



Complementary Learning Systems

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Received 21 November 2010; received in revised form 5 April 2011; accepted 6 April 2011

Abstract

This paper reviews the fate of the central ideas behind the complementary learning systems (CLS) framework as originally articulated in McClelland, McNaughton, and O'Reilly (1995). This framework explains why the brain requires two differentially specialized learning and memory systems, and it nicely specifies their central properties (i.e., the hippocampus as a sparse, pattern-separated system for rapidly learning episodic memories, and the neocortex as a distributed, overlapping system for gradually integrating across episodes to extract latent semantic structure). We review the application of the CLS framework to a range of important topics, including the following: the basic neural processes of hippocampal memory encoding and recall, conjunctive encoding, human recognition memory, consolidation of initial hippocampal learning in cortex, dynamic modulation of encoding versus recall, and the synergistic interactions between hippocampus and neocortex. Overall, the CLS framework remains a vital theoretical force in the field, with the empirical data over the past 15 years generally confirming its key principles.

Keywords: Hippocampus; Neocortex; Learning; Memory; Consolidation; Neural network models

The publication of McClelland, McNaughton, and O'Reilly (1995)—MMO95 hereafter—represented an important turning point in the development of the Parallel Distributed Processing (PDP) framework: it showed that the heretofore relatively abstract principles of connectionist models (e.g., the distributed model of memory from Chapter 17 of the PDP volumes; McClelland & Rumelhart, 1986) could be applied to a biologically detailed domain, in an influential way. This paper also provided the insight of turning what had been widely regarded as the fundamental failing of neural network models into a point of leverage in understanding the functional organization of the brain. Specifically, the phenomenon of *catastrophic interference*, where subsequent learning tended to completely overwrite

earlier learning, was taken by some as an indication that the PDP framework was fatally flawed (McCloskey & Cohen, 1989). MMO95 argued instead that catastrophic interference is an inevitable consequence of systems that employ highly overlapping distributed representations, and furthermore that such systems have a number of highly desirable properties (e.g., the ability to perform generalization and inference; Hinton, McClelland, & Rumelhart, 1986; McClelland & Rumelhart, 1986). Many of these fundamental issues can be addressed by employing a structurally distinct system with complementary learning properties: sparse, non-overlapping representations that are highly robust to interference from subsequent learning. Such a sparse system by itself would be like an autistic savant: good at memorization but unable to perform everyday inferences (McClelland, 2000). But when paired with the complementary highly overlapping system, a much more versatile overall system can be achieved. This core CLS insight, founded in clear, principled understanding of neuron-like processing dynamics at a very general level, proved capable of accounting for a wide range of extant biological, neuropsychological, and behavioral data.

For example, it had long been known that the hippocampus plays a critical role in episodic memory, but the CLS framework provides a clear and compelling explanation for why such a system is necessary, and what its distinctive properties should be relative to the complementary neocortical learning system. One of the most intriguing contributions of the approach was an explanation for the observation that the hippocampus can replay individual memories back to the neocortex. This achieves an *interleaving* of learning experiences, which PDP models showed is capable of eliminating catastrophic interference. This abstract principle of learning made the concrete and seemingly counter-intuitive prediction that *older* memories should be relatively spared with hippocampal damage, because they will have had time to be consolidated through interleaved replay into the distributed neocortical system. Strikingly, retrograde memory gradients from a variety of species appeared to support this prediction, with the further nuance that longer lived species have longer such gradients (with those in humans spanning even for decades). However, this data and its interpretation remain among the most controversial aspects of the CLS framework (Nadel & Moscovitch, 1997; Winocur, Moscovitch, & Bontempi, 2010), as we discuss later.

The main contribution of the MMO95 paper is that it brought together so many different strands under a clear, principled framework. None of the individual pieces themselves were particularly novel, and the core ideas of hippocampal pattern separation versus cortical statistical learning (and even a simple form of hippocampal replay at night) had been articulated as far back as Marr (1972), and considerably developed by McNaughton and Morris (1987), Rolls (1989), but the whole package was greater than the sum of its parts. Unbeknownst to us at the time, Sherry and Schacter (1987) had advanced a very similar idea based on functional tradeoffs leading to an evolutionary pressure to develop multiple memory systems. At a personal level, the ideas behind the MMO95 paper were stimulated by a sabbatical visit by Jay McClelland to Bruce McNaughton's laboratory, combined with Randy O'Reilly's arrival as a new graduate student in Jay's laboratory, with a strong interest in more biologically oriented applications of neural network models. An extensive mathematically oriented investigation of hippocampal encoding and retrieval dynamics (O'Reilly & McClelland, 1994) was another early product of this line of work.

In the 15 years since the publication of MMO95, there has been a huge volume of work examining the functional properties of the hippocampal and neocortical learning systems, and the core principles of the CLS approach seem to have held up well overall. In the remaining sections, we first describe the basic function of the hippocampal system in the CLS framework, including recent data supporting it, then summarize some of the most relevant developments, followed by a brief summary of some recent advances in CLS-based computational modeling.

1. Hippocampal encoding and retrieval

There is broad theoretical agreement about the basic outlines for how the anatomy of the hippocampus and surrounding cortical areas support memory encoding and retrieval, and solid empirical data supporting these basic elements (Fig. 1). The hippocampus sits at the top of a hierarchy of brain areas, so that it can integrate information from all over cortex to form a *conjunctive* representation of an episode or event. The perirhinal cortex funnels information from the ventral visual stream in inferior temporal cortex (representing object category and identity information) into the hippocampus, while the parahippocampal cortex funnels more dorsal pathway spatial information. These inputs converge into the medial entorhinal cortex (EC), which then gives rise to the perforant path projection into the dentate gyrus (DG), CA3, and CA1 of the hippocampus proper.

