Chapter 1

General Introduction
The brain is modular

One of the most striking features of the brain is that it is modular; it consists of often highly specialized areas. The brain can be broadly divided in distinct areas for processing sensory information, areas that are important for storing information and areas important for planning and executing actions. One of the best studied brain regions is the occipital cortex, which is known to be important for processing visual features of the environment. The visual cortex is subdivided in areas specialized for processing basic visual features such as color in V4 (Zeki et al., 1991), shape in the lateral occipital cortex (LOC; Kourtzi & Kanwisher, 2000) and motion in MT/MST (Tootell et al., 1995; Zeki et al., 1991), but also for higher order features, or feature compounds such as faces in the fusiform face area (FFA; Kanwisher, McDermott, Chun, 1997) and houses in the parahippocampal place area (PPA; Epstein & Kanwisher, 1998). Moreover, the processing of visual information can be subdivided into two pathways; a dorsal stream, which contains areas that are specialized in processing spatial and action-related features and a ventral stream, which contains areas that are specialized in non-spatial features (Milner & Goodale, 1995).

Behavioral investigations of feature integration

The modular organization of the brain requires effective communication in order to integrate the information that is represented in distinct brain areas. An example of the necessity to integrate is when the visual field consists of multiple objects. When these objects have different colors and shapes, there needs to be a mechanism that enables the system to associate the correct color with the correct shape. The need for a mechanism that is responsible for integration of information that is represented in distinct brain modules has been commonly referred to as the ‘binding problem’ (Treisman, 1996).

One way to investigate the binding problem is to study the possible behavioral consequences of integrated features. A method that has been used in many studies on the binding problem is the investigation of sequential effects. In a paradigm originally designed by Hommel (1998), subjects are subsequently confronted with two objects that consist of multiple features (for instance shape and location, Figure 1). When subjects have to make a discriminatory response to one of the features of the second object (S2), performance (RTs and error rates) is influenced by the preceding object (S1). More specifically, performance on S2 is generally good (fast RTs and low error rates), when both features are repeated, or when both features are alternated from S1.
to S2. However, performance is impaired (slow RTs and high error rates) when one of the features is repeated, while the other is alternated.

![Diagram of the binding paradigm](image)

**Figure 1.** Example trial of the binding paradigm.

It has been proposed that this behavioral pattern can be explained as a signature of the integration that occurs on S1. If an association is established between two features, repeating one of these features automatically reactivates the previously associated feature in a kind of pattern-completion process. In the case of partial repetition of features, the reactivation of a feature that does not reflect the current sensory input, or ‘event’, and it therefore leads to conflict. The increased reaction times and error rates are thought to reflect this conflict, since additional processing is needed to suppress the erroneously activated feature and remove the association between the two features that were presented on S1, a process that has been called ‘unbinding’ (Colzato, van Wouwe, Lavender, & Hommel, 2006).

These ‘binding costs’ have not only been shown for arbitrary visual features of an object, but also for different sensory domains (Zmigrod & Hommel, 2009) and representations of actions (Colzato, Raffone & Hommel, 2006; Hommel, 1998). The term ‘event-files’ has been coined to describe bindings that involve these different representational domains (Hommel, 1998).

Importantly, integration of features in the above-described paradigm is not necessary for the task that subjects have to perform. Binding costs can thus be seen as a reflection of implicit, automatic integration of features. This does not imply that goal-directed, top-down processes cannot influence the maintenance of relational information between features. Indeed, it has been shown that the amount of attention
devoted to S1 influences binding costs (Colzato, Raffone & Hommel, 2006). Moreover, previous research has shown that binding costs are larger when visual feature conjunctions include images of real objects. The authors suggest that real objects elicit top-down priming due to a conceptual match in long-term memory (Hommel & Colzato, 2009; Colzato, Raffone, and Hommel, 2006).

**How do brain modules communicate?**

It has been proposed that neural synchrony is the underlying brain mechanism that enables feature binding to occur. Originally, it was the work of Engel and Singer on animals (for an overview, see: Engel & Singer, 2001) that spurred theories about the functional relevance of neural synchronization in feature integration. However, many findings have shown that neural synchronization can also be demonstrated in EEG-recordings of human subjects (for an overview, see: Jensen, Kaiser & Lachaux, 2007). Neural synchrony refers to the coherence of neural firing in distinct groups of neurons. When two features that are represented in distinct brain areas are bound together, the groups of neurons that represent these features fire in the same frequency in phase. In this way, an association between two representations can be formed and maintained, even though a physical distance separates the two representations. It has been suggested that neural synchrony reflects a communication window or channel that can overcome the noise of the neural firings that occur between the two groups of neurons (Fries, 2005). In concordance with this theory, it has been proposed that the firing frequency decreases when larger physical distances between neural representations have to be bridged (Varela, Lachaux, Rodriguez & Martinerie, 2001). It has been demonstrated that neural synchrony in the gamma range (~30-100 Hz) occurs when visual features are integrated (Engel & Singer, 2001). In contrast, neural synchronization in the beta range (~12-20Hz) has shown to be important for integration between visual and auditory information (von Stein, Rappelsberger, Sarnthein & Petsche, 1999) and between visual information and motor information (Roelfsema, Engel, Koenig & Singer, 1997).

