Research Proposal

A. Specific Aims

This project seeks to better explain the functional and algorithmic roles of rapid eye movement (REM) sleep in both human and machine learning. To our knowledge, no work has been done computationally modeling a learning system that utilizes both REM and non-REM (NREM) processes. The most popular theories on the function of NREM and REM sleep currently appear at odds with each other, with REM appearing to impede on the benefits thought to emerge during NREM sleep. Assessing plausible REM algorithms in artificial neural networks (ANNs) also demonstrating NREM and waking activity, as well as these ANNs' alignment with human performance, will help refine and specify our understanding of REM sleep, as well as potentially yield new sleep-inspired methods for machine-learners.

We will develop and assess models of REM activity rooted observed in human REM activity and instantiate these models in artificial neural networks (ANNs) concurrently simulating NREM and waking activity. We will examine how these ANNs perform on categorization compared to ANNs not including an REM component. Once we have identified classes of problems that are better solved by either networks with (REM+) or without (REM-) an REM component, we will run human behavioral studies examining whether humans who have experience either normal sleep (REM+) or REM-deprived sleep (REM-) will outperform each other in the same classes of problems. Identifying conditions where agents with an REM component perform both better and worse than those without one, rather than simply demonstrating that those with REM generally perform better, is a necessary step in understanding REM sleep on both a functional and an algorithmic level.

A core idea behind the work being proposed is that REM sleep does not only replay memories from wakefulness, but also generates novel experiences that emerge through neural activation without external sensory feedback. This idea makes the specific prediction that REM will aid a control system (be it biological brain or ANN) in tasks with little training data; as the training set grows, systems without REM should eventually outperform those that have it. Translated into a human task, REM- participants in our experiments should outperform those allowed normal sleep in categorization tasks of novel stimuli in cases where they receive a large amount of training. However, this effect should flip with a small amount of training, and REM+ participants should outperform those deprived of REM sleep. Participants will undertake either a long or short training session, sleep that night under experimenter observation, and partake in a testing session on novel stimuli, which they must attempt to categorize, upon waking the following morning.

Specific Aim 1: Computationally derive more precise functional and computational accounts of REM sleep.

A. Computationally model a control system utilizing both NREM and REM components.

Researches have previously modeled NREM [1] and REM [2-3], but not their co-occurrence in a single network. NREM sleep and REM sleep alternate constantly through sleep, and modeling both processes in tandem rather than independently is a necessary step in deriving a more complete understanding of the function of sleep.

B. Identify task conditions where REM is either beneficial or detrimental.

Previous research has primarily focused on how REM generally aids in memory consolidation, and, to our knowledge, no current work exists explicitly predicting properties of tasks that would yield both better and worse performance in REM+ networks. We will build ANNs that have waking, NREM, and REM components. We will have these ANNs attempt to categorize pattern sets under varying time and sample size constraints. We predict that REM+ networks will be able to reach sufficient testing performance (e.g. ~80-90% accuracy) faster and with smaller training sets than REM- networks, but that REM- networks will have higher asymptotic performance levels compared to REM+ networks.

Specific Aim 2: Demonstrate sufficient and asymptotic performance level difference with or without REM sleep in human participants.

We predict that human performance in categorization tasks after sleep will align with that of computer simulations after a night's rest. We will run multiple experiments, each with one REM+ group and one REM- group. The training session participants receive will vary in duration (short or long) and training set size (small or large). We predict that short sessions and small training sets will benefit REM+ participants. Of particular interest, we make the novel prediction that long sessions and large training sets will benefit REM- participants.

B. Background and Significance

REM sleep and synaptic homeostasis: We humans spend about a third of our lives sleeping. Why we need sleep and what drives actually happens in our heads during sleep remains one of the most enduring questions in psychology. Intuitively, sleep seems to offer a "relaxation" time where our brains "shut down." Over the past decade, the synaptic homeostasis hypothesis (SHH) gained wide acceptance as a useful model of the algorithmic processes and functional outcomes of non-REM (NREM) sleep [1,4-7], and seem to back this "relaxed-state" intuition. The core idea of the SHH is that, through a waking day, synaptic connections are increasingly globally strengthened. Through sleep, particularly slow-wave sleep (SWS) that occurs during NREM, connections are globally reduced to baseline levels for the next day of wakefulness. A main functional outcome of this reduction in synaptic connectivity is the removal of weak coincidental connections made through the day, leaving only well established connections, as well as room for novel ones.

