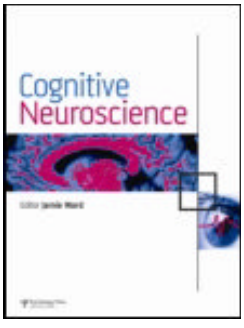

Cognitive Neuroscience
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/pcns20

Predictive coding, precision and synchrony

Karl Friston [a]
[a] The Wellcome Trust Centre for Neuroimaging, University College London, London, UK

Version of record first published: 27 Jul 2012

To cite this article: Karl Friston (2012): Predictive coding, precision and synchrony, Cognitive Neuroscience, 3:3-4, 238-239

To link to this article: http://dx.doi.org/10.1080/17588928.2012.691277

COGNITIVE NEUROSCIENCE, 2012, 3 (3–4), 227–259 (includes Discussion Paper, Commentaries, and Reply)

Discussion Paper

Repetition priming and repetition suppression: A case for enhanced efficiency through neural synchronization

Stephen J. Gotts[1], Carson C. Chow[2], and Alex Martin[1]

[1]Section on Cognitive Neuropsychology, Laboratory of Brain and Cognition, National Institute of Mental Health (NIMH), National Institutes of Health, Bethesda, MD, USA
[2]Laboratory of Biological Modeling, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health, Bethesda, MD, USA

Stimulus repetition in identification tasks leads to improved behavioral performance ("repetition priming") but attenuated neural responses ("repetition suppression") throughout task-engaged cortical regions. While it is clear that this pervasive brain–behavior relationship reflects some form of improved processing efficiency, the exact form that it takes remains elusive. In this Discussion Paper, we review four different theoretical proposals that have the potential to link repetition suppression and priming, with a particular focus on a proposal that stimulus repetition affects improved efficiency through enhanced neural synchronization. We argue that despite exciting recent work on the role of neural synchronization in cognitive processes such as attention and perception, similar studies in the domain of learning and memory —and priming, in particular—have been lacking. We emphasize the need for new studies with adequate spatiotemporal resolution, formulate several novel predictions, and discuss our ongoing efforts to disentangle the current proposals.

Keywords: Repetition priming; Repetition suppression; Synchrony; Prediction; Expectation.

When we repeatedly encounter an object in the environment, we become faster and more accurate at identifying it, a phenomenon referred to as "repetition priming" (see Schacter & Buckner, 1998; Tulving & Schacter, 1990, for review). Repetition priming is stimulus-specific, builds up over several stimulus repetitions (e.g., Logan, 1990; Ostergaard, 1998; Wiggs, Martin, & Sunderland, 1997), and while it attenuates over short delays (e.g., McKone, 1995, 1998), it can be extremely long-lasting with significant residual effects lasting days, months, and even years (e.g., Cave, 1997; Mitchell, 2006; van Turennout, Ellmore, & Martin, 2000). It is also relatively automatic in the sense that it often occurs without subjects' awareness (e.g., Cave & Squire, 1992) and is robust to attentional manipulations (e.g., Kellogg, Newcombe, Kammer, & Schmitt, 1996; Szymanski & MacLeod, 1996) and modest alterations of stimulus form (e.g., Biederman & Cooper, 1991, 1992; Cave, Bost, & Cobb, 1996; Srinivas, 1996). Historically, repetition priming has played an important role in our understanding of the organization of human memory due to its neuropsychological dissociation from more explicit forms of memory in amnesic patients (e.g., Graf, Squire, & Mandler, 1984; Warrington & Weiskrantz, 1974). Amnesic patients with damage to the medial temporal

Correspondence should be addressed to: Stephen J. Gotts, Section on Cognitive Neuropsychology, Laboratory of Brain and Cognition, National Institute of Mental Health (NIMH), National Institutes of Health, Bethesda, MD 20892, USA. E-mail: gottss@mail.nih.gov

The authors would like to thank Nathan Crone, David Plaut, Jay McClelland, David McMahon, Carl Olson, and Avniel Ghuman for helpful discussions. The preparation of this paper was supported by the National Institute of Mental Health, NIH, Division of Intramural Research.

www.psypress.com/cognitiveneuroscience http://dx.doi.org/10.1080/17588928.2012.670617

lobes, including the hippocampus, can exhibit profound impairments in recall and recognition of recent events while at the same time demonstrating normal or nearly normal repetition priming effects (see Squire, 1992, for review). While caution is warranted in attributing priming entirely to implicit as opposed to explicit memory processes (both would typically be expected to contribute in normal individuals—e.g., Henson & Gagnepain, 2010; Voss & Paller, 2008), the basic dissociation has led researchers to focus primarily on the role of neocortical plasticity mechanisms, with priming potentially serving as a window into the formation of long-term knowledge representations that reside primarily in the neocortex (e.g., McClelland, McNaughton, & O'Reilly, 1995; Stark & McClelland, 2000). Indeed, stimulus repetition paradigms in neuroimaging studies (e.g., functional magnetic resonance imaging, or fMRI) are routinely used as a tool to infer the nature of neocortical representations in a variety of cognitive domains (e.g., Andresen, Vinberg, & Grill-Spector, 2009; Bedny, McGill, & Thompson-Schill, 2008; Cant, Large, McCall, & Goodale, 2008; Fairhall, Anzellotti, Pajtas, & Caramazza, 2011; Gold, Balota, Kirchhoff, & Buckner, 2005; Gotts, Milleville, Bellgowan, & Martin, 2011; Konen & Kastner, 2008; Mahon et al., 2007; Piazza, Izard, Pinel, Le Bihan, & Dehaene, 2004). Recent work has identified separate contributions of perceptual, conceptual, and decision/response-related processing to both task performance and priming effects (e.g., Dobbins, Schnyer, Verfaellie, & Schacter, 2004; Horner & Henson, 2008, 2012; Wig, Buckner, & Schacter, 2009; Race, Badre, & Wagner, 2010; Race, Shanker, & Wagner, 2009 Wig, Grafton, Demos, & Kelley, 2005).

While behavioral performance improves with stimulus repetition, neural activity in humans (BOLD fMRI) and monkeys (single-cell firing rates) tends to decrease, a phenomenon often referred to as "repetition suppression" (see Desimone, 1996; Henson, 2003; Grill-Spector, Henson, & Martin, 2006, for reviews). Like priming, repetition suppression is stimulus-specific, builds up over several repetitions (e.g., Jiang, Haxby, Martin, Ungerleider, & Parasuraman, 2000; Miller, Gochin, & Gross, 1991), and has both short-lived and long-lasting components (e.g., Grill-Spector & Malach, 2001; Li, Miller, & Desimone, 1993; van Turennout, Bielamowicz, & Martin, 2003). It occurs relatively automatically (e.g., under anesthesia: Miller et al., 1991) and in a wide range of neocortical brain regions. Indeed, the agreement of the empirical properties of repetition priming and repetition suppression was initially met with enthusiasm that the relationship between the two would clarify the mechanisms underlying priming (e.g., Schacter & Buckner, 1998; Wiggs & Martin, 1998). Given the automatic nature and generality of the two phenomena throughout different cognitive domains, tasks, and brain regions, the promise of understanding this link is that it could pay large dividends in understanding the basic relationships between brain and mind.

However, the relationship between repetition priming and repetition suppression also presents a major puzzle: How is it that reductions in neural activity can mediate better behavioral performance? After all, the propagation of neural activity from sensory areas through to decision- and response-related brain regions (ultimately in motor cortex) is what is thought to mediate performance in an identification task. In studies of repetition priming using common objects and other familiar stimuli, there is little evidence of repetition-related increases in neural activity (see Henson, 2003, for review). So where does the behavioral facilitation come from? Just to highlight how puzzling this basic situation is, it is worth remembering that the major "activation-based" theories of priming that existed prior to the first neuroimaging studies of priming in the mid-1990s (e.g., spreading activation, connectionist models) posited repetition-related accumulation or *increases* in activity in the nodes or units that represented a given stimulus (e.g., Anderson, 1983; Becker, Moscovitch, Behrmann, & Joordens, 1997; Collins & Loftus, 1975; McClelland & Rumelhart, 1985). This issue would also appear to cut across the distinction between implicit versus explicit memory, since both sets of processes are likely to be reflected in some mixture in neural and behavioral repetition effects. One must still explain how less neural activity somehow produces a more effective behavioral response. It is worth noting that in a variety of cognitive domains that do not intrinsically involve stimulus repetition (e.g., attention, visual search, working memory, motion discrimination) better behavioral performance is generally associated with increased rather than decreased activity in cells that prefer a stimulus, location, or response (e.g., Luck, Chelazzi, Hillyard, & Desimone, 1997; Newsome, Britten, & Movshon, 1989; Rainer, Asaad, & Miller, 1998; Schall & Hanes, 1993). Indeed, the basic logic used in mapping visual receptive fields in single-unit studies, in evaluating the results of functional localizers in neuroimaging studies, or in quantitatively comparing neural responses to different experimental conditions, implicitly relies on the assumption that greater activity corresponds to greater involvement in processing. The disconnect with this logic that is represented by the joint observation of repetition priming and repetition suppression makes these phenomena even more important and fundamental to understand. Joint repetition priming/suppression

appears to reflect some kind of improved efficiency mechanism or set of mechanisms that apply over a wide range of repetition lags. While the exact form of these mechanisms is unclear, the need for such mechanisms is clear, given the high energy cost of neural signaling (see Raichle & Mintun, 2006, for review). It is likely that processes of natural selection discovered solutions that optimize both performance and energy use simultaneously (e.g., Aiello & Wheeler, 1995; Allman, 1990). Below, we review four of the main theoretical proposals about what form these solutions might take (see also Grill-Spector et al., 2006).

THEORETICAL MODELS OF REPETITION SUPPRESSION AND PRIMING

Facilitation

The "Facilitation" model (Henson, 2003; James & Gauthier, 2006; James, Humphrey, Gati, Menon, & Goodale, 2000) is perhaps the most straightforward resolution, positing that with repetition, neural activity is advanced in time with a more rapid overall time course (see Figure 1A). In BOLD fMRI experiments, rapid timing differences such as this would be lost due to the slow time course of the BOLD response. This view has received some support in fMRI experiments that either slowed down the time course of a trial by gradually unmasking the stimuli (e.g., James et al., 2000; but see Eger, Henson, Driver, & Dolan, 2007) or attempted to measure BOLD latency differences directly (e.g., Gagnepain et al., 2008; Henson, Price, Rugg, Turner, & Friston, 2002). However, direct electrical recordings of single-cell activity in a variety of brain regions in monkeys (e.g., Anderson, Mruczek, Kawasaki, & Sheinberg, 2008; Freedman, Riesenhuber, Poggio, & Miller, 2006; Li et al., 1993; McMahon & Olson, 2007; Rainer & Miller, 2000; Verhoef, Kayaert, Franko, Vangeneugden, & Vogels, 2008) and in human patients undergoing neurosurgery (e.g., Pedreira et al., 2010) have presented strong counter evidence to this idea under typical stimulus presentation conditions. Firing-rate curves to repeated stimuli show no evidence of advancing in time and are subsumed under the firing-rate curves to novel stimuli. A more sophisticated version of this hypothesis (Bayesian networks and "explaining away") are discussed below.

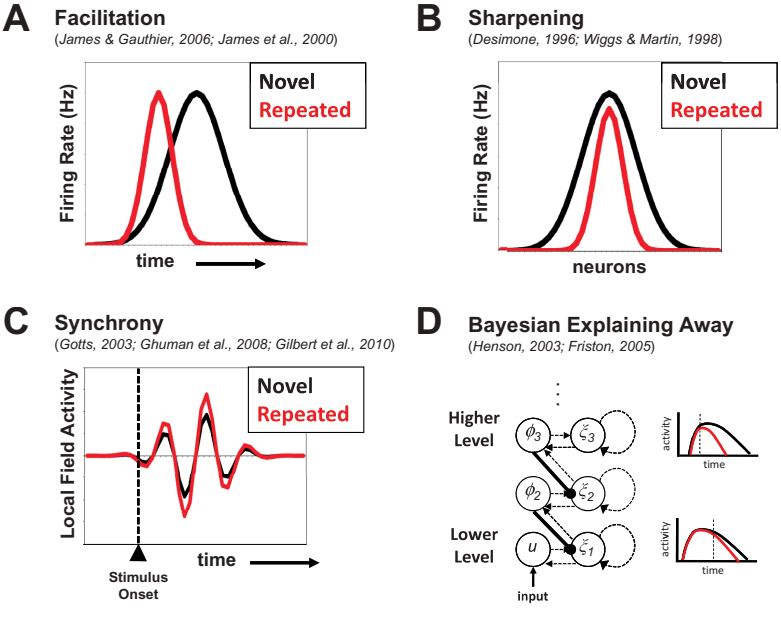

Figure 1. Theories that explain repetition priming in the face of repetition suppression. Graphical depictions of the theories discussed in the text are shown for (A) facilitation, (B) sharpening, (C) synchrony, and (D) Bayesian "explaining away." Hypothetical novel and repeated conditions are shown with black and red curves, respectively. In panel D, suppressive feedback from higher levels to lower levels in the network structure is highlighted by thick black lines, and the earlier separation of novel and repeated conditions in higher levels relative to lower levels is indicated with vertical dashed lines in the activity plots to the right.

Sharpening

A second idea, often referred to as "sharpening" (Desimone, 1996; Wiggs & Martin, 1998), holds that while neural activity is decreasing on the average, the decreases are carried mainly by the cells that are poorly tuned and/or weakly responsive to the repeated stimuli with the "best" cells (i.e., most selective/responsive) instead retaining their activity levels (Figure 1B). If the poorly responsive cells are dropping out while the best-responsive cells keep their responses, the distribution of cell responses over the population is actually more informative about the identity of the stimulus even though the firing rates have decreased overall. In monkeys, there is certainly some evidence consistent with sharpening in single-cell recordings, particularly after lengthy periods of training with the same set of stimuli (e.g., several months: Baker, Behrmann, & Olson, 2002; Freedman et al., 2006; Rainer & Miller, 2000). However, stimulus repetitions that occur solely within a single experimental session have tended to elicit changes in firing-rate that are more consistent with proportional "scaling", in which the "best" responses exhibit the largest decreases (e.g., Li et al., 1993; McMahon & Olson, 2007; Miller, Li, & Desimone, 1993). It is particularly challenging to understand how priming can occur under these circumstances because the cells that are most responsible for driving downstream responses are the ones that are decreasing the most. fMRI studies in humans that have attempted to evaluate sharpening of visual object representations with experience have similarly generated mixed results. Jiang et al. (2007) trained subjects to discriminate between morphed pictures of cars that were assigned to distinct categories. Using an fMRI-adaptation paradigm (see Grill-Spector & Malach, 2001), they found greater release from adaptation with small changes in visual stimulus form in the right lateral occipital cortex after training relative to pre-training, consistent with "sharper," less-overlapping visual form representations. However, another recent fMRI-adaptation study by Weiner, Sayres, Vinberg, and Grill-Spector (2010), using short- and longer-lag repetitions to measure changes in category selectivity, found proportional changes for preferred and non-preferred categories throughout the lateral aspects of ventral occipitotemporal cortex, consistent with proportional "scaling" (i.e., multiplying by a value between 0 and 1) rather than sharpening. Only the more medial aspects of ventral temporal cortex showed larger repetition suppression effects for non-preferred relative to preferred categories, and only for longer-lag repetitions. Similar attempts to use rapid adaptation paradigms to measure tuning changes in single-cell firing rates in monkeys have failed to yield support for sharpening (e.g., De Baene & Vogels, 2010). Even if sharpening were shown to occur robustly in the experimental contexts in which repetition priming is observed, additional assumptions would need to be articulated in order for sharpening to explain priming. For example, when neural representations are distributed over many cells in a "population code" (e.g., Georgopoulos, Schwartz, & Kettner, 1986), each individual cell— even ones that fire at lower rates—could potentially contribute to activating cells in downstream regions that prefer the current stimulus. What is to guarantee that a large loss of firing rate in the poorly responsive cells will not result in weaker or slower onset of firing in the preferred cells downstream? This point highlights another elusive aspect of the sharpening idea. In order for sharpening of firing rate responses to go through as an explanation of priming, there still seems to be a need for an *increase* in firing rate at earlier latencies in the cells that most prefer the repeated stimulus *somewhere* in the brain (akin to the facilitation model). Perhaps this would not occur until the ultimate or penultimate stage of processing in executing a response, but it would still appear to be necessary. Indeed, most neural network models that exhibit sharpening through the application of a supervised learning algorithm predict a mixture of repetition suppression and enhancement effects (e.g., McClelland & Rumelhart, 1985; Norman & O'Reilly, 2003). To date, we still have little or no evidence of such an enhancement occurring, even in lateral prefrontal sites that may play a more central role in decision/response selection (e.g., Rainer & Miller, 2000).

