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Chapter 72

Sleep and Performance Prediction Modeling

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Chapter Highlights

- Sleep loss and circadian misalignment cause neurobehavioral performance impairment and contribute to errors, incidents, and accidents. Biomathematical models may be used to help manage fatigue risk in operational settings.
- Most currently available biomathematical models predict sleepiness or neurobehavioral performance impairment based on three basic components: circadian variation, homeostatic sleep-wake regulation, and sleep inertia.
- Recent advances in biomathematical modeling include accounting for nonlinear interaction between circadian and sleep-wake homeostatic processes, prediction of the cumulative effects of chronic sleep restriction on neurobehavioral performance, and extension of model predictions from group averages to individuals.
- Biomathematical models are gaining acceptance in operational settings as components of fatigue risk management systems.

Alertness and cognitive performance vary as a function of time of day, time awake, and a variety of situational factors. Prescriptive rules for hours of service do not capture these intrinsic temporal influences and therefore do not fully protect against performance deficits. Accordingly, a number of "biomathematical models of fatigue" have been (and continue to be) developed for anticipating and avoiding performance impairment; targeting optimal timing and dosing of countermeasures; improving work schedules, productivity, and safety; and informing accident investigations.

Most biomathematical performance prediction models are based on quantification of two primary and one secondary neurobiologic processes underlying variation in alertness and performance over time: the circadian process and the homeostatic process (see Chapter 37) as well as the sleep inertia process.[1-7] A variety of other factors affecting alertness and performance, including stimulant use, light exposure, distractions, and motivation, are currently not accounted for in most models. Instead, these factors are generally considered to effect transient deviations from the general trend that temporarily mask but do not alter the circadian or homeostatic processes that drive those trends. As such, current biomathematical models are useful for predicting normative performance for specific times of day, durations of time awake, and recent sleep history, with the understanding that actual, moment-to-moment alertness and performance of individuals may vary as a function of a broad array of factors.

One of the primary processes on which physiology-based, biomathematical models are built is the circadian process, which influences both performance and sleep regulation. This process is presumed to reflect physiologic activation apparent in measurements of body core temperature and certain hormones (such as melatonin). Performance increases (improves) with circadian activation, whereas propensity to sleep decreases (and vice versa).

The other primary process tracks the brain's level of sleep debt (level of physiologic need for sleep), which in turn affects alertness and performance capacity such that it is depleted while awake and replenished while asleep. This sleep-wake homeostatic process is dependent on the number of hours of recent sleep obtained (prior day), the number of hours of wakefulness (time since awakening), and current overall sleep debt (which is dependent on the amount of sleep loss that has accumulated over days, weeks, or perhaps longer). Performance capacity decreases (degrades) with homeostatic depletion, and propensity to sleep increases. The circadian and homeostatic processes continuously interact to influence observed performance and propensity to sleep.

A third process, called sleep inertia, reflects the temporary degradation in performance that is seen immediately after awakening. The magnitude of this effect depends primarily on depth of sleep at the time of awakening (which is itself affected by both the circadian and homeostatic processes). Sleep inertia dissipates with time since awakening, and recovery of performance is typically essentially complete within about 20 minutes of awakening.[8]

Recent advances have refined the mathematical representations of these three components, have added interaction terms among the components, and have added factors to account for chronic sleep restriction and dynamic variations in circadian phase (including the influence of light exposure). Additionally, methods have been developed to estimate patterns of sleep under specific work schedules.[5,9-13]

COMPONENTS OF THREE-PROCESS BIOMATHEMATICAL MODELS

To illustrate the modeling approach shared in general form by several three-process models,[2-5] the Sleep, Activity, Fatigue, and Task Effectiveness (SAFTE) model will be used in this

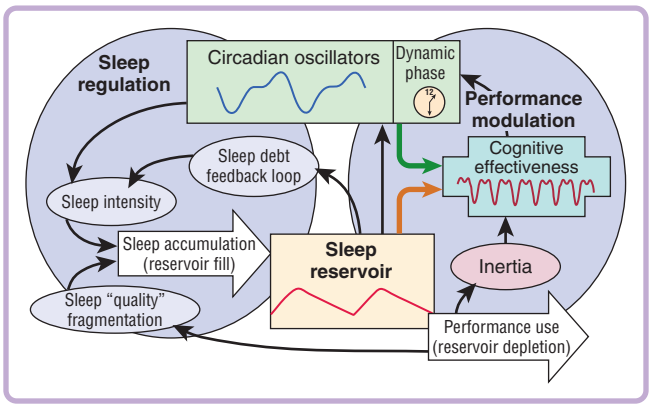

Figure 72-1 Schematic of the Sleep, Activity, Fatigue and Task Effectiveness (SAFTE) model.[5,9]

chapter. The components of this model are diagrammed in Figure 72-1.

Circadian Oscillator

Performance while awake and the drive to sleep are both controlled, in part, by a circadian process.[3,14,15] For a person entrained to a sleep period of 11 PM to 7 AM, performance reaches a peak in the early evening at approximately 7 PM and—if it could be measured during sleep—would fall to a minimum at approximately 4 AM. There is a secondary peak of performance in the morning at about 10 AM, and a secondary minimum (dip) in the early afternoon at about 2 PM. Negatively correlated with this alertness pattern is a tendency to fall asleep, which reaches a peak at about the same time performance and alertness reach a trough.

