Explicitly Acquired Interrelations Among Mental Schema Reduces Cognitive Load and Facilitates Emergence of Novel Responses in Mice and Artificial Neural Networks.

Authors:
Vikram Pal Singh[1], Shruti Shridhar[1], Shankanava Kundu[1], Richa Bhatt[1], Balaji Jayaprakash[1*]

Affiliations:
1. Center for Neuroscience, Indian Institute of Science, Bangalore, India

*Corresponding Author
Email correspondence: jbalaji@iisc.ac.in

Abstract:

Mammalian brain has evolved to infer from past experiences and elicit context relevant novel behavioural responses hitherto unexpressed by the animal. Little is known about if and how prior knowledge affect emergence of such novel responses. Remarkably, our brain not only arrives at these responses through logical inferences but can also preserve these related memories distinctly without catastrophic interference. Often mental schema has been proposed to be the framework for such phenomenon. In this study, using mice as a model animal, we show that schematic networks not only enhance the cognitive load handling capacity (CLHC) preventing catastrophic interference, but also enable the generation of novel responses that are context relevant. Interestingly, when the animals were trained in a paradigm that did not invoke the pre-formed mental schema, we observed neither an enhancement to CLHC nor a generation of novel context relevant responses. Using these principles of mental schema that we discovered from our animal experiments, we develop a neurologically relevant ANN that avoids catastrophic interference and captures all the properties associated with different modes of learning tested in our experiments. The custom architecture of the ANN enables it to generate responses similar to animals in novel scenario.

Keywords:
Mental schema, rodent behaviour, learning and memory, problem-solving

Statements and Declarations
Competing Interests: The authors declare that they have no conflict of interest.

Introduction:

Organisation of information (knowledge structure) in terms of mental schema in the brain has been postulated and studied extensively in humans (Bartlett 1932; Carmichael, Hogan, and Walter 1932). Bartlett (Bartlett 1932) hypothesised that storing the past experiences in organised knowledge structures such as mental schema can help in forming new ideas through "*constructive and predictive processes"*. Few of the studies have investigated the existence of mental schema and their role in system consolidation in various animal species (Farovik et al. 2015; Mao et al. 2021; McKenzie et al. 2014; Tse et al. 2007). These studies have either focused on role of mental schema in rapid acquisition and consolidation or on the brain regions correlated with mental schema. The exact role schema plays in complex cognitive phenomenon such as problem solving and handling higher cognitive load during learning has not been studied explicitly especially in an animal model. In our previous work, we utilize a modification of the mental schema task in rats (Day, Langston, and Morris 2003) to study temporal order memory in mice (Shridhar et al. 2022). Since we had successfully translated the task to mice in our laboratory, we use the same setup with a new experimental design to investigate the implication of such mental constructs in avoidance of catastrophic forgetting and problem solving.

Conventional approach to studying learning and memory focuses on understanding associations that are developed because of stimuli-stimuli or stimulus-response presentations (Heath 1979; Pearce 1987; Pavlov 2010; R. A. Rescorla 1972). While they help to tease out the fundamental principles of learning, they can be limiting when it comes to understanding the abstraction of interstimulus relations that arise upon simultaneous presentation of multiple equally contingent associative pairs (Asch 1969). We reasoned that perhaps a framework like mental schema is a promising candidate that can both expand the cognitive load handling capacity (CLHC) and explain how pre-learned knowledge provide a more efficient learning system. Such system can balance storing the novelty and its relationship to the past information (van Kesteren et al. 2012). Thus, we proposed that mental schema being an organised structure, can serve as a template against which the new incoming information can be compared and stored, thereby enhancing the CLHC. Specifically, we hypothesis and test if prior knowledge in the form of schema facilitates the acquisition of complex information which otherwise would not have been possible. We proceeded to test this hypothesis by designing an event arena-based flavour-place association task for mice.

Results:

Event Arena Based Flavour Place Association Paradigm in Mice:

Our experimental design consists of training the mice in a flavour-place association task in an event arena (*Fig1a*; See methods for complete description). Briefly, the event arena consists of a cuboidal sandbox with 5 sand wells. The task involves animal finding the correct location (sand well) that has the pellet. The animals are allowed to explore the arena for 120s to extract the food pellet from the correct location. The animals need to learn the correspondence between the flavour and the location. Once in event arena, the animal explores and learns to associate the location of the reward sand wells and the corresponding flavour presented at the start of the trial (see methods and Shruthi et al 2022). The locations of the sand wells are chosen to minimise rotational symmetry. The arena has 2 distinct intra-maze cues that defines the context.

Training consists of multiple sessions. Each session consists of 5 trials, one for each flavour-place pair. During the training phase, the animals need to learn 5 distinct flavours and their corresponding locations in the arena. The flavour-location pair is kept unique and consistent throughout the experiment. The sessions are separated by at least 2 days and trials are separated by 45-60 mins. The start boxes as well as order of flavours presentation are randomised, while maintaining a consistent flavour-to-location correspondence across all the trials and sessions.

The performance of the animals is recorded in the form of errors (number of incorrect locations scratched/dug in a trial) they make during training. We observe that the errors progressively reduce across sessions (*Fig1b*). An important measure in learning is the strength of memory. It is typically assessed by measuring the perseverance of the animal in exhibiting the correct response during a probe trial (cued but not rewarded). On the day of the probe trial, the animals are cued with a flavoured pellet outside the arena (just as training), but there is no food reward at the correct location. In practice, we place food pellets corresponding to all the five flavours below a mesh in all the wells to prevent animals being drawn to the location by the odour cues (*Fig1c*; See methods for complete description of flavour pellet preparation and reward well construction). The memory strength of the animals is assessed by estimating the percentage of time they spent digging at the correct location and comparing it with random chance (for 5 wells, chance being 20%). We interspersed probe trials to test the strength of memory on the 11th, 18th and 21st sessions, labelled PT1, PT2 and PT3, respectively. The percentage dig time at the correct location is then compared across different probe trials and with the chance factor. As can be seen from *Fig1d*, the mean percentage dig time at the correct location progressively increased from PT1 to PT3, indicating that the memory strength progressively increases with training (ANOVA, n=55, F-Value=5.5933, p= 0.006307). The animals dug a significantly larger fraction of time at the correct location compared to the random chance on the PT3, while on both PT1 and PT2, the percentage dig time at the correct location is at chance (PT1: t-test, p =0.7684; PT2: 0.7899). Thus, it took approximately 21 training sessions to learn the five flavours and their corresponding locations for mice. Our choice and composition of flavours as well as the sand well locations with respect to two intra maze cues and other cues are such that the animals acquired all these flavours equally well (ANOVA, F-Value=1.0153; p= 0.40421; supplementary information1). From these observations we establish that mice can perform in an open event arena and learn five distinct flavour-place associations bound by the same context. We refer to this configuration of event arena as Map #1.

Prior knowledge facilitates acquisition of new information of equal complexity *only when presented in relation to it:*

In our task, the mice need to learn the association between flavour and sand well locations, and thereby the spatial relationships between these locations within the arena. We note that whenever the mice reach a particular location, the distances from the cues that define that location are reinforced irrespective of it being correct and rewarded or incorrect and hence not rewarded. This owing to the requirements of learning both correct as well as incorrect choices in discrimination training. Thus, we hypothesise that these implicitly acquired relations between locations along with explicit flavour-place pairs can act as *mental schema*. We then argued if this was to be true, then, new information when presented *in relation to prior knowledge* should result in faster acquisition (Tse et al. 2007). Specifically, we asked if schema-based learning can facilitate in acquiring not just a few additional paired associations (as shown by Tse et al. 2007), but rather an entirely new event arena configuration (referred to as Map#2). The configuration of associations in the new context (Map#2) is such that it does not share any common features (intra-maze cues, flavours, reward locations/sand wells) with Map#1. In such a scenario we proceed to test if the animals i) can learn such a new map and

ii) does the rate of learning depends on prior knowledge. There can be three possible outcomes – (a) there is no overlap between old and the new map memories. In that case, the new learning should be like the learning of the initial map (Map#1); (b) Map#1 information content is at the upper limit of cognitive load handling capacity of the animal. This will lead to new learning being impaired; and (c) old memories can assist in learning of the new map at a rapid rate.

In order to test this, we trained animals (that have already learnt Map#1) to learn an additional set of five flavour-place associations in two different routes : (i) **Solitary Learning:** The new set of flavours corresponding to new sand well locations in a new context defined by altogether new visual cues (i.e. Map#2) are presented for training with no explicit reference to Map#1 (ii) **Relational Learning:** Making use of the extensible nature of the behavioural paradigm, Map#2 is arrived through graded changes in Map#1. We introduce a representation to describe such modifications in our various training paradigms. Each arena configuration can be written as a set of alpha-numerals. The alphabets represent the intra-maze cues and the numerals represent the unique flavour-location pair. Thus, the animals having learnt Map#1 (represented as AB12345) are trained on CD67890 directly for solitary learning group. The relational learning group went through AB12367, AB12678, AB67890, AC67890 and then to CD67890. After each of the modification to the map (in relational learning grp), the mice underwent two training sessions on that configuration before the next modification is introduced. The training paradigm and the maps involved are illustrated at the bottom of *Fig2a and Fig 2c*.

