

Summary of the Key Features of Seven Biomathematical Models of Human Fatigue and Performance

MELISSA M. MALLIS, SIG MEJDAL, TAMMY T. NGUYEN*, AND DAVID F. DINGES

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Background: Biomathematical models that quantify the effects of circadian and sleep/wake processes on the regulation of alertness and performance have been developed in an effort to predict the magnitude and timing of fatigue-related responses in a variety of contexts (e.g., transmeridian travel, sustained operations, shift work). This paper summarizes key features of seven biomathematical models reviewed as part of the Fatigue and Performance Modeling Workshop held in Seattle, WA, on June 13–14, 2002. The Workshop was jointly sponsored by the National Aeronautics and Space Administration, U.S. Department of Defense, U.S. Army Medical Research and Materiel Command, Office of Naval Research, Air Force Office of Scientific Research, and U.S. Department of Transportation. **Methods:** An invitation was sent to developers of seven biomathematical models that were commonly cited in scientific literature and/or supported by government funding. On acceptance of the invitation to attend the Workshop, developers were asked to complete a survey of the goals, capabilities, inputs, and outputs of their biomathematical models of alertness and performance. Data from the completed surveys were summarized and juxtaposed to provide a framework for comparing features of the seven models. **Results:** Survey responses revealed that models varied greatly relative to their reported goals and capabilities. While all modelers reported that circadian factors were key components of their capabilities, they differed markedly with regard to the roles of sleep and work times as input factors for prediction: four of the seven models had work time as their sole input variable(s), while the other three models relied on various aspects of sleep timing for model input. Models also differed relative to outputs: five sought to predict results from laboratory experiments, field, and operational data, while two models were developed without regard to predicting laboratory experimental results. All modelers provided published papers describing their models, with three of the models being proprietary. **Conclusions:** Although all models appear to have been fundamentally influenced by the two-process model of sleep regulation by Borbély (6), there is considerable diversity among them in the number and type of input and output variables, and their stated goals and capabilities. **Keywords:** biomathematical models, circadian rhythms, work/rest schedules, sleep, sleep loss, alertness, fatigue, performance.

periods of waking and displaced work schedules result in both subjective and physiological fatigue, cognitive performance decrements and errors, safety risks, and adverse health effects (5,14–17,22,26,27,34–36). For example, pilots on long-haul flight schedules with multiple flight legs and layovers often experience misalignment of the light/dark cycle and sleep/wake cycle (external circadian desynchrony). This desynchronization coupled with fluctuations in the amount and timing of light exposure can affect pilots' ability to sleep, resulting in fatigue and performance decrements (3,19,21), and raises concerns about the cumulative adverse effects such factors may have on their performance over duty days.

In view of the fact that sleep (homeostatic) and circadian processes interact to influence sleep propensity and waking alertness and performance (37), it is essential to accurately quantify the impact of these factors in order to accomplish the following: 1) predict the times at which skilled performance is most likely to be maintained at acceptable levels; 2) establish the times that are most suitable for restful recovery sleep; and 3) determine the cumulative effects of different work/rest schedules on overall performance capability. Predicting biologically dynamic changes in alertness and performance capability is key to developing schedules that are both safe and productive. Biomathematical modeling that predicts the temporally dynamic effects of sleep and circadian neurobiology on performance holds considerable promise for making such predictions, but challenges remain (13).

There are a number of major efforts underway inter-

TECHNOLOGICAL ADVANCEMENTS, the global economy, and military preparedness now require optimal human functioning 24 hours per day, 7 days per week (24/7). Throughout industrialized countries, a growing number of business, transportation, energy, public health, safety, and maintenance sectors now operate 24/7. For the millions of people working in these environments, the timing of sleep often deviates from its biologically natural nocturnal placement, and work demands frequently require alertness and performance when sleep is either reduced or misaligned relative to the endogenous circadian nadir in alertness. Prolonged

* Posthumously.

From the Fatigue Countermeasures Group (M. M. Mallis); Monterey Technologies, Inc. (S. Mejdal); San Jose State University (T. T. Nguyen), NASA Ames Research Center, Moffett Field, CA; and Division of Sleep and Chronobiology, Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, PA (D. A. Dinges).

Address correspondence to: Melissa M. Mallis, Ph.D., who is the Principal Investigator and Team Leader of the Fatigue Countermeasures Group, NASA-Ames Research Center Human Factors Research and Technology Division, Systems Safety Research Branch, MS-262-4 Moffett Field, CA 94035-1000; Melissa.M.Mallis@nasa.gov.

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nationally that focus on the elaboration and application of biomathematical models of fatigue, and the manner in which they can predict sleep and waking neurobehavioral performance in laboratory and/or operational environments, as well as the extent to which they can be packaged in a user-friendly software program and tested by others for their scientific validity and reliability as scheduling tools. The goal of these efforts is to develop convenient biomathematical tools that will be capable of predicting the impact of acute sleep loss, cumulative sleep loss, circadian desynchrony, differential recovery periods, countermeasure effects, and related aspects of work/rest schedules on performance and safety, in order to help minimize fatigue-related events. This report summarizes, for descriptive purposes, the key features of seven biomathematical models currently in development or commercially available as a basis for helping predict and manage human alertness and performance.

METHODS

The National Aeronautics and Space Administration (NASA), U.S. Department of Defense (DoD), U.S. Army Medical Research and Materiel Command, Office of Naval Research, Air Force Office of Scientific Research, and U.S. Department of Transportation joined to sponsor the Fatigue and Performance Modeling Workshop in Seattle, WA, on June 13–14, 2002. The authors of the biomathematical models most commonly published in scientific literature and/or supported by government funding were invited to attend the workshop. Prior to the Workshop, each modeler was asked to complete a descriptive survey (**Appendix A**) on their model and return it no later than March 15, 2002. The survey results for biomathematical models described in this paper are from the authors who participated in the workshop. After compiling the completed surveys into a summarized form, the modelers were given another opportunity to view the summarized form and make any changes or modifications. This manuscript summarizes the results of the models' descriptive key features based on those modified survey responses received no later than June 28, 2002. A summary of the completed descriptive surveys can be viewed at <http://fatigue.anteon.com/model.htm>.

