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[1]Department of Cell Biology, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, Massachusetts 01655, USA. [2]Department of Molecular, Cellular, and Developmental Biology, Yale University, New Haven, Connecticut 06520-8103, USA. E-mail: gregory.pazour@umassmed.edu

Primer

Inner space: Reference frames

Aaron Batista

How are we aware of our surroundings? Somehow, from a pair of tiny, two-dimensional pictures of the visual world – provided by our retinas – our brains are able to render the world as it is, accurately depicting the locations of both a distant mountain range and the camera we are pointing at it. To understand how space is represented in the brain, neurophysiologists have borrowed the useful concept of a *reference frame* (also called a *coordinate frame*) from engineers and physicists. A reference frame, in the mathematical sense, is simply a set of rigid axes that intersect at a point, the origin. These axes are usually perpendicular to each other, and they are marked with gradations. This system allows the location of any object to be described by a set of numbers, called coordinates – its position along each of the axes. How is this notion useful in neuroscience? It allows us to phrase questions about how the brain encodes space in very concrete terms. For example, suppose we wish to understand how it is that a person can catch a baseball. Using reference frames, we can state the question as, 'How does the brain translate the position of the ball from the coordinates of the retinas into its coordinates in a reference frame centered on the left hand?' (Figure 1)

Some modifications to the physicist's concept of a reference frame are needed to apply it in neuroscience. Neurons in the visual system do not report the coordinates of an object. Instead, neurons that encode visual space each represent a very restricted region of space. Cells will respond to stimuli located in one particular location, termed the *response field* of the neuron, or the *receptive field* in cases where the neuron's response is considered to be strictly sensory, and will not respond to the same object positioned somewhere else. (Often, a visual stimulus must have other features in order for a neuron to respond to it, such as a particular color, a direction in which it is moving, or even how the animal intends to respond to that stimulus.) Areas of the brain that represent visual space do so by using a population of neurons with response fields at different locations. Once we locate the response field for a neuron, we can ask in which reference frame that neuron encodes space using some very simple manipulations: by moving one part of the body at a time, we can explore whether the neuron's response field moves along with that body part. If it does, then we have reason to believe that the neuron encodes space in a reference frame anchored to that body part.

Reference frames for vision

The neural signal induced by light in the retina is carried through the thalamus to the primary visual cortex, also called V1 or *striate cortex*, for the pronounced stripe of myelinated input fibers visible in histological sections. Neurons found along this pathway all use a *retinal* reference frame: if the eyes move, the spot in the world to which these cells respond also moves, but it stays fixed with respect to the retina. Retinal coordinates are also the rule throughout the *extrastriate* visual areas, those areas just downstream from the striate cortex. This fact leads to a dramatic realization about the organization of the visual system: every time our eyes move, the visual scene sweeps across our visual areas. Yet, despite this, we somehow perceive that the world remains stable.

To achieve this stability, the brain must factor in information about the position and movements of the eyes. This combination of visual and postural information becomes evident further along in the visual system. For example, area VIP, a multisensory area in the parietal lobe of monkeys, contains a

mixture of head-centered (Figure 2B) and retinal reference frames. Premotor cortex — a region of the frontal lobe that controls some high level aspect of movement planning — also contains neurons that use head-centered reference frames to represent space.

A distinct but easily conflated issue is important to mention here. Neurons within a brain area may be organized *topographically* (or in a *map*), meaning that neurons that are next to each other represent stimuli with similar properties. For example, V1 is *retinotopic*, meaning that neurons near each other in cortical tissue have receptive fields that represent points nearby in visual space. The auditory cortex is *tonotopic*, meaning sounds with similar pitch activate nearby neurons. Topography can be an important clue to the function of an area: if neurons are arrayed according to the value of a particular parameter, then that property might be critical in the processing performed by that area. However, neurons do not *need* to be arranged topographically along the dimensions of the reference frame they employ: in principle, the pattern of wiring from one area to another can disentangle the particular placement of neurons within a cortical area. So, a brain area can encode space in a particular reference frame, even if its neurons do not form a map of that space.

