\)Here, linear means that the right-hand side of Eqs. (1.3.23) and (1.3.24) can be written as a linear combination of the dependent variables $p$ and $u$, and $q$ and $v$, respectively.
Each compartment has an external, time-dependent input, which as before may be linked to either endogenous or exogenous effects on the homeostat. From the compartment perspective, $u_n(t)$ and $v_n(t)$ are more suited to be seen as secondary processes as opposed to their previous definition—upper and lower asymptotes. This means that absolute values of $u_n(t)$ and $v_n(t)$ in relative to $p_n(t)$ and $q_n(t)$ are no longer conceptually relevant.

The coupled set of linear Eqs. (1.3.23) and (1.3.24) has a remarkably rich repertoire of solutions; within days, depending on the eigenvalues of the $\alpha$ and $\sigma$ coefficient matrices,\(^1\) and across days, depending on the eigenvalues of the system of equations for the initial values (analogous to Eqs. (1.1.33) and (1.1.34)) as introduced in the next section. We will focus on the changes in performance across days, and will consider three specific model cases in Section 1.4. However, let’s first examine the general solutions of the MTPM for initial values and states of equilibrium.

\(^1\)We use bold notation to indicate two-dimensional matrices. Here $\alpha = \begin{bmatrix} \alpha_{1,1} & \alpha_{1,2} \\ \alpha_{2,1} & \alpha_{2,2} \end{bmatrix}$ and similarly for the $\sigma$ matrix.
1.3.2 Initial values at wake onset and sleep onset

To derive equations for the initial values at wake and sleep onset for the MTPM, we focus again on the predicted initial values (across days) at wake onset, \( p_n(t_n) \) and \( u_n(t_n) \), and sleep onset, \( q_n(t_n + W_n) \) and \( v_n(t_n + W_n) \). Our derivation is analogous to that of the gTPM (see Appendix C.2). The result is:

\[
\begin{bmatrix}
    p_{n+1}(t_{n+1}) \\
    u_{n+1}(t_{n+1})
\end{bmatrix}
= \Phi_n(t_{n+1}) \Psi_n(t_n + W_n) \begin{bmatrix}
    p_n(t_n) \\
    u_n(t_n)
\end{bmatrix} + F_n, \tag{1.3.25}
\]

\[
\begin{bmatrix}
    q_{n+1}(t_{n+1} + W_{n+1}) \\
    v_{n+1}(t_{n+1} + W_{n+1})
\end{bmatrix}
= \Psi_n(t_{n+1} + W_{n+1}) \Phi_n(t_{n+1}) \begin{bmatrix}
    q_n(t_n + W_n) \\
    v_n(t_n + W_n)
\end{bmatrix} + G_n, \tag{1.3.26}
\]

for all \( T_n, W_n; 0 < W_n \leq T_n \) and \( n = 0, 1, 2, \ldots \), given \([p_0(t_0), u_0(t_0)]^T\) (where \( T \) is standard notation for transposed matrix). Here the two-dimensional matrices \( \Phi_n \) and \( \Psi_n \) are explicitly given in Appendix C.1, Eqs. (C.1-5) and (C.1-6), and \( F_n \) and \( G_n \) in Appendix C.2, Eqs. (C.2-3) and (C.2-5), respectively. Note that \([q_0(t_0 + W_0), v_0(t_0 + W_0)]^T\) can be derived from the initial values \([p_0(t_0), u_0(t_0)]^T\) by using Eqs. (1.3.17) and (C.1-1):

\[
\begin{bmatrix}
    q_0(t_0 + W_0) \\
    v_0(t_0 + W_0)
\end{bmatrix}
= \Psi_0(t_0 + W_0) \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + \Omega_0(t_0 + W_0) - \begin{bmatrix}
    0 \\
    \delta
\end{bmatrix}, \tag{1.3.27}
\]

where \( \Omega_0(t_0 + W_0) \) is given by Eq. (C.1-2).

1.3.3 Model dynamics

Analogous to Eqs. (1.1.36) and (1.1.37) for the gTPM, we can find states of equilibrium for the MTPM by solving:

\[
\begin{bmatrix}
    p_{n+m}(t_{n+m}) \\
    u_{n+m}(t_{n+m})
\end{bmatrix}
= \Phi_n(t_{n+m}) \Psi_n(t_n + W_n) \begin{bmatrix}
    p_n(t_n) \\
    u_n(t_n)
\end{bmatrix} , \tag{1.3.28}
\]

\[
\begin{bmatrix}
    q_{n+m}(t_{n+m} + W_{n+m}) \\
    v_{n+m}(t_{n+m} + W_{n+m})
\end{bmatrix}
= \Psi_n(t_{n+m} + W_{n+m}) \Phi_n(t_{n+m} + W_n) \begin{bmatrix}
    q_n(t_n + W_n) \\
    v_n(t_n + W_n)
\end{bmatrix} , \tag{1.3.29}
\]

where \( m \in \{1, 2, \ldots \} \). To investigate the existence of equilibrium points for the MTPM when \( m = 1 \), let’s consider wake/sleep schedules in which \( T_n = T \) and \( W_n = W \) are constant. In this case, \( \Psi_n(t_n + W_n) = \Psi(t_n + W) \) and \( \Phi_n(t_{n+1}) = \Phi(t_n + T) \) are also constant (see Appendix C.1). We assume that \( \beta_i(t) \) and \( \gamma_i(t) \) are bounded, oscillatory functions, and that the circadian period \( \tau = T \); hence, \( F_n = F \) and \( G_n = G \) are constant as well (see Appendix C.2). Equilibrium points may now be derived by solving Eqs. (1.3.25) and (1.3.26) for
Using the identity matrix $\mathbf{I}$ and solving for $\begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix}$ we obtain the equilibrium point:

\[
\begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix} = (\mathbf{I} - \mathbf{A})^{-1} \begin{bmatrix} F_1 \\ F_2 \end{bmatrix}.
\]  

**Proof.** By definition, a state of equilibrium occurs when, as $n \to \infty$, $p_{n+1}(t_{n+1}) = p_n(t_n)$ and $u_{n+1}(t_{n+1}) = u_n(t_n)$:

\[
\begin{bmatrix} p_{n+1}(t_{n+1}) \\ u_{n+1}(t_{n+1}) \end{bmatrix} = \begin{bmatrix} p_n(t_n) \\ u_n(t_n) \end{bmatrix} = \begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix}.
\]

By substitution we arrive at

\[
\begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix} = \mathbf{A} \begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix} + \begin{bmatrix} F_1 \\ F_2 \end{bmatrix}.
\]

Using the identity matrix $\mathbf{I}$ and solving for $\begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix}$ we obtain the equilibrium point:

\[
\begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix} = \begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix} = \begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix}.
\]

\[
\begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix} = (\mathbf{I} - \mathbf{A})^{-1} \begin{bmatrix} F_1 \\ F_2 \end{bmatrix}.
\]

This results in:

\[
\begin{bmatrix} p(t_n) \\ u(t_n) \end{bmatrix} = [\mathbf{I} - \Phi(t_n + T) \Psi(t_n + W)]^{-1} \mathbf{F},
\]

\[
\begin{bmatrix} q(t_n + W) \\ v(t_n + W) \end{bmatrix} = [\mathbf{I} - \Psi(t_n + W) \Phi(t_n + T)]^{-1} \mathbf{G},
\]

where $\mathbf{I}$ is the two-dimensional identity matrix (see Lemma 1.3.1). The equilibrium point for the onset of wakefulness is given in Eq. (1.3.30) $[p(t_n), u(t_n)]^T$, and the equilibrium
point for the onset of sleep is given in Eq. (1.3.31), \([q(t_n + W), v(t_n + W)]^T\). Here we have dropped the subscripts of the variables, since by definition they do not change at the equilibrium across days. Examination of Eqs. (1.3.35) and (1.3.36) reveals that the existence of an equilibrium state depends on the nonsingularity of

\[ [I - \Phi(t_n + T)\Psi(t_n + W)] \text{, and} \]
\[ [I - \Psi(t_n + W)\Phi(t_n + T)] \text{,} \] (1.3.37) (1.3.38)

respectively (see Appendix C.1). That is, equilibrium points can only exist when:

\[ \det(I - \Phi(t_n + T)\Psi(t_n + W)) \neq 0, \quad \text{and} \]
\[ \det(I - \Psi(t_n + W)\Phi(t_n + T)) \neq 0, \] (1.3.39) (1.3.40)

where \( \det \) is the determinant.\(^k\) We will later discuss specific cases of the model for which equilibrium points exist and for which they do not.

As mentioned in our earlier analysis of the gTPM, stability of equilibrium points for linear or nonlinear systems can be determined by a process called linearization. For the MTPM this is trivial since the system of Eqs. (1.3.25) and (1.3.26) are already linear. In general, however, linearization would be accomplished by finding the Jacobian matrix, \( J \), of
\[ \begin{bmatrix} p_{n+1}(t_n + 1) \\ u_{n+1}(t_n + 1) \end{bmatrix} \] in Eq. (1.3.25) evaluated at the equilibrium point \([p(t_n), u(t_n)]^T\). Here the Jacobian is:

\[ J_{p,u} = \begin{bmatrix} \frac{\partial p_{n+1}(t_n + 1)}{\partial p_n(t_n)} & \frac{\partial p_{n+1}(t_n + 1)}{\partial u_n(t_n)} \\ \frac{\partial u_{n+1}(t_n + 1)}{\partial p_n(t_n)} & \frac{\partial u_{n+1}(t_n + 1)}{\partial u_n(t_n)} \end{bmatrix} p(t_n), u(t_n) \] (1.3.41)

An analogous Jacobian, \( J_{q,v} \), can be derived for \([q_{n+1}(t_n + 1 + W), v_{n+1}(t_n + 1 + W)]^T\) in Eq. (1.3.26) evaluated at the equilibrium point \([q(t_n + W), v(t_n + W)]^T\). Generalizing from Eqs. (1.1.45) and (1.1.46), the equilibrium points are asymptotically stable\(^l\) if all eigenvalues \( \Lambda_i \), derived from the characteristic equation:

\[ \det(J_{p,u} - \Lambda_i I) = 0, \] (1.3.42)

\(^3\)To be able to invert a matrix, as in Eqs. (1.3.35) and (1.3.36), it must be nonsingular or nondegenerate, meaning that its determinant must be non-zero.

\(^k\)The determinant of a matrix \( A \) is \( \det(A) = \det \left( \begin{bmatrix} a & b \\ c & d \end{bmatrix} \right) = (a d - c b) \)

\(^l\)Here, asymptotic stability means that the solution trajectory will eventually converge to the state of equilibrium regardless of the starting points \([p_0(t_0), u_0(t_0)]^T\) and \([q_0(t_0 + W), v_0(t_0 + W)]^T\).
(and similarly for $J_{q,v}$), have magnitudes less than one (Kelly and Peterson, 2001). From Eqs. (1.3.25) and (1.3.26) the Jacobian matrices for the MTPM are:

$$J_{p,u} = \Phi(t_n + T)\Psi(t_n + W), \quad (1.3.43)$$
$$J_{q,v} = \Psi(t_n + W)\Phi(t_n + T). \quad (1.3.44)$$

Thus, the characteristic equations used to determine the eigenvalues are:

$$\det(\Phi(t_n + T)\Psi(t_n + W) - \Lambda I) = 0, \quad (1.3.45)$$
$$\det(\Psi(t_n + W)\Phi(t_n + T) - \Lambda I) = 0. \quad (1.3.46)$$

Since Eqs. (1.3.43) and (1.3.44) are shifted (i.e., $\Phi \Psi$ vs. $\Psi \Phi$, see Appendix C.5), the eigenvalues determined from Eqs. (1.3.45) and (1.3.46) are identical. This tells us that the equilibrium points $[p(t_n), u(t_n)]^T$ and $[q(t_n + W), v(t_n + W)]^T$ are either simultaneously asymptotically stable or simultaneously unstable.

1.3.3.1 Dynamics across days

The characteristic behavior of the model across days can further be analyzed by deriving the closed form of Eq. (1.3.25) for the level of performance at the onset of wakefulness and Eq. (1.3.26) for the nominal level of performance at the onset of sleep. These closed form solutions can be derived based on the following two lemmas.

**Lemma 1.3.2.** Let $A$ be a nonsingular, square, real-valued matrix. Consider $\sum_{i=0}^{n} A^i : i \in \mathbb{N}$. The closed form of the solutions is:

$$\sum_{i=0}^{n} A^i = (I - A)^{-1} \left( I - A^{n+1} \right).$$

**Proof.**

$$\sum_{i=0}^{n+1} A^i = \sum_{i=0}^{n} A^i + A^{n+1}$$
$$= I + A + A^2 + \ldots + A^{n-1} + A^n + A^{n+1}$$
$$= I + A \left( I + A + \ldots + A^{n-1} + A^n \right)$$
$$= I + A \sum_{i=0}^{n} A^i.$$
Therefore
\[ \sum_{i=0}^{n} A^i + A^{n+1} = I + A \sum_{i=0}^{n} A^i, \]
and
\[ \sum_{i=0}^{n} A^i = (I - A)^{-1} (I - A^{n+1}). \]

Lemma 1.3.3. Let
\[
\begin{bmatrix}
    p_{n+1}(t_{n+1}) \\
    u_{n+1}(t_{n+1})
\end{bmatrix}
= A^n \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + F_1 \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix},
\]
where the 2 by 2 coefficient matrix \( A \) and the \( F_i \)'s are constant and the matrix \( I - A \) is nonsingular, be a coupled set of first order linear nonhomogenous DEs. The closed form is then:
\[
\begin{bmatrix}
    p_n(t_n) \\
    u_n(t_n)
\end{bmatrix} = A^n \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + (I - A^n)(I - A)^{-1} \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix},
\]
where \( n \in \mathbb{N} \) and \( I \) is the identity matrix.

Proof. For \( n = 1 \) we have:
\[
\begin{bmatrix}
    p_1(t_1) \\
    u_1(t_1)
\end{bmatrix} = A \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + F_1 \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix}.
\]
Assume
\[
\begin{bmatrix}
    p_k(t_k) \\
    u_k(t_k)
\end{bmatrix} = A^k \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + (I - A^k)(I - A)^{-1} \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix}.
\]

Now consider:
\[
\begin{bmatrix}
    p_{k+1}(t_{k+1}) \\
    u_{k+1}(t_{k+1})
\end{bmatrix} = A \begin{bmatrix}
    p_k(t_k) \\
    u_k(t_k)
\end{bmatrix} + F_1 \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix}
\]
\[
= A \left( A^k \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + (I - A^k)(I - A)^{-1} \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix} \right) + F_1 \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix}
\]
\[
= A^{k+1} \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + A(A^k + A^{k-2} + \ldots + I) \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix} + F_1 \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix}
\]
\[
= A^{k+1} \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + (A^k + A^{k-1} + \ldots + A) \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix} + I \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix}
\]
\[
= A^{k+1} \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + (A^k + A^{k-1} + \ldots + A + I) \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix}
\]
\[
= A^{k+1} \begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix} + (I - A^{k+1})(I - A)^{-1} \begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix}.
\]
where we have used Lemma (1.3.2).

**Lemma 1.3.4.** Let the 2 by 2 matrix \( A \) be diagonalizable with two distinct eigenvalues written as a diagonal matrix:

\[
\Lambda = \begin{bmatrix}
\Lambda_1 & 0 \\
0 & \Lambda_2
\end{bmatrix}.
\]

The matrix product \( A^n \) tends to zero as \( n \to \infty \) if the magnitudes of both eigenvalues \( \Lambda_i \) are less than unity.

**Proof.** Since the matrix \( A \) is diagonalizable we can use a suitable matrix \( U \) and write:

\[
A^n = (U \Lambda U^{-1})^n = U \Lambda U^{-1} U \Lambda U^{-1} \ldots U \Lambda U^{-1} = U \Lambda^n U^{-1} \to 0 \quad \text{as} \quad n \to \infty.
\]

It is instructive to note that in model cases when the magnitudes of the eigenvalues of the matrix \( \Phi_n(t_{n+1})\Psi_n(t_n + W_n) \) (see Eqs. (1.3.25) and (1.3.26)) are less than unity the closed form solution defined by Eqs. (1.3.47) for large \( n \) reduces to the equilibrium point defined by Eq. (1.3.33) (see Lemma 1.3.4).

### 1.3.4 Another look at the generalized ODE system for the ETPM

As a first example of the MTPM and to show the importance of understanding the dynamical behavior of a biomathematical such as the MTPM through the mathematics, we will take another look at the model of Eqs. (1.3.21) and (1.3.22), (the generalized ODE system for the ETPM by Avinash et al. (2005)). Recall this model was formulated by setting the parameters \( \alpha_{2,1} \), \( \alpha_{2,2} \) and \( \sigma_{2,1} \) to zero in the MTPM of Eqs. (1.3.23) and (1.3.24). In this particular model case we impose the condition that \( \sigma_{1,1} \neq \sigma_{2,2} \).\(^n\) We assume that the eigenvalues and independent eigenvectors are real and distinct (reflecting changes within days).\(^n\) For the \( \alpha \) matrix in Eq. (1.3.21) these are:

\[
\lambda_1 = \alpha_{1,1}, \quad \lambda_2 = 0,
\]

\(^n\)This insures that the eigenvalues \( \lambda_1 \) and \( \lambda_2 \) are distinct for this model case.

\(^n\)To reduce notation in our results, we will normalize all non-zero eigenvectors to have the form \( x_i = \begin{bmatrix} x_{i,1} \\ 1 \end{bmatrix} \).
\[ x_1 = \begin{bmatrix} 1 \\ 0 \end{bmatrix}, \quad (1.3.52) \]
\[ x_2 = \begin{bmatrix} -\frac{\alpha_{1,2}}{\alpha_{1,1}} \\ 1 \end{bmatrix}, \quad (1.3.53) \]

and for the \( \sigma \) matrix in Eq. (1.3.22) are:

\[ \lambda_3 = \sigma_{1,1}, \quad (1.3.54) \]
\[ \lambda_4 = \sigma_{2,2}, \quad (1.3.55) \]
\[ x_3 = \begin{bmatrix} 1 \\ 0 \end{bmatrix}, \quad (1.3.56) \]
\[ x_4 = \begin{bmatrix} \sigma_{1,2} \\ \sigma_{2,2}-\sigma_{1,1} \\ 1 \end{bmatrix}. \quad (1.3.57) \]

The linear system of Eqs. (1.3.21) and (1.3.22) is a specific case of the analogous system of compartments in Fig. 1.15, where the parameter \( \alpha_{2,2} \) and both of the feedback parameters \( \alpha_{2,1} \) and \( \sigma_{2,1} \) have been removed. This means that the only way the contents of compartment \( u_n(t) \) can grow or decay is through the nonhomogeneity \( \beta_2(t) \) or the relationship to \( v_n(t) \) using Eq. (1.3.18), whereas during sleep, the contents of compartment \( v_n(t) \) remain influenced by both the constant parameter \( \sigma_{2,2} \) and the nonhomogeneity \( \gamma_2(t) \). The dynamics of the contents of the performance compartment \( p_n(t) \) during wakefulness and \( q_n(t) \) during sleep are governed by the rate constants \( \alpha_{1,1} \) and \( \sigma_{1,1} \), respectively. See Fig. 1.16 for a compartment analogy of this model.

1.3.4.1 Model case dynamics

The dynamics of Eqs. (1.3.21) and (1.3.22) can be seen by using Eqs. (1.3.25) and (1.3.26) to examine when states of equilibrium exist. Per Eqs. (1.3.39) and (1.3.40), and using the eigenvalues and eigenvectors in Eqs. (1.3.50)-(1.3.57), we have:

\[
\det(I - \Phi(t_n + T)\Psi(t_n + W)) \\
= \det\left(I - \begin{bmatrix} x_3 e^{\lambda_3(T-W)} & x_4 e^{\lambda_4(T-W)} \\ x_3 & x_4 \end{bmatrix}^{-1} \begin{bmatrix} x_1 e^{\lambda_1 W} & x_2 e^{\lambda_2 W} \\ x_1 & x_2 \end{bmatrix}^{-1}\right) \\
= \det\left(\begin{bmatrix} 1 - e^{\alpha_{1,1} W} e^{\sigma_{1,1}(T-W)} \\ h_1 \\ 0 \\ 1 - e^{\sigma_{2,2}(T-W)} \end{bmatrix}\right), \quad (1.3.58)
\]
Eqs. (1.3.58) and (1.3.59) are equivalent and imply that a state of equilibrium exists when:

\[ \alpha \text{(1.3.17) and (1.3.18)}. \]

Notice, in this model the two feedback parameters \( q \) and \( p \) performance, described by Eqs. (1.3.21) and (1.3.22). Here we show two separate compartments which describe performance, \( p_n(t) \), and a second process, \( u_n(t) \), during wakefulness, and nominal performance, \( q_n(t) \), and a second process, \( v_n(t) \), during sleep. The two systems are connected across days by Eqs. (1.3.62) no longer holds. This means that specifically for the ETPM (Avinash et al., 2005)

\[ (1.3.63) \]

Figure 1.16: Analogous system of compartments for the generalized ETPM case of the MTPM described by Eqs. (1.3.21) and (1.3.22). Here we show two separate compartments which describe performance, \( p_n(t) \), and a second process, \( u_n(t) \), during wakefulness, and nominal performance, \( q_n(t) \), and a second process, \( v_n(t) \), during sleep. The two systems are connected across days by Eqs. (1.3.62) no longer holds. This means that specifically for the ETPM (Avinash et al., 2005)

\[ (1.3.63) \]

and

\[ \det(I - \Psi(t_n + W) \Phi(t_n + T)) = \det(I - [x_1 e^{\lambda_1 W} x_2 e^{\lambda_2 W}] [x_1 \ x_2]^{-1} [x_3 e^{\lambda_3 (T - W)} x_4 e^{\lambda_4 (T - W)}] [x_3 \ x_4]^{-1}) = \det\left(\begin{bmatrix} 1 - e^{\sigma_{1,1} (T - W)} e^{\alpha_{1,1} W} & h_2 \\ 0 & 1 - e^{\sigma_{2,2} (T - W)} \end{bmatrix}\right), \] (1.3.59)

where

\[ h_1 = \frac{\sigma_{1,2}}{\sigma_{1,1} - \sigma_{2,2}} (e^{\sigma_{1,1} (T - W)} - e^{\sigma_{2,2} (T - W)}) + \frac{\alpha_{1,2}}{\alpha_{1,1}} (e^{\alpha_{1,1} W} - 1) e^{\sigma_{1,1} (T - W)}, \] (1.3.60)

\[ h_2 = \frac{\sigma_{1,2}}{\sigma_{1,1} - \sigma_{2,2}} (e^{\sigma_{1,1} (T - W)} - e^{\sigma_{2,2} (T - W)}) e^{\alpha_{1,1} W} + \frac{\alpha_{1,2}}{\alpha_{1,1}} (e^{\alpha_{1,1} W} - 1) e^{\sigma_{2,2} (T - W)}. \] (1.3.61)

Eqs. (1.3.58) and (1.3.59) are equivalent and imply that a state of equilibrium exists when:

\[ (1 - e^{\sigma_{1,1} (T - W)} e^{\alpha_{1,1} W})(1 - e^{\sigma_{2,2} (T - W)}) \neq 0. \] (1.3.62)

If all parameters \( \sigma_{1,1}, \alpha_{1,1} \) and \( \sigma_{2,2} \) are negative, as is the case for the published parameters for the EPTM (Avinash et al., 2005), then:

\[ 0 < (1 - e^{\sigma_{1,1} (T - W)} e^{\alpha_{1,1} W})(1 - e^{\sigma_{2,2} (T - W)}) < 1, \] (1.3.63)

for all \( T, W: 0 \leq W < T \). However, when \( W = T \) we have \( 1 - e^{\sigma_{2,2} (T - T)} = 0 \) and Eq. (1.3.62) no longer holds. This means that specifically for the ETPM (Avinash et al., 2005)
(i.e., when parameters $\alpha_{1,1}, \sigma_{1,1}$ and $\sigma_{2,2}$ are negative) equilibrium points are always found except in the case of total sleep deprivation.

To determine stability of the state of equilibrium when it does exist, we solve either Eq. (1.3.45) or Eq. (1.3.46) for eigenvalues of the iterative system of Eqs. (1.3.25) and (1.3.26), where we find:

$$\Lambda_1 = e^{\sigma_{1,1}(T-W)}e^{\alpha_{1,1}W},$$  \hspace{1cm} (1.3.64)

$$\Lambda_2 = e^{\sigma_{2,2}(T-W)}.$$  \hspace{1cm} (1.3.65)

Notice that because all parameters are assumed to be negative for the ETPM model case, the equilibrium points are asymptotically stable, because $0 < \Lambda_i < 1$ for both $i$. Therefore, the ETPM predicts exponential convergence of the level of performance at the onset of wake and at the onset of sleep to their respective equilibrium states for all amounts of sleep duration except total sleep deprivation.

The equilibrium point defined in Eqs. (1.3.35) and (1.3.36) can be seen to be dependent on the duration of wakefulness (see Fig. 1.17). Notice that the equilibrium points at the onset of wakefulness increase hyperbolically and tend to infinity as wakefulness is increased toward total sleep deprivation ($W = 24$). That is, the model predicts that as wakefulness is increased linearly, performance at equilibrium increases hyperbolically—each hour less sleep leads to progressively greater performance impairment at the stable equilibrium.

### 1.3.4.2 Dynamics across days

As we have seen, the characteristic behavior of the model across days can be analyzed by deriving the closed form of Eq. (1.3.25) for the level of performance at the onset of wakefulness and Eq. (1.3.26) for the onset of sleep. For the model case of Eqs. (1.3.21) and (1.3.22) and using Eq. (1.3.47) the closed form of Eq. (1.3.25) for the onset of wakefulness can be written:

$$\begin{bmatrix}
p_n(t_n) \\
u_n(t_n)
\end{bmatrix} = e^{\alpha_{1,1}W}e^{\sigma_{1,1}(T-W)}h_1 e^{\sigma_{2,2}(T-W)}
\begin{bmatrix}
h_0(t_0) \\
u_0(t_0)
\end{bmatrix}
+ \left(I - e^{\alpha_{1,1}W}e^{\sigma_{1,1}(T-W)}h_1 e^{\sigma_{2,2}(T-W)}\right)^n
\begin{bmatrix}
1 - e^{\alpha_{1,1}W}e^{\sigma_{1,1}(T-W)}h_1 \\
0
\end{bmatrix}^{-1}
\begin{bmatrix}
F_1 \\
F_2
\end{bmatrix},$$  \hspace{1cm} (1.3.66)
Figure 1.17: Plot showing states of equilibrium for performance level at wake onset versus duration of wakefulness of the ETPM using published parameters (Avinash et al., 2005). The figure shows the dynamics of the states of equilibrium for a continuous range of wakefulness durations: \(p(t_n)\) (solid) and \(u(t_n)\) (dashed). We see for the ETPM model that as wakefulness approaches \(W = 24\) (i.e., the point when the state of equilibrium vanishes and Eqs. (1.3.37) and (1.3.38) become degenerate), the equilibrium state increases hyperbolically toward infinity.

Figure 1.18: Plot showing the magnitude of the eigenvalues \(\Lambda_1\) (solid line) and \(\Lambda_2\) (dashed line) of Eqs. (1.3.64) and (1.3.65), respectively, versus duration of wakefulness using published parameters (Avinash et al., 2005). The vertical line at \(W = 24\) depicts where the stable equilibrium state vanishes. We see that the eigenvalue defined by Eq. (1.3.65) reaches unity exactly at total sleep deprivation.
and the closed form of Eq. (1.3.26) for the onset of sleep can be written as:

$$
\begin{bmatrix}
q_n(t_n + W) \\
v_n(t_n + W)
\end{bmatrix} =
\begin{bmatrix}
e^{\sigma_1(T-W)}e^{\alpha_1 W} & h_2 \\
0 & e^{\sigma_2(T-W)}
\end{bmatrix}^n
\begin{bmatrix}
q_0(t_0 + W) \\
v_0(t_0 + W)
\end{bmatrix}
+ \left( I - \begin{bmatrix}
e^{\sigma_1(T-W)}e^{\alpha_1 W} & h_2 \\
0 & e^{\sigma_2(T-W)}
\end{bmatrix} \right)^{-1}
\begin{bmatrix}
G_1 \\
G_2
\end{bmatrix},
\end{equation}

(1.3.67)

where \(h_1\) and \(h_2\) are given in Eqs. (1.3.60) and (1.3.61), respectively. Notice that at total sleep deprivation (i.e., the bifurcation point for the ETPM) the matrices to be inverted in the right hand side of Eqs. (1.3.66) and (1.3.67) are singular. This means that the closed form solution at total sleep deprivation has a different form than the result from Lemma 1.3.3.

To determine the closed form solution at the bifurcation let us first assume that an infinitesimally small amount of sleep exists between successive days so that Eqs. (1.3.17) and (1.3.18) can still be applied. We find (see Appendix C.3):

$$
\begin{bmatrix}
p_n(t_n) \\
u_n(t_n)
\end{bmatrix} =
\begin{bmatrix}
h_1(W = T) \\
1 - e^{\alpha_1 W}
\end{bmatrix} \begin{bmatrix}
1 - (e^{\alpha_1 W})^n \\
1
\end{bmatrix}
\begin{bmatrix}
p_0(t_0) \\
u_0(t_0)
\end{bmatrix}
+ \frac{n h_1(W = T) F_2(W = T) + (F_1(W = T) - A) \left( \frac{1}{1 - e^{\alpha_1 W}} + (e^{\alpha_1 W})^n \right)}{n F_2(W = T)},
\end{equation}

(1.3.68)

where \(A\) is given in Eq. (C.3-7) and \(h_1(W = T)\) in Eq. (1.3.60). We can see when \(0 < e^{\alpha_1 W} < 1\) (i.e., the ETPM) that Eq. (1.3.68) describes straight lines across days as \(n \to \infty\):

$$
\begin{bmatrix}
p_n(t_n) \\
u_n(t_n)
\end{bmatrix} =
\begin{bmatrix}
h_1(W = T) \\
1 - e^{\alpha_1 W}
\end{bmatrix} \begin{bmatrix}
p_0(t_0) \\
u_0(t_0)
\end{bmatrix}
+ \frac{n h_1(W = T) F_2(W = T) + (F_1(W = T) - A) \left( \frac{1}{1 - e^{\alpha_1 W}} \right)}{n F_2(W = T)},
\end{equation}

(1.3.69)

with slopes:

$$
M_{p,u} = \begin{bmatrix}
h_1(W = T) F_2(W = T) \\
F_2(W = T)
\end{bmatrix},
\end{equation}

(1.3.70)

where in the above equations \(F_1(W = T)\) and \(F_2(W = T)\) are the first and second elements of the nonhomogeneous term \(F(W = T)\) in Eq. (1.3.25), respectively (see also Eq. (C.2-3)). We see from Fig. 1.19 that at total sleep deprivation, the level of performance across

45
days forms a straight line with slope defined by the first element of Eq. (1.3.70). Let us now consider three other model cases of the MTPM.

1.4 Model cases of the MTPM

The generalized model described by Eqs. (1.3.23) and (1.3.24) has a total of eight parameters within the $\alpha$ and $\sigma$ coefficient matrices. By setting certain parameters to zero we can produce several different models, each of which exhibits unique characteristics. In the following sections we analyze two such model cases plus the full model (no assumptions
on the $\alpha_{i,j}$ or the $\sigma_{i,j}$ parameters). In each example we assume that the $\beta_i(t)$ and $\gamma_i(t)$ functions of Eqs. (1.3.23) and (1.3.24) are bounded and periodic with period $\tau = T$, and that the duration of day, $T$, and the daily length of sleep, $T - W$, are constant. In this way $\Psi(t_n + W)$, $\Phi(t_n + T)$, $F$ and $G$ in Eqs. (1.3.35) and (1.3.36) are constant.