Additionally, prior to the Workshop, each modeling team was provided laboratory and operational descriptive scenarios (but not the resulting performance and alertness data) that included some aspect of sleep deprivation and circadian desynchrony (e.g., transmeridian travel, shift work, chronic partial sleep restriction, prolonged work). They were asked to apply their model to the scenarios and provide estimated performance and alertness levels as calculated by their specific fatigue and alertness algorithm. The results, as estimated by each model, were compared against actual data (when they were available) to highlight critical gaps that still remain in the accuracy and validity of models. These data are presented in a separate article (41).

RESULTS

Full survey results were obtained from representatives of seven biomathematical models of human fatigue and performance. Each of these models is described in detail in manuscripts by the modelers and co-authors throughout this special issue of *Aviation, Space, and Environmental Medicine* (1,2,4,23–25,30). The primary purpose of this article was to compare and contrast the modelers' responses to the survey (**Appendix A**). Following a brief description of these models, their similarities and differences as reported via the survey instrument are highlighted based on the data presented in Tables I–V.

Descriptions of the Biomathematical Models as Provided by the Modelers

Presented below are brief overviews of seven models taken directly from information provided in the revised surveys the modelers completed as of June 28, 2002. Specifically, the overviews include the modelers' responses to the following open-end questions: Real-time update capability (question 15), software interface (question 18), conceptual assumptions (question 19), technical assumptions (question 20), and range of validity (question 21). Survey responses collected on their target markets (question 7) and current users (question 8) are also provided. Only those responses specifically provided by the modelers are summarized below.

The descriptions presented in the following sections are based on the surveys that the authors completed. Therefore, these overviews do not necessarily describe the full capabilities of each model. That is, some authors may have provided a more thorough description of their models' capabilities than other authors. We suggest that the modelers be contacted directly to learn more about their specific models.

Two-Process Model and related approaches (1): As noted by the survey respondent, Dr. Achermann, the Two-Process Model (6,7,9) is at the core of many models addressing the regulation of fatigue and performance. The model was created using laboratory data from a number of experiments, including power spectral analysis of electroencephalographic slow wave activity (SWA) during nonREM sleep. According to Achermann, conceptual assumptions of the model include a linear interaction of homeostatic and circadian processes and a sleep inertia component (exponential). There are no technical assumptions except that the simulation starts from a stable state. The modelers also stated that they demonstrated model validity in successful simulations under various sleep conditions.

It was reported that the model was developed for the scientific community of sleep researchers. The respondent stated that the software interface is not standardized, allowing it to be adapted according to specific needs, and at this time, the model does not include a real-time update capability.

Sleep/Wake Predictor 1.4.3.2 Model (2): As reported by the survey respondent, Dr. Åkerstedt, the Sleep/Wake Predictor Model was created using mainly group results from subjective alertness data collected in experi-

ments on altered sleep/wake patterns. The model assumes an exponential fall of alertness during wakefulness, an exponential rise of alertness during sleep, a circadian rhythm of alertness with a peak at 16:48, and an exponential sleep inertia factor. No assumptions are made other than that of a normal 8-h sleep when starting the simulation. According to the survey respondent, the model has been validated in many studies of shift work, mainly as group results, and it has been used to account for diurnal type (morningness-eveningness), and long and short sleep periods.

The target markets identified for use of the Sleep Predictor Model are researchers in sleep/wake regulation and in shift work, companies demanding irregular work hours, and government organizations in charge of safety, health, and work hour regulations. Åkerstedt reported that the model software interface provides screen output including sleep variables (latency, duration, bedtime), alertness and performance curves, accident risk, and percentage of time at sleepiness risk, as well as printer file outputs for all curves and start and end times of all sleep periods. Modification of the software allows for a real-time update capability with use of an external device. The model has been further refined using "accident risk" and shift worker alertness ratings data to link the phase of the circadian component to the wake-up time. The authors use an algorithm generated from laboratory experiments to predict sleep times and durations.

System for Aircrew Fatigue Evaluation (SAFE 2.09) Model (4): As reported by the survey respondent, Mr. Spencer, the SAFE Model is being developed primarily for use in aviation operations. The model was developed based on laboratory experiments and, later, was adjusted based on data collected during actual long-haul flights. The model can be described as a combination of a sinusoidal component in time of day and a cubic trend in time since sleep. The modelers stated that validation studies are being conducted that involve collection of alertness data during actual flights. Currently, airline standby situations are not included, and neither are augmented flights, if part of a multi-sector duty.

Spencer reported that the United Kingdom Civil Aviation Authority is currently using the SAFE Model. According to the survey, the software interface allows for input information to be entered directly on the screen. Results are displayed graphically in two-week time frames and estimates of sleep times are an optional display. Alertness levels during duty periods are color-coded. The current version of the model does not allow for real-time updates.

Interactive Neurobehavioral Model (24)[†]: As reported by the survey respondent, Dr. Jewett, the Interactive Neurobehavioral Model estimates neurobehavioral performance, which is determined by a linear combination of circadian, homeostatic, and sleep inertia components. Unless otherwise stated, initial conditions are assumed to be 8 h of sleep in darkness from 00:00–08:00 and 16 h

of wakefulness in 150 lux. A circadian period of 24.2 is assumed with no missing input data. The modelers reported that validation assessments have been performed in comparisons of model predictions with neurobehavioral data collected in human subjects laboratory studies involving varying light patterns, simulated jet lag, sleep deprivation, and non-24 h schedules. As reported, the model currently does not account for illness, sleep disorders, consumption of alcohol, caffeine, or other drugs.

Jewett reported that model development was targeted for scientific researchers; NASA; DoD schedulers; shift/duty schedulers in trucking, aviation and railway industry; and agencies that regulate duty hours, such as the Federal Aviation Administration. Current users are reported to include scientific NASA and DoD researchers. The model's software is reported to work on a personal computer (PC) and allows the user to input both light levels and sleep/wake times for the specific schedule to be simulated. Text output files, which can be read in any graphical program, are generated to predict performance and alertness levels and minimum core body temperature. The modelers also stated that a revised version of the software is being finalized to generate graphs of the input protocol and output results. An existing version of the model allows for real-time update capability via information directly from an Actiwatch-L (Mini Mitter, Inc., Bend, OR), which can easily be edited to allow for connection with other actigraphy and light sensors.