Enhanced neural synchronization

A very different proposal that may help to resolve this puzzle is that as cells are firing at lower overall rates, they are firing more synchronously with one another, leading to more efficient neural processing (Gilbert, Gotts, Carver, & Martin, 2010; Gotts, 2003) (Figure 1C). Neurons are not only sensitive to the average firing rates of their inputs—they are also sensitive to the relative timing of their input spikes due to the passive membrane property of "capacitance" (e.g., Koester & Siegelbaum, 2000). Input spikes only transiently depolarize a receiving cell, after which the membrane voltage decays back toward the resting potential at a rate dictated by the membrane time constant. Small depolarizations that occur simultaneously (i.e., synchronously) in a receiving cell will be much

more likely to sum above the voltage threshold needed to evoke an action potential. Biophysical models and *in vitro* physiology experiments on cortical cells have substantiated this relationship, demonstrating separate contributions of input firing rate and synchrony to a receiving cell's responses (e.g., Reyes, 2003; Salinas & Sejnowski, 2000, 2001). In the extreme, volleys of single spikes could travel along reliably through a processing pathway from sensory to motor, perhaps only requiring a few spikes to generate an appropriate response. Note that this mechanism would also not require elevated firing rates in downstream areas for priming to occur, potentially allowing for decreases in firing rate throughout the entire system. In this view, what increases is the likelihood of generating a single post-synaptic spike when a pre-synaptic spike occurs. It predicts that stimulus repetition should be accompanied by larger fluctuations in local measures of neural population activity (e.g., local field voltages and magnetic field measurements, multi-neuron firing rate binned over short time windows, etc.; e.g., Gilbert et al., 2010), as well as greater phase-locking/coherence between task-engaged cortical sites (e.g., Ghuman, Bar, Dobbins, & Schnyer, 2008).

In a simplified neocortical circuit model that incorporated biologically proportionate numbers of excitatory and inhibitory cells and short-term plasticity mechanisms, Gotts (2003) showed that it was possible to simultaneously address short-lag repetition suppression and priming effects through enhanced synchronization. The model included synaptic depression, an attenuation of transmitter release following spiking activity (e.g., Abbott, Varela, Sen, & Nelson, 1997; Tsodyks & Markram, 1997), and spike-frequency adaptation, the spike-dependent activation of K^+ currents that hyperpolarize the membrane post-synaptically and decrease the membrane resistance (e.g., Constanti & Sim, 1987; Madison & Nicoll, 1984), both parameterized to independent *in vitro* and *in vivo* physiological recordings of neocortical cells (e.g., Ahmed, Allison, Douglas, Martin, & Whitteridge, 1998; Varela, Song, Turrigiano, & Nelson, 1999). The model was able to address short-term (i.e., a few seconds) repetition suppression effects quantitatively as well as qualitatively in a variety of monkey single-cell recording and human fMRI experiments (e.g., Grill-Spector & Malach, 2001; Jiang et al., 2000; Miller et al., 1991; Miller et al., 1993), and it naturally produced "scaling" of the firing-rate distributions as observed in several experiments (e.g., MacMahon & Olson, 2007; Miller et al., 1993; Weiner et al., 2010). Importantly, as the model's firing rates decreased with repetition, the synchronization of the spike times simultaneously increased. This enhanced synchronization could be propagated between separate simulated regions in the model, and it was robust to expected synaptic delays and a modest amount of variability in the firing-rate distribution. Simulating reaction time as the amount of time required for a single receiving output cell to reach a threshold number of spikes, the model also produced repetition priming effects as synchronization increased. Repetition priming that occurs through enhanced synchronization—and in the face of firing-rate decreases—constitutes a particular form of neural efficiency mechanism. A model quite similar to the Gotts (2003) model has also been applied to account for repetition-related decreases in firing rate and enhanced spike synchronization in the insect antennal lobe (olfaction) with good success (Bazhenov, Stopfer, Sejnowski, & Laurent, 2005). While the cellular mechanisms in these models would not enhance synchronization over the much longer repetition lags discussed above, good candidates would include longer-term synaptic plasticity mechanisms such as spike-timing-dependent, long-term potentiation and depression (LTP/LTD) (e.g., Bi & Poo, 1998; Markram, Lubke, Frotscher, & Sakmann, 1997; Sjöstrom, Turrigiano, & Nelson, 2001). With repetition, spike-timing-dependent LTP/LTD mechanisms have the potential to improve and coordinate the timing of spikes across cells, permitting enhanced local and long-range synchronization among task-engaged brain regions.

Despite the promise that the synchrony model holds for resolving the puzzle of repetition priming and repetition suppression, there are relatively few studies that have evaluated it empirically. A burgeoning literature on neural synchronization has developed over the last 10–15 years in domains such as attention and perceptual binding (see Engel, Fries, & Singer, 2001; Fries, 2005; Gregoriou, Gotts, Zhou, & Desimone, 2009b, for reviews). However, only a handful of studies involving stimulus repetition in the neocortex have used multi-electrode recording techniques that are capable of measuring spike synchronization directly. For example, von Stein, Chiang, and Konig (2000) recorded simultaneously from areas 17 and 7 in cat visual cortex while the cats performed a go/no-go task. When they compared trained to novel stimuli, they found greater phase-locking between the two visual areas in the alpha frequency range (8–12 Hz) for trained stimuli. Two recent recording studies by Dragoi and colleagues in monkeys, one in V1, using multi-contact, cross-laminar electrodes (Hansen & Dragoi, 2011), and another in V4, using multiple single electrodes (Wang, Iliescu, Ma, Josić, & Dragoi, 2011), examined local changes in synchronization after brief visual

adaptation (duration = 300 ms) to oriented sine-wave gratings. In both studies, firing rates were reduced to a test grating presented 100 ms after the adaptor. Spikes elicited by the test grating were simultaneously more synchronized with the local field potential (LFP) (spike-LFP coherence) in the gamma frequency range (30–80 Hz) relative to a control condition in which the adapting grating was replaced with a random dot patch of matched luminance. The increases in gamma synchronization in both studies were associated with improvement in neuronal orientation discrimination performance of the test gratings. For the study in V1, for which laminar information was available, the improvement in neuronal orientation discrimination performance was only associated with increases in gamma synchronization within the superficial cortical layers that serve as output to subsequent visual areas. In models, it is not clear whether synchronization effects should have a different impact at higher versus lower frequencies, since similar benefits can be observed over a range of frequencies (e.g., Salinas & Sejnowski, 2000, 2001). However, given that the brain's activity dynamics are generally weighted toward lower frequencies (e.g., He, Zempel, Snyder, & Raichle, 2010), one might expect changes in lower frequencies to have a larger impact relative to higher frequencies that have weaker overall amplitudes (such as gamma).

A few additional studies using single electrodes have provided relevant data for evaluating the synchrony model. Anderson et al. (2008) exposed monkeys to novel and familiar images during passive viewing while recording both multi-unit spiking activity and LFPs in inferior temporal cortex. In addition to observing repetition suppression effects in firing rate to the familiar images, they simultaneously observed larger low-frequency fluctuations in the LFPs (~5–10 Hz) that were phase-locked to the stimulus onset (i.e., larger evoked responses). In a related study, Peissig, Singer, Kawasaki, and Sheinberg (2007) observed a similar pattern in LFPs that they recorded with transcranial electrodes implanted over occipitotemporal sites. They first trained monkeys to classify a set of bird and object pictures. During testing, the monkeys performed the same classifications on both previously trained and novel pictures. Behaviorally, they observed repetition priming effects for trained relative to novel pictures (faster reaction time and improved accuracy), while they observed larger low-frequency fluctuations in the LFPs that were particularly prominent at 170 ms after stimulus onset. In a different study aimed at evaluating changes in stimulus selectivity to familiar pictures, Freedman et al. (2006) analyzed the firing-rate responses of a large number of single cells (~300) in inferior temporal cortex (area TE) to familiar and novel stimuli during passive viewing. They observed increases in stimulus selectivity to familiar pictures (consistent with the sharpening model), while also observing a hint of periodicity in the firing rate curves to familiar stimuli, with fluctuations at approximately 5–10 Hz (see their Figure 8). Closer inspection of the firing rate curves reported for the three monkeys in Anderson et al. (2008, their Figure 4) also reveals a similar tendency for periodicity. Taken together, these studies all provide evidence that supports the basic premise of the synchrony model, namely that cells should fire in a more synchronous and temporally coordinated manner following stimulus repetition, both locally and in inter-areal interactions among task-engaged cortical sites. It is important to note that such evidence is not limited to monkeys and other mammals. Striking similarities also exist in electrode recordings in insects during stimulus repetition. For example, Stopfer and Laurent (1999) repeatedly presented odor puffs to the antennae of locusts and recorded spikes and LFP responses in the antennal lobe (i.e., the insect equivalent of the olfactory bulb in mammals). Across a series of repetitions presented at a rate of one stimulus per 10 s, they found repetition suppression in firing rates, as well as increased synchrony between the spikes and the LFPs in the 20–30-Hz frequency range. In a separate conditioning experiment in honeybees, Stopfer, Bhagavan, Smith, and Laurent (1997) were able to pharmacologically block odor-selective synchronous firing while leaving odor-selective firing rates intact. Under these conditions, the bees' odor discrimination was impaired, demonstrating a causal role of synchrony in their behavior.

Having just reviewed many of the microelectrode recording studies in animals that are relevant to the evaluation of the synchrony model, what relevant data exist for humans and in repetition priming tasks? In most human studies, measurements of neural activity are restricted to noninvasive neuroimaging methods such as fMRI, magnetoencephalography (MEG), and electroencephalography/event-related potentials (EEG/ERP). The most extensive literature in humans that employs a method with the appropriate temporal resolution is the EEG/ERP literature on repetition priming (e.g., Bentin & Peled, 1990; Henson et al., 2003; Henson, Rylands, Ross, Vuilleumier, & Rugg, 2004; Kiefer, 2005; Olichney et al., 2000; Paller & Gross, 1998; Rugg, Brovedani, & Doyle, 1992; Rugg, Mark, Gilchrist, & Roberts, 1997; Swick, 1998). While scalp EEG/ERP studies have occasionally found evidence consistent with larger evoked responses to repeated stimuli for select electrode sites (e.g., Schendan & Kutas, 2003;

Scott, Tanaka, Sheinberg, & Curran, 2006), most studies have failed to find such evidence or have even reported attenuated ERPs with repetition (e.g., Fiebach, Gruber, & Supp, 2005; Gruber & Muller, 2005; Race et al., 2010). The discrepancy with the results reviewed above for electrode-recording studies with animals could occur for several reasons: (1) there is a species difference with humans, and larger ERPs with repetition are simply not occurring (i.e., the synchrony model is wrong); (2) the timing of fluctuations in the ERPs, such as those in the alpha to gamma frequency range (~8–80 Hz), are somewhat idiosyncratic from subject to subject and group-averaging across subjects (or low-pass filtering the voltage signals below 20 Hz) washes these differences away; or (3) the spatial resolution of scalp EEG signals is too coarse and requires source estimation to see spatially localized effects, particularly for those in deeper sources that may carry the largest effects (e.g., the fusiform gyrus). Two recent source-localized MEG studies of repetition priming in humans suggest that the answer may be one of the last two reasons (Ghuman et al., 2008; Gilbert et al., 2010). Gilbert et al. (2010) asked subjects to covertly name pictures of common objects by pressing a response button when they knew the correct name, with randomly intermixed novel and repeated trials. They measured evoked power (i.e., phase-locked to the stimulus onset) in source-estimated data by an event-related beamformer approach, that is, event-related synthetic aperture magnetometry ("ER-SAM") (Cheyne, Bostan, Gaetz, & Pang, 2007), focusing the analyses on brain regions known to exhibit repetition suppression in fMRI studies (e.g., extrastriate visual cortex, the fusiform gyrus, and the lateral prefrontal cortex). In order to retain phase information in the MEG signals, source-estimated responses in different frequency bands (5–15 Hz: theta/alpha; 15–35 Hz: beta; 35–60 Hz: gamma) were first averaged in the time domain across trials, either novel or repeated. Evoked power estimates were calculated in 100-ms bins around the stimulus onset. Gilbert et al. (2010) observed increases in low-frequency evoked power (5–15 Hz) for repeated stimuli in the right fusiform gyrus and right lateral prefrontal cortex, with the earliest effects occurring between 100 and 200 ms post-stimulus onset in the fusiform gyrus. Similar results were observed in striate/extrastriate visual cortex, albeit in a slightly higher frequency range (beta: 15–35 Hz). Ghuman et al. (2008) measured changes in phase-locking between distant cortical sites in lateral prefrontal and occipitotemporal cortex while subjects made size judgments about novel and repeated objects. They found increases in fronto-temporal phase-locking between 10 and 15 Hz for repeated relative to novel objects. Importantly, the latency of the phase-locking increase predicted the magnitude of repetition priming for individual subjects. Taken together, these studies suggest that stimulus repetition in humans indeed leads to similar changes to those observed in electrode recording studies in animals. Repetition leads to larger local fluctuations in neural activity, as well as increased coupling between distant task-engaged sites, providing support for the synchrony model.

Bayesian networks and "explaining away"

The final proposal that we will consider is a more sophisticated variant of the facilitation model proposed by Friston and Henson (Friston, 2005; Henson, 2003; see Grill-Spector et al., 2006, for further discussion). In this proposal, the cortex is cast as a form of hierarchical generative Bayesian statistical model (see also Dayan, Hinton, Neal, & Zemel, 1995; Lee & Mumford, 2003; Lewicki & Sejnowski, 1996; Mumford, 1992; Rao & Ballard, 1999). Perceptual inference occurs as a progressive interaction between bottom-up sensory input ("evidence") and top-down expectations ("prediction") throughout the cortical hierarchy. A critical aspect of this view is that top-down predictions serve to inhibit or suppress the bottom-up sensory evidence, with residual activity in the lower levels of the cortical hierarchy serving as "prediction error" that is, in turn, relayed back toward the higher levels. The learning mechanism (expectation maximization—EM—algorithm) improves the top-down predictions in the service of reducing prediction error, leading to reductions in neural activity in lower levels with stimulus repetition (i.e., repetition suppression) (see Figure 1D). This process is commonly referred to in the literature on Bayesian networks as "explaining away" (e.g., Pearl, 1988), since as the appropriate causes of the sensory evidence are learned, the incorrect causes (i.e., prediction error) are reduced and explained away. The proposal bears similarity to the simple facilitation model in that stimulus repetition leads to progressively earlier termination of activity, potentially supporting earlier and improved behavioral identification/discrimination.

The Bayesian "explaining away" model makes a number of novel predictions in stimulus repetition paradigms. Given that repetition suppression in a certain brain region results from top-down input and that this input can be further propagated to progressively lower levels, the model predicts the following: (1) repetition suppression effects should tend to occur earlier in higher-level regions than in lower-level regions, (2) repetition should lead to stronger top-down causal interactions as assessed by methods such as Grainger causality and dynamic causal modeling (DCM)

(Friston, Harrison, & Penny, 2003), and (3) the nature of those stronger top-down causal interactions should be suppressive/inhibitory (i.e., negative coupling). One relatively novel feature of the Bayesian view is that higher levels of the processing hierarchy can track the likelihood of encountering particular objects, as well as more abstract variables such as the likelihood of object repetition in a stream of stimuli. This feature leads to a fourth prediction: a high likelihood of stimulus repetition in an experimental session (or block of trials) should produce a stronger top-down expectation/prediction from brain regions representing this more abstract contextual information (possibly in prefrontal regions). Hence, larger repetition suppression effects should be observed in brain regions receiving this kind of input (perhaps in object or category selective cortex in the temporal lobes). This last prediction has been evaluated in several recent experiments. Summerfield, Trittschuh, Monti, Mesulam, and Enger (2008) embedded short-term repetitions of face pictures in blocks of trials in which repetitions were either frequent (60% of trials) or infrequent (20% of trials). They found that repetition-suppression effects in the fusiform face area (FFA) were stronger when repetitions were expected, with similar recent results reported in EEG/ERP (Summerfield, Wyart, Johnen, & de Gardelle, 2011) and MEG (Todorovic, van Ede, Maris, & de Lange, 2011). In contrast, a study of repetition suppression in monkey TE by Kaliukhovich and Vogels (2011) failed to find evidence of this kind of contextual sensitivity in single-cell firing rates or in LFP gamma band power. Another recent fMRI study in humans, while able to replicate the effect of repetition expectation on repetition-suppression magnitude, found that this expectation effect disappeared when subjects had their attention diverted away from the stimuli (Larsson & Smith, 2012). This would appear to rule out the extreme version of the "explaining away" view in which all repetition-suppression effects are explained by relatively high-level repetition expectation. However, it is important to keep in mind that this extreme version probably had few adherents to start with, since earlier, more perceptual levels in the Bayesian hierarchy would not be expected to be influenced directly by more abstract variables such as the frequency of stimulus repetition. Taken together, these results provide partial support for a role of high-level expectation in modulating short-term repetition suppression effects, at least at particular points along the cortical processing hierarchy. The first three predictions listed above have been evaluated less thoroughly. However, one recent study by Ewbank et al. (2011) has provided some support for the prediction that top-down causal interactions should be stronger following stimulus repetition. They used DCM in fMRI to investigate changes in causal interactions between the fusiform body area (FBA) and the extrastriate body area (EBA) while subjects viewed pictures of human bodies. Pictures were either repetitions of the same body identity or different identities, shown in blocked conditions. They also evaluated the effect of varying picture size and viewpoint on repetition suppression and causal interactions. They found repetition suppression in both EBA and FBA to all viewing conditions (the same identity evoked less activity than different identities). Simultaneously, the DCM analyses revealed increased top-down causal interactions from FBA to EBA for same-identity relative to different-identity blocks in all conditions, with the same size/same view condition also showing greater causal interactions in the bottom-up direction. The fact that repetition suppression and greater top-down causal interactions occurred in the same experimental circumstances is consistent with prediction no. 2 listed above. However, these authors did not evaluate the more direct association between the strength of top-down coupling from FBA to EBA and the magnitude of repetition suppression in EBA, nor did they focus discussion on the apparently positive sign of the top-down coupling (relevant to prediction no. 3 listed above; for another study evaluating positive versus negative causal interactions with DCM, see a recent paper by Cardin, Friston, & Zeki, 2011). Positive coupling suggests an excitatory rather than inhibitory top-down influence on the lower-level activity, inconsistent with the "explaining away" account of repetition suppression but potentially consistent with the synchrony model (e.g., Ghuman et al., 2008). The use of a blocked design also brings with it issues of interpretation, due to potential differences in attentional state and processing strategy (see below for further discussion). Nevertheless, these preliminary results provide some partial support for the Bayesian "explaining away" proposal. Future experiments will need to focus on how proposals such as the synchrony model and "explaining away" might be further teased apart.

