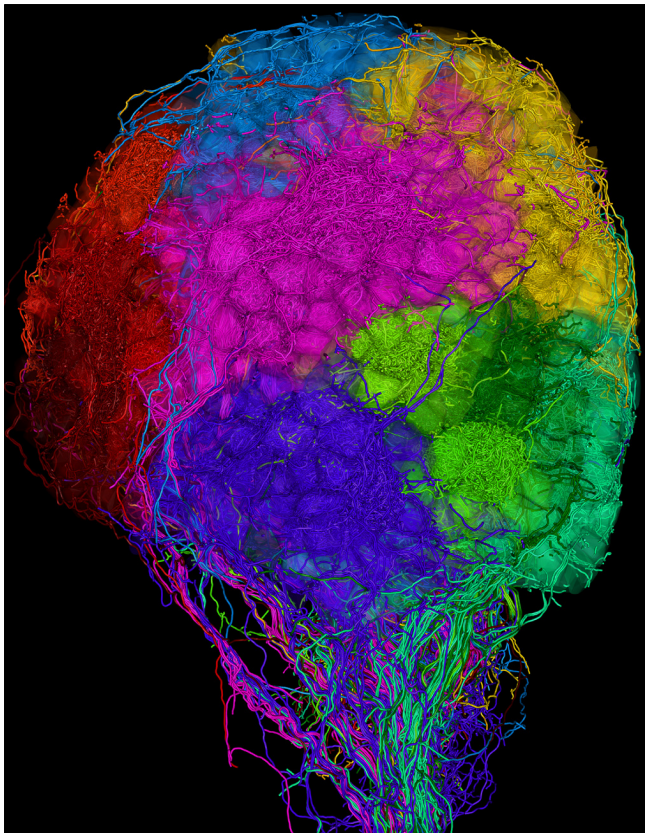

Figure 1 Rendering of a reconstruction of all mitral cells in the larval zebrafish olfactory bulb. Cells are colored according to the glomerulus they innervate. The seven colors correspond to seven broad groups of glomeruli, as identified by molecular markers and shared patterns of interneuron connectivity. Image courtesy of Adrian Wanner, Friedrich Miescher Institute for Biomedical Research.

the granule cells, which at later stages become the most abundant neuronal type in the bulb. The authors noted that, at this stage, the fish bulb resembles the antennal lobe of insects.

Second, four cells of previously unreported types were identified, two of which project out of the bulb and two of which are intrabulbar cells of unusually large size and extensive innervation. Uncovering the function of these neurons promises to be a worthwhile task.

Third, inhibitory neurons innervated several, but typically not all, glomeruli; moreover, the inhibitory neurons could be divided into clear modules, collections of neurons that possessed similar glomerular innervation patterns (**Fig. 1**). Innervation patterns were predicted better by glomerular identity than by distance, indicating that wiring is driven by molecular cues and/or functional similarity more than just by constraints on neurite length.

The interpretation of anatomy both informs and benefits from functional studies. In this case, two of the inhibitory neuron modules correspond to groups of glomeruli that have been shown to respond to distinct classes of chemical cues (amino acids for a lateral group, bile acids for a medial group)[6–8]. Consequently, one possible function of these modules is to normalize responses among neurons tuned to a particular portion of chemical space. However, it remains possible that these modules are involved in more intricate forms of computation. Intriguingly, the organization of glomeruli changes over the course of development in an experience-dependent manner[9].

Neuroanatomy may be one of the oldest disciplines in neuroscience, but recent years have witnessed an explosion of interest in new anatomical questions, approaches and applications. Techniques based on electron microscopy are demanding. But in the case of the larval zebrafish olfactory bulb, Wanner *et al.*[2] have exploited a literal silver lining to improve image quality and perform a substantive big-picture analysis of the organization of a local circuit. Such studies, coupled with measurements of their function, promise to achieve a new level of mechanistic understanding of circuit function.

COMPETING FINANCIAL INTERESTS
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What stays the same in orbitofrontal cortex

Erin L Rich & Jonathan D Wallis

Researchers show that orbitofrontal neurons perform the same value-related computations across different decisions. Value computations are therefore a critical feature around which orbitofrontal representations are organized.

