

# A Multi-state Model of Cortical Memory

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**Abstract**— A fundamental property of cortical pathways is the ability to retain information beyond time-delimited environmental events. Here, we propose that the neural connectivity between different regions of cortex directly contributes to the preservation of memory traces. A structural network of macaque cortex was obtained from the CoCoMac database. A computational model was then employed to simulate the flow of information between regions of interest (ROIs). This model assigned discrete states to each of 47 ROIs, and allowed exchanges between ROIs as well as random memory decay over time. The rate at which memory decayed over time depended on the network topology; it was found to be markedly less in primate cortex than in a random connectivity that preserved the experimental degree distribution. These results suggest that evolutionary constraints may promote a large-scale cortical anatomy that is optimized for the continuity of memory in time.

## I. INTRODUCTION

According to the classic conception of memory, synaptic plasticity drives the formation of representations in the brain that are stable over time [1, 2]. However, recent findings of spontaneous, activity-driven plasticity at individual synapses challenge this view, and suggest that memories are perpetually vulnerable to decay [3].

In the cerebral cortex, a region of central importance for memory [4-6], spontaneous synaptic modifications occur at a rate of once per 10-100 secs [7]. An essential question is thus: what neural mechanisms are responsible for the preservation of memories across time? Further, how can highly detailed memories be maintained over years and decades, reaching as far back as early childhood [8, 9]?

Because it is impossible to record continuously from the human cortex for days and months, many researchers rely on physiologically informed computer models to address these questions [10-12]. In these models, memory storage depends on long-term synaptic plasticity, which induces lasting changes in neural excitability.

However, extant models fail to take into account known aspects of neuroanatomical connectivity that may play a pivotal role in memory maintenance [13-15]. Synaptically-stored information may be maintained by information

exchanges across distinct cortical regions, thus preventing the permanent loss of a memory trace. Crucially, this idea depends on the ability of cortical circuits to communicate in efficient and systematic ways – pointing to the role of precisely organized structural connectivity.

Here, we provide a proof-of-principle for the idea that fundamental aspects of cortical connectivity directly contribute to the maintenance of memory. To this end, we combine empirical data on primate cortical connectivity with a simple computer model of information exchanges among cortical regions. Here, we define “memory” not in a strict cognitive sense, but rather as a concept that outlines the capacity of neuronal circuits to store representations over extended periods of time (e.g., through long-term potentiation and depression acting on local synaptic networks). In this sense, the concept is applicable both to sensory memory of stimuli as well as motor-related memory for rehearsed patterns of movement.

In the remainder of this paper, we first provide an overview of the structural connectivity obtained from the CoCoMac database. Then, we describe a computer model that combines this connectivity with a simple set of rules for information exchange across brain regions. Finally, we provide comparisons of different forms of connectivity on the ability of the model to store representations over time, and speculate that particular aspects of cortical connectivity may have been selected by evolution partly because of their pivotal role in memory.

## II. METHODS

### A. CoCoMac Database

The macaque data were obtained from the CoCoMac database, as previously described [14], and included 47 neocortical areas of visual, sensory, and motor regions linked by 505 pathways identified by anatomical tracing (Fig.1).

The CoCoMac database employed here consists of a binary connectivity matrix of brain regions linked together by interregional pathways [16]. We employed a manually-collated matrix from previous work [14]. Regions of interest (ROIs) include motor, visual, and somatosensory regions. The connectivity matrix featured 47 nodes and 505 connections. Each ROI comprised a large number of individual synapses. Because of the nature of the imaging approach, the resulting matrix cannot be used to infer the directionality of anatomical connections. Only cortico-cortical connectivity was considered, therefore excluding subcortical circuits. All simulation results are compared to those obtained with a randomly shuffled connectivity matrix

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that preserves the degree sequence and weight distribution of the original matrix.

### B. Multi-state Model

Given a whole-cortex connectivity matrix as described above, a computer model was designed to examine information exchanges between different cortical sites.