GOING FORWARD

Having reviewed four basic proposals as to how repetition suppression might afford repetition priming, the only view that we consider definitively ruled out by current data is the facilitation model, at least in its existing form. Firing-rate recordings in a variety of areas in monkeys and even in humans (e.g., Pedreira et al., 2010) have shown that the onset of neural responses in typical stimulus viewing conditions is not temporally advanced. In many experimental

circumstances used to measure priming, particularly those in which stimulus repetitions occur within a single experimental session, tests of the sharpening model have also yielded a surprising lack of support. At present, we view the synchrony model as the most promising. Recent experiments in a variety of cognitive domains in animals and humans have provided converging support for the role of neural synchronization in behavior. However, the Bayesian "explaining away" model has received experimental support, as well, and neither the synchrony nor "explaining away" model has been run through a full gauntlet of experimental tests. Below we lay out three basic experimental methods, that, if applied, should help to bring about more clarity to the relationship between repetition suppression and priming.

Spike-LFP recordings in animals and human patients

The most direct way to evaluate the synchrony model would be to measure single-unit and/or multi-unit spiking responses, along with LFPs, in several task engaged cortical regions. For example, monkeys could be trained to perform a discrimination task on visual stimuli with responses indicated through eye movements, taking behavioral measures of response time and accuracy (as in McMahon & Olson, 2007). Responses could then be recorded simultaneously in object/form-selective temporal regions such as the TE and areas involved in the execution of eye movements such as the frontal eye fields (FEF). The synchrony model would predict that spike-LFP coherence, possibly in lower frequencies such as alpha (8–12 Hz) or beta (13–30 Hz), should be greater for repeated stimuli within areas as well as across areas (for an example of this type of experiment in visual attention, see Gregoriou, Gotts, Zhou, & Desimone, 2009a). Furthermore, this increased coherence should predict the magnitude of repetition priming. Interestingly, the Bayesian "explaining away" model would also predict increased coherence between spikes in higher-level areas, such as FEF, and LFPs in lower-level areas (e.g., TE, in this case, due to suppression by top-down predictions). Both models would expect similar results in other paired locations within the ventral visual pathway that are involved in object form processing (e.g., V1, V2, V4, and TEO). The "explaining away" model would posit a further relationship between coherence increases and the magnitude of repetition suppression in the more bottom-up region of a pair of recording sites (with larger repetition suppression expected for larger coherence). Taking measures of causality in LFP-LFP recordings between two connected regions (e.g., Grainger causality, DCM, etc.), the "explaining away" model clearly predicts that the directionality of the interactions should flow more in the top-down direction for repeated stimuli compared to novel stimuli. Repetition-suppression effects should also occur earlier in top-down regions than in bottom-up regions. The quantitative relationship between repetition suppression and increased synchronization, as well as the direction of information flow following repetition, is less constrained in the synchrony model, potentially allowing for somewhat independent effects and symmetrical top-down/bottom-up causal interactions (see discussion below). However, the synchrony and "explaining away" proposals differ critically in which cells should show the increased coupling. The synchrony model posits that task-engaged cells that carry information critical for task performance are the ones that are synchronizing, activating each other more reliably and effectively with single spikes. The prediction that follows is that cells that prefer a repeated stimulus are the ones that should synchronize (relative to those that are weakly tuned or weakly responsive). In contrast, the Bayesian "explaining away" proposal holds that there are two separate subpopulations of cells, cells that encode the conditional expectation of perceptual causes (f_i) and those encoding prediction error (ξ_i) (see Figure 1D and Friston, 2005, p. 826, for discussion). After learning, the "error" cells are the ones that are suppressed by top-down predictions, and it is the firing of these cells that should carry the effects of the more strongly negative top-down coupling (perhaps exhibiting hyperpolarized voltages following spiking in higher-level areas representing predictions). Occasionally, experiments of this type (i.e., recording spikes and LFPs with microelectrodes) can be conducted in human patients undergoing brain surgery (e.g., Kraskov, Quiroga, Reddy, Fried, & Koch, 2007), and the same sorts of predictions would be expected to hold in these contexts.

Intracranial EEG in humans

While we view recent source-estimated MEG experiments in humans as supporting the synchrony model (and potentially the Bayesian "explaining away" model), source-estimation procedures are forced to make many assumptions in order to provide an inverse solution, and the algorithms are complex. Direct electrical recordings with good spatial resolution (<1–2 cm) would be useful for verifying the basic pattern of results observed in these MEG experiments, as well as for testing further predictions of the two

models. Such measures are currently available in intracranial EEG studies in human patients who are undergoing surgery for intractable epilepsy; this is referred to as electrocorticography (EcoG) (e.g., Canolty et al., 2006; Puce, Allison, & McCarthy, 1999). While the subdural electrodes used in these studies typically do not allow the recordings of spikes, they permit recordings of field voltages directly from the cortical surface and often provide coverage over a large extent of one cerebral hemisphere, recording signals from up to 100 electrodes simultaneously per patient. We have reported preliminary results of one such study utilizing an object-naming task in two patients with coverage of the lateral surface of the left frontal and temporal lobes (Gotts, Crone, & Martin, 2010, Society for Neuroscience Abstracts, Program 94.11). We found that stimulus repetition led to repetition priming in both patients and increases in low-frequency evoked power (1–15 Hz) for virtually all task-engaged electrodes (i.e., those that exhibited significant evoked responses), replicating the basic pattern of Gilbert et al. (2010). Like Ghuman et al. (2008), we also observed increases in phase-locking (LFP-LFP coherence) between task-engaged frontal and temporal electrodes in the alpha (8–12 Hz) and low beta (12–18 Hz) frequency ranges. With additional patients, we should have the ability to test several of the predictions discussed above for the spike-LFP experiments, such as the timing and directionality of changes in the top-down and bottom-up directions, as well as the association between coherence changes and the magnitude of repetition priming. While the inability to record spikes in single cells will necessarily create some ambiguity in interpretation with respect to the exact form that changes in synchronization take (e.g., spike synchrony versus rapid co-modulation of firing rates), the advantage of this method over the spike-LFP recordings is the nearly whole-hemisphere coverage that it provides. To our knowledge, only one other ECoG study to date in humans has examined the effect of stimulus repetition on local field activity (Puce et al., 1999). However, this study examined only short-term repetitions in ventral temporal cortex during passive viewing (as in Miller et al., 1991), and no measures of repetition priming were taken.

Connectivity methods in fMRI

One large downside in using source-estimated MEG or ECoG to assess changes in neural synchronization is that the analog of repetition suppression in these methods is unclear. Fluctuations in field activity, either magnetic or electrical, may eventually be found to have a reliable correlate in terms of overall neural activity level, but this relationship is currently unknown. The two types of measures could theoretically be unrelated in the same manner that the mean and variance of a random variable can be independent and separate quantities. For example, a firing rate that is uniformly distributed in time may have no detectable effect on field fluctuations, resulting in a blindness to certain sorts of changes in activity level when taking field measurements. In order to relate repetition suppression, repetition priming, and changes in synchrony, it would be best to measure these phenomena in the same experiments. While this should be possible for the spike-LFP recording methods in animals, it might also be possible in coarser methods that are available to more researchers, such as fMRI in humans. First emphasized by Friston and colleagues (Friston et al., 1997, 2003), fMRI studies that measure patterns of temporal covariation in the BOLD response across pairs or collections of brain regions have become commonplace following the advent of resting-state functional connectivity methods (see Fox & Raichle, 2007, for review). If cells in two brain regions are engaging in more synchronous interactions with increased coupling while processing repeated compared to novel stimuli, one might expect the magnitudes of the corresponding BOLD responses to co-vary at higher levels, as well. This idea suggests a relatively straightforward fMRI experiment in which it should be possible to evaluate the separate effects of stimulus repetition on the mean BOLD response versus on the magnitude of BOLD covariation between pairs of task-engaged voxels/regions. However, there is at least one main stumbling block to carrying out this experiment. When novel and repeated stimuli are randomly intermixed in a typical rapid event-related design, standard analysis methods do a good job at estimating the mean BOLD response to each condition, even with a great deal of overlap of the slow responses to individual stimuli as long as baseline periods are appropriately interleaved. However, the same is not true of estimating the variation around the mean to each individual stimulus. This is what would be necessary in order to measure a condition-specific change in correlation/coupling cleanly, with correlation/coupling between two brain regions being calculated over the set of individual stimulus responses in each experimental condition (e.g., novel versus repeated). One solution would be to use a blocked design with no temporal overlap of the novel and repeated conditions, although that has well-known downsides, creating problems of interpretation with respect to strategic effects and differences in attentional state (e.g., D'Esposito, Zarahn, & Aguirre, 1999; Hamburger & Slowiaczek, 1998). A better

solution would be to space individual stimuli far enough apart such that the peaks of the BOLD responses are no longer overlapping (~8–10 s, closer to a "slow" event-related design; e.g., Bandettini & Cox, 2000), still permitting randomly interleaved conditions. In an experiment such as this (currently underway in our laboratory), the synchrony model predicts that while the mean BOLD response is decreased to repeated stimuli (repetition suppression), correlations of the response magnitudes to individual repeated stimuli across task-engaged voxels should *increase*. Furthermore, beta weights or causal model parameters (e.g., DCM) that assess the strength of inter-regional coupling should be more positive and facilitatory for repeated compared to novel stimuli. The Bayesian "explaining away" model makes at least two novel predictions in this experiment: (1) methods of assessing causality (e.g., Grainger, DCM) should reveal a greater top-down flow of information (see discussion of Ewbank et al., 2011, above), and (2) beta weights or DCM model parameters between two connected brain regions should be *negative*, rather than positive as in the synchrony model, between top-down and bottom-up areas for repeated stimuli. The magnitude of this negative coupling should be associated with the magnitude of repetition suppression in the bottom-up areas.

A FINAL NOTE ON REPETITION SUPPRESSION AND THE SYNCHRONY MODEL

The synchrony model posits that stimulus repetition should lead to enhanced local and long-range synchronization among task-engaged cortical regions, and this, in turn, should lead to improved accuracy and more rapid response times. What does this model have to say about repetition suppression? In the Gotts (2003) neural network model, short-term repetitions produced repetition suppression and synchronization in a more or less unitary fashion, through short-term plasticity mechanisms of synaptic depression and spike-frequency adaptation. However, these mechanisms recover over tens of seconds and do not apply at the longer lags used to study repetition suppression in many experiments. At longer lags, long-term plasticity mechanisms, such as LTP/LTD, are likely to be responsible for any observed changes in synchronization, perhaps through spike-timing-dependent plasticity (e.g., Bi & Poo, 1998; Markram et al., 1997; Sjöstrom et al., 2001), which improves the timing relations among cells that prefer the repeated stimulus. It is further possible that LTD dominates the changes such that activities will be reduced overall, producing repetition suppression, but how this would relate to changes in synchrony is quite unclear. We would tentatively suggest that the mechanisms producing changes in synchronization and those resulting in overall activity decreases may be at least partially independent, possibly explaining the lack of relationship between repetition suppression and repetition priming that has occasionally been observed (e.g., McMahon & Olson, 2007; Race et al., 2009; Xu, Turk-Browne, & Chun, 2007). Partial independence would require at least two mechanisms that would tend to be engaged when stimuli are repeatedly encountered in the service of improving neural processing efficiency. With more data in spike-LFP and slow event-related fMRI experiments, the relative importance of repetition suppression and synchronization in explaining priming may be put to the appropriate tests.

Commentaries

Predictive coding, precision and synchrony

Karl Friston
The Wellcome Trust Centre for Neuroimaging, University College London, London, UK
E-mail: k.friston@fil.ion.ucl.ac.uk

http://dx.doi.org/10.1080/17588928.2012.691277

Abstract: Gotts, Chow and Martin provide a very nice review of repetition priming and suppression that reaches a compelling conclusion—we need to look more closely at synchronization in learning and priming. Indeed, current modeling work focuses on this issue—namely, the dynamic causal modeling of electrophysiological responses to address the role of synchrony in Bayesian explaining away. This commentary revisits the nature and relationships among the four theories in Gotts et al. and nuances some of their empirical predictions. In particular, I emphasize *precision* or uncertainty in predictive coding as a unifying consideration.

I think that we are closer to understanding the computational anatomy of repetition and priming than might be thought. This optimism rests upon casting the theories reviewed in Gotts et al. as complementary perspectives on the same problem: *Facilitation* and *sharpening* are phenomena that are fully consistent with *Bayesian explaining away*, which is mediated by *synchronization*. In other words, explaining away is a theory about *what* the brain is doing and synchronization is a proposal about *how* the brain does it. In one sense, the Bayesian brain hypothesis is almost certainly correct—in the sense that our capacity for near-optimal perceptual inference means that we must be performing some form of approximate Bayesian (probabilistic) inference. The real question is how this approximate inference is implemented neuronally. At present, the most popular implementation is *predictive coding* that involves reciprocal message-passing between hierarchically deployed cortical areas (Mumford, 1992; Rao & Ballard, 1999). There is a vast amount of neurobiological evidence in support of this scheme, which can be derived—in a fairly straightforward way—from (approximate) Bayesian optimality principles (Friston, 2008). So, can predictive coding explain the phenomena of *facilitation* and *sharpening*; and does it admit a role for *synchrony*?

This work was funded by the Wellcome Trust.

Predictive coding

Predictive coding relies upon the optimization of top-down predictions—thought to originate in deep pyramidal cells—that try to suppress or explain away prediction errors, encoded by superficial pyramidal cells in lower hierarchical levels (Mumford, 1992; Friston, 2008). Prediction errors are then broadcast over forward connections to adjust predictions at higher levels. Crucially, top-down predictions are not just about the *content* of lower-level representations but also about our *confidence* in those representations. This confidence may be mediated by modulating the post-synaptic gain of superficial pyramidal cells encoding prediction error—to boost their influence on higher levels. Mathematically, this gain corresponds to the precision (inverse variance) of prediction errors and provides a nice metaphor for attention (Feldman & Friston, 2010).

It is fairly straightforward to explain *facilitation* and *sharpening* within this framework: Facilitation involves a speeding of evoked neuronal responses, which—in the context of predictive coding—speaks to an increase in synaptic rate constants that is formally identical to increases in synaptic gain (encoding precision or confidence). This boosts prediction errors that inform the best hypothesis about the cause of sensory input (Gregory, 1980), while suppressing alternative hypotheses; namely *it sharpens neuronal representations*. On exposure to repeated stimuli, plastic changes in forward (and backward) connections enable a more efficient facilitation and sharpening (see Henson et al., 2012). In short, this scheme accounts for repetition priming and suppression and the phenomena of facilitation and sharpening. So where does synchrony come in?

Synchronous gain and predictive coding

An obvious candidate for controlling post-synaptic gain is synchronization of pre-synaptic inputs—a phenomena referred to as *synchronous gain* (Chawla, Lumer, & Friston, 1999). This means that the selection of prediction errors—that drive higher-level representations—almost certainly involves synchronization. Indeed, there is current interest in the possibility that bottom-up messages—from superficial pyramidal cells—are mediated by fast (gamma) frequencies, while top-down messages from deep pyramidal cells may be mediated by slower (beta) frequencies (Buffalo, Fries, Landman, Buschman, & Desimone, 2011). It is this hypothesis that current collaborations with Pascal Fries and colleagues hope to test—using dynamic causal modeling (Bastos et al., 2012).

Empirical predictions

Finally, I will reiterate the importance of formal theories and modeling—as emphasized by Gotts et al.—by commenting on the empirical predictions made by predictive coding. First, repetition suppression rests on optimizing connection strengths that mediate predictions. Crucially, these change (anti-symmetrically) the efficacy of *both forward and backward* connections (Friston, 2008). Second, because predictive coding minimizes prediction error, it is based upon feedback dynamics. This means that either forward or backward connections must be (effectively) inhibitory. The fact that both forward and backward connections are excitatory (Glutamatergic) has exercised us a little. Current thinking is that *explaining away* is mediated by local inhibitory interneurons (Bastos et al., 2012). Finally, repetition suppression is expressed throughout the hierarchy (in high and low areas) *at the same time*. This is because message-passing is recurrent and suppression of prediction error emerges concurrently at all levels. Repetition suppression to high-level attributes will clearly occur later but it will be expressed at lower levels. This phenomenon has been studied extensively in the context of the simplest repetition suppression—namely the mismatch negativity (Garrido, Kilner, Stephan, & Friston, 2009).