The relational group progressed with faster acquisition of Map#2 compared to the solitary learning group (*Fig2a and Fig2c*). We conducted a probe trial to compare the memory strength after 6 training trials before changing the visual cues for relational learning group. Our probe trial results (*Fig2b PT1*) showed that the animals learnt new flavour place associations in the relational learning group (n=8, t-test, p=0.03806). Following this, we changed the intra maze cues to eliminate any residual relationships from Map#1 thus resulting in a Map#2 configuration. At this point, it is important to note that both solitary and relational groups have the identical maps (Map#2 with CD67890 configuration). *Fig2b PT2* shows the percent dig time for the probe trials conducted at the end of 10 trials. The animals that underwent relational learning dig 29.4 % at PT 1 and 33.5% at PT 2 conducted before and after change of visual cues, indicating that they dig preferentially at the correct locations and perform above chance. On the other hand, the solitary group animals dig 24.18 % at PT 1 and 23.9% at PT 2 (conducted after equal number of sessions as that of the relational learning group). We see that the solitary learning groups dig at correct locations only by chance (*Fig2d*), as the mean % dig at correct location is not significantly different from the chance factor of 20% (n=7, t-test, p=0.535). This demonstrates that the animals acquire the new Map#2 faster only when presented in relation to the previously acquired Map#1 (in a graded manner). This suggests not only that mental schema can facilitate faster acquisition of related information, but also that new information only when presented in relation to pre-existing schema (relational group) and not otherwise (solitary group) can facilitate acquisition of a complex multitude of new information.

Graded Presentation is not Sufficient to Facilitate the Acquisition of Schema:

Next, we reasoned that the enhanced CLHC we observed in the relational group could have originated from the novel information presented in smaller "chunks" rather than being assisted by previous learning as we hypothesised earlier. To test this, we ran another group where the animals (that are handled, habituated and shaped along the other group) are directly trained for flavour-place associative pairs of Map#2 in a graded manner with the key difference of never undergoing training for Map#1. Note this mimics the relational learning group's training process. As per the experimental design, for the first two trials, the animals were

presented with two flavours (ABxxx67), followed by addition of one more novel flavour pair (ABxx678) on the 3rd and 4th trial and finally having all the five flavours (AB67890) during 5th and 6th trial (similar to the relational learning group *except no prior schema for Map#1*). We argued if the prior memory were not to play an effect and the presentation of new information in small chunks was sufficient for rapid learning, we should see faster and complete acquisition of all five flavour-place associations in this control group.

Fig3a shows the performance of these mice scored using the error measure as function of sessions. We observed a rapid initial learning followed by a plateau and then a decline in their performance. We assessed the strength of memory using probe trials similar to the other (relational and solitary) experimental groups. The animals learnt to associate the flavour and their location during the initial two trials. When probed for their flavour-location memory, the animals were able to retrieve the two paired-associates remarkably well (n=10, t-test, p=0.001) and their performance was well above chance (*Fig3b PT1*). However, training the animals on subsequent days with additional flavours resulted in an initial plateauing followed by the decline in their performance at the end of session #6 (*Fig3a)*. We conducted a probe trial following 6 sessions of training on this regime. As shown in *Fig3b PT2*, the performance of these animals after training for all five paired associates dropped to chance (n=9, t-test, p=0.532). We were surprised to find the performance at the second probe trial to be at chance given the above-chance performance of these animals during the first probe trial. So, we segregated our second probe trial performance data in two sets (i) for the initially presented flavours for which the animals had memory during PT1(in Session#1 and Session#2) and ii) for the remaining three flavours. Since our training paradigm involved extensive randomisation of the order of presentation of flavours and start box locations, both these sets comprised of all flavour and location identities and devoid of flavour/location identity specific effects. Much to our surprise we observed that the performance for even the old flavours (that the animals have shown memory for during the first probe trial) was at chance at the end of incremental training (*Fig3c*| n=8, ANOVA, t-statistics=1.2957, p=0.237). This suggests that the increase in the number of flavours in subsequent trials probably resulted in memory interference. Put together, our results indicate that presentation of new information in small chunks did help initially but was not sufficient to encode the entire set of five associations in mice. Further, we also conclude that training in small chunks without any assistance from preformed schema is prone to interference.

This together with our results from relational and solitary training studies argues that the faster learning we see for a subset of flavour pair associates could be due to the "chunking" but they fail to encode any subsequent associations. Given these observations we infer that schema avoids catastrophic forgetting by helping the animal encode multitude of information while still preserving recently acquired prior knowledge.

Generalisation does not reduce the CLHC:

Generalisation is thought to be mechanism to reduce the memory overload through formation of a representation that abstracts and represents many related memory event (Reinert et al. 2021). This phenomenon has been postulated as one of the ways in which our brain links different life experiences together hence making learning similar information easier (Richards et al. 2014). Here we investigated if providing enough time for a small chunk of a complex memory to consolidate (Anagnostaras, Maren, and Fanselow 1999) can help in enhancing the cognitive load handling capacity for subsequent learning without a need for a preformed mental schema. We trained a group of animals in two flavour place association for two days and tested their memory in probe trails administered on third day (*Fig3d*). *Fig3e PT1* shows the above chance performance of the animals in the probe trial (n=8, t-test, p<0.001). Following this, the animals were let to rest in their home cage for 20 days. After 20 days, the animals were tested

for the remote retrieval following a one session of reminder training. Following the reminder, the animals clearly showed distinct and above chance digging at the correct location as compared to incorrect locations (*Fig3e PT2;* n=10, t-test, $p<0.001$). Following this, we trained the animals on the incremental training regime wherein the map is populated with new flavour-place associates every 2 days. When tested for memory of these flavour pairs after 4 days of training, their performance was at chance (*Fig3e PT3;* n=9, t-test, p=0.287). This trend was similar to the Incremental learning group discussed earlier. These results illustrates that a long rest period (for memory consolidation) does not help with rapid learning in future if the learnt set was not rich/complex enough (just 2 PAs). When we persisted with the training of this group of animals for a similar duration to our original Map#1 training, the animals exhibited above chance performance for all the 5 flavour pairs (*Fig3e PT5;* n=8, t-test, p=0.008).

Generation of Context Relevant Novel Responses:

Having shown that prior schema plays a facilitating role when acquiring new information, we wanted to ask if the same framework can be used to help animals navigate in novel scenarios derived from previous experiences. This sets a platform for thinking about "problem-solving like behaviour" in rodent research. Specifically, we were interested in knowing if the animals can deduce the correct location of the food pellet in a novel hitherto unknown schematic layout that is implicitly related to previously exposed maps.

To test this, we exposed relational and solitary learning groups (that were exposed to both Map#1 and Map#2 equally) to a new configuration (CD12345; Map#3). This is a new map that the animals have not experienced before however, this can be derived from information from the previous Maps. We generated this map by taking the flavour-location pairs of Map#1 (xx12345) and then placing them in the context of Map#2 (CDxxxxx), thereby making a new hybrid configuration to which the animals have never been exposed before (*Fig4e*). This will let us test if any of the experimental group be able to reorient themselves with respect to new cues and dig at the correct food location with no prior training on this map. The rationale behind such experimental design and setup is that both the groups have learned Map#1 and have been exposed to Map#2 equally (10 sessions). We proceeded by performing probe trials for flavours #4 and #5 while training the mice in flavours 1 to 3 to prime and reduce anxiety caused because of a novel map.

We discovered that the animals from relational learning paradigm were able to solve the hybrid configuration by visiting the correct location significantly more often than the incorrect location (*Fig4b*; n = 8, Mann-Whitney U Test, U-value =14, critical value of U at $p<0.05$ = 15, Z score = 1.83787, p =0.03288). This trend of performance was absent in the animals that underwent solitary learning paradigm (*Fig4b*; n = 7, Mann-Whitney U Test, U-value =17, critical value of U at $p<0.05$ = 11, Z score = -0.89443, p =0.18673). We wanted to further substantiate if this performance is due to animals' ability to relate the new visual cues with the Map#1 flavour-location associates or through other cues. This is critical to our hypothesis. One way to test this is through removing the visual cues and testing for their performance. When the visual cues were removed, both the relational as well as solitary learning group animals failed to perform the task. Specifically, the relational learning group went significantly less to the correct location (n = 8, Mann-Whitney U Test, U-value =14, critical value of U at $p<0.05$ = 15, Z score = 1.83787, p =0.03288) and the solitary leaning group animals went to the correct location not any different from incorrect and not different from when the visual cues were present (n = 7, Mann-Whitney U Test, U-value =14, critical value of U at $p<0.05$ = 11, Z score = -1.27775, p =0.10027). These results demonstrate that the relational group animals are indeed using the intra maze landmarks from Map#2 to solve the problem while the solitary group animals, although trained for same duration on Map#1 and Map#2 are unable to do so.

We reasoned that if the animals were really using the cues to reorient themselves apart from showing a dependence on the visual cue, the errors they make should have the signature of them solving through reorienting themselves in space. In other words, since the animals are learning the remapping of the locations in space, we argued the digging pattern should reflect the animal's confidence in a reward location. This can be tested by measuring the time they spent digging at different locations as a function of distance from the correct reward location. In order to do so, we ranked the different reward locations on the basis of their distance from the correct location (rank refers to spatial proximity). Upon analysis, we can clearly see a progressive downward trend for the relational learning group (*Fig4c*), reflecting a convergent behavioural strategy, where the confidence of the animals on different location goes down as we move further away from the correct location. However, in the solitary learning group, the animals did not exhibit such linear decrease in digging percentage as a function of spatial ranks (*Fig4d*). In fact, it seems that in this problem-solving task, the animals give equal weightage to every location (*Fig4d*). Next, we probed if such relationship is true when distance in measured in continuous space. We did this through generating residence time maps (heatmaps) that represent the time the animal spent in each spatial location with the correct location being the origin. The resulting heatmaps (*Fig4e*) for relational and solitary group clearly demonstrate the selective search exhibited by the animals (the bright centre spot) and progressive decline in the intensity of these search in space.