In the proposed model, each cortical site can take on an arbitrary large (but finite) number of states (default: 100 states). We assume that these states are storing memory representations, without any additional assumptions regarding the specific synaptic mechanisms involved; we also make no specific assumption as to the cognitive content of those traces. One interpretation is that states refer to particular configurations of synaptic strengths within a cortical site. An important advantage of this highly abstracted model is its simplicity; the model can be run for extensive periods of time (up to 10 million time-steps as described in Results), providing results that cannot be achieved with more detailed models [15].

The state of each site in the model is initially set at random between  $s \in [1, \dots, S]$ . Then, the model evolves through discrete time-steps. At each time-step, the following is performed:

- 1) a single cortical site  $n \in [1, \dots, N]$  is chosen at random, with the constraint that all sites must be chosen once before the same site can be chosen again. The probability of that site changing its state to a new, randomly chosen state is given by a fixed parameter  $p_{random}$  (with a default value of  $p_{random} = 0.01$ ).

- 2) with a certain probability of  $p_{connection} = 0.7$ , the state of these other sites is changed to that of site  $n$ . One assumption here is that cortico-cortical connectivity is bi-directional [17].

This model is equivalent to a Markov process where the probability of transitioning from one state to another depends on the connectivity among sites. In the model, the probability that a site will remain in a given state depends on the probability of randomly transitioning to a new state as well as the state of sites to which the site is connected.

The above-described model is a variant of the “forest fire model”, a model for examining brain dynamics under simplified conditions [18]. Several other variants of the model (results not shown), lead to similar conclusions as the ones described next. Similar results were also obtained with various numbers of discrete states, from 2 (representing a “worst-case scenario”; [11, 19]) to 500.

## III. RESULTS

### A. Memory Decay is Slower with Cortical Connectivity Compared to Random Connectivity

In order to examine the evolution of a memory trace over time, we begin with a simulation that keeps track of what sites maintain their initial state over time, and what sites spontaneously alter their state. Given that all states have the same probability of randomly changing state over time ( $p_{random}$ ), the only factor that differentiates one site from another is its connectivity to the rest of cortex. Therefore, over several independent runs, each with different randomly-chosen initial state conditions, it is possible to determine the influence of connectivity on the maintenance of memory (defined as the ability to remain in the same state over time).

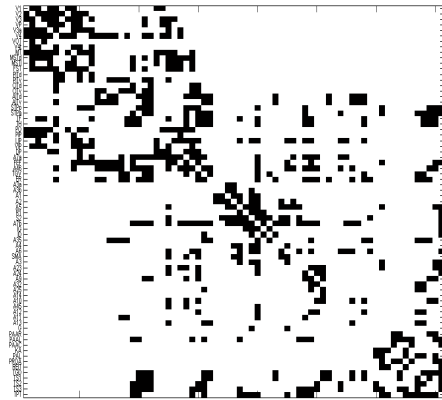


Figure 1. Cortical connectivity based on the CoCoMac database. Each filled square indicates the presence of a connection between two ROIs (self-connections were excluded).

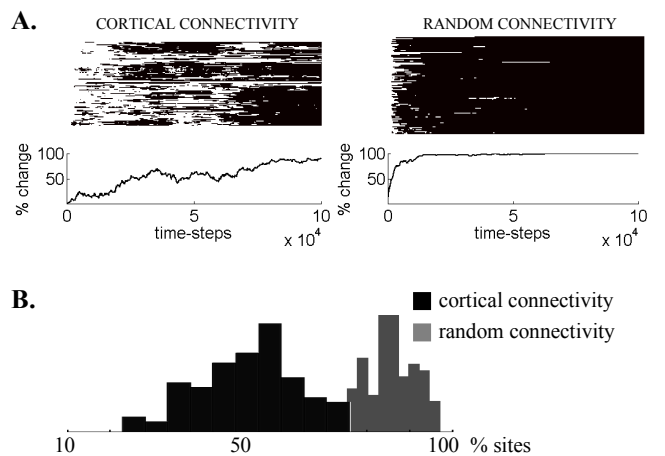


Figure 2. Cortical connectivity contributes to memory maintenance over time. A. Degradation of an activation trace in a version of the model based on cortical connectivity. Top panel: ROIs that have maintained their initial state (white) or switched to a different state (black). Bottom panel: Percentage of sites that have changed their state during the course of the simulation. B. Histogram of the percentage of sites that have changed their state at the end of a simulation lasting 100,1000 time-steps (averaged over 100 independent runs of the model).