Sleep, Activity, Fatigue, and Task Effectiveness (SAFTE) Model (23): As reported by the survey respondent, Dr. Hursh, the conceptual assumption for the SAFTE Model includes a sleep reservoir, circadian rhythm, and sleep inertia component that combine additively. Sleep times and duration are generated based on either real world data or an "auto sleep" algorithm. The only technical assumption is that sleep occurs between 22:00–06:00. These times can be adjusted in the software interface to represent actual sleep schedules. The developers stated that the model has been validated against literature and laboratory-conducted sleep deprivation research and that their plans include validation against actual performance of railroad engineers. Although the current version of the model is based on data collected on college-aged students during laboratory studies, a translation function for aviation pilots is available. Currently, the SAFTE Model does not include the effects of physical work, workload, or level of interest in task.

According to Hursh, the SAFTE Model was developed for use in both military and industrial settings, and current users include the U.S. Air Force and Federal Railroad Administration. Additionally, he reported that the SAFTE Model has been applied to the construction of a Fatigue Avoidance Scheduling Tool (FAST) (18), which is designed to help optimize the operational management of aviation ground and flight crews, but is not limited to this application. As reported, the software interface provides the schedule input and predictions in graphical and tabular form, parameter tables used for adjusting the model, and description boxes for schedules and events.

[†] While the Interactive Neurobehavioral Model by Jewett was presented at the Workshop, the manuscript was not received in time to be included in these Proceedings.

Fatigue Audit InterDyne (FAID) 1 W13E Model (30): As indicated by the survey respondent, Dr. Roach, the FAID Model was created from existing research collected during controlled laboratory experiments on the performance-diminishing effects of wakefulness and the restorative effects of sleep. However, the model does not use sleep time as an input (it is an output). Instead, the developers included a linear “recency of shift” effect into the model, as well as the duration of a 7-d work shift history and its corresponding interaction with the time of day. The model’s one conceptual assumption is in determining the fatigue level by a balance between fatigue accumulated during work periods and the amount of recovery obtained during time off from work. The fatigue levels of work periods and the recovery values of rest periods are determined by their timing, duration, and history over the 7 d preceding work history, provided the input is complete. The prediction of sleep is generated from “real world databases relating sleep duration to the time of the break onset and the hours before the next shift starts.”

Roach reported that the model was developed for organizations that employ shift workers, industry regulators, and accident investigators. The respondent indicated the FAID Model is currently used by the Australian Transport Safety Bureau, the Civil Aviation Safety Authority, Qantas (maintenance engineers), Queensland Rail, and Australian Western Railroad. The model’s real-time update capability requires work hours as input. It was reported that the model can be linked to an organization’s roster/schedule engine such that fatigue levels can be determined in real-time for any past, present, or future work schedules. The three software interfaces are input, analysis, and output with an adjustable parameter of 1-, 2-, and 7-d sleep targets.

Circadian Alertness Simulator (CAS) Model (25): As reported by the survey respondent, Dr. Heitmann, the CAS Model conceptually assumes both a circadian homeostatic component and different time constants for varying types of activity. The model is able to generate output with missing data, but only by assuming initial alertness values, which is also performed at the beginning of any record. Heitmann indicated that model validation assessments had been performed in sleep and alertness studies in workers with irregular, regular, and/or rotating work schedules; comparisons of simulated and actual sleep and alertness; and correlations between a fatigue index and accident rates in transportation. It was also reported that the model is currently not able to incorporate effects of light or phase shifting, but efforts are underway to update the model to include phase shifting. According to the respondent, due to technical assumptions, accuracy of estimations is somewhat compromised at the beginning of the record and for 2–3 d after extended periods of missing data.

As stated in the survey response, the CAS Model was originally developed for use in 24 h-transportation and shift work operations and is currently tailored for irregular work schedules in the transportation industry. Future versions of the model will include regular rotating schedules and jetlag applications. Development of the current version of the CAS Model was for use by Cir-

cadian Technologies, Inc., (Lexington, MA) as an integral part of their consulting services, including projects being conducted with Canadian National Roadway, Amtrak, and the Federal Railroad Administration. It was also reported that the model is incorporated in crew optimization software for freight railroads, and that a future model will be developed for industrial shift work. As reported by Heitmann, the CAS Model software interface provides a double plot of an individual’s activity and sleep pattern; a plot of an individual’s alertness curve; histograms of both activity and alertness for an individual or group; both individual and group statistics for alertness and daily sleep duration; plots for individual or group work pattern statistics; and a fatigue index group histogram. The developers reported that although real-time updates are conceptually possible using actigraphy data, these have not yet been implemented.

Comparisons of the Biomathematical Models

The full survey (Appendix A) responses provided by the modelers are presented in Tables I-V.

Prediction goals of the models: **Table I** summarizes the broad prediction goals of each of the seven models, as well as goals in terms of predicting various types of laboratory experiments on altered work/rest patterns and field operations on altered work/rest patterns (survey questions 10 and 11). In terms of each model’s broad prediction goals, the majority of models seek to predict some aspects of subjective fatigue or sleepiness ($n = 6$); performance ($n = 5$); physiological sleepiness/alertness ($n = 4$); or the impact of countermeasures such as naps and caffeine ($n = 5$). In contrast, few are concerned with predicting accident risk ($n = 2$); optimal work/rest schedules ($n = 3$); circadian phase ($n = 3$); or specific performance task parameters ($n = 2$). The Two-Process Model, Sleep/Wake Predictor Model, Interactive Neurobehavioral Model, SAFTE Model, and CAS Model are each focused on predicting five or more outcomes; whereas the SAFE Model is focused exclusively on subjective outcomes, and the FAID Model on subjective outcomes and performance.