As shown in Fig. 1, the flow of information to be encoded in the hippocampus culminates in the activation of neurons in areas CA3 and CA1, and memory encoding amounts to

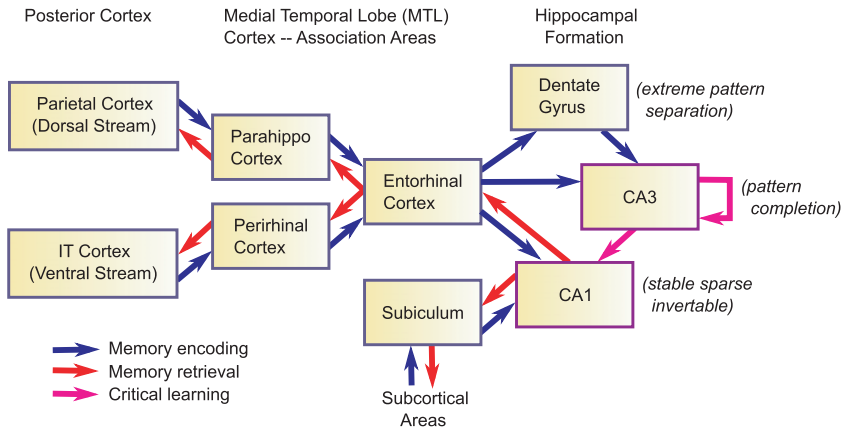


Fig. 1. Hippocampal memory formation, showing how information is encoded and retrieved. The critical learning takes place in the CA3 Schaffer collateral projections that interconnect CA3 neurons with themselves, and in the projections between the CA3 and the CA1. CA3 and CA1 represent the highest levels of encoding in the system (where the blue arrows end), and memory encoding amounts to strengthening the associations between the active neurons within these regions, while memory retrieval involves pattern completion within CA3 driving reactivation of the associated CA1 pattern, which then feeds back down to reactivate the original activity patterns throughout the cortex. IT, inferior temporal.

strengthening the associations between active neurons in these areas. Memory retrieval occurs when a cue triggers completion of the original CA3 activity pattern (i.e., *pattern completion*), which in turn drives CA1 (via the strengthened associations), and results in a cascade of activation that reactivates the original activity patterns throughout cortex.

The system avoids interference from new learning by the process of *pattern separation*, due especially to the DG. Because the DG has very sparse levels of activity (few neurons active at any given time), it provides an exceptional degree of pattern separation to encode new information while avoiding interference with existing memories. This relationship between sparseness and pattern separation was originally articulated by Marr (1972) and analyzed extensively in O'Reilly and McClelland (1994). Considerable recent data acquired using a variety of techniques (including multi-unit recordings in rats and high-resolution fMRI in humans) supports this pattern-separation theory (Bakker, Kirwan, Miller, & Stark, 2008; Clelland et al., 2009; Gilbert, Kesner, & Lee, 2001; Leutgeb, Leutgeb, Moser, & Moser, 2007; McHugh et al., 2007). Area CA3 has less sparse activity levels, but its representations are still highly non-overlapping due to the impact of the DG. An elegant genetic knock-out study in mice shows that CA3 is required for episodic memory learning (Nakashiba, Young, McHugh, Buhl, & Tonegawa, 2008), with a similar study also showing the crucial role of DG (McHugh et al., 2007).

The above account provides a clear unique role for every area in the system, except for area CA1—*what is the unique role of CA1?* This question often goes underappreciated. In the original CLS work, including McClelland and Goddard (1997), we theorized that CA1 is critical for developing a sparse, invertible mapping. This means that activity patterns produced by incoming cortical activity during encoding are capable of re-creating those same cortical activity patterns during retrieval. The critical point that many researchers fail to appreciate about this function of the CA1 is that without it, the problem of catastrophic interference would remain, regardless of how effective the pattern separation is within the CA3. To see why, consider what would happen if CA3 projected directly back into EC. Because the CA3 pattern is highly pattern separated and thus unrelated to anything else the system has seen before, the EC neurons would need to rapidly learn to associate this novel CA3 pattern with the current activity pattern, reflecting the cortical inputs. However, because the EC has high levels of overall activity, the same EC neurons are involved in a large number of different memories. Thus, when a new memory is encoded, the synaptic changes required to learn the associated novel CA3 pattern would have a reasonable chance of interfering with a previously encoded memory. In contrast, because the CA1 has a relatively sparse level of activity, its neurons participate in comparatively fewer overall memories, and thus engender significantly less interference.

Although the CA1 invertible mapping may seem like a relatively trivial function, it turns out that this kind of mapping actually takes significant amounts of learning to develop, especially to establish a representational system that can apply to novel input patterns. Meeting this challenge requires a *combinatorial* or *componential* code, where novel input patterns can be represented as a recombination of existing representational elements (e.g., O'Reilly, 2001). In our existing computational models we typically just establish this code in advance, through the design and pretraining of the model. A long-standing, still unsatisfied, goal is to

develop a more realistic understanding of how this representation gets established in the real system. Recent developments discussed in the final section below suggest a potentially promising avenue.