### 1.4.1 A model case with a bifurcation

The model described in Eqs. (1.3.15) and (1.3.16) predicted adaptation for all constant sleep schedules except total sleep deprivation. However, experimental observations (Belenky et al., 2003; Van Dongen and Dinges, 2003a) put this into question, in particular for daily sleep amounts of less than approximately 4 h. To accommodate a qualitative difference between moderate sleep restriction ($>\approx 4$ h sleep/day) and severe sleep restriction ($<\approx 4$ h sleep/day), we present the first of three new model cases. This model case, as published in McCauley et al. (2009a), can be written as a system of linked ODEs by setting only parameters $\alpha_{2,1}$ and $\sigma_{2,1}$ to zero into Eqs. (1.3.23) and (1.3.24):

\[
\begin{bmatrix}
\dot{p}_n \\
\dot{u}_n
\end{bmatrix} =
\begin{bmatrix}
\alpha_{1,1} & \alpha_{1,2} \\
0 & \alpha_{2,2}
\end{bmatrix}
\begin{bmatrix}
p_n \\
u_n
\end{bmatrix} +
\begin{bmatrix}
\beta_1(t) \\
\beta_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n, t_n + W_n],
\]

\[
\begin{bmatrix}
\dot{q}_n \\
\dot{v}_n
\end{bmatrix} =
\begin{bmatrix}
\sigma_{1,1} & \sigma_{1,2} \\
0 & \sigma_{2,2}
\end{bmatrix}
\begin{bmatrix}
q_n \\
v_n
\end{bmatrix} +
\begin{bmatrix}
\gamma_1(t) \\
\gamma_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}],
\]

where we impose the condition that $\alpha_{1,1} \neq \alpha_{2,2}$ and $\sigma_{1,1} \neq \sigma_{2,2}$. The real and distinct eigenvalues and a suitable set of eigenvectors (reflecting changes within days) for the $\alpha$ matrix in Eq. (1.4.1) are:

\[
\lambda_1 = \alpha_{1,1},
\]

\[
\lambda_2 = \alpha_{2,2},
\]

\[
x_1 = \begin{bmatrix} 1 \\ 0 \end{bmatrix},
\]

\[
x_2 = \begin{bmatrix} \frac{\alpha_{1,2}}{\alpha_{2,2} - \alpha_{1,1}} \\ \alpha_{2,2} - \alpha_{1,1} \end{bmatrix},
\]

and for the $\sigma$ matrix in Eq. (1.4.2) are:

\[
\lambda_3 = \sigma_{1,1},
\]

\[
\lambda_4 = \sigma_{2,2},
\]

\[
x_3 = \begin{bmatrix} 1 \\ 0 \end{bmatrix},
\]
Figure 1.20: Analogous system of compartments for the case of the MTPM with a bifurcation. Here we show two panels each with two separate compartments. The system shown in the left panel (panel a) describes performance, $p_n(t)$, interconnected with a secondary process, $u_n(t)$, during wakefulness. The system shown in the right panel (panel b) describes nominal performance, $q_n(t)$, interconnected with a secondary process, $v_n(t)$, during sleep. As compared to the full model shown in Fig. 1.15, we have removed only the two feedback parameters $\alpha_2,1$ and $\sigma_2,1$. The two systems are connected across days by Eqs. (1.3.17) and (1.3.18).

\[
x_4 = \begin{bmatrix} \sigma_{1,2} \\ \sigma_{2,2} - \sigma_{1,1} \\ 1 \end{bmatrix}.
\] (1.4.10)

The linear system of Eqs. (1.4.1) and (1.4.2) can be described as a special case of the system of two interconnected chambers or compartments seen in Fig. 1.15. Notice for this model case, in Fig. 1.18, we have removed the $\alpha_2,1$ and $\sigma_2,1$ paths which are directed from the performance chambers during wakefulness and sleep into the secondary chambers. In this way we assume that there are no feedback mechanisms from $p_n(t)$ into $u_n(t)$ or from $q_n(t)$ into $v_n(t)$.

### 1.4.1.1 Model case dynamics

Let us now consider the dynamics of Eqs. (1.3.25) and (1.3.26). First we examine when states of equilibrium exist. Per Eqs. (1.3.39) and (1.3.40), and using the eigenvalues and eigenvectors defined by Eqs. (1.4.3) through (1.4.10) we have:

\[
\det(I - \Phi(t_n + T) \Psi(t_n + W))
= \det\left(I - \begin{bmatrix} x_3 e^{\lambda_3(T-W)} & x_4 e^{\lambda_4(T-W)} \\ \end{bmatrix} [x_3 \ x_4]^{-1} \begin{bmatrix} x_1 e^{\lambda_1 W} & x_2 e^{\lambda_2 W} \end{bmatrix} [x_1 \ x_2]^{-1}\right)
= \det\left(\begin{bmatrix} 1 - e^{\alpha_{1,1} W} e^{\sigma_{1,1}(T-W)} & h_1 \\ 0 & 1 - e^{\alpha_{2,2} W} e^{\sigma_{2,2}(T-W)} \end{bmatrix}\right),
\] (1.4.11)
\[ \text{det}(I - \Psi(t_n + W)\Phi(t_n + T)) \]
\[ = \text{det} \left( I - \left[ x_1 e^{\lambda_1 T} x_2 e^{\lambda_2 W} \right] \begin{bmatrix} x_1 & x_2 \\ 1 - e^{\alpha_1 W} & 1 - e^{\alpha_2 W} \end{bmatrix}^{-1} \left[ x_3 e^{\lambda_3 T} x_4 e^{\lambda_4 W} \right] \begin{bmatrix} x_3 & x_4 \end{bmatrix}^{-1} \right) \]
\[ = \text{det} \left( \begin{bmatrix} 1 - e^{\sigma_1 (T-W)} e^{\alpha_1 W} & h_2 \\ 0 & 1 - e^{\sigma_2 (T-W)} e^{\alpha_2 W} \end{bmatrix} \right), \] (1.4.12)

where
\[ h_1 = \frac{\sigma_{1,2}}{\sigma_{1,1} - \sigma_{2,2}} \left( e^{\sigma_{1,1} (T-W)} - e^{\sigma_{2,2} (T-W)} \right) e^{\alpha_{2,2} W} + \frac{\alpha_{1,2}}{\alpha_{1,1} - \alpha_{2,2}} \left( e^{\alpha_{1,1} W} - e^{\alpha_{2,2} W} \right) e^{\sigma_{1,1} (T-W)} , \] (1.4.13)
\[ h_2 = \frac{\sigma_{1,2}}{\sigma_{1,1} - \sigma_{2,2}} \left( e^{\sigma_{1,1} (T-W)} - e^{\sigma_{2,2} (T-W)} \right) e^{\alpha_{1,1} W} + \frac{\alpha_{1,2}}{\alpha_{1,1} - \alpha_{2,2}} \left( e^{\alpha_{1,1} W} - e^{\alpha_{2,2} W} \right) e^{\sigma_{2,2} (T-W)} . \] (1.4.14)

Eqs. (1.4.11) and (1.4.12) are equivalent (see Appendix C.6), and imply that a state of equilibrium exists for:
\[ (1 - e^{\sigma_{1,1} (T-W)} e^{\alpha_{1,1} W}) (1 - e^{\sigma_{2,2} (T-W)} e^{\alpha_{2,2} W}) \neq 0. \] (1.4.15)

We see that when the four parameters \( \alpha_{1,1}, \alpha_{2,2}, \sigma_{1,1} \) and \( \sigma_{2,2} \) are negative, Eq. (1.4.15) is always satisfied, since
\[ 0 < (1 - e^{\sigma_{1,1} (T-W)} e^{\alpha_{1,1} W}) (1 - e^{\sigma_{2,2} (T-W)} e^{\alpha_{2,2} W}) < 1, \] (1.4.16)
for all \( T, W: 0 < W \leq T \). This means that when these four parameters are negative, equilibrium points exist for all daily sleep durations including total sleep deprivation. However, by relaxing the condition that all parameters are negative, we may have a situation where Eq. (1.4.15) is no longer held.

To examine this, let us assume parameters \( \alpha_{1,1}, \sigma_{1,1} \) and \( \sigma_{2,2} \) to be negative, but parameter \( \alpha_{2,2} \) to be positive. For this case, the requirement for the existence of equilibrium points, Eq. (1.4.15), is not always held. We can see this by examining the product \( e^{\sigma_{2,2} (T-W)} e^{\alpha_{2,2} W} \) in Eq. (1.4.15). Here, \( e^{\sigma_{2,2} (T-W)} < 1 \), while \( e^{\alpha_{2,2} W} > 1 \). That is, for a particular combination of \( \sigma_{2,2} \) and \( \alpha_{2,2} \), and by varying the amount of wakefulness \( W \), this product may change from \( e^{\sigma_{2,2} (T-W)} e^{\alpha_{2,2} W} < 1 \) to \( e^{\sigma_{2,2} (T-W)} e^{\alpha_{2,2} W} > 1 \). At unity, the state of equilibrium does not exist (i.e., Eqs. (1.3.37) and (1.3.38) become degenerate).
To determine stability of equilibrium points when they do exist, we solve either Eq. (1.3.45) or Eq. (1.3.46) for eigenvalues of the iterative system of Eqs. (1.3.25) and (1.3.26):

\begin{align*}
\Lambda_1 &= e^{\sigma_{1,1}(T - W)} e^{\alpha_{1,1} W}, \\
\Lambda_2 &= e^{\sigma_{2,2}(T - W)} e^{\alpha_{2,2} W}.
\end{align*}

Notice, in the case when all parameters are negative, the equilibrium points (which exist for all cases of sleep duration including total sleep deprivation) are asymptotically stable. This is because $0 < \Lambda_i < 1$ for both $i$. Just as we showed for the gTPM of Chapter 1.1, in the case when $\alpha_{2,2}$ is positive there are three possibilities for $\Lambda_2$ (for each $0 < \Lambda_1 < 1$). For $\Lambda_2 < 1$, the system has a stable equilibrium point. For $\Lambda_2 > 1$ there is also an equilibrium point, but it is unstable (recall that for stability both eigenvalues must have magnitudes less than unity). For $\Lambda_2 = 1$, the state of equilibrium disappears altogether (i.e., Eq. (1.4.15) no longer holds). Thus, we can see that when changing the amount of sleep, $T - W$, a bifurcation occurs where the system dynamics change qualitatively: from stable (performance level tends exponentially toward a fixed asymptote) to a condition with no equilibrium point to unstable (performance level tends exponentially away from the fixed asymptote).

Let us determine the relationship between $\alpha_{2,2}$ and $\sigma_{2,2}$ by setting $\Lambda_2$ to unity in Eq. (1.4.18) and derive a formula for the critical amount of daily wakefulness $W_c$ beyond which asymptotic stability is no longer achieved:

\[ W_c = \frac{\sigma_{2,2}}{\sigma_{2,2} - \alpha_{2,2}} T, \]

for all $T, W_c : 0 < W_c \leq T$. This expression can also be written as follows:

\[ \frac{W_c}{T - W_c} = \frac{-\sigma_{2,2}}{\alpha_{2,2}}, \]

which reveals whether the bifurcation occurs as a function of the ratio of wakefulness ($W$) to sleep ($T - W$). If the ratio of wakefulness to sleep falls below the critical ratio of Eq. (1.4.20), then this model predicts exponential convergence to the state of equilibrium. If the ratio of wakefulness to sleep exceeds the critical ratio, it diverges away from the state of equilibrium. Both convergence and divergence occur at the rate specified by the matrix product $\Phi \Psi$ of Eq. (1.3.25) for onset of wake and $\Psi \Phi$ of Eq. (1.3.26) for onset of sleep.

Depending on the signs of the parameters $\alpha_{1,1}$, $\alpha_{2,2}$, $\sigma_{1,1}$ and $\sigma_{2,2}$, the case could exist where the eigenvalue $\Lambda_1$ of Eq. (1.4.18) could also change from less than unity to greater
than unity. Suppose $\alpha_{1,1}$ is positive and $\sigma_{1,1}$ is negative. Then an equation can be written analogous to that of Eq. (1.4.19), but in terms of $\alpha_{1,1}$ and $\sigma_{1,1}$, which again predicts the critical amount of wakefulness:

$$W_c = \frac{\sigma_{1,1}}{\sigma_{1,1} - \alpha_{1,1}} T.$$  \hfill (1.4.21)

Recall that the trajectory across days becomes unstable with only one eigenvalue having a magnitude of greater than one. This means that, depending on the signs of the parameters $\alpha_{1,1}, \alpha_{2,2}, \sigma_{1,1}$ and $\sigma_{2,2}$, either eigenvalue could cause the bifurcation.

1.4.1.2 Dynamics across days

The characteristic behavior of this case of the MTPM across days can be seen by deriving the closed form of the solution of Eq. (1.3.25) for the level of performance at the onset of wakefulness and Eq. (1.3.26) for the onset of sleep. For the model case of Eqs. (1.4.1) and (1.4.2), and using Eq. (1.3.47), the closed form of the solution of Eq. (1.3.25) for the onset of wakefulness, and Eq. (1.3.26) for the onset of sleep, can be written as:

$$\begin{bmatrix} p_n(t_n) \\ u_n(t_n) \end{bmatrix} = \begin{bmatrix} e^{\alpha_{1,1}W} e^{\sigma_{1,1}(T-W)} & h_1 \\ 0 & e^{\alpha_{2,2}W} e^{\sigma_{2,2}(T-W)} \end{bmatrix}^n \begin{bmatrix} p_0(t_0) \\ u_0(t_0) \end{bmatrix} + \left( I - \begin{bmatrix} e^{\alpha_{1,1}W} e^{\sigma_{1,1}(T-W)} & h_1 \\ 0 & e^{\alpha_{2,2}W} e^{\sigma_{2,2}(T-W)} \end{bmatrix} \right)^n \times \begin{bmatrix} 1 - e^{\alpha_{1,1}W} e^{\sigma_{1,1}(T-W)} & h_1 \\ 0 & 1 - e^{\alpha_{2,2}W} e^{\sigma_{2,2}(T-W)} \end{bmatrix}^{-1} \begin{bmatrix} F_1 \\ F_2 \end{bmatrix}, \hfill (1.4.22)$$

and

$$\begin{bmatrix} q_n(t_n + W) \\ v_n(t_n + W) \end{bmatrix} = \begin{bmatrix} e^{\sigma_{1,1}(T-W)} e^{\alpha_{1,1}W} & h_2 \\ 0 & e^{\sigma_{2,2}(T-W)} e^{\alpha_{2,2}W} \end{bmatrix}^n \begin{bmatrix} q_0(t_0 + W) \\ v_0(t_0 + W) \end{bmatrix} + \left( I - \begin{bmatrix} e^{\sigma_{1,1}(T-W)} e^{\alpha_{1,1}W} & h_2 \\ 0 & e^{\sigma_{2,2}(T-W)} e^{\alpha_{2,2}W} \end{bmatrix} \right)^n \times \begin{bmatrix} 1 - e^{\sigma_{1,1}(T-W)} e^{\alpha_{1,1}W} & h_2 \\ 0 & 1 - e^{\sigma_{2,2}(T-W)} e^{\alpha_{2,2}W} \end{bmatrix}^{-1} \begin{bmatrix} G_1 \\ G_2 \end{bmatrix}, \hfill (1.4.23)$$

respectively. Here $h_1$ is given in Eq. (1.4.13), and $h_2$ is given in Eq. (1.4.14). At the bifurcation point defined by $\Lambda_2 = 1$ in Eq. (1.4.18), the matrices to be inverted in the right hand side of Eqs. (1.4.22) and (1.4.23) are singular and therefore the closed form solution has a different form than that of the result from Lemma 1.3.3. We find that at the onset of
wakefulness across days the predictions become (see Appendix C.3):

\[
\begin{bmatrix}
    p_n(t_n) \\
    u_n(t_n)
\end{bmatrix}
= \begin{bmatrix}
    \left( e^{\alpha_1 W_c} e^{\sigma_{1,1}(T-W_c)} \right)^n & \frac{h_1(W=W_c)}{1-e^{\alpha_1 W_c} e^{\sigma_{1,1}(T-W_c)}} \left( 1 - \left( e^{\alpha_1 W_c} e^{\sigma_{1,1}(T-W_c)} \right)^n \right) \\
    0 & 1
\end{bmatrix}
\begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix}
+ \begin{bmatrix}
    \frac{n h_1(W=W_c)}{1-e^{\alpha_1 W_c} e^{\sigma_{1,1}(T-W_c)}} F_2(W = W_c) \\
    n F_2(W = W_c)
\end{bmatrix}
+ \begin{bmatrix}
    (F_1(W = W_c) - A) \left( \frac{1}{1-e^{\alpha_1 W_c} e^{\sigma_{1,1}(T-W_c)}} + \left( e^{\alpha_1 W_c} e^{\sigma_{1,1}(T-W_c)} \right)^n \right) \\
    0
\end{bmatrix}, \quad (1.4.24)
\]

and predictions at the onset of sleep become:

\[
\begin{bmatrix}
    q_n(t_n + W) \\
    v_n(t_n + W)
\end{bmatrix}
= \begin{bmatrix}
    \left( e^{\sigma_{1,1}(T-W_c)} e^{\alpha_1 W_c} \right)^n & \frac{h_1(W=W_c)}{1-e^{\sigma_{1,1}(T-W_c)} e^{\alpha_1 W_c}} \left( 1 - \left( e^{\sigma_{1,1}(T-W_c)} e^{\alpha_1 W_c} \right)^n \right) \\
    0 & 1
\end{bmatrix}
\begin{bmatrix}
    q_0(t_0 + W_c) \\
    v_0(t_0 + W_c)
\end{bmatrix}
+ \begin{bmatrix}
    \frac{n h_2(W=W_c)}{1-e^{\sigma_{1,1}(T-W_c)} e^{\alpha_1 W_c}} F_2(W = W_c) \\
    n F_2(W = W_c)
\end{bmatrix}
+ \begin{bmatrix}
    (G_1(W = W_c) - A) \left( \frac{1}{1-e^{\sigma_{1,1}(T-W_c)} e^{\alpha_1 W_c}} + \left( e^{\sigma_{1,1}(T-W_c)} e^{\alpha_1 W_c} \right)^n \right) \\
    0
\end{bmatrix}. \quad (1.4.25)
\]

Here \( A \) (see also analogously Eq. (C.3-7)) is:

\[
A = \frac{h_1(W = W_c)}{1-e^{\sigma_{1,1}(T-W_c)} e^{\alpha_1 W_c}} F_2(W = W_c), \quad (1.4.26)
\]

and \( h_1(W = W_c) \) and \( h_2(W = W_c) \) can be determined from Eqs. (1.4.13) and (1.4.14), respectively. We can see that when \( 0 < e^{\sigma_{1,1}(T-W_c)} e^{\alpha_1 W_c} < 1 \), Eqs. (1.4.24) and (1.4.25) become straight lines across days as \( n \to \infty \) (see Appendix C.3 for an analogous proof):

\[
\begin{bmatrix}
    p_n(t_n) \\
    u_n(t_n)
\end{bmatrix}
= \begin{bmatrix}
    0 & \frac{h_1(W=W_c)}{1-e^{\alpha_1 W_c} e^{\sigma_{1,1}(T-W_c)}} \\
    0 & 1
\end{bmatrix}
\begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix}
+ \begin{bmatrix}
    \frac{n h_1(W=W_c)}{1-e^{\alpha_1 W_c} e^{\sigma_{1,1}(T-W_c)}} F_2(W = W_c) + (F_1(W = W_c) - A) \left( \frac{1}{1-e^{\alpha_1 W_c} e^{\sigma_{1,1}(T-W_c)}} \right) \\
    n F_2(W = W_c)
\end{bmatrix}, \quad (1.4.27)
\]
and

\[
\begin{bmatrix}
q_n(t_n + W) \\
v_n(t_n + W)
\end{bmatrix} = \begin{bmatrix}
0 & \frac{h_2(W = W_c)}{1 - e^{\alpha_{1,1}(T - W_c)} e^{\alpha_{1,1} W_c}} \\
0 & 1
\end{bmatrix}
\begin{bmatrix}
q_0(t_0 + W) \\
v_0(t_0 + W)
\end{bmatrix} \\
+ \begin{bmatrix}
n \frac{h_2(W = W_c)}{1 - e^{\alpha_{1,1}(T - W_c)} e^{\alpha_{1,1} W_c}} G_2(W = W_c) \\
n G_2(W = W_c)
\end{bmatrix}
\begin{bmatrix}
(t_0 + W) \\
W_c - (T - W_c) e^{\alpha_{1,1} W_c}
\end{bmatrix},
\]

(1.4.28)

with slopes:

\[
M_{p,u} = \begin{bmatrix}
\frac{h_1(W = W_c)}{1 - e^{\alpha_{1,1} W_c}} F_2(W = W_c) \\
F_2(W = W_c)
\end{bmatrix},
\]

(1.4.29)

and

\[
M_{q,v} = \begin{bmatrix}
\frac{h_2(W = W_c)}{1 - e^{\alpha_{1,1} W_c}} G_2(W = W_c) \\
G_2(W = W_c)
\end{bmatrix},
\]

(1.4.30)

respectively. Here \(F_1(W = W_c)\) and \(F_2(W = W_c)\) are the first and second elements of the nonhomogeneous term \(F(W = W_c)\) in Eq. (1.3.25) (see also Eq. (C.2-3)), and similarly for the elements of \(G\). We see from Fig. 1.21 that at the bifurcation point, predictions across days form straight lines with slopes defined by the first elements of Eq. (1.4.29) at the onset of wakefulness and Eq. (1.4.30) at the onset of sleep. From the compartmental point of view shown in Fig. 1.20 and at the bifurcation, the contents of the compartments grow linearly—performance impairment increases by the same amount each day.

In Fig. 1.21 we show performance predictions from the bifurcation model of Eqs. (1.4.1) and (1.4.2) for five wake/sleep schedules with different amounts of nocturnal sleep, using the published parameters from McCauley et al. (2009a). For convenience we show the \(\alpha_{i,j}\) and \(\sigma_{i,j}\) parameters in Table 1.2.

<table>
<thead>
<tr>
<th>parameter</th>
<th>mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\alpha_{1,1})</td>
<td>-0.0135</td>
</tr>
<tr>
<td>(\alpha_{1,2})</td>
<td>0.000929</td>
</tr>
<tr>
<td>(\alpha_{2,2})</td>
<td>0.00743</td>
</tr>
<tr>
<td>(\sigma_{1,1})</td>
<td>-2.17</td>
</tr>
<tr>
<td>(\sigma_{1,2})</td>
<td>0.872</td>
</tr>
<tr>
<td>(\sigma_{2,2})</td>
<td>-0.0397</td>
</tr>
</tbody>
</table>

Table 1.2: Published parameter estimates for the \(\alpha\) and \(\sigma\) matrices from McCauley et al. (2009a).
Using Table 1.2 and Eq. (1.4.19), we determine that the mean value of the bifurcation point $W_c$ is 20.2 h of wakefulness (i.e., 3.8 h of sleep). From Fig. 1.21 we see that when the duration of daily wakefulness is less than the critical amount, performance impairment tends to a state of equilibrium. We would expect that for all wake durations greater than the critical amount of wakefulness, performance impairment should exhibit a diverging pattern, exponentially escalating across days (e.g., the 2 h TIB schedule shown in Fig. 1.21). However, the predictions seen in the figure appear to converge for total sleep deprivation. This model behavior is due in part to the secondary process $u_n$ and can be understood by observing the interaction of the compartments in Fig. 1.20 (panel a), as well as considering
the published parameter estimates for the $\alpha$ matrix in Eq. (1.4.1) used for the predictions (McCauley et al., 2009a) (see Table 1.2). The contents of the $p_n$ compartment are consumed by a process with the rate constant $\alpha_{1,1}$ and resupplied by a process with a much smaller rate constant, $\alpha_{1,2}$. However, because the $u_n$ compartment is growing exponentially, by a process with the positive rate constant $\alpha_{2,2}$, its sheer magnitude will eventually be enough to reverse the consumption of $p_n$. The result is that performance impairment is predicted to increase across days, but initially in a decelerating manner (McCauley et al., 2009a).

1.4.2 A model case with feedback

Another model case can be formulated by setting only parameter $\sigma_{2,1}$ to zero into Eqs. (1.3.23) and (1.3.24):

$$\begin{bmatrix} \dot{p}_n \\ \dot{u}_n \end{bmatrix} = \begin{bmatrix} \alpha_{1,1} & \alpha_{1,2} \\ \alpha_{2,1} & \alpha_{2,2} \end{bmatrix} \begin{bmatrix} p_n \\ u_n \end{bmatrix} + \begin{bmatrix} \beta_1(t) \\ \beta_2(t) \end{bmatrix}, \quad \text{for } t \in [t_n, t_n + W_n],$$  \hfill (1.4.31)

$$\begin{bmatrix} \dot{q}_n \\ \dot{v}_n \end{bmatrix} = \begin{bmatrix} \sigma_{1,1} & \sigma_{1,2} \\ 0 & \sigma_{2,2} \end{bmatrix} \begin{bmatrix} q_n \\ v_n \end{bmatrix} + \begin{bmatrix} \gamma_1(t) \\ \gamma_2(t) \end{bmatrix}, \quad \text{for } t \in [t_n + W_n, t_{n+1}],$$  \hfill (1.4.32)

where we impose the condition that $\sigma_{1,1} \neq \sigma_{2,2}$. The real and distinct eigenvalues and eigenvectors (reflecting changes within days) for the $\alpha$ matrix in Eq. (1.4.31) are:

$$\lambda_1 = \frac{\alpha_{1,1} + \alpha_{2,2}}{2} + \frac{\sqrt{4 \alpha_{1,2} \alpha_{2,1} + (\alpha_{1,1} - \alpha_{2,2})^2}}{2},$$  \hfill (1.4.33)

$$\lambda_2 = \frac{\alpha_{1,1} + \alpha_{2,2}}{2} - \frac{\sqrt{4 \alpha_{1,2} \alpha_{2,1} + (\alpha_{1,1} - \alpha_{2,2})^2}}{2},$$  \hfill (1.4.34)

$$\mathbf{x}_1 = \begin{bmatrix} 2\alpha_{1,2} \\ \alpha_{2,2} - \alpha_{1,1} + \sqrt{4 \alpha_{1,2} \alpha_{2,1} + (\alpha_{1,1} - \alpha_{2,2})^2} \\ 1 \end{bmatrix},$$  \hfill (1.4.35)

$$\mathbf{x}_2 = \begin{bmatrix} 2\alpha_{1,2} \\ \alpha_{2,2} - \alpha_{1,1} - \sqrt{4 \alpha_{1,2} \alpha_{2,1} + (\alpha_{1,1} - \alpha_{2,2})^2} \\ 1 \end{bmatrix},$$  \hfill (1.4.36)

and for the $\sigma$ matrix in Eq. (1.4.32) are:

$$\lambda_3 = \sigma_{1,1},$$  \hfill (1.4.37)

$$\lambda_4 = \sigma_{2,2},$$  \hfill (1.4.38)

$$\mathbf{x}_3 = \begin{bmatrix} 1 \\ 0 \end{bmatrix},$$  \hfill (1.4.39)

$$\mathbf{x}_4 = \begin{bmatrix} \sigma_{1,2} \\ \sigma_{2,2} - \sigma_{1,1} \end{bmatrix}.$$  \hfill (1.4.40)
Figure 1.22: Analogous system of compartments for the case of the MTPM with feedback. We show two panels each with two separate compartments. The left system (panel a) describes performance, \( p_n(t) \), interconnected with a secondary process, \( u_n(t) \), during wakefulness. The right system (panel b) describes nominal performance, \( q_n(t) \), interconnected with a secondary process, \( v_n(t) \), during sleep. In this model case we have removed only one of the feedback parameters. This case assumes a feedback mechanism where the contents of compartment \( u_n(t) \) changes depending on the contents of compartment \( p_n(t) \) by the constant rate parameter \( \alpha_{2,1} \). Like the model case of Section 1.4.1 the two systems are connected across days by Eqs. (1.3.17) and (1.3.18).

The linear system of Eqs. (1.4.31) and (1.4.32) can also be described as a system of two interconnected chambers or compartments (see Fig. 1.22). We see in this model case that there is a feedback mechanism during wakefulness, from \( p_n(t) \) into \( u_n(t) \), but no equivalent mechanism during sleep.

### 1.4.2.1 Model case dynamics

Let us now consider the dynamics of Eqs. (1.3.25) and (1.3.26) for this particular model case of the MTPM. As we have done before, we will first examine when the states of equilibrium exist. Per Eqs. (1.3.39) and (1.3.40), and using the eigenvalues and normalized eigenvectors in Eqs. (1.4.33) through (1.4.40) we have:

\[
\begin{align*}
\det (I - \Phi(t_n + T)\Psi(t_n + W)) \\
&= \det \left( I - \begin{bmatrix} x_3 e^{\sigma_{1,1}(T-W)} & x_4 e^{\sigma_{2,2}(T-W)} \\ x_3 & x_4 \end{bmatrix} \begin{bmatrix} x_3 & x_4 \end{bmatrix}^{-1} \begin{bmatrix} x_1 e^{\lambda_1 W} & x_2 e^{\lambda_2 W} \end{bmatrix} \begin{bmatrix} x_1 & x_2 \end{bmatrix}^{-1} \right) \\
&= \det \left( \begin{bmatrix} 1 - e^{\sigma_{1,1}(T-W)} B_3 + x_4 B_1 B_2 & x_1 x_2 e^{\sigma_{1,1}(T-W)} B_1 - x_4 B_2 B_4 \\ -e^{\sigma_{2,2}(T-W)} B_1 & 1 + e^{\sigma_{2,2}(T-W)} B_4 \end{bmatrix} \right), \\
&= (1.4.41)
\end{align*}
\]
and

\[
\det (I - \Psi(t_n + W) \Phi(t_n + T)) = \det \left( I - \begin{bmatrix} x_1 e^{\lambda_1 W} & x_2 e^{\lambda_2 W} \\ x_1 & x_2 \end{bmatrix} \begin{bmatrix} x_1 x_2 \end{bmatrix}^{-1} \begin{bmatrix} x_3 e^{\sigma_{1,1}(T-W)} & x_4 e^{\sigma_{2,2}(T-W)} \end{bmatrix} \begin{bmatrix} x_3 & x_4 \end{bmatrix}^{-1} \right) = \det \left( \begin{bmatrix} 1 - e^{\sigma_{1,1}(T-W)} B_3 & x_4 B_2 B_3 + x_1 x_2 e^{\sigma_{2,2}(T-W)} B_1 \\ -e^{\sigma_{1,1}(T-W)} B_1 & 1 + x_4 B_2 + e^{\sigma_{2,2}(T-W)} B_4 \end{bmatrix} \right),
\]

(1.4.42)

where

\[
B_1 = \frac{e^{\lambda_1 W} - e^{\lambda_2 W}}{x_1 - x_2},
\]

(1.4.43)

\[
B_2 = e^{\sigma_{1,1}(T-W)} - e^{\sigma_{2,2}(T-W)},
\]

(1.4.44)

\[
B_3 = \frac{x_1 e^{\lambda_1 W} - x_2 e^{\lambda_2 W}}{x_1 - x_2},
\]

(1.4.45)

\[
B_4 = \frac{x_2 e^{\lambda_1 W} - x_1 e^{\lambda_2 W}}{x_1 - x_2}.
\]

(1.4.46)

The determinants in Eqs. (1.4.41) and (1.4.42) can be shown to be equivalent (see Appendix C.6). Let us use Eq. (1.4.41) where we see that a state of equilibrium exists when:

\[
(1 - e^{\sigma_{1,1}(T-W)} B_3)(1 + e^{\sigma_{2,2}(T-W)} B_4) + \left(x_4 B_2 + x_1 x_2 e^{\sigma_{2,2}(T-W)} e^{\sigma_{1,1}(T-W)} B_1\right) B_1 \neq 0.
\]

(1.4.47)

In Section 1.6.2 where we produce parameter estimations and model predictions for this model case, we will numerically determine the roots of Eq. (1.4.47) which determine exactly where the model bifurcates.

Stability of an equilibrium state when it does exist can be determined by finding the eigenvalues of the matrix products \(\Phi(t_n + T)\Psi(t_n + W)\) or \(\Psi(t_n + W)\Phi(t_n + T)\). Recall that we have shown that because these are shifted matrices (i.e., \(\Phi\Psi\) vs. \(\Psi\Phi\)), the eigenvalues are identical (see Appendix C.5). Let us consider the first of these two matrix products (e.g., the coefficient matrix of Eqs. (1.3.25)):

\[
\Phi(t_n + T)\Psi(t_n + W) = \begin{bmatrix} e^{\sigma_{1,1}(T-W)} B_3 + x_4 B_2 B_3 & -x_1 x_2 e^{\sigma_{1,1}(T-W)} B_1 + x_4 B_2 B_4 \\ e^{\sigma_{2,2}(T-W)} B_1 & -e^{\sigma_{2,2}(T-W)} B_4 \end{bmatrix}.
\]

(1.4.48)

Using Eq. (1.3.45) we can find the two eigenvalues, \(\Lambda_i\) where \(i = \{1, 2\}\), of Eq. (1.4.48):

\[
\Lambda_i = \text{Tr}(\Phi(t_n + T)\Psi(t_n + W)) 
\pm \sqrt{\text{Tr}(\Phi(t_n + T)\Psi(t_n + W))^2 - 4 \det(\Phi(t_n + T)\Psi(t_n + W))},
\]

(1.4.49)
where \( \text{det} \) is the determinant and \( \text{Tr} \) is the trace. We will numerically solve these in Section 1.6.2 to determine stability of the equilibrium states. When the magnitude of both eigenvalues are less than unity the equilibrium state is stable, otherwise the equilibrium state is unstable.