The existence of both a major and a minor peak in performance with corresponding troughs between them is often modeled as the result of two linked harmonic oscillations (cosine functions), one with a period of 24 hours and the other with a period of 12 hours. This results in a combined function of the form shown in Figure 72-2.[16] More dynamic models of the circadian process use a limit cycle or Van der Pol oscillator that yields a function of similar form.[17]

A simplifying assumption of most biomathematical models is that the same underlying arousal oscillator drives the variations in both cognitive performance and sleep propensity. The amplitude of the circadian process is dependent on the level of sleep debt modeled by the sleep-wake homeostatic process.[6,18,19] The phase (timing) of the circadian process is driven largely by environmental factors, most notably the timing of sunlight exposure,[12,20] but also has an individual trait component expressed as morningness and eveningness.[21]

Sleep-Wake Homeostatic Regulation

The control of sleep and its influence on cognitive capacity is usually modeled as a homeostatic process.[15,22-24] One way to conceptualize this process is through a sleep reservoir (see Figure 72-1). A fully rested person has a certain performance capacity (represented by the sleep reservoir capacity). During wakefulness, units are subtracted from the sleep reservoir according to a use function. During sleep, units are added to the sleep reservoir and the capacity to perform and be alert is restored.

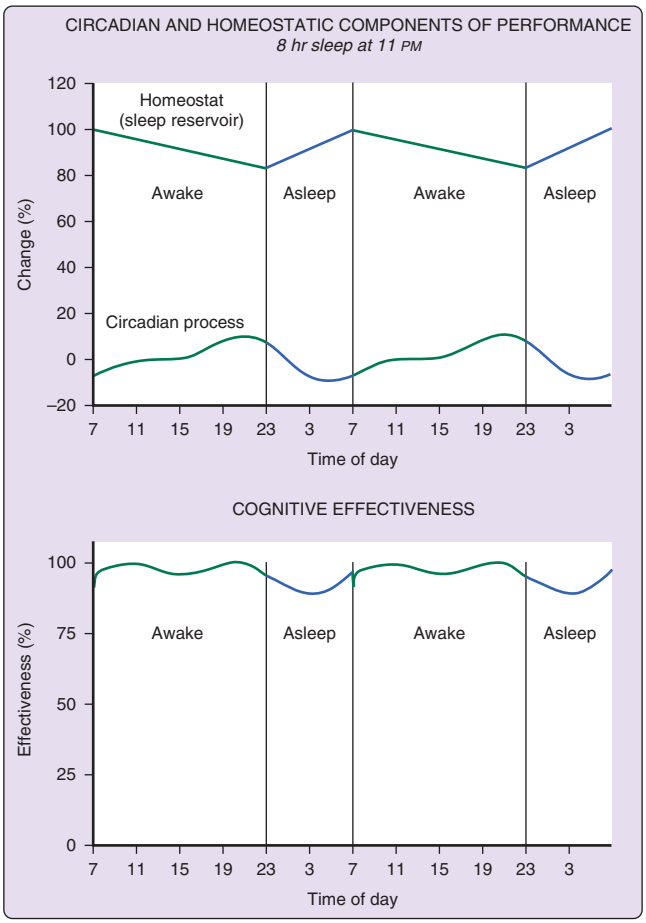

Figure 72-2 The sleep-wake homeostatic (*top*) and circadian (*middle*) processes affecting performance (cognitive effectiveness, *bottom*). Graphs are based on SAFTE model simulations of a 16-hour wake/8 hour sleep schedule, with sleep starting at 11 PM. (Performance predictions during sleep are suppositional because they cannot actually be observed during the sleep state.)

The rate of unit accumulation during sleep is driven by two factors: circadian variation and current overall sleep deficit, which is the shortage in the current level of the reservoir. Because the rate of unit accumulation is in part regulated by the current level of the reservoir, the process is homeostatic. The top panel of Figure 72-2 shows the decrease in performance units during wakefulness and the increase during sleep.

Results from laboratory studies have revealed that chronic sleep restriction (anything less than approximately 8 hours per 24 hours) leads to cumulative alertness and performance deficits.[25-27] For sleep durations of more than 4 hours per night, performance declines across days but eventually reaches a suboptimal plateau or equilibrium level.[13,26] The achievement of this suboptimal equilibrium state implies a feedback-modulated control system. Modeling this phenomenon has led to much new activity in model development.[5,11,13,28,29] In the SAFTE model, this phenomenon is implemented by reducing the reservoir capacity each time sleep restriction occurs (see later).

Accumulation of performance units does not start immediately on falling asleep. There is a 5-minute delay from sleep onset until performance units begin to accumulate. This delay

accounts for the approximate time required to return to restorative sleep following a brief arousal and results in a penalty during recuperation (see Figure 72-1) in an environment that leads to frequent interruptions (sleep fragmentation).

Sleep Inertia

A third factor diagrammed in Figure 72-1 is the transient performance impairment that often occurs immediately following awakening (i.e., sleep inertia).[8,22] It is typically modeled as an exponentially decreasing performance deficit.[5,30,31] Because of the relatively short duration of sleep inertia, it is relevant mainly in operational contexts in which individuals may be required to perform immediately on awakening (e.g., first responders), and therefore it is not included in some biomathematical models.[6,10,32]

COMBINED EFFECTS: PREDICTED PERFORMANCE

Alertness and performance are modeled as the combined effect (in most models calculated as the sum) of the mathematical functions for the circadian oscillator, the sleep-wake homeostatic reservoir, and sleep inertia immediately following awakening. The sum of the homeostatic process with the circadian process produces a performance function with two nadirs, one in the late night to early morning and a smaller one in the early afternoon. These two processes are shown in the top panel of Figure 72-2. Their combined effects on performance are shown in the bottom panel of Figure 72-2.