A typical simulation of a model with 100 states, run for

100,000 time-steps, is shown in Figure 2A. Despite random fluctuations influencing the model across time, not all sites alter their initial state; rather, at any given time, a proportion of 20-30% of sites occupied their initial state. This proportion is significantly greater in a model with randomized connectivity; indeed we found a statistically reliable difference between a model with cortical connectivity versus random connectivity, when comparing the average proportion of decayed sites across time for 100 independent runs of each model (Student's  $t$ -test,  $t(198) = 7.71, p < .0001$ ) (Fig.2B).

To further illustrate the relationship between structural connectivity and the maintenance of memory traces in the cortical connectivity model, we examined the time-lagged auto-correlation of the model, indicative of the rate at which information is altered. When compared to a model with randomized connectivity, the cross-correlation obtained with cortical connectivity was markedly higher as the time-lag increased, suggesting a slow time course of decay (Fig.3C). In separate simulations, we tested a total of 100 versions of networks with randomized connectivity, and qualitatively similar results were obtained.

### B. Cat Cortical Connectivity

The above results are not confined to primate data; a memory advantage was also found with cortical connectivity obtained from the cat [20]. When compared to an appropriate random control that preserved degree distribution, the cat cortical connectivity yielded a significantly smaller proportion of decayed sites across time (100 independent runs) ( $t(198) = 1.9720, p < .042$ ).

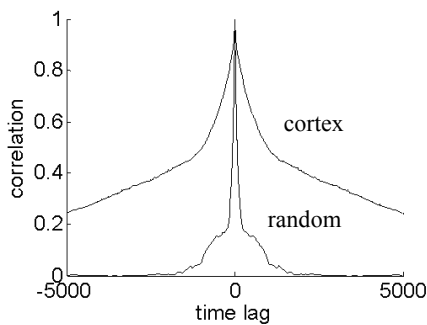


Figure 3. Mean cross-correlation function across all sites of the cortical and random models (normalized between 0-1).

### C. Dominant Modes of Connectivity Are Related to Memory

What properties of cortical connectivity account for this effect? A recent proposal is that the eigenvectors of the structural connectivity's covariance matrix (i.e., "dominant modes") may be related to network attractors observed in the dynamics of the model [21]. Conceptually, spontaneous activity in the model can be described as a series of random transitions between attractors that are formed by the dominant modes. When these modes have high values, the

attractors have a strong influence on network dynamics, and exert a pull that does not allow activity to stray very far from an initial state. A direct prediction is therefore that dominant modes should be much stronger in cortical connectivity than a randomized control. This result is clearly confirmed (Fig.4), consistent with the idea that the maintenance of a memory trace over extended periods of time is influenced by attractors resulting from the structural connectivity of cortex.

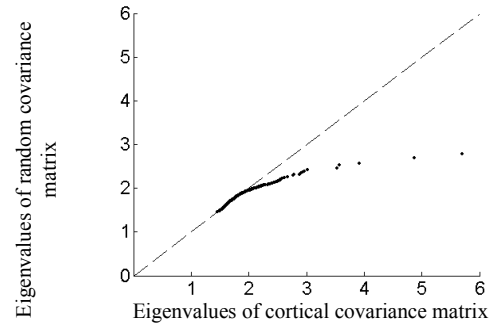


Figure 4. Eigenvalues of the cortical connectivity covariance, compared to eigenvalues obtained after randomizing the connectivity. The dashed line is a slope of unity.

### D. Longevity of a Memory

Exactly how long can memory traces be maintained in the model? A rough estimate can be obtained on the basis of known rates of spontaneous plasticity in cortex. In a conservative scenario, let us assume a constant rate of one synaptic change per 10 sec [7]. Let us further assume that any single change alters the state of an entire ROI in the model; this is a very conservative scenario, as some individual synapses may not contribute significantly to the state of a cortical site. If the probability of a random state transition is  $p_{random} = 0.01$ , then a single time-step would be roughly 100 ms. In a model without any connectivity between cortical sites, the probability of decay is  $N/p_{random}$ , and therefore the model is expected to decay fully after approximately 10,000 iterations (2 hrs 42 min). By contrast, after running the model for 10 million time-steps (equivalent to roughly 100 days of cortical activity) some sites of the model had still retained their initial state. In a less conservative scenario that considers a rate of spontaneous plasticity on the order of 100 sec (resulting in a time step of 1 sec), 10 million time-steps would be equivalent to roughly 3.2 years. Of course, the above correspondence between state changes and spontaneous plasticity is highly abstracted, and is meant only to illustrate the robustness of memory traces over time. Nevertheless, our results indicate that cortical neuroanatomy may be designed in a way that promotes memory maintenance.