In conclusion, I think Gotts et al. raise a number of fascinating questions that may herald some important advances in our understanding of computational architectures in the brain, over the next few years.

* * *

Explaining away repetition effects via predictive coding

Michael P. Ewbank and Richard N. Henson
MRC Cognition and Brain Sciences Unit, Cambridge, UK
E-mail: michael.ewbank@mrc-cbu.cam.ac.uk

http://dx.doi.org/10.1080/17588928.2012.689960

Abstract: Gotts, Chow and Martin summarize Predictive Coding models in which repetition-related decreases in neural activity reflect an "Explaining Away" of stimulus-driven neural activity. Here we elaborate the subtleties of testing such models, particularly with fMRI.

The "Explaining Away" model described by Gotts et al. is really the application of a more general doctrine in neuroscience—that of "predictive coding" (Friston, 2012)—to the case of repetition effects. The key idea is that neurons receive predictions from higher layers of a hierarchical network, with any difference between those predictions and the input from lower layers producing a prediction error in that layer. Synaptic change serves to reduce future prediction error (i.e., improve predictions), resulting in reduced activity in those neurons coding the prediction error when a stimulus is repeated.

In the specific instantiation of predictive coding discussed by Gotts et al., each layer contains three types of neurons: Not just those coding prediction error, but also those coding predictions (from higher layers) and input (prediction errors from lower layers). Yet the relative contribution of these different types of neurons to a hemodynamic measure like BOLD is uncertain (see Egner, Monti, & Summerfield, 2010), making such models difficult to test with fMRI. Testing may be easier with EEG/MEG though, given that Friston (2008) makes a specific claim that the cortical neurons coding prediction error are the large, supragranular pyramidal neurons, thought to make the dominant contribution to the EEG/MEG signal.

Regarding experimental paradigms to test predictive coding, it is important to note that the recent debate about whether expectation of repetition does, on the basis of human fMRI and EEG (e.g., Summerfield, Wyart, Johnen, & de Gardelle, 2011), or does not, on

This work was supported by the UK Medical Research Council (MC_A060_5PR10) and (MC_A060_5PQ50).

the basis of monkey single-cell recording (Kaliukhovich & Vogels, 2011), modulate repetition suppression is actually somewhat parenthetical to predictive coding. This is because the "predictions" manipulated in the Summerfield et al. paradigm are likely to be conscious/strategic (and so may be less prevalent in monkeys). Yet the "predictions" in predictive coding theory are automatic, intrinsic properties of the brain networks that do not necessarily depend on conscious expectation. Thus while the effects of higher-order expectancy are clearly interesting and important (and probably generated by prefrontal regions that act on the ventral stream), the lack of such expectancy effects in other paradigms (Kaliukhovich & Vogels, 2011; Larsson & Smith, 2012) should not be used to reject predictive-coding models.

Another approach used to support predictive coding models of repetition suppression is to examine changes in connectivity between brain regions. Our own work, for example, has used Dynamic Causal Modelling (DCM) of fMRI data to show that repetition of bodies (Ewbank et al., 2011) or faces (Ewbank, Henson, Rowe, Stoyanova, & Calder, in press), at least across different images, modulates backward connections from "higher" regions in fusiform cortex to "lower" regions in extrastriate occipital cortex. Gotts et al. wondered why this modulation by repetition reflected a more positive coupling parameter in the DCM, when according to predictive coding, one might expect a more negative coupling associated with the suppression of prediction error in lower regions by higher regions. Again, however, the precise interpretation is more subtle because we do not know which types of excitatory/inhibitory neurons contribute to the BOLD signal. Moreover, due to high interdependency between parameters in such recurrent DCMs, inference is often more appropriate at the level of model selection rather than model parameters (Rowe, Hughes, Barker, & Owen, 2010). Thus, although we discussed our results in terms of predictive coding, the main conclusion of the Ewbank et al. papers (which were based on model selection) is that repetition suppression is not purely a local phenomenon (such as sharpening or even neuronal fatigue; Grill-Spector, Henson, & Martin, 2006), but also entails interactions between brain regions. This claim is consistent with both predictive coding and synchrony theories.

A further reason why DCM for fMRI may be limited in its ability to distinguish theories like predictive coding and synchrony is that the modulatory inputs (repetition in this case) need to be sustained over several seconds in order to have an appreciable impact on the network dynamics (Henson, Wakeman, Phillips, & Rowe, 2012). This is why we used a blocked design in the Ewbank et al. studies, where the modulation was assumed to operate throughout blocks. As Gotts et al. observe, such designs are undesirable from a behavioral perspective (e.g., encouraging use of conscious expectancies like those discussed above). Randomized designs (e.g., Henson, 2012) are clearly preferable, but in order to test for changes in effective connectivity as defined by dynamic models like DCM, data with higher temporal resolution are needed (e.g., Garrido, Kilner, Stephan, & Friston, 2009). Thus we agree with Gotts et al. that an exciting future direction is to examine connectivity, perhaps via synchrony, between regions using methods like EEG/MEG.

* * *

Repetition accelerates neural dynamics: In defense of facilitation models

Richard N. Henson
MRC Cognition and Brain Sciences Unit, Cambridge, UK
E-mail: rik.henson@mrc-cbu.cam.ac.uk

http://dx.doi.org/10.1080/17588928.2012.689962

Abstract: Gotts, Chow and Martin give an excellent contemporary summary of the neural mechanisms that have been proposed to underlie the effects of stimulus repetition on brain and behavior. Here I comment on their Facilitation mechanism, and provide EEG evidence that repetition can accelerate neural processing.

Gotts et al. (2012) review four types of neural mechanism that might underlie the reduced brain response associated with repetition of a stimulus: Facilitation, Sharpening, Synchrony and Explaining Away. In particular, they make a case for mechanisms based on

This work was supported by the UK Medical Research Council (MC_US_A060_0046).

Synchrony, while questioning the cases for Facilitation and Sharpening. However, it is important to note that these mechanisms are not mutually exclusive. For example, it is possible that predictive coding is a general property of the brain (Friston, 2012; Ewbank & Henson, 2012), and that the associated *explaining away* of stimulus-driven activity is achieved by *synchronous* activity between hierarchical brain regions, such that repetition causes *sharper* (sparser) spatial patterns of activity, and a *facilitation* (acceleration) of the dynamics of that activity. So below, I caution against the premature dismissal of Facilitation.

From a dynamical perspective, the brain's response to an external perturbation (stimulus) is likely to entail a period of higher energy (activity) that lasts several hundred milliseconds until a new, stable state of lower energy is reached (an attractor). As in many recurrent neural network models, this state-change is likely to trigger synaptic change, so as to widen/deepen the basin of attraction. When that stimulus is repeated therefore, there will be a faster settling (stabilization) of the network dynamics, i.e., a shorter duration of above-baseline neural activity (possibly despite negligible change in the onset of that activity). A shorter duration of neural activity will reduce the magnitude of response recorded by hemodynamic methods like fMRI that integrate over seconds of activity (i.e., cause *repetition suppression*; Henson, 2003).

The tension that Gotts et al. observe between faster behavioral responses (repetition priming) and reduced neural activity does not apply to Facilitation models, because both are the consequence of accelerated neural processing. However Facilitation is not really a mechanism, but rather a description of what happens at the neural level (to produce a reduced response at the hemodynamic level). Nonetheless, it remains distinct from the other mechanisms considered, in that Facilitation could occur with, or without, any concomitant change in Sharpness, Synchrony or Explaining Away.

Gotts et al. dismiss Facilitation models because of a lack of direct electrophysiological evidence. However, such evidence may be abundant in human EEG/MEG studies; just rarely conceptualized as such. Figure 1, for example, shows that the ERP to the repeated presentation of a face can be parsimoniously described as an accelerated version of the ERP to its initial presentation. Though such extracranial ERPs could originate from multiple neural sources (as Gotts et al. warn), it is unclear how this multiple determinacy would produce such a simple

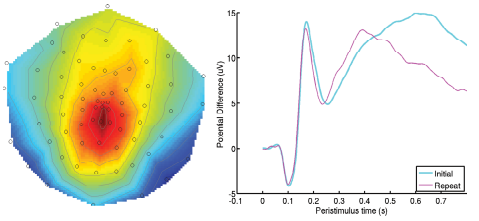

Figure 1. EEG data recorded from 70 electrodes (Henson, Wakeman, LItvak, & Friston, 2011) show that the ERP to the immediate (after ~3 seconds) yet unpredictable repetition of a face (magenta) is accelerated relative to that for its initial presentation (cyan). The topography (left; nose upward) and timecourse (right) are the first, dominant spatial and temporal components of a singular-value decomposition (SVD) of the (temporally-concatenated) trial-averaged ERPs, averaged over 18 participants. The scaling (zoom) of the time-axis for the temporal component of the initial presentation was systematically varied to minimize the RMSE between it and that for the repeat presentation. The mean acceleration factor was 92%, which was significantly less than 100% across participants, $t(17) = 3.18$, $p < .01$ (two-tailed).

temporal scaling. Since EEG/MEG data relate directly to LFPs from a population of neurons, the puzzle, as Gotts et al. observe, is why this apparent acceleration has not been observed at the level of spiking rates.

Looking forward, I fully support Gotts et al.'s proposals for future research, which can be divided into better data and better modeling. In addition to concurrent recording of local field and action potentials, to address the puzzle above, better data will come from recording from neurons in different layers of cortex, to relate to specific predictive coding models (e.g., Friston, 2008), and to establish which of these neurons contribute to M/EEG and fMRI signals. Data with high temporal resolution (such as M/EEG) is critical to test for dynamical changes over the few hundred milliseconds post-stimulus onset, for example, in terms of within- and/or across-frequency changes in power and/or phase of oscillations. In terms of better models, computational instantiations of some the above ideas are vital (e.g., the important work of Gotts, 2003), to relate both spatial (e.g., sharpness) and temporal (e.g., synchrony) dimensions of data, and to relate single-neuron data to population responses like fMRI; particularly, as noted above, if those ideas are not mutually exclusive and all turn out to reflect aspects of reality.

* * *

Learning-induced sharpening of neuronal tuning and adaptation: Not "mixed"

Maximilian Riesenhuber
Laboratory for Computational Cognitive Neuroscience, Department of Neuroscience, Georgetown University Medical Center, Washington, USA
E-mail: mr287@georgetown.edu

http://dx.doi.org/10.1080/17588928.2012.689970

Abstract: Gotts et al. present an attractive model of how priming can arise from neuronal adaptation effects. Their very satisfying account helps to demystify adaptation effects. In fact, adaptation effects are even less mysterious than portrayed: While Gotts et al. state that "fMRI studies in humans that have attempted to evaluate sharpening of visual object representations with experience have … generated mixed results", referring to fMRI adaptation (fMRI-A) studies by our group and others, the results described in the cited papers are in fact entirely compatible, further establishing the usefulness of fMRI-A to probe neuronal tuning in humans.

To review, Weiner, Sayres, Vinberg and Grill-Spector (2010) investigated fMRI adaptation effects across the brain for different object classes, with subjects viewing images belonging to categories such as flowers, cars, or guitars. For short lag adaptation paradigms (where prime and target immediately follow each other, with no intervening images), they report that adaptation consisted of a scaling of fMRI responses, i.e., a response reduction that was proportional to the initial response, in line with neurophysiological results in non-human primates (De Baene & Vogels, 2010; McMahon & Olson, 2007). This response scaling effect of adaptation is what is exploited by studies using fMRI rapid adaptation techniques (fMRI-RA) to estimate neuronal tuning specificity: In fMRI-RA, the response to a pair of stimuli presented in rapid succession is measured for pairs similar or different in a specific perceptual aspect (e.g., viewpoint or shape), and the difference between the two response amplitudes is interpreted as an index of stimulus representational dissimilarity at the neuronal level. For instance, we previously used fMRI-RA to test our model of face neurons in the fusiform face area, the FFA (Jiang et al., 2006). Specifically, the model predicted that viewing a particular face should be associated with a sparse activation pattern over face neurons sharply tuned to faces similar to the currently viewed face, with little activation of neurons sharply tuned to dissimilar faces. Thus, in an fMRI-RA paradigm that varies the similarity between two face images shown successively in a single trial, the BOLD-contrast signal in the FFA for increasing within-pair face dissimilarity should progressively increase as the two faces activate increasingly disjoint subpopulations of neurons (causing increasingly lower amounts of neuronal adaptation), up to where the two images activate different subpopulations of neurons, at which point the response level should asymptote and not increase for further increases in face dissimilarity. Correspondingly, at the behavioral level, this model predicts that the ability to discriminate specific faces is directly related to the dissimilarity of the neuronal activation patterns associated with these faces in the FFA and thus the response level in the adaptation paradigm. These predictions were confirmed experimentally (Jiang et al., 2006).

This ability to probe neuronal selectivity with fMRI-RA opens the door to using adaptation effects to measure how perceptual and task learning *change* neuronal selectivity. A common prediction (with ample support from animal studies, as pointed out by Gotts et al.) of computational models is that perceptual learning involves sharpening of neuronal stimulus representations. The goal of Jiang et al. (2007) was to use fMRI-RA to test the core prediction that perceptual learning also sharpens neuronal stimulus representations in humans. To this end, we trained subjects to categorize morphed car shapes (Jiang et al., 2007), and probed the selectivity of car-selective stimulus representations using fMRI-RA before and after training. We reasoned that if categorization training leads to sharpened neuronal selectivity to car images, then the overlap of neuronal activations caused by two sequentially presented car images differing by a fixed amount of shape change would decrease following training, resulting in an increase of BOLD-contrast response in brain regions selective for the car shapes (independently identified in lateral occipital cortex, the LOC). Indeed, we found that categorization training induced a significant release from adaptation for small shape changes in LOC irrespective of category membership, compatible with the sharpening of a representation coding for physical appearance (while an area in lateral prefrontal cortex showed sensitivity post-training to explicit changes in category membership, as predicted by a computational model).

Supported by NSF grants 0749986 and 1026934 and NIH grant HD067884.

When applying fMRI-RA in this way, i.e., to probe changes in neuronal selectivity induced by intervening task training, it would be highly problematic if probing the stimulus representation with fMRI-RA itself affected the selectivity of the underlying representation (e.g., by sharpening of neuronal tuning), which would raise the question of whether the changes observed in the adaptation paradigm were due to training or were due to probing with fMRI-RA. However, in the same study (Jiang et al., 2007), we conducted a control experiment that established that repeated fMRI-RA without intervening training did *not* cause a change in release from adaptation. Similarly, a recent monkey electrophysiology study showed that stimulus repetition did not affect neuronal shape selectivity (De Baene & Vogels, 2010). Nevertheless, special care needs to be taken when designing fMRI-A paradigms to control factors such as differences in attention or task difficulty for particular stimuli or trials that might cause modulations of stimulus responses independent of adaptation effects and could thus complicate the interpretation of the experimental results (see also Krekelberg, Boynton, & van Wezel, 2006).

Thus, in summary, (Weiner et al., 2010) and (Jiang et al., 2007) did not produce mixed results but rather paint a consistent picture, that adaptation techniques, when used carefully, can be used as a powerful tool to finely probe the selectivity of neuronal tuning with fMRI .

* * *

Synchrony upon repetition: One or multiple neural mechanisms?

Kevin S. Weiner[1] and Kalanit Grill-Spector[1,2]
[1]Department of Psychology, Stanford University, Stanford, USA
[2]Neuroscience Institute, Stanford University, Stanford, USA
E-mail: kweiner@stanford.edu

http://dx.doi.org/10.1080/17588928.2012.689973

Abstract: A central goal of cognitive neuroscience is to understand the relationship between repetition suppression (RS) and priming. Gotts and colleagues propose a new model examining this relationship where stimulus repetition produces increased neural synchronization, thus increasing the efficiency of neural responses and potentially explaining the characterizing features of both RS and priming. While synchrony is an appealing new model, we suggest that further constraints are necessary to account for qualitatively different types of RS and priming yet to be considered by the present implementation.

This work was supported by NSF BCS grant 0920865.

Gotts et al. propose a new model to explain a puzzling enigma in cognitive neuroscience: How does stimulus repetition generate reduced neural responses (repetition suppression; RS) as well as faster and more accurate behavioral responses (priming)? The authors suggest that along with the commonly reported RS, stimulus repetition also increases neural synchronization locally within neurons of a brain region, as well as globally among regions in a task-engaged cortical network. In turn, this increased synchrony leads to increased precision of neural responses by shortening the time it takes downstream neurons to reach firing threshold, which then expedites behavioral responses. Two new ideas are appealing about the synchrony model. First, it suggests an unconsidered direction where joint coupling of neural responses may be the key link between RS and priming. Second, synchrony predicts that in order to understand the neural mechanisms of RS and priming, researchers need to consider not only the firing rate or overall responses of a neural population, but also the coherence among neural firing patterns.