2. Characterizing hippocampal representations: Conjunctive versus elemental

A central claim of the CLS framework is that the hippocampus encodes information in a qualitatively different way than the neocortex. Specifically, to minimize interference, the hippocampus must keep representations highly separated from each other, so that different neurons participate in encoding memories of even similar events or places. This can be achieved through very sparse levels of activation (e.g., 0.05% in the DG of the hippocampus, compared to roughly 15% in the cortex)—this was Marr's original insight into what was special about the hippocampus (Marr, 1972). So what exactly are the implications of these sparse, pattern-separated representations?

Sutherland and Rudy (1989) established a clear connection between theoretical ideas about hippocampal representations and specific behavioral tasks in rats that could be used to test these ideas. For example, a task that required learning to associate a different outcome to the *conjunction* of two stimuli (A and B) from each stimulus independently (i.e., an *elemental* representation) should depend critically on the hippocampus. However, it turned out that this simple story did not hold up in the data (Rudy & Sutherland, 1996), and a more nuanced account was needed (O'Reilly & Rudy, 2001). This new account preserved the essential idea that hippocampal representations should be conjunctive in nature, but it also recognized that neocortical learning systems were sufficiently flexible as to learn conjunctive codes too, when specifically forced to do so via task contingencies. Thus, the key prediction of this account is that *rapid, incidental* conjunctive learning is the truly unique province of the hippocampus. The paradigmatic example of this in rats is the context preexposure effect in fear conditioning, where briefly exposing a rat to the context in which it will subsequently be shocked leads to a substantial elevation in measured fear conditioning compared to non-preexposed controls. Indeed, the data show that rats rapidly and automatically form hippocampally mediated encodings of novel environments (Rudy & O'Reilly, 1999).

3. Complementary contributions to human recognition memory

One of the most important applications of the CLS approach has been in the domain of human recognition memory, where the issue of *recollection* versus *familiarity* contributions has had a long and controversial history. Norman and O'Reilly (2003) demonstrated that a computational model with hippocampal and cortical components could account for a range of relevant phenomena in this domain, and that the hippocampal system accorded well with the general characterizations in the literature of recollection, while the cortical system was a good match for familiarity. In particular *dual process* models of recognition memory

(Yonelinas, 2002) posit that recollection is a process that involves the explicit recall of the studied item (typically along with associated episodic context), and when this occurs, people can respond “old” to a probe item with a high level of confidence. In contrast, the familiarity process is driven by some kind of *global match* between the probe and stored memory items, which results in a much more graded, continuous memory signal that is typically not accompanied by the explicit recall of specific content information.

The conjunctive, pattern-separated nature of hippocampal representations is consistent with the episodic nature of recollection, with pattern separation (and other features of the hippocampal system; Norman & O'Reilly, 2003) making it unlikely that recollective memory will be invalid (i.e., such memories are deserving of high confidence). In contrast, the overlapping distributed representations in the cortex naturally compute something like a global-match familiarity signal, which produces continuous levels of a recognition signal, and does not yield the recall of specific episodic details.

Ken Norman has published a recent review on how the CLS model of recognition memory has held up over the years (Norman, 2010), so we would not dwell on this topic much here. However, a few key points from the articles contained in the associated special issue of the journal *Hippocampus* (Voss & Paller, 2010) struck us as particularly salient:

- There appears to be widespread agreement across a range of authors on the qualitative properties of the hippocampal memory system, which align well with the characterization provided by the CLS framework. That is, everyone seems to agree that it supports conjunctive pattern-separated representations that encode information in a more contextualized, episodic manner.
- There is general agreement that the surrounding cortical areas (e.g., perirhinal cortex) support less of this kind of conjunctive pattern-separated encoding; however, the best way of characterizing the nature of the differences between the hippocampus proper versus surrounding cortical areas remains in contention, and it is unclear if relevant data exist to decide definitively among the alternatives. Some authors emphasize a more qualitative difference (Yonelinas, Aly, Wang, & Koen, 2010), while others focus on a more quantitative difference (Cowell, Bussey, & Saksida, 2010; Shimamura, 2010; Wixted, Mickes, & Squire, 2010). The CLS model makes a clear prediction based on the unique anatomical features of the hippocampal system that give rise to its pattern-separation properties (O'Reilly & McClelland, 1994)—the hippocampus is significantly more conjunctive and driven toward pattern separation than surrounding cortical areas. However, as Norman (2010) emphasizes, the CLS model does predict that these distinctions will be reduced or eliminated if the memories are highly overlapping, such that they overwhelm even the hippocampal pattern-separation system. This is consistent with available data (e.g., Barense et al., 2005; Elfman, Parks, & Yonelinas, 2008; Yotsumoto, Kahana, Wilson, & Sekuler, 2007). Thus, as is often the case, simple verbal labels fail to capture the subtlety of the underlying neural mechanisms. Perhaps further progress can be obtained by developing clear contrasting predictions from different implemented models, and testing those empirically.

- The hierarchical relational binding theory (hRBT) of Shimamura and Wickens (2009) provides a conceptually unified abstract framework that bridges the quantitative versus qualitative divide. It does so by proposing a consistent process (relational binding) for all areas of medial temporal lobe (MTL), which nevertheless results in hippocampus being somewhat special by virtue of being at the top of the hierarchy. Furthermore, multiple stages of relational binding in their model produce non-linear effects, such that higher areas tend to be much more sensitive to bindings than lower areas. Shimamura (2010) argues that hRBT maps onto the CLS model, and we generally agree, in the sense that it is a more abstract, process-based model that exhibits similar overall behavior to the CLS model. But although familiarity is well described by standard (Gaussian) signal-detection theory (Hintzman, 1988; Yonelinas, Dobbins, Szymanski, Dhaliwal, & King, 1997), one of the major points of the Norman and O'Reilly (2003) paper was that abstract models that are constrained largely by their ability to fit such data may be degenerate (there are many such models that will fit the data equally well). In contrast, by incorporating biological data at multiple levels of analysis, in addition to fitting signal-detection curves, the CLS model may provide a more constrained and satisfying overall theory.