During the first part of a daytime waking period, the circadian process increases (growing activation) and the homeostatic process decreases (reservoir depletion). When summed, the changes in these two processes are approximately offsetting each other, leading to relatively constant daytime performance. After the 7 PM (approximately) evening peak in the circadian process, both the circadian process and homeostatic process decline, leading to a precipitous loss of alertness and performance at approximately 11 PM that facilitates sleep onset.

During nighttime sleep, the circadian process continues to decrease (declining activation, which facilitates sleep maintenance) and the homeostatic process increases (restoration of reservoir level). After the early morning nadir in the circadian process, both the circadian and homeostatic processes rise, culminating in spontaneous awakening at approximately 7 AM.[1] Combined (summated), the two processes produce the performance profile depicted in the bottom panel of Figure 72-2.

QUANTIFYING RECUPERATION DURING SLEEP

During sleep, the sleep reservoir is replenished. In the SAFTE model, the rate at which the reservoir is filled depends on the prior long-term sleep debt (as reflected in the current level of the reservoir). A large reservoir deficit leads to an increased rate of replenishment; a small deficit leads to a reduced rate of replenishment. The rate of replenishment also appears to be modulated by the circadian variation in sleep propensity[33] and may follow the circadian pattern of sleep propensity[34,35] (the inverse of the circadian pattern of activation in the top panel of Figure 72-2). The net effect is a near-linear homeostatic reservoir accumulation through a normal night (see top panel of Figure 72-2), which is in line with results that show an approximately linear relationship between sleep duration and performance recuperation.[25,36]

The homeostatic regulation of sleep[37] leads to equilibrium states under certain conditions of chronic sleep restriction.[8] If a subject is scheduled to take less than an optimal amount of sleep each night (defined here as approximately 8 hours) and instead obtains, for example, 5 hours per day, the reservoir initially loses more units during the waking period than are made up during the sleep period. This results in a sleep debt at the end of the sleep period that accumulates over days.[24,25] However, because the rate of accumulation during sleep increases with sleep debt, eventually the rate of accumulation increases so that 5 hours of sleep makes up for 19 hours of wakefulness. At this point, the reservoir reaches an equilibrium state over days, and no further debt is accumulated. However, the reservoir remains at less than 100% replenished as long as the person remains on this reduced sleep schedule.

The sleep-wake homeostatic process is not infinitely elastic, and results show that there is a limit to the rate of accumulation and thus to whether a given sleep-wake schedule permits equilibrium. In the SAFTE model, any schedule that provides less than 4 hours of sleep per day will not reach an equilibrium state, and performance capacity will gradually deplete entirely. Results of biomathematical model analyses have provided further evidence that there is such a bifurcation (i.e., qualitative change in behavior) for the homeostatic process when sleep is reduced to below approximately 4 hours.[8]

The long-lasting effects of chronic sleep restriction on performance impairment and reduced capacity to recuperate[24,25] suggest that some aspect of sleep-wake homeostasis undergoes a gradual change that is slow to recover.[2,27] This phenomenon has prompted modelers to revise the sleep-wake homeostatic process by adding a long-term process.[2,8,27,28,38,39] Within the context of the SAFTE model, this process is instantiated as a gradual downregulation of the sleep reservoir capacity during chronic sleep restriction. When sleep durations return to the nominal value of approximately 8 hours per day, the downregulation of the reservoir capacity is gradually reversed.

The implication is that after a period of chronic sleep restriction, it takes multiple days of recovery sleep to restore performance to baseline levels.[8,24] Laboratory evidence has shown that extending sleep to more than 8 hours per day for an extended period of time provides some resilience to the effects of subsequent sleep restriction.[33] This recent finding implies that it should also be possible to moderately increase the capacity of the sleep reservoir.[6] In the SAFTE model, more than 8 hours of sleep per day will hasten the recovery of the reservoir set point to the full value but will not increase capacity beyond the nominal limit for a person consistently sleeping 8 hours per day, so the findings that sleep extension confers performance benefits during subsequent sleep restriction may require further model refinement (as has already been pursued in another model[6]).

The time of day also affects the recuperative potential of a sleep period. For an individual given 8 hours of sleep per day from 11 AM until 7 PM, waking performance reaches a peak about 4 hours after awakening (9 PM). It then rapidly declines during the late night and early morning hours to a