Development of Physiologically Relevant ANN that Emulates Mental Schema Formation: Our observations from the above experiments showed that future learning can utilise/benefit from pre-existing organised memory frameworks. The key component in high cognitive load handling was avoiding interference. This is analogous to catastrophic forgetting in artificial neural networks (ANNs) (French 1999; McCloskey and Cohen 1989). Hwu et. al. proposed a contrastive Hebbian learning ANN that is physiologically closer to neural communication as opposed to backpropagation based ANNs (Hwu and Krichmar 2020; Baldi and Pineda 1991; Movellan 1991; O'Reilly 1996; Ororbia and Mali 2019). In principle, they achieved this by allowing only a few nodes to participate in a learning for a specific kind of stimulus. This is inspired from the idea of different engrams differentially encoding various associations (Cai et al. 2016). We adapted their network architecture to recapitulate the behavioural results we obtained in our experiments. Such an experiment inspired theoretical framework can help us design more targeted intervention studies in future. The architecture and training protocols are explained in supplementary information 2.

In short, the ANN oscillates between 2 phases namely- (a) a fast-learning "*hippocampus stream*" which operates on Hebbian update for learning and (b) a slow learning "*schema/cortical stream"* with contrastive Hebbian updates and hippocampus activation from the fast-learning phase as the teacher signal. The whole architecture of the network is made up of multiple layers and their utilization is dependent on the active stream and the learning phase of the network (*Fig5a*). The network has 3 inputs to it: a context pattern (representing the contextual configuration of the task), a flavour, and the correct location associated with that flavour. The input context pattern (equivalent to the learning Map in our animal studies) is represented by a 2-dimensional grid with 25 elements (5 x 5). The unique reward locations along with all their relations with other elements are represented as an input value of 1 and the landmarks are represented with an activation value of 2 since landmarks have a significant influence on the context representation. All the remaining grid locations are set to a value of 0. The flavour is an 18-element array with each active element representing one of the 10 flavours used throughout the task. The action layer is similar in dimension to the context pattern with the difference that it only represents the correct location for a given trial as 1 while remaining locations are set to null. For more detailed description of the network architecture and training

regime, please refer to supplementary information 2. For our simulations, we started with 20 virtual mice assigned to 2 different groups (Relational learning and solitary learning). We allowed the animals to learn Map1 configuration for 21 days (same as our mice study) with probe trials conducted after same session as in our animal study. We then subjected them to two different training protocols as mentioned above. We observed that the network used the same nodes (during the CHL cortical stream) for the new map in case of relational learning and was able to assimilate the new information much faster (*Fig5c*). At the end of 10 sessions (to achieve Map2), similar to our results from earlier experiments, the virtual animals participating in solitary learning regime performed poorly as compared to the relational learning group (*Fig5d PT4*; n=10; paired t-test; n=10; t-statistics: -4.8413; $p<0.0001$). Moreover, when tested on the problem-solving configuration (Map3; flavour-location pairs from Map1 and intra-maze cues from Map2), we see similar results as that in our behavioural experiments (*Fig5d PT6*). The Relational learning group was superior in performance as compared to solitary learning group (n =10; paired t-test; t-statistics: -4.36769; p=0.0018). These comparable results are encouraging and can be used to formulate better invention studies in future that could look at the role of engrams in learning and memory in such complex task.

Discussion:

We establish a novel event arena based behavioural paradigm in rodents to test role of prior knowledge and adoption of different learning strategies on the acquisition of new information. We find that learning in relation to what is known already prevented the catastrophic interference and helped in problem solving task in mice. Heavy cognitive load has been shown to impede new learning (Kolibius, Born, and Feld 2020; Feld, Weis, and Born 2016). Our experiments show that the animals can learn a complex (> 5 paired associates as against 1 or 2) open maze paradigm only when it is presented in relation to prior knowledge.

Although different aspects of schema have been demonstrated in rats (Tse et al. 2007; Alonso et al. 2021; Wang and Morris 2010), here for the first time we test and show that mental schema facilitates acquiring a completely new map that is equal in content and complexity. We note this is quite different from acquiring just a couple of new paired associates. We reason this to be the plausible explanation for the animals initially having the memory for 2 flavours acquired just after 2 training sessions and losing them once new flavours are introduced. However, when the same scheme of training is provided for the animals that had prior learning, they are able to not only acquire faster but also were able to retain all the 5 paired associates. We interpret such an effect as demonstration of that mental schema enhancing cognitive load handling of an animal.

In the process of demonstrating the above, we also establish an event arena based task for investigating flavour place/location associations. Our setup consisted of a 1.4 m x 1.4 m arena with 5 reward wells and 2 intra-maze cues. Each well was associated with a uniquely flavoured food pellet and the animal was cued with the same flavour pellet outside the arena before the start of a trial. Over the course of the experimentation, with the help of probe (cued but unrewarded) trials, we show that mice were able to learn the maze and associate the cued flavour to its respective location in the arena by using the intra-maze cues.

Once the animals acquired the initial configuration of flavour-location associations with respect to the intra-maze cues (Map1), we tested the utility of a *"mental schema"* in these animals by gradually modifying Map1 to achieve a completely new configuration Map2

(termed relational learning). As a control, we also ran another group that, after learning Map1, was directly transferred to Map2 (termed solitary learning). This will allow us to understand the difference in learning with and without referencing acquired memories. We observed that the relational learning group acquired Map2 rapidly while solitary learning group remained at chance for the same duration of training on new map.

Since our relational learning group was presented with only few changes per trial, the rapid learning behaviour can be result of chunking (Burtis 1982; Gobet and Clarkson 2004). To investigate role of chunking, we designed the *"Incremental learning group*". Please note that this is a naïve experimental group that was never trained on Map1. We started by giving the animals only 2 associations in the arena which they learnt rapidly. Following this, we added 3 more unique associations (while keeping the old associations intact). Once the animals were trained for 2 days on the final configuration (similar to the training procedure for relational learning group), we performed another probe trial. Careful dissection of probe trial revealed that not only the animals failed to learn all the 5 flavour-place associations, but they also seem to have forgotten the previously learnt 2 flavour place association. These results suggest catastrophic forgetting due to memory interference (Navarro Lobato et al. 2023).

Put together the result from relational, solitary and incremental learning group we argue that having a rich memory association network allows for faster acquisition, increases high cognitive load handling capacity and avoids memory interference from similar associations acquired in close temporal windows.

Since incremental learning group was successful in learning the initial 2 association pairs quickly, we were intrigued to test if this coupled with system consolidation was enough to have the effects observed in relational learning group. We trained a group of animals on 2 flavour-place associations and then gave them a long rest (20 days). In rodent literature, this duration has been shown to be tightly associated with system consolidation (Li et al. 2023; Bonaccorsi et al. 2013; Terranova et al. 2023; Frankland and Bontempi 2005; Kim and Fanselow 1992). Following the rest period, the animals were brought back to the arena, given a reminder training and tested for their memory of the task. The animals performed above chance for the task. We proceeded with the next additions of new flavour-location associations (similar to that in incremental learning and relational learning paradigm) and observed the same result as that in incremental learning paradigm. The animals not only failed to acquire the new flavour-location association, but it seems that the already acquired associations were compromised as well. This leads us to conclude that the effect we see in relational learning group cannot simply be explained by system consolidation or chunking but in fact must be some higher order cognitive framework like mental schema. Although we acknowledge that it requires meticulous intervention studies in future to truly understand the role of system consolidation in this group. To rule out the possibility that this maybe an animal group that may be incapable of learning a complex arena setup like this, we kept on training these animals on the Map1 configurations and eventually after 20 sessions, we could demonstrate that the animal group could acquire the new map and perform above chance during probe trials.

Mental schema has been postulated to be the framework for knowledge and has been implied in decision making and problem solving (van Kesteren et al. 2012; Sweller 1988; Brewer and Treyens 1981; Lewis and Anderson 1985). Since our results suggest that mice might be using similar abstract structure, we wanted to investigate if our 2 groups (one

presented/trained explicitly in relation to prior knowledge i.e. relational learning group and another without explicitly making this relation apparent i.e. solitary learning group) can exhibit differences in problem-solving scenarios. We created a hybrid map by merging visual cues from Map2 with flavour-place associations with Map1. We observed that the relational learning group performed significantly better in solving this hybrid map as compared to solitary learning group. Furthermore, when intra maze cues were removed from the arena, performance of both the groups dropped to chance. This argues that the animals were using the visual cues from another map to orient themselves in this hybrid configuration.

It has been postulated and substantially shown that different engrams are formed for perceptually and cognitively different learnings while similar engrams encode seemingly similar cues overlapping in time. Inspired from this literature, Hwu et. al. (Hwu and Krichmar 2020) created a contrastive Hebbian learning based artificial neural network that tries to recapitulate the behavioural results of Tse et. al. (Tse et al. 2007) work for mental schema and memory consolidation. The major advantage of this architecture and mode of learning was two-fold. Firstly, the network adjusts for the errors without backpropagation and unlike back propagation it is more biologically plausible. Secondly, the network suggests a solution for catastrophic forgetting problem by ensuring that different artificial engrams encode for starkly different/ novel information. We leveraged this network with a few modifications to test on our dataset. We demonstrate that we were able to engage the same artificial engram for relational learning group while our engram switched for solitary learning group. Moreover, we were also able to demonstrate that this network can perform problem solving with a hybrid map just like our experimental animals for relational learning group. This is especially encouraging since it is consistent with the current narrative of how engrams encode new information and paves the way for future histological and intervention studies. Finally, the complexity and prolonged nature of the task rendered our attempts to investigate the neurological underpinnings through lesions futile. Studies in the future could discern out the brain regions involved in behaviour through passive observational studies that involves less invasive procedures.