### 1.4.2.2 Dynamics across days

The characteristic behavior for this case of the MTPM model across days can be further analyzed by deriving the closed form of the solution of Eq. (1.3.25). For the model case of Eqs. (1.4.31) and (1.4.32), and using Eq. (1.3.47), the closed form of the solutions of Eq. (1.25) for the onset of wakefulness and Eq. (1.3.26) for the onset of sleep can be written as:

\[
\begin{bmatrix}
    p_n(t_n) \\
    u_n(t_n)
\end{bmatrix}
\begin{bmatrix}
    e^{\sigma_{1,1}(T-W)}B_3 - x_{4,1}B_1B_2 & -x_{1,1}x_{2,1}e^{\sigma_{1,1}(T-W)}B_1 + x_{4,1}B_2B_4 \\
    e^{\sigma_{2,2}(T-W)}B_1 & -e^{\sigma_{2,2}(T-W)}B_4
\end{bmatrix}^n
\begin{bmatrix}
    p_0(t_0) \\
    u_0(t_0)
\end{bmatrix}
\]

\[
+ \left( I - \begin{bmatrix}
    e^{\sigma_{1,1}(T-W)}B_3 - x_{4,1}B_1B_2 & -x_{1,1}x_{2,1}e^{\sigma_{1,1}(T-W)}B_1 + x_{4,1}B_2B_4 \\
    e^{\sigma_{2,2}(T-W)}B_1 & -e^{\sigma_{2,2}(T-W)}B_4
\end{bmatrix}^n \right)
\]

\[
\times \begin{bmatrix}
    1 - e^{\sigma_{1,1}(T-W)}B_3 + x_{4,1}B_1B_2 & x_{1,1}x_{2,1}e^{\sigma_{1,1}(T-W)}B_1 - x_{4,1}B_2B_4 \\
    -e^{\sigma_{2,2}(T-W)}B_1 & 1 + e^{\sigma_{2,2}(T-W)}B_4
\end{bmatrix}^{-1}
\begin{bmatrix}
    F_1 \\
    F_2
\end{bmatrix},
\]

(1.4.50)

during wakefulness, and

\[
\begin{bmatrix}
    q_n(t_n + W) \\
    v_n(t_n + W)
\end{bmatrix}
\begin{bmatrix}
    e^{\sigma_{1,1}(T-W)}B_3 & -x_{4,1}B_2B_3 - x_{1,1}x_{2,1}e^{\sigma_{2,2}(T-W)}B_1 \\
    e^{\sigma_{1,1}(T-W)}B_1 & -x_{4,1}B_1B_2 - e^{\sigma_{2,2}(T-W)}B_4
\end{bmatrix}^n
\begin{bmatrix}
    q_0(t_0 + W) \\
    v_0(t_0 + W)
\end{bmatrix}
\]

\[
+ \left( I - \begin{bmatrix}
    e^{\sigma_{1,1}(T-W)}B_3 & -x_{4,1}B_2B_3 - x_{1,1}x_{2,1}e^{\sigma_{2,2}(T-W)}B_1 \\
    e^{\sigma_{1,1}(T-W)}B_1 & -x_{4,1}B_1B_2 - e^{\sigma_{2,2}(T-W)}B_4
\end{bmatrix}^n \right)
\]

\[
\times \begin{bmatrix}
    1 - e^{\sigma_{1,1}(T-W)}B_3 + x_{4,1}B_2B_3 + x_{1,1}x_{2,1}e^{\sigma_{2,2}(T-W)}B_1 \\
    -e^{\sigma_{1,1}(T-W)}B_1 & 1 + x_{4,1}B_1B_2 + e^{\sigma_{2,2}(T-W)}B_4
\end{bmatrix}^{-1}
\begin{bmatrix}
    G_1 \\
    G_2
\end{bmatrix},
\]

(1.4.51)

during sleep, where the \( B_i \)'s are given in Eqs. (1.4.43) through (1.4.46) and the eigenvalues and eigenvectors in Eqs. (1.4.33) through (1.4.40).

\[^{\text{a}}\text{The trace of a matrix } A = \text{Tr} \left( \begin{bmatrix} a & b \\ c & d \end{bmatrix} \right) = (a + d)\]
1.4.3 The full model

This model case uses all of the parameters in Eqs. (1.3.23) and (1.3.24). For convenience let us rewrite this system:

\[
\begin{bmatrix}
\dot{p}_n \\
\dot{u}_n
\end{bmatrix} =
\begin{bmatrix}
\alpha_{1,1} & \alpha_{1,2} \\
\alpha_{2,1} & \alpha_{2,2}
\end{bmatrix}
\begin{bmatrix}
p_n \\
u_n
\end{bmatrix} +
\begin{bmatrix}
\beta_1(t) \\
\beta_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n, t_n + W_n],
\]

(1.4.52)

\[
\begin{bmatrix}
\dot{q}_n \\
\dot{v}_n
\end{bmatrix} =
\begin{bmatrix}
\sigma_{1,1} & \sigma_{1,2} \\
\sigma_{2,1} & \sigma_{2,2}
\end{bmatrix}
\begin{bmatrix}
q_n \\
v_n
\end{bmatrix} +
\begin{bmatrix}
\gamma_1(t) \\
\gamma_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}],
\]

(1.4.53)

where the real and distinct eigenvalues and suitable eigenvectors for the \( \alpha \) matrix in Eq. (1.4.52) are:

\[
\lambda_1 = \frac{\alpha_{1,1} + \alpha_{2,2}}{2} + \sqrt{\frac{4 \alpha_{1,2} \alpha_{2,1} + (\alpha_{1,1} - \alpha_{2,2})^2}{2}},
\]

(1.4.54)

\[
\lambda_2 = \frac{\alpha_{1,1} + \alpha_{2,2}}{2} - \sqrt{\frac{4 \alpha_{1,2} \alpha_{2,1} + (\alpha_{1,1} - \alpha_{2,2})^2}{2}},
\]

(1.4.55)

\[
x_1 = \begin{bmatrix}
\frac{2\alpha_{1,2}}{\alpha_{2,2} - \alpha_{1,1} + \sqrt{4 \alpha_{1,2} \alpha_{2,1} + (\alpha_{1,1} - \alpha_{2,2})^2}} \\
1
\end{bmatrix},
\]

(1.4.56)

\[
x_2 = \begin{bmatrix}
\frac{2\alpha_{1,2}}{\alpha_{2,2} - \alpha_{1,1} - \sqrt{4 \alpha_{1,2} \alpha_{2,1} + (\alpha_{1,1} - \alpha_{2,2})^2}} \\
1
\end{bmatrix},
\]

(1.4.57)

and for the \( \sigma \) matrix in Eq. (1.4.53) are:

\[
\lambda_3 = \frac{\sigma_{1,1} + \sigma_{2,2}}{2} + \sqrt{\frac{4 \sigma_{1,2} \sigma_{2,1} + (\sigma_{1,1} - \sigma_{2,2})^2}{2}},
\]

(1.4.58)

\[
\lambda_4 = \frac{\sigma_{1,1} + \sigma_{2,2}}{2} - \sqrt{\frac{4 \sigma_{1,2} \sigma_{2,1} + (\sigma_{1,1} - \sigma_{2,2})^2}{2}},
\]

(1.4.59)

\[
x_3 = \begin{bmatrix}
\frac{2\sigma_{1,2}}{\sigma_{2,2} - \sigma_{1,1} + \sqrt{4 \sigma_{1,2} \sigma_{2,1} + (\sigma_{1,1} - \sigma_{2,2})^2}} \\
1
\end{bmatrix},
\]

(1.4.60)

\[
x_4 = \begin{bmatrix}
\frac{2\sigma_{1,2}}{\sigma_{2,2} - \sigma_{1,1} - \sqrt{4 \sigma_{1,2} \sigma_{2,1} + (\sigma_{1,1} - \sigma_{2,2})^2}} \\
1
\end{bmatrix}.
\]

(1.4.61)

Recall that the analogous system of two interconnected chambers or compartments for Eqs. (1.4.52) and (1.4.53) is shown in Fig. 1.15.

1.4.3.1 Model case dynamics

The dynamics of Eqs. (1.3.25) and (1.3.26) for this particular model case of the MTPM can be examined by determining when states of equilibrium exist. Per Eqs. (1.3.39) and
(1.3.40) and using the eigenvalues and normalized eigenvectors in Eqs. (1.4.54) through (1.4.61), we have:

$$\det \left( I - \Phi(t_n + T) \Psi(t_n + W) \right)$$

$$= \det \left( I - \begin{bmatrix} x_1 e^{\lambda_1 (T-W)} & x_4 e^{\lambda_4 (T-W)} \\ 1 - B_3 B_5 + x_{3,1} x_{4,1} B_1 B_2 & x_{1,1} x_{2,1} B_1 B_3 - x_{3,1} x_{4,1} B_2 B_6 \\ B_1 B_4 - B_2 B_5 & 1 - B_4 B_6 + x_{1,1} x_{2,1} B_1 B_2 \end{bmatrix} \right),$$

$$\text{(1.4.62)}$$

$$\det \left( I - \Psi(t_n + W) \Phi(t_n + T) \right)$$

$$= \det \left( I - \begin{bmatrix} x_1 e^{\lambda_1 W} & x_2 e^{\lambda_2 W} \\ 1 - B_3 B_5 + x_{1,1} x_{2,1} B_1 B_2 & -x_{1,1} x_{2,1} B_1 B_4 + x_{3,1} x_{4,1} B_2 B_5 \\ B_2 B_6 - B_1 B_3 & 1 - B_4 B_6 + x_{3,1} x_{4,1} B_1 B_2 \end{bmatrix} \right),$$

$$\text{(1.4.63)}$$

where

$$B_1 = \frac{e^{\lambda_1 W} - e^{\lambda_2 W}}{(x_{1,1} - x_{2,1})(x_{3,1} - x_{4,1})},$$

$$B_2 = e^{\lambda_3 (T-W)} - e^{\lambda_4 (T-W)},$$

$$B_3 = x_{3,1} e^{\lambda_3 (T-W)} - x_{4,1} e^{\lambda_4 (T-W)},$$

$$B_4 = x_{4,1} e^{\lambda_3 (T-W)} - x_{3,1} e^{\lambda_4 (T-W)},$$

$$B_5 = \frac{x_{1,1} e^{\lambda_1 W} - x_{2,1} e^{\lambda_2 W}}{(x_{1,1} - x_{2,1})(x_{3,1} - x_{4,1})},$$

$$B_6 = \frac{x_{2,1} e^{\lambda_1 W} - x_{1,1} e^{\lambda_2 W}}{(x_{1,1} - x_{2,1})(x_{3,1} - x_{4,1})}.$$

It can again be shown that the determinants in Eqs. (1.4.62) and (1.4.63) are equivalent. From Eq. (1.4.62), we see that a state of equilibrium exists when:

$$(1 - B_3 B_5 + x_{3,1} x_{4,1} B_1 B_2)(1 - B_4 B_6 + x_{1,1} x_{2,1} B_1 B_2) - (B_1 B_4 - B_2 B_5)(x_{1,1} x_{2,1} B_1 B_3 - x_{3,1} x_{4,1} B_2 B_6) \neq 0.$$  

$$\text{(1.4.70)}$$

Because of the complexity of the inequality of Eq. (1.4.70), numerical methods would be appropriate to determine the roots of Eq. (1.4.70), to find where the model bifurcates.

Stability of an equilibrium state when it does exist can be determined by finding the two eigenvalues of the matrix product:

$$\Phi(t_n + T) \Psi(t_n + W) = \begin{bmatrix} B_3 B_5 - x_{3,1} x_{4,1} B_1 B_2 & -x_{1,1} x_{2,1} B_1 B_3 + x_{3,1} x_{4,1} B_2 B_6 \\ -B_1 B_4 + B_2 B_5 & B_4 B_6 - x_{1,1} x_{2,1} B_1 B_2 \end{bmatrix},$$

$$\text{(1.4.71)}$$
or equivalently the eigenvalues of the matrix product $\Psi(t_n + W)\Phi(t_n + T)$ (see Appendix C.5). Using Eq. (1.3.45) we find these eigenvalues by deriving the determinant and trace of the matrix of Eq. (1.4.71) (cf. Eq. (1.4.49)). When the magnitudes of these two eigenvalues are less than unity the equilibrium state is stable, otherwise it is unstable.

### 1.4.3.2 Dynamics across days

The characteristic behavior of this case of the MTPM model across days can be seen by again deriving the closed form of the solution of Eq. (1.3.25). For the model case of Eqs. (1.4.52) and (1.4.53), and using Eq. (1.3.47), the closed forms of the solutions of Eq. (1.3.25) for the onset of wakefulness and Eq. (1.3.26) for the onset of sleep can be written as:

\[
\begin{bmatrix}
p_n(t_n) \\
u_n(t_n)
\end{bmatrix} = 
\begin{bmatrix}
B_3B_5 - x_{1,1}x_{4,1}B_1B_2 & -x_{1,1}x_{2,1}B_1B_3 + x_{3,1}x_{4,1}B_2B_6 \\
-B_1B_4 + B_2B_5 & B_4B_6 - x_{1,1}x_{2,1}B_1B_2
\end{bmatrix}^n
\begin{bmatrix}
p_0(t_0) \\
u_0(t_0)
\end{bmatrix}
+ \left(I - 
\begin{bmatrix}
B_3B_5 - x_{1,1}x_{4,1}B_1B_2 & -x_{1,1}x_{2,1}B_1B_3 + x_{3,1}x_{4,1}B_2B_6 \\
-B_1B_4 + B_2B_5 & B_4B_6 - x_{1,1}x_{2,1}B_1B_2
\end{bmatrix}
\right)^n
\times
\begin{bmatrix}
1 - B_3B_5 + x_{3,1}x_{4,1}B_1B_2 & x_{1,1}x_{2,1}B_1B_3 - x_{3,1}x_{4,1}B_2B_6 \\
B_1B_4 - B_2B_5 & 1 - B_4B_6 + x_{1,1}x_{2,1}B_1B_2
\end{bmatrix}^{-1}
\begin{bmatrix}
F_1 \\
F_2
\end{bmatrix},
\]

(1.4.72)
during wakefulness, and

\[
\begin{bmatrix}
q_n(t_n + W) \\
v_n(t_n + W)
\end{bmatrix} = 
\begin{bmatrix}
B_3B_5 - x_{1,1}x_{2,1}B_1B_2 & x_{1,1}x_{2,1}B_1B_4 - x_{3,1}x_{4,1}B_2B_5 \\
-B_2B_6 + B_1B_3 & B_4B_6 - x_{3,1}x_{4,1}B_1B_2
\end{bmatrix}^n
\begin{bmatrix}
q_0(t_0 + W) \\
v_0(t_0 + W)
\end{bmatrix}
+ \left(I - 
\begin{bmatrix}
B_3B_5 - x_{1,1}x_{2,1}B_1B_2 & x_{1,1}x_{2,1}B_1B_4 - x_{3,1}x_{4,1}B_2B_5 \\
-B_2B_6 + B_1B_3 & B_4B_6 - x_{3,1}x_{4,1}B_1B_2
\end{bmatrix}
\right)^n
\times
\begin{bmatrix}
1 - B_3B_5 + x_{1,1}x_{2,1}B_1B_2 & -x_{1,1}x_{2,1}B_1B_4 + x_{3,1}x_{4,1}B_2B_5 \\
B_2B_6 - B_1B_3 & 1 - B_4B_6 + x_{3,1}x_{4,1}B_1B_2
\end{bmatrix}^{-1}
\begin{bmatrix}
G_1 \\
G_2
\end{bmatrix},
\]

(1.4.73)
during sleep. Here the $B_i$’s are given by Eqs. (1.4.64) through (1.4.69), and the eigenvalues and eigenvectors by Eqs. (1.4.54) through (1.4.61).

### 1.5 Oscillatory behavior

In the MTPM cases discussed thus far all eigenvalues of the $\alpha$ and $\sigma$ matrices were real and distinct, which produced solutions involving exponential increases and decreases within periods of wakefulness and sleep (just like in the TPM). In the case when these
eigenvalues are complex, the solutions will be combinations of sines and cosines (see Appendix C.7), meaning that the solutions will oscillate within days. We can derive conditions for the generalized two-dimensional model of Eqs. (1.3.23) and Eqs. (1.3.24) to exhibit this type of behavior. For Eq. (1.3.23), the eigenvalues of the $\alpha$ matrix are complex if:

$$(\alpha_{1,1} + \alpha_{2,2})^2 < 4(\alpha_{1,1}\alpha_{2,2} - \alpha_{2,1}\alpha_{1,2})$$

(1.5.1)

(see Eq. (C.7-2)). For Eq. (1.3.24), the eigenvalues of the $\sigma$ matrix are complex if:

$$(\sigma_{1,1} + \sigma_{2,2})^2 < 4(\sigma_{1,1}\sigma_{2,2} - \sigma_{2,1}\sigma_{1,2})$$. 

(1.5.2)

Notice in Eq. (1.5.1), if either $\alpha_{1,2} = 0$ or $\alpha_{2,1} = 0$, then by solving the remaining inequality one would find that $(\alpha_{1,1} - \alpha_{2,2})^2$ must be negative, which cannot be true. The same occurs for $\sigma_{1,2}$ or $\sigma_{2,1}$. Therefore, to have complex eigenvalues and thus oscillatory behavior within days, $\alpha_{1,2}, \alpha_{2,1}, \sigma_{1,2}$ and $\sigma_{2,1}$ must be non-zero parameters.

Complex eigenvalues come in conjugate pairs $a \pm i\omega$ (see Appendix C.7). Here, $a$ is the real part of the eigenvalue which represents the rate of growth/decay of the sinusoidal curve within days. If $a = 0$ the sinusoidal curve has constant amplitude. If $a > 0$ the system will be oscillatory with an amplitude that grows, whereas if $a < 0$ it will be oscillatory with an amplitude that decays. The parameter $\omega$ is the imaginary part of the eigenvalue and represents the frequency ($\omega = 2\pi/T$) of the oscillation. These complex eigenvalues can be used to model the oscillations of the circadian rhythm. In Chapter 4 we will see how to use such model behavior for realignment of the biological clock with the changing environment (i.e., entrainment).

1.6 Parameter estimates and predictions for the MTPM

Parameter estimates from the model described by Eqs. (1.4.1) and (1.4.2) can be found by numerically solving the system of ODEs (e.g., using a Matlab solver). This approach, used by McCauley et al. (2009a) for the case of the MTPM in Section 1.4.1, resulted in the estimation of an optimal set of parameter values. In this thesis, and as we did for the gTPM, we will enlist the MCMC (Haario et al., 2005) to obtain parameter distributions and predictive plots for the MTPM. The MTPM requires searching across a significantly larger space than the gTPM. This motivates the derivation of an exact analytical solution to the system of ODEs, so as to avoid numerical error and uses significantly less computational resources, thereby making possible to iterate through millions of parameter sets.
The analytical solution depends on the specific form of the nonhomogeneities $\beta(t)$ and $\gamma(t)$. Let us assume a specific form for nonhomogeneities $\beta_i(t)$ and $\gamma_i(t)$ and obtain predictions from the model described by Eqs. (1.4.1) and (1.4.2):

$$\begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix} = \begin{bmatrix} \kappa c(t) + \mu \\ 0 \end{bmatrix}, \quad (1.6.1)$$

$$\begin{bmatrix} \gamma_1 \\ \gamma_2 \end{bmatrix} = \begin{bmatrix} \kappa c(t) + \mu \\ 0 \end{bmatrix}, \quad (1.6.2)$$

where the circadian rhythm $c(t)$, is described by Eq. (1.1.5). Here we have assumed that the time-dependent processes $u(t)$ and $v(t)$ are unaffected by the nonhomogeneities. The parameter $\kappa$ is the amplitude of the oscillatory circadian component, and $\mu$ is a constant.

In the following two sections we show results from fitting the same data used in the gTPM analysis (see Section 1.2.1) to obtain parameter estimates for the first two MTPM cases described in Chapter 1.4. We will discuss the third example case in Chapter 3.

### 1.6.1 Parameter estimates and predictions for the model case with a bifurcation

In this section we obtain parameter estimates and predictions from the model described by Eqs. (1.4.1) and (1.4.2) (see Fig. (1.23)). Let us first derive the analytical solution for the specific form of the nonhomogeneities $\beta(t)$ and $\gamma(t)$ given in Eqs. (1.6.1) and (1.6.2).
1.6.1.1 Analytical solution within days

Using eigenvalues and eigenvectors Eqs. (1.4.3) through (1.4.10) we can readily write the analytical solution to Eqs. (1.4.1) and (1.4.2) (see Appendix C.4). During wakefulness we find:

\[
\begin{bmatrix}
  p_n(t) \\
  u_n(t)
\end{bmatrix} =
\begin{bmatrix}
  e^{\alpha_{1,1}(t-t_n)} & \frac{\alpha_{1,2}}{\alpha_{2,2} - \alpha_{1,1}}
  \\
  0 & e^{\alpha_{2,2}(t-t_n)}
\end{bmatrix}
\begin{bmatrix}
  e^{\alpha_{2,2}(t-t_n)} - e^{\alpha_{1,1}(t-t_n)} \\
  e^{\alpha_{2,2}(t-t_n)}
\end{bmatrix} + \mathbf{\Omega}_n(t),
\]

where

\[
\mathbf{\Omega}_n(t) = \begin{bmatrix} 1 & 0 \end{bmatrix} \left( \kappa \sum_{k=1}^{5} a_k e^{\alpha_{1,1}(t-t_n)} \frac{2k\pi}{\tau} \cos \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - \cos \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)
\]

\[
\mathbf{\Omega}_n(t) + \mathbf{\mathcal{K}} \mathbf{\mathcal{L}}(t),
\]

and during sleep:

\[
\begin{bmatrix}
  q_n(t) \\
  v_n(t)
\end{bmatrix} =
\begin{bmatrix}
  e^{\sigma_{1,1}(t-(t_n+W_n))} & \frac{\sigma_{1,2}}{\sigma_{2,2} - \sigma_{1,1}}
  \\
  0 & e^{\sigma_{2,2}(t-(t_n+W_n))}
\end{bmatrix}
\begin{bmatrix}
  e^{\sigma_{1,1}(t-(t_n+W_n))} - e^{\sigma_{1,1}(t-(t_n+W_n))} \\
  e^{\sigma_{2,2}(t-(t_n+W_n))}
\end{bmatrix} + \mathbf{\Theta}_n(t),
\]

where

\[
\mathbf{\Theta}_n(t) = \begin{bmatrix} 1 & 0 \end{bmatrix} \left( \kappa \sum_{k=1}^{5} a_k e^{\sigma_{1,1}(t-(t_n+W_n))} \frac{2k\pi}{\tau} \cos \left( \frac{2k\pi}{\tau} (t_n + W_n - \phi) \right) - \cos \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)
\]

\[
\mathbf{\Theta}_n(t) + \mathbf{\mathcal{K}} \mathbf{\mathcal{L}}(t),
\]

1.6.1.2 Initial performance level

To utilize Eqs. (1.6.3) or (1.6.5) one must have the initial values \([p_0(t_0), u_0(t_0)]^T\) (when initiating model predictions at the onset of wakefulness) or \([q_0(t_0 + W_0), v_0(t_0 + W_0)]^T\)
(when initiating model predictions at the onset of sleep). Assuming stable baseline conditions, and assuming without loss of generality, we begin with performance predictions at the onset of wakefulness, we can use the equilibrium equation for the onset of wakefulness in Eq. (1.3.35). The initial values \([p_0(t_0), u_0(t_0)]^T\) for a particular amount of baseline wakefulness, \(W_b\), is:

\[
\begin{bmatrix} p_0(t_0) \\ u_0(t_0) \end{bmatrix} = \left( I - \begin{bmatrix} x_3 e^{\lambda_3(T-W_b)} & x_4 e^{\lambda_4(T-W_b)} \\ 1-e^{\alpha_1 W_b} e^{\sigma_1(T-W_b)} & 0 \end{bmatrix} \right)^{-1} \begin{bmatrix} \frac{e^{\sigma_1(T-W_b)}}{1-e^{\alpha_1 W_b} e^{\sigma_1(T-W_b)}} \right) \begin{bmatrix} \Omega(t_n + W_b) \\ \Theta(t_n + T) \end{bmatrix} + \begin{bmatrix} \frac{e^{\sigma_2(T-W_b)}}{1-e^{\alpha_2 W_b} e^{\sigma_2(T-W_b)}} \right) \begin{bmatrix} \delta \end{bmatrix}, \quad (1.6.7)
\]

where \(h_1(W = W_b)\) is given in Eqs. (1.4.13), and \(\Omega(t_n + W_b)\) and \(\Theta(t_{n+1})\) can be obtained using Eqs. (1.6.4) and (1.6.6), respectively.

### 1.6.1.3 Parameter estimates and model predictions

Parameter estimates and predictions for the model case defined by the ODE system Eqs. (1.4.1) and (1.4.2) can now be obtained using the MCMC algorithm. The results are shown in Table 1.3 and Figs. 1.24 through 1.31. The figures show that the model

<table>
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<th>parameter</th>
<th>mean</th>
<th>standard error</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\alpha_{1,1})</td>
<td>0.0085</td>
<td>0.007</td>
</tr>
<tr>
<td>(\alpha_{1,2})</td>
<td>-0.0096</td>
<td>0.003</td>
</tr>
<tr>
<td>(\alpha_{2,2})</td>
<td>0.012</td>
<td>0.001</td>
</tr>
<tr>
<td>(\kappa)</td>
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<td>0.07</td>
</tr>
<tr>
<td>(\phi)</td>
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<td>0.4</td>
</tr>
<tr>
<td>(\sigma_{2,2})</td>
<td>-0.065</td>
<td>0.007</td>
</tr>
<tr>
<td>(\delta)</td>
<td>22</td>
<td>3</td>
</tr>
<tr>
<td>(\mu)</td>
<td>0.69</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Table 1.3: Parameter estimates and standard errors for the case of the MTPM with a bifurcation described by Eqs. (1.4.1) and (1.4.2) using 676 data points from two laboratory sleep deprivation experiments (Belenky et al., 2003; Van Dongen et al., 2003).
Figure 1.24: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the $\alpha_{1,1}$, $\alpha_{1,2}$ and $\sigma_{2,2}$ parameters in Eq. (1.4.1) for the case of the MTPM with a bifurcation. Contour curves represent the 50% and 90% probability levels. The parameters are well defined by the data and have near-Gaussian distributions.

Figure 1.25: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the $\alpha_{1,1}$, $\alpha_{1,2}$, $\alpha_{2,2}$ and $\sigma_{2,2}$ parameters in Eqs. (1.4.1) and (1.4.2) for the case of the MTPM with a bifurcation. Contour curves represent the 50% and 90% probability levels. The parameters are well defined by the data and have near-Gaussian distributions.
Figure 1.26: Projections of MCMC chains are shown for the parameter pair $\sigma_{1,1}$ and $\sigma_{1,2}$ in Eq. (1.4.2) for the case of the MTPM with a bifurcation. We see a strong linear correlation between these two parameters.

Figure 1.27: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the parameters $\kappa$, $\phi$, $\delta$, and $\mu$ in Eqs. (1.4.1) and (1.4.2) for the case of the MTPM with a bifurcation. Contour curves represent the 50% and 90% probability levels. We see that these parameters are well defined by the data and have near-Gaussian distributions.
parameters $\alpha_{1,1}$, $\alpha_{1,2}$, $\alpha_{2,2}$, $\kappa$, $\phi$, $\sigma_{2,2}$, $\delta$ and $\mu$ in Eqs. (1.4.1) and (1.4.2) are well defined by the data. However $\sigma_{1,1}$ and $\sigma_{1,2}$ are seen to be strongly linearly correlated (see Fig. 1.26). This suggests that the experimental data (Belenky et al., 2003; Van Dongen et al., 2003) do not define these particular model parameters well, probably due to the lack of experimental data during sleep. These parameters might be better determined using data from experiments with schedules that include napping (Mollicone et al., 2008) (see also Chapter 3 of this thesis), as will be considered in future research.

Using Eq. (1.4.19) and Table 1.3 we determine that the bifurcation point, $W_c$, is 20.2 h.
Figure 1.29: Model predictions for the case of the MTPM with a bifurcation for four laboratory sleep deprivation conditions (Belenky et al., 2003). The upper-left panel shows 7 days with 9 h TIB per day; the upper-right panel shows 7 days with 7 h TIB per day; the lower-left panel shows 7 days with 5 h TIB per day; and the lower-right panel shows 7 days with 3 h TIB per day. Each schedule is followed by 3 days with 8 h TIB per day. Grey regions represent 90% confidence bands for the predicted means. Dots are grouped average PVT lapses data (Belenky et al., 2003).

(i.e., 3.8 h of sleep) All wake/sleep schedules with daily wakefulness above the bifurcation point show diverging performance patterns, whereas all schedules with wakefulness below the bifurcation converge (see Figs. 1.28 and 1.29).

Using the parameter estimates of Table 1.3 let us now take a look at the equilibrium dynamics at the bifurcation point, and see what happens as the amount of wakefulness approaches $W_c$ from both directions. From the equilibrium state defined in Eqs. (1.3.35) and (1.3.36) we can see in Fig. 1.30 that the equilibrium point increases hyperbolically, tending to infinity as wakefulness is increased toward $W_c$; and decreases hyperbolically, tending to negative infinity as wakefulness is decreased toward $W_c$. Exactly at the bifurcation point,
Figure 1.30: Plot showing states of equilibrium of performance level versus duration of wakefulness for the case of the MTPM with a bifurcation. The figure shows the dynamics of the states of equilibrium for a continuous range of wakefulness durations: p (solid) and u (dashed). The vertical dotted line represents the bifurcation defined by Eq. (1.4.19) where the equilibrium state vanishes. We see as wakefulness approaches $W_c$ from the left the equilibrium state increases hyperbolically toward infinity. As wakefulness approaches $W_c$ from the right side the equilibrium state decreases hyperbolically toward negative infinity. However, the equilibrium state becomes positive as wakefulness increases toward the duration of day, $T$.

Figure 1.31: Plot showing the magnitude of the eigenvalues $\Lambda_1$ (solid line) and $\Lambda_2$ (dashed line) of Eqs. (1.4.17) and (1.4.18), respectively, versus duration of wakefulness for the case of the MTPM with a bifurcation. The vertical dotted line represents the bifurcation defined by Eq. (1.4.19) where the equilibrium state vanishes.
a) During wakefulness

b) During sleep

Figure 1.32: Analogous system of compartments for the case of the MTPM with feedback and with specific nonhomogeneities given in Eqs. (1.6.1) and (1.6.2). The left system (panel a) describes performance, \( p(t) \), interconnected with a secondary process, \( u(t) \), during wakefulness. The right system (panel b) describes nominal performance, \( q(t) \), interconnected with a secondary process, \( v(t) \), during sleep.

\[ A_2 \text{ defined in Eq. (1.4.18) reaches unity, resulting in the qualitative change in model behavior from stability to instability (see Fig. 1.31). However, notice that unlike the gTPM, the equilibrium state no longer remains negative as wakefulness increases from the bifurcation point upwards toward the duration of day, } T \text{ (see McCauley et al., 2009a).} \]

From Table 1.3 we see that the parameter \( \alpha_{1,1} \) has a mean of 0.0085 and a standard error of 0.007. Therefore, the 90% probability region contains negative values for the parameter. This means that either Eq. (1.4.19) or Eq. (1.4.21) could define the bifurcation.

### 1.6.2 Parameter estimates and predictions for the model case with feedback

In this section we obtain parameter estimates and predictions from the model described by Eqs. (1.4.31) and (1.4.32) using the nonhomogeneities given in Eqs. (1.6.1) and (1.6.2).

#### 1.6.2.1 Analytical solution within days

Using the eigenvalues and eigenvectors in Eqs. (1.4.33) through (1.4.36) we can immediately write the analytical solutions within days to Eqs. (1.4.31) during wakefulness (see Appendix C.4):

\[
\begin{bmatrix}
  p_n(t) \\
  u_n(t)
\end{bmatrix} =
\begin{bmatrix}
  x_{1,1}e^{\lambda_1 (t-t_n)} - x_{2,1}e^{\lambda_2 (t-t_n)} & -x_{1,1}x_{2,1} \left( e^{\lambda_1 (t-t_n)} - e^{\lambda_2 (t-t_n)} \right) \\
  e^{\lambda_1 (t-t_n)} - e^{\lambda_2 (t-t_n)} & x_{1,1}e^{\lambda_2 (t-t_n)} - x_{2,1}e^{\lambda_1 (t-t_n)}
\end{bmatrix}
\frac{1}{(x_{1,1} - x_{2,1})} \begin{bmatrix}
  p_n(t_n) \\
  u_n(t_n)
\end{bmatrix} + \Omega_n(t),
\]

(1.6.8)
where

\[
\Omega_n(t) = \sum_{i=1}^{2} \frac{1}{(x_{1,1} - x_{2,1})}\left[ \frac{x_{i,1}}{1} \right]
\]

\[
\left( \kappa \sum_{k=1}^{5} A_k \left( e^{i\lambda_k(t-t_0)} \cos \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - \cos \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right) + \kappa \sum_{k=1}^{5} \lambda_k \tau^2 \left( e^{i\lambda_k(t-t_0)} \sin \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - \sin \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right) + \frac{\mu}{\lambda_i} \left( e^{\lambda_i(t-t_0)} - 1 \right) \right) \quad (1.6.9)
\]

During sleep the solution within days is unchanged from the model case of the MTPM with a bifurcation (see Eqs. (1.6.5) with Eq. (1.6.6)).