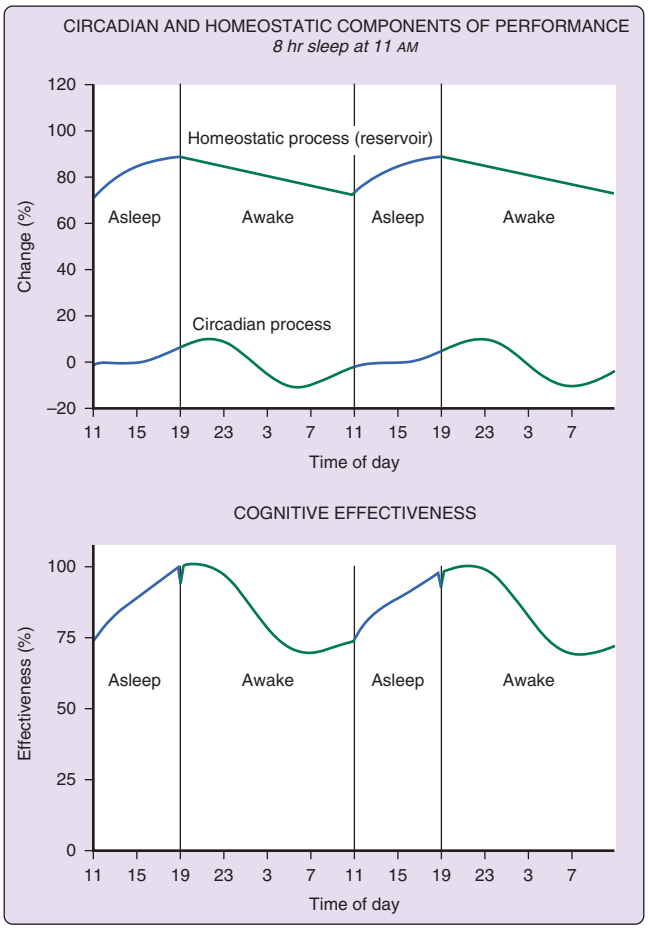

Figure 72-3 The sleep-wake homeostatic (*top*) and circadian (*middle*) processes affecting performance (cognitive effectiveness, *bottom*) when 8 hours of sleep occurs during the day starting at 11 AM. Graphs are based on SAFTE model simulations.

deep minimum at about 5 AM, as illustrated in the bottom panel of Figure 72-3. This pattern is substantially different from the performance pattern seen after nighttime sleep (see Figure 72-2) for two reasons. First, owing to the circadian rhythm in sleep propensity, daytime sleep periods exhibit less physiologic sleep and therefore less homeostatic reservoir replenishment, that is, the reservoir level does not return to 100% (see Figure 72-3, top panel). Second, circadian activation reaches its minimum in the early morning hours, at the same time that the sleep-wake homeostatic reservoir is increasingly depleted.

This pattern has negative implications for performance under shift schedules that require daytime sleep. It is well documented that most mistakes on the night shift occur during the early morning hours,[34,35] and biomathematical models predict this outcome. Note also that the pattern illustrated in Figure 72-3 is likely to be a "best case scenario" in that it was presumed that 8 hours of sleep was achieved during the 8-hour daytime sleep period. However, results indicate that shift workers seldom achieve 8 hours of sleep during the daytime hours even if they are sleep deprived. That is, sleep propensity (debt) tends to be insufficient to completely overcome countervailing circadian wake drive and environmental factors such as daylight and social activities.[36,37]

SLEEP ESTIMATION

The accuracy of biomathematical model predictions is dependent on accurate measurement or prediction of sleep times and durations. Sleep timing and duration can be estimated mathematically using the two-process model of sleep regulation[38] (see Chapter 36) and detailed models of sleep neurobiology.[40,41] However, these models do not account for social and other nonbiologic constraints on sleep.[42] For this reason, in situations in which biomathematical models are applied to work schedules, it may be necessary to make use of an alternative method for estimating potential sleep given the available sleep opportunities.

One approach to developing a sleep estimation algorithm involves modeling the observed likelihood of sleep from results of field studies in the operational environment in which sleep was recorded by means of diaries or actigraphy.[43] In the SAFTE model, it is assumed that the occurrence of major sleep episodes is largely the result of a decision to go to bed, conditioned by the person's typical need for sleep and opportunities to sleep, reflective of social, cultural, and professional factors. A sleep estimation algorithm simulates the decision process that governs when a person chooses to sleep. Sleep is assumed not to occur during work or commuting to work because these periods limit sleep opportunities.

Within sleep opportunities, further decisions about when to sleep are made based on sleep habits. These habits might include such factors as the preferred bedtime, the normal duration of sleep on work and rest days, the minimum duration of a nap, and any time during the day that a person normally uses for personal activities and not sleep. The sleep estimation algorithm combines these parameters with circadian factors (described earlier) to generate estimates of the timing and duration of sleep during opportunities afforded by the work schedule.[11,42]

In recent studies with airline pilots (36 domestic and 15 international) and shift workers (147 workers with fixed and rotating shift patterns with irregular shift extensions and overtime), the algorithm was trained on actigraphically recorded sleep-wake to achieve 85% to 87% accuracy for predicting sleep and wakefulness for individual subjects. The algorithm estimated average total sleep per 24 hours to within 1 minute of the actual group average.[44] Although there remained considerable individual differences in sleep patterns, from an aggregate risk assessment perspective, the SAFTE model predictions based on such data were as good as inputting actual wrist actigraphy data. The optimal settings of the algorithm were nearly identical for these two very different work populations, a function of the fact that the sleep-wake behaviors of all humans are governed by essentially the same physiologic and environmental factors.

CIRCADIAN PHASE SHIFTING

When people move to another time zone or alter work patterns so that sleep and wake consistently occur systematically at new times of day, the internal circadian oscillator that modulates alertness and performance shifts to this new schedule. During this period, individuals experience performance degradation, disrupted mood, and feelings of dysphoria, collectively termed jet lag (see Chapters 35 and 37).[45-48] Several models simulate this process and adjust the phase of the

circadian rhythm to coincide with the new activity pattern. This feature is critical for the accurate prediction of the effects of moving to a new time zone or changing to a new and regular work schedule, such as changing from the day shift to the night shift.[37]

The factors that mediate phase shifts vary across models. Research suggests that a major driver of circadian phase is exposure to sunlight or bright light[49]—especially the blue part of the spectrum[50] (see Chapter 35). In some models, direct measurements of light exposure are required as input and are used to predict changes in circadian phase.[3] Other models use a surrogate for sunlight measurement.[5,9,11,51]

In the SAFTE model, it is assumed that the probability of bright light exposure is proportional to the time spent awake during daytime hours. Hence, the model adjusts the rate of phase change based on the proportion of waking time that occurs during daytime hours. This simplification eliminates the need to take continuous measurements of light to drive the circadian process, but it also means that there is no mechanism to input light exposure as a deliberate countermeasure.[52-54] Given that the interaction between the circadian oscillator and the sleep-wake homeostatic process appears to be bidirectional,[18] the timing of the sleep period may in and of itself also contribute to circadian adjustment.[11,55]

PERFORMANCE PREDICTION

As illustrated in Figures 72-2 and 72-3, biomathematical performance prediction models simulate the dynamic interplay of circadian variation in alertness and sleep propensity, homeostatic sleep-wake regulation supporting performance capacity, and short-term sleep inertia following awakening. Specific models differ in the manner in which these three factors are represented and mathematically combined. The predictions of such models also depend on the metrics (units) of the models. For example, the units expressed by the SAFTE model are percent changes in cognitive speed from baseline performance when fully rested (i.e., 8 hours of sleep per 24 hours) and diurnally oriented (i.e., sleep from 11 PM to 7 AM). Cognitive speed corresponds to speed of response on a psychomotor vigilance test (PVT).[56] Studies that have included other cognitive tests along with the PVT have shown them to be highly correlated, with the PVT showing the greatest sensitivity to daily sleep amounts.[57]

When predicting group averages (but not individual performance[41]), translation functions can be used to calculate other performance metrics such as lapse likelihood, reaction time, and mean cognitive throughput (correct responses per unit of time) on other cognitive tests, such as serial addition-subtraction, choice reaction time, logical reasoning, and code substitution. Figure 72-4 shows output from a translation function that expresses performance as PVT lapse likelihood, which increases with time awake and mirrors response speed.

To illustrate the potential of these models to accurately predict performance under a variety of sleep-wake-work schedules, two examples are offered. The first example concerns performance changes on a variety of cognitive tasks during a period of total sleep deprivation in a laboratory.[58] As depicted in Figure 72-5, these measures were compared with model predictions and found to conform to the group means of the performance observations with 98% of the variance explained.

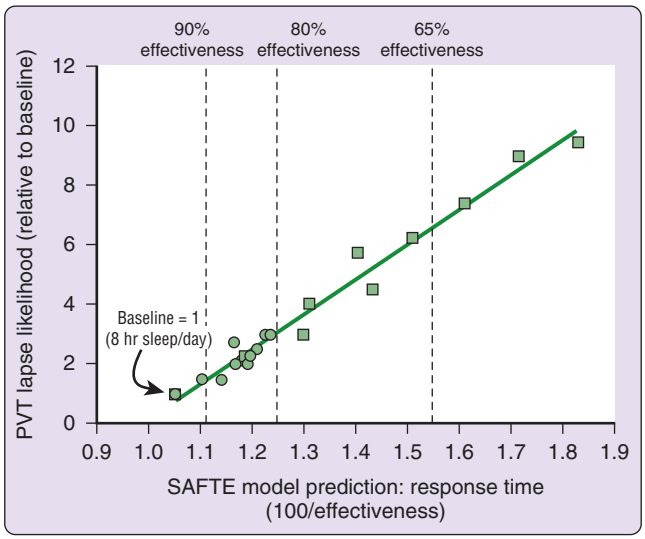

Figure 72-4 Linear relationship of lapse likelihood on a psychomotor vigilance test (PVT) to predicted response time (100/effectiveness) from the SAFTE model. PVT data were recorded during days of chronic sleep restriction to 3 hours per day (○) or 5 hours per day (■).[26]

The second example deals with chronic sleep restriction as encountered in demanding schedules that allow for less than optimal nightly sleep durations over extended periods of time. Figure 72-6 shows performance observations (daytime averages) obtained during a laboratory dose-response study involving 7 days of sleep restricted to 3, 5, 7, or 9 hours per day, preceded by 3 baseline days and followed by 3 recovery days, each with 8 hours of time in bed per night.[26] As shown in the figure, the group means of the objective performance measures were compared with the predictions of the model and found to explain 94% of the variance.

Biomathematical models may predict performance on a selected, standardized performance task, such as the PVT, or on an abstract performance metric, such as a sleepiness scale from, say, 0 to 100. Mathematical modeling may be applied to make absolute predictions, which are compared against a threshold (e.g., that distinguishes acceptable from unacceptable performance[59]). In these applications, the specific performance metric used and the value of the threshold are crucially important.

More commonly, biomathematical modeling is used to make relative comparisons of predicted performance during two or more alternative sleep-wake or work scheduling options. In such cases, modeling enables selection of the scheduling alternative that is less fatiguing, or less fatiguing as well as more productive or cost-effective.[60] In this application, the specific performance metric used is not critical. However, there is debate about whether "better versus worse" should be quantified based on maximum or minimum level of the metric (i.e., highest risk) or on some other calculation such as a combination of both level and duration of performance impairment (i.e., risk exposure).[61]

Ongoing mathematical modeling efforts are aimed toward predicting, in greater detail, the effects of sleep loss on performance on a diverse range of tasks.[62,63]

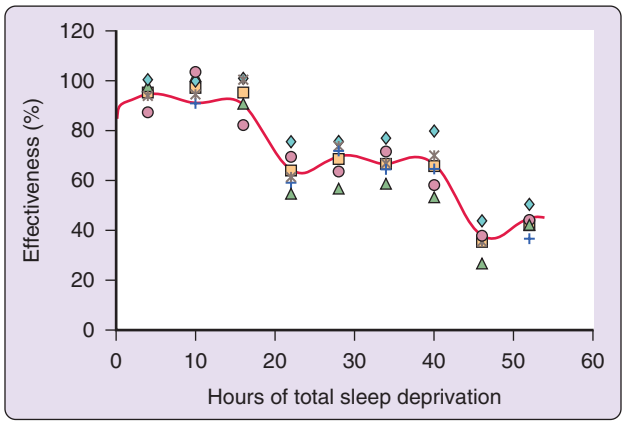

Figure 72-5 Fatigue model predictions for group-average (n = 12) cognitive performance during 54 hours of total sleep deprivation (beginning at 7 AM) compared with actual observations[58] for several cognitive measures (different symbols) and mean cognitive performance (*squares*) expressed relative to baseline. Model predictions were made with the SAFTE model (*solid line*) with a reservoir depletion rate of 1.1% per hour.[5] ◆, Serial reaction time; +, decoding problem performance; ж, encoding problem performance; ●, auditory vigilance; ▲, logical reasoning.