REM sleep, where EEG activity levels can reach and even exceed waking levels [8], has forced psychologists to understanding the role of sleep in learning as more than restfulness. With respect to the SSH, the removal of weak connections seems at odds with activity observed during REM sleep. Electroencephalogram (EEG) activity observed during REM sleep is remarkably similar to that observed during wakefulness, with the most accepted theory of activity being the replay of waking experience [9]. If this was the case, this activity would hinder the down-regulation of memories performed during NREM. Resolving this apparent incompatibility between prominent functions of NREM and REM sleep can help us better understand the function of sleep as a whole.

Towards a falsifiable account of REM sleep: Falsification has long been at the core of effective scientific research [13]. Current theories of REM function face a conundrum in that they primarily focus solely on the advantages of REM, particularly how REM can yield better memory consolidation [3,14-15]. Various computational models [e.g. 2,3] have already demonstrated plausible REM algorithms that improve memory retention. However, there are many ways an algorithm could plausibly increase memory retention. Much stronger support for a viable REM algorithm would be that one not only benefits cognition as in humans, but also *hinders* cognition as in humans. REM sleep is not always beneficial: there is a rich field dedicated to the study of REM-deprivation and its benefits to depressed patients [26] and to emotional well-being in general [24]. The connection between depression and REM sleep demonstrates that, whatever algorithm occurs during REM, it is not ubiquitously beneficial. To quantitatively identify the set of control system and/or environmental conditions that leads to REM being a hinderance would provide substantial insight into its actual algorithmic and functional instantiations.

Evidence for a REM improving short-term performance at the expense of asymptotic performance: Sleep's observation-resistant nature makes overt evidence of actual sleep algorithms hard to find. However, there is evidence from biology, psychology, and computer science suggesting that REM may aid cognition by generating virtual samples during sleep on which the brain can train. Besides waking-like spectral activity, REM-sleep is also characterized by dramatic non-sensitivity to external stimuli [10-11]. This means that, whatever occurs during REM most likely could only occur via extended neural activation without sensory input. Evidence is also mounting showing that, beyond general memory consolidation, REM is particularly important for emotional and procedural memory consolidation, both fundamentally implicit processes [27]. These two features of REM align remarkably well with algorithms derived in computer science for what is known as *virtual sample generation* (VSG) [17,28]. Programmers developed VSG to achieve better performance on tasks where the system does not have enough actual training data to effectively solve a problem. VSG works by combining and warping previously seen training data into novel patterns that, once resolved/classified by the system, most likely have benefitted the system. It is, essentially, an attempt at imagination in machines. The tradeoff comes when there is a large amount of training data. If this is the case, then virtual samples are unnecessary and the risk it takes treating a virtual training sample as a true sample may hinder the system. Through the following experiments, we hope to show that the advantages and disadvantages of virtual sample generation align with, and may illuminate, the advantages and disadvantages REM-sleep yields in humans.

C. Research Design and Methods

Specific Aim 1: Computationally model a control system utilizing both NREM and REM components and identify task conditions where REM is either beneficial or detrimental.

<u>Rationale:</u> To our knowledge, there has not yet been research modeling a learning system with a waking, NREM, and REM component. These models are necessary for evaluating proposed NREM and REM functions; NREM and REM sleep occur in an alternating cycle [12], suggesting that the functions of the two processes may rely on said alternation. This work will be the first to directly examine how the two processes' alternations affect learning in machine learners. This research will will be the first to attempt to identify problem domains where systems would be both be either benefitted or hindered by the inclusion of an REM component. Identifying these domains is essential for obtaining a specific algorithmic account of REM sleep, rather than the general claim that it is beneficial. **In Aim 1A we seek to build an artificial control system that utilizes both REM and NREM processes. In Aim 1B we seek to identify what classes of problem result in the system being aided by, as well as which classes will result in the system being hurt by, an REM sleep component.**

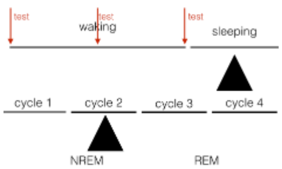

Figure 1: Schematic of a "day" of training for a network. During "waking," all networks will see the exact same stream of hand-drawn digits from two digit classes. Network performance will be tested three times each day: once immediately following sleep, once halfway through waking training, and once immediately before sleep. Each sleep section will have four NREM-REM cycles.

For both subaims, we will build ANNs of various architecture classes, all containing various implementations of previously proposed and novel NREM and REM algorithms. We will use an experimental design that will enable us to inspect and assess categorization performance of ANNs across a variety of task constraints at every time point in training. The analyses we will use will examine both internal network organization as well as network performance.