4. Consolidation of hippocampal memories in cortex

One of the most compelling ideas explored in MMO95 was that the hippocampus trains the cortex by replaying memories, giving the slower learning cortex a chance to integrate newer memories without overwriting the older ones. One of the signature indicators of such a *consolidation* process is the presence of retrograde memory gradients, where recent memories are actually more impaired by hippocampal damage than more remote ones (contrary to the typical forgetting function). Considerable work has been done in this area in the last 15 years, but the evidence is perhaps less clear now than it seemed to be back in 1995.

A full and insightful review of the current status of this literature is provided by Winocur et al. (2010), along with a welcome clarification of the critical issues in this domain. Winocur et al. (2010) end up converging on a view of consolidation that is actually quite close to that originally envisioned in MMO95, although unfortunately that original article did not state these key ideas with the precision and clarity that Winocur et al. (2010) achieve with their *transformation* model of consolidation. Specifically, the nature of the memories that become consolidated in neocortex is significantly different from those that were originally encoded by the hippocampus, by virtue of the complementary nature of these memory systems. Whereas the hippocampus encodes a crisp, contextualized, episodic memory, the neocortex extracts a highly semanticized, generalized “gist” representation that integrates over many different episodes. This difference is exactly as expected from the CLS framework. Winocur et al. (2010) also argue that the original episodic memory *remains in the hippocampus* for as long as the memory can be considered to be retained at all. In other words, there is not a literal “transfer” of information *out* of the hippocampus to the cortex,

but rather the cortex learns its own, more distributed, version of what the hippocampus had originally encoded. This new cortical representation captures a similarity structure that was not initially present in the hippocampal representation, and it allows for a generalization of the memory trace to other similar cortical representations. Although the original MMO95 paper adopted a more transient view of hippocampal memory, based largely on data that are now much less certain, there is nothing in the basic CLS framework that requires it to be transient—the model is essentially agnostic about this issue. Finally, Winocur et al. (2010) emphasize that there is a dynamic interplay between hippocampal and neocortical memory systems, such that one or the other may be dominant depending on the circumstances. We take up this issue of dynamic interplay in the next section, describing very recent CLS modeling work.

Some of the most controversial data in the consolidation domain concern the retrograde gradients, which are found in some cases but not others (see Sutherland, O'Brien, & Lehmann, 2008 for a review). Sutherland et al. (2008) present comprehensive, well-controlled data from fear conditioning in rats, which has been a widely used paradigm to explore the consolidation hypothesis (and rats represent a simpler, more reliable system to study than primates, including humans). Their data are inconsistent with both standard consolidation theory (which predicts the retrograde gradients), and an important alternative theory proposed by Nadel and Moscovitch (1997), which posits that multiple traces of a given original memory are encoded in the hippocampus, with new traces encoded as that episodic memory is reactivated. This multiple trace theory (MTT) predicts that the size of the hippocampal lesion will determine the extent of the retrograde gradient, with more of a gradient for smaller lesions (because more traces will remain intact), but Sutherland et al. (2008) found no such effect (gradients were flat for all lesion sizes, with just a main effect of better memory overall for smaller lesions). Furthermore, other data taken to support MTT are equally consistent with the transformation view described above; for example, Viard et al. (2010) show that the hippocampus plays a key role in memories throughout the life span but also that it does so in rich interaction with other cortical areas.

4.1. Neuronal replay

Another very active area of work in the consolidation domain focuses on one of the primary mechanisms thought to underlie the ability of the hippocampus to teach the cortex: the nightly replay of memories learned during the day (see Fig. 2). There have been a number of papers that demonstrate this kind of hippocampal replay dynamic by showing that the statistics of neural coactivity during sleep recapitulate that evident during an earlier learning activity. For example, Wilson and McNaughton (1994) reported that rats in slow-wave sleep (SWS) repeat daytime hippocampal place cell activity patterns. Stickgold (2005) cites similar procedural memory consolidation in humans, and Susanne and Jan (2010) provide a review of declarative memory consolidation in humans.

A leading theory for how this hippocampal replay works involves the phenomenon of *sharp waves* during sleep or quiet waking (Euston & McNaughton, 2006; Karlsson & Frank, 2009; Lee & Wilson, 2002; Nadasdy, Hirase, Czurko, Csicsvari, & Buzsaki, 1999), where

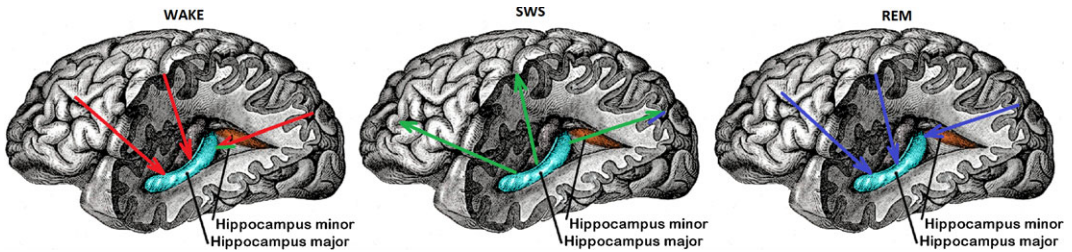


Fig. 2. The hippocampus is thought to play a central role in information transfer during wake/sleep cycles for memory consolidation. Information from the neocortex flows into the hippocampus during waking periods, out from the hippocampus and targeting neocortex during waking periods, out from the hippocampus and targeting neocortex during SWS, and back into the hippocampus from the neocortex during REM. REM, rapid eye movement; SWS, slow-wave sleep.

