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Review article

What's in a context? Cautions, limitations, and potential paths forward

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HIGHLIGHTS

- Contexts must be stable over time along an experiential dimension.
- Contexts must be at least moderately complex in nature and their representations must be modifiable or adaptable.
- Contexts must have some behavioral relevance (be it overt or incidental) so that its role can be measured.

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ABSTRACT

The purpose of memory is to guide current and future behavior based on previous experiences. Part of this process involves either discriminating between or generalizing across similar experiences that contain overlapping conditions (such as space, time, or internal state), which we often conceptualize as "contexts". In this review, we highlight major challenges facing the field as we attempt a neuroscience-based approach to the study of context and its impact on learning and memory. Here, we review some of the methodologies and approaches used to investigate context in both animals and humans, including the neurobiological mechanisms involved. Finally, we propose three tenets for operationalizing context in the experimental setting: 1) contexts must be stable over time along an experiential dimension; 2) contexts must be at least moderately complex in nature and their representations must be modifiable or adaptable, and 3) contexts must have some behavioral relevance (be it overt or incidental) so that its role can be measured.

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1. What constitutes a context?

Contextual information plays a key role in investigations of learning and memory, but is notoriously difficult to operationalize and study. A typical view of context is that it sets up expectations or contingencies that themselves can serve as ways of organizing information or as cues for retrieval. Take, for example, the "butcher on the bus" phenomenon often used to exemplify familiarity-based recognition memory [1]. A person (e.g., the butcher) on the bus looks familiar, but without the relevant features of the familiar context (e.g., the butcher shop), the identity of this individual can be difficult to retrieve. This example illustrates the power of context in providing a rich set of retrieval cues, which can range from an emotional state to a physical space. In the laboratory setting, context is present in all of our experiments, even if it is not parametrically varied or specifically examined. When given a yes/no recognition test for a list of words, the question is not whether "window" has ever been seen, but rather whether it was seen in the context of the experiment or a particular study list. When asked for a free associate of "hand", it is not an entirely free-association, but an association bound by or at least informed by the context of the study episode. For example, if the study list contained semantically related words such as "time, dial, alarm", one might freely associate with "clock" whereas if the list contained words such as "arm, leg, body", one might respond with "finger". Every time we repeat items on a study list, each experience is different from the last despite the fact that we call it a "repetition" as the context has changed. Even if the same items are presented before and after, eliciting a repetition of a sequence of events, the "temporal context" is different and the second set of items will quite likely be viewed as a "second set", altering the context in which they are being viewed. Thus, the test participant is now different and the experiential history is different, leading in some ways to a different context. Yet, at the same time, these potentially minor alterations may well be subsumed over a more general context common to the events. Thus, in addition to space and time, experiential history, emotional state, motivational state, hormonal state, circadian rhythm, attentional fluctuations, and many other factors contribute to context. Given the ever present and pervasive nature of "context" in the study of memory (and more broadly, any cognitive or behavioral task), it can be difficult to isolate and define in operational terms what makes up a context in any situation.

The hippocampus has long been implicated in contextual processing, with data from lesions and electrophysiological recordings in rodents to functional neuroimaging in humans. A review of this literature reveals a multitude of paradigms and approaches to investigating context, with as many variations on what constitutes context. Generally, as we will discuss at length, a common thread appears to be the processing of associations. Here, we review how context has been examined in studies of episodic memory and attempt to distill the key components of context and the issues that need to be addressed to make progress in understanding context, its instantiation in the brain, and the role it plays in memory.

First, we survey approaches to operationalizing and studying context in the literature and then evaluate the neurobiological mechanisms involved in representing context. Next, we explore the notion that simple perceptual information (be it driven from the external environment or from retrieval or imagery) could be driving many of the effects observed in extant studies, which complicate our attempts to isolate broader contextual representations. To make progress in this domain, future studies must go further to mitigate the possibility that observed effects are purely from associative memory or from perceptual confounds. Finally, we propose three tenets for operationalizing context in the experimental setting: 1) contexts must be stable over time along an experiential dimension; 2) contexts must be at least moderately complex in nature and their representations must be modifiable or adaptable, and 3) contexts must have some behavioral relevance (be it overt or incidental) so that their role can be measured. Thus, while we believe that there is a meaningful representation to "context" in the brain, more research is necessary to establish and differentiate contextual processing from an association of features, no matter how complex.

It is important to note that in this discussion, we are not attempting to draw lines around what context is in an absolute sense. Indeed, the elements of an experience that form a context can vary, leaving ample room for gray areas. The three tenets we describe are rather intended to aid in an effective operational definition, which can make for clearer contrasts in experimental designs. Thus, we urge the reader to bear in mind that we are considering context as a gradient or continuum, and are offering avenues of thought that can assist in determining which experimental conditions and contrasts might optimize the operationalization of context to better understand its role in learning, memory, and behavior.

2. Cornucopia of contextual conditions

Context has been operationalized and studied in a variety of different ways in the extant literature. One very common experimental design used in rodent studies is contextual fear conditioning. Briefly, this paradigm introduces an aversive stimulus, typically a shock, to an animal in a particular chamber. Later, the animal is returned to that chamber in the absence of the aversive stimulus (sometimes different chambers with no aversive pairings are also used as control conditions). The freezing response is measured, which is taken as evidence that the animal remembers the negative association between the chamber and the aversive stimulus [2]. The amygdala, hippocampus, and prefrontal cortex are often found to be critical for this type of fear conditioning [3] (more on the roles of these regions in the Neurobiological Mechanisms Underlying Context section). Though this is a simple operationalization of a context, it satisfies basic conditions of unchanging or relatively stable information (i.e., the spatial layout of the chamber) and behavioral relevance. However, it must be noted that the presence or absence of freezing does not necessarily inform one as to what an animal *remembers*. For example, lesions to the amygdala, which eliminate freezing, do not necessarily eliminate other indices of fear memory (e.g., avoidance) in conditioned animals [4]. Despite complications in interpreting freezing, this paradigm has been a powerful tool for assessing the contributions of different brain regions to context-dependent memory. For instance, it was recently demonstrated that freezing behaviors can be 'transferred' to an unconditioned chamber by optogenetically reactivating certain hippocampal neurons that were active in a conditioned chamber [5].

As with fear conditioning, many experimental uses of context hinge on "where + what" associations. Importantly, this is not simply memory for spatial locations or for items, but memory for specific item-location pairings. These paradigms have emphasized the importance of medial temporal lobe regions in establishing item-location or item-scene associations across rodents [6–8] and primates [9,10]. Similar approaches have been taken in humans, such as objects encoded against a background image [11,12] or in different on-screen locations [13,14]. In this type of experimental design, non-human animals are often tasked with exhibiting a specific behavior in the event of specific pairings of items and locations to demonstrate memory for spatial context. This response-contingency approach is also used in humans, though some studies have queried subjects more subjectively by asking them to indicate the extent to which they "recollect" the spatial context in which an item was encountered [15]. Beyond static