Models also differed markedly relative to their focus on prediction of various types of laboratory experiments on altered work/rest patterns (survey question 11, subsection 1). Similar to prediction goals, the Two-Process Model, Sleep/Wake Predictor Model, Interactive Neurobehavioral Model, and the SAFTE Model all seek to predict laboratory experimental results for each of the five altered work/rest patterns in the survey (i.e., simulated shift work; simulated sustained or continuous operations; chronic partial sleep deprivation; simulated jet lag; and the effects of countermeasures). In contrast, neither the SAFE Model nor the CAS Model targets prediction of any of the five laboratory simulations of altered work/rest patterns. The FAID Model is focused on prediction of laboratory simulation of shift work and sustained operations.

Models also segregated into two groups relative to the extent to which they focused on prediction of various types of field operations involving altered work/rest patterns (survey question 11, subsection 2). Again,

TABLE I. CURRENT PREDICTION GOALS OF BIOMATHEMATICAL MODELS OF FATIGUE AND PERFORMANCE.

	Two-Process Model	Sleep/Wake Predictor Model	SAFE Model	Interactive Neurobehavioral Model	SAFTE Model	FAID Model	CAS Model
Q.10 - Broad categorizations of what model seeks to predict							
<i>Key aspects of:</i>							
Subjective state (e.g., fatigue, sleepiness)	✓	✓	✓	✓		✓	✓
Performance (e.g., cognitive, physical)	✓	✓		✓	✓	✓	
Physiology (e.g., physiological alertness or physiological sleepiness)	✓	✓		✓			✓
Accident risk		✓					✓
Optimal work/rest schedules		✓			✓		✓
Impact of specific countermeasures (e.g., nap, caffeine)	✓	✓		✓	✓		✓
Other: (open-ended question)							
Biocompatibility of work schedules							✓
Circadian phase		✓		✓	✓		
Effects of non-linear metric	✓						
Homeostatic and circadian interaction	✓						
Specific task parameters		✓			✓		
Q.11 - Model's prediction goals/current focus							
<i>Prediction of results from laboratory experiments on altered work/rest patterns:</i>							
Simulated shift work	✓	✓		✓	✓	✓	
Simulated sustained or continuous operations	✓	✓		✓	✓	✓	
Chronic partial sleep deprivation	✓	✓		✓	✓		
Simulated jet lag	✓	✓		✓	✓		
Effects of countermeasures (behavioral, pharmacological, technological)	✓	✓		✓	✓		
Other: (open-ended question)							
Circadian effects of light exposure				✓			
Circadian phase					✓		
Effects of sleep deprivation	✓						
Sleep fragmentation/times					✓		
<i>Prediction of results from field operations:</i>							
Length of shift work		✓		✓	✓		✓
Shift work/night work operations		✓		✓	✓	✓	✓
Sustained or continuous operations		✓		✓	✓		✓
Jet lag	✓	✓		✓	✓		
Other: (open ended question)							
Accident risk in transportation							✓
Army, Navy watch systems		✓					
Civil air operations		✓	✓			✓	
Effects of irregular work schedules							✓
Non-24 h schedules				✓			
Sleep environment					✓		
Space mission scheduling	✓						
Time of sleep					✓		

all models, except the SAFE Model and the FAID Model, sought to predict outcomes in various domains. The latter models were limited to civil air operations (SAFE Model and FAID Model) and shift work (FAID Model).

Parameters estimated by models: **Table II** summarizes the modelers' responses to a query on which of each of nine capabilities is currently implemented in each model (survey question 12). According to their responses, every one of the models (n = 7) provides estimates of the "recovery potential of sleep (e.g., sleep timing, sleep duration)," and most provide estimates of "changes as a function of time awake" (n = 6); of "endogenous circadian parameters (e.g., period, phase)" (n = 5); of "sleep inertia" (n = 5); and of "cumulative sleep debt" (n = 5). In contrast, only a minority of the models focus on estimates of "changes as a function of work time or time on task" (n = 3); estimates of "type of work (e.g., cognitive or physical)" (n = 2); estimates of "individual variability" (n = 3); or estimates of "effects of environmental variables (e.g.,

light, temperature, noise)" (n = 3). While six of the models provided estimates of at least six or more of the nine areas, the FAID Model was again the exception, focusing on estimates of two categories ("recovery potential of sleep" and "changes as function of work time or time on task").

Required inputs for models: **Table III** summarizes the required inputs for each model in response to an open-ended question (survey question 13). There was no consistency among models in response to this query. "Work hours" was a required input for a majority (n = 4) (Sleep/Wake Predictor Model, SAFE Model, FAID Model, and CAS Model) of the seven models. Sleep/wake time was a required input for the remaining three models (Two-Process Model, Interactive Neurobehavioral Model, and SAFTE Model). Interestingly, "work hours" was the only required input for the Sleep/Wake Predictor Model, FAID Model, and the CAS Model. Consistent with its sole focus on commercial aviation, the SAFE Model required specification of four aviation-specific inputs.

TABLE II. CAPABILITIES CURRENTLY IMPLEMENTED IN THE MODELS.

	<i>Two-Process Model</i>	<i>Sleep/Wake Predictor Model</i>	<i>SAFE Model</i>	<i>Interactive Neurobehavioral Model</i>	<i>SAFTE Model</i>	<i>FAID Model</i>	<i>CAS Model</i>
Q.12 - Capabilities currently implemented							
<i>Estimates of:</i>							
Changes as a function of time awake	✓	✓	✓	✓	✓		✓
Changes as a function of work time or time on task			✓			✓	✓
Type of work (e.g., cognitive vs. physical)		✓					✓
Recovery potential of sleep (e.g., sleep timing, sleep duration)	✓	✓	✓	✓	✓	✓	✓
Endogenous circadian parameters (e.g., period, phase)	✓		✓	✓	✓		✓
Sleep inertia	✓	✓	✓	✓	✓		✓
Cumulative sleep debt	✓	✓		✓	✓		✓
Individual variability in any of above parameters		✓	✓				✓
Effects of environmental variables (e.g., light, temperature, noise)	✓			✓	✓		
*Other: (open ended question)							