sequences of events that might have stretched for seconds during wakefulness are compressed into a matter of a few tens of milliseconds (a notion nicely captured in the recent movie *Inception*). There is converging neurophysiological evidence supporting this theory. For example, sharp waves were shown to emanate from the CA1 region in the primate hippocampus, more frequently during sleep, with similarities to rat and human EEG data (Skaggs et al., 2007). Learning induces both greater frequency and magnitude of sharp-wave complexes during postlearning SWS in an odor-reward association task in rats (Eschenko, Ramadan, Molle, Born, & Sara, 2008) and other tasks (Peyrache, Khamassi, Benchenane, Wiener, & Battaglia, 2009). Sharp waves in hippocampus, sleep spindles in neocortex, and spiking activity in both are correlated during SWS (Ji & Wilson, 2007; Qin, McNaughton, Skaggs, & Barnes, 1997). Their co-occurrence may be indicative of consolidation in neocortex for memories initially encoded in the hippocampus (Siapas & Wilson, 1998). However, although these correlated activations are statistically significant, they are also rather weak in overall magnitude. For example, in Ji and Wilson (2007), only nine instances of coordinated cortical and hippocampal activations were observed, out of 366 (cortex), and 121 (hippocampus) significant replay events total. Furthermore, these significant replay events themselves were relatively rare, with 5,808 (cortex) and 1,555 (hippocampus) total candidate events (where such candidate events reflect a selected subset of the full set of events, meeting various minimal criteria). Thus, it remains unclear how much actual consolidation this level of actual replay could support.

Despite these concerns in the correlational data, tests of a more causal nature seem to indicate an important role for SWS and sharp waves in particular. For example, Girardeau, Benchenane, Wiener, Buzsaki, and Zugaro (2009) interfered with sharp-wave activity by stimulating in rat hippocampus at the onset of these waves, and produced degraded performance in a radial maze task, relative to a yoked control with the same stimulation not tied to sharp-wave onset. Furthermore, subsequent memory performance in humans has been shown to be related to hippocampal replay (Peigneux et al., 2004; Rasch & Born, 2007), as well as hippocampal coordination with cortex (Tambini, Ketz, & Davachi, 2010).

A CLS-based model of memory reactivation during sleep was presented by Norman, Newman, and Perotte (2005). This model highlighted the replay of recent experiences during SWS as described above, but it additionally focused on the replay of already well-learned patterns of activity during rapid eye movement (REM) sleep as a means for reduced forgetting. This mechanism is generally compatible with the transformation model of consolidation described above. Mechanistically, this model depends on oscillatory learning triggered by the theta rhythm, which strengthens weak memories and weakens conflicting ones. During one phase of learning, the inhibition is lower, allowing neural units from potentially competing memory traces to become active—these units have their synaptic weights reduced. During another phase, inhibition is higher, which causes neurons that should be active to turn off—these units have their synaptic weights increased. This oscillation of inhibition effectively re-encodes memories to reduce interference from overlap, complementary to how the hippocampus reduces interference through its architecture.

Similarly, memory protection in the hippocampus may occur during REM sleep. Studies have implicated that the information flow is directed from neocortical areas to the hippocampus during REM, where a complementary process to SWS for consolidating hippocampal memory may be at play (Buzsaki, 2002; Louie & Wilson, 2001; Wilson & McNaughton, 1994). Moreover, it has been proposed that the endogenous activity of CA3 units equalizes the strengths of existing memories relative to newly added ones (Norman et al., 2005; Robins & McCallum, 1999). Indeed, neocortically and endogenously driven replay, to and within the hippocampus, may act together for the consolidation of newer memories and the protection of old ones.

5. Dynamics in CLS models

There is an important conundrum stemming from the idea that the hippocampus is continuously and automatically encoding new episodic memories: When does it ever get a chance to recall old information? More generally, there is a fundamental issue in switching between encoding and recall modes of operation. In the early work associated with the CLS model, we found that various parameters of the anatomy and physiology of the hippocampal formation are well suited for optimizing a tradeoff between encoding (which benefits from maximal pattern separation) and recall (which benefits from maximal pattern completion) (O'Reilly & McClelland, 1994). Because pattern separation and pattern completion pull the system in opposite directions, parameters of the system that optimize one will impair the other, and vice-versa. Thus, some kind of compromise needs to be struck, and the specific features of the hippocampal circuitry appear to strike a particularly good compromise. For example, Hebbian synaptic modification (LTP) facilitates completion but reduces separation, unless the strength of synapses from inactive presynaptic units to postsynaptic units is reduced (LTD). Also, multiple layers, as in EG to DG to CA3, allow the compounding of pattern separation, but not pattern completion (O'Reilly & McClelland, 1994).