Materials and methods:

Animals:

We used adult (5–6-month-old) C57BL/6J male mice from this study acquired from the Central Animal Facility, Indian Institute for Science. The animals were housed in pairs on a 12-h light/dark cycle. Before starting the experiment, one of the animals from each cage was briefly anaesthetized using 2% isoflurane and ear marked by making a small wedge cut on right ear. This helps us to identify them during the experimental run. The study is performed in accordance with the animal protocol approved by the Institute Animal Ethics Committee, Indian Institute for Science, Bengaluru.

Event Arena:

The main design of the event arena was inspired form the study by Tse et. al (Science, 2007). We adapted their design and made significantly design changes to adapt the setup to our experiments in rodents. Event arena consists of a 104 x 104 x 15 cm roofless cuboid box with 4 entry/starting boxes in the middle of each side. The floor of the arena is covered with fresh sand up to a height of 1-2 cm. The arena is held on metal frame and enclosed with an outer larger box to avoid animals using any external cues from the room. Animals' behaviour was recorded using a HD camera mounted on the roof of the external box. The reward wells (digging sites for animal to acquire reward) were placed in arena to avoid any rotational symmetry. The position and number of these reward wells and intra-maze landmarks depends on the experimental run.

Habituation:

The mice are handled twice daily on top of their home cage for (6–10 days) to wean off any anxious escape behaviours and acclimate them to human handling. Following this, the animals are allowed to explore the arena with food pellets randomly scattered throughout the arena. Habituation is deemed complete once the animals stop wall hugging and freely exploring the centre of the arena.

Food restriction:

The food restriction was implemented in a gradual manner with restricting them to two pellets per mouse per day for 1st week and then tapering it down to 1 pellet per mouse per day for next few days. Once the experimenters are sure that the animals have acclimated to the regime, the animals were started on shaping and training protocols. On experiment days, the animals are given only 1 pellet per mouse outside of the experimental arena while on off days they are fed 2 pellets per day. Experimenter kept a close watch on the animal behaviour and if any animal exhibited lethargy and hunching, the animal was given more food and excluded from the experimental run till recovery.

Shaping:

Our experimental design relies on the animals to dig the favoured pellet from under the sand. To induce digging behaviour in the animals, we perform shaping. To begin with, the animals are presented with food reward on the top of sand wells. Note that there is no flavour present in the food pellets for shaping trials. The food pellet is then gradually lowered into the sand

well on subsequent shaping sessions. The shaping is considered completed when the food pellet reaches the bottom of the sand well (3 cm deep) and the mice are able to retrieve the pellets.

Flavour pellet:

The flavoured food pellets were prepared inhouse by mixing flavours to ground up rodent feed (NutriLab Rodent Feed, Provimi) and then extruding the paste into pellets of desired sizes. The pellets were allowed to dry in an oven for 4 hours. All the procedures were performed in a semi-sterile environment. Fresh pellets were made every week. The pellets were labelled and stored in air-tight containers and stored in dry and dark conditions. The various flavours used for the experiment are as follows:

S. No	Flavour	Supplier	Concentration (w/w)
1.	Basil	Snapin, Duval enterprises Pvt. Ltd.	1%
2.	Cassia	Arvind Trading Company	0.50%
3.	Cocoa	WeikField, Weikfield foods Pvt. Ltd.	1%
4.	Cumin	Everest, S. Narendrakumar & Co.	1%
5.	Dry Mango	Everest, S. Narendrakumar & Co.	1%
6.	Elaichi	Arvind Trading Company	1%
7.	Fenugreek	Eastern, Eastern Condiments Pvt. Ltd.	1%
8.	Ginger	Snapin, Duval enterprises Pvt. Ltd.	1%
9.	Rosewhite	Bush, International Flavors and fragrances India Pvt. Ltd.	1% (v/w)
10.	Thyme	Keya, Keya Foods International Pvt. Ltd.	0.50%

Training protocol:

Every experimental run is called a session which comprises of 5 individual trials with non-repeating pseudo-randomly assigned flavour-place pair per trial. Note that the relationship between a flavour and its corresponding location in the arena never changes over the course of the experiment while the sequence in which the pairs are presented and site of entry to arena is randomized per session per mice. At the start of a trial, the animal is presented with the cue flavoured pellet and allowed to consume the pellet for about 20 sec. Following this, the animal is dropped at the randomly assigned site of entry and the session begins as soon as the animal leaves the start box and enters the arena. The mice are given 120 seconds to find the correct pellet and if the animal fails, the experimenters suggest the correct location and give then an extra 30 seconds to retrieve the pellets. After the mouse has dug and retrieved the pellet, it has 10–15 s to consume the food reward before it is returned to the home cage. Once the trial is over, next correct reward well is baited and all the reward wells are replaced with fresh ones. The sand is sprayed with 70% alcohol, sand is shuffled and flattened to remove any odour or visual track cues.

In general, the experiments are run such that there is at least 45 min delay between each trial for any given mouse.

Cued probe trials:

We test the strength of the memory using cued probe trials wherein the animal is cued while the correct location is devoid of any food reward. This ensures that there are no olfactory cues helping the animal arrive at the correct location. If the animal is certain of the correct location, they revisit the location over and over and spend significantly more time digging at the location despite no food pellet being there. To avoid extinction, the probe trials are run for only 60 sec and the experiments rewards the animal at the correct location with the correct flavoured pellet at the end of the probe trial. Performance during probe trial is measured as the percentage of digging time at the correct location over the total digging time for the trial.

Artificial Neural Network training:

The neural network was custom written in MATLAB 2014 and was run on a i5-32GB-CPU. The data input for various learning setups is provided in supplementary information 2.

Data and code sharing

Data and code for the study can be shared after acceptance of the manuscript upon a reasonable request to the authors.

References:

Alonso, Alejandra, Levan Bokeria, Jacqueline van der Meij, Anumita Samanta, Ronny Eichler, Ali Lotfi, Patrick Spooner, Irene Navarro Lobato, and Lisa Genzel. 2021. "The HexMaze: A Previous Knowledge Task on Map Learning for Mice." *ENeuro* 8 (4): ENEURO.0554-20.2021.

Anagnostaras, S. G., S. Maren, and M. S. Fanselow. 1999. "Temporally Graded Retrograde Amnesia of Contextual Fear after Hippocampal Damage in Rats: Within-Subjects Examination." *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 19 (3): 1106–14.

Asch, Solomon E. 1969. "A Reformulation of the Problem of Associations." *The American Psychologist* 24 (2): 92–102.

Baldi, Pierre, and Fernando Pineda. 1991. "Contrastive Learning and Neural Oscillations." *Neural Computation* 3 (4): 526–45.

Bartlett, Frederic Charles. 1932. "Remembering: A Study in Experimental and Social Psychology." *Https://Psycnet.Apa.Org › Recordhttps://Psycnet.Apa.Org › Record* 317. https://psycnet.apa.org/fulltext/1995-98505-000.pdf.

Bonaccorsi, Joyce, Simona Cintoli, Rosa Mastrogiacomo, Sigrid Baldanzi, Chiara Braschi, Tommaso Pizzorusso, Maria Cristina Cenni, and Nicoletta Berardi. 2013. "System Consolidation of Spatial Memories in Mice: Effects of Enriched Environment." *Neural Plasticity* 2013 (July): 956312.

Brewer, William F., and James C. Treyens. 1981. "Role of Schemata in Memory for Places." *Cognitive Psychology* 13 (2): 207–30.

Burtis, P. J. 1982. "Capacity Increase and Chunking in the Development of Short-Term Memory." *Journal of Experimental Child Psychology* 34 (3): 387–413.

Cai, Denise J., Daniel Aharoni, Tristan Shuman, Justin Shobe, Jeremy Biane, Weilin Song, Brandon Wei, et al. 2016. "A Shared Neural Ensemble Links Distinct Contextual Memories Encoded Close in Time." *Nature* 534 (7605): 115–18.

Carmichael, L., H. P. Hogan, and A. A. Walter. 1932. "An Experimental Study of the Effect of Language on the Reproduction of Visually Perceived Form." *Journal of Experimental Psychology* 15 (1): 73–86.

Day, M., R. Langston, and R. G. M. Morris. 2003. "Glutamate-Receptor-Mediated Encoding and Retrieval of Paired-Associate Learning." *Nature* 424 (6945): 205–9.

Farovik, Anja, Ryan J. Place, Sam McKenzie, Blake Porter, Catherine E. Munro, and Howard Eichenbaum. 2015. "Orbitofrontal Cortex Encodes Memories within Value-Based Schemas and Represents Contexts That Guide Memory Retrieval." *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 35 (21): 8333–44.

Feld, Gordon B., Patrick P. Weis, and Jan Born. 2016. "The Limited Capacity of Sleep-Dependent Memory Consolidation." *Frontiers in Psychology* 7 (September): 1368.

Frankland, Paul W., and Bruno Bontempi. 2005. "The Organization of Recent and Remote Memories." *Nature Reviews. Neuroscience* 6 (2): 119–30.

French, Robert M. 1999. "Catastrophic Forgetting in Connectionist Networks." *Trends in Cognitive Sciences* 3 (4): 128–35.

Gobet, Fernand, and Gary Clarkson. 2004. "Chunks in Expert Memory: Evidence for the Magical Number Four ... or Is It Two?" *Memory (Hove, England)* 12 (6): 732–47.

Heath, Richard A. 1979. "A Model for Discrimination Learning Based on the Wagner-Rescorla Model." *Australian Journal of Psychology* 31 (3): 193–99.

Hwu, Tiffany, and Jeffrey L. Krichmar. 2020. "A Neural Model of Schemas and Memory Encoding." *Biological Cybernetics* 114 (2): 169–86.