### 1.6.2.2 Initial performance level

To utilize Eqs. (1.6.8) or (1.6.5) one must be given the initial value \([p_0(t_0), u_0(t_0)]^T\) or \([q_0(t_0 + W_0), v_0(t_0 + W_0)]^T\), respectively. We can derive these initial values for any set of parameters as we did for the model case of Section 1.4.1.

Assuming stable baseline conditions, and assuming that we begin with performances predictions at the onset of wakefulness, we can use the equilibrium equation for the onset of wakefulness in Eq. (1.3.35). The initial values \([p_0(t_0), u_0(t_0)]^T\) for a particular amount of baseline wakefulness, \(W_b\), is:

\[
\begin{pmatrix}
  p_0(t_0) \\
  u_0(t_0)
\end{pmatrix}
= \left( I - \begin{bmatrix}
  x_3 e^{\lambda_3(T-W_b)} & x_4 e^{\lambda_4(T-W_b)} \\
  x_3 & x_4
\end{bmatrix}^{-1} \begin{bmatrix}
  x_1 e^{\lambda_1 W_b} & x_2 e^{\lambda_2 W_b} \\
  x_1 & x_2
\end{bmatrix} \right)^{-1} F
\]

\[
= \left( \begin{bmatrix}
  1 - e^{\sigma_{1,1} W_b} B_3 + x_{4,1} B_1 B_2 \\
  -e^{\sigma_{2,2} (T-W_b)} B_1
\end{bmatrix} x_{1,1} x_{2,1} e^{\sigma_{1,1} (T-W_b)} B_1 - x_{4,1} B_2 B_4
\right)^{-1}
\]

\[
\begin{pmatrix}
  e^{\sigma_{1,1} (T-W_b)} \\
  0
\end{pmatrix} \frac{\sigma_{1,2}}{\sigma_{2,2} - \sigma_{1,1}} \begin{bmatrix}
  e^{\sigma_{2,2} (T-W_b)} - e^{\sigma_{1,1} (T-W_b)} \\
  e^{\sigma_{2,2} (T-W_b)} - e^{\sigma_{1,1} (T-W_b)}
\end{bmatrix} \Omega(t_n + W_b)
\]

\[
+ \Theta(t_n + T) + \begin{pmatrix}
  \frac{\sigma_{1,2}}{\sigma_{2,2} - \sigma_{1,1}} \\
  1 - e^{\sigma_{2,2} (T-W_b)}
\end{pmatrix} \begin{bmatrix}
  e^{\sigma_{2,2} (T-W_b)} - e^{\sigma_{1,1} (T-W_b)} \\
  e^{\sigma_{2,2} (T-W_b)} - e^{\sigma_{1,1} (T-W_b)}
\end{bmatrix} \delta
\]

\quad (1.6.10)

where the \(B_i\)'s are given in Eqs. (1.4.43) through (1.4.46), and \(\Omega(t_n + W_b)\) and \(\Theta(t_n + 1)\) can be obtained using Eqs. (1.6.9) and (1.6.6), respectively.
Figure 1.33: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the parameters $\alpha_{1,1}$, $\alpha_{1,2}$ and $\alpha_{2,2}$ in Eqs. (1.4.31) and (1.4.32) for the case of the MTPM with feedback. Contour curves represent the 50% and 90% probability levels. The parameters are well defined by the data.

### 1.6.2.3 Parameter estimates and model predictions

Parameter estimates and predictions for the MTPM defined by Eqs. (1.4.31) and (1.4.32) can now be obtained. The results are shown in Figs. 1.33 through 1.41 and in Table 1.4.

<table>
<thead>
<tr>
<th>parameter</th>
<th>mean</th>
<th>standard error</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_{1,1}$</td>
<td>$-0.00096$</td>
<td>$0.0009$</td>
</tr>
<tr>
<td>$\alpha_{1,2}$</td>
<td>$0.00076$</td>
<td>$0.0003$</td>
</tr>
<tr>
<td>$\alpha_{2,1}$</td>
<td>$-0.24$</td>
<td>$0.03$</td>
</tr>
<tr>
<td>$\alpha_{2,2}$</td>
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<td>$0.006$</td>
</tr>
<tr>
<td>$\kappa$</td>
<td>$0.84$</td>
<td>$0.05$</td>
</tr>
<tr>
<td>$\phi$</td>
<td>$22$</td>
<td>$0.2$</td>
</tr>
<tr>
<td>$\sigma_{2,2}$</td>
<td>$-0.049$</td>
<td>$0.004$</td>
</tr>
<tr>
<td>$\delta$</td>
<td>$7.6$</td>
<td>$1$</td>
</tr>
<tr>
<td>$\mu$</td>
<td>$0.35$</td>
<td>$0.01$</td>
</tr>
</tbody>
</table>

Table 1.4: Parameter estimates and standard errors for the case of the MTPM with feedback described by Eqs. (1.4.31) and (1.4.32) using 676 data points from two laboratory sleep deprivation experiments (Belenky et al., 2003; Van Dongen et al., 2003).

The bifurcation for this particular model case is estimated at 20.8 h of wakefulness (i.e., 3.2 h of sleep). Let us again consider what happens to the equilibrium dynamics at the bifur-
Figure 1.34: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the parameters $\alpha_{1,1}$, $\alpha_{1,2}$, $\alpha_{2,1}$, and $\sigma_{2,2}$ in Eqs. (1.4.31) and (1.4.32) for the case of the MTPM with feedback. Contour curves represent the 50% and 90% probability levels. The parameters are well defined by the data.

Figure 1.35: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the parameters $\alpha_{1,1}$, $\alpha_{1,2}$, $\alpha_{2,1}$, and $\sigma_{2,2}$ in Eqs. (1.4.31) and (1.4.32) for the case of the MTPM with feedback. Contour curves represent the 50% and 90% probability levels. The parameters are well defined by the data.
Figure 1.36: Projections of MCMC chains are shown for the parameter pair \(\sigma_{11}\) and \(\sigma_{12}\) in Eq. (1.4.32) for the case of the MTPM with a bifurcation. Again, and as expected, we see a strong linear correlation between these two parameters.

Figure 1.37: Projections of MCMC chains and estimated boundaries of reliability regions are shown for the parameters \(\kappa, \phi, \delta,\) and \(\mu\) in Eqs. (1.4.31) and (1.4.32) for the case of the MTPM with feedback. Contour curves represent the 50% and 90% probability levels. As we expect, these parameters are well defined by the data and have near-Gaussian distributions.
cation point as the amount of wakefulness approaches $W_c$ from both directions. From the equilibrium state defined in Eqs. (1.3.35) and (1.3.36), and using the parameters in Table 1.4, we can see from Fig. 1.40 that the equilibrium point increases hyperbolically, tending to infinity as wakefulness is increased toward $W_c$ and decreases hyperbolically, tending to negative infinity as wakefulness is decreased toward $W_c$. However the equilibrium state remains negative as wakefulness approaches duration of a day.

Figure 1.38: Model predictions for the case of the MTPM with feedback for four laboratory sleep deprivation conditions (Van Dongen et al., 2003). The upper-left panel shows 16 days with 8 h TIB per day; the upper-right panel shows 14 days with 6 h TIB per day followed by 2 days with 8 h TIB per day; the lower-left panel shows 14 days with 4 h TIB per day followed by 2 days with 8 h TIB per day; and the lower-right panel shows total sleep deprivation for 88 h. Grey regions represent 90% confidence bands for the predicted means. Dots are grouped average PVT lapses data (Van Dongen et al., 2003).
Figure 1.39: Model predictions for the case of the MTPM with feedback for four laboratory sleep deprivation conditions (Belenky et al., 2003). The upper-left panel shows 7 days with 9 h TIB per day; the upper-right panel shows 7 days with 7 h TIB per day; the lower-left panel shows 7 days with 5 h TIB per day; and the lower-right panel shows 7 days with 3 h TIB per day. Each schedule is followed by 3 days with 8 h TIB per day. Grey regions represent 90% confidence bands for the predicted means. Dots are grouped average PVT lapse data (Belenky et al., 2003).
Figure 1.40: Plot showing states of equilibrium of performance level versus duration of wakefulness for the case of the MTPM with feedback. The figure shows the dynamics of the states of equilibrium for a continuous range of wakefulness durations: p (solid) and u (dashed). The vertical dotted line represents the bifurcation defined by the inequality of Eq. (1.4.47) where the equilibrium state vanishes. We see as wakefulness approaches $W_c$ from the left the equilibrium state increases hyperbolically toward infinity. As wakefulness approaches $W_c$ from the right side the equilibrium state decreases hyperbolically toward negative infinity. In this example, we see that the equilibrium state remains negative as wakefulness increases from the bifurcation toward the duration of a day, $T$.

Figure 1.41: Plot showing the magnitude of the eigenvalues $\Lambda_1$ and $\Lambda_2$ of Eq. (1.4.49) versus duration of wakefulness for the case of the MTPM with feedback. Here we see that one of the eigenvalues is nearly zero. The vertical dotted line represents the bifurcation defined by the inequality of Eq. (1.4.47) where the equilibrium state vanishes.
Chapter 2

Modeling Repeating Wake/Sleep Schedules

The analysis of the dynamics of the MTPM for constant, consolidated daily sleep durations revealed the presence of a qualitative change in model behavior which occurs at a specific duration of daily sleep. This so-called "bifurcation" reflected observations seen in laboratory studies (Van Dongen et al., 2003; McCauley et al., 2009a) of the neurobehavioral effects of total sleep deprivation and chronic sleep restriction. For the case of the MTPM discussed in Section 1.4.1, the bifurcation, defined by Eq. (1.4.19), was estimated to occur just under 4 hours time in bed. For chronic sleep restriction down to the bifurcation point we predicted that performance deficits increase but eventually stabilize, at a (suboptimal) state of equilibrium. For sleep restriction less than the bifurcation point, including total sleep deprivation, we predicted that performance deficits escalate, away from an unstable equilibrium.

These results completely described the behavior of the MTPM for fixed wake/sleep schedules across days of consolidated daily sleep. In real-life situations, wake/sleep schedules typically have daily sleep durations that vary from day to day, or in clusters of days. These types of schedules often repeat across several days or weeks, and may include days with severely restricted sleep opportunities followed by recovery days intended to restore performance to near-baseline levels. In this chapter, we examine the dynamics of the MTPM for such repeating schedules.
2.1 Analysis of the MTPM for repeating wake/sleep schedules

Here we reinvestigate the MTPM of Eqs. (1.3.23) and (1.3.24) for wake/sleep schedules that are repetitive across a constant number of days or weeks.

2.1.1 Initial values at wake onset and sleep onset

Recall that our analysis of the MTPM was constructed by deriving the iterative equations for the onset of wake and the onset of sleep (see Eqs. (1.3.25) and (1.3.26), respectively). For our analysis for repeating schedules that repeat every \(m\)th day, let us consider an analogous approach. Here, the iterative equations predicting every \(m\)th onset of wakefulness and every \(m\)th onset of sleep (see Appendix D.1) are written as follows:

\[
\begin{bmatrix}
    p_{n+m}(t_{n+m}) \\
    u_{n+m}(t_{n+m})
\end{bmatrix} = \prod_{k=1}^{m} \Phi_{n+m-k}(t_{n+m-k+1}) \Psi_{n+m-k}(t_{n+m-k} + W_{n+m-k}) \begin{bmatrix}
    p_{n}(t_{n}) \\
    u_{n}(t_{n})
\end{bmatrix} + \bar{F}_n,
\]

(2.1.1)

\[
\begin{bmatrix}
    q_{n+m}(t_{n+m} + W_{n+m}) \\
    v_{n+m}(t_{n+m} + W_{n+m})
\end{bmatrix} = \prod_{k=1}^{m} \Psi_{n+m-k+1}(t_{n+m-k+1} + W_{n+m-k+1}) \Phi_{n+m-k}(t_{n+m-k}) \begin{bmatrix}
    q_{n}(t_{n} + W_{n}) \\
    v_{n}(t_{n} + W_{n})
\end{bmatrix} + \bar{G}_n,
\]

(2.1.2)

where \(\bar{F}_n\) and \(\bar{G}_n\) are given in Eqs. (D.1-10) and (D.1-12), respectively. Here, the first day of each repeated cluster of days, starting with day \(n\), is \(n, n + m, n + 2m, \ldots\). The wake/sleep schedule across day 1 through day \(m\) repeat every \(m\) number of days.

Let us now investigate the existence of equilibrium points for the case in which length of day is constant (i.e., \(T_{n+m-k} = T\), typically 24 h) and by definition the duration of wakefulness for each \(m\)th day of the repeating schedule is constant (i.e., \(W_{n+m-k} = W_{m-k}\) where \(k = \{1 \ldots m\}\)). In this case, \(\Psi_{n+m-k}(t_{n+m-k} + W_{n+m-k}) = \Psi_{m-k}(t_{n+m-k} + W_{m-k})\) and \(\Phi_{n+m-k}(t_{n+m-k+1}) = \Phi_{m-k}(t_{n+m-k+1})\) are also constant across the repeated schedules (see Appendix C.1). Like before, we assume that \(\beta_i(t)\) and \(\gamma_i(t)\) are bounded, oscillatory functions, and that the circadian period \(\tau = T\); hence, \(\bar{F}_n = \bar{F}\) and \(\bar{G}_n = \bar{G}\) are constant as well (see Appendix C.2).
### 2.1.2 Model dynamics

Under conditions of fixed repeating schedules, states of equilibrium for Eqs. (2.1.1) and (2.1.2) can be derived, per Eqs. (1.3.28) and (1.3.29):

\[
\begin{bmatrix}
    p(t_{n+m}) \\
    u(t_{n+m})
\end{bmatrix}
= \left[ I - \prod_{k=1}^{m} \Phi_{m-k}(t_{n+m-k} + T) \Psi_{m-k}(t_{n+m-k} + W_{m-k}) \right]^{-1} \tilde{F},
\]

\[
\begin{bmatrix}
    q(t_{n+m} + W_{m}) \\
    v(t_{n+m} + W_{m})
\end{bmatrix}
= \left[ I - \prod_{k=1}^{m} \Psi_{m-k+1}(t_{n+m-k+1} + W_{m-k+1}) \Phi_{m-k}(t_{n+m-k} + T) \right]^{-1} \tilde{G},
\]

where \( I \) is the two-dimensional identity matrix and where we have used \( t_{n+m-k+1} = t_{n+m-k} + T \). Here, \([p(t_{n+m}), u(t_{n+m})]^T\) and \([q(t_{n+m} + W_{m}), v(t_{n+m} + W_{m})]^T\) represent the equilibrium state for the onset of wakefulness and for the onset of sleep every \( m \)th day, respectively. Examination of Eqs. (2.1.3) and (2.1.4) reveals that the existence of a state of equilibrium depends on the nonsingularity of:

\[
\begin{bmatrix}
    I - \prod_{k=1}^{m} \Phi_{m-k}(t_{n+m-k} + T) \Psi_{m-k}(t_{n+m-k} + W_{m-k}) \\
    I - \prod_{k=1}^{m} \Psi_{m-k+1}(t_{n+m-k+1} + W_{m-k+1}) \Phi_{m-k}(t_{n+m-k} + T)
\end{bmatrix},
\]

(see Appendix C.1). That is, a state of equilibrium across \( m \) days can only exist when:

\[
\det(I - \prod_{k=1}^{m} \Phi_{m-k}(t_{n+m-k} + T) \Psi_{m-k}(t_{n+m-k} + W_{m-k})) \neq 0, \quad \text{and}
\]

\[
\det(I - \prod_{k=1}^{m} \Psi_{m-k+1}(t_{n+m-k+1} + W_{m-k+1}) \Phi_{m-k}(t_{n+m-k} + T)) \neq 0.
\]

Recall that stability of equilibrium points for linear or nonlinear systems can be determined by linearization, which in the case of repeating schedules requires finding the Jacobian matrix, \( J \), of \([p_{n+m}(t_{n+m}), u_{n+m}(t_{n+m})]^T\) in Eq. (2.1.1) evaluated at the equilibrium point \([p(t_n), u(t_n)]^T\). Analogously, the Jacobian matrix can be derived for \([q_{n+m}(t_{n+m} + W_m), v_{n+m}(t_{n+m} + W_m)]^T\) in Eq. (2.1.2) evaluated at the equilibrium point \([q(t_n + W_m), v(t_n + W_m)]^T\). For the MTPM with fixed repeating schedules, the Jacobian matrices are explicitly written as:

\[
J_{p,u} = \prod_{k=1}^{m} \Phi_{m-k}(t_{n+m-k} + T) \Psi_{m-k}(t_{n+m-k} + W_{m-k}),
\]

\[
J_{q,v} = \prod_{k=1}^{m} \Psi_{m-k+1}(t_{n+m-k+1} + W_{m-k+1}) \Phi_{m-k}(t_{n+m-k} + T).
\]
The equilibrium points are asymptotically stable if the eigenvalues $\Lambda_i$ of the Jacobian matrix have magnitudes less than unity (Kelly and Peterson, 2001). Here the characteristic equations used to determine the eigenvalues are written as follows:

\[
\det \left( \prod_{k=1}^{m} \Phi_{m-k}(t_{n+m-k}+T) \Psi_{m-k}(t_{n+m-k}+W_{m-k}) - \Lambda I \right) = 0, \quad (2.1.11)
\]
\[
\det \left( \prod_{k=1}^{m} \Psi_{m-k+1}(t_{n+m-k+1}+W_{m-k+1}) \Phi_{m-k}(t_{n+m-k}+T) - \Lambda I \right) = 0. \quad (2.1.12)
\]

Notice that the matrix products in Eqs. (2.1.11) and (2.1.12) are of the form:

\[
\Phi_{m-1} \Psi_{m-1} \Phi_{m-2} \Psi_{m-2} \cdots \Phi_0 \Psi_0, \quad (2.1.13)
\]

and

\[
\Psi_m \Phi_{m-1} \Psi_{m-1} \Phi_{m-2} \cdots \Psi_1 \Phi_0, \quad (2.1.14)
\]

respectively. Since the wake/sleep schedule repeats every $m^{th}$ day, we readily notice that:

\[
\Psi_m = \Psi_0. \quad (2.1.15)
\]

Therefore, using Eq. (2.1.15) and the fact that eigenvalues of a shifted set of matrices (e.g., $ABC \to CAB$, where $A$, $B$ and $C$ are square matrices; see Appendix C.5) are the same, we see that the eigenvalues determined from Eqs. (2.1.11) and (2.1.12) and of the form of Eqs. (2.1.13) and (2.1.14) are also identical. This tells us that the equilibrium points $[p(t_{n+m}), u(t_{n+m})]^T$ and $[q(t_{n+m}+W_m), v(t_{n+m}+W_m)]^T$ are either both asymptotically stable or both unstable. We will now examine repetitive wake/sleep schedules in the MTPM for bifurcation properties.

### 2.2 A model case of the MTPM for repeating wake/sleep schedules and with a bifurcation

Let us consider the model case described in Section 1.4.1 for repeating wake/sleep schedules. Recall that this model case was constructed by setting the parameters $\alpha_{2,1}$ and $\sigma_{2,1}$ to zero into Eqs. (1.3.23) and (1.3.24). As before, we will impose the condition that $\alpha_{1,1} \neq \alpha_{2,2}$ and $\sigma_{1,1} \neq \sigma_{2,2}$. The real and distinct eigenvalues and eigenvectors are given in Eqs. (1.4.3) through (1.4.10).
2.2.1 Model case dynamics

Analogous to our derivation in Section 1.4.1, we can determine when a state of equilibrium exists for a repeating wake/sleep schedule. Per Eqs. (2.1.7) and (2.1.8) we have:

\[
\det \left( I - \prod_{k=1}^{m} \Phi_{m-k}(t_{n+m-k} + T) \Psi_{m-k}(t_{n+m-k} + W_{m-k}) \right) 
= \det \left( \begin{bmatrix}
1 - \prod_{k=1}^{m} e^{\alpha_{1,1} W_{m-k} e^{\sigma_{1,1}(T-W_{m-k})}} & h_1 \\
0 & 1 - \prod_{k=1}^{m} e^{\alpha_{2,1} W_{m-k} e^{\sigma_{2,1}(T-W_{m-k})}} 
\end{bmatrix} \right),
\]

(2.2.1)

\[
\det \left( I - \prod_{k=1}^{m} \Psi_{m-k+1}(t_{n+m-k+1} + W_{m-k+1}) \Phi_{m-k}(t_{n+m-k} + W_{m-k}) \right) 
= \det \left( \begin{bmatrix}
1 - \prod_{k=1}^{m} e^{\alpha_{1,1}(T-W_{m-k}) e^{\sigma_{1,1} W_{m-k}}} & h_2 \\
0 & 1 - \prod_{k=1}^{m} e^{\alpha_{2,1} W_{m-k} e^{\sigma_{2,2}(T-W_{m-k})}} 
\end{bmatrix} \right),
\]

(2.2.2)

where

\[
h_1 = \sum_{j=1}^{m} \left( \left( \prod_{k=1}^{j} e^{\alpha_{1,1} W_k e^{\sigma_{1,1}(T-W_k)}} \right) h_{1,k} \left( \prod_{k=j+1}^{m} e^{\alpha_{2,2} W_k e^{\sigma_{2,2}(T-W_k)}} \right) \right),
\]

(2.2.3)

\[
h_2 = \sum_{j=1}^{m} \left( \left( \prod_{k=1}^{j} e^{\sigma_{1,1}(T-W_k) e^{\alpha_{1,1} W_k}} \right) h_{2,k} \left( \prod_{k=j+1}^{m} e^{\alpha_{2,1} W_k e^{\sigma_{2,1}(T-W_k)}} \right) \right),
\]

(2.2.4)

with

\[
h_{1,k} = \frac{\sigma_{1,2}}{\sigma_{1,1} - \sigma_{2,2}} \left( e^{\sigma_{1,1}(T-W_k) e^{\sigma_{2,2}(T-W_k)}} - e^{\sigma_{2,2}(T-W_k)} \right) e^{\alpha_{2,2} W_k}
+ \frac{\alpha_{1,2}}{\alpha_{1,1} - \alpha_{2,2}} \left( e^{\alpha_{1,1} W_k e^{\sigma_{2,2}(T-W_k)}} - e^{\sigma_{2,1}(T-W_k)} \right),
\]

(2.2.5)

\[
h_{2,k} = \frac{\sigma_{1,2}}{\sigma_{1,1} - \sigma_{2,2}} \left( e^{\sigma_{1,1}(T-W_k) e^{\alpha_{1,1} W_k}} - e^{\sigma_{2,2}(T-W_k)} \right) e^{\sigma_{1,1} W_k}
+ \frac{\alpha_{1,2}}{\alpha_{1,1} - \alpha_{2,2}} \left( e^{\alpha_{1,1} W_k e^{\sigma_{2,2}(T-W_k)}} - e^{\sigma_{2,2}(T-W_k)} \right),
\]

(2.2.6)

(see Appendix D.2). Eqs. (2.2.1) and (2.2.2) are equivalent (see Appendix C.6 for a proof), and imply that fixed points exist for:

\[
(1 - e^{\sigma_{1,1}(mT - \sum_{k=1}^{m} W_k) e^{\sigma_{1,1} \sum_{k=1}^{m} W_k}})(1 - e^{\sigma_{2,2}(mT - \sum_{k=1}^{m} W_k) e^{\alpha_{1,1} \sum_{k=1}^{m} W_k}}) \neq 0.
\]

(2.2.7)
We see that when all parameters are negative, Eq. (2.2.7) is always satisfied, since
\[ 0 < (1 - e^{\sigma_{1,1} (mT - \sum_{k=1}^{m} W_k)} e^{\sigma_{1,1} \sum_{k=1}^{m} W_k}) (1 - e^{\sigma_{2,2} (mT - \sum_{k=1}^{m} W_k)} e^{\sigma_{2,2} \sum_{k=1}^{m} W_k}) < 1, \] (2.2.8)for all \( T, W_k; 0 < W_k \leq T \). This means that for the case with strictly negative parameters, fixed points exist for all daily sleep durations including total sleep deprivation. However, by relaxing the condition that all parameters are negative, we may produce a situation as in Section 1.4.1 where Eq. (2.2.7) does not hold.

To derive conditions necessary for a bifurcation to occur let us assume, as we did before, that the parameters \( \alpha_{1,1}, \sigma_{1,1} \) and \( \sigma_{2,2} \) are negative, and the parameter \( \alpha_{2,2} \) is positive. For this case, the requirement for the existence of a state of equilibrium, Eq. (2.2.7), is not always satisfied. Analogous to what we did in Section 1.4.1 we examine the product \( e^{\sigma_{2,2} (mT - \sum_{k=1}^{m} W_k)} e^{\sigma_{2,2} \sum_{k=1}^{m} W_k} \) in Eq. (2.2.7). Here, \( e^{\sigma_{2,2} (mT - \sum_{k=1}^{m} W_k)} < 1 \), while \( e^{\sigma_{2,2} \sum_{k=1}^{m} W_k} > 1 \). This means that for a particular combination of \( \sigma_{2,2} \) and \( \alpha_{2,2} \), and by varying the total amount of wakefulness \( \sum_{k=1}^{m} W_k \) that has accumulated through the repeating wake/sleep schedule, this product may change from \( e^{\sigma_{2,2} (mT - \sum_{k=1}^{m} W_k)} e^{\sigma_{2,2} \sum_{k=1}^{m} W_k} < 1 \) to \( e^{\sigma_{2,2} (mT - \sum_{k=1}^{m} W_k)} e^{\sigma_{2,2} \sum_{k=1}^{m} W_k} > 1 \), where at unity the equilibrium point vanishes.

To determine stability of the equilibrium points when they exist, we solve either Eq. (2.1.11) or Eq. (2.1.12) for eigenvalues of the coefficient matrices of the iterative system of Eqs. (2.1.1) and (2.1.2). We find:
\[ \Lambda_1 = e^{\sigma_{1,1} (mT - \sum_{k=1}^{m} W_k)} e^{\sigma_{1,1} \sum_{k=1}^{m} W_k}, \] (2.2.9)
\[ \Lambda_2 = e^{\sigma_{2,2} (mT - \sum_{k=1}^{m} W_k)} e^{\sigma_{2,2} \sum_{k=1}^{m} W_k}. \] (2.2.10)
In the case when \( \alpha_{2,2} \) is positive, there are again three possibilities for \( \Lambda_2 \) for each \( 0 < \Lambda_1 < 1 \). For \( \Lambda_2 < 1 \), the system has a stable equilibrium state. For \( \Lambda_2 > 1 \), there is also an equilibrium state, but it is unstable. For \( \Lambda_2 = 1 \), the equilibrium point disappears altogether (substitution of Eq. (2.2.10) into Eq. (2.2.7)).

We can see that by changing the total amount of sleep accumulated through the \( m \) days of the wake/sleep schedule, \( mT - \sum_{k=1}^{m} W_k \), a bifurcation can occur where the system dynamics change qualitatively across repeated \( m \)-day schedules, that is, from a stable condition (performance level referenced at each \( i \)th day tends exponentially toward a fixed asymptote), to a condition with no equilibrium point, to an unstable condition (performance level referenced at each \( i \)th day tends exponentially away from a fixed asymptote). This result is distinct from the analysis of Section 1.4.1 in that it shows that a repeating
wake/sleep schedule can have unstable segments (see Fig. 2.1), while the schedule across
days or weeks as a whole is stable.

Similar to the critical wakefulness formula of Eq. (1.4.19), we can determine the rela-
tionship between $\alpha_{2,2}$ and $\sigma_{2,2}$ by setting $\Lambda_2$ to unity in Eq. (2.2.10) and derive a formula
for the critical amount of accumulated daily wakefulness beyond which asymptotic stability
is no longer achieved:

$$\left( \sum_{k=1}^{m} W_k \right)_{c} = \frac{-\sigma_{2,2}}{\alpha_{2,2} - \sigma_{2,2}} m T,$$  \hspace{1cm} (2.2.11)

for all $T, W_k : 0 < (\sum_{k=1}^{m} W_k)_{c} \leq T$. This expression can also be written in the form:

$$\bar{W}_c = \frac{-\sigma_{2,2}}{\alpha_{2,2} - \sigma_{2,2}} T,$$  \hspace{1cm} (2.2.12)

or

$$\frac{\bar{W}_c}{T - \bar{W}_c} = \frac{-\sigma_{2,2}}{\alpha_{2,2}},$$  \hspace{1cm} (2.2.13)

where

$$\bar{W}_c = \frac{\left( \sum_{k=1}^{m} W_k \right)_{c}}{m}$$  \hspace{1cm} (2.2.14)

is the average daily wakefulness across the $m$ days. Here, Eq. (2.2.13) reveals that whether
or not bifurcation occurs is a function of the ratio of the average daily wakefulness, $\bar{W}_c$, to the average daily sleep, $T - \bar{W}_c$, during the repeating wake/sleep schedule. If this ratio
of average daily wakefulness to average daily sleep falls below the critical ratio of Eq. (2.2.13), then the model predicts exponential convergence to a fixed asymptote. If the ratio
of average daily wakefulness to average daily sleep exceeds the critical ratio, the model
predicts divergence away from a fixed asymptote. Both convergence and divergence occur
at the rate specified by the matrix products described in Eq. (2.1.13).

Fig. 2.1 shows three examples of 7-day schedules repeated 3 times. The schedule with
2 h TIB for the first five days (diamonds) appears to diverge both across the first five days
daily TIB is less than the predicted bifurcation point of $T - \bar{W}_c = 3.8$ h TIB, where we
have used the published parameters in McCauley et al. (2009a)) and across the entire 7-day schedule (the average daily TIB for the whole repeating schedule (i.e., $T - \bar{W} = 3.71$ h) is
less than the bifurcation point defined in Eq. (2.2.11)). The schedule with 3 h TIB (squares)
also appears to diverge across the first five days of the schedule. However this schedule, as
a whole, converges to a state of equilibrium defined by Eq. (2.1.3) ($m = 7$). This is because
average daily TIB across the whole 7-day schedule (i.e., $T - \bar{W} = 4.42$ h) is greater than
Figure 2.1: Plot showing performance predictions for three repeating schedules using the case of the MTPM with a bifurcation, Eqs. (1.3.15) through (1.3.20). The figure shows three different repeating schedules each of which repeats 3 times every \( m = 7 \) days \( (n \in \{0, \ldots, 20\}) \). Each day has constant duration \( T = 24 \) h. The schedules are as follows: sleep restriction days one through five have 2 h TIB (diamonds), 3 h TIB (squares) and 6 h TIB (circles) and recovery days six and seven have 8 h TIB. The average amount of daily wakefulness across the three repeating schedules is: \( T - \bar{W} = 3.71 \) h, 4.42 h, and 6.57 h, respectively. The circadian process is assumed to have the same period as the length of day, \( \tau = 24 \) h and wakefulness begins at 07:30 each day. Parameters used are those published in McCauley et al. (2009a). Solid lines are performance predictions within days. The nominal predictions during sleep are not shown as to reduce clutter.

The schedule with 6 h TIB for the first five days converges for all individual days and across the entire schedule.
Chapter 3

Modeling Split Sleep Schedules

In many operational settings, splits sleep schedules (i.e., multiple sleep episodes in a day) are common, and optimal scheduling (timing and duration) of split sleep is important to minimize fatigue and maintain performance, productivity and safety. Here we investigate the dynamics of the MTPM of Eqs. (1.3.23) and (1.3.24) for split sleep scenarios.