Going beyond the structural properties of the hippocampus, Hasselmo and colleagues have explored various ways in which the hippocampal system could *dynamically* switch

between encoding and retrieval modes (Hasselmo, 1999; Hasselmo, Bodelon, & Wyble, 2002; Hasselmo, Schnell, & Barkai, 1995; Molyneaux & Hasselmo, 2002; Wyble, Linster, & Hasselmo, 2000). These ideas involve a dynamic modulation of the strength of one or more pathways in the system, and the specifics of the different proposals vary in the locus and agent of this modulation. Recent work on the CLS model has led us to adopt (with some modifications) the version of dynamic modulation that depends on differential phase relationships within the theta cycle (4–8 Hz) (Hasselmo et al., 2002). In Hasselmo's proposal (Fig. 3), the EC has a strong influence at the phase of the theta rhythm when the CA3 has a weak influence. This corresponds to encoding, because it allows input information represented in the EC to strongly influence CA3 and CA1, without the confounding influence of CA3 pattern completion and subsequent activation of CA1, which are associated with recall. In the opposite phase of theta, the opposite dynamic holds, such that a strong CA3 dominates over a weak EC, and the system is much more likely to recall than encode. This theta-phase model has been tested and supported in several experiments (Colgin et al., 2009; Manns, Zilli, Ong, Hasselmo, & Eichenbaum, 2007; Rizzuto et al., 2003). Perhaps the most important feature of the Hasselmo theta-phase model is that it oscillates between encoding and retrieval *constantly* (a few times per second), which contrasts with the prevalent notion that the system switches relatively infrequently, and in a strategic, controlled manner between encoding and recall modes.

Within the context of the Leabra model of biologically plausible learning (O'Reilly, 1998; O'Reilly & Munakata, 2000), which is used to implement the CLS models, this rapid switching suggests a possible augmentation to the hippocampal architectural strengths already in place: The hippocampus could be leveraging these theta-phase dynamics to perform error-driven learning. Specifically, the system is constantly attempting to recall information relevant to the current situation, and then learning based on the encoding phase

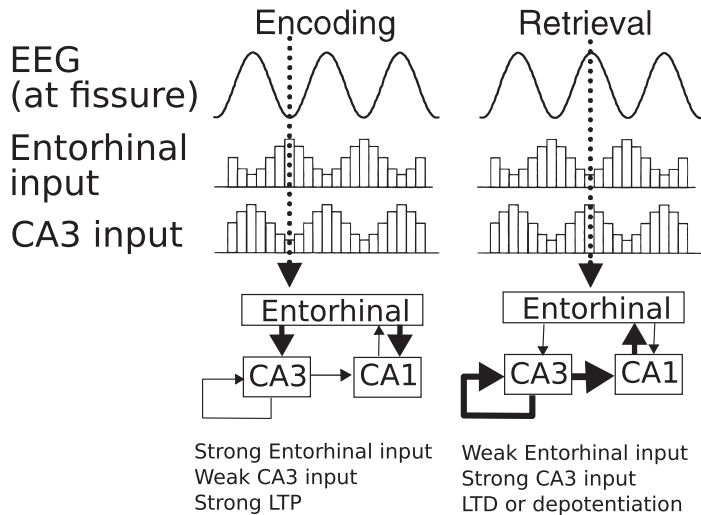


Fig. 3. Hasselmo's proposal for theta-phase modulation of hippocampal encoding versus retrieval. LTD, long-term depression; LTP, long-term potentiation.

that follows immediately thereafter how the recall differed from the actual current inputs. Learning is based on the delta or difference between these two phases, which correspond in Leabra to the expectation or minus phase (recall) versus the outcome or plus phase (encoding) (O'Reilly, 1996). Simulation studies reveal that this error-driven learning dynamic can lead to enhanced hippocampal learning, compared to the purely Hebbian form of learning typically used in CLS models (O'Reilly & Rudy, 2001).

A somewhat different take on the theta-phase oscillation dynamics within the overall CLS framework was explored by Ken Norman and colleagues (Norman, Newman, & Detre, 2007; Norman, Newman, Detre, & Polyn, 2006). In this model, the sign of synaptic plasticity changes during the different phases of the theta cycle, leading to a learning dynamic that “stress tests” representations and reinforces weak elements, while also differentiating from nearby competitors. This work was an important precursor to the computational modeling of memory equalization during sleep stages in (Norman et al., 2005) (discussed above).

5.1. Synergy between the neocortex and hippocampus

Using the phase-based learning version of the CLS model described in the previous section, we have recently shown that more than being merely complementary, the neocortex and hippocampus can actually be quite synergistic, even within the domain of episodic memory (Bhattacharyya, Howard, & O'Reilly, unpublished data). Fig. 4 shows our integrated model of hippocampus and MTL during recall of missing elements in a presented

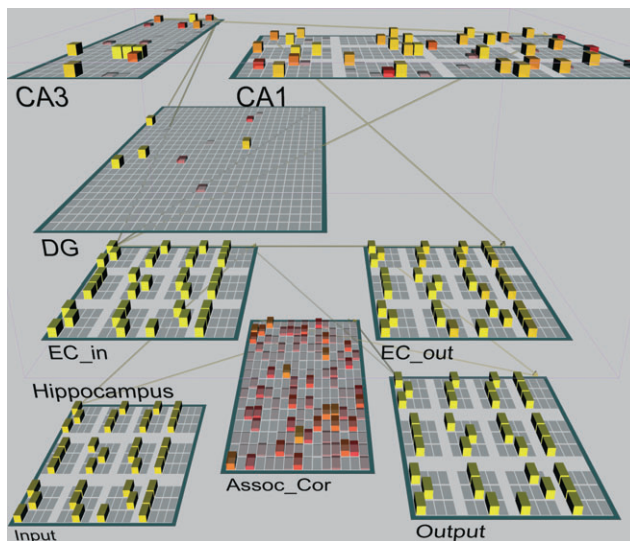


Fig. 4. Integrated hippocampal/cortical model in the Emergent neural simulation. The neocortical pathway maps directly between input and output, while the hippocampus operates on top of that using patterns mapped into EC_in, with hippocampal output from EC_out projecting directly to the output layer. In this example, the “B” associate is missing from the input (second column of inputs) but is recalled on the output via combined contributions of hippocampus and neocortex. DG, dentate gyrus; EC, entorhinal cortex.