### E. Correlation Between Memory and Network Connectivity

The above results suggest that the topology of cortical connectivity in primate brains may support the persistence of

activity states across time. This view can serve as the starting point for several novel predictions on the relationship between cortical connectivity and memory.

The following simulations were performed in order to relate different aspects of connectivity to the propensity of ROIs to occupy their initial state over time. First, we performed 100 independent runs of the model, each with different initial states and lasting 100,000 time-steps. Then, for each ROI, we computed a “memory index” by taking the average number of time-steps spent in their respective initial state, over all time-steps of all runs. A similar protocol was performed using random connectivity. In order to determine, for each ROI, whether cortical connectivity played a role in memory maintenance, we performed repeated *t*-tests with Bonferroni correction for multiple ROIs (leading to a criterion of  $p < .01/N = 10^{-5}$ ) comparing cortical versus random models.

Results showed that, in the cortical model, several ROIs spent significantly more time in their initial state when compared to the random model (Fig.5A). Overall, while a majority of sites spend less than 30% of the time in their initial state, a small proportion of sites rarely (if ever) strayed from their initial state (Fig.5B).

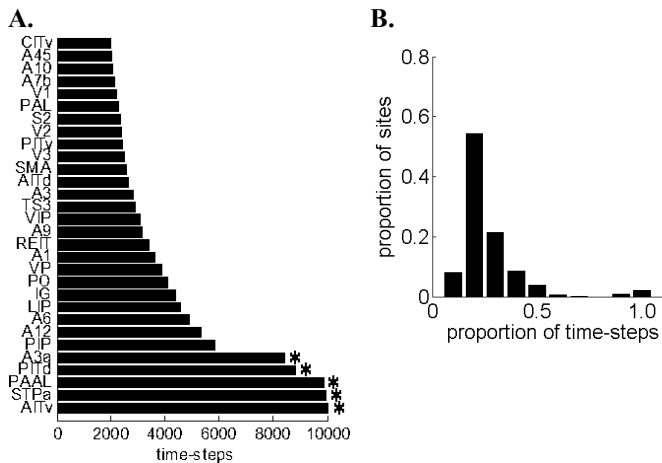


Figure 5. Topographical distribution of ROIs that occupy their initial state for marked periods of time. A. ROIs that occupy their initial state significantly more often with cortical compared to random connectivity (shown in red), as determined by repeated *t*-tests (see main text). \* =  $p < .01/N = 10^{-5}$ . B. Proportion of time-steps where each ROI occupied its initial state (obtained after 100 independent runs of the model, 100,000 time-steps each).

Do sites with a marked propensity towards switching state have certain structural properties that set them apart from other sites? To address this question, we correlated the memory indices of all ROIs with different aspects of cortical connectivity. We found statistically reliable correlations between these memory indices and several network measures, including mean path length (Pearson’s correlation,  $r = 0.40$ ,  $p < .0001$ ), clustering coefficient ( $r = -0.31$ ,  $p < .0001$ ), betweenness-centrality ( $r = -0.33$ ,  $p < .001$ ), and mean incoming/outgoing strength ( $r = -0.74$ ,  $p < .001$ ). From

these findings, we conclude that: 1) cortical regions that are isolated from the rest of the network (in terms of path length) decayed slower; 2) regions with a higher degree of clustering decayed faster; 3) regions that are more central to a network, effectively acting as “hubs”, exhibit more decay; 4) regions with stronger incoming and outgoing connectivity exhibit more decay.