Though both priming and RS are widespread phenomena, there are qualitatively different types of each yet to be considered by the present implementation of the synchrony model. Researchers have identified dissociable forms of priming linked with RS in specific regions either cortically distant from one another (e.g., in frontal and temporal cortex; Schacter, Dobbins, & Schnyer, 2004; Race, Shanker, & Wagner, 2009) or cortically proximate (e.g., within left lateral frontal cortex; Race et al., 2009). Further, though the authors use evidence of RS from striate and extrastriate regions across species in support of the synchrony model, RS dynamics are not cortically uniform, but are region-specific and time scale dependent. For instance, different types of RS matriculate in early and high-level visual regions: RS occurs after a single presentation of a stimulus and is sustained across many intervening stimuli in high-level ventral temporal cortex (VTC), but not in primary visual cortex (V1; Sayres and Grill-Spector, 2006). Indeed, in order to induce RS in V1, one needs continual stimulus repetitions for an

extended time period and to "top-it-up" with later repetitions in order to extend its effects even over a handful of intervening stimuli (Boynton and Finney, 2003; Fang, Murray, Kersten, & He, 2005). Additionally, even within VTC, medial and lateral aspects display differential RS effects across time scales: RS in lateral VTC manifests as scaling of neural responses across immediate and long-lagged repetitions, whereas RS in medial VTC exhibits scaling for immediate repetitions and sharpening for long-lagged repetitions (Weiner et al., 2010). We give examples from the visual system, but these concerns of regional specificity and time scale dependency are general concerns of RS across cortical systems and species (van Turennout, Ellmore, & Martin, 2000; Schacter et al., 2004; Verhoef, Kayaert, Franko, Vangeneugden, & Vogels, 2008; Race et al., 2009). As timing parameters within and across task-engaged regions are central to the authors' idea of synchronization, it is essential to consider at least two alternatives that may account for the regional specificity of RS. One possibility is that synchrony can generate many types of RS for different ranges and combinations of model parameters (e.g., synaptic depression and spike-frequency adaptation). Alternatively, differential neural mechanisms underlie differential RS effects across regions and time scales where synchrony alone cannot explain a multitude of RS effects. Simulating interactions among model parameters will be a useful stepping-stone for testing the feasibility of these alternative hypotheses.

Gotts et al. further propose that increased synchrony of neural responses with repetition occurs both locally within a region and globally across regions. However, local and inter-areal synchrony are fundamentally different and are associated with different types of neural signatures. Long-range coupling is associated with local field potential (LFP) power in lower frequencies (alpha range, 8–20 Hz), whereas local spiking activity is associated with LFP power in higher frequencies (high gamma range, > 60Hz). As decreased local firing is the defining feature of RS, intuitively then, high gamma power tends to decrease with repetition (De Baene and Vogels, 2010). On the other hand, additional findings show increases in alpha power with repetition (Ghuman, Bar, Dobbins, & Schnyer, 2008; Gilbert, Gotts, Carver, & Martin, 2010), suggesting increased inter-areal synchrony of neural responses. These data suggest an anticorrelated relationship between local and inter-areal synchrony as a function of repetition, which is at odds with the present description of the model. Thus, we suggest that a productive future direction will be to make explicit predictions about what aspects of the model relate to local synchrony vs. inter-areal synchrony, and to test these hypotheses empirically by examining coherence in spiking activity and LFPs.

In sum, the synchrony model suggests important new directions for understanding RS, priming, and their relationship. Future consideration of computational factors accounting for the multitude of RS and priming effects, as well as their effects on local and inter-areal synchrony, will determine either the ubiquity or specificity of the synchrony model of repetition.

* * *

All in the timing: Priming, repetition suppression, and synchrony

David B. T. McMahon

Section on Cognitive Neurophysiology and Imaging, Laboratory of Neuropsychology, National Institute of Mental Health, National Institutes of Health, Bethesda, USA

E-mail: mcmahond@mail.nih.gov

http://dx.doi.org/10.1080/17588928.2012.689969

Abstract: The terms "priming" and "repetition suppression" are commonly used to refer to phenomena occurring on time scales that can differ by several orders of magnitude, ranging from seconds to days or even years. The models discussed by Gotts et al. provide a thought-provoking theoretical framework for relating neuronal and behavioral plasticity. I argue that whereas both the sharpening and the Bayesian models may mediate the gradual acquisition of perceptual expertise, they are unlikely to account for more rapid behavioral changes. The synchrony model, however, could potentially operate within the timing constraints imposed by the fastest forms of repetition priming.

The author is supported by the NIMH Intramural Research Program.

With regard to the sharpening hypothesis, it is noteworthy that the evidence for enhanced selectivity in monkey inferotemporal (IT) cortex comes from prolonged training periods across many days, if not weeks (Baker, Behrmann, & Olson, 2002; Freedman, Riesenhuber, Poggio, & Miller, 2006; De Baene, Ons, Wagemans, & Vogels, 2008). By contrast, studies of visual response plasticity that were expressed over time scales relevant to the fastest priming effects found the opposite of sharpening, namely scaling reductions of firing rates (Li, Miller, & Desimone, 1993; McMahon and Olson, 2007; De Baene and Vogels, 2010). These findings support the idea that gradually acquired perceptual expertise could be mediated by sharpening, but some other mechanism is needed to explain more rapidly induced behavioral changes such as priming.

According to the Bayesian model, perceptual learning is mediated by priors represented in high-level cortical areas that become more efficient at predicting representations in lower-level sensory areas. Consistent with this notion, recent physiological evidence shows that IT visual responses are reduced when the appearance of a stimulus is reliably predicted by an antecedent stimulus, but this effect is only evident after many days of training (Meyer and Olson, 2011). A similar effect is not observed when prior expectation is based on experience with predictable stimulus pairings during a single block within a recording session (Kaliukhovich and Vogels, 2011). These two studies together provide an upper and lower bound on the time scale over with a mechanism of Bayesian "explaining away" could be instantiated in the brain.

An appeal of the synchrony model is that it could operate on a fast enough time scale to account for priming. In monkeys trained to report a perceptual decision with eye movements (McMahon and Olson, 2007), the observed distribution of saccadic reaction times fell between 220 and 490ms (Figure 2A, inset). In the same study, repetition suppression was evident in visual responses of neurons in IT cortex at a latency of 150ms (Figure 2A). These results constrain the time range within which synchrony (or any neural mechanism of priming) would need to operate: Certainly some time after the visual response, perhaps after the repetition suppression, but before the behavioral responses.

How do these timing constraints compare with the candidate mechanisms proposed for the synchrony model? Gotts et al. focus on examples of reduced spiking responses that were accompanied by low-frequency (4–8 Hz) oscillations (Freedman,

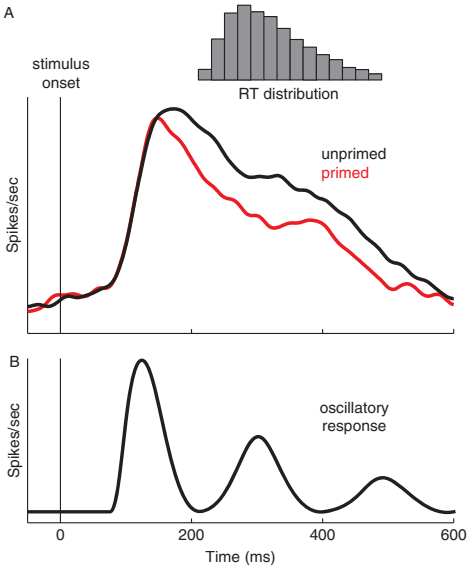

Figure 2. Timing constraints on neural mechanisms of priming. **A**, Spiking responses to primed and unprimed visual stimuli recorded from single units in IT cortex. Inset, distribution of saccadic reaction times irrespective of priming (2.5% — 97.5% percentile range, based on McMahon and Olson, 2007). **B**. Schematic of oscillatory spiking response evoked from IT neurons (based on Rollenhagen and Olson, 2005; Mirpour and Esteky, 2009).

Riesenhuber, Poggio, & Miller, 2006, Anderson, Mruczek, Kawasaki, & Sheinberg, 2008), a schematic of which is shown in Figure 2B.

Strong rhythmic activity in this range is prevalent in IT cortex (Rollenhagen and Olson, 2005; Mirpour and Esteky, 2009). A recent study further showed that, in monkeys performing a delayed match to sample task, low-frequency oscillations recorded simultaneously in V4 and prefrontal cortex became more coherent during the delay period (Liebe, Hoerzer, Logothetis, & Rainer, 2012). This result lends plausibility to the proposal by Gotts et al. that modulation of low-frequency oscillations could act as a mechanism for enhanced long-range coupling between cortical areas. The relative time scales of behavioral priming, repetition suppression, and rhythmic spiking illustrated here suggest a behavioral approach for testing of the synchrony model: If enhanced neuronal synchrony leads to faster reaction times, then it should be possible to manipulate behavioral responses using stimuli that

match (or interfere with) the resonance frequency of the oscillation in the spiking responses.

* * *

Focusing on the frontal cortex

Aidan J. Horner[1,2]
[1] UCL Institute of Cognitive Neuroscience, London, UK
[2] UCL Institute of Neurology, London, UK
E-mail: a.horner@ucl.ac.uk

http://dx.doi.org/10.1080/17588928.2012.689959

Abstract: Gotts et al. provide a timely review of the major neural models of repetition suppression (RS) and priming. They justifiably call on researchers to focus their attention on the extent to which these phenomena can be explained by changes in synchrony between cortical regions. They are relatively agnostic as to which regions may be critical to RS and priming. Here I argue we should devote more attention to the role of frontal regions, and suggest that there is a need to engage with more cognitive accounts of priming in order to develop a comprehensive neurocognitive account of priming and RS.

Gotts et al. present four neural models designed to capture the complex relationship between repetition suppression (RS) and behavioral priming (henceforth referred to as priming). They support the idea that synchrony, temporally correlated neural firing that allows for increased efficiency of communication between spatially distinct cortical regions, underlies this relationship. I strongly support Gotts et al.'s call for more research focusing on the interaction between cortical regions following stimulus repetition. Their discussion, however, was relatively agnostic concerning the cortical regions we should focus on in order to understand such interactions. I would argue that the prefrontal cortex, more specifically the inferior frontal gyrus (IFG), and its interactions with more posterior perceptual regions, should be the focus of our attention.

Firstly, the IFG has been perhaps the only region that has consistently demonstrated RS across multiple stimulus types including visual objects (e.g., Koutstaal et al., 2001), faces (e.g., Henson et al., 2003), and written (e.g., Barton, Fox, Sekunova, & Iaria, 2010) and spoken (e.g., Gagnepain et al., 2008) words. Secondly, the IFG has consistently been shown to correlate with priming (e.g., Dobbins, Schnyer, Verfaellie, & Schacter, 2004). Thirdly, transcranial magnetic stimulation to the IFG has been shown to disrupt priming and RS (Wig, Grafton, Demos, & Kelley, 2005). Finally, using magnetoencephalography, visual object repetition has been shown to increase synchrony between frontal and occipitotemporal regions (Ghuman, Bar, Dobbins, & Schnyer, 2008).

It seems the IFG plays a critical and causal role in the production of priming and is therefore a key region on which to focus our attention. Two questions emerge from this discussion: (1) Why has the IFG been relatively overlooked despite this evidence and (2) What role does the IFG play in priming and RS? With regard to the former question, the first possible reason is due to the legacy of particular cognitive accounts of priming, which were largely adopted by the neuroimaging community, that suggest priming relates to the modification of perceptual (and conceptual) representations (Henson, 2003). The second reason is that RS, as measured by fMRI, is often maximal in occipitotemporal perceptual regions. Thus, regions known to be involved in perceptual processing, such as lateral occipital and fusiform regions in the case of object recognition, were (and still are) the predominant cortical regions of focus.

What role does the IFG play in priming and RS? In recent years, there has been a resurgence of interest in the idea that bindings between a stimulus (e.g., a visual object) and a response (e.g., a "yes" decision) can facilitate response selection processes (Logan, 1990). Such stimulus-response (S-R) contributions have now been shown to drive RS in frontal regions (Horner & Henson, 2012). Furthermore, S-R learning has been shown to explain a large proportion of priming variance during long-lag visual classification studies (Horner & Henson, 2009). As such, it seems the IFG may play an important role in the selection of task-appropriate responses, possibly integrating information from multiple cortical sources including, though not limited to, posterior perceptual regions. Importantly, given the localization of S-R contributions to frontal regions and the dominant role it plays in priming, it would seem appropriate to focus our efforts on understanding RS in frontal regions, and how this region communicates with more posterior perceptual regions.

Finally, the above discussion serves to highlight the need to embed cognitive theories of priming and RS (e.g., episodic vs. abstractionist accounts) within

models of the neural mechanisms that underlie such effects (e.g., sharpening vs. synchrony). For example, not only do we need to state how RS results in priming but also what information is being learned (i.e., what representations are being encoded/modified) in order for such phenomena to manifest. Each level of account should serve to shape and constrain the other, allowing for a fuller understanding of the neurocognitive mechanisms that give rise to RS and priming.

* * *

Repetition suppression and repetition priming are processing outcomes

Gagan S. Wig
Department of Neurology, Washington University School of Medicine, St Louis, USA
E-mail: gwig@npg.wustl.edu

http://dx.doi.org/10.1080/17588928.2012.689964

Abstract: There is considerable evidence that repetition suppression (RS) is a cortical signature of previous exposure to the environment. In many instances RS in specific brain regions is accompanied by improvements in specific behavioral measures; both observations are outcomes of repeated processing. In understanding the mechanism by which brain changes give rise to behavioral changes, it is important to consider what aspect of the environment a given brain area or set of areas processes, and how this might be expressed behaviorally.

Different structures of the brain engage in different forms of information processing. One way of defining the function of a specific brain structure is to examine its methods of computation in service of learning (e.g., Doya, 1999). There is considerable anatomical, neurophysiological, and theoretical evidence to suggest that the cerebral cortex engages in unsupervised learning to reflect the statistics of the environment by forming efficient cortical representations of the organism's experiences. Moreover, different areas of the cerebral cortex learn the statistics of distinct features of the environment, and RS may be a neural signature of this statistical learning. Identifying a mechanism by which RS produces the behavioral changes that typically accompany repeated processing (i.e., repetition priming) necessitates careful consideration of how RS reflects the processing outcomes of a specific area or set of areas, and what the appropriate behavioral metric for this processing outcome may be.

Drawing from empirical and theoretical sources, Gotts and colleagues describe four potential mechanisms for how RS may result in repetition priming. The authors provide clear and testable predictions for evaluating how these mechanisms may link RS to behavioral facilitation. Their article will be a key source of reference in moving forward with this important endeavor.

In studying the mechanism by which RS may result in repetition priming, it is imperative to remember that both RS and repetition priming are independent measurements of the processing outcomes of repeated experience. It is not necessary that observations of RS in a collection of areas be clearly linked to changes in the observed behavior, or any clear or measureable behavioral measures for that matter. If RS is a neural signature of cortical learning, it is likely that RS observed in different areas is a consequence of different processing outcomes. As such, different areas may reveal that they've learned the statistics of the environment via distinct behavioral measures.

As an example, speeded response times following repeated semantic classification of visually responsive objects is typically accompanied by RS within numerous brain areas including regions of the inferior frontal gyrus, inferior temporal lobes, and occipital cortex. While the behavioral improvements may be a product of increased synchrony between a subset of regions that are involved in decision processes (e.g., between areas within the frontal and temporal cortex; see Ghuman, Bar, Dobbins, & Schnyer, 2008), other regions exhibiting RS need not be directly linked to the measured classification-time improvements.

RS can be eliminated or diminished in certain regions using transient disruption (i.e., TMS; Wig, Grafton, Demos, & Kelley, 2005) or changes in stimulus-to-decision mapping (e.g., Dobbins, Schnyer, Verfaellie, & Schacter, 2004; Horner & Henson, 2008; Wig, Buckner, & Schacter, 2009). The disruption of RS is also accompanied by reductions in the observed behavioral improvements (e.g., response time during semantic classification). However, despite these region-specific reductions in RS, RS is still prominent in other regions that are likely involved in task performance (e.g., regions of the visual cortex—see Figure 4 of Wig

et al., 2005). Does this mean that the neural changes in the visual cortex are "epiphenomenal", unrelated to any form of learning, or mediated by a distinct mechanism? Not necessarily: An alternate explanation is that the visual cortex has learned some statistics related to the experimental paradigm and that this has resulted in neural changes reflecting this learning (i.e., RS), but that an appropriate behavioral marker of the statistical learning in these regions has not been sufficiently measured.

In understanding how RS may lead to behavioral facilitation, and evaluating one mechanism for this relationship over the other, we need to carefully identify the appropriate behavioral metrics that may signify cortical learning for the specific area or set of areas that are the focus of investigation. Investigations of repetition priming have a long and rich history and have described a variety of behavioral changes that reveal past exposure to the environment (e.g., Roediger, 1990; Schacter, 1987). RS may be a consequence of the mechanism by which the brain indexes past exposure, and it will be essential to identify appropriate measures to quantify the ways in which the brain and its substructures might retain and express information related to previous experience.

* * *

Task, time and context as potential mediators of repetition priming effects

Benjamin J. Dyson[1] and Claude Alain[2]
[1] Department of Psychology, Ryerson University, Toronto, Canada
[2] Rotman Research Institute, Toronto, Canada
E-mail: ben.dyson@psych.ryerson.ca

http://dx.doi.org/10.1080/17588928.2012.689961

Abstract: In apparent conflict with the synchronicity model, we consider three types of evidence from the auditory literature (negative priming, perceptual learning, sensory gating) that reveal stimulus repetition can be associated with decreased rather than increased early evoked responses. The difficulty with consolidating a wide range of tasks in adjudicating between theories of repetition priming might be because the potentially critical roles of task, time and context are neglected.

Gotts, Chow and Martin provide a stimulating review regarding one of cognitive neuroscience's most pervasive double-takes: Processing facilitation at a behavioral level expressed as activation suppression at a neural level. Attempting to consolidate studies on perception, attention and memory across a number of different species inevitably leads to spatially and temporally diffuse patterns of activation, which threaten to cloud the evaluation of some already relatively complex hypotheses regarding repetition priming. Limiting our discussion to the interpretation of event-related potentials, Gotts et al. appeal to the observation of repeated stimuli with "larger low-frequency fluctuations in the LFPs (~ 5–10 Hz) that were phase-locked to the stimulus onset (i.e., larger evoked responses)" in support of the synchronicity model, citing novel versus familiar (or trained) image exposure paradigms in monkeys. We will discuss additional evidence from the human auditory evoked response literature and consider the potentially critical roles of task, time and context.

The negative priming paradigm provides one example of how stimulus repetition interacts with task demands. Typically, the requirement for participants to respond to a target stimulus that was designated as a distractor stimulus on the previous trial leads to less efficient responding. When evoked potentials associated with auditory negative priming are considered, negative priming trials were associated with *reduced* N1 amplitude, a negative deflection at about 100ms post-stimulus, relative to standard control trials in which neither the target nor distractor on the previous trials was repeated (Mayr, Niedeggen, Buchner, & Pietrowks, 2003). Similar reductions in N1 amplitude were also observed in repetition control trials, where the target on the previous trial became the distractor on the current trial. In this case, reduced N1 amplitude to repeated stimuli appear to counter the claims of the synchronicity model and suggest that task and/or response demands may be critical in determining the direction of the repetition priming effect.

Studies into the neural correlates of perceptual learning also offer insights into how the brain responds to stimulus repetition over longer periods of time. For instance, learning to identify different speech tokens has been associated with *reductions* in early auditory evoked responses that take place within the first hour of training (N1 and P2, a positive deflection at about

180ms post-stimulus; Alain, Campeanu, & Tremblay, 2009; Ben-David, Campeanu, Tremblay, & Alain, 2011). These amplitude reductions were apparent within the same block of trials as well as between blocks of trials within the recording session. These studies raise the concern that stimulus spacing may also modulate the direction of the repetition priming effect (see Gotts et al. discussion of achieving uncontaminated BOLD response). The concern that longer temporal intervals may decrease the likelihood of facilitation with respect to repeated stimuli is supported by the data on inhibition of return (IOR). IOR is a temporal constraint of repetition priming in that the behavioral processing facilitation observed at short intervals reverses to inhibition at longer intervals ("longer" in the context of auditory processing can be as short as 750ms; Mondor, Breau, & Milliken, 1998).

A final example of reduced evoked responses to stimulus repetition is provided by the sensory gating literature. Here, the amplitude of a positive-going deflection 50ms after sound onset (labeled P1 or P50) is typically *reduced* for the second presentation of an identical sound (e.g., Kisley, Noecker, & Guinther, 2004). Importantly, the presence and absence of P1 attenuation is used to adjudicate between non-schizophrenic and schizophrenic samples, respectively, and so the interpretation of neural activity at these early stages has clear clinical implications. What is critical to note though is in sensory gating paradigms, participants tend to be exposed to sounds under passive listening conditions. Therefore, the frequency of repetition and change in the environment may be a third influence on the direction of the repetition priming effect (see current discussion of Summerfield et al., 2008, 2011) even in the absence of task. We argue that a consideration of the perceptual and cognitive demands within repetition priming paradigms is required to disambiguate the currently disparate literatures.

* * *

 http://dx.doi.org/10.1080/17588928.2012.697054

Reply to Commentaries

Repetition priming and repetition suppression: Multiple mechanisms in need of testing

Stephen J. Gotts[1], Carson C. Chow[2], and Alex Martin[1]

[1]Section on Cognitive Neuropsychology, Laboratory of Brain and Cognition, National Institute of Mental Health (NIMH), National Institutes of Health, Bethesda, MD 20892, USA
[2]Laboratory of Biological Modeling, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health, Bethesda, MD 20892, USA

In our Discussion Paper, we reviewed four theoretical proposals that have the potential to link the neural and behavioral phenomena of Repetition Suppression and Repetition Priming. We argued that among these proposals, the Synchrony and Bayesian Explaining Away models appear to be the most promising in addressing existing data, and we articulated a series of predictions to distinguish between them. The commentaries have helped to clarify some of these predictions, have highlighted additional evidence supporting the Facilitation and Sharpening models, and have emphasized dissociations by repetition lag and brain location. Our reply addresses these issues in turn, and we argue that progress will require the testing of Repetition Suppression, changes in neural tuning, and changes in synchronization throughout the brain and over a variety of lags and task contexts.

Keywords: Repetition priming; Repetition suppression; Synchrony; Prediction; Bayesian.

BAYESIAN EXPLAINING AWAY MODEL

Both Friston's and Henson's commentaries make the point that the Facilitation, Sharpening, Synchrony, and Bayesian Explaining Away models are not mutually exclusive. This is a point that we failed to clarify and that we fully endorse. The ideas are certainly mechanistically distinct, but they could all coexist with one another simultaneously, perhaps making separate contributions in explaining repetition priming. Efforts should be focused on assessing the contribution of any/all (none?) of these in a given experimental situation.

Friston's commentary clarifies his positions on the experimental predictions that we articulated. He re-emphasizes his commitment to anti-symmetrical bottom-up and top-down interactions, while he is less enthusiastic about the relative timing predictions. Between-region anti-symmetry is the central claim of this model. It predicts that top-down causal interactions should be more negative after stimulus repetition and that repetition suppression in lower-level areas should be due to feedback from higher-level areas. Friston also stresses the presence of repetition-dependent changes in the feed-forward direction with stimulus repetition,

Correspondence should be addressed to: Stephen J. Gotts, Section on Cognitive Neuropsychology, Laboratory of Brain and Cognition, National Institute of Mental Health (NIMH), National Institutes of Health, Bethesda, MD 20892, USA. E-mail: gottss@mail.nih.gov

We would like to thank the authors for their commentaries and excellent feedback on our Discussion Paper. A number of important clarifications and issues have been raised, to which we provide some brief responses.

The preparation of this paper was supported by the National Institute of Mental Health, NIH, Division of Intramural Research.

although with an inverse valence to the feedback effects (implementing a negative feedback loop). We view these clarifications as quite reasonable but differ with Friston on other aspects of his argument. Friston claims that near-optimal perceptual inference lends support to a Bayesian brain hypothesis in which top-down/bottom-up interactions are anti-symmetrical. We believe that it is difficult in principle and practice to distinguish between near-optimal and satisfactory inference given a set of stimuli to be identified and tasks to be performed. Many neural network models demonstrate good performance over a range of learning problems. For example, the Boltzmann machine (e.g., Ackley, Hinton, & Sejnowski, 1985) utilizes a "contrastive" Hebbian algorithm to modify synaptic strengths as the model is exposed to a set of patterns to be associated. The learning algorithm, often heralded for its "biologically plausibility" (e.g., O'Reilly, 1998), leads this model to improve gradually with experience, develop similarity-based internal representations, and perform "linearly inseparable" mappings such as the XOR problem (e.g., Minsky & Papert, 1969). It does all of this while developing *symmetrical* weights between units in higher- and lower-level pools of units. Influential models such as Adaptive Resonance Theory (e.g., Grossberg, 1976), the Interactive Activation Model (McClelland & Rumelhart, 1981), and the Biased Competition Model (Desimone & Duncan, 1995) all predict a symmetrical coding scheme. These models exploit the flexible advantages of top-down, selective excitation in domains ranging from perception to working memory, visual attention/search, and imagery. It will be interesting to see if the Bayesian brain hypothesis can be extended into these domains using a more anti-symmetrical scheme. We would also note that attempts to test the anti-symmetrical property of Mumford's (1992) Bayesian theory in single-cell recordings with monkeys have found support for feedback excitation rather than feedback inhibition (e.g., Lee & Mumford, 2003). This is not necessarily problematic for Friston's proposal, because the cells encoding the conditional expectation of perceptual causes are distinct from those encoding prediction error. Nevertheless, we do not believe that it is self-evident that the brain behaves in its details as a Bayesian neural network model, at least one that relies on anti-symmetrical coupling in the feed-forward versus feedback directions.

Ewbank and Henson appear to take issue with our use of the label "Explaining Away" when referring to Friston's Bayesian model, preferring instead "Predictive Coding". Our rationale was simply to use a label that better distinguished the anti-symmetrical property in this model from the variety of models that utilize "prediction" in very different ways (e.g., Elman nets, Temporal Difference learning, forward models, etc.). Ewbank and Henson emphasize the difficulty in testing subtle predictions about brain connectivity using fMRI methods when the separate contributions of different cell types to the BOLD signal are unknown. We certainly agree that local estimates of the BOLD response in a given voxel will reflect an unknown mixture of various influences (a small fraction of which are neural). However, given the importance of the anti-symmetrical property to the Bayesian model articulated above, we think that it would be unwise to dispatch with this prediction prematurely. Causal modeling approaches that are capable of assessing directional influences between anatomically connected cortical regions (e.g., DCM, Grainger, etc.) should detect net inhibitory coupling in the feedback direction—even when local activity represents an average over different cell types that are present in unknown proportions. If the feedback is net excitatory, what would serve as the basis of repetition suppression? If the problem is the ability of causal modeling approaches to infer directional influences appropriately among interrelated variables, then this problem will apply in a similar manner to the analyses of experiments using alternative methods such as EEG/MEG (e.g., Kiebel, Garrido, Moran, & Friston, 2008). However, we agree that EEG/MEG studies of inter-areal interactions constitute a promising direction for future research.

FACILITATION AND SHARPENING MODELS: THE SHORT AND LONG OF IT

In his separate commentary, Henson makes the case that it is too soon to dismiss the Facilitation model. While he admits that supporting evidence from single-cell recordings has been lacking, he raises the possibility that accelerated neural responses may be commonplace in EEG/MEG. We concur with him about the basic puzzle: How is it that electrical/magnetic field data can become decoupled from spike data? This decoupling extends even to the basic latency of stimulus-evoked responses in microelectrode recordings from occipital areas in animals (firing-rate latencies ranging from 30–50ms, whereas field measurements often show onsets closer to 70–100ms). Our best guess for a resolution is that it involves some form of field cancellation of the earliest responses. In any case, accelerated responses at the single-cell level should be obtainable if the Facilitation model is to hold. Having said that, a very recent study (since the submission of our paper) has provided some more direct support for the Facilitation

model, as well as the Sharpening model, in recordings from monkey inferior temporal cortex (Woloszyn & Sheinberg, 2012). This study involved an extensive training period of several months (like other studies providing support for Sharpening), but it still suggests that Facilitation may apply in some cases. We are therefore happy to concede the point to Henson that it is too early to dismiss the Facilitation model.

The Riesenhuber, Weiner and Grill-Spector, and McMahon commentaries all mention the issue of how repetition lag (short versus long) relates to the observation of proportional scaling versus Sharpening. Riesenhuber makes the case that evidence on long-lag repetitions and Sharpening is not mixed but paints a consistent picture, with proportional scaling effects limited to lags typically involved in fMRI rapid adaptation paradigms (repetitions separated by a few seconds). We agree that results from experiments employing very long lags (and/or practice durations) versus very short lags have been reliably associated with Sharpening and scaling, respectively (see also McMahon's commentary). However, results for lags of an intermediate range (minutes or longer within a single testing session) do not fit cleanly into this picture. For example, Li et al. (1993) showed independent effects of short- and long-lag repetitions on single-cell firing rates in monkey inferior temporal cortex, with proportional scaling observed for long-lag repetitions ($\sim$ tens of minutes). As noted by Weiner and Grill-Spector, Weiner et al. (2010) found results in human fMRI for long lags that were consistent with proportional scaling in all but one of the regions that they examined (medial ventral temporal cortex). Given that these more intermediate lags are the ones involved in most repetition priming studies, the evidence supporting the involvement of Sharpening in repetition priming does indeed appear to be mixed. Even if we were to grant a larger role to Sharpening at these lags, additional assumptions would still be required to explain Repetition Priming. We concur with McMahon that the Synchrony model is well situated to explain priming at the shorter lags that tend to produce scaling, and it may participate at longer lags (and/or practice durations) as well.

DIFFERENT LOCATIONS DO NOT NECESSARILY IMPLY DIFFERENT MECHANISMS

The Weiner and Grill-Spector, Horner, and Wig commentaries all highlight the fact that studies of Repetition Suppression often report findings that vary by brain location. Weiner and Grill-Spector note the challenges facing the Synchrony model in explaining the region- and lag-dependent nature of Repetition Suppression in occipital and temporal brain regions. While no model can currently explain this range of data, we agree that this should be the goal. We would note that while synchrony is a mechanism at one level of description, it is also an emergent phenomenon with multiple possible underlying mechanisms that can apply differentially at different lags and potentially in different brain regions (e.g., spike-frequency adaptation and synaptic depression, electrical synapses between interneurons, spike-timing-dependent plasticity, etc.). Our current experimental focus is simply to detect whether synchronization is occurring in the appropriate experimental contexts and whether it is quantitatively related to the magnitude of repetition priming. In his commentary, Horner rightly makes the point that Repetition Suppression is most strongly related to priming in the prefrontal cortex and that this central issue should not be lost in the discussion. Wig counters, appropriately in our view, that just because occipital Repetition Suppression is more weakly related to repetition priming in certain tasks does not imply that it is irrelevant to priming magnitudes in all tasks. Would a task that emphasizes information represented in occipital areas (e.g., fine shape discriminations) yield a stronger association between occipital Repetition Suppression and priming (see also Martin & Gotts, 2005)? More generally, we would argue that Repetition Suppression effects that are dissociable by brain region or task do not necessarily imply qualitatively distinct lower-level mechanisms. Future experiments will need to clarify the region- and lag-dependence of Repetition Suppression, changes in neural tuning properties, as well as changes in Synchrony. One issue raised by Weiner and Grill-Spector that we would dispute is the exclusive role of high versus low frequency oscillations in local versus long-distance cortical interactions, respectively. Modulations of local synchrony can be in lower frequencies (theta, alpha, beta: E.g., Anderson et al., 2008; Gilbert et al., 2010; Gregoriou, Gotts, & Desimone, 2012) and modulations of long-distance synchrony can be in higher frequencies (gamma: E.g., Buschman & Miller, 2007; Gregoriou et al., 2009a).

NEGATIVE PRIMING AND OTHER PARADIGMS

In the final commentary, Dyson and Alain argue that our proposal has failed to consider the influences of task, time, and context on repetition priming. They cite evidence from EEG/ERP studies in the auditory modality, noting conflicting evidence from negative

priming, perceptual learning of speech tokens, and sensory gating. Some of the differences with our literature review may involve genuine differences between visual and auditory modalities. However, we would reiterate the difficulty of using scalp EEG/ERP measurements to rule out a proposal cast at the level of underlying neural sources. Too many ambiguities are present. Results from paradigms such as negative priming that involve multiple simultaneous stimuli and additional processes (selective attention) may also not be directly comparable to simple identification paradigms with sequentially presented single stimuli.

The Commentaries offered in response to our Discussion Paper highlight the importance and interest in uncovering the mechanism(s) linking Repetition Suppression to one of nature's most powerful learning phenomena, Priming. We again thank our colleagues for their thoughtful and thought-provoking comments on our proposal.

References from the Discussion Paper, the Commentaries, and the Reply

Abbott, L. F., Varela, J. A., Sen, K., & Nelson, S. B. (1997). Synaptic depression and cortical gain control. *Science*, *275*, 220–224.

Ackley, D. H., Hinton, G. E., & Sejnowski, T. J. (1985). A learning algorithm for Boltzmann machines. *Cognitive Science*, *9*, 147–169.

Ahmed, B., Allison, J. D., Douglas, R. J., Martin, K. A. C., & Whitteridge, D. (1998). Estimates of the net excitatory currents evoked by visual stimulation of identified neurons in cat visual cortex. *Cerebral Cortex*, *8*, 462–476.

Aiello, L. C., & Wheeler, P. (1995). The expensive tissue hypothesis: The brain and digestive system in human and primate evolution. *Current Anthropology*, *36*, 199–221.

Alain, C., Campeanu, S., & Tremblay, K. (2009). Changes in sensory evoked responses coincide with rapid improvement in speech identification performance. *Journal of Cognitive Neuroscience*, *22*, 392–403.

Allman, J. M. (1990). The origin of the neocortex. *Seminars in the Neurosciences*, *2*, 257–262.

Anderson, B., Mruczek, R. E., Kawasaki, K., & Sheinberg, D. (2008). Effects of familiarity on neural activity in monkey inferior temporal lobe. *Cerebral Cortex*, *18*, 2540–2552.

Anderson, J. R. (1983). *The architecture of cognition*. Cambridge, MA: Harvard University Press.

Andresen, D. R., Vinberg, J., & Grill-Spector, K. (2009). The representation of object viewpoint in human visual cortex. *NeuroImage*, *45*, 522–536.

Baker, C. I., Behrmann, M., & Olson, C. R. (2002). Impact of learning on representation of parts and wholes in monkey inferotemporal cortex. *Nature Neuroscience*, *5*(11), 1210–1216.