Kesteren, Marlieke T. R. van, Dirk J. Ruiter, Guillén Fernández, and Richard N. Henson. 2012. "How Schema and Novelty Augment Memory Formation." *Trends in Neurosciences* 35 (4): 211–19.

Kim, J. J., and M. S. Fanselow. 1992. "Modality-Specific Retrograde Amnesia of Fear." *Science (New York, N.Y.)* 256 (5057): 675–77.

Kolibius, Luca D., Jan Born, and Gordon B. Feld. 2020. "Vast Amounts of Encoded Items Nullify but Do Not Reverse the Effect of Sleep on Declarative Memory." *Frontiers in Psychology* 11: 607070.

Lewis, Matthew W., and John R. Anderson. 1985. "Discrimination of Operator Schemata in Problem Solving: Learning from Examples." *Cognitive Psychology* 17 (1): 26–65.

Li, Zengmin, Dilsher Athwal, Hsu-Lei Lee, Pankaj Sah, Patricio Opazo, and Kai-Hsiang Chuang. 2023. "Locating Causal Hubs of Memory Consolidation in Spontaneous Brain Network in Male Mice." *Nature Communications* 14 (1): 5399.

Mao, Dun, Eric Avila, Baptiste Caziot, Jean Laurens, J. David Dickman, and Dora E. Angelaki. 2021. "Spatial Modulation of Hippocampal Activity in Freely Moving Macaques." *Neuron* 109 (21): 3521-3534.e6.

McCloskey, Michael, and Neal J. Cohen. 1989. "Catastrophic Interference in Connectionist Networks: The Sequential Learning Problem." In *Psychology of Learning and Motivation*, edited by Gordon H. Bower, 24:109–65. Academic Press.

McKenzie, Sam, Andrea J. Frank, Nathaniel R. Kinsky, Blake Porter, Pamela D. Rivière, and Howard Eichenbaum. 2014. "Hippocampal Representation of Related and Opposing

Memories Develop within Distinct, Hierarchically Organized Neural Schemas." *Neuron* 83 (1): 202–15.

Movellan, Javier R. 1991. "Contrastive Hebbian Learning in the Continuous Hopfield Model." In *Connectionist Models*, edited by David S. Touretzky, Jeffrey L. Elman, Terrence J. Sejnowski, and Geoffrey E. Hinton, 10–17. Morgan Kaufmann.

Navarro Lobato, Irene, Adrian Aleman-Zapata, Anumita Samanta, Milan Bogers, Shekhar Narayanan, Abdelrahman Rayan, Alejandra Alonso, et al. 2023. "Increased Cortical Plasticity Leads to Memory Interference and Enhanced Hippocampal-Cortical Interactions." *ELife* 12 (May): e84911.

O'Reilly, Randall C. 1996. "Biologically Plausible Error-Driven Learning Using Local Activation Differences: The Generalized Recirculation Algorithm." *Neural Computation* 8 (5): 895–938.

Ororbia, Alexander G., and Ankur Mali. 2019. "Biologically Motivated Algorithms for Propagating Local Target Representations." *Proceedings of the AAAI Conference on Artificial Intelligence* 33 (01): 4651–58.

Pavlov, P. Ivan. 2010. "Conditioned Reflexes: An Investigation of the Physiological Activity of the Cerebral Cortex." *Annals of Neurosciences* 17 (3): 136–41.

Pearce, J. M. 1987. "A Model for Stimulus Generalization in Pavlovian Conditioning." *Psychological Review* 94 (1): 61–73.

R. A. Rescorla, A. R. Wagner. 1972. "Theory of Pavlovian Conditioning: Variations in the Effectiveness of Reinforcement and Nonreinforcement." In *Classical Conditioning II: Current Research and Theory*, edited by W. F. Prokasy A. H. Black, 64–99.

Reinert, Sandra, Mark Hübener, Tobias Bonhoeffer, and Pieter M. Goltstein. 2021. "Mouse Prefrontal Cortex Represents Learned Rules for Categorization." *Nature* 593 (7859): 411–17.

Richards, Blake A., Frances Xia, Adam Santoro, Jana Husse, Melanie A. Woodin, Sheena A. Josselyn, and Paul W. Frankland. 2014. "Patterns across Multiple Memories Are Identified over Time." *Nature Neuroscience* 17 (7): 981–86.

Shridhar, Shruti, Vikram Pal Singh, Richa Bhatt, Sankhanava Kundu, and J. Balaji. 2022. "A New Paradigm for Investigating Temporal Order Memory Shows Higher Order Associations Are Present in Recent but Not in Remote Retrieval." *Experimental Brain Research. Experimentelle Hirnforschung. Experimentation Cerebrale* 240 (2): 611–29.

Sweller, John. 1988. "Cognitive Load during Problem Solving: Effects on Learning." *Cognitive Science* 12 (2): 257–85.

Terranova, Joseph I., Jun Yokose, Hisayuki Osanai, Sachie K. Ogawa, and Takashi Kitamura. 2023. "Systems Consolidation Induces Multiple Memory Engrams for a Flexible Recall Strategy in Observational Fear Memory in Male Mice." *Nature Communications* 14 (1): 3976.

Tse, Dorothy, Rosamund F. Langston, Masaki Kakeyama, Ingrid Bethus, Patrick A. Spooner, Emma R. Wood, Menno P. Witter, and Richard G. M. Morris. 2007. "Schemas and Memory Consolidation." *Science* 316 (5821): 76–82.

Wang, Szu-Han, and Richard G. M. Morris. 2010. "Hippocampal-Neocortical Interactions in Memory Formation, Consolidation, and Reconsolidation." *Annual Review of Psychology* 61 (1): 49–79, C1-4.

Explicitly Acquired Interrelations Among Mental Schema Reduces Cognitive Load and Facilitates Emergence of Novel Responses in Mice and Artificial Neural Networks.

Authors:
Vikram Pal Singh[1], Shruti Shridhar[1], Shankanava Kundu[1], Richa Bhatt[1], Balaji Jayaprakash[1*]

Affiliations:
1. Center for Neuroscience, Indian Institute of Science, Bangalore, India

*Corresponding Author
Email correspondence: jbalaji@iisc.ac.in

Figures and legends:

Fig1:

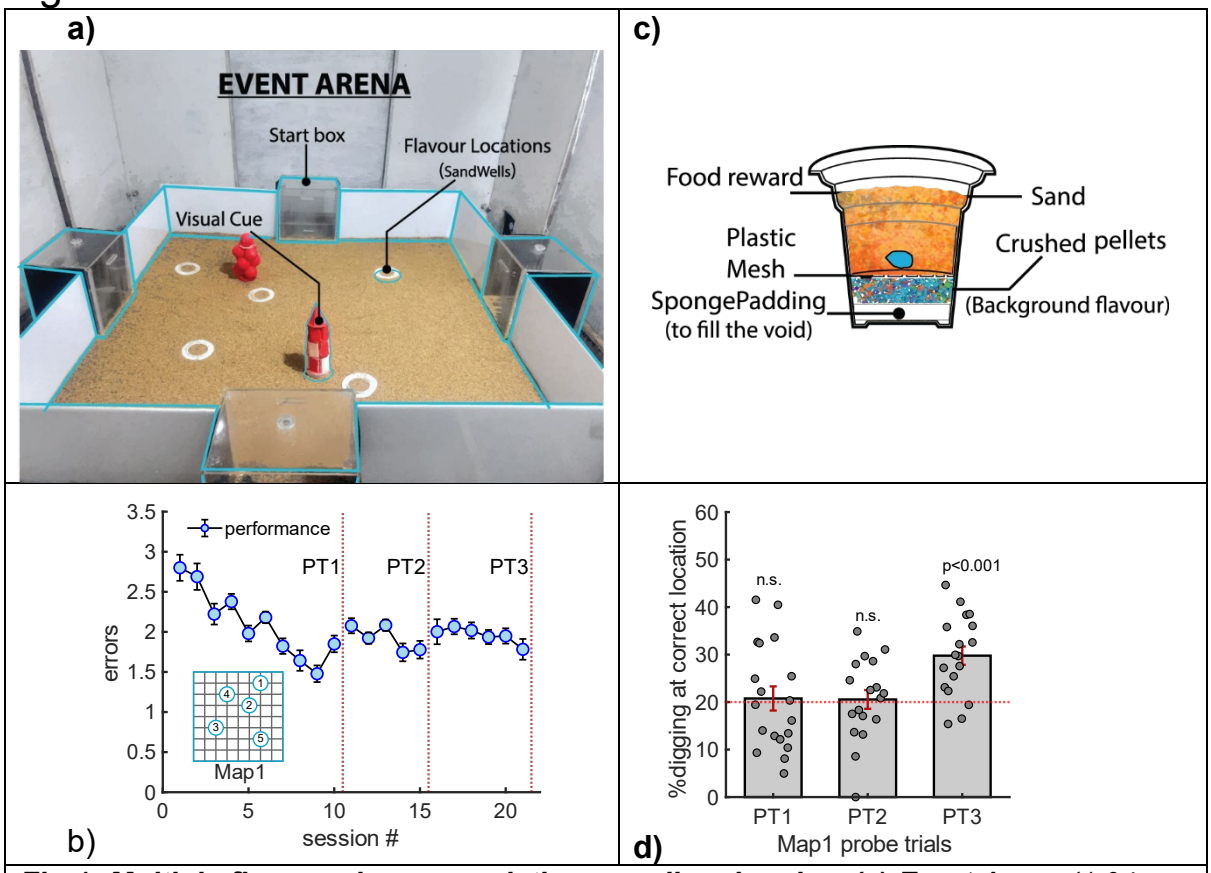


Fig 1: Multiple flavour-place association paradigm in mice. (a) *Event Arena (1.04 m x 1.04 m) with 5 sand wells accessible at any given point from the start boxes decided by the experimenter.* ***(c)*** *The custom designed sand wells with the base filled with crushed flavour pellets excluding the flavour on the mesh so as to produce same background odour across all the sand wells.* ***(b)*** *Acquisition of paired associates over a period of 21 sessions. Red dashed lines indicate the sessions corresponding to probe trials. The inset illustrates the configuration of flavour locations for Map#1.* ***(d)*** *The performance of the animals improves over time in a cued recall probe trial with performance significantly above chance after session 21 in PT3 (n=18, One Sample t-test, t-Statistics 4.91525, p=1.308 x 10^{-4}).*

Fig 2:

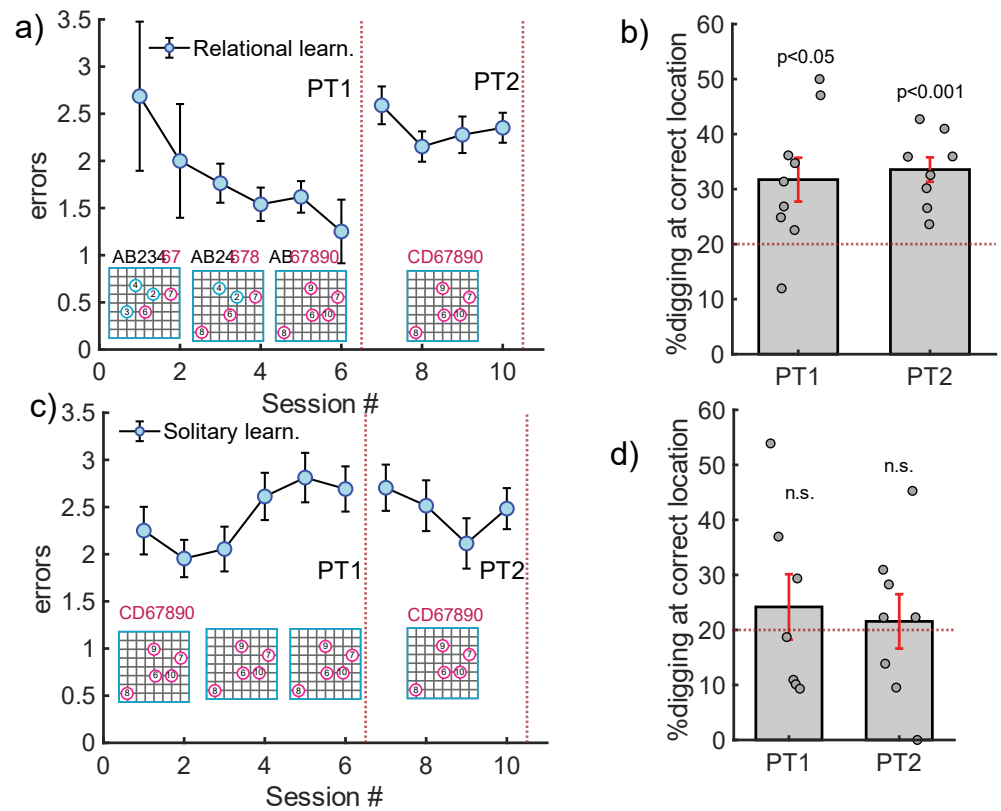


Fig 2: Acquisition of new flavour-location configuration (Map#2) *by the two groups of mice that were trained using two different approaches.* ***(a)****Schematic representation of the training protocol followed to train two performance matched group of animals on new flavour-place configuration (Map2). For one group, Map1 was gradually morphed into Map2 (Relational Learning) while other group was trained on new map from the beginning (Solitary Learning).* ***(b)*** *Performance of relational learning and solitary learning group. The red dashed lines indicate the sessions corresponding to the probe trials. (c)Relational learning group performs significantly above chance during the probe trial for the new map with old cues (n=8, unpaired t-test, t-statistics=2.55077, p=0.03806) and with new cues (n=8, unpaired t-test, t-statistics=5.75607, p=0.000694074). The solitary learning group was unable to acquire the new map after 10 days. This was confirmed by performing probe trials on day 6 (n=7, unpaired t-test, t-statistics=0.65832, p=0.53476) and day 10 (n=7, unpaired t-test, t-statistics= 0.72277, p=0.49702) of the training sessions.*

Fig3:

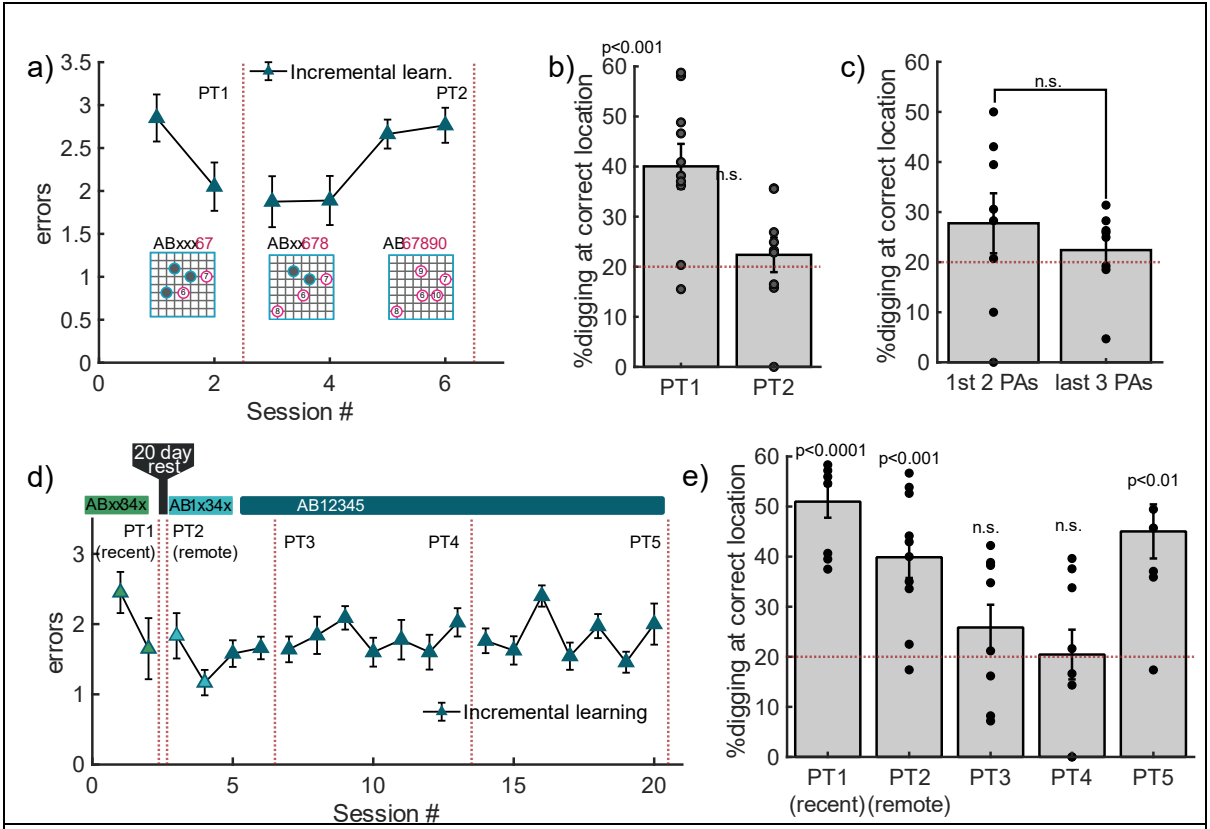


Fig 3. Acquisition of new flavour-place configuration (Map2) by incremental learning group mice. (a) *Performance of the incremental learning group. The red dashed lines indicate site of probe trial.* ***(b) The*** *incremental learning group performs significantly above chance after training for two flavour-location associations for two days (n=10, unpaired t-test, t-statistics= 4.46688, p=0.00156), but are unable to acquire the other 3 flavour-location associations which were presented over the next 6 days (n=9, unpaired t-test, t-statistics=0.6517, p=0.53287).* ***(c)*** *When we assessed their performance on the second probe trial, we could clearly see that the new flavour-location associations have not been acquired. (d)(e)*

Fig 4:

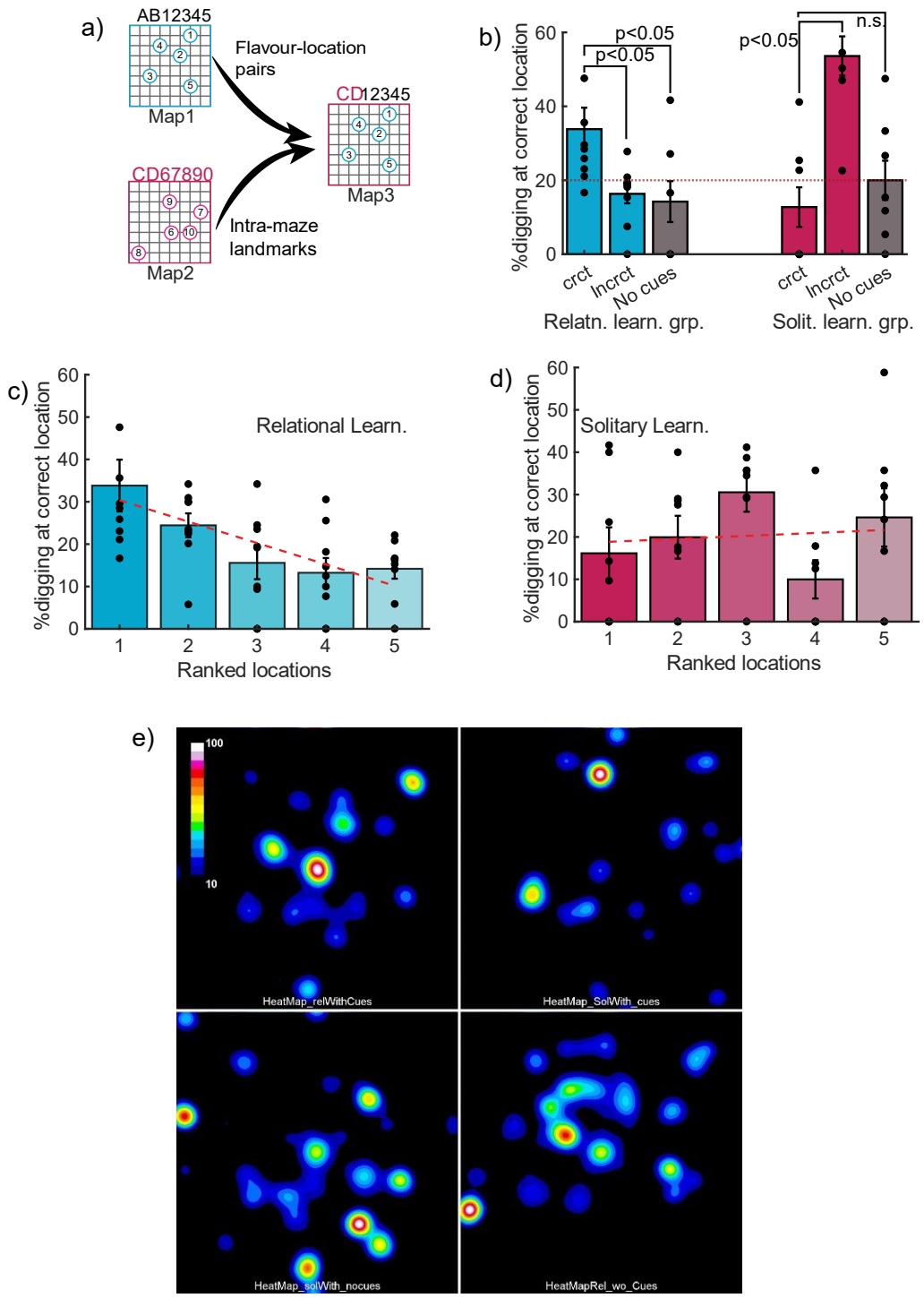


Fig 4: ***Performance of mice in a problem-solving task (a)*** *Schematic representation of the design for problem solving task. The favour-location associations were borrowed from Map#1 as it is the map learnt by both the group and visual cues were borrowed from Map#2.* ***(b)*** *The relational learning group mice visit the correct location significantly more often than the incorrect locations (n=8, Mann-Whitney U Test, U-value = 14, critical value of U at p<0.05 = 15, Z-Score = 1.83787, p=0.03288). Also, the difference in the animals' performance with and without cue is significant (n=8, Mann-Whitney U Test, U-value = 14, critical value of U at p<0.05 = 15, Z-Score 1.83787, p=0.03288), suggesting that animals*

indeed use the visual cues to navigate and arrive at the correct location. For the solitary learning group of mice, there is no significant difference in their visit to correct and incorrect locations; either with (n=7, Mann-Whitney U Test, U-value = 17, critical value of U at p<0.05 = 11, Z-Score = -0.89443, p=0.18673) or without cue (n=7, Mann-Whitney U Test, U-value = 14, critical value of U at p<0.05 = 11, Z-Score = -1.27775, p=0 .10027). ***(c)*** *Distance-wise ranking of flavour locations with respect to correct location in relational learning shows a downward trend suggesting that the animals follow neigh rest neighbour search pattern.; while* ***(d)*** *in case of solitary learning, they visit all the locations equally with no preference to the nearest neighbours.*

The residence time heat map during problem solving trial. The individual trials of the mice are tracked and re-oriented such that the center of the image (512, 512) corresponds to the correct food pellet location. As can be seen from the map the group of animals that were trained in relation to prior memory (top left) not only search more at the correct location compared to animals trained in solitary group with (top right) and without visual cues (bottom left) and relative group without the visual cues (bottom right). they search in the vicinity of the correct location. Each spot represents location of one or more search center where food well was located. After reorienting the map to have the correct location at 512, 525, the residence times were added at each pixel and entire image was normalised for highest occupancy.

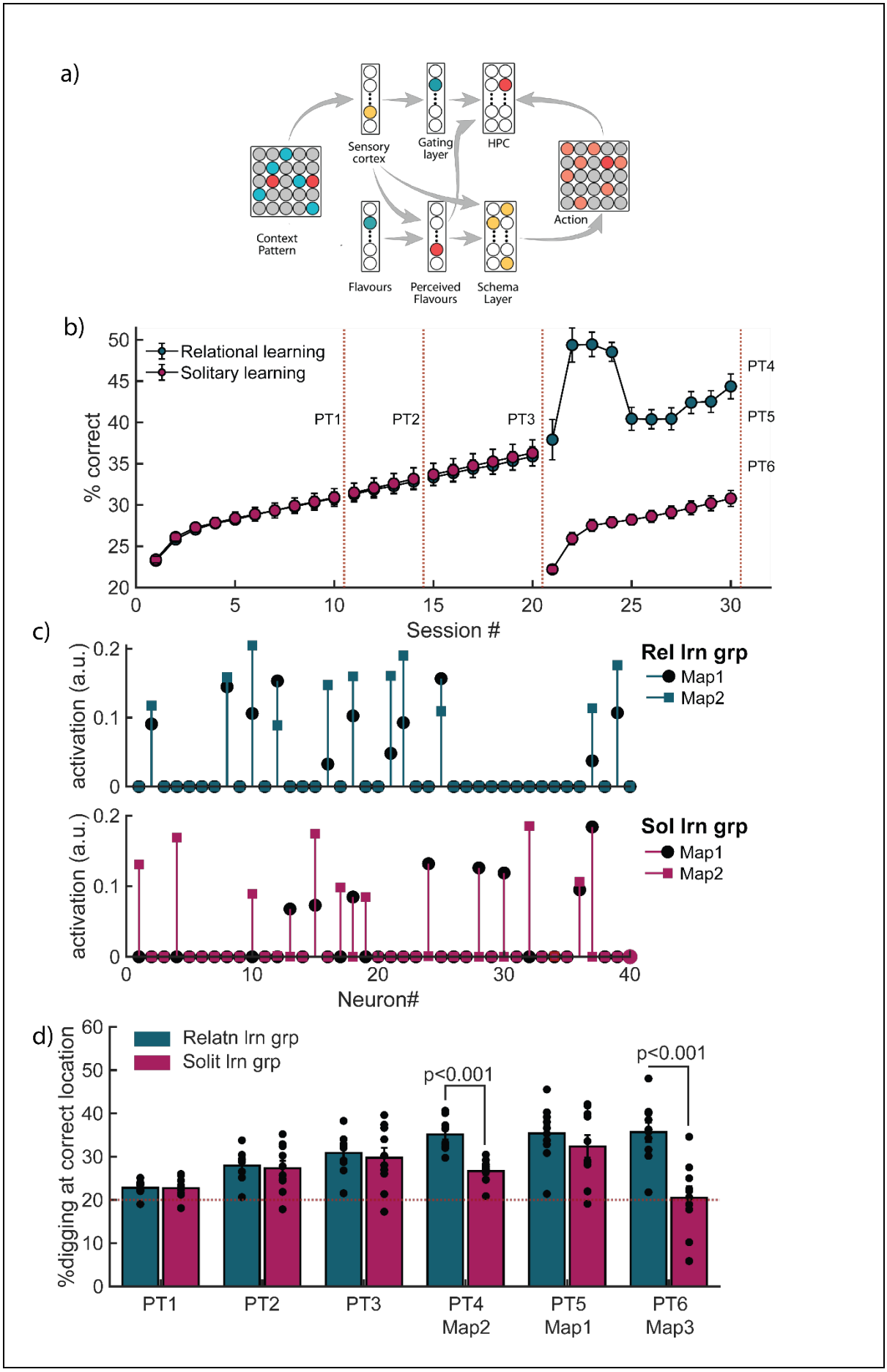
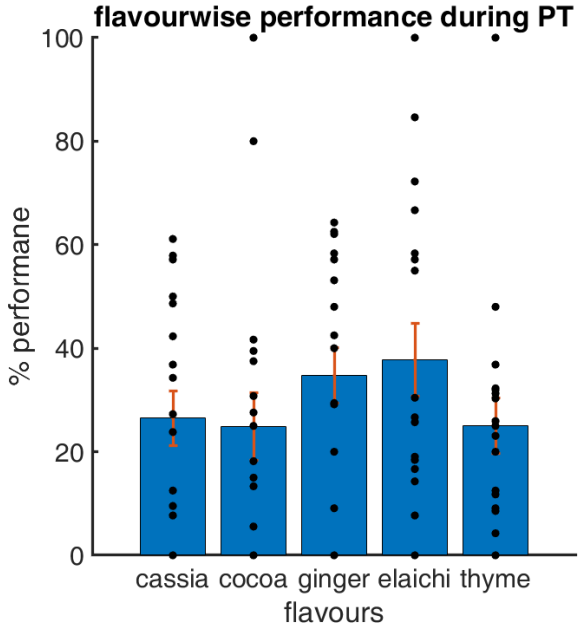

a)
Sensory cortex
Gating layer
HPC
Context Pattern
Action
Flavours
Perceived Flavours
Schema Layer
b)
Relational learning
Solitary learning
% correct
Session #
PT1
PT2
PT3
PT4
PT5
PT6
c)
activation (a.u.)
Rel lrn grp
Map1
Map2
Sol lrn grp
Map1
Map2
Neuron#
d)
%digging at correct location
Relatn lrn grp
Solit lrn grp
p<0.001
p<0.001
PT1
PT2
PT3
PT4
Map2
PT5
Map1
PT6
Map3