* No responses from modelers on this category

Primary outputs generated by models: **Table IV** summarizes the primary outputs generated by each model in response to an open-ended question (survey question 16). With the exception of the SAFTE Model, all six remaining models provided primary output information on subjective alertness and/or subjective fatigue levels/scores. There was no consistency among the models relative to their specific generation of either circadian (e.g., estimated phase) or sleep outcomes (e.g., sleep accumulated), but five models did include at least one primary output in the circadian-sleep area. The same was the case for generation of primary performance outcomes (e.g., cognitive performance, lane tracking, performance effectiveness, reaction time, vigilance, violations based on risk thresholds)—four of the seven models had at least one primary performance

output (Sleep/Wake Predictor Model, Interactive Neurobehavioral Model, SAFTE Model, and FAID Model). The Sleep/Wake Predictor Model offered by far the largest number of primary outputs (n = 9), while all other models generated three primary outputs (Two-Process Model, Interactive Neurobehavioral Model, FAID Model, and CAS Model) or only one primary output (SAFE Model and SAFTE Model).

Model information: **Table V** displays information on each model's status relative to patent, proprietary access, commercialization, and target market (survey questions 1,2,4-7). Although only the CAS Model is patented, the SAFTE Model has a patent pending, and there is an intention to patent the Interactive Neurobehavioral Model. The SAFE Model, FAID Model, and CAS Model are all proprietary. The SAFTE Model,

TABLE III. REQUIRED INPUTS TO MODELS.

	<i>Two-Process Model</i>	<i>Sleep/Wake Predictor Model</i>	<i>SAFE Model</i>	<i>Interactive Neurobehavioral Model</i>	<i>SAFTE Model</i>	<i>FAID Model</i>	<i>CAS Model</i>
Q.13 - Types of required input for each model (open ended question)							
<i>Aviation specific variables:</i>							
Bunk availability			✓				
Number of pilots working			✓				
Number of sectors			✓				
Pilot augmentation			✓				
<i>Environmental variables:</i>							
Light levels	✓			✓			
Location(s)			✓				
<i>Sleep variables:</i>							
Sleep length					✓		
Sleep quality					✓		
Sleep/wake time	✓			✓	✓		
Time allotted for sleep				✓			
<i>Work variables:</i>							
Work hours		✓	✓			✓	✓

TABLE IV. PRIMARY OUTPUTS FOR MODELS.

	<i>Two-Process Model</i>	<i>Sleep/Wake Predictor Model</i>	<i>SAFE Model</i>	<i>Interactive Neurobehavioral Model</i>	<i>SAFTE Model</i>	<i>FAID Model</i>	<i>CAS Model</i>
Q.16 - Types of primary output generated by each model (open ended question)							
<i>Circadian/sleep variables:</i>							
Circadian phase/period	✓			✓			
Estimate of sleep accumulated		✓				✓	
Sleep latency		✓					
Sleep start/end		✓					✓
<i>Objective performance variables:</i>							
Cognitive throughput				✓			
Lane drifting (driving simulator)		✓					
Performance effectiveness		✓			✓		
Reaction time		✓					
Vigilance performance		✓					
Violations based on risk threshold levels						✓	
<i>Subjective variables:</i>							
Alertness ratings	✓	✓	✓	✓			✓
Fatigue level/scores	✓	✓				✓	✓

TABLE V. MODEL INFORMATION.

	<i>Two-Process Model</i>	<i>Sleep/Wake Predictor Model</i>	<i>SAFE Model</i>	<i>Interactive Neurobehavioral Model</i>	<i>SAFTE Model</i>	<i>FAID Model</i>	<i>CAS Model</i>
Q.2 - Model name and version	Two-Process Model and related approaches	Sleep/Wake Predictor 1.4.3.2	System for Aircrew Fatigue Evaluation 2.09	Interactive Neurobehavioral Model	Sleep, Activity, Fatigue, & Task Effectiveness Model	Fatigue Audit InterDyne 1W13E	Circadian Alertness Simulator
Q.1 - Survey respondent	Peter Achermann	Torbjorn Akerstedt	Mick Spencer	Megan Jewett	Steven Hursh	Greg Roach	Anneke Heitmann
Q.4 - Patent information							✓
Model patented							USA
Country of patent							Moore-Ede, Mitchell
Patent holder							7/18/1995
Patent date							5,433,223
Patent number					✓		
Patent pending					✓		✓
Intending to patent							
Q.5 - Proprietary information			✓				✓
Model proprietary							
Q.6 - Commercial information					✓	✓	✓
Model commercially available							
Available from					NTI, SAIC	Interdynamics	Circadian Technologies
Q.7 - Target market (open ended question)							
<i>Aviation specific:</i>							
Airlines			✓				
Boeing/Airbus ultra-long range plane developers				✓			
Civil aviation regulators			✓				
<i>24/7 operations:</i>							
Companies with irregular work hours		✓					✓
24-h transportation operations							✓
Industrial settings/regulators		✓			✓		
<i>Research:</i>							
Scientific community	✓						
NASA/DOD scientists				✓			
Organizations/operations/researchers with shiftworkers		✓				✓	✓
Scientific/sleep/wake regulation researchers	✓	✓		✓			
<i>Other:</i>							
Accident investigators						✓	
Military settings					✓		

FAID Model, and CAS Model are commercially available. According to these survey responses, it appears that only the Two-Process Model, and the Sleep/Wake Predictor Model are completely accessible and freely available for public use and scrutiny. In terms of target markets, the models have a broad and varied user/customer target population, as previously described.

DISCUSSION

Survey responses revealed that models varied greatly relative to their reported prediction goals and capabilities. The majority of models sought validation through prediction of either laboratory experiments or field operations on altered work/rest patterns (i.e., simulated shift work; simulated sustained or continuous operations; chronic partial sleep deprivation; simulated jet lag; and the effects of countermeasures). The Two-Process Model, Sleep/Wake Predictor Model, Interactive Neurobehavioral Model, and the SAFTE Model all seek to predict outcomes from such venues, whereas the CAS Model, FAID Model, and SAFE Model have much less focus on predictions and improvements based on laboratory and field data sets. To the extent that laboratory and field data sets can provide data that permit validation of model predictions based on known changes in sleep and circadian-mediated physiology, and objectively obtained performance outcomes, it is critical that all models focus to some extent on continued validation and improvement through these contexts.