How do we make an infinite number of decisions with a finite number of neurons? Neurons in prefrontal cortex are characterized by a remarkable degree of diversity in their response properties and are seemingly capable of encoding any arbitrary relationship that might be behaviorally relevant[1]. But this flexibility must be balanced against a stable organization to efficiently exchange information with other brain areas. Revealing the structure guiding responses of prefrontal neurons has been a challenge. In this issue of *Nature Neuroscience*, Xie and Padoa-Schioppa[2] investigate neuron responses in orbitofrontal cortex (OFC), a prefrontal region critical for value-based decision-making[3–5]. They show that, like other prefrontal neurons, OFC neurons exhibit a great deal of heterogeneity.

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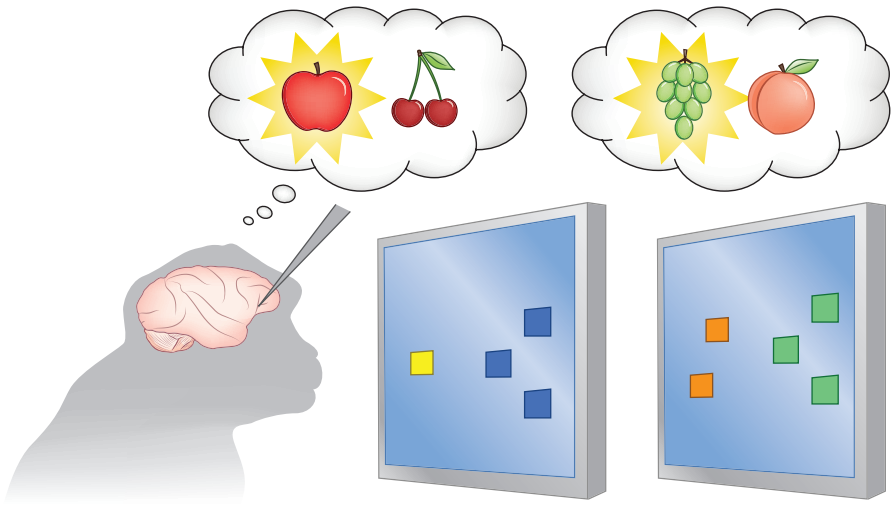

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Figure 1 Monkeys were trained to make choices between different offers of juice reward. Each offer was represented by colored squares, where the number of squares indicated the amount of juice on offer and the color of the squares indicated the type of juice. In the first trial block, animals chose between two juices, such as apple and cherry (juices A and B). In the second trial block, they chose between two different juices, C and D. The authors found that OFC neurons remapped from block 1 to block 2 to encode the different rewards. However, neural tuning for decision information was consistent, maintaining the organization of the decision-making circuit.

However, their responses are organized in a consistent manner with respect to the encoding of economic decision variables.

In their experiment, monkeys were allowed to choose between two juice rewards of varying amounts, each referred to as an offer. For instance, in one trial the animal might choose between 2 drops of apple juice and 5 drops of cherry juice. The extent to which it preferred apple to cherry, or any pairing of two juices A and B, was determined by varying the amounts of A and B on offer. If the animal was offered equal amounts of A and B, it would consistently choose the juice it preferred; for example, juice A. However, if offered a sufficiently large quantity of juice B, it would choose B instead. Based on repeated choices, one can determine the relative value of the two options. For example, 1 drop of apple juice might equal 3 drops of cherry juice for a particular monkey. Previous work has shown that neurons in OFC encode variables relevant to making these decisions[6]. Some neurons encode the value of one of the offers ('offer value' neurons)—for example, the value of apple juice being offered. Other neurons encode the value of the offer that the animal chooses, regardless of which juice it is ('chosen value' neurons). And still others encode the identity of the chosen juice, regardless of its value ('chosen juice' neurons).

The key question was how these neurons would respond if the animal were presented with a different choice—for example, if juices A and B were switched to C and D. Neurons that encode 'offer values' and 'chosen juice' do so with respect to a specific reward. Would these neurons simply go silent when their preferred reward was not an option? Or would they 'remap' and encode a new reward? If they remap, is there any consistent structure guiding their responses, or would they remap arbitrarily, embodying the archetypal prefrontal flexibility? To test this, the researchers recorded the same neurons while animals made choices in two trial blocks. In the first block, they chose between varying amounts of juice rewards A and B, and in the second block they performed the same task but chose between juices C and D (**Fig. 1**).