Bandettini, P. A., & Cox, R. W. (2000). Event-related fMRI contrast when using constant interstimulus interval: Theory and experiment. *Magnetic Resonance in Medicine*, *43*, 540–548.

Barton, J. J. S., Fox, C. J., Sekunova, A., & Iaria, G. (2010). Encoding in the visual word form area: An fMRI adaptation study of words versus handwriting. *Journal of Cognitive Neuroscience*, *22*(8), 1649–1661. doi: 10.1162/jocn.2009.21286

Bastos, A. M., Usrey, W. M., Adams, R. A., Mangun, G. R., Fries, P., & Friston, K. J. (under review). Canonical microcircuits for predictive coding.

Bazhenov, M., Stopfer, M., Sejnowski, T. J., & Laurent, G. (2005). Fast odor learning improves reliability of odor responses in the locust antennal lobe. *Neuron*, *46*, 483–492.

Becker, S., Moscovitch, M., Behrmann, M., & Joordens, S. (1997). Long-term semantic priming: A computational account and empirical evidence. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *23*, 1059–1082.

Bedny, M., McGill, M., & Thompson-Schill, S. L. (2008). Semantic adaptation and competition during word comprehension. *Cerebral Cortex*, *18*, 2574–2585.

Ben-David, B. M., Campeanu, S., Tremblay, K., & Alain, C. (2011). Auditory evoked potentials dissociate rapid perceptual learning from task repetition without learning. *Psychophysiology*, *48*, 797–807.

Bentin, S., & Peled, B. S. (1990). The contribution of task-related factors to ERP repetition effects at short and long lags. *Memory & Cognition*, *18*, 359–366.

Bi, G. Q., & Poo, M. M. (1998). Synaptic modifications in cultured hippocampal neurons: Dependence on spike timing, synaptic strength, and postsynaptic cell type. *Journal of Neuroscience*, *18*, 10464–10472.

Biederman, I., & Cooper, E. E. (1991). Evidence for complete translational and reflectional invariance in visual object recognition. *Perception*, *20*, 585–593.

Biederman, I., & Cooper, E. E. (1992). Size invariance in visual object priming. *Journal of Experimental Psychology: Human Perception and Performance*, *18*, 121–133.

Boynton, G. M., & Finney, E. M., (2003). Orientation-specific adaptation in human visual cortex. *Journal of Neuroscience*, *23*, 8781–8787.

Buffalo, E. A., Fries, P., Landman, R., Buschman, T. J., & Desimone, R. (2011). Laminar differences in gamma and alpha coherence in the ventral stream. *Proceedings of the National Academy of Sciences*, *108* (27), 11262.

Buschman, T. J., & Miller, E. K. (2007). Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. *Science*, *315*, 1860–1862.

Canolty, R. T., Edwards, E., Dalal, S. S., Soltani, M., Nagarajan, S. S., Kirsch, H. E., et al. (2006). High gamma power is phase-locked to theta oscillations in human neocortex. *Science*, *313*, 1626–1628.

Cant, J. S., Large, M. E., McCall, L., & Goodale, M. A. (2008). Independent processing of form, colour, and texture in object perception. *Perception*, *37*, 57–78.

Cardin, V., Friston, K. J., & Zeki, S. (2011). Top-down modulations in the visual form pathway revealed with dynamic causal modeling. *Cerebral Cortex*, *21*, 550–562.

Cave, C. B. (1997). Very long-lasting priming in picture naming. *Psychological Science*, *8*, 322–325.

Cave, C. B., Bost, P. R., & Cobb, R. E. (1996). Effects of color and pattern on implicit and explicit picture memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *22*, 639–653.

Cave, C. B., & Squire, L. R. (1992). Intact and long lasting repetition priming in amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *18*, 509–520.

Chawla, D., Lumer, E. D., & Friston, K. J. (1999). The relationship between synchronization among neuronal populations and their mean activity levels. *Neural Computation*, *11*(6), 1389–411.

Cheyne, D., Bostan, A. C., Gaetz, W., & Pang, E. W. (2007). Event-related beamforming: A robust method for presurgical functional mapping using MEG. *Clinical Neurophysiology*, *118*, 1691–1704.

Collins, A. M., & Loftus, E. F. (1975). A spreading-activation theory of semantic processing. *Psychological Review*, *82*, 407–428.

Constanti, A., & Sim, J. A. (1987). Calcium-dependent potassium conductance in guinea-pig olfactory cortex neurones invitro. *Journal of Physiology (London)*, *387*, 173–194.

Dayan, P., Hinton, G. E., Neal, R. M., & Zemel, R. S. (1995). The Helmholtz machine. *Neural Computation*, *7*, 889–904.

D'Esposito, M., Zarahn, E., & Aguirre, G. K. (1999). Event-related functional MRI: Implications for cognitive psychology? *Psychological Bulletin*, *125*, 155–164.

De Baene, W., Ons, B., Wagemans, J., & Vogels, R. (2008). Effects of category learning on the stimulus selectivity of macaque inferior temporal neurons. *Learning and Memory*, *15*(9), 717–727.

De Baene, W., & Vogels, R. (2010). Effects of adaptation on the stimulus selectivity of macaque inferior temporal spiking activity and local field potentials. *Cerebral Cortex*, *20*(9), 2145–2165.

Desimone, R. (1996). Neural mechanisms for visual memory and their role in attention. *Proceedings of the National Academy of Sciences of the United States of America*, *93*, 13494–13499.

Desimone, R., & Duncan, J. (1995). Neural mechanisms of selective visual attention. *Annual Review of Neuroscience*, *18*, 193–222.

Dobbins, I. G., Schnyer, D. M., Verfaellie, M., & Schacter, D. L. (2004). Cortical activity reductions during repetition priming can result from rapid response learning. *Nature*, *428*, 316–319.

Doya, K. (1999). What are the computations of the cerebellum, the basal ganglia and the cerebral cortex? *Neural Networks*, *12*(7–8), 961–974.

Eger, E., Henson, R. N., Driver, J., & Dolan, R. J. (2007). Mechanisms of top-down facilitation in perception of visual objects studied by fMRI. *Cerebral Cortex*, *17*, 2123–2133.

Egner, T., Monti, J. M., & Summerfield, C. (2010). Expectation and surprise determine neural population responses in ventral visual stream. *Journal of Neuroscience*, *30*, 16601–16608.

Engel, A. K., Fries, P., & Singer, W. (2001). Dynamic predictions: Oscillations and synchrony in top-down processing. *Nature Reviews Neuroscience*, *2*, 704–716.

Ewbank, M., & Henson, R. N. (2012). Explaining away repetition effects via predictive coding. *Cognitive Neuroscience, 3*(3–4), 239–240.

Ewbank, M. P., Henson, R., Rowe, J., Stoyanova, R., & Calder, A. (in press). Different neural mechanisms within occipitotemporal cortex underlie repetition suppression across same and different-size faces. *Cerebral Cortex.*

Ewbank, M. P., Lawson, R. P., Henson, R. N., Rowe, J. B., Passamonti, L., & Calder, A. J. (2011). Changes in "top-down" connectivity underlie repetition suppression in the ventral visual pathway. *Journal of Neuroscience*, *31*, 5635–5642.

Fairhall, S. L., Anzellotti, S., Pajtas, P. E., & Caramazza, A. (2011). Concordance between perceptual and categorical repetition effects in the ventral visual stream. *Journal of Neurophysiology*, *106*, 398–408.

Fang, F., Murray, S. O., Kersten, D., & He, S. (2005). Orientation-tuned fMRI adaptation in human visual cortex. *Journal of Neurophysiology*, *94*, 4188–4195.

Feldman, H., & Friston, K. J. (2010). Attention, uncertainty, and free-energy. *Frontiers in Human Neuroscience*, *4*, 215.

Fiebach, C. J., Gruber, T., & Supp, G. G. (2005). Neuronal mechanisms of repetition priming in occipitotemporal cortex: Spatiotemporal evidence from functional magnetic resonance imaging and electroencephalography. *Journal of Neuroscience*, *25*, 3414–3422.

Fox, M. D., & Raichle, M. E. (2007). Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nature Reviews Neuroscience*, *8*, 700–711.

Freedman, D. J., Riesenhuber, M., Poggio, T., & Miller, E. K. (2006). Experience-dependent sharpening of visual shape selectivity in inferior temporal cortex. *Cerebral Cortex*, *16*(11), 1631–1644.

Fries, P. (2005). A mechanism for cognitive dynamics: Neuronal communication through neuronal coherence. *Trends in Cognitive Sciences*, *9*, 474–480.

Friston, K. (2005). A theory of cortical responses. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *360*, 815–836.

Friston, K. (2008). Hierarchical models in the brain. *PLoS Computational Biology*, *4*(11), e1000211.

Friston, K. (2012). Predictive coding, precision and synchrony. *Cognitive Neuroscience*, *3*(3–4), 238–239.

Friston, K. J., Buechel, C., Fink, G. R., Morris, J., Rolls, E., & Dolan, R. J. (1997). Psychophysiological and modulatory interactions in neuroimaging. *NeuroImage*, *6*, 218–229.

Friston, K. J., Harrison, L., & Penny, W. (2003). Dynamic causal modeling. *NeuroImage*, *19*, 1273–1302.

Gagnepain, P., Chételat, G., Landeau, B., Dayan, J., Eustache, F., & Lebreton, K. (2008). Spoken word memory traces within the human auditory cortex revealed by repetition priming and functional magnetic resonance imaging. *Journal of Neuroscience*, *28*, 5281–5289.

Garrido, M. I., Kilner, J. M., Stephan, K. E., & Friston, K. J. (2009). The mismatch negativity: A review of underlying mechanisms. *Clinical Neurophysiology*, *120*(3), 453–63.

Georgopoulos, A. P., Schwartz, A. B., & Kettner, R. E. (1986). Neuronal population coding of movement direction. *Science*, *233*, 1416–1419.

Ghuman, A. S., Bar, M., Dobbins, I. G., & Schnyer, D. M. (2008). The effects of priming on frontal-temporal communication. *Proceedings of the National Academy of Sciences*, *105*(24), 8405–8409.

Gilbert, J. R., Gotts, S. J., Carver, F. W., & Martin, A. (2010). Object repetition leads to local increases in the temporal coordination of neural responses. *Frontiers in Human Neuroscience*, *4*, 30.

Gold, B. T., Balota, D. A., Kirchhoff, B. A., & Buckner, R. L. (2005). Common and dissociable activation patterns associated with controlled semantic and phonological processing: Evidence from fMRI adaptation. *Cerebral Cortex*, *15*, 1438–1450.

Gotts, S. J. (2003). *Mechanisms underlying enhanced processing efficiency in neural systems*. Pittsburgh, PA: Carnegie Mellon University Press.

Gotts, S. J., Chow, C. C., & Martin, A. (2012). Repetition priming and repetition suppression: A case for enhanced efficiency through neural synchronization. *Cognitive Neuroscience*, *3*(3–4), 227–237.

Gotts, S. J., Milleville, S. C., Bellgowan, P. S. F., & Martin, A. (2011). Broad and narrow conceptual tuning in the human frontal lobes. *Cerebral Cortex*, *21*, 477–491.

Graf, P., Squire, L. R., & Mandler, G. (1984). The information that amnesic patients do not forget. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *10*, 164–178.

Gregoriou, G. G., Gotts, S. J., & Desimone, R. (2012). Cell-type-specific synchronization of neural activity in FEF with V4 during attention. *Neuron*, *73*, 581–594.

Gregoriou, G. G., Gotts, S. J., Zhou, H., & Desimone, R. (2009a). High-frequency, long-range coupling between prefrontal and visual cortex during attention. *Science*, *324*, 1207–1210.

Gregoriou, G. G., Gotts, S. J., Zhou, H., & Desimone, R. (2009b). Long-range neural coupling through synchronization with attention. *Progress in Brain Research*, *176*, 35–45.

Gregory, R. L. (1980). Perceptions as hypotheses. *Philosophical Transactions of the Royal Society London B*, *290*, 181–197.

Grill-Spector, K., Henson, R., & Martin, A. (2006). Repetition and the brain: Neural models of stimulus-specific effects. *Trends in Cognitive Science*, *10*, 14–23.

Grill-Spector, K., & Malach, R. (2001). fMR-adaptation: A tool for studying the functional properties of human cortical neurons. *Acta Psychologica*, *107*, 293–321.

Grossberg, S. (1976). Adaptive pattern classification and universal recoding: II. Feedback, expectation, olfaction, and illusions. *Biological Cybernetics*, *23*, 187–202.

Gruber, T., & Muller, M. M. (2005). Oscillatory brain activity dissociates between associative stimulus content in a repetition priming task in the human EEG. *Cerebral Cortex*, *15*, 109–116.

Hamburger, M., & Slowiaczek, L. M. (1998). Repetition priming and experimental context effects. *American Journal of Psychology*, *111*, 1–31.

Hansen, B. J., & Dragoi, V. (2011). Adaptation-induced synchronization in laminar cortical circuits. *Proceedings of the National Academy of Sciences of the United States of America*, *108*, 10720–10725.

He, B. J., Zempel, J. M., Snyder, A. Z., & Raichle, M. E. (2010). The temporal structures and functional significance of scale-free brain activity. *Neuron*, *66*, 353–369.

Henson, R. (2003). Neuroimaging studies of priming. *Progress in Neurobiology*, *70*(1), 53–81.

Henson, R. (2012). Repetition accelerates neural dynamics: Indefense of facilitation models. *Cognitive Neuroscience*, *3* (3–4), 240–241.

Henson, R. N., & Gagnepain, P. (2010). Predictive, interactive multiple memory systems. *Hippocampus*, *20*, 1315–1326.

Henson, R. N., Goshen-Gottstein, Y., Ganel, T., Otten, L. J., Quayle, A., & Rugg, M. D. (2003). Electrophysiological and haemodynamic correlates of face perception, recognition and priming. *Cerebral Cortex*, *13*, 793–805.

Henson, R. N., Price, C. J., Rugg, M. D., Turner, R., & Friston, K. J. (2002). Detecting latency differences in event-related BOLD responses: Application to words versus nonwords and initial versus repeated face presentations. *NeuroImage*, *15*, 83–97.

Henson, R. N., Rylands, A., Ross, E., Vuilleumier, P., & Rugg, M. D. (2004). The effect of repetition lag on electrophysiological and haemodynamic correlates of visual object priming. *NeuroImage*, *21*, 1674–1689.

Henson, R. N., Wakeman, D. G., Litvak, V., & Friston, K. J. (2011). A parametric empirical Bayesian framework for the EEG/MEG inverse problem: Generative models for multisubject and multimodal integration. *Frontiers in Human Neuroscience*, *5*, 76, 1–16.

Henson, R., Wakeman, D., Phillips, C., & Rowe, J. (2012). Effective connectivity between OFA and FFA during face perception: DCM of evoked MEG, EEG and fMRI responses. *Abstract accepted for Human Brain Mapping 2012*.

Horner, A. J., & Henson, R. N. (2008). Priming, response learning and repetition suppression. *Neuropsychologia*, *46*(7), 1979–1991.

Horner, A. J., & Henson, R. N. (2009). Bindings between stimuli and multiple response codes dominate long-lag repetition priming in speeded classification tasks. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *35*(3), 757–779.

Horner, A. J., & Henson, R. N. (2012). Incongruent abstract stimulus-response bindings result in response interference: FMRI and EEG evidence from visual object classification priming. *Journal of Cognitive Neuroscience*, *24*(3), 760–773.

James, T. W., & Gauthier, I. (2006). Repetition-induced changes in BOLD response reflect accumulation of neural activity. *Human Brain Mapping*, *27*, 37–45.

James, T. W., Humphrey, G. K., Gati, J. S., Menon, R. S., & Goodale, M. A. (2000). The effects of visual object priming on brain activation before and after recognition. *Current Biology*, *10*, 1017–1024.

Jiang, X., Bradley, E., Rini, R. A., Zeffiro, T., VanMeter, J., & Riesenhuber, M. (2007). Categorization training results in shape—and category-selective human neural plasticity. *Neuron*, *53*(6), 891–903.

Jiang, X., Rosen, E., Zeffiro, T., VanMeter, J., Blanz, V., & Riesenhuber, M. (2006). Evaluation of a shape-based model of human face discrimination using FMRI and behavioral techniques. *Neuron*, *50*(1), 159–72.

Jiang, Y., Haxby, J. V., Martin, A., Ungerleider, L. G., & Parasuraman, R. (2000). Complementary neural mechanisms for tracking items in human working memory. *Science*, *287*, 643–646.

Kaliukhovich, D. A., & Vogels, R. (2011). Stimulus repetition probability does not affect repetition suppression in macaque inferior temporal cortex. *Cerebral Cortex*, *21*(7), 1547–1558.

Kellogg, R. T., Newcombe, C., Kammer, D., & Schmitt, K. (1996). Attention in direct and indirect memory tasks with short- and long-term probes. *American Journal of Psychology, 109*, 205–217.

Kiebel, S. J., Garrido, M. I., Moran, R. J., & Friston, K. J. (2008). Dynamic causal modelling for EEG and MEG. *Cognitive Neurodynamics*, *2*, 121–136.

Kiefer, M. (2005). Repetition priming modulates category-related effects on event-related potentials: Further evidence for multiple cortical semantic systems. *Journal of Cognitive Neuroscience*, *17*, 199–211.