pattern. The model is implemented using the Leabra framework (O'Reilly & Munakata, 2000) in the Emergent neural simulation system (Aisa, Mingus, & O'Reilly, 2008). Fig. 5 shows effects of the phase modulation on training for a challenging classification task that we trained the model on, demonstrating that the resulting error-driven learning dynamic in the hippocampus improves learning considerably.

Somewhat surprisingly, instead of dragging the hippocampus down on episodic memory tasks to which it is not particularly well suited, the neocortex can actually end up providing a performance benefit. The critical insight for how this can happen is that the neocortical system can start to settle into an attractor state that is somewhat close to the target memory to be recalled, and this then puts the hippocampus into a much better zone for producing the full recall. Going back to the anatomical simulations from O'Reilly and McClelland (1994), we have known that the hippocampus is very sensitive to the extent of partial cue information that is available to trigger pattern completion. The neocortex thus can have significant benefits by just completing some of the information in a very coarse way.

To explore this synergistic dynamic, Bhattacharyya et al. (unpublished data) tested networks on the AB-AC task (Barnes & Underwood, 1960), which has typically been used to illustrate the phenomenon of catastrophic interference (McCloskey & Cohen, 1989; O'Reilly & Munakata, 2000). This is a particularly challenging test case for any synergy to emerge, because we know that the neocortical system on its own will suffer catastrophic interference when stimulus dataset A is first trained with associations to a B dataset, and subsequently trained with new associations to a C dataset. Interestingly, we find that although the neocortical interference can indeed be very significant, it is reduced when coupled with the hippocampus—the original AB associates remain lurking just below the surface, and the hippocampal system can still pull them out quite effectively. Fig. 6 shows the key results.

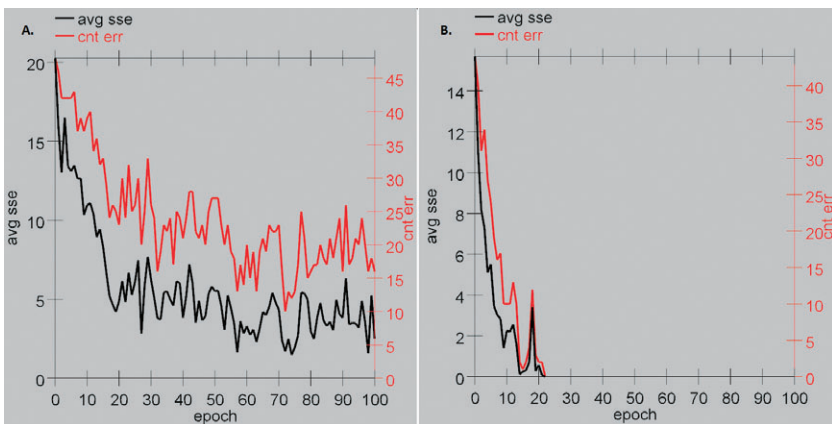


Fig. 5. Effect of phase modulation on learning. (A) Training performance on a challenging classification task for a hippocampal network with no phase modulation, so that it cannot take advantage of error-driven learning. (B) Marked improvement in ability to learn (lower recall error), by attenuating the strength of EC's connection to CA1 during the recall phase. Shown are average sum-squared error (SSE, black line, and left axis) and number of trials that cannot be recalled perfectly (red line, right axis). EC, entorhinal cortex.

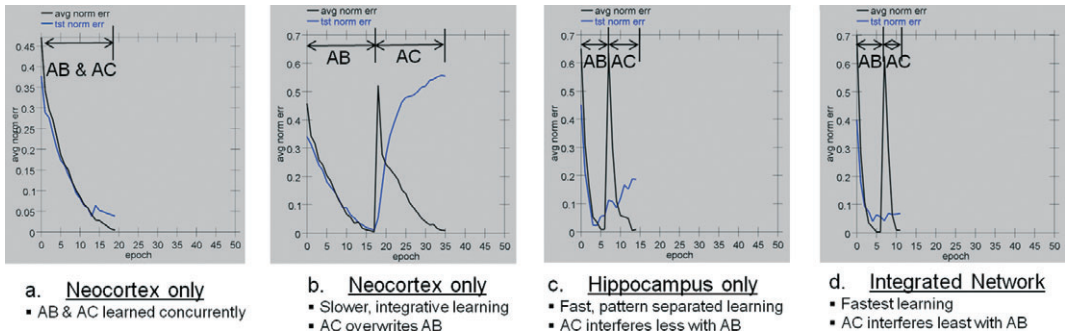


Fig. 6. AB-AC interference experiments: A cortex-only network (a) is able to learn a concatenated AB + AC dataset. This demonstrates that network capacity is not an issue. But when AB-only training and testing are followed by AC-only training, the cortical network shows catastrophic interference (b). A hippocampal network (c) has much less interference. Most notably, when the two are integrated (d), the network learns faster and has even less interference. Average normalized error (in black) measures training error as the associates are learned. Blue line shows the same metric while testing against AB each epoch as the two associations are learned.