In sum, the memory decay of any given cortical site is largely caused by interactions with other sites. This result seems in contradiction with the finding that memory decay is more pronounced when no connectivity is present. Thus, there may be a conflict between the propensity of regions to connect to each other (enhancing global memory), and the propensity of regions to become disconnected (enhancing local memory). One potential way to resolve this conflict can be referred to as a “modularity trade-off”, whereby cortical sites tend to interact strongly with nearby neighbors, and weakly with more distant ones. Such trade-off is a potential origin of the “small-world” connectivity observed in the cortex of several species, and also found in the current cortical data [22]. This small-world effect describes how remarkably few intermediate steps are required to transfer information across a network, and how clusters of highly interconnected neighbors tend to form amongst sites.

Our results are consistent with the idea that networks with small-world properties can maintain memories over time in spite of ongoing synaptic plasticity; comparisons to an appropriate random control which preserves degree distribution but not small-world properties showed more pronounced decay than cortical connectivity matrices (Fig.2).

#### IV. DISCUSSION

The current work incorporated data on cortical structural connectivity with a large-scale computational model of interactions between different ROIs. Our main finding is that the global architecture of primate cortex contributes to the preservation of memory across time. By comparison to an appropriate random connectivity, memory traces decayed at a markedly slow rate. Furthermore, precise quantitative aspects of cortical connectivity (including clustering coefficient, path length, centrality, and connection strength) were related to the ability of individual ROIs to preserve memory traces across time.

In the context of numerous studies on the synaptic correlates of memory [23], our work raises the possibility that cortical structure as a whole contributes to the capacity of the brain to store information over remarkable periods of time [8]. Such extensive capacity poses an important problem when memory is examined at a cellular level, given that individual synapses are susceptible to spontaneous plasticity at a rate of once every 10-100 sec [7]. Our work suggests that this problem is best addressed by considering the large-scale connectivity of primate cortex.

Our main finding of a relationship between the global structure of cortex and the preservation of memory is in line

with recent work on diffusion tensor imaging [24, 25]. A particularly striking instance of such relationship is found in patients with multiple sclerosis, where the extent of memory impairment correlates with white matter damage between distal cortical areas [24].

Going beyond anatomical considerations, our model proposes that memories are preserved by continuous exchanges of information among cortical sites. These exchanges constitute a potential origin of ongoing fluctuations in cortex, observed even when the brain is not actively involved in a task [26]. A partial confirmation of this idea comes from neuroimaging work relating spontaneous activity to memory processes [27, 28].

Findings of a memory advantage in our model suggest that cortical connectivity may have been shaped by evolution that has promoted memory as a strategy of fundamental importance. Over the course of evolution, memory may have provided advantages for the survival of entire species as well as competition amongst individual members of a species sharing limited resources. Because we found a similar memory advantage in the macaque and cat cortices, these evolutionary constraints may originate from early phylogenetic developments of the brain. Analyses of the large-scale neural connectivity of further species – as well as in humans – would be informative to substantiate this claim.

Speculatively, it is possible that the capacity to form lasting memories has emerged as a by-product of constraints on cortical connectivity [29]. For instance, a trade-off between minimizing the cost of wiring length and maximizing information exchanges in cortex may have biased the cortex towards a small-world architecture [30]. In such architecture, synaptic wiring is mostly local, with a small proportion of long-range connections responsible for exchanges of information among weakly connected regions. Both the human and macaque cortex possess a small-world structure; the co-evolution of memory and small-world connectivity is a likely possibility.

In future work, the proposed model will be combined with more detailed synaptic mechanisms [15] in order to examine the neural contributions of memory maintenance in cortex. Such approach, however, will discard an important advantage of the highly abstracted model presented here, which allows us to examine large-scale cortical dynamics over extended periods of time (e.g., up to 10 million time-steps in the results presented here).

Further work would also be required to examine the contribution of hippocampus, thalamus, basal ganglia, and other structures to the storage, maintenance, and retrieval of memories over time. Finally, further studies using the proposed model could reach beyond an investigation of the time-course of memory maintenance, and examine how many individual items can be stored at once and to what degree they will interfere with one another [9].

In conclusion, our results support the emerging perspective that memory can be understood as a large-scale process, involving distributed networks of neurons that

participate in the active maintenance of even our most distant past.

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