The authors found that OFC adapted to the change by remapping neural responses to new rewards while maintaining the overall structure of encoding in relation to decision variables in the task. That is, a neuron that encoded an offer value in the first block continued to encode an offer value in the second block, even though the specific juice on offer was different. The same was true for chosen juice and chosen value encoding. Not only was this structure upheld, but the animal's subjective preference was the key feature dictating which reward a neuron remapped to. For example, if the animal preferred juice A over juice B and C over D, then neurons encoding the offer value of juice A would consistently remap to encode the offer value of juice C. Similarly, neurons encoding juice B offers would remap to encode juice D. In fact, preference-based consistency of neural responses recorded in the AB-CD design was indistinguishable from that recorded in a control condition where the second block was identical to the first (AB-AB design). Therefore, OFC neurons maintain their functional roles when the animal is presented with new decisions to make, and their responses are organized by subjective preference.

To emphasize this point, the authors recorded neurons in another condition. As before, block 1 consisted of choices between juices A and B, in which A was the preferred juice, but block 2 consisted of choices between C and A, where C was the preferred juice. Therefore, juice A was the same in both blocks but was the preferred option in the first block and the non-preferred in the second. In this case, neurons again remapped in block 2 according to the animal's preference. Neurons selective for the value or identity of A in the first block were selective for the value or identity of C in the second block, even though juice A was still an available option. This is strong evidence that OFC neurons do not encode the sensory features of rewards, such as taste, but the evaluation of that taste in the context of the current decision.

These results suggest that, at least in one area of prefrontal cortex, neurons do not arbitrarily map to task parameters. Rather, there are specific dimensions along which information in OFC is organized and these dimensions remain consistent across task conditions. By analogy to the visual system, a neuron in inferior temporal cortex may be tuned to respond to specific objects, but this tuning will be consistent, or invariant, across a variety of object sizes and positions with respect to the viewer[7,8]. In the same way, OFC neurons appear to be tuned to respond to decision parameters, but are invariant with respect to the specific properties of the goods under consideration. This is in contrast to recent results suggesting that higher cortical areas such as prefrontal and posterior parietal cortex encode category-free combinations of task parameters[9].

The ability of OFC circuits to represent a diversity of information in a structured way could be an efficient means of dealing with the many decisions an animal is likely to encounter. Similar choice tasks have shown that OFC neurons are capable of 'quantitative adaptation', rescaling their responses when the offered juice amounts cover larger or smaller ranges across conditions[10,11]. Xie and Padoa-Schioppa[2] demonstrate that OFC neurons can also show 'qualitative adaptation'. That is, the population adapts to contexts in which different items are available. A critical question for future work is how far one can push this adaptation while still retaining the same representational structure. How would these

same neurons respond in foraging tasks where the choice is between accepting or rejecting a given offer? How would they respond in multi-step decisions, where some choices do not lead directly to reward?

These questions are timely, since another line of research suggests that OFC is critical for constructing internal models of the environment, or task structure, to determine optimal behaviors that will yield specific outcomes. These studies have proposed that OFC represents one's place in a 'cognitive map' of the task space[12]. Information contributing to this cognitive map is likely distributed in the brain, but a distinct role for OFC may be in disambiguating perceptually similar situations that differ in an unseen variable[12]—for example, if the intended goal or presently unavailable options require different actions. Indeed, OFC responses differ depending on knowledge of rewards that are possible in the current environment but not presently available. When qualitatively different rewards are offered on interleaved rather than blocked trials in a similar choice task, neurons do not adapt in the same way, but encode decision variables relative to all potential offers[13]. Thus, task relevant but unobservable features of the environment are reflected in OFC, consistent with the idea that these representations are based on a model, or cognitive map, of the task.

One drawback of the cognitive map theory is that it allows any task-relevant information to be represented within OFC, so that a given neuron might encode arbitrary variables under different task conditions. While some have argued that heterogeneity is beneficial for encoding complex information[1], the study by Xie and Padoa-Schioppa[2] places concrete constraints on this flexibility. OFC neurons extract key decision-related variables, and do so in a consistent manner across different choices. These results suggest a path forward in understanding the nature of OFC processing. Determining the degree to which information encoded by a given neuron remains invariant across different situations could help to define the critical parameters around which representations in OFC are constructed. This organizational stability could enable other brain areas, as well as other components of the decision-making circuit within OFC, to interact with specific populations of neurons that perform the same computation across multiple contexts.

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