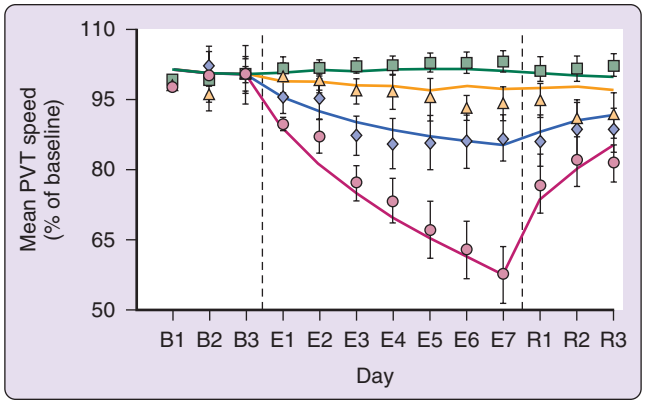

Figure 72-6 Fatigue model predictions for group-average psychomotor vigilance test (PVT) performance (averaged within each day) across 3 baseline days (B1–B3) with 8 hours time for sleep; 7 experimental days (E1–E7) with daily sleep restricted to 3 hours (●, n = 13), 5 hours (◆, n = 13), 7 hours (▲, n = 14), or 9 hours (■, n = 16); and 3 recovery days (R1–R3) with 8 hours time for sleep.[26] Model predictions were made with the SAFTE model (*solid line*).[5]

MODELING APPLIED TO OPERATIONAL SETTINGS

Most biomathematical performance prediction models are optimized to predict changes in cognitive performance as measured by standard laboratory tests performed under controlled laboratory conditions. It is assumed that these tests measure changes in the fundamental capacity to perform a variety of tasks that rely, more or less, on the cognitive skills of attention, detection, discrimination, reaction time, mental processing, reasoning, or decision making. However, the extent to which any specific operational task relies on these cognitive skills is generally not known. Thus deficits in cognitive capacity seen in the laboratory may not always predict deficits in the capacity to perform different operational tasks.

It is reasonable to assume, however, that changes in task performance will be correlated with changes in underlying

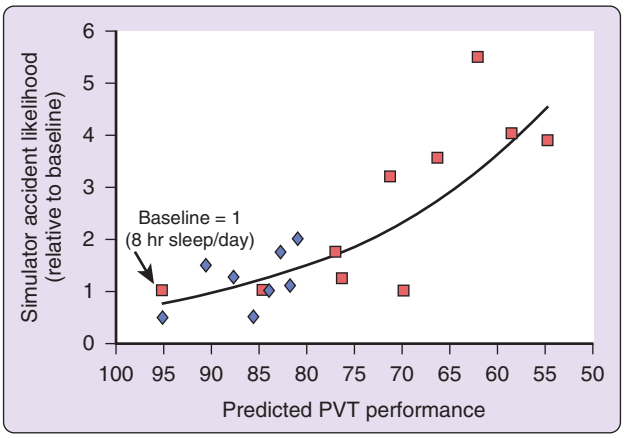

Figure 72-7 Systematic relationship (*solid line*) between model predictions optimized to predict psychomotor vigilance test (PVT) performance and group-average accidents observed in a driving simulator.[64] Model predictions were made with the SAFTE model.[5] ■, 3 hours sleep per day (n = 13); ◆, 5 hours sleep per day (n = 13).

cognitive capacity and therefore that changes in one task will be correlated with changes in another task if both tasks tap the same underlying capacity. The validity of this assumption has been demonstrated in job task simulator experiments. For example, Figure 72-7 illustrates that there is a systematic relationship between predicted performance for the PVT (generated from SAFTE) and driving simulator accident data from subjects given varying amounts of daily sleep for a week.[64]

Biomathematical modeling (prediction) of operational task performance could be used to design better work schedules, alter the timing of critical tasks to coincide with periods of predicted optimal performance, or time the application of countermeasures to prevent errors and accidents. Unlike prescriptive hours-of-service regulations, these models provide physiology-based, flexible, and quantifiable ways to optimize safety and performance in operational environments.

Current uses of biomathematical modeling alone or as a component of fatigue risk management systems in operational settings include the following:

- Prediction of risk for impairment associated with a given work-rest or wake-sleep schedule, allowing for selection of optimal duty scheduling
- Guidance for effective implementation of countermeasures
- To inform, supplement, or substitute hours-of-service policies and regulations
- As an aid in post hoc incident or accident investigations to determine the extent to which fatigue may have been a contributing factor
- As an educational tool for understanding the operational consequences of insufficient sleep and circadian misalignment

A relatively new application of biomathematical modeling involves the use of model predictions as a surrogate for performance measurements in settings where sleep can be measured (e.g., with actigraphy) but measuring performance would interfere with performance of critical tasks.