3.1 Extending the MTPM for split sleep schedules

The framework of the MTPM can be extended to track homeostatic and circadian influences for any set of nocturnal or diurnal wake/sleep episodes. Let us rewrite the general class of linear nonhomogeneous first-order ODEs, Eqs. (1.3.23) and (1.3.24), for any set of daily wake/sleep episodes (see Fig. 3.1):

\[
\begin{bmatrix}
\dot{p}_{n,k_n} \\
\dot{u}_{n,k_n}
\end{bmatrix} =
\begin{bmatrix}
\alpha_{1,1} & \alpha_{1,2} \\
\alpha_{2,1} & \alpha_{2,2}
\end{bmatrix}
\begin{bmatrix}
p_{n,k_n} \\
u_{n,k_n}
\end{bmatrix}
+ \begin{bmatrix}
\beta_1(t) \\
\beta_2(t)
\end{bmatrix}, \quad \text{for } t \in [t_{n,k_n}, t_{n,k_n} + W_{n,k_n}],
\]

(3.1.1)

\[
\begin{bmatrix}
\dot{q}_{n,k_n} \\
\dot{v}_{n,k_n}
\end{bmatrix} =
\begin{bmatrix}
\sigma_{1,1} & \sigma_{1,2} \\
\sigma_{2,1} & \sigma_{2,2}
\end{bmatrix}
\begin{bmatrix}
q_{n,k_n} \\
v_{n,k_n}
\end{bmatrix}
+ \begin{bmatrix}
\gamma_1(t) \\
\gamma_2(t)
\end{bmatrix}, \quad \text{for } t \in [t_{n,k_n} + W_{n,k_n}, t_{n,k_n+1}],
\]

(3.1.2)

where \(k_n = 0, 1, 2, \ldots, k_n^*\) specify the wake/sleep episodes within the \(n^{\text{th}}\) day. As before, \(\alpha_{i,j}\) and \(\sigma_{i,j}\) are constant parameters, \(\beta_i(t)\), and \(\gamma_i(t)\) are time-dependent nonhomogeneities, and the initial conditions, \([p_{0,0}(t_{0,0}), u_{0,0}(t_{0,0})]^T\), are assumed to be given. Coupling within days from a wake episode to a sleep episode, and from a sleep episode to a wake episode is determined by:

\[
\begin{bmatrix}
q_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \\
v_{n,k_n}(t_{n,k_n} + W_{n,k_n})
\end{bmatrix} = \begin{bmatrix}
p_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \\
u_{n,k_n}(t_{n,k_n} + W_{n,k_n}) - \delta
\end{bmatrix},
\]

(3.1.3)
Figure 3.1: Plot showing an example of linking multiple daily wake/sleep episodes with the new model formulation, Eqs. (3.1.1) and (3.1.2). The figure shows three days \((n = 0, 1, 2)\). Each day is 24 h in duration. The first two days each have two wake/sleep episodes, i.e., one diurnal and one nocturnal \((k = 0, 1)\). The third day has three wake/sleep episodes \((k = 0, 1, 2)\). Performance is modeled as \(p(t)\) during wakefulness (solid curves) and \(q(t)\) during sleep (dotted curves). The predictions during sleep (gray areas) are virtual and as we have assumed before would only be meaningful if the sleeping person were woken up to probe performance (and no sleep inertia occurred). The dashed vertical lines show the transition points from sleep to wakefulness across days, where \(q_{n,k} (t_{n,k} + T_{n,k})\) and \(p_{n+1,0}(t_{n+1,0})\) are linked per Eq. (3.1.5). The dash-dotted vertical lines show the transition points from wakefulness to sleep within days, where \(p_{n,k}(t_{n,k} + W_{n,k})\) and \(q_{n,k}(t_{n,k} + W_{n,k})\) are linked per Eq. (3.1.3) and the dotted vertical lines show the transition from sleep to wakefulness within days, where \(q_{n-1,k}(t_{n-1,k} + W_{n-1,k})\) and \(p_{n,k}(t_{n,k} + W_{n,k})\) are linked per Eq. (3.1.4).

\[
\begin{bmatrix}
    p_{n,k} (t_{n,k}) \\
    u_{n,k} (t_{n,k})
\end{bmatrix}
= \begin{bmatrix}
    q_{n,k-1}(t_{n,k-1} + T_{n,k-1}) \\
    v_{n,k-1}(t_{n,k-1} + T_{n,k-1}) + \delta
\end{bmatrix}.
\]  

(3.1.4)
where the parameter $\delta$ is a free parameter. Coupling across days (i.e., when $k_n = k_n^*$ which specifies the last wake/sleep episode of the $n^{th}$ day) is given by:

\[
\begin{bmatrix}
q_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*}) \\
v_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})
\end{bmatrix} =
\begin{bmatrix}
p_{n+1,0}(t_{n+1,0}) \\
u_{n+1,0}(t_{n+1,0}) - \delta
\end{bmatrix}.
\]

(3.1.5)

### 3.1.1 Initial values at wake onset and sleep onset

To understand how the model predicts trends across days and weeks, we extend the idea used in our analyses of the MTPM, where we utilized the onset of wakefulness and the onset of sleep as anchor points. Without loss of generality, let us focus on the equations for the initial values of wake and sleep onsets for the first (i.e., $0^{th}$) wake/sleep episode of each day. We will then focus on these predicted initial values of wake onset $p_{n,0}(t_{n,0})$ and $u_{n,0}(t_{n,0})$, and sleep onset, $q_{n,0}(t_{n,0} + W_{n,0})$ and $v_{n,0}(t_{n,0} + W_{n,0})$ and predict their dynamics across days. Our derivation is analogous to that of the generalized model of Eqs. (1.3.23) (see Appendix E.1). The result is:

\[
\begin{bmatrix}
p_{n+1,0}(t_{n+1,0}) \\
u_{n+1,0}(t_{n+1,0})
\end{bmatrix} = \prod_{k_n=0}^{k_n^*} \Phi_{n,k_n}(t_{n,k_n} + T_{n,k_n}) \Psi_{n,k_n} \left( t_{n,k_n} + W_{n,k_n} \right) \begin{bmatrix}
p_{n,0}(t_{n,0}) \\
u_{n,0}(t_{n,0})
\end{bmatrix} + \tilde{F}_{n,0}.
\]

(3.1.6)

\[
\begin{bmatrix}
q_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \\
v_{n+1,0}(t_{n+1,0} + W_{n+1,0})
\end{bmatrix} = \prod_{k_n=0}^{k_n^*} \Psi_{n,k_n+1}(t_{n,k_n+1} + W_{n,k_n+1}) \Phi_{n,k_n} \left( t_{n,k_n} + T_{n,k_n} \right) \begin{bmatrix}
q_{n,0}(t_{n,0} + W_{n,0}) \\
v_{n,0}(t_{n,0} + W_{n,0})
\end{bmatrix} + \tilde{G}_{n,0}.
\]

(3.1.7)

for all $T_{n,k_n}, W_{n,k_n}: 0 < W_{n,k_n} \leq T_{n,k_n}$ and $n \in \{0, 1, 2, \ldots \}$ given $[p_{0,0}(t_{0,0}), u_{0,0}(t_{0,0})]^T$. Here the two-dimensional matrices $\Phi_{n,k_n}$ and $\Psi_{n,k_n}$ are explicitly given in Appendix C.1, Eqs. (C.1-5) and (C.1-6), and $\tilde{F}_{n,0}$ and $\tilde{G}_{n,0}$ in Appendix E.1, Eqs. (E.1-12) and (E.1-17), respectively. Note that $[q_{0,0}(t_{0,0} + W_{0,0}), v_{0,0}(t_{0,0} + W_{0,0})]^T$ can be formulated in terms of the initial values $[p_{0,0}(t_{0,0}), u_{0,0}(t_{0,0})]^T$ by using Eqs. (3.1.3) and (E.1-1):

\[
\begin{bmatrix}
q_{0,0}(t_{0,0} + W_{0,0}) \\
v_{0,0}(t_{0,0} + W_{0,0})
\end{bmatrix} = \Psi_{0,0}(t_{0,0} + W_{0,0}) \begin{bmatrix}
p_{0,0}(t_{0,0}) \\
u_{0,0}(t_{0,0})
\end{bmatrix} + \Omega_{0,0}(t_{0,0} + W_{0,0}) - \begin{bmatrix}
0 \\
\delta
\end{bmatrix},
\]

(3.1.8)

where $\Omega_{0,0}(t_{0,0} + W_{0,0})$ can be derived from Eq. (E.1-2).
3.1.2 Model dynamics

Analogous to the MTPM in Section 1.3, Eqs. (3.1.6) and (3.1.7) have states of equilibrium when:

\[
\begin{bmatrix}
    p_{n+m,k_n+m}(t_{n+m,k_n+m}) \\
    u_{n+m,k_n+m}(t_{n+m,k_n+m}) \\
    q_{n+m,k_n+m}(t_{n+m,k_n+m}+W_{k_n+m}) \\
    v_{n+m,k_n+m}(t_{n+m,k_n+m}+W_{k_n+m})
\end{bmatrix} =
\begin{bmatrix}
    p_{n,k_n}(t_{n,k_n}) \\
    u_{n,k_n}(t_{n,k_n}) \\
    q_{n,k_n}(t_{n,k_n}+W_{k_n}) \\
    v_{n,k_n}(t_{n,k_n}+W_{k_n})
\end{bmatrix},
\]

(3.1.9)

\[
\begin{bmatrix}
    p_{n+1,k}(t_{n+1,k}) \\
    u_{n+1,k}(t_{n+1,k}) \\
    q_{n+1,k}(t_{n+1,k}+W_k) \\
    v_{n+1,k}(t_{n+1,k}+W_k)
\end{bmatrix} =
\begin{bmatrix}
    p_{n,k}(t_{n,k}) \\
    u_{n,k}(t_{n,k}) \\
    q_{n,k}(t_{n,k}+W_k) \\
    v_{n,k}(t_{n,k}+W_k)
\end{bmatrix},
\]

(3.1.10)

where \( m = 1, 2, \ldots \). To investigate the existence of a state of equilibrium for the MTPM with our extended notation, let’s consider fixed daily wake/sleep schedules in which \( k_n = k \) \((k \in \{0, 1, 2, \ldots , k^*\})\), and \( T_{n,k_n} = T_k \) and \( W_{n,k_n} = W_k \) are constant. In this case, \( \Psi_{n,k_n}(t_{n,k_n}+W_{n,k_n}) = \Psi_k(t_{n,k_n}+W_k) \) and \( \Phi_{n,k_n}(t_{n+1,k}) = \Phi_k(t_{n,k_n}+T_k) \) are also constant (see Appendix C.1). As before we assume that \( \beta_i(t) \) and \( \gamma_i(t) \) are bounded, oscillatory functions, and that the circadian period \( \tau = T_k \); hence, \( \tilde{F}_{n,k_n} = \tilde{F}_k \) and \( \tilde{G}_{n,k_n} = \tilde{G}_k \) are constant as well (see Appendix E.1). States of equilibrium are derived by solving Eqs. (3.1.6) and (3.1.7) for \( p(t_{n,k_n}), u(t_{n,k_n}), q(t_{n,k_n}+W_k) \) and \( v(t_{n,k_n}+W_k) \) by setting:

\[
\begin{align*}
p_{n+1,k}(t_{n+1,k}) &= p_{n,k}(t_{n,k}) = p(t_{n,k}), \\
u_{n+1,k}(t_{n+1,k}) &= u_{n,k}(t_{n,k}) = u(t_{n,k}), \\
q_{n+1,k}(t_{n+1,k}+W_k) &= q_{n,k}(t_{n,k}+W_k) = q(t_{n,k}+W_k), \quad \text{and} \\
v_{n+1,k}(t_{n+1,k}+W_k) &= v_{n,k}(t_{n,k}+W_k) = v(t_{n,k}+W_k).
\end{align*}
\]

This results in:

\[
\begin{bmatrix}
    p(t_{n,0}) \\
    u(t_{n,0})
\end{bmatrix} =
\begin{bmatrix}
    I - \prod_{k=0}^{k^*} \Phi_k(t_{n,k}+T_k) \Psi_k(t_{n,k}+W_k)
\end{bmatrix}^{-1} \tilde{F}_0,
\]

(3.1.11)

\[
\begin{bmatrix}
    q(t_{n,0}+W_0) \\
    v(t_{n,0}+W_0)
\end{bmatrix} =
\begin{bmatrix}
    I - \prod_{k=0}^{k^*} \Psi_{k+1}(t_{n,k+1}+W_{k+1}) \Phi_k(t_{n,k}+T_k)
\end{bmatrix}^{-1} \tilde{G}_0,
\]

(3.1.12)

where \( I \) is the two-dimensional identity matrix. Here, \([p(t_{n,0}), u(t_{n,0})]^T\) is the equilibrium point for the onset of wakefulness and \([q(t_{n,0}+W_0), v(t_{n,0}+W_0)]^T\) is the equilibrium point for the onset of sleep for the first wake/sleep episode of the day. Examination of Eqs.

\[\text{In Chapter 2 we analyzed the MTPM for repeating schedules. With little effort that analysis can be used in conjunction with our extended notation to include repeating schedules with multiple daily wake/sleep episodes. An example is shown in Fig. 3.2.}\]
(3.1.11) and (3.1.12) reveals that the existence of a state of equilibrium depends on the nonsingularity of

\[
I - \prod_{k=0}^{k^*} \Phi_k(t_{n,k} + T_k) \Psi_k(t_{n,k} + W_k), \quad \text{and} \quad \tag{3.1.13}
\]

\[
I - \prod_{k=0}^{k^*} \Psi_{k+1}(t_{n,k+1} + W_{k+1}) \Phi_k(t_{n,k} + T_k), \quad \tag{3.1.14}
\]

respectively (see Appendix C.1). That is, an equilibrium can only exist when:

\[
\det \left( I - \prod_{k=0}^{k^*} \Phi_k(t_{n,k} + T_k) \Psi_k(t_{n,k} + W_k) \right) \neq 0, \quad \text{and} \quad \tag{3.1.15}
\]

\[
\det \left( I - \prod_{k=0}^{k^*} \Psi_{k+1}(t_{n,k+1} + W_{k+1}) \Phi_k(t_{n,k} + T_k) \right) \neq 0. \quad \tag{3.1.16}
\]

We determine stability by finding the Jacobian matrices, \( J \), of \( [p_{n+1,0}, u_{n+1,0}]^T \) in Eq. (3.1.6) evaluated at the equilibrium point \( [p(t_{n,0}), u(t_{n,0})]^T \), and \( [q_{n+1,0}, v_{n+1,0}]^T \) in Eq. (3.1.7) evaluated at the equilibrium point \( [q(t_{n,0} + W_0), v(t_{n,0} + W_0)]^T \). For the MTPM with constant split sleep schedules the Jacobian matrices are explicitly given by:

\[
J_{p,u} = \prod_{k=0}^{k^*} \Phi_k(t_{n,k} + T_k) \Psi_k(t_{n,k} + W_k), \quad \tag{3.1.17}
\]

\[
J_{q,v} = \prod_{k=0}^{k^*} \Psi_{k+1}(t_{n,k+1} + W_{k+1}) \Phi_k(t_{n,k} + T_k). \quad \tag{3.1.18}
\]

The equilibrium points are asymptotically stable if all eigenvalues \( \Lambda_j \) of the Jacobian matrix have magnitudes less than one (Kelly and Peterson, 2001). The characteristic equations used to determine the eigenvalues are written as follows:

\[
\det \left( \prod_{k=0}^{k^*} \Phi_k(t_{n,k} + T_k) \Psi_k(t_{n,k} + W_k) - \Lambda I \right) = 0, \quad \tag{3.1.19}
\]

\[
\det \left( \prod_{k=0}^{k^*} \Psi_{k+1}(t_{n,k+1} + W_{k+1}) \Phi_k(t_{n,k} + T_k) - \Lambda I \right) = 0. \quad \tag{3.1.20}
\]

The matrix products in Eqs. (3.1.17) and (3.1.18) are of the form:

\[
\Phi_{k^*} \Psi_{k^*} \Phi_{k^* - 1} \Psi_{k^* - 1} \ldots \Phi_0 \Psi_0, \quad \tag{3.1.21}
\]

and

\[
\Psi_{k^* + 1} \Phi_k \Psi_{k^*} \Phi_{k^* - 1} \ldots \Psi_1 \Phi_0, \quad \tag{3.1.22}
\]

91
respectively. Since the wake/sleep episodes repeat every day, we notice that:

\[ \Psi_{k^* + 1} = \Psi_0. \tag{3.1.23} \]

Therefore, using Eq. (3.1.23) and the fact that eigenvalues of a shifted set of matrices (e.g., \( ABC \rightarrow CAB \), where \( A, B \) and \( C \) are square matrices; see Appendix C.5) are the same, we can see that the eigenvalues determined from Eqs. (3.1.19) and (3.1.20) and of the form of Eqs. (3.1.21) and (3.1.22) are also identical. This tells us that the equilibrium points can see that the eigenvalues determined from Eqs. (3.1.19) and (3.1.20) and of the form \( E(t_{n,0}) \) are either both asymptotically stable or both unstable. We will now examine the MTPM with the extended notation to include multiple daily wake/sleep episodes for bifurcation properties in a similar manner as we did for the case of the MTPM of Eqs. (1.4.1) and (1.4.2).

### 3.2 A model case of the MTPM for split sleep schedules and with a bifurcation

The model case of the MTPM with a bifurcation, discussed in Section 1.4.1, can be rewritten with notation that incorporates multiple wake/sleep episodes per day:

\[
\begin{bmatrix}
\dot{p}_{n,k} \\
\dot{u}_{n,k}
\end{bmatrix} = \begin{bmatrix}
\alpha_{1,1} & \alpha_{1,2} \\
0 & \alpha_{2,2}
\end{bmatrix} \begin{bmatrix}
p_{n,k} \\
u_{n,k}
\end{bmatrix} + \begin{bmatrix}
\beta_1(t) \\
\beta_2(t)
\end{bmatrix}, \quad \text{for } t \in [t_{n,k}, t_{n,k} + W_{n,k}],
\tag{3.2.1}
\]

\[
\begin{bmatrix}
\dot{q}_{n,k} \\
\dot{v}_{n,k}
\end{bmatrix} = \begin{bmatrix}
\sigma_{1,1} & \sigma_{1,2} \\
0 & \sigma_{2,2}
\end{bmatrix} \begin{bmatrix}
q_{n,k} \\
v_{n,k}
\end{bmatrix} + \begin{bmatrix}
\gamma_1(t) \\
\gamma_2(t)
\end{bmatrix}, \quad \text{for } t \in [t_{n,k} + W_{n,k}, t_{n,k} + 1],
\tag{3.2.2}
\]

where we impose the condition that \( \alpha_{1,1} \neq \alpha_{2,2} \) and \( \sigma_{1,1} \neq \sigma_{2,2} \). The real and distinct eigenvalues and eigenvectors are given in Eqs. (1.4.3) through (1.4.10).

#### 3.2.1 Model case dynamics

We can now investigate the dynamics of this extended model and determine when equilibrium points exist. Per Eqs. (3.1.15) and (3.1.16) we have:

\[
\det \left( I - \prod_{k=0}^{k^*} \Phi_k(t_{n,k} + T_k) \Psi_k(t_{n,k} + W_k) \right) = \det \left( \begin{bmatrix}
1 - \prod_{k=0}^{k^*} e^{\alpha_{1,1} W_k e^{\sigma_{1,1} (T_k - W_k)}} & h_1 \\
0 & 1 - \prod_{k=0}^{k^*} e^{\alpha_{2,2} W_k e^{\sigma_{2,2} (T_k - W_k)}}
\end{bmatrix} \right) 
= \det \left( \begin{bmatrix}
1 - e^{\alpha_{1,1} \sum_{k=0}^{k^*} W_k e^{\sigma_{1,1} (T - \sum_{k=0}^{k^*} W_k)}} & h_1 \\
0 & 1 - e^{\alpha_{2,2} \sum_{k=0}^{k^*} W_k e^{\sigma_{2,2} (T - \sum_{k=0}^{k^*} W_k)}}
\end{bmatrix} \right),
\tag{3.2.3}
\]

92
and

\[
\det \left( I - \prod_{k=0}^{k^*} \Psi_{k+1}(t_{n,k+1} + W_{k+1}) \Phi_k(t_{n,k} + T_k) \right)
\]

\[
= \det \left( \begin{bmatrix}
1 - \prod_{k=0}^{k^*} e^{\sigma_{1,1}(T_k - W_k)} e^{\alpha_{1,1} W_k} & h_2 \\
0 & 1 - \prod_{k=0}^{k^*} e^{\sigma_{2,2}(T_k - W_k)} e^{\alpha_{2,2} W_k}
\end{bmatrix} \right)
\]

\[
= \det \left( \begin{bmatrix}
1 - e^{\sigma_{1,1} \left( T - \sum_{k=0}^{k^*} W_k \right)} e^{\alpha_{1,1} \sum_{k=0}^{k^*} W_k} & h_2 \\
0 & 1 - e^{\sigma_{2,2} \left( T - \sum_{k=0}^{k^*} W_k \right)} e^{\alpha_{2,2} \sum_{k=0}^{k^*} W_k}
\end{bmatrix} \right),
\]

(3.2.4)

where we have used \( \sum_{k=0}^{k^*} T_k = T \) which is constant and where

\[
h_1 = e^{\alpha_{2,2} \sum_{k=0}^{k^*} W_k} h_{1,1} + e^{\sigma_{1,1} \left( T - \sum_{k=0}^{k^*} W_k \right)} h_{1,2},
\]

(3.2.5)

\[
h_2 = e^{\alpha_{1,1} \sum_{k=0}^{k^*} W_k} h_{1,1} + e^{\sigma_{2,2} \left( T - \sum_{k=0}^{k^*} W_k \right)} h_{1,2},
\]

(3.2.6)

with

\[
h_{1,1} = \frac{\sigma_{1,2}}{\sigma_{1,1} - \sigma_{2,2}} \left( e^{\sigma_{1,1} \left( T - \sum_{k=0}^{k^*} W_k \right)} - e^{\sigma_{2,2} \left( T - \sum_{k=0}^{k^*} W_k \right)} \right),
\]

(3.2.7)

\[
h_{1,2} = \frac{\alpha_{1,2}}{\alpha_{1,1} - \alpha_{2,2}} \left( e^{\alpha_{1,1} \sum_{k=0}^{k^*} W_k} - e^{\alpha_{2,2} \sum_{k=0}^{k^*} W_k} \right),
\]

(3.2.8)

Eqs. (3.2.3) and (3.2.4) are equivalent (see Appendix C.6 for a proof), and imply that equilibrium points exist for:

\[
(1 - e^{\sigma_{1,1} \left( T - \sum_{k=0}^{k^*} W_k \right)} e^{\alpha_{1,1} \sum_{k=0}^{k^*} W_k}) (1 - e^{\sigma_{2,2} \left( T - \sum_{k=0}^{k^*} W_k \right)} e^{\alpha_{2,2} \sum_{k=0}^{k^*} W_k}) \neq 0.
\]

(3.2.9)

We see that when all parameters are negative, Eq. (3.2.9) is always satisfied, since

\[
0 < (1 - e^{\sigma_{1,1} \left( T - \sum_{k=0}^{k^*} W_k \right)} e^{\alpha_{1,1} \sum_{k=0}^{k^*} W_k}) (1 - e^{\sigma_{2,2} \left( T - \sum_{k=0}^{k^*} W_k \right)} e^{\alpha_{2,2} \sum_{k=0}^{k^*} W_k}) < 1,
\]

for all \( T; \sum_{k=0}^{k^*} W_k; 0 < \sum_{k=0}^{k^*} W_k \leq T \). This means that for the case with strictly negative parameters, equilibrium points exist for all amounts of total daily sleep \( (T - \sum_{k=0}^{k^*} W_k) \) including total sleep deprivation (i.e., \( \sum_{k=0}^{k^*} W_k = T \)). However, if we relax the condition that all parameters are negative we may have a situation we have seen before, where Eq. (3.2.9) no longer holds.

Let us assume parameters \( \alpha_{1,1}, \sigma_{1,1} \) and \( \sigma_{2,2} \) to be negative, but parameter \( \alpha_{2,2} \) to be positive. For this case, the requirement for the existence of a state of equilibrium, Eq. (3.2.9), is not always satisfied, which can be seen by examination of the product
\[ e^{\sigma_{2,2} \Sigma_{k=0}^{k^*} (T_k - W_k)} e^{\alpha_{2,2} \Sigma_{k=0}^{k^*} W_k} \]. Here, \( e^{\sigma_{2,2} \Sigma_{k=0}^{k^*} (T_k - W_k)} < 1 \), while \( e^{\alpha_{2,2} \Sigma_{k=0}^{k^*} W_k} > 1 \). This means for a particular combination of \( \sigma_{2,2} \) and \( \alpha_{2,2} \), and by varying the amount of wakefulness \( W_k \) that this product may change from the case when \( e^{\sigma_{2,2} \Sigma_{k=0}^{k^*} (T_k - W_k)} e^{\alpha_{2,2} \Sigma_{k=0}^{k^*} W_k} < 1 \) to the case when \( e^{\sigma_{2,2} \Sigma_{k=0}^{k^*} (T_k - W_k)} e^{\alpha_{2,2} \Sigma_{k=0}^{k^*} W_k} > 1 \). And, as we know from our previous analyses, at unity the equilibrium point does not exist.

To determine stability of states of equilibrium when they do exist, we solve either Eq. (3.1.19) or Eq. (3.1.20) for eigenvalues of the iterative system of Eqs. (3.1.6) and (3.1.7):

\[
\Lambda_1 = e^{\sum_{k=0}^{k^*} (T_k - W_k)} e^{\alpha_{1,1} \Sigma_{k=0}^{k^*} W_k}, \\
\Lambda_2 = e^{\sum_{k=0}^{k^*} (T_k - W_k)} e^{\alpha_{2,2} \Sigma_{k=0}^{k^*} W_k}. 
\]

Notice that in the case when all parameters are negative, the equilibrium points (which exist for all cases of sleep duration including total sleep deprivation) are asymptotically stable. This is because \( 0 < \Lambda_i < 1 \) for both \( i \). In the case when \( \alpha_{2,2} \) is positive, we again have three possibilities for \( \Lambda_2 \) (while for each \( 0 < \Lambda_1 < 1 \)). For \( \Lambda_2 < 1 \), the system has a stable state of equilibrium. For \( \Lambda_2 > 1 \) there is a state of equilibrium, but it is unstable. For \( \Lambda_2 = 1 \), the equilibrium state disappears. By changing the amount of daily sleep, \( T - \sum_{k=0}^{k^*} W_k \), we see that a bifurcation can occur, just like in our analysis of the model case of Section 1.4.1.

Let us now determine a relationship between \( \alpha_{2,2} \) and \( \sigma_{2,2} \) by setting \( \Lambda_2 \) to unity in Eq. (3.2.11) and derive a formula for the critical amount of daily wakefulness \( \left( \sum_{k=0}^{k^*} W_k \right)_c \) beyond which asymptotic stability is no longer achieved:

\[
\left( \sum_{k=0}^{k^*} W_k \right)_c = \frac{-\sigma_{2,2}}{\alpha_{2,2} - \sigma_{2,2}} T, 
\]

for all \( T, \left( \sum_{k=0}^{k^*} W_k \right)_c : 0 < \left( \sum_{k=0}^{k^*} W_k \right)_c \leq T \). This expression can also be written as follows:

\[
\frac{\left( \sum_{k=0}^{k^*} W_k \right)_c}{T - \left( \sum_{k=0}^{k^*} W_k \right)_c} = \frac{-\sigma_{2,2}}{\alpha_{2,2}},
\]

which reveals that whether or not a bifurcation occurs is a function of the ratio of total daily wakefulness \( \left( \sum_{k=0}^{k^*} W_k \right)_c \) to total daily sleep \( T - \left( \sum_{k=0}^{k^*} W_k \right)_c \). If the ratio of total daily wakefulness to total daily sleep falls below the critical ratio of Eq. (3.2.13), then the model predicts exponential convergence to the fixed asymptote. If the ratio of total daily wakefulness to total daily sleep exceeds the critical ratio, then the model predicts divergence away from a fixed asymptote. Both convergence and divergence occur at the rate specified by the
Figure 3.2: Plot showing performance predictions for three repeating schedules using the case of the MTPM with a bifurcation and with extended notation for multiple wake/sleep episodes (Eqs. (3.1.1) and (3.1.2)). The figure shows three different repeating schedules each of which repeats 3 times every $m = 7$ days ($n = 0, 1, \ldots, 20$). Each day has constant duration $T = 24$ h. Each day, wakefulness begins at 07:30 (solid markers), and there is a scheduled nap wake-up time at 13:30 every day (open markers). The schedules are as follows: Sleep restriction days one through five have a 1 h TIB diurnal nap and 1 h TIB nocturnal nap (diamonds), 1.5 h diurnal nap and 1.5 h nocturnal nap (squares), or 3 h diurnal nap and 3 h nocturnal (circles), and recovery days six and seven have 8 h nocturnal TIB only. The average amount of daily wakefulness across each seven-day repeating cycle is: $W = 3.71$ h, 4.42 h, and 6.57 h, respectively. The circadian process is assumed to have the same period as the length of day, $\tau = 24$ h. Parameters used are those published in McCauley et al. (2009a). Solid lines are performance predictions within days. Markers show predictions at the onset of wakefulness for the first wake episode $p_{n,0}(t_{n,0})$ as predicted by Eq. (3.1.6). Nominal predictions during sleep are not shown as to reduce clutter.

The model further predicts that the bifurcation threshold remains the same across days of equal total sleep duration. However, the associated equilibrium states for different tim-
Figure 3.3: Expanded view of Figs. 2.1 and 3.2 for days 11 through 19, showing the subtle differences between the predictions for consolidated sleep (dashed lines) versus an example of split sleep (solid lines). The pairs of superimposed conditions have the same total sleep duration by day, and thus the same average sleep duration across the repeating schedule. However, there is a small benefit in performance during the mid-day from splitting sleep as compared to consolidating sleep. For more severely restricted sleep schedules, the differences are increasingly smaller.

ings of sleep episodes (Eqs. (3.1.11) and (3.1.12)) may be different, due to the different integration limits in $\tilde{F}_n,0$ and $\tilde{G}_n,0$ (see Eqs. (E.1-12) and (E.1-17), respectively). Recall that in the model case of Section 1.4.1, $F$ and $G$ in Eqs. (1.3.35) and (1.3.36), were constant for a given consolidated sleep duration. Yet, in the new model formulation, $\tilde{F}_0$ and $\tilde{G}_0$ in Eqs. (E.1-12) and (E.1-17) are dependent on the timing of the daily multiple wake/sleep episodes. This means that predicted asymptotic performance may be influenced by changing the timing of split sleep episodes without changing the total amount of time invested in sleep.

At the bifurcation, (where the equilibrium point vanishes), the MTPM with the extended notation predicts, as did the model case of Section 1.4.1 for consolidated sleep, that
the change in level of performance at the onset of wake and the onset of sleep (i.e., the first wake/sleep episode), across days, will be constant for large $n$. These slopes are not necessarily equal for the onsets of wake and sleep, nor are they necessarily the same for different timings of the sleep episodes (see Figs. 3.2 and 3.3).
Chapter 4

Modeling Shift Work Schedules

Shift work can lead to a desynchronization between the circadian rhythm of the biological clock and the (imposed) light/dark cycle of the environment. Resynchronization of the circadian rhythm takes place in response to light exposure, as governed by a dose response curve (Boivin et al., 1994), and according to a phase response curve (Jewett et al., 1994). That is, the strength and timing of light exposure determine how fast a desynchronized circadian rhythm can shift back to a state of synchronization with the environment. In the following work we utilize our previous results on complex eigenvalues (see Section 1.5), and discuss a modeling approach which may be used to resynchronize the biological clock with the environment after a perturbation, such as may result from shifted work schedules.

4.1 A modeling approach for realignment of the circadian pacemaker with the environment

We begin by recalling the performance equations during wakefulness and sleep for the MTPM of Eqs. (3.1.1) and (3.1.2), which include the extended notation developed in Chapter 3. In this system of ODEs the $\beta$ and $\gamma$ functions in part represent the circadian rhythm, where we require only that these functions be bounded and oscillatory. Even so, these nonhomogeneities imply that the biological clock is synchronized with the environment.

Let us introduce a new system of ODEs which may relax this assumption may provide a realignment feature for the circadian rhythm in the face of shifted wake/sleep schedules:

\[
\begin{bmatrix}
\dot{c}(t) \\
\dot{r}(t)
\end{bmatrix} =
\begin{bmatrix}
-\eta & 1 \\
-(\frac{2\pi}{T})^2 & 0
\end{bmatrix}
\begin{bmatrix}
c(t) \\
r(t)
\end{bmatrix}
+ \begin{bmatrix}
\eta z(t) \\
0
\end{bmatrix},
\]

(4.1.1)

where \( z(t) = \sin\left(\frac{2\pi}{T} (t - \phi)\right) \) is the sinusoidal function that represents the external influence...
from the environment, and \( c(t) \) is the internal circadian rhythm. Further, \( T \) is the length of the wake/sleep cycle and \( \tau \) is the period of the environment. The parameter \( \eta \) is the rate of realignment, which may be estimated using appropriate experimental data.

Recall that in Section 1.5, we showed that when the eigenvalues for an ODE system such as Eq. (4.1.1) are complex, the solutions will be combinations of sines and cosines (see Appendix C.7). This means that the system solutions will oscillate within days. Eigenvalues for Eq. (4.1.1) are easily obtained by solving the characteristic equation:

\[
det \left( \begin{bmatrix} -\eta & 1 \\ -\left(\frac{2\pi}{T}\right)^2 & 0 \end{bmatrix} - \Lambda I \right) = 0. \tag{4.1.2}
\]

When \( \eta = 0 \) (meaning that there is no external influence from the environment) we find the two complex eigenvalues:

\[
\Lambda_1 = i \frac{2\pi}{T}, \tag{4.1.3}
\]
\[
\Lambda_2 = -i \frac{2\pi}{T}, \tag{4.1.4}
\]

where \( \frac{2\pi}{T} \) is the angular frequency of the oscillatory solution (see also Appendix C.7). For the case when \( \eta \neq 0 \) we find, provided that \( \eta^2 < 4 \left(\frac{2\pi}{T}\right)^2 \), that the eigenvalues are complex:

\[
\Lambda_1 = -\frac{\eta}{2} + i \frac{\sqrt{\eta^2 - 4 \left(\frac{2\pi}{T}\right)^2}}{2}, \tag{4.1.5}
\]
\[
\Lambda_2 = -\frac{\eta}{2} - i \frac{\sqrt{\eta^2 - 4 \left(\frac{2\pi}{T}\right)^2}}{2}, \tag{4.1.6}
\]

meaning that the solution will be oscillatory (see Section 1.5). When \( \eta > 0 \) (i.e., the real part of the eigenvalue, \( -\frac{\eta}{2} \), is negative), the amplitude of the oscillations decays, which means that over time (e.g., days) the circadian rhythm, \( c(t) \), becomes synchronized with the external environment, \( z(t) \).