Fig. 6a shows that if the different associates are trained concurrently, the cortex is forced to learn weights that distinguish between them. This experiment also illustrates that network capacity is not an issue; it is large enough to hold all the AB and AC data. But critically, when AC-only data are trained *after* AB-only data are learned, the cortex has no architectural features to direct the new association to different units. This results in catastrophic interference (Fig. 6b), where more than half of the AB trials are wrong. On the other hand, the pattern-separation abilities of the hippocampal system largely avoid interference (Fig. 6c), retaining about 70%–80% of the AB associates after acquiring the AC ones. But the most interesting result is that when the cortex and hippocampus are integrated, the network learns slightly faster and suffers even less interference (Fig. 6d).

So by virtue of pattern separation, the hippocampus is able to avoid interference between overlapping memories; yet despite its confusion over dueling associations, the cortex helps the hippocampus in a way we have yet to clearly identify. We are currently exploring the dueling dynamics of this synergy, by comparing neural activation patterns *during* recall. Note that neuronal replay, mentioned above, is another mechanism for avoiding this kind of cortical interference; like in Fig. 6a, it would allow old memories and new to be reexperienced.

6. Future directions of hippocampal research

The central tenants of the CLS framework seem to have held up well under subsequent testing, providing a useful basis to consider what are the currently most pressing questions and problems for understanding hippocampal contributions to learning, memory, and cognition more broadly. Within the hippocampal formation itself, we highlighted above that the specific contribution of the CA1 is relatively less well understood—providing empirical

tests of the idea that it provides a sparse invertible encoding of the EC would be an exciting development. However, exactly how to design and conduct those tests would require considerable more thought, with specific simulation tests conducted to explicate the predictions of our model. Similarly, a better understanding of the functional roles of the subiculum is needed—it likely plays a similar role as CA1 but also interfaces with important subcortical structures and plays a more “limbic” role (O’Mara, Sanchez-Vives, Brotons-Mas, & O’Hare, 2009).

Perhaps the most pressing issues for future research lie outside the hippocampus proper, involving instead the interactions with other brain areas. For example, to what extent, and how, does hippocampal encoding and recall support the kind of working memory and executive functions that are commonly attributed to the prefrontal cortex (PFC)? Recent data suggest that cognitive control can frequently be applied in a *reactive* fashion that requires recall of prior task context, instead of sustained active maintenance (subserved by the PFC), which produces a more *proactive* control dynamic (Braver et al., 2001; Chatham, Frank, & Munakata, 2009; Reynolds, Braver, Brown, & van der Stigchel, 2006). The rapid encoding and retrieval functions of the hippocampus provide a natural fit for this reactive control ability, but more research is needed on this link (Hasselmo & Stern, 2006). The PFC also plays a strong role in directing the encoding and retrieval of information in the hippocampus (Blumenfeld & Ranganath, 2007)—understanding this interaction in greater detail is an important topic of future research. One intriguing idea is that the PFC may modulate theta-phase dynamics (discussed above) to influence hippocampal encoding versus retrieval—some suggestive evidence is consistent with this idea (Jones & Wilson, 2005), but more of this difficult work recording simultaneously in PFC and hippocampus needs to be done.

The other major domain of cortical interactions involves the hippocampus and posterior cortical areas, which have been explored more extensively in the context of consolidation (reviewed above), and other domain-specific memory phenomena (e.g., spatial maps and grid cells; Hafting, Fyhn, Molden, Moser, & Moser, 2005; Hafting, Fyhn, Bonnevie, Moser, & Moser, 2008; and the role of the perirhinal cortex relative to other cortical areas in memory and object recognition; Winters, Saksida, & Bussey, 2008; Cowell et al., 2010). The new simulation work described above highlights more general forms of potential synergistic interactions between hippocampus and posterior neocortex, which could potentially be tested empirically. One suggestive idea is that the hippocampal theta-phase modulation for error-driven learning might play a role in supporting error-driven learning in the neocortex as well. This might provide an interesting new wrinkle in the consolidation story, to the extent that such a dynamic plays out during sleep as well.

Another example of hippocampal/cortical synergy comes from a recent model by Kumaran and McClelland (2010) that shows how recurrent interactions between hippocampus and cortex can support various forms of generalization over specific exemplars (e.g., in the transitive inference task; Dusek & Eichenbaum, 1997—in a way that complements a learning-based dynamic within the CLS framework as explored in Frank, Rudy, and O’Reilly 2003).

7. Conclusions

In conclusion, the CLS framework remains a vital, core theoretical framework for understanding how learning and memory are specialized in the brain. The central ideas from the MMO95 paper remain as relevant today as they were 15 years ago. Of course, considerable progress has been made, and many of these core ideas have been developed and refined over the years, but the essential framework remains remarkably intact. Stepping back from all the specifics of this area, one striking conclusion can be drawn from the success of this approach: The core ideas behind the CLS framework are based on very basic principles of learning in neuron-like processing systems as articulated in the PDP volumes—the predictive validity of these principles in explaining a wide and ever-expanding range of data strongly suggests that the brain can indeed be well described using the basic computational language of neural network models. Thus, in accord with the theme of this special issue, the PDP framework was indeed revolutionary in shaping how we think about cognition and neural processing, and it also has a remarkable ability to remain relevant for 25 years, and beyond.

Acknowledgments

Supported by DARPA STO under Contract No. HR0011-10-C-0014 to HRL.

Thanks to Ken Norman, Jay McClelland, and Tim Rodgers for valuable comments during manuscript review.

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