It is noteworthy that the only input or output parameter that is included in all seven models was output estimates of the "recovery potential of sleep (e.g., sleep timing, sleep duration)." This is surprising, if for no other reason than there has been scant scientific data on the precise mathematical nature of the neurobehavioral (e.g., performance, risk, fatigue level) recovery function relative to sleep duration. Other than assuming more sleep is better than less sleep, it is not clear how accurate any of the model estimates are relative to this critical factor (41). It is a testament to the importance all models placed on estimating recuperation from sleep that recovery sleep potential is present in all of them. The same cannot be said for circadian phase estimates, which are outputs only of the Two-Process Model and Interactive Neurobehavioral Model.

In contrast to the recovery potential of sleep, the majority of models appear to ignore the one factor that governments and regulatory bodies most often seek to limit when it comes to fatigue and work hours—namely, work duration itself (i.e., time on task) in relation to type of work. This may have to do with the fact that remarkably little is known about how important work time is relative to wake time, and whether or not the type of work determines the rate of fatigue development independent of, or in interaction with, wake time (11,20,28). Some models appear to treat wake time as comparable to work time, while others focus exclusively on work hours, regardless of wake time. Models that appear to have a relatively strong application goal oriented toward industry (FAID Model, CAS Model,

Sleep/Wake Predictor Model, SAFE Model) appear to utilize estimates of work time and type of work.

Few models attempt estimates of "individual variability" or estimates of "effects of environmental variables (e.g., light, temperature, noise)." This is interesting because these two factors are precisely what many workers feel are the most salient in determining the response to a fatiguing work schedule (32,40).

In terms of primary outputs generated by the seven biomathematical models, the most common was subjective alertness and/or subjective fatigue levels/scores. It has long been controversial in scientific studies of fatiguing sleep/wake schedules and work/rest schedules as to whether subjective ratings of sleepiness and alertness are reliable markers of actual behavioral capability (8,10,42). As many studies find subjective ratings of sleepiness and alertness are not reliable as find that they are reliable (29,31,39). Some models did not generate circadian and/or sleep outcomes, while other modelers indicated they offered no generation of primary performance outcomes (Two-Process Model, SAFE Model, CAS Model), which is surprising since performance capability is ultimately the outcome most relevant to safety and production.

Despite their differences, these seven biomathematical models have a fundamental similarity—they make somewhat comparably broad assumptions about the decay of functional capability with elevating sleep drive, and the recovery of function with sleep, as well as the circadian modulation of sleep and waking. These assumptions reflect the seminal role the Two-Process Model has played in the subsequent development of the other six models. However, the models vary considerably in the manner in which the underlying two processes (i.e., homeostatic drive for sleep and endogenous circadian timing) are modeled. All the models have an underlying curve describing the attenuation of performance while awake, the replenishment of performance while asleep, and an oscillating curve representing the circadian effect on performance. It is in the modeling of these curves that the model divergence can best be seen. For instance, the attenuation and replenishment curves for wake and sleep, respectively, are modeled in a variety of ways—linearly, exponentially, as a polynomial, or as a sigmoid. Similarly, the circadian effect is modeled as a sinusoid, a skewed sinusoidal, a combination of sinusoids with different periods, or modeled using Van der Pol oscillators.

Although all the models are based on the homeostatic drive for sleep and the endogenous circadian system, they differ markedly in their inclusion of other factors that potentially can impact fatigue and performance. For instance, only the Interactive Neurobehavioral Model uses specific estimates of the light received by the individual and the corresponding effect it is expected to have on phase shifting the circadian clock. Some models include a sleep inertia effect that lowers performance for the first few hours after awakening (12,33,38). The effects of pharmacological agents such as alcohol and caffeine are not included in all of the models. Some models embed in the algorithms another model specifically designed for the prediction of sleep

onset and duration, while others use databases of actual sleep from prior studies in order to estimate these important sleep parameters. It is not known whether these approaches are comparable.

Predicting fluctuations in alertness and performance is the key to developing schedules that are both safe and productive, and to identify when to optimally apply countermeasures to prevent performance-impairing fatigue. The seven biomathematical modeling teams that participated in this survey were generous in their time and responses. Details of their models and their modeling strategies and goals may have advanced some since this survey was taken. We refer the reader to their respective articles in this volume, as well as the comments of others on those articles and supporting publications.

APPENDIX A.

Biomathematical Model Survey, Fatigue and Performance Modeling Workshop, June 13–14, 2002

Dear modeler:

The information that you provide in this survey is critical to a productive and successful Workshop and serves several important purposes. First, your responses will become part of a compendium of public information about the models presented at the Workshop. This compendium will be made available at the meeting. Second, the data collected here will be used to provide you with several scenarios for which you will be requested to make model predictions before and during the meeting. The information you provide will help ensure these scenarios are realistic and fall within the domain of your model. Finally, the survey data collected here also will ensure realistic expectations about what the models will yield. For these reasons, it is important that your responses be as complete and accurate as possible.

Please complete this survey no later than 15 March 2002. If you have more than one model, please complete a separate survey for each one. If you have questions about how to answer any portion of the survey, please contact Dr. David Neri (nerid@onr.navy.mil) or Dr. Roy Vigneulle (RVigneulle@anteon.com). Thank you.