To solve the system of Eqs. (4.1.1), either numerically or analytically, we must be given initial values \( c(t_0) \) and \( z(t_0) \). Let us assume that at \( t = t_0 \), the biological clock and the environment are completely synchronized. As such, we can derive initial conditions which would produce a trajectory where the circadian rhythm is immediately and persistently synchronized, and the amplitude of the biological clock at \( t = t_0 \) is the same as that of the environment:

\[
c(t_0) = \sin \left( \frac{2\pi}{\tau} (t_0 - \phi) \right). \tag{4.1.7}
\]
Figure 4.1: Plot showing the dynamics of Eq. (4.1.1) for the resynchronization of the circadian rhythm (solid lines) with the environment (dashed lines). We arbitrarily set the rate of realignment to $\eta = .1$. The duration of the wake/sleep cycle $T = 24$ h is equal to the period of the environment, $\tau$. For the first two days in all panels they are synchronized. At the beginning of day two a phase shift of 0, 4 or 8 h (upper panels from left to right) or 12, 16, or 20 h (lower panels from left to right) occurs in the environment. We see that the biological clock and the environment resynchronize (in both phase and amplitude) in approximately the same amount of time regardless of the amount of the initial phase shift.

The initial condition for the function $z(t)$ in Eq. (4.1.1) can be determined by explicitly solving the homogeneous equation for $\dot{r}(t)$ using the requirement for synchronization (i.e., $c(t) = \sin(\omega (t - \phi)))$. Setting $t = t_0$ into the result we find:

$$r(t_0) = \frac{2\pi}{\tau} \cos \left( \frac{2\pi}{\tau} (t_0 - \phi) \right).$$

Using the initial conditions from Eqs. (4.1.7) and (4.1.8), we can derive the time-dependent solution of Eq. (4.1.1), where we introduce the two-dimensional matrix $\xi(t)$.
Figure 4.2: Plot showing the dynamics of Eq. (4.1.1) for the resynchronization of the circadian rhythm (solid lines) with the environment (dashed lines). The rate of realignment is set at $\eta = 0.1$. The duration of wake/sleep cycle $T = 24 \text{ h}$ is equal to the period of the environment, $\tau$. The phase shift in this figure is set at 12 h for all panels, but the phase shift starting time changes; at the beginning of the second day and at 4-hour increments thereafter: 0, 4, or 8 h after the beginning of day 2 (upper panels from left to right) or 12, 16, or 20 h after the beginning of day 2 (lower panels from left to right). As in Fig. 4.1, we see that the biological clock and the environment resynchronize (in both phase and amplitude) in approximately the same amount of time regardless of the amount of the starting time of the initial phase shift.

as the fundamental solution of the homogeneous part (Derrick and Grossman, 1997):

$$
\begin{align*}
\begin{bmatrix}
c(t) \\
r(t)
\end{bmatrix} &= \xi(t)\xi^{-1}(t_0) \begin{bmatrix}
c(t_0) \\
r(t_0)
\end{bmatrix} + \int_{t_0}^{t} \xi(t)\xi^{-1}(s) \begin{bmatrix}
\eta \sin\left(\frac{2\pi}{\tau}(s - \phi)\right) \\
0
\end{bmatrix} ds \\
&= \xi(t)\xi^{-1}(t_0) \begin{bmatrix}
\sin\left(\frac{2\pi}{\tau}(t_0 - \phi)\right) \\
\frac{2\pi}{\tau} \cos\left(\frac{2\pi}{\tau}(t_0 - \phi)\right)
\end{bmatrix} + \int_{t_0}^{t} \xi(t)\xi^{-1}(s) \begin{bmatrix}
\eta \sin\left(\frac{2\pi}{\tau}(s - \phi)\right) \\
0
\end{bmatrix} ds,
\end{align*}
$$

(4.1.9)

In Figs. 4.1 and 4.2, numerical solutions to the system of ODEs of Eqs. (4.1.1) are
shown for some example simulations. In these simulations the internal biological clock and
the environment are initially aligned. Fig. 4.1 shows the effect of shifting phase between
the environment by various amounts and the biological clock. Fig. 4.2 shows the same,
but changing the timing of the phase shift. By setting the rate of realignment at $\eta = .1$ the
realignment appears to take up to 3 to 4 days; by fitting experimental data to the model this
parameter can be properly estimated in future research.
Conclusion

For more than 25 years the Two-Process Model (Borbély, 1982) has served to accurately describe and predict human sleep timing, duration and structure, as well as sleep electroencephalographic (EEG) power spectra, under a wide variety of laboratory and field conditions (Achermann, 2004; Borbély and Achermann, 1999). However, predicting waking cognitive performance with the TPM has been only partially successful, and new modeling approaches have been needed to capture the effects of chronic sleep restriction (Van Dongen et al., 2003) and other interventions (Dinges, 2004) on cognitive functioning. In keeping with the correspondence principle (Bohr, 1920) held in various areas of science, we aimed to build such a new approach on the foundation of the TPM (McCauley et al., 2009a). Preserving what has already been accomplished with the TPM, this could ultimately yield a model encompassing both sleep physiology and waking cognitive performance. In the present thesis, we have developed a mathematical framework that may make this possible.

We showed that the TPM (Borbély, 1982) and recent expansions and variations of the model (Avinash et al., 2005; Johnson et al., 2004) for the prediction of performance impairment belong to a generalized class of coupled, linear, nonhomogeneous, first-order ordinary differential equations (ODEs) with a remarkably rich repertoire of dynamic behaviors. We introduced the new biomathematical model as the Modulating Two-Process Model (MTPM). We replaced the one-dimensional equations for the homeostatic process in the TPM, which have two parameters (one for wake and one for sleep), by two-dimensional equations with up to eight parameters (four for wake and four for sleep). The two-dimensional equations contain the homeostatic process as is already included in the TPM, and a new process modulating the homeostat over longer time constants (days to weeks). Experimental observations indicated the need for such a modulating process (Van Dongen et al., 2003; Belenky et al., 2003), although the underlying physiology remains to be elucidated.
In trying to find what can be learned from our mathematical results, it can be instructive to consider analogous systems described by the same types of ODEs. The linear systems considered here are also seen in the mathematics describing a system of two interconnected chambers or compartments, each filled with a time-dependent volume of liquid or concentration of some compound in a medium (see, e.g., Figs. 1.2 and 1.15). If this analogy holds, then the underlying mechanisms for the homeostatic process and the long-term modulating process could, for instance, involve the build-up (during wake) and dissipation (during sleep) of two distinct compounds, each representing the time-limiting factor in their own cascade of biochemical reactions. We have proposed that these compounds may be part of the regulatory process in the adenosinergic system (McCauley et al., 2009a).

In this thesis, we first examined the dynamic properties of our generalized class of ODEs for performance prediction in the context of consolidated daily sleep episodes, and determined the existence of states of equilibrium and the stability thereof. We derived a number of strictly mathematical results (McCauley et al., 2009a). One key finding is that with specific ranges of parameter values, the generalized ODE system of Eqs. (1.3.23) and (1.3.24), with bounded, periodic nonhomogeneity, produces a bifurcation whereby daily wake durations extended up to a critical value lead to adaptation (i.e., global convergence of performance impairment for given time of day toward an asymptote), whereas daily wake durations extended beyond the critical value lead to escalating performance degradation over days (see Fig. 1.28 and 1.29). There is evidence from laboratory experiments that this model behavior may reflect the actual effects of chronic sleep restriction, and that the critical value may be between 20 and 21 hours of wakefulness (Belenky et al., 2003; Van Dongen and Dinges, 2003b). Such empirical evidence, if confirmed in future studies, helps to constrain the parameter values of the \( \alpha \) and \( \sigma \) matrices (see Eq. (1.4.20)).

Using the analysis of the MTPM as a foundation, we examined varying wake/sleep schedules that repeat across days. We discovered that the underlying characteristic behavior of the model was fundamentally unchanged. We found that the bifurcation point was now defined by the average duration of daily wakefulness across the length of the repetitive schedule (see Eq. (2.2.11)). For schedules where the average daily wake duration was less than the bifurcation threshold, the model predicted that performance deficits across the repeating cycle increase but eventually stabilize to a stable, albeit suboptimal, state of equilibrium (McCauley et al., 2009b). For schedules with average daily wakefulness greater
than the bifurcation threshold, the model predicted that performance deficits escalate, diverging from an unstable equilibrium state. We saw that, even though within the repeating cycle (i.e., across a shorter segment of days) performance may diverge away from an unstable state of equilibrium (daily wakefulness is greater than the bifurcation point), when the average daily wakefulness becomes less than the bifurcation point, performance across the repeating schedule as a whole is predicted to converge toward an equilibrium state.

In further work, we extended the MTPM framework for wake/sleep schedules that could include multiple wake/sleep segments in a single day. Using this new model formulation we again explored the dynamics of the MTPM. We found that a bifurcation was again present, and mathematically defined by the average amount of daily sleep (Eq. (3.2.12)). It was of particular interest that the bifurcation point was the same no matter how sleep was distributed during the day. However, the equilibrium states are predicted to be dependent on when the sleep occurs (due to the integration limits in $\tilde{F}_{n,0}$, see Eq. E.1-12). This means that the timing of nap sleep could play a role in determining performance level at an equilibrium state. Nonetheless, the overall duration of the combined sleep periods per day appeared to be the predominant mediator of performance in the model predictions, as has also been found in experimental data (Mollicone et al., 2008).

Finally, we briefly considered what might be a good modeling strategy for when the internal circadian rhythm becomes desynchronized relative to the environment such as may occur during shift work. Using the same general ODE system, but focusing on the complex eigenvalues, we introduce a set of equations (Eqs. (4.1.1) for the circadian rhythm resynchronization in response to light exposure (or other environmental cues). Further work is needed to fully examine the dynamics of these equations.

We provided a variety of proofs, closed-form equations, and other results pertaining to the generalized class of coupled, linear, nonhomogeneous, first-order ODEs (see Appendices). We found that the characteristic behavior of the model is unchanged for any bounded, periodic nonhomogeneity. This means that the shape of the changes in performance within days—the overt circadian rhythm resulting from the nonhomogeneity—does not fundamentally affect the characteristic behavior of the model across days. In other words, although the homeostatic and circadian components of performance regulation interact (Dijk and Czeisler, 1995; Van Dongen and Dinges, 2003a); they can nevertheless be treated separately from a mathematical and experimental point of view. As such, our
approach using the level of performance at the onset of wakefulness and the onset of sleep as a reference point for prediction across days should generalize to all time points of the wake/sleep cycle.

The MTPM as a set of linear ODEs models the dynamics of the homeostatic regulation of performance for a variety of wake/sleep schedules within and across days or weeks. The same ODEs can also generate oscillatory behavior within wake/sleep cycles, thus the ODE system we introduced in this thesis may provide a comprehensive basis for a new, broadly applicable tool for the prediction of performance impairment due to sleep loss and circadian misalignment.
Appendix A

Proofs for the generalized Two-Process Model (gTPM)

A.1 Derivation of the difference equations for initial values at the onset of wakefulness and the onset of sleep in the gTPM

We begin with Eq. (1.1.16) and substitute into the left-hand side the solution, Eq. (1.1.26), evaluated at the onset of wakefulness $t_{n+1}$:

$$p_{n+1}(t_{n+1}) = q_n(t_{n+1})$$

$$= e^{\sigma(t_{n+1}-(t_n+W_n))} q_n(t_n + W_n) + \int_{t_n + W_n}^{t_{n+1}} e^{\sigma(t_{n+1}-s)} \eta(s) ds$$

$$= e^{\sigma(T_n-W_n)} q_n(t_n + W_n) + \int_{t_n + W_n}^{t_n + T_n} e^{\sigma((t_n+T_n)-s)} \eta(s) ds. \quad (A.1-1)$$

Here, we have used the relation $t_{n+1} = t_n + T_n$. Now we can use Eq. (1.1.15) and substitute the solution, Eq. (1.1.25), evaluated at the beginning of sleep, $t_n + W_n$, to obtain the desired result where $p_{n+1}(t_{n+1})$ is in terms of $p_n(t_n)$:

$$p_{n+1}(t_{n+1}) = e^{\sigma(T_n-W_n)} \left[ e^{\alpha(t_n+W_n-t_n)} p_n(t_n) + \int_{t_n}^{t_n + W_n} e^{\alpha((t_n+T_n)-s)} \beta(s) ds \right]$$

$$+ \int_{t_n + W_n}^{t_n + T_n} e^{\sigma((t_n+T_n)-s)} \gamma(s) ds$$

$$= e^{\sigma(T_n-W_n)} e^{\alpha W_n} p_n(t_n) + F_n, \quad (A.1-2)$$

where

$$F_n = e^{\sigma(T_n-W_n)} \int_{t_n}^{t_n + W_n} e^{\alpha((t_n+T_n)-s)} \beta(s) ds + \int_{t_n + W_n}^{t_n + T_n} e^{\sigma((t_n+T_n)-s)} \gamma(s) ds. \quad (A.1-3)$$
Similarly, we can derive the difference equations for level of performance at the onset of sleep:

\[ q_{n+1}(t_{n+1} + W_{n+1}) = e^{\alpha W_{n+1}} q_n(t_{n+1}) + \int_{t_{n+1}}^{t_{n+1}+W_{n+1}} e^{\alpha((t_{n+1}+W_{n+1})-s)} \beta(s) \, ds \]

\[ = e^{\alpha W_{n+1}} e^{\sigma(T_n-W_n)} q_n(t_n + W_n) + G_n, \]

where

\[ G_n = e^{\alpha W_{n+1}} \int_{t_n + W_n}^{t_{n+1} + W_{n+1}} e^{\sigma((t_n+T_n)-s)} \gamma(s) \, ds + \int_{t_{n+1}}^{t_{n+1}+W_{n+1}} e^{\alpha((t_{n+1}+W_{n+1})-s)} \beta(s) \, ds. \]  

(A.1-5)

### A.2 Periodic form of the nonhomogeneous part of the iterative equations for the initial values in the gTPM

When the length of day \( T \) and the period \( \tau \) of the oscillatory nonhomogeneity, both assumed constant, are related by \( T/\tau = b/m \), where the ratio \( b/m \in \mathbb{Q} \) is reduced to its lowest terms, the functions \( F_n \) and \( G_n \) in Eqs. (1.1.33) and (1.1.34) become \( m \) periodic. For Eq. (1.1.33) this can be shown by proving \( F_{n+m} = F_n \) where \( m \in \{1, 2, \ldots\} \):

\[ F_n = e^{\sigma(T-W)} \int_{t_n}^{t_{n+W}} e^{\alpha((t_n+W)-s)} \beta(s) \, ds + \int_{t_{n+W}}^{t_{n+mT}} e^{\sigma((t_n+W)-s)} \gamma(s) \, ds \]

\[ = e^{\sigma(T-W)} \int_{t_n + mT}^{t_{n+mT}} e^{\alpha((t_n+W+b\tau)-s)} \beta(s) \, ds + \int_{t_{n+mT}}^{t_{n+mT+mT}} e^{\sigma((t_n+W+b\tau)-s)} \gamma(s) \, ds \]

\[ = e^{\sigma(T-W)} \int_{t_{n+m}}^{t_{n+m+mT}} e^{\alpha((t_n+m-W)-s)} \beta(s) \, ds + \int_{t_{n+m+mT}}^{t_{n+m+mT+mT}} e^{\alpha((t_n+m-W)-s)} \gamma(s) \, ds \]

\[ = F_{n+m}, \]  

(A.2-1)

where we have used \( t_n + mT = t_{n+m} \). Since \( F_n \) is \( m \) periodic, Eq. (1.1.33) with constant coefficient \( \Phi(t_n + T)\Psi(t_n + W) \) must also be \( m \) periodic. The proof for Eq. (1.1.34) is analogous.

### A.3 Asymptotic stability of the equilibrium state in the gTPM

Eqs. (1.1.45) and (1.1.46) can be proven by using a Taylor series expansion. For example using Eq. (1.1.33) for wakefulness, we expand \( p_{n+1}(p_n) \), where \( p_n \) is considered in
a neighborhood of the fixed point \( p \) and \( |p_n - p| \to 0: \)
\[
|p_{n+1}(p_n) - p_{n+1}(p)| = \left| \frac{dp_{n+1}}{dp_n} \right|_p |p_n - p| + \frac{1}{2!} \left| \frac{d^2 p_{n+1}}{dp_n^2} \right|_p |p_n - p|^2 + \ldots \quad (A.3-1)
\]
All terms of higher order than the first are negligible around \( p \), so that Eq. (A.3-1) can be approximated by
\[
|p_{n+1}(p_n) - p_{n+1}(p)| = \left| \frac{dp_{n+1}}{dp_n} \right|_p |p_n - p|. \quad (A.3-2)
\]
This result implies that if \( \left| \frac{dp_{n+1}}{dp_n} \right|_p > 1 \), then the distance between \( p_{n+1}(p_n) \) and \( p_n(p) \) increases for each iteration, which makes the fixed point unstable. If \( \left| \frac{dp_{n+1}}{dp_n} \right|_p < 1 \), then the distance decreases for each iteration, so that \( p_{n+1} \) eventually reaches the fixed point. This is referred to as asymptotically stable. If all higher order derivatives are exactly zero, as is the case for all linear models, and \( \left| \frac{dp_{n+1}}{dp_n} \right|_p < 1 \) regardless of \( p_n \), then the fixed point is globally asymptotically stable. This means that no matter what the initial value is the model solution will always converge to the fixed point.

## A.4 Asymptotic stability of the periodic fixed points in the gTPM

When the length of day \( T \) and period of the nonhomogeneity \( \tau \), both constant, are related by \( T/\tau = d/m \), where the ratio \( d/m \in \mathbb{Q} \) is reduced to its lowest terms, the functions \( F_n \) and \( G_n \) are \( m \) periodic (see Appendix A.2). Hence, upon iteration of \( p_{n+1} \) and \( q_{n+1} \), \( m \) times, one returns to the fixed points \( p_{(k)} \) and \( q_{(k)} \) where \( k \in \{0, \ldots, m-1\} \) (see Eqs. (1.1.42) and (1.1.43)). We can produce an inductive equation that selects every different iterate of Eq. (1.1.33), as follows (for this proof we use the simplified notation \( \Psi_n(t_n + W_n) = \Psi_n \) and \( \Phi_n(t_n + T_n) = \Phi_n \):)
\[
p_{n+1}(t_{n+1}) = \Phi_n \Psi_n p_n(t_n) + F_n,
\]
\[
p_{n+2}(t_{n+2}) = \Phi_{n+1} \Psi_{n+1} p_{n+1}(t_{n+1}) + F_{n+1}
\]
\[
= \Phi_{n+1} \Phi_{n+1} (\Phi_n \Psi_n p_n(t_n) + F_n) + F_{n+1},
\]
\[
\vdots
\]
\[
p_{n+m}(t_{n+m}) = (\Phi_{n+m-1} \Psi_{n+m-1} \cdots \Phi_n \Psi_n) p_n(t_n) + (\Phi_{n+m-1} \Psi_{n+m-1} \cdots \Phi_{n+1} \Psi_{n+1}) F_n
\]
\[
+ (\Phi_{n+m-1} \Psi_{n+m-1} \cdots \Phi_{n+2} \Psi_{n+2}) F_{n+1} + \cdots + (\Phi_{n+m-1} \Psi_{n+m-1}) F_{n+m-2}
\]
\[
+ F_{n+m-1},
\]
which can be written in condensed form:

\[
p_{n+m}(t_{n+m}) = \left( \prod_{k=0}^{m-1} \Phi_{n+k} \Psi_{n+k} \right) p_n(t_n) + \sum_{j=1}^{m-1} \left( \prod_{k=j}^{m-1} \Phi_{n+k} \Psi_{n+k} \right) F_{n+j-1} + F_{n+m-1}.
\]  

(A.4-1)

Eq. (A.4-1) represents \( m \) unique iterative equations, which differ by their initial values: \( p_0(t_0), p_1(t_1) \) to \( p_{m-1}(t_{m-1}) \).

We assume \( p_0(t_0) \) is given, and the others can be derived using Eq. (1.1.33). Since we consider the case of constant length of day and duration of sleep, \( \Psi_{n+k} = \Psi \) and \( \Phi_{n+k} = \Phi \) are constant. This results in the simplified equation:

\[
p_{n+m}(t_{n+m}) = (\Phi \Psi)^m p_n(t_n) + \sum_{j=1}^{m-1} (\Phi \Psi)^{j-1} F_{n+m-j}.
\]  

(A.4-2)

We now find periodic fixed points by setting \( p_{n+m} = p_n = p \) and \( F_{n+m-j} = F_{n-j} = F_j \) (see Appendix A.2):

\[
p = \frac{\sum_{j=0}^{m-1} (\Phi \Psi)^j F_j}{1 - (\Phi \Psi)^m}.
\]  

(A.4-3)

To determine stability of these fixed points we take the derivative of \( p_{n+m} \) with respect to \( p_n \) in Eq. (A.4-2) (cf. A.3). It follows that:

\[
\left| \frac{dp_{n+m}}{dp_n} \right| = (\Phi \Psi)^m.
\]  

(A.4-4)

Since in the TPM both parameters \( \alpha \) and \( \sigma \) are negative, the product of \( \Phi \) and \( \Psi \) (Eqs. (1.1.30) and (1.1.29), respectively) is such that \( 0 < \Phi \Psi < 1 \), which also means \( 0 < (\Phi \Psi)^j < 1 \) for all \( j \geq 1 \). Therefore, each of the fixed points \( p(k) \) with \( k \in \{0, \ldots, m-1\} \) are asymptotically stable fixed points of their respective equations \( p_{n+k} \). Similarly, we find that the fixed points \( q(k) \) are asymptotically stable fixed points of \( q_{n+k} \).

### A.5 Analytical solutions for a gTPM model case

Using Eq. 1.1.5 for the circadian rhythm, the nonhomogeneities \( \beta(t) \) and \( \gamma(t) \) shown in Eq. (1.2.1) and (1.2.2), respectively can be explicitly written:

\[
\beta(s) = \kappa c(t) + \mu = \kappa \sum_{k=1}^{5} A_k \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) + \mu,
\]  

(A.5-1)

(A.5-2)
\[ \gamma(s) = \kappa c(t) + \mu = \kappa \sum_{k=1}^{5} A_k \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) + \mu. \]  

(A.5-3)

Here we have assumed the same form for the forcing functions during wakefulness and during sleep, which would imply that \( \beta(t) = \gamma(t) \). However, their actual forms are unknown and is an important direction for our future research. Using Eqs. (1.1.29) and (1.1.30) we can explicitly write Eqs. (1.1.27) and (1.1.28):

\[ \Psi_n(t) = e^{\alpha(t-t_n)} \]  
\[ \Phi_n(t) = e^{\sigma(t-(t_n+W_n))}. \]  

(A.5-4)

(A.5-5)

Now using these results we can explicitly write Eqs. (1.1.31) and (1.1.32) for this particular model case of the gTPM:

\[ \Omega_n(t) = \int_{t_n}^{t} \Psi_n(t)\Psi_n^{-1}(s)\beta(s) ds, \]
\[ = e^{\alpha\tau} \kappa \sum_{k=1}^{5} A_k \int_{t_n}^{t} e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) ds + e^{\alpha\tau} \mu \int_{t_n}^{t} e^{-\alpha s} ds, \]  

(A.5-6)

\[ \Theta_n(t) = \int_{t_n+W_n}^{t} \Phi_n(t)\Phi_n^{-1}(s)\gamma(s) ds, \]
\[ = e^{\sigma\tau} \kappa \sum_{k=1}^{5} A_k \int_{t_n+W_n}^{t} e^{-\sigma s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) ds + e^{\sigma\tau} \mu \int_{t_n+W_n}^{t} e^{-\sigma s} ds. \]  

(A.5-7)

The definite integrals in Eqs. (A.5-6) and (A.5-7) can be analytically solved by the method of integration by parts. Let us first derive the integrals in Eq. (A.5-6):

\[ \int_{t_n}^{t} e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) ds \]
\[ = -\frac{\tau e^{-\alpha s} \cos \left( \frac{2k\pi}{\tau} (s - \phi) \right)}{2k\pi} \bigg|_{t_n}^{t} - \frac{\alpha \tau}{2k\pi} \int_{t_n}^{t} e^{-\alpha s} \cos \left( \frac{2k\pi}{\tau} (s - \phi) \right) ds \]
\[ = -\frac{\tau e^{-\alpha s} \cos \left( \frac{2k\pi}{\tau} (s - \phi) \right)}{2k\pi} \bigg|_{t_n}^{t} - \frac{\alpha \tau^2}{4k^2\pi^2} e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) \bigg|_{t_n}^{t} \]
\[ - \frac{\alpha^2 \tau^2}{4k^2\pi^2} \int_{t_n}^{t} e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) ds. \]  

(A.5-8)
Thus,

\[
\int_{t_n}^{t} e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) \, ds \\
= \frac{-\tau e^{-\alpha} \cos \left( \frac{2k\pi}{\tau} (s - \phi) \right) \bigg|^t_{t_n} - \frac{\alpha\tau^2}{4k^2\pi^2} e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) \bigg|^t_{t_n}}{1 + \frac{\alpha^2\tau^2}{4k^2\pi^2}} \\
= -\frac{2k\pi\tau e^{-\alpha} \cos \left( \frac{2k\pi}{\tau} (s - \phi) \right) \bigg|^t_{t_n} - \alpha\tau^2 e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) \bigg|^t_{t_n}}{4k^2\pi^2 + \alpha^2\tau^2} \\
= \frac{2k\pi\tau \left( e^{-\alpha_n} \cos \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - e^{-\alpha} \cos \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)}{4k^2\pi^2 + \alpha^2\tau^2} \\
\quad + \frac{\alpha\tau^2 \left( e^{-\alpha_n} \sin \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - e^{-\alpha} \sin \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)}{4k^2\pi^2 + \alpha^2\tau^2}.
\]  

(A.5-9)

And for the last integral term in the right hand side of Eq. A.5-7:

\[
\int_{t_n}^{t} e^{-\alpha} \, ds = -\frac{e^{-\alpha s}}{\alpha} \bigg|^t_{t_n} \\
= \frac{e^{-\alpha_n} - e^{-\alpha}}{\alpha}.
\]  

(A.5-10)

Similarly we can also derive the integrals in Eq. (A.5-7):

\[
\int_{t_n + W_n}^{t} e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) \, ds \\
= -\frac{\tau e^{-\alpha} \cos \left( \frac{2k\pi}{\tau} (s - \phi) \right) \bigg|^t_{t_n + W_n} - \frac{\sigma\tau}{2k\pi} \int_{t_n + W_n}^{t} e^{-\alpha s} \cos \left( \frac{2k\pi}{\tau} (s - \phi) \right) \, ds} \\
= -\frac{\tau e^{-\alpha} \cos \left( \frac{2k\pi}{\tau} (s - \phi) \right) \bigg|^t_{t_n + W_n} - \frac{\sigma\tau^2}{4k^2\pi^2} e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) \bigg|^t_{t_n + W_n}}{4k^2\pi^2 + \alpha^2\tau^2} \\
\quad - \frac{\sigma^2\tau^2}{4k^2\pi^2} \int_{t_n + W_n}^{t} e^{-\alpha s} \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) \, ds.
\]  

(A.5-11)
Using these results we can easily write the complete time-dependent solutions $p_n(t)$ and $q_n(t)$:

$$p_n(t) = e^{\alpha(t-t_n)} p_n(t_n)$$

$$+ \kappa \sum_{k=1}^{5} A_k \frac{2k\pi \tau \left(e^{\alpha(t-t_n)} \cos \left(\frac{2k\pi}{\tau} (t_n - \phi)\right) - \cos \left(\frac{2k\pi}{\tau} (t - \phi)\right)\right)}{4k^2\pi^2 + \alpha^2\tau^2}$$

$$+ \kappa \sum_{k=1}^{5} A_k \frac{\alpha \tau^2 \left(e^{\alpha(t-t_n)} \sin \left(\frac{2k\pi}{\tau} (t_n - \phi)\right) - \sin \left(\frac{2k\pi}{\tau} (t - \phi)\right)\right)}{4k^2\pi^2 + \alpha^2\tau^2}$$

$$+ \frac{\mu}{\alpha} \left(e^{\alpha(t-t_n)} - 1\right).$$  \hspace{1cm} (A.5-14)

$$q_n(t) = e^{\sigma(t-(t_n+W_n))} q_n(t_n + W_n)$$

$$+ \kappa \sum_{k=1}^{5} A_k \frac{2k\pi \tau \left(e^{\sigma(t-(t_n+W_n))} \cos \left(\frac{2k\pi}{\tau} (t_n + W_n - \phi)\right) - \cos \left(\frac{2k\pi}{\tau} (t - \phi)\right)\right)}{4k^2\pi^2 + \sigma^2\tau^2}$$

$$+ \kappa \sum_{k=1}^{5} A_k \frac{\sigma \tau^2 \left(e^{\sigma(t-(t_n+W_n))} \sin \left(\frac{2k\pi}{\tau} (t_n + W_n - \phi)\right) - \sin \left(\frac{2k\pi}{\tau} (t - \phi)\right)\right)}{4k^2\pi^2 + \sigma^2\tau^2}$$

$$+ \frac{\mu}{\sigma} \left(e^{\sigma(t-(t_n+W_n))} - 1\right).$$  \hspace{1cm} (A.5-15)
A.6 Analytical solution for initial value of performance at the onset of wakefulness and the onset of sleep

To utilize Eqs. (A.5-14) or (A.5-15) one must have the initial value \( p_0(t_0) \) or \( q_0(t_0 + W_0) \), respectively. Let us assume we begin with performance predictions at the onset of wakefulness and that performance predictions are assumed in a state of equilibrium (e.g., baseline) at a constant wakefulness duration, \( W_b \), each day and length of day, \( T \), is constant. We will derive the initial values \( p_0(t_0) \) in terms of parameters for the gTPM using the nonhomogeneities in Eqs. (A.5-1) and (A.5-3).

Recall the equations for predicting performance for the onset of wakefulness at the state of equilibrium are given by Eqs. (1.1.42). Using Eqs. (A.5-4) and (A.5-5) we can write the equilibrium equation for onset of wakefulness and at a particular duration of wakefulness, \( W_b \):

\[
p(t_n) = \left( 1 - e^{\sigma(T-W_b)} e^{\alpha W_b} \right)^{-1} F. \tag{A.6-1}
\]

The last term on the right hand side of Eq. (A.6-1) is given by Eq. (A.1-3):

\[
F_n = e^{\sigma(T-W_b)} \Omega_n(t_n + W_b) + \Theta_n(t_n + T). \tag{A.6-2}
\]

where \( \Omega_n(t_n + W_b) \) and \( \Theta_n(t_n + T) \) using Eqs. (A.5-6) and (A.5-7), respectively, are given by:

\[
\Omega_n(t_n + W_b) = \kappa \sum_{k=1}^{5} A_k \frac{2k\pi \tau \left( e^{\alpha W_b} \cos \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - \cos \left( \frac{2k\pi}{\tau} (t_n + W_b - \phi) \right) \right)}{4k^2\pi^2 + \alpha^2\tau^2} \\
+ \kappa \sum_{k=1}^{5} A_k \frac{\alpha^2 \left( e^{\alpha W_b} \sin \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - \sin \left( \frac{2k\pi}{\tau} (t_n + W_b - \phi) \right) \right)}{4k^2\pi^2 + \alpha^2\tau^2} \\
+ \frac{\mu}{\alpha} \left( e^{\alpha W_b} - 1 \right), \tag{A.6-3}
\]

\[
\Theta_n(t_n + T) = \kappa \sum_{k=1}^{5} A_k \frac{2k\pi \tau \left( e^{\sigma(T-W_b)} \cos \left( \frac{2k\pi}{\tau} (t_n + W_b - \phi) \right) - \cos \left( \frac{2k\pi}{\tau} (t_n + T - \phi) \right) \right)}{4k^2\pi^2 + \sigma^2\tau^2} \\
+ \kappa \sum_{k=1}^{5} A_k \frac{\sigma^2 \left( e^{\sigma(T-W_b)} \sin \left( \frac{2k\pi}{\tau} (t_n + W_b - \phi) \right) - \sin \left( \frac{2k\pi}{\tau} (t_n + T - \phi) \right) \right)}{4k^2\pi^2 + \sigma^2\tau^2} \\
+ \frac{\mu}{\sigma} \left( e^{\sigma(T-W_b)} - 1 \right). \tag{A.6-4}
\]
Appendix B

Mathematical models that insure invariance to choice of time step in difference equations

B.1 The model by Johnson and colleagues (2004) as a system of coupled nonhomogeneous first-order differential equations

Mathematical models used to predict fatigue and performance are often formulated as a system of difference equations (DEs) in which a value of a model variable at the next time point is expressed in terms of the value(s) at the previous time point(s). A typical form of such DEs is:

$$y(t + \Delta t) = y(t) + f(\Delta),$$  \hspace{1cm} (B.1-1)

where $f(t)$ is a function of time (or a constant). An important criterion for such equations is that they must be invariant to choice of the time step. That is, the prediction for a given time point should not change if it is derived from more fine-grained predictions with smaller time steps.