Biomathematical modeling plays a key role in the approval of exceptions to flight and duty time limitations under the fatigue risk management system approval process of the U.S. Federal Aviation Administration (FAA) as implemented in

2014.[65] Using a multistep approval process, the FAA accepts applications for exceptions to prescriptive flight and duty time limitations that combine longer duties with offsetting rest and time-of-day limitations. To obtain final approval, the aviation certificate holder must collect data to verify that sleep and performance under the alternative means of compliance (AMOC) are equivalent to what might be observed under the prescriptive rules.

To gain temporary approval to conduct operations to collect the necessary data, the aviation certificate holder is allowed to provide biomathematical modeling results or actual sleep and performance data (when available) to the FAA in order to establish a safety case for the AMOC. The FAA bases its final approval for the AMOC on statistical equivalence[66,67] of actual sleep and performance findings compared with a control condition (i.e., one that meets the prescriptive limitations). The integration of biomathematical modeling into a regulatory framework that allows for AMOC reflects the demonstrated utility of modeling for simultaneously enhancing both fatigue risk management or operational safety and efficiency of flight operations.

INDIVIDUAL DIFFERENCES

Individual differences in responses to sleep loss and circadian timing (e.g., in shift work)[68] represent a substantial source of error variance in most biomathematical models, which were developed first and foremost to predict group-average performance. Individual differences can be accounted for broadly by reflecting the expected distribution of performance outcomes in the model predictions, based on the individual variability of performance changes observed in laboratory studies.[11,69] This approach provides information on the range of effects to be expected under a specific sleep-wake-work schedule, but it does not provide information about where any specific individual would fall within that range.

Individual differences in vulnerability to sleep loss have been demonstrated to be traitlike[70] and thus predictable on a subject-specific basis.[71] Two complementary strategies could be implemented to enhance individual-level prediction.[41] The first is to incorporate predictors of performance vulnerability, such as morningness-eveningness,[72] basal sleep need,[73] or specific genetic polymorphisms,[74-76] into the model equations.[77] To date, none of these predictors has been demonstrated to account for a substantial portion of interindividual variability, but research efforts are ongoing[76,78] and novel candidate predictors continue to be identified.

The second strategy is to tailor the parameters of the model to the individual based on real-time or near-real-time performance observations obtained from the individual. Algorithms for this have been developed,[41,79,80] with confidence intervals indicating the statistical certainty level of the predictions.[79]

LIMITATIONS OF BIOMATHEMATICAL MODELS

Biomathematical modeling has become a valuable tool for fatigue risk management (see Chapter 71). However, it is also based on evolving science, and thus there are limitations that should be noted.[77,81,82] Some limitations to consider when evaluating a model include the following:

- Accuracy of model predictions relative to observations obtained from laboratory versus field studies
- Generalizability, that is, to what extent the model is applicable to sleep-wake-work scenarios not used in its development
- Balance between sensitivity and specificity, that is, the extent to which predictions are liberal or conservative with regard to identifying periods with meaningfully increased or decreased performance

These and other modeling issues were discussed at the international Fatigue and Performance Modeling Workshop (June 13 to 14, 2002, Seattle, Wash.) and were documented in the proceedings of that meeting.[83] Since then, biomathematical models have undergone further development, rendering some of the information in the proceedings outdated. Nevertheless, the volume continues to provide valuable documentation of biomathematical modeling as a developing science.

The accuracy of a model depends on the accuracy of the major inputs to that model. A key input is the pattern of sleep-wake under a given work schedule. In laboratory studies, precise polysomnographic quantification of sleep-wake is possible. Such data are seldom available in operational settings, but a variety of other techniques can be used to obtain sleep data, such as wrist actigraphy (see Chapter 73), sleep diaries, or an algorithmic sleep estimator (discussed previously). Although algorithmic sleep estimation can be useful for prediction of elevated accident risk,[84] the accuracy of such predictions depends on the accuracy of the sleep estimates that serve as input to the model. Such estimates may suffice when the goal is prediction of the average performance of large groups of workers, but they may be problematic when the goal is prediction of individual performance.

Similarly, as noted previously, measures of circadian rhythm are rarely available in the operational environment, and thus estimates of the phase and amplitude of the circadian process must be generated from the timing of sleep, light exposure, or other environmental drivers of biologic rhythms. Again, such estimates may suffice for large groups but are likely to be less useful for predicting the performance of individuals who may, for example, be extreme morning or evening types.[72] Additional information (e.g., recent sleep-wake history) would be required to reduce this source of error.

Another major input to performance prediction models is "initial state." This refers to the sleep debt (reservoir level), circadian phase, and (depending on the specific model) other relevant variables that provide the starting point from which predictions are made. If the initial states are unknown, assumptions regarding the likely sleep-wake history and circadian phase need to be made. The accuracy of these assumptions initially determines the accuracy of the model predictions. However, the influence of the initial state estimates diminishes over time,[85] and the accuracy of the model improves as actual daily sleep measures (e.g., actigraphic sleep measurements) or work schedule–based sleep estimates accrue and are used as input to the model.

CONCLUSION

Biomathematical models predict physiology-based cognitive capacity as a function of sleep-wake history, circadian rhythm, and sleep inertia. Cognitive capacity affects the ability to perform specific tasks and thereby affects the risk for making an error or the probability of rare events like accidents.[84]

It is important to understand assumptions underlying biomathematical models. In most three-process models, it is assumed that the rate and magnitude of cognitive performance impairment are independent of the nature of activities performed while awake (e.g., task load, work pace). However, it is known that performance decreases as a function of time on task,[86,87] the number of flight segments during an aircrew duty period,[88] successive duty periods in shift work,[89] and other factors. Conversely, performance is temporarily restored by rest breaks and sustained by days off.[39,90] Current performance prediction models do not account for these factors, nor do they account for the effects of pharmacologic countermeasures (e.g., caffeine, although model development to address caffeine is underway[91]).