Fig. 5 a) Architecture of the artificial neural network. Context patterns and flavours are the inputs for the system and the action is the output layer. The different routes of flow of information are shown with grey arrows. b) Performance of the artificial neural network on 5 flavour-location associations till session 21. After this, half of the population was run through relational learning regime (cyan) and rest through the solitary learning (pink). C) ***Probe trial performance of the artificial neural network****. The neural network learns Map#1 for 21 sessions during which we do not see any difference in the two populations of virtual animals (relational and solitary). After being trained for Map#2 as per the two different training regimes, we observe a significant difference in the performance of the two groups (PT4; Paired Sample t-Test; mean(rel) = 35.11364; mean(sol) = 26.65462; SD(rel)=3.62235; SD(sol)=2.7199; t Statistics = -4.8413; n = 10; p=9.19359 x 10^{-4}) while their previous learning seems to be comparable (PT5 (relational); One Sample t-Test; mean(rel) = 35.36566; SD(rel)=6.451; t Statistics =7.53224; n = 10; p= 3.57012 x 10^{-5}; PT5 (solitary); One Sample t-Test; mean(sol) = 32.35482; SD(sol)=8.27343; t Statistics =4.72227; n = 10; p=0.00109). These groups, when subjected to a problem-solving configuration, exhibited similar results as our mice studies wherein the relational learning group performed significantly better than the solitary learning group (PT6 (problem-solving); Paired Sample t-Test; mean(rel)= 35.68079; mean(sol)=20.51432; SD(rel)=7.03243; SD(sol)= 8.1939; t Statistics =-4.36769; n = 10; p=0.0018).*

Explicitly Acquired Interrelations Among Mental Schema Reduces Cognitive Load and Facilitates Emergence of Novel Responses in Mice and Artificial Neural Networks.

Supplementary information and figures:

Supplementary information 1: ***Performance of animals split by flavour during PT3 Map1***

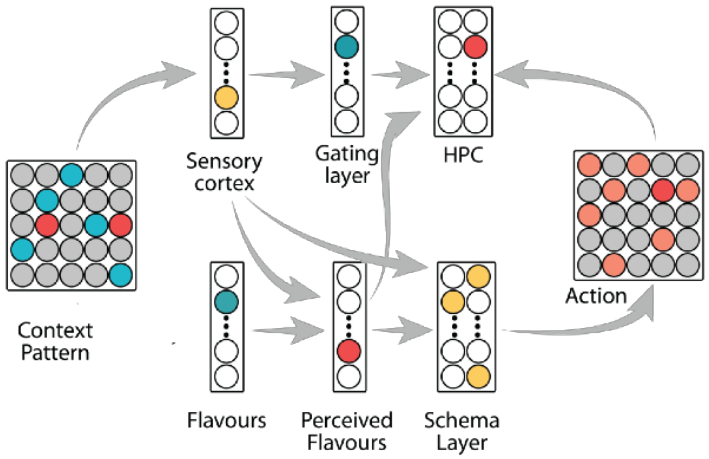


Supplementary fig 1: flavour-wise performance of mice on PT3 for Map1

	SumOfSquares	DF	MeanSquares	F	pValue
Flavours	2619.9	4	654.97	1.0153	0.40421
Error	54834	85	645.11		
Total	57454	89			

Supplementary information 2: ***ANN architecture***

a) ANN architecture:



Supplementary fig 2: ANN architecture.

b) Initialization of different layers:

The various layers are initialized as follows:

I. Context Pattern:

Schema A	**[0,0,1,0,0;0,1,0,0,0;0,2,0,1,2;1,0,0,0,0;0,0,0,0,1]**
Map1_1 (Relational learn.)	**[0,1,0,0,0;0,0,1,0,0;0,2,0,1,2;1,0,0,0,0;0,0,0,0,1];**
Map1_2 (Relational learn.)	**[0,1,0,0,0;0,0,1,0,0;0,2,0,1,2;1,0,0,0,0;1,0,0,0,0];**
Map2 (Relational learn.)	**[0,1,0,0,0;0,0,1,0,0;1,2,0,0,2;0,0,0,1,0;1,0,0,0,0];**
Map2 (relational learning with new landmark position)	**[0,1,0,2,0;0,0,1,0,0;1,0,0,0,0;0,0,0,1,0;1,0,2,0,0];**
Map2 (Solitary learn)	**[0,1,0,2,0;0,0,1,0,0;1,0,0,0,0;0,0,0,1,0;1,0,2,0,0];**

II. Cue sets:

Schema A	**[1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0;];**
Map1_1 (Relational learn.)	**[0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0;...**

	0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0;];
Map1_2 (Relational learn.)	**[0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0;... 0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0;];**
Map2 (Relational learn.)	**[0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0;];**
Map2 (Relational learning with new landmark position)	**[0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0;];**
Map2 (Solitary learn)	**[0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0;];**

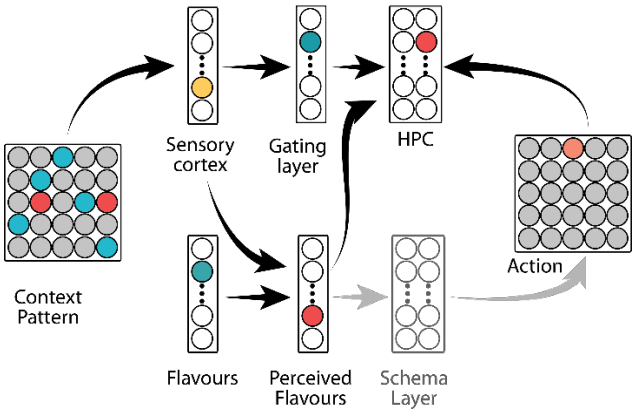
III. Action/output layer:

Schema A	**[0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1;];**
Map1_1 (Relational learn.)	**[0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1;];**
Map1_2 (Relational learn.)	**[0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0;];**
Map2 (Relational learn.)	**[0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0;];**
Map2 (Relational learning with new	**[0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0;...**

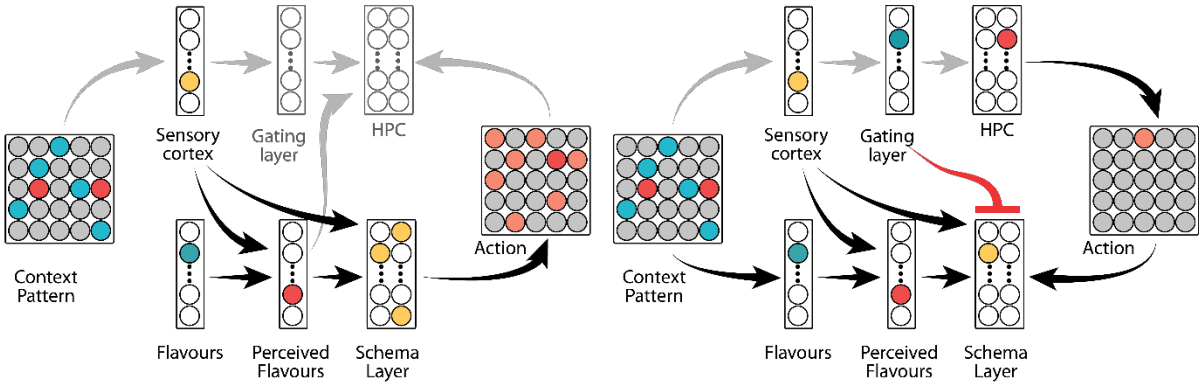
landmark position)	**0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0;];**
Map2 (Solitary learn)	**[0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0,0,0;... 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,0,0,0,0;];**

c) **Initial weights for each layer to contribute to other layers is randomized.**

d) Training protocol:

- The dHPC layer receives three inputs during the hippocampal learning stream: the contextual pattern (via sensory layer and gating layer); the perceived flavour (the perceived flavour is the product of the sensory layer activation and the flavour layer. This is done to account for the effect of the context on the perceived information); and the corresponding correct location for the task from the action layer (*supplementary fig. 3*).
- 

Supplemetary fig 3: Hippocampal training architecture

- The network goes through multiple epochs, and once the activity of each layer converges, the network enters the cortical learning stream where the weight updates happen via contrastive Hebbian Learning.
- The contrastive Hebbian learning depends on the difference in the weights in the two phases of any network i.e. a free phase and a teacher phase (*supplementary fig 4*).
- 

Supplementary fig 4: Left: free phase; Right: teacher phase

- The cortical stream begins with the free phase where the schema layer receives two inputs: the context pattern and flavour (via same layers as the hippocampal stream) and is allowed to produce a correct location in the action layer. This is followed by a teacher phase where the dHPC active neuron (from the previous dHPC learning phase for a particular flavour-location trial) acts as a teacher for the correct location to the schema layer. During this phase, the schema layer receives 3 inputs (context pattern, flavours and correct location). Additionally, in this phase, the nodes in schema layers are gated in a manner where only a few nodes can participate in this learning. This is to emulate the fact that not all the cells participate in every learning and only a subset of neurons encode the incoming information. This is achieved by using a gating layer to project negative inhibitory weights to the schema layer with a few elements of the inhibitory matrix set to zero (not affecting the downstream layer).
- The performance of the cortical stream in the two phases is used to implement contrastive Hebbian weight updates for every layer. Another feature of this ANN is that at each trial it calculates the familiarity of the context pattern and modulates the number of learning epochs (see supplementary information). This implementation allows us to detect schema with consistent and inconsistent information.