Even though neural synchrony has been deemed important for many cognitive functions, such as (visual) awareness, short-term memory, long-term memory and attention, all of these functions rely on communication and integration of information represented in distinct brain areas. In the case of (visual) awareness, neural synchrony in the gamma range has been associated directly with binding processes. In other words, binding through neural synchrony has been proposed to be a necessary condition for awareness (Engel & Singer, 2001). Short-term memory and attention have also been associated with neural synchronization in the gamma range and can
be seen as the way frontal brain areas, which are associated with top-down control, influence local representations of for instance sensory information. It has also been shown that increases of synchronization in the gamma band reflect the ‘bias-signal’, which facilitates processing of attended sensory information (Fell, Fernández, Klaver, Elger & Fries, 2003). Moreover, increased synchronization in the gamma band reflects can reflect the retention of (sensory) information in short-term memory (Tallon-Baudry & Bertrand, 1999). Again, top-down control may be responsible for influencing local representations during short-term memory retention.

Finally, the role of neural synchronization in long-term episodic memory has also been demonstrated (Klimesch, 1999; Sederberg, Kahana, Howard, Donner & Madsen, 2003). It has been shown that synchronization in the both the gamma (~30-100 Hz) and theta range (4-8 Hz) are related to encoding and retrieval of episodic information in long-term memory. Multiple brain regions are involved in long-term memory processes. The most well-known brain area that is important for the formation of episodic memory traces is the medial temporal, which includes the hippocampus (Squire, Stark & Clark, 2004). Second, research has shown that (pre)frontal areas are important for top-down control of consolidation and retrieving of episodic information (Simons & Spiers, 2003). Finally, there is evidence that the posterior parietal cortex is involved in the attentional processing demands that accompany retrieval of episodic memory traces (Cabeza, Ciaramelli, Olson & Moscovitch, 2008). During encoding or retrieval of information in long-term memory, all these areas must communicate effectively with each other, but also with brain areas that represent the to-be-encoded or to-be-retrieved information; communication which may be supported by neural synchronization.

**Beyond correlations, tools for investigating the functional relevance of neural synchronization**

Even though many studies have demonstrated correlations between neural synchronization and feature integration, the functional relevance of neural synchronization in feature binding is still under heated debate, on a theoretical level (Ghose & Maunsell, 1999; Reynolds & Desimone, 1999; Shadlen & Movshon, 1999; Treisman, 1999) and due to empirical studies showing an absence of neural synchrony during integration demanding situations (Lamme & Spekreijse, 1998), contour grouping (Roelfsema, Lamme & Spekreijse, 2004) and motion coherence (Thiele & Stoner, 2003). One of the core arguments against the functional relevance of neural synchronization is based on the fact that many of the supporting empirical findings are correlational. This leaves the possibility that neural synchronization is epiphenomenal;
it may co-occur during feature integration, but it does not reflect the underlying mechanism that is responsible for feature integration.

In order to investigate the functional relevance of neural synchronization in feature binding and other cognitive processes, methods are required that enable experimental manipulation of neural synchronization itself. In this way, the effects of altered neural synchronization on feature integration and other cognitive processes can be measured, resulting in greater explanatory power than the demonstration of mere correlations.

There are several techniques, with which neural synchronization can be experimentally manipulated. First, neural synchronization can be manipulated indirectly using psychopharmacological substances that are known to influence neural synchronization via neurotransmitter systems. The muscarinic-cholinergic neurotransmitter system is known to be directly related to neural synchronization in the gamma range, especially in the visual cortex (Rodriguez-Bermudez, Kallenbach, Singer & Munk, 2004). Findings on human subjects have shown that psycho-active drugs that are known to manipulate the muscarinic-cholinergic neurotransmitter system, such as alcohol and caffeine have profound effects on feature integration (Colzato, Erasmus, & Hommel, 2004; Colzato, Fagioli, Erasmus, & Hommel, 2005). These effects have later been replicated with more specific muscarinic-cholinergic agonists and antagonists (Botly & De Rosa, 2007; Botly & De Rosa, 2008).

Promising methods that have been used to manipulate neural synchrony directly are repetitive transcranial magnetic stimulation (rTMS), the presentation of visual flicker stimuli and neurofeedback.