DEs that meet these criteria can be transformed into a continuous system formulated as ordinary differential equations (ODEs). We recently formulated a system of ODEs (McCauley et al., 2009a) for the sleep/wake homeostatic aspect of neurobehavioral performance, which represents a generalized framework for a variety of previously published models (Mallis et al., 2004). Here we consider this ODE system in the context of the homeostatic model of Johnson et al. (2004). We show that this model is not invariant to choice
of time step, and we use our ODE-based model (McCauley et al., 2009a) to propose a way to fix this.

The model by Johnson et al. (2004) predicts changes in fatigue and performance across days by coupling two processes: a conventional homeostatic process ("homeostat") representing a buildup of pressure for sleep during wakefulness and a dissipation of this pressure during sleep (Borbély and Achermann, 1999), and a newly proposed regulatory process modulating the homeostat. Across days, predictions of performance are posited to be proportional to the predicted level of the homeostat.

Let us begin by writing the Johnson et al. (2004) in notation used in (McCauley et al., 2009a). The predicted level of performance on day \( n \), \( p_n(t) \), and the state of the new regulatory process on day \( n \), \( u_n(t) \), during wakefulness are given by:

\[
\begin{align*}
p_n(t + \Delta t) &= p_n(t) - \kappa_d \Delta t, \\
u_n(t + \Delta t) &= u_n(t) - \mu_d \Delta t,
\end{align*}
\]

(B.1-2), (B.1-3) for \( t \in [t_n, t_{n+1}] \), and

\[
\begin{align*}
q_n(t + \Delta t) &= v_n(t) + (q_n(t) - v_n(t)) e^{-\kappa_r \Delta t}, \\
v_n(t + \Delta t) &= 100 + (v_n(t) - 100) e^{-\mu_r \Delta t},
\end{align*}
\]

(B.1-4), (B.1-5) for \( t \in [t_n + W_n, t_{n+1}] \), where \( \kappa_d \), \( \mu_d \), \( \kappa_r \) and \( \mu_r \) are model parameters. Eqs. (B.1-2) and (B.1-3) can be written equivalently as a system of first-order ODEs:

\[
\begin{align*}
\frac{dp_n}{dt} &= -\kappa_d, \\
\frac{du_n}{dt} &= -\mu_d,
\end{align*}
\]

(B.1-6), (B.1-7) with appropriate initial conditions. Eq. (B.1-5) can also be written as a first-order ODE:

\[
\frac{dv_n}{dt} = -\mu_r (v_n - 100).
\]

(B.1-8)

This is easily confirmed by comparing the analytical solution (Derrick and Grossman, 1997) of Eq. (B.1-8):

\[
v_n(t) = 100 + (v_n(t_0) - 100) e^{-\mu_r t},
\]

(B.1-9) which can be written in iterative form as Eq. (B.1-5) for any step size \( \Delta t \). However, to find an ODE to represent Eq. (B.1-4) we must proceed in a slightly different manner. Let us
first iterate Eqs. (B.1-4) and (B.1-5) from \( t = 0 \) to \( t = 2\Delta t \) for two different-size time steps, \( \Delta t \) and \( 2\Delta t \), and compare the result for each at time \( t = 2\Delta t \). We first iterate by \( \Delta t \) twice:

\[
\begin{align*}
q_n(\Delta t) &= v_n(0) + (q_n(0) - v_n(0))e^{-\kappa_1\Delta t}, \\
v_n(\Delta t) &= 100 + (v_n(0) - 100)e^{-\mu_1\Delta t},
\end{align*}
\]  

(B.1-10)

(B.1-11)

and

\[
\begin{align*}
q_n(2\Delta t) &= v_n(\Delta t) + (q_n(\Delta t) - v_n(\Delta t))e^{-\kappa_2\Delta t}, \\
v_n(2\Delta t) &= 100 + (v_n(\Delta t) - 100)e^{-\mu_2\Delta t}.
\end{align*}
\]  

(B.1-12)

(B.1-13)

By substitution of Eqs. (B.1-10) and (B.1-11) into Eqs. (B.1-12) and (B.1-13), we obtain:

\[
q_n(2\Delta t) = 100 + (v_n(0) - 100)e^{-\mu_2\Delta t} \\
+ \left( v_n(0) + (q_n(0) - v_n(0))e^{-\kappa_2\Delta t} - (100 + (v_n(0) - 100)e^{-\mu_2\Delta t}) \right) e^{-\kappa_2\Delta t},
\]

(B.1-14)

\[
v_n(2\Delta t) = 100 + (100 + (v_n(0) - 100)e^{-\mu_2\Delta t} - 100)e^{-\mu_2\Delta t}.
\]

(B.1-15)

Now let us iterate with only one step of size \( 2\Delta t \):

\[
\begin{align*}
q_n(2\Delta t) &= v_n(0) + (q_n(0) - v_n(0))e^{-\kappa_2\Delta t}, \\
v_n(2\Delta t) &= 100 + (v_n(0) - 100)e^{-\mu_2\Delta t}.
\end{align*}
\]  

(B.1-16)

(B.1-17)

Eq. (B.1-15) and (B.1-17) can be shown to be equivalent. However, Eq. (B.1-14) and (B.1-16) are not, implying that Eq. (B.1-4) is not invariant to the choice of time step \( \Delta t \).

One way to find a modification of Eq. (B.1-4) that is invariant to \( \Delta t \) and amendable to transformation into an ODE is to subtract \( q_n(t) \) from both sides of Eq. (B.1-4):

\[
q_n(t + \Delta t) - q_n(t) = v_n(t) - q_n(t) + (q_n(t) - v_n(t))e^{-\kappa_1\Delta t},
\]

(B.1-18)

\[
= (q_n(t) - v_n(t)) \left( e^{-\kappa_1\Delta t} - 1 \right).
\]

Let’s divide by \( \Delta t \) and take the limit as \( \Delta t \to 0 \):

\[
\lim_{\Delta t \to 0} \frac{q_n(t + \Delta t) - q_n(t)}{\Delta t} = \lim_{\Delta t \to 0} \frac{(q_n(t) - v_n(t))}{\Delta t} \left( e^{-\kappa_1\Delta t} - 1 \right).
\]

(B.1-19)

The left-hand side of Eq. (B.1-19) represents the definition of \( dq_n/dt \). Since the right-hand side has as its limit \( 0/0 \), we can enlist L’Hôpital’s rule and take the derivative of the numerator and denominators with respect to \( \Delta t \):

\[
\frac{dq_n}{dt} = \lim_{\Delta t \to 0} \frac{-\kappa_1(q_n(t) - v_n(t))e^{-\kappa_1\Delta t}}{1}.
\]

(B.1-20)
This limit can be taken, where the result is:

\[
\frac{dq_n}{dt} = -\kappa_r(q_n - v_n).
\]  
(B.1-21)

Let us now find the analytical solution to this ODE (Derrick and Grossman, 1997):

\[
q_n(t) = 100 + \left( q_n(t_0) - \frac{(v_n(t_0) - 100)}{\kappa_r - \mu_r} - 100 \right) e^{-\kappa_r t} \\
+ \left( \frac{(v_n(t_0) - 100)\kappa_r}{\kappa_r - \mu_r} \right) e^{-\mu_r t}.
\]  
(B.1-22)

We can also write this as an iterative equation for any time step size \(\Delta t\):

\[
q_n(t + \Delta t) = 100 + \left( q_n(t) - \frac{(v_n(t) - 100)}{\kappa_r - \mu_r} - 100 \right) e^{-\kappa_r \Delta t} \\
+ \left( \frac{(v_n(t) - 100)\kappa_r}{\kappa_r - \mu_r} \right) e^{-\mu_r \Delta t}.
\]  
(B.1-23)

This is not exactly the same as Eq. (B.1-4); Eq. (B.1-4) only converges to Eq. (B.1-23) as \(\Delta t\) approaches zero.

Thus, to make the model by Johnson et al.(2004) invariant to the choice of \(\Delta t\), Eq. (B.1-4) could be replaced by Eq. (B.1-23). The model can then be expressed in our framework of coupled ODEs as follows:

\[
\begin{bmatrix}
\dot{p}_n \\
\dot{u}_n
\end{bmatrix}
= 
\begin{bmatrix}
\beta_1(t) \\
\beta_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n, t_n + W_n],
\]  
(B.1-24)

\[
\begin{bmatrix}
\dot{q}_n \\
\dot{v}_n
\end{bmatrix}
= 
\begin{bmatrix}
\sigma_{1,1} & \sigma_{1,2} \\
0 & \sigma_{2,2}
\end{bmatrix}
\begin{bmatrix}
q_n \\
v_n
\end{bmatrix}
+ 
\begin{bmatrix}
\gamma_1(t) \\
\gamma_2(t)
\end{bmatrix}, \quad \text{for} \quad t \in [t_n + W_n, t_{n+1}].
\]  
(B.1-25)
Appendix C

Proofs for the Modulated Two-Process Model (MTPM)

C.1 Analytical solutions for the generalized model

The general solution of Eqs. (1.3.23) and (1.3.24) is given by

\[
\begin{bmatrix}
p_n(t) \\
u_n(t)
\end{bmatrix} = \Psi_n(t) \begin{bmatrix}
p_n(t_n) \\
u_n(t_n)
\end{bmatrix} + \Omega_n(t),
\]

(C.1-1)

where

\[
\Omega_n(t) = \int_{t_n}^{t} \Psi_n(t) \psi^{-1}_n(s) \begin{bmatrix}
\beta_1(s) \\
\beta_2(s)
\end{bmatrix} ds,
\]

(C.1-2)

for all \( t \in [t_n, t_n + W_n] \) and

\[
\begin{bmatrix}
q_n(t) \\
v_n(t)
\end{bmatrix} = \Phi_n(t) \begin{bmatrix}
q_n(t_n + W_n) \\
v_n(t_n + W_n)
\end{bmatrix} + \Theta_n(t),
\]

(C.1-3)

where

\[
\Theta_n(t) = \int_{t_n + W_n}^{t} \phi_n(t) \phi^{-1}_n(s) \begin{bmatrix}
\gamma_1(s) \\
\gamma_2(s)
\end{bmatrix} ds,
\]

(C.1-4)

for all \( t \in [t_n + W_n, t_{n+1}] \). Here

\[
\Psi_n(t) = \psi_n(t) \psi^{-1}_n(t_n),
\]

(C.1-5)

\[
\Phi_n(t) = \phi_n(t) \phi^{-1}_n(t_n + W_n),
\]

(C.1-6)

are the principal matrix solutions, and \( \psi_n(t) \) and \( \phi_n(t) \) are the fundamental solutions of the homogeneous part of Eqs. (1.3.23) and (1.3.24), respectively (Derrick and Grossman,
1997). In general, computing the inverse of a matrix function, such as found under the integrals of Eqs. (C.1-1) and (C.1-3) can be quite tedious. However by assuming the coefficient matrices $\alpha$ and $\sigma$ are constant, we can use the equality (Derrick and Grossman, 1997):

\[
\Psi_n^{-1}(t) = \Psi_n(-t), \tag{C.1-7}
\]
\[
\Phi_n^{-1}(t) = \Phi_n(-t). \tag{C.1-8}
\]

The form of the fundamental solutions is dependent on the eigenvalues (either real or complex conjugate) and the corresponding eigenvectors (either one or two linearly independent eigenvectors) of the coefficient matrices $\alpha$ and $\sigma$.

For the case when eigenvalues are real and distinct or complex conjugate with two linearly independent eigenvectors, the general form of the fundamental $2 \times 2$ matrix solutions $\Psi_n(t)$ and $\Phi_n(t)$ of Eqs. (C.1-1) and (C.1-3), respectively, are given by (Derrick and Grossman, 1997):

\[
\psi_n(t) = \begin{bmatrix} x_1 e^{\lambda_1 t} & x_2 e^{\lambda_2 t} \end{bmatrix}, \tag{C.1-9}
\]
\[
\phi_n(t) = \begin{bmatrix} x_3 e^{\lambda_3 t} & x_4 e^{\lambda_4 t} \end{bmatrix}. \tag{C.1-10}
\]

Let us consider the solution for the wake equation, Eq. (C.1-9). Here the eigenvalues $\lambda_1$ and $\lambda_2$ are the roots to the characteristic equations $\det(\alpha - \lambda I) = 0$. The linearly independent eigenvectors $x_i$ for $i \in \{1, 2\}$ are determined as non-trivial solutions (Derrick and Grossman, 1997) to

\[
(\alpha - \lambda_i I)x_i = 0. \tag{C.1-12}
\]

However, when eigenvalues are pairwise identical and there is only one independent eigenvector, the fundamental matrix solution $\Psi_n(t)$ is:

\[
\psi_n(t) = [x \ (y + xr)] e^{\lambda t}. \tag{C.1-11}
\]

In this case, $x$ is the only linearly independent eigenvector of the coefficient matrix $\alpha$. Any vector $y$ that satisfies:

\[
(\alpha - \lambda I)x = 0, \tag{C.1-12}
\]
\[
(\alpha - \lambda I)y = x, \tag{C.1-13}
\]

is called a generalized eigenvector of $\alpha$. It works the same way for the sleep equation.
C.2 Derivation of the difference equations for initial values in the generalized model

To derive the difference equations for the level of performance at the onset of wakefulness, we begin with Eq. (1.3.18) and substitute into the left-hand side the solution, Eq. (C.1-3), evaluated at the beginning of wakefulness \( t_n+1 \):

\[
\begin{bmatrix}
p_{n+1}(t_{n+1}) \\
u_{n+1}(t_{n+1})
\end{bmatrix} = \begin{bmatrix}
q_n(t_{n+1}) \\
v_n(t_{n+1}) + \delta
\end{bmatrix}
= \Phi_n(t_{n+1}) \begin{bmatrix}
q_n(t_n + W_n) \\
v_n(t_n + W_n)
\end{bmatrix} + \Theta_n(t_{n+1}) + \begin{bmatrix}
0 \\
\delta
\end{bmatrix}.
\] (C.2-1)

By using Eq. (1.3.17) we can substitute the solution, Eq. (C.1-1), evaluated at the beginning of sleep, \( t_n + W_n \), to obtain the desired result where \( p_{n+1}(t_{n+1}) \) and \( u_{n+1}(t_{n+1}) \) are now in terms of \( p_n(t_n) \) and \( u_n(t_n) \):

\[
\begin{bmatrix}
p_{n+1}(t_{n+1}) \\
u_{n+1}(t_{n+1})
\end{bmatrix} = \Phi_n(t_{n+1}) \begin{bmatrix}
p_n(t_n + W_n) \\
u_n(t_n + W_n) - \delta
\end{bmatrix} + \Theta_n(t_{n+1}) + \begin{bmatrix}
0 \\
\delta
\end{bmatrix}
= \Phi_n(t_{n+1}) \begin{bmatrix}
p_n(t_n + W_n) \\
u_n(t_n + W_n)
\end{bmatrix} + \Theta_n(t_{n+1}) + (I - \Phi_n(t_{n+1})) \begin{bmatrix}
0 \\
\delta
\end{bmatrix}
= \Phi_n(t_{n+1}) \Psi_n(t_n + W_n) \begin{bmatrix}
p_n(t_n) \\
u_n(t_n)
\end{bmatrix} + F_n,
\] (C.2-2)

where

\[
F_n = \Phi_n(t_{n+1}) \Omega_n(t_n + W_n) + \Theta_n(t_{n+1}) + (I - \Phi_n(t_{n+1})) \begin{bmatrix}
0 \\
\delta
\end{bmatrix}.
\] (C.2-3)

Similarly, we can derive the difference equations for the level of performance at the onset of sleep:

\[
\begin{bmatrix}
q_{n+1}(t_{n+1} + W_{n+1}) \\
v_{n+1}(t_{n+1} + W_{n+1})
\end{bmatrix} = \Psi_{n+1}(t_{n+1} + W_{n+1}) \Phi_n(t_{n+1}) \begin{bmatrix}
q_n(t_n + W_n) \\
v_n(t_n + W_n)
\end{bmatrix} + G_n,
\] (C.2-4)

where

\[
G_n = \Psi_{n+1}(t_{n+1} + W_{n+1}) \Theta_n(t_{n+1}) + \Omega_n(t_{n+1} + W_{n+1}) - [I - \Psi_{n+1}(t_{n+1} + W_{n+1})] \begin{bmatrix}
0 \\
\delta
\end{bmatrix}.
\] (C.2-5)

C.3 Closed form solution in total sleep deprivation for the ETPM

Recall that the general form of the ETPM case of the MTPM was formulated by setting the parameters \( \alpha_{2,1} \), \( \alpha_{2,2} \) and \( \sigma_{2,1} \) to zero in Eqs. (1.3.23) and (1.3.24). The corresponding
performance equations at the onset of wake, given in Eqs. (1.3.25), at total sleep deprivation
\( W = T \) are of the form:

\[
\begin{bmatrix}
  p_{n+1}(t_{n+1}) \\
  u_{n+1}(t_{n+1})
\end{bmatrix}
= \begin{bmatrix}
  e^{\alpha_1 W} & h_1(W = T) \\
  0 & 1
\end{bmatrix}
\begin{bmatrix}
  p_n(t_n) \\
  u_n(t_n)
\end{bmatrix}
+ \begin{bmatrix}
  F_1(W = T) \\
  F_2(W = T)
\end{bmatrix},
\]

(C.3-1)

where \( F_1(W = T) \) and \( F_2(W = T) \) are constants, and the initial conditions \( p_0(t_0) \) and \( u_0(t_0) \) are presumed given. Here, the closed form for \( u_{n+1}(t_{n+1}) \) can be written as follows:

\[
u_n(t_n) = n F_2(W = T) + u_0(t_0). \tag{C.3-2}
\]

The closed form for \( p_{n+1}(t_{n+1}) \) can also be determined. Let us first assume the form of the solution:

\[
p_n(t_n) = p_n^H + p_n^N, \tag{C.3-3}
\]

where \( p_n^H \) is the solution of the corresponding homogeneous equation and \( p_n^N \) is the particular solution of the nonhomogeneous equation. The homogeneous solution is of the form:

\[
p_n^H = C (e^{\alpha_1 W})^n, \tag{C.3-4}
\]

where \( C \) is a constant determined from the initial condition \( p_0(t_0) \). We will assume the particular solution takes the form:

\[
p_n^N = nA + B. \tag{C.3-5}
\]

By substitution of Eqs. (C.3-2) and (C.3-5) into Eq. (C.3-1) for \( p_{n+1}(t_{n+1}) \), we obtain:

\[
nA(1 - e^{\alpha_1 W}) + A + B - e^{\alpha_1 W} B = h_1(W = T)u_0(t_0) + F_1(W = T)
+ nh_1(W = T)F_2(W = T). \tag{C.3-6}
\]

Now by comparing constants and coefficients of \( n \) on the right and left-hand side of Eq. (C.3-6) we can determine both \( A \) and \( B \):

\[
A = \frac{h_1(W = T)}{1 - e^{\alpha_1 W}} F_2(W = T), \tag{C.3-7}
\]

\[
B = \frac{1}{1 - e^{\alpha_1 W}} \left( h_1(W = T)u_0(t_0) + F_1(W = T) - A \right). \tag{C.3-8}
\]

We can also determine the constant \( C \) by setting \( n = 0 \) in Eq. (C.3-3) using Eqs. (C.3-4) and (C.3-5):

\[
C = p_0(t_0) - B. \tag{C.3-9}
\]
Substitution of Eqs. (C.3-4) and (C.3-5) into Eq. (C.3-3), with Eqs. (C.3-7), (C.3-8) and (C.3-9), gives the closed form for \( p_n(t_n) \):

\[
p_n(t_n) = \left( p_0(t_0) - \frac{1}{1 - e^{\alpha_1 t}} (h_1(W = T)u_0(t_0) + F_1(W = T) - A) \right) (e^{\alpha_1 t})^n
\]

\[
+ n \frac{h_1(W = T)}{1 - e^{\alpha_1 t}} F_2(W = T) + \frac{1}{1 - e^{\alpha_1 t}} (h_1 u_0(t_0) + F_1(W = T) - A).
\] (C.3-10)

### C.4 Analytical solutions for the MTPM within days

Using Eqs. (C.1-9) and (C.1-10) we can explicitly write the matrices of Eqs. (C.1-5) and (C.1-6):

\[
\Psi_n(t) = \Psi_n(t)\Psi_n^{-1}(t_n),
\]

\[
= \begin{bmatrix}
  x_1e^{\lambda_1 t} & x_2e^{\lambda_2 t} \\
  x_1e^{\lambda_1 (t_n)} & x_2e^{\lambda_2 (t_n)}
\end{bmatrix}^{-1}
\]

\[
= \begin{bmatrix}
  x_1e^{\lambda_1 (t-t_n)} & x_2e^{\lambda_2 (t-t_n)} \\
  x_1 & x_2
\end{bmatrix}^{-1}
\] (C.4-1)

\[
\Phi_n(t) = \Phi_n(t)\Phi_n^{-1}(t_n + W_n),
\]

\[
= \begin{bmatrix}
  x_3e^{\lambda_3 t} & x_4e^{\lambda_4 t} \\
  x_3e^{\lambda_3 (t_n+W_n)} & x_4e^{\lambda_4 (t_n+W_n)}
\end{bmatrix}^{-1}
\]

\[
= \begin{bmatrix}
  x_3e^{\lambda_3 (t-(t_n+W_n))} & x_4e^{\lambda_4 (t-(t_n+W_n))} \\
  x_3 & x_4
\end{bmatrix}^{-1}
\] (C.4-2)

We can also explicitly write Eqs. (C.1-2) and (C.1-4) for the MTPM:

\[
\Omega_n(t) = \int_{t_n}^{t} \Psi_n(t)\Psi_n^{-1}(s) \begin{bmatrix}
  \beta_1(s) \\
  \beta_2(s)
\end{bmatrix} ds,
\]

\[
= \frac{1}{(x_{1,1}x_{2,2}-x_{1,2}x_{2,1})} \begin{bmatrix}
  x_{1,1}e^{\lambda_1 t} & x_{2,1}e^{\lambda_2 t} \\
  x_{1,2}e^{\lambda_1 t} & x_{2,2}e^{\lambda_2 t}
\end{bmatrix}
\]

\[
\times \begin{bmatrix}
  x_{2,2} \int_{t_n}^{t} e^{\lambda_1 s} \beta_1(s) ds - x_{2,1} \int_{t_n}^{t} e^{\lambda_1 s} \beta_2(s) ds \\
  -x_{1,2} \int_{t_n}^{t} e^{\lambda_2 s} \beta_1(s) ds + x_{1,1} \int_{t_n}^{t} e^{\lambda_2 s} \beta_2(s) ds
\end{bmatrix}
\] (C.4-3)

and similarly \( \Theta_n(t) \) can be derived:

\[
\Theta_n(t) = \int_{t_n+W_n}^{t} \Phi_n(t)\Phi_n^{-1}(s) \begin{bmatrix}
  \gamma_1(s) \\
  \gamma_2(s)
\end{bmatrix} ds,
\]

\[
= \frac{1}{(x_{3,1}x_{4,2}-x_{3,2}x_{4,1})} \begin{bmatrix}
  x_{3,1}e^{\lambda_3 t} & x_{4,1}e^{\lambda_4 t} \\
  x_{3,2}e^{\lambda_3 t} & x_{4,2}e^{\lambda_4 t}
\end{bmatrix}
\]

\[
\times \begin{bmatrix}
  x_{4,2} \int_{t_n+W_n}^{t} e^{\lambda_3 s} \gamma_1(s) ds - x_{4,1} \int_{t_n+W_n}^{t} e^{\lambda_3 s} \gamma_2(s) ds \\
  -x_{3,2} \int_{t_n+W_n}^{t} e^{\lambda_4 s} \gamma_1(s) ds + x_{3,1} \int_{t_n+W_n}^{t} e^{\lambda_4 s} \gamma_2(s) ds
\end{bmatrix}
\] (C.4-4)
By assuming the form of $\beta_i(t)$ and $\gamma_i(t)$ shown in Eqs. (1.6.1) and (1.6.2):

$$
\begin{bmatrix}
\beta_1(s) \\
\beta_2(s)
\end{bmatrix} = \left[ \kappa \sum_{k=1}^{5} A_k \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) + \mu \right] 
$$

(C.4-5)

$$
\begin{bmatrix}
\gamma_1(s) \\
\gamma_2(s)
\end{bmatrix} = \left[ \kappa \sum_{k=1}^{5} A_k \sin \left( \frac{2k\pi}{\tau} (s - \phi) \right) + \mu \right] 
$$

(C.4-6)

where we have used Eq. 1.1.5 for the circadian rhythm, the definite integrals in Eqs. (C.4-3) and (C.4-4) can be analytically solved by the method of integration by parts (see the derivations for the gTPM in Appendix A.5). Similar to the results of the gTPM we can easily write the complete time-dependent solutions $[p_n(t) u_n(t)]$ and $[q_n(t) v_n(t)]$:

$$
\begin{bmatrix}
p_n(t) \\
u_n(t)
\end{bmatrix} = \begin{bmatrix}
x_1 e^{\lambda_1(t-t_n)} \\
x_2 e^{\lambda_2(t-t_n)}
\end{bmatrix} \begin{bmatrix}
x_1 & x_2
\end{bmatrix}^{-1} \begin{bmatrix}
p_n(t_n) \\
u_n(t_n)
\end{bmatrix} + \frac{1}{(x_1 x_2, 2 - x_1 x_2, 1)} \times 
\begin{bmatrix}
x_1 x_2 e^{\lambda_1 t} \int_{t_n}^{t} e^{-\lambda_1 s} \beta_1(s)ds - x_1 x_2 e^{\lambda_2 t} \int_{t_n}^{t} e^{-\lambda_2 s} \beta_1(s)ds \\
x_1 x_2 e^{\lambda_1 t} \int_{t_n}^{t} e^{-\lambda_1 s} \beta_1(s)ds - x_1 x_2 e^{\lambda_2 t} \int_{t_n}^{t} e^{-\lambda_2 s} \beta_1(s)ds
\end{bmatrix} 
\begin{bmatrix}
x_1 & x_2
\end{bmatrix}^{-1} \begin{bmatrix}
p_n(t_n) \\
u_n(t_n)
\end{bmatrix} 
$$

$$
+ \sum_{i=1}^{2} (-1)^{i+1} \frac{x_{3-i, 2}}{(x_1 x_2, 2 - x_1 x_2, 1)} \xi_i 
\times \left( \kappa \sum_{k=1}^{5} A_k \frac{2k\pi \tau \left( e^{\lambda_i(t-t_n)} \cos \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - \cos \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)}{4k^2 \pi^2 + \lambda_i^2 \pi^2} 
+ \kappa \sum_{k=1}^{5} A_k \frac{\lambda_i \tau^2 \left( e^{\lambda_i(t-t_n)} \sin \left( \frac{2k\pi}{\tau} (t_n - \phi) \right) - \sin \left( \frac{2k\pi}{\tau} (t - \phi) \right) \right)}{4k^2 \pi^2 + \lambda_i^2 \pi^2} 
+ \frac{\mu}{\lambda_i} \left( e^{\lambda_i(t-t_n)} - 1 \right) \right), 
$$

(C.4-7)
\[
\begin{bmatrix}
q_n(t) \\
v_n(t)
\end{bmatrix}
= \begin{bmatrix}
x_3e^{\lambda_3(t-(n+W_n))} \\
x_4e^{\lambda_4(t-(n+W_n))}
\end{bmatrix}
\begin{bmatrix}
x_3 & x_4
\end{bmatrix}^{-1}
\begin{bmatrix}
q_n(t_n+W_n) \\
v_n(t_n+W_n)
\end{bmatrix}
\]
\[
+ \frac{1}{(x_{1,1}x_{2,2}-x_{1,2}x_{2,1})}
\times
\begin{bmatrix}
x_3,1 x_4,2 e^{\lambda_3 t} \int_{t_n+W_n}^{t_n} e^{-\lambda_3 s} \gamma_1(s)ds - x_3,2 x_4,1 e^{\lambda_4 t} \int_{t_n+W_n}^{t_n} e^{-\lambda_4 s} \gamma_1(s)ds \\
x_3,2 x_4,2 e^{\lambda_3 t} \int_{t_n+W_n}^{t_n} e^{-\lambda_3 s} \gamma_1(s)ds - x_3,2 x_4,2 e^{\lambda_4 t} \int_{t_n+W_n}^{t_n} e^{-\lambda_4 s} \gamma_1(s)ds
\end{bmatrix}
\]
\[
= \begin{bmatrix}
x_3e^{\lambda_3(t-(n+W_n))} \\
x_4e^{\lambda_4(t-(n+W_n))}
\end{bmatrix}
\begin{bmatrix}
x_3 & x_4
\end{bmatrix}^{-1}
\begin{bmatrix}
q_n(t_n+W_n) \\
v_n(t_n+W_n)
\end{bmatrix}
\]
\[
+ \sum_{i=3}^{4} (-1)^{i+1} \frac{x_{7-i,2}}{(x_{3,1} x_{4,2}-x_{3,2} x_{4,1})} x_i
\times
\left( \kappa \sum_{k=1}^{5} A_k \frac{2k \pi \tau \left( e^{\lambda_i (t-t_n)} \cos \left( \frac{2k \pi}{\tau} (t_n+W_n-\phi) \right) - \cos \left( \frac{2k \pi}{\tau} (t-\phi) \right) \right)}{4k^2 \pi^2 + \lambda_i^2 \tau^2}
\right.
\]
\[
+ \kappa \sum_{k=1}^{5} A_k \frac{\lambda_i \tau^2 \left( e^{\lambda_i (t-(n+W_n))} \sin \left( \frac{2k \pi}{\tau} (t_n+W_n-\phi) \right) - \sin \left( \frac{2k \pi}{\tau} (t-\phi) \right) \right)}{4k^2 \pi^2 + \lambda_i^2 \tau^2}
\]
\[
+ \frac{\mu}{\lambda_i} \left( e^{\lambda_i (t-(n+W_n))} - 1 \right),
\]
\] \hspace{1cm} (C.4-8)

**C.5 Proof that eigenvalues of shifted matrices are identical**

A shifted matrix product is of the form:

\[
A_0 A_1 A_2 \ldots A_{m-1} A_m \quad \text{and} \quad A_1 A_2 \ldots A_{m-1} A_m A_0,
\]
\] \hspace{1cm} (C.5-1)

where a new matrix product is formed by moving one matrix (e.g., \(A_j\)) from the front of the matrix product to the end of the matrix product (or visa versa). Notice that repeating this operation \(m\)-times would result in the original matrix product.

Let us now consider the matrix product \(\prod_{i=1}^{m} A_i\) in the characteristic equation:

\[
\det \left( \prod_{i=1}^{m} A_i - \lambda I \right) = 0.
\] \hspace{1cm} (C.5-2)

If the \(A_i\)'s are 2x2 matrices, then the eigenvalues \(\lambda\) from Eq. (C.5-2) can be found from the roots of the quadratic equation:

\[
\det \left( \prod_{i=1}^{m} A_i \right) - \lambda \left( \text{Tr} \left( \prod_{i=1}^{m} A_i \right) \right) + \lambda^2 = 0.
\] \hspace{1cm} (C.5-3)
Expanding the first term from Eq. (C.5-3) we see that

$$\det\left(\prod_{i=1}^{m} A_i\right) = \det(A_1A_2A_3...A_m).$$  \hspace{1cm} (C.5-4)

Using the rules of determinants, we can rewrite Eq. (C.5-4):

$$\det\left(\prod_{i=1}^{m} A_i\right) = \det A_1 \det A_2 \det A_3...\det A_m,$$

$$= \left(\prod_{i=1}^{m} \det(A_i)\right).$$  \hspace{1cm} (C.5-5)

Looking at the trace function in Eq. (C.5-3), we know by definition that \(\text{Tr}(AB) = \text{Tr}(BA)\) and that \(\text{Tr}(ABC) = \text{Tr}(CAB)\) for square matrices. This cyclic property of the trace function is expandable up to \(m\) matrices:

$$\text{Tr}\left(\prod_{i=1}^{m} A_i\right) = \text{Tr}(A_1A_2A_3...A_m)$$

$$= \text{Tr}(A_mA_1A_2...A_{m-1})$$

$$= \text{Tr}(A_{m-1}A_mA_1...A_{m-2})$$

$$\vdots$$

$$= \text{Tr}(A_2A_3...A_mA_1).$$  \hspace{1cm} (C.5-6)

By virtue of both Eq. (C.5-5) and Eq. (C.5-6), Eq. (C.5-3) becomes:

$$\left(\prod_{i=1}^{m} \det(A_i)\right) - \lambda(\text{Tr}\left(\prod_{i=1}^{m} A_i\right)) + \lambda^2 = 0.$$  \hspace{1cm} (C.5-7)

Because of the communicative property of multiplication of the determinants in Eq. (C.5-5) and the cyclic property of the trace function in Eq. (C.5-6), we conclude that the eigenvalues \(\lambda\) of Eq. (C.5-7) are identical regardless of the shift in the product order of the matrices.