- 1. Name of survey respondent: _____
- 2. Model name and version: _____
- 3. Model authors/modeling team members:
 Name: _____
 Address: _____
 Phone: _____
 Email: _____
 Name: _____
 Address: _____
 Phone: _____
 Email: _____

etc. (allow for entry of unspecified number of people)

- 4. Patent information:
 Model patented: no yes
 If yes, country of patent: _____
 If yes, patent holder: _____
 If yes, patent date: _____
 If yes, patent number(s): _____
 Patent pending: no yes
 Intending to patent: no yes
- 5. Is your model proprietary? no yes
- 6. Is your model commercially available? no yes
 If yes, from whom? _____
- 7. What is the target market for your model? _____
- 8. List current users for your model: _____
- 9. What agency(ies), if any, supported the development of your model? _____
- 10. Broadly categorize what your model currently seeks to predict: (Check all that apply.)
 Key aspects of subjective state (e.g., fatigue, sleepiness)

- Key aspects of performance (e.g., cognitive, physical).
- Key aspects of physiology (e.g., physiol. alertness or physiol. sleepiness).
- Key aspects of accident risk.
- Key aspects of optimal work/rest schedules.
- Impact of specific countermeasures (e.g., nap, caffeine).
- Other (please describe): _____

Additional comments/details: _____

- 11. Describe the current focus or goals of your model: (Check all that apply.)
 Prediction of results from laboratory experiments on altered work/rest patterns:
 simulated shift work
 simulated sustained or continuous operations
 chronic partial sleep deprivation
 simulated jet lag
 effects of countermeasures (behavioral, pharmacological, technological)
 other (please describe: _____)
 Prediction of results from field operations.
 length of work shift
 shift work/night work operations
 sustained or continuous operations
 jet lag
 other (please describe: _____)
 Additional comments/details: _____
- 12. Which of the following capabilities are currently implemented in your model ? (Check all that apply.)
 Estimates changes as a function of time awake
 Estimates changes as a function of work time or time on task
 Estimates type of work (e.g., cognitive vs. physical)
 Estimates the recovery potential of sleep (e.g., sleep timing, sleep duration)
 Estimates endogenous circadian parameters (e.g., period, phase)
 Estimates sleep inertia
 Estimates cumulative sleep debt
 Estimates individual variability in any of the above parameters
 Estimates effects of environmental variables (e.g., light, temperature, noise)
 Please specify which environmental variables: _____
 Other (please specify: _____)
- 13. List ALL types of REQUIRED INPUT for your model: (Include technical details such as file format and structure and describe any content details such as required header info, item syntax, etc.)
- 14. List ALL types of OPTIONAL INPUT for your model: (Include technical details such as file format and structure and describe any content details such as required header info, item syntax, etc.)
- 15. Describe any REAL-TIME UPDATE CAPABILITY of your model using other technology input (e.g., wrist actimeter, physiologic sensor, light sensor, etc.): _____
- 16. List ALL types of PRIMARY OUTPUT that your model generates: (Include technical details such as file format and structure and describe any content details such as required header info, item syntax, etc.)
- 17. List ALL types of OTHER OUTPUT that your model generates: (Include here output that you consider non-primary. This might or might not include parameter estimates, statistical assessments, estimates of prediction error, inter-individual variability, or a log file. Include technical details such as file format and structure and describe any content details such as required header info, item syntax, etc.)
- 18. Briefly describe your modeling software interface: (e.g., screen output, printer output, etc. Focus on describing content rather than technical or graphical details.) _____
- 19. Describe the essential CONCEPTUAL ASSUMPTIONS underlying your model: (List conceptual assumptions that are mathematically expressed in the model, e.g., a particular feature is based on an exponential decay function with a time constant of ____; light exposure information is required to be known, etc.) _____
- 20. Describe the essential TECHNICAL ASSUMPTIONS underlying your model: (e.g., no missing information; at least one event every 24 h; initial values required to be known; etc.) _____
- 21. Describe the RANGE OF VALIDITY of your model: (Describe conditions for which the model prediction is not accurate, e.g., no

- sleep deprivation longer than 48 h; model predictions not appropriate for representing individual performance but rather only average group performance, etc.)
22. List ALL the adjustable parameters included in your model:
 23. Describe any aspects of sleepiness or fatigue that your model does not cover or otherwise excludes.
 24. List all validation studies, parameter sensitivity analyses, or other validity assessments performed for your model.
 25. List KEY REFERENCES ONLY for published papers describing your model, its application, and its validation.

- A. Publications on model description:
- B. Publications on model application to laboratory or field data sets or schedules:
- C. Publications on model validation:

IMPORTANT: As the final step in this survey, please email both a sample input file and a sample output file to _____.

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Tammy Thientam Nguyen, senior research associate in the Fatigue Countermeasures Group, NASA Ames Research Center, passed away at the age of 42 on August 13, 2003 after a tragic scuba diving accident in Monterey. She received both her B.A. (1998) and her M.A. (2001) degrees in Experimental Psychology from San Jose State University with an emphasis in stress-related factors and quality of sleep. Tammy's research in the Fatigue Countermeasures Group focused on the effects of sleep loss and night work on human neurobehavioral functioning, circadian rhythms, and fatigue and alertness of airline pilots. Tammy's enthusiasm, laughter, confidence, and knowledge will be truly missed by family, friends, and colleagues.