<u>Methods</u>:

Task: We will train ANNs to solve various categorization problems. Training of the networks will consist of "days," where each day has a waking and sleep component. During a waking component, each network will be presented the same 100 training examples. Each sleep component will feature four alternating NREM and REM components, as four is a typical number of human sleep cycles [20]. In line with previous work [1,4], NREM will simply be a global percentage-wise reduction of weights. As it is reported that global connectivity reduces approximately 18-20% in humans overnight [4], reduction will be 5% for each cycle for a total of ~19% through sleep. REM accounts for about 20% of sleep in adults [21], which is in turn about a half as long as wakefulness, and so REM will consist of 0.5*0.2*100=10 REM-generated virtual samples. See **Figure 1** for a schematic of a "day" for an ANN. These ANNs will have identical network architectures, identical waking and NREM update algorithms, and experience identical data streams during wakefulness. Networks will only differ in their REM-components. Rather than train networks until a stopping criterion has been reached, will will obtain richer network performance metrics by presenting a test dataset before, at the midpoint of, and at the end of each waking period. As we will be taking continuous performance measurements through each "day" of training until performance hits asymptotic levels, we do not need to run separate experiments accounting for short and long training periods. However, we will run experiments with varying training-set sizes. Training-set size will vary in experiments from very small (e.g. 2 training examples per category) to very large (e.g. thousands of examples per category). If a given training-set is too small, a network may never reach sufficient performance on a testing set no matter how many times the training-set is presented to the network.

Stimuli: For these experiments, we will use the MNIST online database of handwritten digits [16]. MNIST consists of tens of thousands of samples of handwritten numbers zero through nine, has is a trusted and nearly ubiquitous dataset for the assessment of categorization algorithms. For each experiment, a random pair of digits will be chosen as the stimuli that the networks must learn to categorize.

Network architecture: We will use Restricted Boltzmann Machines (RBMs) [22], a class of artificial network, as our machine learners through these experiments. RBMs are particularly good fit for modeling the effects of REM sleep for a number of reasons. First, RBMs are unsupervised networks. This means that they do not need to be given the correct category of an experienced sample in order to learn from it, making it more in line with biological learning. RBMs' unsupervised nature are especially crucial for multiple candidate REM algorithms we will be assessing (see <u>REM Algorithms</u> section below), as there would be no biological analogue to a categorization label being presented during REM to a network, and the principles that justify REM sample-generation described below do not apply to generating categorization labels. Each network will have a visible layer of 784 units (28x28, the size of a single MNIST example). Hidden layer size will be derived as the smallest size possible for the REM- control network to reach 90% asymptotic performance. Learning rate will be set at a constant 0.1, a typical learning rate. The networks will not incorporate momentum, as momentum in itself affects network updating and can obscure the effects of the network architecture choices. RBMs are also "shallow," meaning that they only have one hidden layer. We chose a shallow architecture over a more complex deep one because, though powerful, analysis of deep architectures is still not yet well understood [19]. For a description of network

Figure 2: Example REM-generated samples. These samples all created from a training set of twos and fives. From left to right: a) REM-S, b) REM-R, c) REM-RN, d) REM-N, e) REM-MN.

REM Algorithms: Five different REM algorithms will be assessed (see **Figure 2** for examples). Each algorithm serves either as an experiment constraint or as an implementation of proposed neural activation during REM. **a) Synthesis (REM-S)**: REM-S is meant to model the average neural activation of a brain not being constrained by sensory feedback. The algorithm generates samples by taking a recency-weighted average activation of each visible unit during the preceding waking period and stochastically firing each unit with a probability equal to that average activation. **b) Replay (REM-R)**: REM-R will randomly represent a sample seen that day with a recency-weighted probability. This is the most basic instantiation of the popular replay function claimed of REM. Note that this algorithm does not actually generate novel examples, and so may also be interpreted as a REM- algorithm. **c) Replay+Noise (REM-RN)**: REM-RN is a compromise between the pure replay of REM-R, and the non-sensory-constrained product of REM-S. It replays waking samples with noise added to each unit to represent a more mild lack of sensory constraint. **d) Random Noise (REM-N)**: REM-N is a control condition to verify that the preceding REM algorithms are doing something more interesting than introducing noise into the system. REM-N fires every visible unit with uniform probability. **e) Sparsity-Matched Noise (REM-MN)**: REM-MN is the same as REM-N, except it fires each visible unit with a probability equal to the average activation of the whole network. This is a further control to ensure that other REM algorithms are useful beyond noise. **f) No REM (REM-)**: REM- networks will experience no REM-generated samples, and will instead only have global synaptic weight reduced 5% four times.