### C.6 Proof that determinants of shifted matrices are identical

Consider the matrix product \(\prod_{i=1}^{m} A_i\) in the determinant:

$$\det\left(I - \prod_{i=1}^{m} A_i\right).$$  \hspace{1cm} (C.6-1)
If the $A_i$'s are 2x2 matrices, then Eq. (C.6-1) can be written as:

$$\det \left( \prod_{i=1}^{m} A_i \right) - \left( \text{Tr} \left( \prod_{i=1}^{m} A_i \right) \right) + 1.$$  \hspace{1cm} (C.6-2)

By the results in Appendix C.5 (i.e., the communicative property of multiplication of the determinants and the cyclic property of the trace function) we find that Eq. (C.6-2) is invariant to shifted matrices.

C.7 Oscillatory condition for the generalized model

Let’s consider the characteristic equation for the eigenvalues of the $\alpha$ matrix of Eq. (1.3.23):

$$\det \left( \begin{bmatrix} \alpha_{1,1} & \alpha_{1,2} \\ \alpha_{2,1} & \alpha_{2,2} \end{bmatrix} - \lambda I \right) =$$

$$\left( \begin{array}{c} \alpha_{1,1} - \lambda \\ \alpha_{2,1} - \lambda \end{array} \right) \left( \begin{array}{c} \alpha_{2,2} - \lambda \\ \alpha_{1,2} \end{array} \right) - \alpha_{2,1} \alpha_{1,2} =$$

$$\lambda^2 - (\alpha_{1,1} + \alpha_{2,2}) \lambda + (\alpha_{1,1} \alpha_{2,2} - \alpha_{2,1} \alpha_{1,2}) = 0.$$  \hspace{1cm} (C.7-1)

Using the quadratic formula we find the eigenvalues $\lambda_1$ and $\lambda_2$:

$$\lambda_{1,2} = \frac{1}{2} \left( (\alpha_{1,1} + \alpha_{2,2}) \pm \sqrt{(\alpha_{1,1} + \alpha_{2,2})^2 - 4(\alpha_{1,1} \alpha_{2,2} - \alpha_{2,1} \alpha_{1,2})} \right).$$  \hspace{1cm} (C.7-2)

The eigenvalues are complex conjugate $\lambda_{1,2} = a \pm i\omega$ when the term under the square root is negative:

$$(\alpha_{1,1} + \alpha_{2,2})^2 < 4(\alpha_{1,1} \alpha_{2,2} - \alpha_{2,1} \alpha_{1,2}).$$  \hspace{1cm} (C.7-3)

The fundamental solution to the system of Eqs. (1.3.23) with complex eigenvalues is given in Eq. (C.1-9). It is useful to express the exponential terms in Eq. (C.1-9), with complex exponents as sines and cosines using Euler’s formula Euler (1748):

$$e^{(a + i\omega)t} = e^{at} (\cos(\omega t) + i \sin(\omega t)).$$  \hspace{1cm} (C.7-4)

From Eq. (C.7-4) we see that the angular frequency $\omega$ of the oscillations produced is given by the imaginary part of the eigenvalue:

$$\omega = \frac{1}{2} \sqrt{[(\alpha_{1,1} + \alpha_{2,2})^2 - 4(\alpha_{1,1} \alpha_{2,2} - \alpha_{2,1} \alpha_{1,2})]}.$$  \hspace{1cm} (C.7-5)

Likewise, the growth or decay rate of the amplitude is given by the real part of the eigenvalue:

$$a = \frac{(\alpha_{1,1} + \alpha_{2,2})}{2}.$$  \hspace{1cm} (C.7-6)
By assuming the amplitude remains constant ($\alpha_{1,1} = -\alpha_{2,2}$) we can simplify Eq. (C.7-5) to obtain an expression for the period of oscillation:

$$T = \frac{2\pi}{\sqrt{|\alpha_{1,1}^2 + \alpha_{2,1}\alpha_{1,2}|}}, \quad (C.7-7)$$

where $-\alpha_{1,1}^2 < \alpha_{2,1}\alpha_{1,2} < 0$ must be true for oscillations to occur during wakefulness. Conditions for oscillatory behavior during sleep are found analogously.
Appendix D

Proofs for the MTPM for repeating wake/sleep schedules

D.1 Derivation of the difference equations for initial values in the generalized model for repeating wake/sleep schedules

To derive the difference equations for the level of performance at the onset of wakefulness for every repeating $m$th day, we begin by extending Eq. (1.3.18) to reflect a repeating wake/sleep schedule:

$$
\begin{bmatrix}
  p_{n+m}(t_n + m + W_{n+m}) \\
  u_{n+m}(t_n + m + W_{n+m}) \\
  q_{n+m-1}(t_n) \\
  v_{n+m-1}(t_n)
\end{bmatrix}
= \Phi_{n+m-1}(t_n)
$$

$$
\begin{bmatrix}
  q_{n+m}(t_n + m + W_{n+m}) \\
  v_{n+m}(t_n + m + W_{n+m} + \delta)
\end{bmatrix},
$$

(D.1-1)

$$
\begin{bmatrix}
  q_{n+m-1}(t_n) \\
  v_{n+m-1}(t_n)
\end{bmatrix}
= \Phi_{n+m-1}(t_n)
$$

(D.1-2)

We now substitute into the left-hand side of Eq. (D.1-2) the solution, Eq. (C.1-3), evaluated at the beginning of wakefulness $t_{n+m}$:

$$
\begin{bmatrix}
  p_{n+m}(t_n + m) \\
  u_{n+m}(t_n + m)
\end{bmatrix}
= \Phi_{n+m-1}(t_n)
$$

$$
\begin{bmatrix}
  q_{n+m-1}(t_n + m) \\
  v_{n+m-1}(t_n + m) + \delta
\end{bmatrix},
$$

(D.1-3)

By using Eq. (D.1-1) we can substitute the solution, Eq. (C.1-1), evaluated at the beginning of sleep, $t_{n+m-1} + W_{n+m-1}$, to obtain the result where $p_{n+m}(t_n + m)$ and $u_{n+m}(t_n + m)$ are in
terms of \( p_{n+m-1}(t_{n+m-1}) \) and \( u_{n+m-1}(t_{n+m-1}) \):

\[
\begin{bmatrix}
p_{n+m-1}(t_{n+m}) \\
u_{n+m-1}(t_{n+m})
\end{bmatrix}
= \Phi_{n+m-1}(t_{n+m})
\begin{bmatrix}
p_{n+m-1}(t_{n+m-1} + W_{n+m-1}) \\
u_{n+m-1}(t_{n+m-1} + W_{n+m-1}) - \delta
\end{bmatrix}
+ \Theta_{n+m-1}(t_{n+m})
+ (I - \Phi_{n+m-1}(t_{n+m}))
\begin{bmatrix}
0 \\
\delta
\end{bmatrix}
\]

= \Phi_{n+m-1}(t_{n+m})
\begin{bmatrix}
p_{n+m-1}(t_{n+m-1} + W_{n+m-1}) \\
u_{n+m-1}(t_{n+m-1} + W_{n+m-1})
\end{bmatrix}
+ \Theta_{n+m-1}(t_{n+m})
+ (I - \Phi_{n+m-1}(t_{n+m}))
\begin{bmatrix}
0 \\
\delta
\end{bmatrix}
\]

= \Phi_{n+m-1}(t_{n+m}) \Psi_{n+m-1}(t_{n+m-1} + W_{n+m-1})
\begin{bmatrix}
p_{n+m-1}(t_{n+m-1}) \\
u_{n+m-1}(t_{n+m-1})
\end{bmatrix}
+ F_{n+m-1}.

(D.1-4)

where

\[
F_{n+m-1} = \Phi_{n+m-1}(t_{n+m}) \Omega_{n+m-1}(t_{n+m-1} + W_{n+m-1}) + \Theta_{n+m-1}(t_{n+m})
+ (I - \Phi_{n+m-1}(t_{n+m}))
\begin{bmatrix}
0 \\
\delta
\end{bmatrix}.
\]

(D.1-5)

Assuming \( m > 1 \) let us again use Eq. (D.1-2) and follow similar steps to obtain the result

where \( p_{n+m}(t_{n+m}) \) and \( u_{n+m}(t_{n+m}) \) of Eq. (D.1-4) are now in terms of \( p_{n+m-2}(t_{n+m-2}) \) and \( u_{n+m-2}(t_{n+m-2}) \):

\[
\begin{bmatrix}
p_{n+m}(t_{n+m}) \\
u_{n+m}(t_{n+m})
\end{bmatrix}
= \Phi_{n+m-1}(t_{n+m}) \Psi_{n+m-1}(t_{n+m-1} + W_{n+m-1})
\begin{bmatrix}
p_{n+m-1}(t_{n+m-1}) \\
u_{n+m-1}(t_{n+m-1})
\end{bmatrix}
+ F_{n+m-1}
\]

= \Phi_{n+m-1}(t_{n+m}) \Psi_{n+m-1}(t_{n+m-1} + W_{n+m-1})
\begin{bmatrix}
p_{n+m-2}(t_{n+m-2}) \\
u_{n+m-2}(t_{n+m-2}) + \delta
\end{bmatrix}
+ F_{n+m-1}
\]

= \Phi_{n+m-1}(t_{n+m}) \Psi_{n+m-1}(t_{n+m-1} + W_{n+m-1})
\begin{bmatrix}
p_{n+m-2}(t_{n+m-2}) + \delta \\
u_{n+m-2}(t_{n+m-2} + W_{n+m-2})
\end{bmatrix}
+ (I - \Phi_{n+m-2}(t_{n+m-1}))
\begin{bmatrix}
0 \\
\delta
\end{bmatrix} + F_{n+m-1}.

(D.1-6)
Substituting the solution Eq. (C.1-1) evaluated at the beginning of sleep \( t_{n+m-2} + W_{n+m-2} \), we obtain the result where \( p_{n+m}(t_{n+m}) \) and \( u_{n+m}(t_{n+m}) \) are in terms of \( p_{n+m-2}(t_{n+m-2}) \) and \( u_{n+m-2}(t_{n+m-2}) \):

\[
\begin{bmatrix}
  p_{n+m}(t_{n+m}) \\
  u_{n+m}(t_{n+m})
\end{bmatrix} = \Phi_{n+m-1}(t_{n+m}) \Psi_{n+m-1}(t_{n+m-1} + W_{n+m-1}) \times (\Phi_{n+m-2}(t_{n+m-1}) (\Psi_{n+m-2}(t_{n+m-2} + W_{n+m-2}) \\
\times \begin{bmatrix}
  p_{n+m-2}(t_{n+m-2}) \\
  u_{n+m-2}(t_{n+m-2})
\end{bmatrix}
\times \Omega_{n+m-2}(t_{n+m-2} + W_{n+m-2}) + \Theta_{n+m-2}(t_{n+m-1}) + (I - \Phi_{n+m-2}(t_{n+m-1})) \begin{bmatrix}
  0 \\
  \delta
\end{bmatrix}
\right) + F_{n+m-1},
\]

where \( F_{n+m-1} \) is from Eq. (D.1-4) and

\[
F_{n+m-2} = \Phi_{n+m-2}(t_{n+m-1}) \Omega_{n+m-2}(t_{n+m-2} + W_{n+m-2}) + \Theta_{n+m-2}(t_{n+m-1}) + (I - \Phi_{n+m-2}(t_{n+m-1})) \begin{bmatrix}
  0 \\
  \delta
\end{bmatrix}.
\]

By continuing this process \( m \) times we can arrive at the desired results where \( p_{n+m}(t_{n+m}) \) and \( u_{n+m}(t_{n+m}) \) are expressed in terms of \( p_n(t_n) \) and \( u_n(t_n) \):

\[
\begin{bmatrix}
  p_{n+m}(t_{n+m}) \\
  u_{n+m}(t_{n+m})
\end{bmatrix} = \prod_{k=1}^{m} \Phi_{n+m-k}(t_{n+m-k+1}) \Psi_{n+m-k}(t_{n+m-k} + W_{n+m-k}) \begin{bmatrix}
  p_n(t_n) \\
  u_n(t_n)
\end{bmatrix} + \tilde{F}_n,
\]

where

\[
\tilde{F}_n = \sum_{j=1}^{m-1} \left( \prod_{k=1}^{j} \Phi_{n+m-k}(t_{n+m-k+1}) \Psi_{n+m-k}(t_{n+m-k} + W_{n+m-k}) \right) F_{n+m-j-1} + F_{n+m-1}.
\]

Similarly, we can derive the difference equations for the level of performance at the onset of sleep:

\[
\begin{bmatrix}
  q_{n+m}(t_{n+m} + W_{n+m}) \\
  v_{n+m}(t_{n+m} + W_{n+m})
\end{bmatrix} = \prod_{k=1}^{m} \Psi_{n+m-k+1}(t_{n+m-k+1} + W_{n+m-k+1}) \Phi_{n+m-k}(t_{n+m-k+1} + W_{n+m-k+1}) \begin{bmatrix}
  q_n(t_n + W_n) \\
  v_n(t_n + W_n)
\end{bmatrix} + \tilde{G}_n,
\]

(D.1-11)
where
\[
\tilde{G}_n = \sum_{j=1}^{m-1} \left( \prod_{k=1}^{j} \Psi_{n+m-k+1} (t_{n+m-k+1} + W_{n+m-k+1}) \Phi_{n+m-k} (t_{n+m-k+1}) \right) G_{n+m-j-1} + G_{n+m-1} 
\]  
(D.1-12)

D.2 Producing terms from Eqs. 2.2.3 and 2.2.4

As examples for producing terms from Eqs. 2.2.3 and 2.2.4, we explicitly write the first 3 cases \((m = 1, 2, 3)\):

For \(m = 1\),
\[
\begin{align*}
 h_1 &= h_{1,1}, \\
 h_2 &= h_{2,1}.
\end{align*}
\]

For \(m = 2\),
\[
\begin{align*}
 h_1 &= e^{\alpha_1 W_1} e^{\sigma_1 (T-W_1)} h_{1,2} + h_{1,1} e^{\alpha_2 W_2} e^{\sigma_2 (T-W_2)}, \\
 h_2 &= e^{\sigma_1 (T-W_1)} e^{\alpha_1 W_1} h_{2,2} + h_{2,1} e^{\sigma_2 (T-W_2)} e^{\alpha_2 W_2}.
\end{align*}
\]

For \(m = 3\)
\[
\begin{align*}
 h_1 &= e^{\alpha_1 W_1} e^{\sigma_1 (T-W_1)} e^{\alpha_1 W_2} e^{\sigma_1 (T-W_2)} h_{1,3} \\
 &\quad + \left( e^{\alpha_1 W_1} e^{\sigma_1 (T-W_1)} h_{1,2} + h_{1,1} e^{\alpha_2 W_2} e^{\sigma_2 (T-W_2)} \right) e^{\alpha_2 W_3} e^{\sigma_2 (T-W_3)}, \\
 h_2 &= e^{\sigma_1 (T-W_1)} e^{\alpha_1 W_1} e^{\sigma_1 (T-W_2)} e^{\alpha_1 W_2} h_{2,3} \\
 &\quad + \left( e^{\sigma_1 (T-W_1)} e^{\alpha_1 W_1} h_{2,2} + h_{2,1} e^{\sigma_2 (T-W_2)} e^{\alpha_2 W_2} \right) e^{\sigma_2 (T-W_3)} e^{\alpha_2 W_3},
\end{align*}
\]

where the \(h_{1,k}\)’s and \(h_{2,k}\)’s are determined from Eqs. (2.2.5) and (2.2.6), respectively.
Appendix E

Proof for the MTPM for split sleep schedules

E.1 Derivation of the difference equations for initial values in the generalized model for any set of daily wake/sleep episodes

In this section we derive the difference equations which predict the first (e.g., the $0^{\text{th}}$) daily onset of wakefulness and the onset of sleep for the generalized model for any set of daily wake/sleep episodes. Let us begin by rewriting the analytical solutions Eqs. (C.1-1) and (C.1-3) using generalized wake/sleep episodes $k_n \in \{0, 1, 2, \ldots, k_n^*\}$:

\[
\begin{bmatrix}
    p_{n,k_n}(t) \\
    u_{n,k_n}(t)
\end{bmatrix}
= \Psi_{n,k_n}(t)
\begin{bmatrix}
    p_{n,k_n}(t_{n,k_n}) \\
    u_{n,k_n}(t_{n,k_n})
\end{bmatrix}
+ \Omega_{n,k_n}(t),
\]

where

\[
\Omega_{n,k_n}(t) = \int_{t_{n,k_n}}^{t} \Psi_{n,k_n}(s)\Psi_{n,k_n}^{-1}(s)\begin{bmatrix}
    \beta_1(s) \\
    \beta_2(s)
\end{bmatrix}ds,
\]

for all $t \in [t_{n,k_n}, t_{n,k_n} + W_{n,k_n}]$ and

\[
\begin{bmatrix}
    q_{n,k_n}(t) \\
    v_{n,k_n}(t)
\end{bmatrix}
= \Phi_{n,k_n}(t)
\begin{bmatrix}
    q_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \\
    v_{n,k_n}(t_{n,k_n} + W_{n,k_n})
\end{bmatrix}
+ \Theta_{n,k_n}(t),
\]

where

\[
\Theta_{n,k_n}(t) = \int_{t_{n,k_n} + W_{n,k_n}}^{t} \Phi_{n,k_n}(s)\Phi_{n,k_n}^{-1}(s)\begin{bmatrix}
    \gamma_1(s) \\
    \gamma_2(s)
\end{bmatrix}ds,
\]

for all $t \in [t_{n,k_n} + W_{n,k_n}, t_{n+1,k_n}]$. Here

\[
\Psi_{n,k_n}(t) = \Psi_{n,k_n}(t_{n,k_n})\Psi_{n,k_n}^{-1}(t_{n,k_n}),
\]

\[
\Phi_{n,k_n}(t) = \Phi_{n,k_n}(t_{n,k_n})\Phi_{n,k_n}^{-1}(t_{n,k_n} + W_{n,k_n}),
\]
are the principal matrix solutions for each of the $k_n^* + 1$ wake/sleep episodes within the $n^{th}$ day, and $\Psi_{n,k_n}(t)$ and $\Phi_{n,k_n}(t)$ are the fundamental solutions of the homogeneous part of Eqs. (1.3.23) and (1.3.24), respectively (see analogous derivation in Appendix C.1).

To derive the difference equations for the level of performance at the onset of wakefulness for the $0^{th}$ wake/sleep cycle, we begin with Eq. (3.1.5) and substitute into the left-hand side the solution Eq. (E.1-3), evaluated at the end of the $k_n^*$ sleep episode $t_{n,k_n^*} + T_{n,k_n^*}$:

$$
\begin{bmatrix}
    p_{n+1,0}(t_{n+1,0}) \\
    u_{n+1,0}(t_{n+1,0})
\end{bmatrix}
= \begin{bmatrix}
    q_{n,k_n^*} (t_{n,k_n^*} + T_{n,k_n^*}) \\
    v_{n,k_n^*} (t_{n,k_n^*} + T_{n,k_n^*}) + \delta
\end{bmatrix}
= \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})
\begin{bmatrix}
    q_{n,k_n^*} (t_{n,k_n^*} + W_{n,k_n^*}) \\
    v_{n,k_n^*} (t_{n,k_n^*} + W_{n,k_n^*})
\end{bmatrix}
+ \Theta_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})
\begin{bmatrix}
    0 \\
    \delta
\end{bmatrix},
$$

where we have used $t_{n+1,0} = t_{n,k_n^*} + T_{n,k_n^*}$. Note also that the $\sum_{k_n=0}^{k_n^*} T_{n,k_n} = T_n$, where $T_n$ is the duration of the $n^{th}$ day. By using Eq. (3.1.3) we can substitute Eq. (E.1-1) evaluated at the beginning of the $k_n^*$ sleep episode $t_{n,k_n^*} + W_{n,k_n^*}$, to obtain the result where $p_{n+1,0}(t_{n+1,0})$ and $u_{n+1,0}(t_{n+1,0})$ are now in terms of $p_{n,k_n^*}(t_{n,k_n^*})$ and $u_{n,k_n^*}(t_{n,k_n^*})$:

$$
\begin{bmatrix}
    p_{n+1,0}(t_{n+1,0}) \\
    u_{n+1,0}(t_{n+1,0})
\end{bmatrix}
= \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})
\begin{bmatrix}
    p_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \\
    u_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) - \delta
\end{bmatrix}
+ \Theta_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})
\begin{bmatrix}
    0 \\
    \delta
\end{bmatrix}
= \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})
\begin{bmatrix}
    p_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \\
    u_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*})
\end{bmatrix}
+ \Theta_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})
\begin{bmatrix}
    0 \\
    \delta
\end{bmatrix}
+ (I - \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*}))
\begin{bmatrix}
    0 \\
    \delta
\end{bmatrix}
= \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})\Psi_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*})
\begin{bmatrix}
    p_{n,k_n^*}(t_{n,k_n^*}) \\
    u_{n,k_n^*}(t_{n,k_n^*})
\end{bmatrix}
+ \Theta_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})
\begin{bmatrix}
    0 \\
    \delta
\end{bmatrix},
$$

(E.1-7)

where

$$
F_{n,k_n^*} = \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})\Omega_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*})
+ \Theta_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})
\begin{bmatrix}
    0 \\
    \delta
\end{bmatrix},
$$

(E.1-8)

Assuming $k_n^* > 0$, we continue by substitution of Eq. (3.1.4) into Eq. (E.1-7) and follow
analogous steps used to produce Eq. (E.1-7):

\[
\begin{align*}
&= \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})\Psi_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \\
&\times \left[ q_{n,k_n^*-1}(t_{n,k_n^*} + T_{n,k_n^*}) \nu_{n,k_n^*-1}(t_{n,k_n^*} + T_{n,k_n^*}) + \delta \right] + F_{n,k_n^*} \\
&= \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})\Psi_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \\
&\times \left[ \Phi_{n,k_n^*-1}(t_{n,k_n^*} + T_{n,k_n^*}) \left[ \begin{array}{c}
p_{n,k_n^*-1}(t_{n,k_n^*} + W_{n,k_n^*}) \\
u_{n,k_n^*-1}(t_{n,k_n^*} + W_{n,k_n^*}) \end{array} \right] \right] + F_{n,k_n^*} \\
&= \prod_{k=k_n^*}^{k_n} \Phi_{n,k_n}(t_{n,k_n} + T_{n,k_n})\Psi_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \left[ \begin{array}{c}p_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \\
u_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \end{array} \right]
\end{align*}
\]  

(E.1-9)

Again, by using Eq. (3.1.3) we can substitute the solution Eq. (E.1-1) evaluated at the beginning of the \(k_n^* - 1\) sleep episode \(t_{n,k_n^*} + W_{n,k_n^*}\), to obtain the result where \(p_{n+1.0}(t_{n+1.0})\) and \(u_{n+1.0}(t_{n+1.0})\) are now in terms of \(p_{n,k_n^*}(t_{n,k_n^*})\) and \(u_{n,k_n^*}(t_{n,k_n^*})\):

\[
\begin{align*}
&= \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*})\Psi_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \\
&\times \left[ \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*}) \left[ \begin{array}{c}
p_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \\
u_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \end{array} \right] \right] + F_{n,k_n^*} \\
&= \prod_{k=k_n}^{k_n^*} \Phi_{n,k_n}(t_{n,k_n} + T_{n,k_n})\Psi_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \left[ \begin{array}{c}p_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \\
u_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \end{array} \right]
\end{align*}
\]  

(E.1-10)

By continuing this process \(k_n^*\) times we can arrive at the desired results where \(p_{n+1.0}(t_{n+1.0})\) and \(u_{n+1.0}(t_{n+1.0})\) are in terms of \(p_{n,0}(t_{n,0})\) and \(u_{n,0}(t_{n,0})\):

\[
\begin{align*}
&= \prod_{k_n=0}^{k_n^*} \Phi_{n,k_n}(t_{n,k_n} + T_{n,k_n})\Psi_{n,k_n}(t_{n,k_n} + W_{n,k_n}) \left[ \begin{array}{c}p_{n,0}(t_{n,0}) \\
u_{n,0}(t_{n,0}) \end{array} \right] + \tilde{F}_{n,0}.
\end{align*}
\]  

(E.1-11)

where

\[
\tilde{F}_{n,0} = \sum_{j=0}^{k_n^*-1} \left( \prod_{k_n=0}^{k_n^*-k_n} \left[ \Phi_{n,k_n} + T_{n,k_n} \right] \Psi_{n,k_n} + W_{n,k_n^*} \right) F_{n,k_n^* - j - 1} + F_{n,k_n^*}.
\]  

(E.1-12)
The process is similar for derivation of the difference equations for the level of performance at the onset of sleep for the $0^{th}$ wake/sleep cycle. However, because of the complexity in notation let us explicitly show the steps. Here, we begin with Eq. (3.1.3) and substitute into the left-hand side the solution Eq. (E.1-1), evaluated at the end of the $0^{th}$ wake episode $t_{n+1,0} + W_{n+1,0}$:

\[
\begin{bmatrix}
q_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \\
v_{n+1,0}(t_{n+1,0} + W_{n+1,0})
\end{bmatrix}
= \begin{bmatrix}
p_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \\
u_{n+1,0}(t_{n+1,0} + W_{n+1,0})
\end{bmatrix}
- \begin{bmatrix}
0 \\
\delta
\end{bmatrix}
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \begin{bmatrix}
p_{n+1,0}(t_{n+1,0}) \\
u_{n+1,0}(t_{n+1,0})
\end{bmatrix}
+ \Omega_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \begin{bmatrix}
0 \\
\delta
\end{bmatrix}
\]

By using Eq. (3.1.5) we can substitute Eq. (E.1-3) evaluated at the end of the $k_n^*$ sleep episode $t_{n,k_n^*} + T_{n,k_n^*}$, to obtain the result where $q_{n+1,0}(t_{n+1,0} + W_{n+1,0})$ and $v_{n+1,0}(t_{n+1,0} + W_{n+1,0})$ are now in terms of $q_{n,k_n^*} (t_{n,k_n^*} + W_{n,k_n^*})$ and $v_{n,k_n^*} (t_{n,k_n^*} + W_{n,k_n^*})$:

\[
\begin{bmatrix}
q_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \\
v_{n+1,0}(t_{n+1,0} + W_{n+1,0})
\end{bmatrix}
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \begin{bmatrix}
q_{n,k_n^*} (t_{n,k_n^*} + T_{n,k_n^*}) \\
v_{n,k_n^*} (t_{n,k_n^*} + T_{n,k_n^*})
\end{bmatrix}
+ \Omega_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \begin{bmatrix}
0 \\
\delta
\end{bmatrix}
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \begin{bmatrix}
q_{n,k_n^*} (t_{n,k_n^*} + T_{n,k_n^*}) \\
v_{n,k_n^*} (t_{n,k_n^*} + T_{n,k_n^*})
\end{bmatrix}
+ \Omega_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \begin{bmatrix}
0 \\
\delta
\end{bmatrix}
- (I - \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0})) \begin{bmatrix}
0 \\
\delta
\end{bmatrix}
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \Phi_{n,k_n^*} (t_{n,k_n^*} + T_{n,k_n^*})
\times \begin{bmatrix}
q_{n,k_n^*} (t_{n,k_n^*} + W_{n,k_n^*}) \\
v_{n,k_n^*} (t_{n,k_n^*} + W_{n,k_n^*})
\end{bmatrix}
+ G_{n,k_n^*},
\]

where

\[
G_{n,k_n^*} = \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \Phi_{n,k_n^*} (t_{n,k_n^*} + T_{n,k_n^*})
+ \Omega_{n+1,0}(t_{n+1,0} + W_{n+1,0}) - (I - \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0})) \begin{bmatrix}
0 \\
\delta
\end{bmatrix}.
\]

Assuming $k_n^* > 0$, we continue by substitution of Eq. (3.1.3) into Eq. (E.1-11) and
follow analogous steps used to produce Eq. (E.1-11):

\[
\begin{bmatrix}
q_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \\
v_{n+1,0}(t_{n+1,0} + W_{n+1,0})
\end{bmatrix}
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*}) \left[ \begin{array}{c}
p_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \\
u_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \end{array} \right] - \frac{\delta}{\delta} + G_{n,k_n^*}
\]

\[
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*}) \left( \Psi_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \left[ \begin{array}{c}
p_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \\
u_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \end{array} \right] + G_{n,k_n^*}
\right)
\]

Again, we can substitute the solution Eq. (E.1-3) evaluated at the end of the $k_n^* - 1$ sleep episode $t_{n,k_n^* - 1} + T_{n,k_n^* - 1}$, to obtain the result where $q_{n+1,0}(t_{n+1,0})$ and $v_{n+1,0}(t_{n+1,0})$ are now in terms of $q_{n,k_n^* - 1}(t_{n,k_n^* - 1})$ and $v_{n,k_n^* - 1}(t_{n,k_n^* - 1})$:

\[
\begin{bmatrix}
q_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \\
v_{n+1,0}(t_{n+1,0} + W_{n+1,0})
\end{bmatrix}
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*}) \left[ \begin{array}{c}
q_{n,k_n^* - 1}(t_{n,k_n^* - 1} + W_{n,k_n^* - 1}) \\
v_{n,k_n^* - 1}(t_{n,k_n^* - 1} + W_{n,k_n^* - 1}) \end{array} \right] + G_{n,k_n^*}
\]

\[
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*}) \left( \Psi_{n,k_n^*}(t_{n,k_n^*} + W_{n,k_n^*}) \left[ \begin{array}{c}
q_{n,k_n^* - 1}(t_{n,k_n^* - 1} + W_{n,k_n^* - 1}) \\
v_{n,k_n^* - 1}(t_{n,k_n^* - 1} + W_{n,k_n^* - 1}) \end{array} \right] + G_{n,k_n^*}
\right)
\]

\[
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*}) \left[ \begin{array}{c}
q_{n,k_n^* - 1}(t_{n,k_n^* - 1} + W_{n,k_n^* - 1}) \\
v_{n,k_n^* - 1}(t_{n,k_n^* - 1} + W_{n,k_n^* - 1}) \end{array} \right] + G_{n,k_n^*}
\]

\[
= \Psi_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \Phi_{n,k_n^*}(t_{n,k_n^*} + T_{n,k_n^*}) \left[ \begin{array}{c}
q_{n,k_n^* - 1}(t_{n,k_n^* - 1} + W_{n,k_n^* - 1}) \\
v_{n,k_n^* - 1}(t_{n,k_n^* - 1} + W_{n,k_n^* - 1}) \end{array} \right] + G_{n,k_n^*}
\]
where for clarity let us show the specific form of $G_{n,k_n^*-1}$:

$$G_{n,k_n^*-1} = \Psi_{n,k_n^*}(t_n,k_n^* + W_n,k_n^*) \Theta_{n,k_n^*-1}(t_n,k_n^*-1 + T_n,k_n^*-1) + \Omega_{n,k_n^*}(t_n,k_n^* + W_n,k_n^*) - (I - \Psi_{n,k_n^*}(t_n,k_n^* + W_n,k_n^*)) \begin{bmatrix} 0 \\ \delta \end{bmatrix}. \quad (E.1-15)$$

By continuing this process $k_n^*$ times we can arrive at the desired results where $q_{n+1,0}(t_{n+1,0} + W_{n+1,0})$ and $v_{n+1,0}(t_{n+1,0} + W_{n+1,0})$ are in terms of $q_{n,0}(t_{n,0} + W_{n,0})$ and $v_{n,0}(t_{n,0} + W_{n,0})$:

$$\begin{bmatrix} q_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \\ v_{n+1,0}(t_{n+1,0} + W_{n+1,0}) \end{bmatrix} = \prod_{k_n=0}^{k_n^*-1} \Psi_{n,k_n^*+1}(t_n,k_n^*+1 + W_n,k_n^*+1) \Phi_{n,k_n^*-1}(t_n,k_n^*-1 + T_n,k_n^*-1) \times \begin{bmatrix} q_{n,0}(t_{n,0} + W_{n,0}) \\ v_{n,0}(t_{n,0} + W_{n,0}) \end{bmatrix} + \tilde{G}_{n,0}, \quad (E.1-16)$$

where

$$\tilde{G}_{n,0} = \sum_{j=0}^{k_n^*-1} \prod_{k_n=0}^{j} \Psi_{n,k_n^*-k_n^*+1}(t_n,k_n^*-k_n^*+1 + W_n,k_n^*-k_n^*+1) \Phi_{n,k_n^*-k_n^*-1}(t_n,k_n^*-k_n^*-1 + T_n,k_n^*-k_n^*-1) G_{n,k_n^*+j-1} + G_{n,k_n^*}, \quad (E.1-17)$$

Also, notice that we use notation:

$$\Phi_{n,k_n^*+1}(t_n,k_n^*+1 + T_n,k_n^*+1) = \Phi_{n+1,0}(t_{n,0} + T_{n,0})$$

$$\Psi_{n,k_n^*+1}(t_n,k_n^*+1 + W_n,k_n^*+1) = \Psi_{n+1,0}(t_{n,0} + W_{n,0}).$$
Poster presentations and publications


References


Euler, L. (1748). Introductio in analysin infinitorum. Lausanne, 1:104.