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REFERENCES

1. Achermann P. The two-process model of sleep regulation revisited. *Aviat Space Environ Med* 2004; 75(3,Suppl.):A37-48.
2. Åkerstedt T, Folkard S, Portin C. Predictions from the three process model of alertness. *Aviat Space Environ Med* 2004; 75(3,Suppl.):A75-83.
3. Beljan JR, Rosenblatt LS, Hetherington NW, et al. Human performance in the aviation environment: Final report. Hampton, VA: NASA-Langley Research Center 1972; NASA Contract No. NAS2-6657.
4. Belyavin AJ, Spencer MB. Modeling performance and alertness: the QinetiQ approach. *Aviat Space Environ Med* 2004; 75(3,Suppl.):A93-103.
5. Bonnet MH. Differentiating sleep continuity effects from sleep stage effects. *J Sleep Res* 2000; 9:403-6.
6. Borbély AA. A two-process model of sleep regulation. *Hum Neurobiol* 1982; 1:195-204.
7. Borbély AA, Achermann P. Sleep homeostasis and models of sleep regulation. *J Biol Rhythms* 1999; 14:557-68.
8. Brown ID. Prospects for technological countermeasures against driver fatigue. *Accident Analysis Prevent* 1997; 29:525-31.
9. Daan S, Beersma D, Borbély A. Timing of human sleep: recovery process gated by a circadian pacemaker. *Am J Physiol* 1984; 246:R161-78.
10. Dinges DF. The nature of sleepiness: causes, contexts and consequences. In: Stunkard A, Baum A, eds. *Perspectives in behavioral medicine: eating, sleeping and sex*. Hillsdale, NJ: Erlbaum; 1989; 147-80.
11. Dinges DF. An overview of sleepiness and accidents. *J Sleep Res* 1995; 4(Suppl:2):4-11.
12. Dinges DF. Are you awake? Cognitive performance and reverie during the hypnopompic state. In: Bootzin RR, Kihlstrom JF, Schacter D, eds. *Sleep and cognition*. Washington, DC: American Psychological Association; 1990; 159-75.
13. Dinges DF, Achermann P. Commentary: future considerations for models of human neurobehavioral function. *J Biol Rhythms* 1999; 14:598-601.
14. Dinges DF, Kribbs NB. Performing while sleepy. Effects of experimentally-induced sleepiness. In: Monk TH, ed. *Sleep, sleepiness and performance*. Chichester: John Wiley & Sons; 1991; 97-128.
15. Dinges DF, Pack F, Williams K, et al. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4-5 hours per night. *Sleep* 1997; 20:267.
16. Doran SM, Van Dongen HP, Dinges DF. Sustained attention performance during sleep deprivation: evidence of state instability. *Arch Ital Biol* 2001; 139:253-67.
17. Drummond SP, Brown GG, Stricker JL, et al. Sleep deprivation-induced reduction in cortical functional response to serial subtraction. *Neuroreport* 1999; 10(18):3745-8.
18. Eddy DR, Hursh SR. Fatigue Avoidance Scheduling Tool (FAST). Brooks AFB, TX: AFRL/HEOA; 2001; Report No: AFRL-HEBR-TR-2001-0140.
19. Graeber RC. Aircrew fatigue and circadian rhythmicity. In: Wiener EL, Nagel DC, eds. *Human factors in aviation*. San Diego, CA: Academic Press; 1988; 305-44.
20. Hamelin P. Lorry drivers' time habits in work and their involvement in traffic accidents. *Ergonomics* 1987; 30:1323-33.
21. Hawkins F. *Human factors in flight*. Brookfield, VT: Gower; 1987.
22. Horne JA. Human sleep, sleep loss, and behaviour. Implications for prefrontal cortex and psychiatric disorder. *Br J Psychiatr* 1993; 162:413-9.
23. Hursh SR, Redmond DP, Johnson ML, et al. Fatigue models for applied research in warfighting. *Aviat Space Environ Med* 2004; 75(3,Suppl.):A44-53.
24. Jewett ME, Kronauer RE. Interactive mathematical models of subjective alertness and cognitive throughput in humans. *J Biol Rhythms* 1999; 14:588-97.
25. Moore-Ede M, Heitmann A, Croke D, et al. Circadian alertness simulator for fatigue risk assessment in transportation: application to reduce frequency and severity of truck accidents. *Aviat Space Environ Med* 2004; 75(3,Suppl.):A107-18.
26. Naitoh P. Sleep deprivation in humans. In: Venables, PH, Christie, MJ eds. *Research in psychophysiology*. London: John Wiley; 1975.
27. Rogers NL, Szuba M, Staab JP, et al. Neuroimmunologic aspects of sleep and sleep loss. *Semin Clin Neuropsychiatr* 2001; 6:295-307.
28. Rosa RR. Extended work shifts and excessive fatigue. *J Sleep Res* 1995; 4(Suppl:2):51-6.
29. Rosa RR. Report of chronic insomnia of poor EEG sleep. *Psychosomatic Medicine* 2000; 62:474-82.
30. Roach GD, Fletcher A, Dawson D. A model to predict work-related fatigue based on hours of work. *Aviat Space Environ Med* 2004; 75(3, Suppl.):A61-9.
31. Rosekind MR, Graeber RC, Dinges DF, et al. Crew factors in flight operations IX: Effects of planned cockpit rest on crew performance and alertness in long-haul operations. Moffett Field, CA: NASA Ames Research Center; 1994; NASA Technical Memorandum 108839.
32. Rosekind MR, Miller DL, Gregory KB, et al. Crew factors in flight operations XII: A survey of sleep quantity and quality in on-board crew rest facilities. Moffett Field, CA: NASA Ames Research Center; 2000; NASA Technical Memorandum 2000-20961.
33. Rosekind MR, Smith RM, Miller DL, et al. Alertness management: strategic naps in operational settings. *J Sleep Res* 1995; 4(Suppl: 2):62-6.
34. Shearer WT, Reuben JM, Mullington JM, et al. Soluble TNF-alpha receptor 1 and IL-6 plasma levels in humans subjected to the sleep deprivation model of spaceflight. *J Allergy Clin Immunol* 2001; 107:165-170.
35. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet* 1999; 354:1435-9.
36. Thomas M, Sing H, Belenky G, et al. Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. *J Sleep Res* 2000; 9:335-52.
37. Van Dongen HPA, Dinges DF. Circadian rhythms in fatigue, alertness and performance. In: Kryger MH, Roth T, Dement

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- WC, eds. Principles and practice of sleep medicine, 3rd ed. Philadelphia: Saunders; 2000; 391–9.
38. Van Dongen HPA, Price NJ, Mullington JM, et al. Caffeine eliminates psychomotor vigilance lapses from sleep inertia. *Sleep* 2001; 24:813–9.
39. Van Dongen HPA, Maislin, G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep* 2003; 26:117–26.
40. Van Dongen HPA, Rogers NL, Dinges DF. Sleep debt: theoretical and empirical issues. *Sleep Biol Rhythms* 2003; 1:5–13.
41. Van Dongen HPA. Comparison of model predictions to experimental data: rectifying false impressions. *Aviat Space Environ Med* 2004; 75(3,Suppl.):A122–4.
42. Wylie CD, Shultz T, Miller JC, et al. Commercial motor vehicle driver fatigue and alertness study: Project report. Washington, DC: Federal Highway Administration, U S Department of Transportation; 1996 Report No; FHWA-MC-97-002.