Kisley, M. A., Noecher, T. L., & Guinther, P. M. (2004). Comparison of sensory gating to mismatch negativity and self-reported perceptual phenomena in healthy adults. *Psychophysiology*, *41*, 604–612.

Koester, J., & Siegelbaum, S. A. (2000). Membrane potential. In E. R. Kandel, J. H. Schwartz, & T. M. Jessell (Eds.), *Principles of neural science* (4th ed., pp. 125–139). New York, NY: McGraw-Hill.

Konen, C. S., & Kastner, S. (2008). The hierarchically organized neural systems for object information in human visual cortex. *Nature Neuroscience*, *11*, 224–231.

Koutstaal, W., Wagner, A. D., Rotte, M., Maril, A., Buckner, R. L., & Schacter, D. L. (2001). Perceptual specificity in visual object priming: Functional magnetic resonance imaging evidence for a laterality difference in fusiform cortex. *Neuropsychologia*, *39*(2), 184–199.

Kraskov, A., Quiroga, R. Q., Reddy, L., Fried, I., & Koch, C. (2007). Local field potentials and spikes in the human medial temporal lobe are selective to category. *Journal of Cognitive Neuroscience*, *19*, 479–492.

Krekelberg, B., Boynton, G. M., & van Wezel, R. J. (2006). Adaptation: From single cells to BOLD signals. *Trends in Neurosciences*, *29*(5), 250–6.

Larsson, J., & Smith, A. T. (2012). fMRI repetition suppression: Neuronal adaptation or stimulus expectation? *Cerebral Cortex*, *22*, 567–576.

Lee, T. S., & Mumford, D. (2003). Hierarchical Bayesian inference in the visual cortex. *Journal of the Optical Society of America*, *20*, 1434–1448.

Lewicki, M. S., & Sejnowski, T. J. (1996). Bayesian unsupervised learning of higher order structure. *Advances in Neural Information Processing Systems*, *9*, 529–535.

Li, L., Miller, E. K., & Desimone, R. (1993). The representation of stimulus familiarity in anterior inferior temporal cortex. *Journal of Neurophysiology*, *69*(6), 1918–1929.

Liebe, S., Hoerzer, G. M., Logothetis, N. K., & Rainer, G. (2012). Theta coupling between V4 and prefrontal cortex predicts visual short-term memory performance. *Nature Neuroscience*, *15*(3), 456–462.

Logan, G. D. (1990). Repetition priming and automaticity: Common underlying mechanisms? *Cognitive Psychology*, *22*, 1–35.

Luck, S. J., Chelazzi, L., Hillyard, S. A., & Desimone, R. (1997). Neural mechanisms of spatial selective attention in areas V1, V2, and V4 of macaque visual cortex. *Journal of Neurophysiology*, *77*, 24–42.

Madison, D. V., & Nicoll, R. A. (1984). Control of the repetitive discharge of rat CA1 pyramidal neurones invitro. *Journal of Physiology (London)*, *354*, 319–331.

Mahon, B. Z., Milleville, S. C., Negri, G. A. L., Rumiati, R. I., Alfonso, C., & Martin, A. (2007). Action-related properties shape object representations in the ventral stream. *Neuron*, *55*, 507–520.

Markram, H., Lubke, J., Frotscher, M., & Sakmann, B. (1997). Regulation of synaptic efficacy by coincidence of postsynaptic APs and EPSPs. *Science*, *275*, 213–215.

Martin, A., & Gotts, S. J. (2005). Making the causal link: Frontal cortex activity and repetition priming. *Nature Neuroscience*, *8*, 1134–1135.

Mayr, S., Niedeggen, M., Buchner, A., & Pietrowsky, R. (2003). ERP correlates of auditory negative priming. *Cognition, 90*, B11–B21.

McClelland, J. L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review*, *102*, 419–457.

McClelland, J. L., & Rumelhart, D. E. (1981). An interactive activation model of context effects in letter perception: Part 1. An account of basic findings. *Psychological Review*, *88*, 375–407.

McClelland, J. L., & Rumelhart, D. E. (1985). Distributed memory and the representation of general and specific information. *Journal of Experimental Psychology: General*, *114*, 159–188.

McKone, E. (1995). Short-term implicit memory for words and nonwords. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *21*, 1108–1126.

McKone, E. (1998). The decay of short-term implicit memory: Unpacking lag. *Memory & Cognition*, *26*, 1173–1186.

McMahon, D. B., & Olson, C. R. (2007). Repetition suppression in monkey inferotemporal cortex: Relation to behavioral priming. *Journal of Neurophysiology*, *97*, 3532–3543.

Meyer, T., & Olson, C. R. (2011). Statistical learning of visual transitions in monkey inferotemporal cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(48), 19401–19406.

Miller, E. K., Gochin, P. M., & Gross, C. G. (1991). Habituation-like decrease in the responses of neurons in inferior temporal cortex of the macaque. *Visual Neuroscience*, *7*, 357–362.

Miller, E. K., Li, L., & Desimone, R. (1993). Activity of neurons in anterior inferior temporal cortex during a short-term memory task. *Journal of Neuroscience*, *13*, 1460–1478.

Minsky, M., & Papert, S. (1969). *Perceptrons*. Cambridge, MA: MIT Press.

Mirpour, K., & Esteky, H. (2009). State-dependent effects of stimulus presentation duration on the temporal dynamics of neural responses in the inferotemporal cortex of macaque monkeys. *Journal of Neurophysiology*, *102*(3), 1790–1800.

Mitchell, D. B. (2006). Nonconscious priming after 17 years: Invulnerable implicit memory? *Psychological Science*, *17*, 925–929.

Mondor, T. A., Breau, L. M., & Milliken, B. (1998). Inhibitory processes in auditory selective attention: Evidence of location-based and frequency-based inhibition of return. *Perception & Psychophysics*, *60*, 296–302.

Mumford, D. (1992). On the computational architecture of the neocortex. II. The role of cortico-cortical loops. *Biological Cybernetics*, *66*, 241–251.

Newsome, W. T., Britten, K. H., & Movshon, J. A. (1989). Neuronal correlates of a perceptual decision. *Nature*, *341*, 52–54.

Norman, K. A., & O'Reilly, R. C. (2003). Modeling hippocampal and neocortical contributions to recognition memory: A complementary learning-systems approach. *Psychological Review*, *110*, 611–646.

Olichney, J. M., Van Petten, C., Paller, K. A., Salmon, D. P., Iragui, V. J., & Kutas, M. (2000). Word repetition in amnesia: Electrophysiological measures of impaired and spared memory. *Brain*, *123*, 1948–1963.

O'Reilly, R. C. (1998). Six principles for biologically based computational models of cortical cognition. *Trends in Cognition Science*, *2*, 455–462.

Ostergaard, A. L. (1998). The effects on priming of word frequency, number of repetitions, and delay depend on the magnitude of priming. *Memory & Cognition*, *26*, 40–60.

Paller, K. A., & Gross, M. (1998). Brain potentials associated with perceptual priming vs explicit remembering during

the repetition of visual word-form. *Neuropsychologia*, *36*, 559–571.

Pearl, J. (1988). *Probabilistic reasoning in intelligent systems: Networks of plausible inference*. San Mateo, CA: Morgan Kaufmann.

Pedreira, C., Mormann, F., Kraskov, A., Cerf, M., Fried, I., Koch, C., et al. (2010). Responses of human medial temporal lobe neurons are modulated by stimulus repetition. *Journal of Neurophysiology*, *103*, 97–107.

Peissig, J. J., Singer, J., Kawasaki, K., & Sheinberg, D. L. (2007). Effects of long-term object familiarity on event-related potentials in the monkey. *Cerebral Cortex*, *17*, 1323–1334.

Piazza, M., Izard, V., Pinel, P., Le Bihan, D., & Dehaene, S. (2004). Tuning curves for approximate numerosity in the human intraparietal sulcus. *Neuron*, *44*, 547–555.

Puce, A., Allison, T., & McCarthy, G. (1999). Electrophysiological studies of human face perception. III. Effects of top-down processing on face-specific potentials. *Cerebral Cortex*, *9*, 445–458.

Race, E. A., Badre, D., & Wagner, A. D. (2010). Multiple forms of learning yield temporally distinct electrophysiological repetition effects. *Cerebral Cortex*, *20*, 1726–1738.

Race, E. A., Shanker, S., & Wagner, A. D. (2009). Neural priming in human frontal cortex: Multiple forms of learning reduce demands on the prefrontal executive system. *Journal of Cognitive Neuroscience*, *21*, 1766–1781.

Raichle, M. E., & Mintun, M. A. (2006). Brain work and brain imaging. *Annual Review of Neuroscience*, *29*, 449–476.

Rainer, G., Asaad, W. F., & Miller, E. K. (1998). Selective representation of relevant information by neurons in the primate prefrontal cortex. *Nature*, *393*, 577–579.

Rainer, G., & Miller, E. K. (2000). Effects of visual experience on the representation of objects in the prefrontal cortex. *Neuron*, *27*, 179–189.

Rao, R. P., & Ballard, D. H. (1999). Predictive coding in the visual cortex: A functional interpretation of some extra-classicalreceptive-field effects. *Nature neuroscience*, *2*(1), 79–87.

Reyes, A. D. (2003). Synchrony-dependent propagation of firing rate in iteratively constructed networks invitro. *Nature Neuroscience*, *6*, 593–599.

Roediger, H. L. (1990). Implicit memory retention without remembering. *American Psychologist*, *45*, 1043–1056.

Rollenhagen, J. E., & Olson, C. R. (2005). Low-frequency oscillations arising from competitive interactions between visual stimuli in macaque inferotemporal cortex. *Journal of Neurophysiology*, *94*(5), 3368–3387.

Rowe, J. B., Hughes, L. E., Barker, R. A., & Owen, A. M. (2010). Dynamic causal modelling of effective connectivity from fMRI: Are results reproducible and sensitive to Parkinson's disease and its treatment? *Neuroimage*, *52*, 1015–1026.

Rugg, M. D., Brovedani, P., & Doyle, M. C. (1992). Modulation of event-related potentials (ERPs) by word repetition in a task with inconsistent mapping between repetition and response. *Electroencephalography and Clinical Neurophysiology*, *84*, 521–531.

Rugg, M. D., Mark, R. E., Gilchrist, J., & Roberts, R. C. (1997). ERP repetition effects in indirect and direct tasks: Effects of age and interitem lag. *Psychophysiology*, *34*, 572–586.

Salinas, E., & Sejnowski, T. J. (2000). Impact of correlated synaptic input on output firing rate and variability in simple neuronal models. *Journal of Neuroscience*, *20*, 6193–6209.

Salinas, E., & Sejnowski, T. J. (2001). Correlated neuronal activity and the flow of neural information. *Nature Reviews Neuroscience*, *2*, 539–550.

Sayres, R., & Grill-Spector, K. (2006). Object-selective cortex exhibits performance-independent repetition suppression. *Journal of Neurophysiology*, *95*, 995–1007.

Schacter, D. L. (1987). Implicit memory—History and current status. *Journal of Experimental Psychology: Learning, Memory, & Cognition*, *13*(3), 501–518.

Schacter, D. L., & Buckner, R. L. (1998). Priming and the brain. *Neuron*, *20*, 185–195.

Schacter, D. L., Dobbins, I. G., & Schnyer, D. M. (2004). Specificity of priming: A cognitive neuroscience perspective. *Nature Reviews: Neuroscience*, *5*, 853–862.

Schall, J. D., & Hanes, D. P. (1993). Neural basis of saccade target selection in frontal eye field during visual search. *Nature*, *366*, 467–469.

Schendan, H. E., & Kutas, M. (2003). Time course of processes and representations supporting visual object identification and memory. *Journal of Cognitive Neuroscience*, *15*, 111–135.

Scott, L. S., Tanaka, J. W., Sheinberg, D. L., & Curran, T. (2006). A reevaluation of the electrophysiological correlates of expert object processing. *Journal of Cognitive Neuroscience*, *18*, 1453–1465.

Sjöstrom, P. J., Turrigiano, G. G., & Nelson, S. B. (2001). Rate, timing, and cooperativity jointly determine cortical synaptic plasticity. *Neuron*, *32*, 1149–1164.

Squire, L. R. (1992). Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans. *Psychological Review*, *99*, 195–231.

Srinivas, K. (1996). Size and reflection effects in priming: A test of transfer-appropriate processing. *Memory & Cognition*, *24*, 441–452.

Stark, C. E., & McClelland, J. L. (2000). Repetition priming of words, pseudowords, and nonwords. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *26*, 945–972.

Stopfer, M., Bhagavan, S., Smith, B. H., & Laurent, G. (1997). Impaired odour discrimination on desynchronization of odour-encoding neural assemblies. *Nature*, *390*, 70–74.

Stopfer, M., & Laurent, G. (1999). Short-term memory in olfactory network dynamics. *Nature*, *402*, 664–648.

Summerfield, C., Trittschuh, E. H., Monti, J. M., Mesulam, M. M., & Egner, T. (2008). Neural repetition suppression reflects fulfilled perceptual expectations. *Nature Neuroscience*, *11*, 1004–1006.

Summerfield, C., Wyart, V., Johnen, V. M., & de Gardelle, V. (2011). Human scalp electroencephalography reveals that repetition suppression varies with expectation. *Frontiers in Human Neuroscience*, *5*, 67. doi: 10.3389/fnhum.2011.00067.

Swick, D. (1998). Effects of prefrontal lesions on lexical processing and repetition priming: An ERP study. *Cognitive Brain Research*, *7*, 143–157.

Szymanski, K. F., & MacLeod, C. M. (1996). Manipulation of attention at study affects an explicit but not an implicit test of memory. *Consciousness and Cognition: An International Journal*, *5*, 165–175.

Todorovic, A., van Ede, F., Maris, E., & de Lange, F. P. (2011). Prior expectation mediates neural adaptation to repeated sounds in the auditory cortex: An MEG study. *Journal of Neuroscience*, *31*, 9118–9123.

Tsodyks, M. V., & Markram, H. (1997). The neural code between cortical pyramidal neurons depends on neurotransmitter release probability. *Proceedings of the National Academy of Sciences of the United States of America*, *94*, 719–723.

Tulving, E., & Schacter, D. L. (1990). Priming and human memory systems. *Science*, *247*, 301–306.

van Turennout, M., Bielamowicz, L., & Martin, A. (2003). Modulation of neural activity during object naming: Effects of time and practice. *Cerebral Cortex*, *13*, 381–391.

van Turennout, M., Ellmore, T., & Martin, A. (2000). Long-lasting cortical plasticity in the object naming system. *Nature Neuroscience*, *3*, 1329–1334.

Varela, J. A., Song, S., Turrigiano, G. G., & Nelson, S. B. (1999). Differential depression at excitatory and inhibitory synapses in visual cortex. *Journal of Neuroscience*, *19*, 4293–4304.

Verhoef, B.-E., Kayaert, G., Franko, E., Vangeneugden, J., & Vogels, R. (2008). Stimulus similarity-contingent neural adaptation can be time and cortical area dependent. *Journal of Neuroscience*, *28*, 10631–10640.

von Stein, A., Chiang, C., & Konig, P. (2000). Top-down processing mediated by interareal synchronization. *Proceedings of the National Academy of Sciences of the United States of America*, *97*, 14748–14753.

Voss, J. L., & Paller, K. A. (2008). Brain substrates of implicit and explicit memory: The importance of concurrently acquired neural signals of both memory types. *Neuropsychologia*, *46*, 3021–3029.

Wang, Y., Iliescu, B. F., Ma, J., Josić, K., & Dragoi, V. (2011). Adaptive changes in neuronal synchronization in macaque V4. *Journal of Neuroscience*, *31*, 13204–13213.

Warrington, E. K., & Weiskrantz, L. (1974). The effect of prior learning on subsequent retention in amnesic patients. *Neuropsychologia*, *12*, 419–428.

Weiner, K. S., Sayres, R., Vinberg, J., & Grill-Spector, K. (2010). fMRI-adaptation and category selectivity in human ventral temporal cortex: Regional differences across time scales. *Journal of Neurophysiology*, *103*, 3349–3365.

Wig, G. S., Buckner, R. L., & Schacter, D. L. (2009). Repetition priming influences distinct brain systems: Evidence from task-evoked data and resting-state correlations. *Journal of Neurophysiology*, *101*(5), 2632–2648.

Wig, G. S., Grafton, S. T., Demos, K. E., & Kelley, W. M. (2005). Reductions in neural activity underlie behavioral components of repetition priming. *Nature Neuroscience*, *8*(9), 1228–1233.

Wiggs, C. L., & Martin, A. (1998). Properties and mechanisms of perceptual priming. *Current Opinion in Neurobiology*, *8*, 227–233.

Wiggs, C. L., Martin, A., & Sunderland, T. (1997). Monitoring frequency of occurrence without awareness: Evidence from patients with Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology*, *19*(*2*), 235–244.

Woloszyn, L., & Sheinberg, D. L. (2012). Effects of long-term visual experience on responses of distinct classes of single units in inferior temporal cortex. *Neuron*, *74*, 193–205.

Xu, Y., Turk-Browne, N. B., & Chun, M. M. (2007). Dissociating task performance from fMRI repetition attenuation in ventral visual cortex. *Journal of Neuroscience*, *27*, 5981–5985.