<u>Analysis</u>: Internal network organization as well as behavioral performance will be assessed three times per

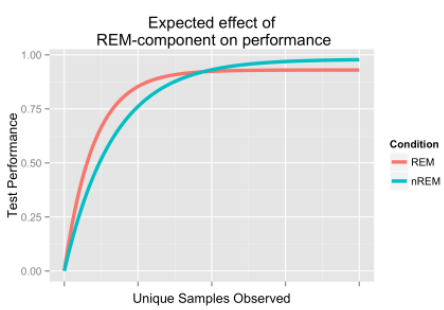

Figure 3: As the number of unique examples observed increases, the performance benefits of REM are expected to decrease until a point where it is then more beneficial to not have an REM-component. Note that "unique samples observed is a type of summary statistic that is a function of total unique samples in the data set and total samples observed so far

Equation 1: $p(t) = C+(1-e^{-kt})$, where C is asymptotic performance rate, k is rate of improvement, and t is time (or, here, number of unique examples observed). In the example shown in Figure 2, C is higher for REM- but lower for k.

each training cycle.

Identifying how metrics vary as a function of time, sample size, and time of day: We will measure how each of the metrics described below change as a function of time, and sample size, and time of day. We will fit exponential learning curves to derive both asymptotic performance as well as improvement-rate values for each network under varying REM conditions (see **Figure 3** and **Equation 1**). We will find these values over averages of each day's testing as well as for each individual testing point in order to see whether REM conditions affect performance through different at different points in the day.

Network free energy: Unsupervised networks learn via a process called *contrastive divergence.* The goal of contrastive divergence is to minimize the distance between initial neural activation on first seeing a

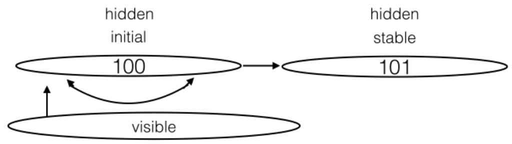

Figure 3: Simple example of assessing network energy in a network with 3 hidden units. Initial pattern activation is passed from the visible to the hidden layer through synaptic weights, resulting in neural activation 1-0-0. The hidden layer activates the synapses between its own weights until it stabilizes on the neural pattern 1-0-1. Thus, the free energy of this visual pattern is 1.

pattern, and activation after the network stabilizes. (see **Figure 3**). This distance between initial and stable neural state is know as *free energy*. Typically, lower average free energy marks a better-organized network [22].

Neural distance: Beyond general energy levels, a well-organized categorization network should learn to bring the neural representations of items in the same category closer, and drive representations of items of different classes farther from each other [23]. We will calculate average within-and between-category Euclidean distances of neural representations of test stimuli as another metric of network performance.

Error-rate: internal organization of a network is only as good as the performance it ultimately yields. We will place a linear classifier on top of the hidden layer of each network and make each attempt to classify training stimuli. The percentage of incorrectly classified test samples will be compared across networks.

<u>Predicted Outcomes</u>:

Condition x Time Interaction: Given a sufficiently large training-set, we predict that REM+ algorithms will initially outperform REM- conditions. A smaller training set necessarily means there is a higher chance for a network to converge on a poor categorization boundary [17-18]. Even with a large training set, early in training, a network will have experienced few unique training examples and so be susceptible to converging on suboptimal categorization boundaries. REM+ algorithms can address this lack of data by warping previously seen examples into potentially task-relevant examples. As time passes and the networks see more examples, REM- algorithms are expected to converge on a more optimal solution than REM+ algorithms, as REM+ generates only potentially useful samples, which may ultimately steer the network from more optimal performance.

Condition x Training-Set Size Interaction: We mention above how, given a large enough training set, a REM- network is expected to eventually see enough unique examples to outperform an REM+ network. However, if the training set is sufficiently small, a network may get caught in the idiosyncrasies of a training set no matter how many times it sees each sample, and so may reach lower asymptotic performance levels than REM+ networks.

Control networks: We expect REM-S and REM-RN networks to generally outperform REM-N and REM-MN networks on both asymptotic performance and improvement rate. While the noise conditions may serve to rattle networks out of local minima, REM-S and REM-RN go farther and are expected to keep networks from local minima *and* update the network in a direction relevant to the task they are trying to solve.