It has been shown that rTMS can influence neural synchronization in frequencies such as the alpha band (8-12 Hz) and beta band (14-30 Hz; for an overview, see Thut & Miniussi, 2009). However, much research on the use of rTMS is needed, since there currently does not seem to be a one-to-one relationship between the frequency of magnetic stimulation that is used and the frequency band that is influenced (Thut & Miniussi, 2009).

Presenting oscillating visual stimuli have shown to ‘entrain’ the firing frequency of neurons in the visual cortex (Herrmann, 2001). In other words, neural synchronization in particular frequency bands can be studied by presenting oscillating visual stimuli in the frequency that is under investigation. Indeed, a recent study by Bauer, Cheadle, Parton, Müller and Usher (2009) showed that subliminal visual flicker that oscillated in the gamma range (at 50 Hz) facilitated the processing of an upcoming target stimulus, possibly by mimicking the top-down bias-signal that is known to occur in the gamma range.
Finally, neurofeedback has been shown to be effective in increasing and decreasing neural synchronization directly in specific frequency bands (Bird, Newton, Sheer, & Ford, 1978; Vernon et al., 2003). Neurofeedback has mainly been studied as a possible treatment method for psychological and neurological disorders that are associated with impairments of neural synchrony, such as ADHD (Fuchs, Birbaumer, Lutzenberger, Gruzelier, & Kaiser, 2003), migraine (Kropp, Siniatchkin, & Gerber, 2002), and epilepsy (Kotchoubey, Strehl, Holzapfel, Blankenhorn, Fröscher, & Birbaumer, 1999). However, recent studies by Egner & Gruzelier (2001, 2003, 2004) and Vernon et al. (2003) have shown that neurofeedback can be used to manipulate neural synchronization and study its effects on cognitive processes.

Outline of the thesis

Chapter 2 describes a study in which we investigated whether binding can occur between features that are processed in the dorsal stream and features that are processed in the ventral stream. It has been hypothesized that the dorsal stream of visual information processing operates exclusively online and has no access to memory (Cant, Westwood, Valyeara, & Goodale, 2005; Milner & Goodale, 1995). If this is indeed the case, sequential effects of binding, which reflect a memory trace of previous communication, should not be expected between dorsal and ventral features. Our results are inconsistent with this view; we showed that binding can occur between objects that are known to be processed in the ventral stream (faces and houses) and motion, which is known to be processed in the dorsal stream.

Chapter 3 investigates one of the core assumptions regarding the neural basis of the sequential effects of feature integration. As described above, partial repetition of features is thought to result in performance costs due to automatic reactivation of a previously associated, now inappropriate feature. Using an event-related fMRI study, we provided direct evidence for this mechanism. The results showed that perceiving a face moving in the same direction as a just-perceived house increased activation in the PPA.

Chapter 4 explores whether binding can occur in true absence of top-down signals and investigates the relationship between implicit, automatic binding and explicit binding. First, our results show that binding between visual features does occur in the absence of task-relevant information, but only between real objects and not between arbitrary features. This in accordance of a previous study which showed that binding costs are larger when real objects are included (Colzato, Raffone, and Hommel, 2006; Hommel & Colzato, 2009), due to top-down priming resulting from a conceptual match in long-term memory. Our findings show that top-down priming
resulting from a match in long-term memory is sufficient to elicit binding costs (experiment 1a and 1b). Second, the results of experiment 2a and 3a showed that explicit storage of visual relations in short-term memory does not result in binding effects of arbitrary features in the absence of task-relevant information (Experiment 2a), suggesting that the absence of binding costs can be attributed to an absence of retrieval processes. Interestingly, binding effects disappeared between real objects as a result of explicit storage (Experiment 2b), which points to interference of top-down related retrieval processes by short-term memory processes.

Chapter 5 investigates neurofeedback as a possible method for studying the functional role of gamma band activity (GBA) in feature binding. The results showed that subjects are indeed able to enhance occipital GBA in the course of 8 neurofeedback sessions. Moreover, enhanced GBA resulted in a decrease of visual binding costs, but not of visuo-motor binding costs. We hypothesize that enhanced occipital GBA reflects increased top-down control, which leads to increased flexibility in the handling of event files. This conclusion is supported by the finding that the change in GBA correlated positively with the change of fluid intelligence, which is arguably related to control processes.

Chapter 6 replicates the findings of chapter 5 in that increased GBA causes a decrease in binding costs. The results of this study suggest that increased occipital GBA is caused by an increase of frontal GBA, which again points to enhanced top-down control as a result of GBA-enhancing neurofeedback. Moreover, the results of this study showed that increased GBA led to an increase of the ability to retrieve contextual information from long-term memory, which has also been associated with frontal control mechanisms.

Chapter 7 contains the summary and conclusions.

The following references correspond with chapters 2-6 of this thesis:


