

# Stirred, Not Shaken: Motor Control with Partially Mixed Selectivity

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In this issue of *Neuron*, Zhang et al. (2017) demonstrate that neurons in human parietal cortex represent effector responses functionally segregated, while other movement variables are associated in a subordinated fashion. Such partially mixed selectivity facilitates efficient motor control in various behavioral contexts.

The brain combines a multitude of sensory and cognitive signals to accurately control and guide our movements in an ever-changing complex world. This computation is distributed across many brain areas that are specialized for specific functions or movement features.

To better understand the neuronal coding of particular brain areas, traditional neurophysiology went at great length to explore the properties of individual single neurons while animals performed specific motor behaviors. This classical work led to fundamental insights into the coding pattern of brain areas with respect to specific movement parameters, like the movement direction of hand movements or the applied force (Evarts, 1968; Georgopoulos et al., 1982).

Together with lesion and inactivation studies, specific brain areas of the fronto-parietal network have been identified to be causally relevant for sensory, motor, or cognitive functions, and corresponding single-unit studies have ascribed specific functional properties to individual neurons and neuronal populations. Such characterizations of cortical areas and subareas have been further supplemented by anatomical investigations demonstrating the specific connectivity patterns between these networks (Rizzolatti and Luppino, 2001).

Investigating the representations of sensory and motor signals in specific brain areas has been tremendously helpful for understanding the underlying coding schemes. In many of these studies, individual neurons represent not only one sensory or motor feature, but a multitude of them. For example, neurons in the

anterior intraparietal cortex (area AIP) of macaque monkeys encode not only specific features of the object that the animal intends to grasp, including its shape, size, and orientation, but also the spatial position of the object or the subject's gaze position (Janssen and Scherberger, 2015). Such multiple or mixed selectivity for sensory and motor features is surprising at the level of individual neurons, since it makes neural coding complicated and hard to interpret. Nevertheless, such mixed selectivity seems necessary to fulfill the computational requirements of the brain.

How does a brain area achieve its computations? Clearly, many individual neurons are simultaneously selective for a multitude of distinct features. However, the activity patterns across individual neurons are highly variable, leading to a large variety of mixed selectivity in the neuronal population. This makes clear-cut neuronal classifications in a population rather difficult (e.g., visual, visuo-motor, or motor neurons in AIP). However, neuronal diversity and heterogeneity might provide an important computational advantage. Recent theoretical and modeling considerations have led to the conclusion that mixed selectivity, i.e., the combined representation of multiple features in individual neurons of the network, is most flexible and supportive to perform easy, i.e., linear, computations at subsequent processing stages (Fusi et al., 2016). Therefore, the question of to what extent this computational concept is generally implemented in the neuronal populations of humans and animals is important.

In the present issue of *Neuron*, Zhang et al. (2017) investigate the coding of several types of motor variables in the neuronal population of human AIP of a tetraplegic patient 7 years after injury. This investigation provides a unique opportunity to examine single neuron activity in a human subject and to compare these results, in particular, with previous non-human primate studies.

The patient is instructed to imagine or attempt either a left or a right arm movement, which is either a shoulder shrug or hand squeeze. While paralyzed patients are clearly handicapped in executing specific movements, they can still imagine or attempt such movements. All three movement features—body part (hand or shoulder), effector side (left or right arm), and cognitive strategy (imagined or attempted)—are co-varied, which leads to eight distinct movement conditions that are instructed in random order. Then, while the patient executes this task, populations of single neurons are recorded from a small patch (4 × 4 mm) of human AIP using a chronically implanted 10 × 10 array of recording electrodes.

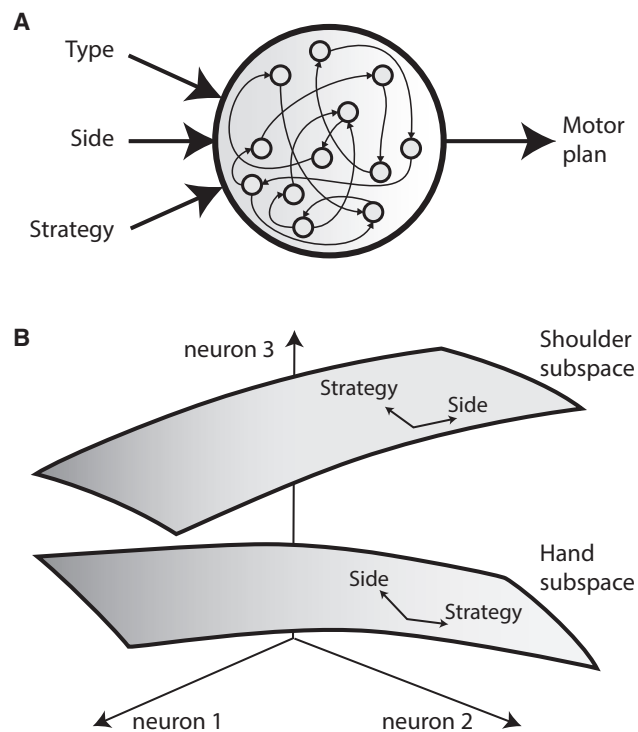
An important first observation is that significant fractions of neurons recorded from this small, circumscribed area are selective for each of the eight task conditions, therefore demonstrating that human AIP represents these movement features in a combined fashion, similar to previous findings demonstrating the combined representation of reaching and grasping movements in monkey AIP (Lehmann and Scherberger, 2013).

But how are the three movement features (body part, side, and strategy)

encoded in human AIP? For this, Zhang et al. (2017) develop and subsequently test four distinct hypotheses: (1) the resulting eight movement conditions could be functionally segregated, i.e., represented in distinct, non-overlapping subnetworks of AIP; (2) each of the three movement features could be encoded in anatomically segregated networks; (3) movement features could be encoded in a mixed selectivity, i.e., with individual neurons being tuned to various combinations of the encoded movement parameters; and (4) finally, the neural network could be organized in a partially mixed fashion, with some movement features being segregated and others being mixed in a subordinate fashion. Results from this study confirm a partially mixed selectivity of human AIP (hypothesis 4) with a segregated encoding of body part (shoulder versus hand) and a subordinate, mixed encoding of body side and cognitive strategy (Figure 1).

More specifically, the segregated encoding of body part is neither spatially nor otherwise topographically segregated in human AIP, not even between separate classes of AIP neurons. Instead, many neurons responding to shoulder movements also respond, to some extent, to hand movements, and vice versa. Computation of a specificity index between the two movement types reveals a continuum of neurons, ranging from favoring one or the other movement type to responding equally well to both. This continuum of neural preference at the level of individual neurons is also observed for the other movement features: body side and movement strategy.

However, movement features appear strikingly different at the population level. Pairwise correlations of neuronal activity reveal a hierarchical structure that separates shoulder from hand movement encoding in the population. In contrast, correlations associated with differing body



**Figure 1. Schematic Illustration of Partially Mixed Selectivity in Human AIP**

(A) Neuronal population receives input of movement features (type, side, and strategy) and outputs a motor plan.

(B) In the neuronal population, movement type (shoulder or hand) is represented in distinct subspaces (gray surfaces). Other movement features (movement side and strategy) are encoded separately in each subspace (small coordinate frames). Population space is shown only for three dimensions (neurons 1–3); however, full dimensionality equals the number of neurons in the population.

side or movement strategy are significantly higher. Furthermore, a generalization analysis confirms these results, in which a decoder of motor features is first trained on a subset of conditions and then tested on the remaining ones. Zhang et al. (2017) find that such decoders generalize well across body side and movement strategy, but not across body part, thus further emphasizing the functional segregation for body part, but not of body side and movement strategy, in human AIP.

These results are remarkable for several reasons. First, from a motor control point of view, one might expect that body side (left versus right) might be the most distinctive feature, perhaps followed by movement type (shoulder versus hand) and strategy (attempted versus imagined movement). However, this was not the case. Movement type

was most distinctive, followed by side and strategy. This emphasizes the role of AIP and the parietal association cortex as a higher-order planning area that is remote to the details of motor execution but linked to more abstract motor plans and object affordances (Schaffelhofer and Scherberger, 2016).

Second, the presence of shoulder movement signals in human AIP, in addition to hand movement signals, does not imply that AIP is causally involved in the execution of shoulder movements. In fact, a previous inactivation study of monkey AIP produced only deficits in hand grasping, but not in arm reaching (Gallese et al., 1994). This suggests a more complex role of these segregated shoulder movement signals in AIP. More research is needed to resolve this question.

Third, the finding of functionally, not anatomically, segregated representations of motor actions suggests that human AIP encodes these movements in distinct neuronal subspaces within

the neuronal population space (Figure 1). Such specialized neuronal subspaces have recently been postulated in macaque motor cortex, e.g., for the distinct encoding of movement preparation and execution (Kaufman et al., 2014) and for describing the neural constraints on motor learning (Sadtlter et al., 2014). At this point, it remains an open, but testable, hypothesis, whether the functional segregation and subordinate mixed selectivity of movement features in human AIP can also be regarded as an instance of subspace coding. If so, such unified concepts might help better understand the building blocks of neural movement control and neural computation in general.

Finally, Zhang et al. (2017) provide first evidence on the neuronal population structure of human posterior parietal cortex. It is reassuring that these findings are in rather good agreement with previous

findings in monkeys (Andersen and Buneo, 2002; Janssen and Scherberger, 2015). This congruence allows us to gain fundamental insights about human brain functions already from very few patient studies, which will considerably ease the development of future clinical applications, like neural prosthetics.

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