As a rule of thumb, biomathematical model predictions should be interpreted as representing the fundamental cognitive capacity of a group or person unaided by pharmacologic countermeasures, that is, a cap on performance as determined by underlying brain physiology. However, actual performance will depend on additional factors, such as the nature of the tasks being performed and the circumstances at hand,[92] which are not accounted for in the model prediction.

CLINICAL PEARL

Sleep loss and circadian misalignment produce deficits in cognitive performance. Biomathematical models that predict performance based on these factors are valuable tools that are increasingly being applied in both operational and nonoperational settings. For personal use, these models can be applied to determine the effects of sleep-wake duration and timing on performance and alertness and thus serve to guide clinical, professional, and personal decision making regarding sleep habits and use of countermeasures. For employers, regulatory agencies, and practitioners in occupational medicine, these models are useful to guide the design of better work schedules, reduce performance errors and accidents, improve the health and well-being of employees, and advance public safety.

SUMMARY

Because insufficient sleep (which is prevalent in modern society) leads to lapses of attention, slowed reaction time, and impaired reasoning and decision making, it is a major proximate cause of errors and accidents in both industrial and military operational settings. Biomathematical models have been developed to predict sleep- and alertness-mediated performance in laboratory and field environments. Such models are already being incorporated into scheduling tools to anticipate and avoid performance impairment in operational settings. Most available models predict performance based on three basic components: circadian variation in alertness and sleep propensity, homeostatic sleep-wake regulation, and sleep inertia. These processes vary over time as a function of sleep-wake patterns and combine to produce changes in subjective alertness and cognitive performance capacity. Current models provide accurate predictions of average performance of groups under variations in sleep opportunities or work schedules. Efforts are underway to further refine these biomathematical models to enhance accuracy of prediction for individuals.

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REVIEW QUESTIONS

1. Which of the following are the component physiologic processes of three-process models of performance?
   A. REM sleep, non-REM sleep, and wakefulness
   B. Subjective, objective, and physiologic sleepiness
   C. Circadian rhythm, homeostatic sleep-wake regulation, and sleep inertia
   D. Sleep, duty hours, and light exposure
2. Which of the following contributes to accident risk?
   A. Duty hours
   B. Sleep homeostasis
   C. Task duration
   D. All of the above
3. An individual's pattern of performance impairment over time can be predicted on the basis of which of the following?
   A. Subjective sleepiness
   B. The interaction of homeostatic sleep drive and circadian rhythm
   C. Aggregate records of incidents and accidents
   D. It cannot be predicted.
4. Which factor does *not* increase the likelihood of human error?
   A. Hours-of-service regulations
   B. Consecutive work shifts
   C. High cognitive task demands
   D. Circadian misalignment
5. Which of the following is *not* an effective way to apply fatigue models in operational fatigue risk management?
   A. Predict risk for impairment associated with a given work-rest or wake-sleep schedule to allow for selection of optimal duty scheduling
   B. Predict which specific operational tasks will be most susceptible to the effects of sleep deprivation
   C. Inform, supplement, or substitute for hours-of-service policies and regulations
   D. Aid post-hoc incident or accident investigations to allow for root cause analysis and determine the extent to which fatigue may have been a contributing factor
6. Which of the following is a strategy for accounting for individual differences in fatigue predictions from mathematical models of fatigue?
   A. Incorporate a sleep homeostat into the model.
   B. Ignore individual differences because they are unstable from situation to situation.
   C. Aggregate records of incidents and accidents.
   D. Tailor the parameters of the model to each individual based on real-time or near-real-time feedback of performance observations.
7. Which of the following is *not* a major limiting factor for fatigue models?
   A. Uncertainty about the sleep patterns of individual workers
   B. Uncertainty about the phase and amplitude of an individual's circadian rhythm
   C. Errors in the "initial state" of the model with catastrophic effects on predictions many weeks in the future
   D. A group-average model should not be used to predict the level of performance capability of a specific individual

ANSWERS

1. **C.** Most of the available biomathematical models predict sleepiness or performance impairment based on three basic components: circadian variation in alertness, homeostatic sleep-wake regulation, and sleep inertia.
2. **D.** Accident risk increases with hours awake (and thus with duty hours) through the buildup of sleep homeostatic pressure, in interaction with time on task (and thus task duration).
3. **B.** Biomathematical models predict performance impairment by tracking homeostatic sleep drive and circadian rhythmicity.
4. **A.** Hours-of-service regulations prescribe maximal duty hours and minimal rest breaks to help reduce the likelihood of human error. That said, biomathematical models can be more effective in this regard because they account for the dynamics of sleepiness over time, which hours-of-service regulations do not do (or do not do well).
5. **B.** Most fatigue models are optimized to predict changes in cognitive skills as measured by standard laboratory tests performed under controlled laboratory conditions. The extent to which any specific operational tasks rely on these cognitive skills is generally not known. Thus deficits in cognitive capacity seen in the laboratory may not always produce identical deficits in the capacity to perform different operational tasks.
6. **D.** Individual differences in susceptibility to performance impairment due to fatigue constitute a trait and are therefore predictable. This makes it possible to tailor the parameters of the model to an individual based on real-time or near-real-time feedback of performance observations.
7. **C.** An important input to fatigue models is the "initial state," and the accuracy of the assumptions for initial state initially determines the accuracy of the model predictions. However, the influence of initial state diminishes over time, and the accuracy of the model improves as actual daily sleep assessments (e.g., actigraphic sleep measurements) or work schedule–based sleep estimates accrue and are used as input to the model.