<u>Issues of Concern</u>: The primary concern of these experiments is the large number of free parameters that must be arbitrarily fixed in any ANN experiment. While we have chosen parameters that are either standard in ANN research or an experimentally derived as possible, it is always possible that performance may be sensitive to learning rate, momentum rate, synaptic transfer function, or even general architecture choice. Further, these REM algorithms externally generate samples to present to the network, rather than having these activations emerge naturally in the system. It may be possible that circuit dynamics could change network behavior. Still, these are issues that plague any ANN study, and there is still a great deal to be learned from this design.

Specific Aim 2: Demonstrate sufficient and asymptotic performance level difference with or without REM sleep in human participants.

<u>Rationale</u>: The work proposed for Specific Aim 1 expects to find an intriguing trade-off that REM provides to a system - better performance initially and with less opportunity for training at the expense of asymptotic performance. The next clear step for validating this bound on the effects of REM sleep is to find such a tradeoff in human participants.

<u>Methods</u>: Neurologically healthy participants (n=80) with typical sleeping habits (bedtime 10pm-12am; waking time 6-8am) will partake in 5-night sleep study. Participants will be divided, without their knowledge, into REM+ or REM- groups, then further subdivided into either a long (L) or short (S) training group. The first four nights,

all participants will arrive at 9pm, where they will undergo laboratory acclimation as used in a recently published study [24]. On arrival, participants will be fitted and recorded via polysomnography (PSG; recorded with Grass 8-20 polygraph), electroencephalography (EEG; 1 and 70 Hz filtering), and electromyogram (EMG 10 and 70 Hz filtering), and electrooculogram (EOG; 0.3 and 15 Hz filtering) while sleeping in the laboratory overnight. Participants will be instructed not to consume caffeine, alcohol, or any other foreign substances for the duration of the study. On the fifth night, participants will arrive at the laboratory at 8pm and undergo training on a categorization task. Participants will sit at a computer and passively observe stimuli from one of two sets of shapes. Category membership will be a function of three features: height, width, and luminosity. The category boundary being a combination of three features will ensure that participants should have to learn category in an implicit rather than rule-based manner [25], better aligning their learning process with the passive nature of the RBMs used in the ANN experiments. Participants in both L groups will partake in a 1-hour training session, and those in the S groups will complete a short, 10-minute training session (S). During training, participants will not actively guess category membership; they will only view trials. Each trial consists of 1000ms of fixation on a fixation cross on a blank screen, followed by 2000ms of sample presentation, in turn followed by another 1000ms of sample presentation with the category label displayed above the sample. In order to control for boredom effects, subjects will receive a probe trial every 30 presentations. Probe trials will be the same as training trials, except, rather than being presented with the shape category, participants will press a computer key to indicate which category s/he believes the sample belongs to. This yields a total of 870 training trials and 30 probe trials for the L group, and 145 training trials and 5 probe trials for the S group. After training, subjects will be prepared for recording and sleep. Sleep stages will be identified using standard procedure specified in [26] using 30s blocks. REM+ participants will be allowed to sleep undistrubed. If a REM- participant is scored to be in REM sleep, we will gently awaken the subject, ask him/her benign questions for two minutes to ensure REM sleep was ended, and let him/her immediately resume sleep. 30 minutes after waking (in order to avoid drowsiness effects) subjects will attempt to categorize a novel set of stimuli consistent with the training set for one hour for, again, a total of 900 trials.

Analysis: We will run a 2 by 2 mixed-factor ANOVA to assess whether sleep condition and training duration affected participant ability to categorize novel items. We will then examine individual differences in percentages of REM-sleep in the REM- conditions to see if individual proportions of REM sleep contributed to performance.

Predicted Outcomes: Should human behavioral results align with expected modeling outcomes, we expect a cross interaction between REM and training-length conditions. Short training means an impoverished training set, which, in turn, we expect to result in REM+ participants outperforming REM- participants in the S group. Conversely, those who had long training should have experiences a rich enough training set such that REM could actually generate virtual samples that corrupt learned categorization, and so we would expect REM- to outperform REM+ in the L group. Further, in the REM+ groups, we may even find correlations between amount of time spent in REM sleep and task performance, with the prediction that amount of REM will be positively correlated with performance in subjects from the S group and negatively correlated with subjects from the S group.

Issues of Concern: Primary issues are issues of subject sample size and alignment with ANN experiment data. Quality of data gathered per subject is essential for effectively researching something as subtle as the effects of sleep, and so study participation is quite intense, which practically means relatively small sample sizes per condition. The networks in our first experiments learn a dataset of hand-drawn digits, which humans know, and so we cannot use the same categorization stimulus set; conversely, solving the shape-categorization task for the RBMs would be very easy for them, as ANNs typically thrive on finding high-dimensional category boundaries.

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