Reference frames for movement

A central question in systems neuroscience is how the brain can use sensory information to plan and perform a movement. Transforming an object's location from sensory reference frames into the reference frames that can specify a movement is one of the critical components of sensory-guided movement processing. (Some of the other important components of sensory–motor processing are, how the decision to act is made, and how the timing of the movement is coordinated.) For example, if an animal wants to pick up a piece of apple in front of it, information about the apple's location enters the brain in a retinal reference frame. However, the command to reach must ultimately take a form that can cause a pattern of muscular contractions. The object's position in retinal coordinates must be elaborated by information about body position: the positions of the eyes in the head, the head on the body, and the arm with respect to the body (Figure 1).

Several recent studies have helped to elucidate how this process maps onto specific regions of the cortex. The visual cortex is the starting point for the visuomotor transformation, and primary motor cortex (also called M1, one of the major sources of projections from the cortex to the brainstem and spinal cord) is the final cortical stage. Several areas in between comprise a dedicated reach pathway. Reach plans are represented in a retinal coordinate frame in area MIP of the parietal cortex (Figure 2C), an area which receives inputs from a variety of extrastriate visual areas. Area 5 is a nearby cortical field that combines visual information with *proprioceptive* inputs — signals from the body's joints and muscles that inform the brain about the positions of body parts. Neurons in area 5 employ a combined eye-centered and hand-centered coordinate frame to represent target location. This suggests the area helps to perform a direct transformation from a retinal representation of a reach plan to a hand-centered representation. Such a representation exists in the premotor cortex. In addition to the neurons mentioned above that use head-centered coding in premotor cortex, some cells represent visual targets in an arm-centered reference frame (Figure 2D). These neurons comprise a very intuitive phase in reach planning: targets are represented visually with respect to the arm's current position, thereby yielding a direct mapping from the arm's current position to its desired position.

The nervous system's command to the arm must specify a pattern of muscular contractions to move the arm to its goal. There has been considerable debate over whether

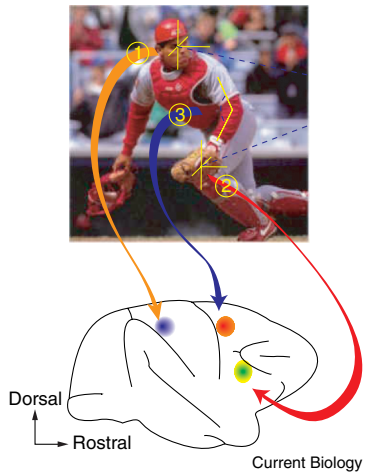

Figure 1.
When we catch a baseball the position of the ball is first registered in a retinal reference frame (1). The brain computes its position with respect to the hand (2), then determines the muscle contractions needed to rotate the joints of the arm and shoulder (3) in order to bring the glove on target with the ball. These three phases of the reach map onto distinct areas of the cerebral cortex, as highlighted in the sketch of the monkey brain.

the primary motor cortex itself encodes these commands to the muscles, or alternatively, specifies the trajectory of the hand through space, which would leave it up to the brainstem and spinal cord to compute the required muscular contractions. Although conceptually these are dramatically different reference frames (sometimes referred to as *intrinsic* and *extrinsic* coordinates, respectively) it has been very difficult to dissociate them experimentally. Evidence exists to support both possibilities, and it may be that M1 actually performs the transformation from extrinsic to intrinsic coordinates. The resolution of this issue has important implications for the design of neural prosthetics that could help paralyzed humans.

Coordinate transformations

As this survey shows, many areas participate in planning a reach. These areas employ reference frames which indicate that they occupy various stages of the sensory–motor transform. How does the brain convert spatial representations from one reference frame to another? It

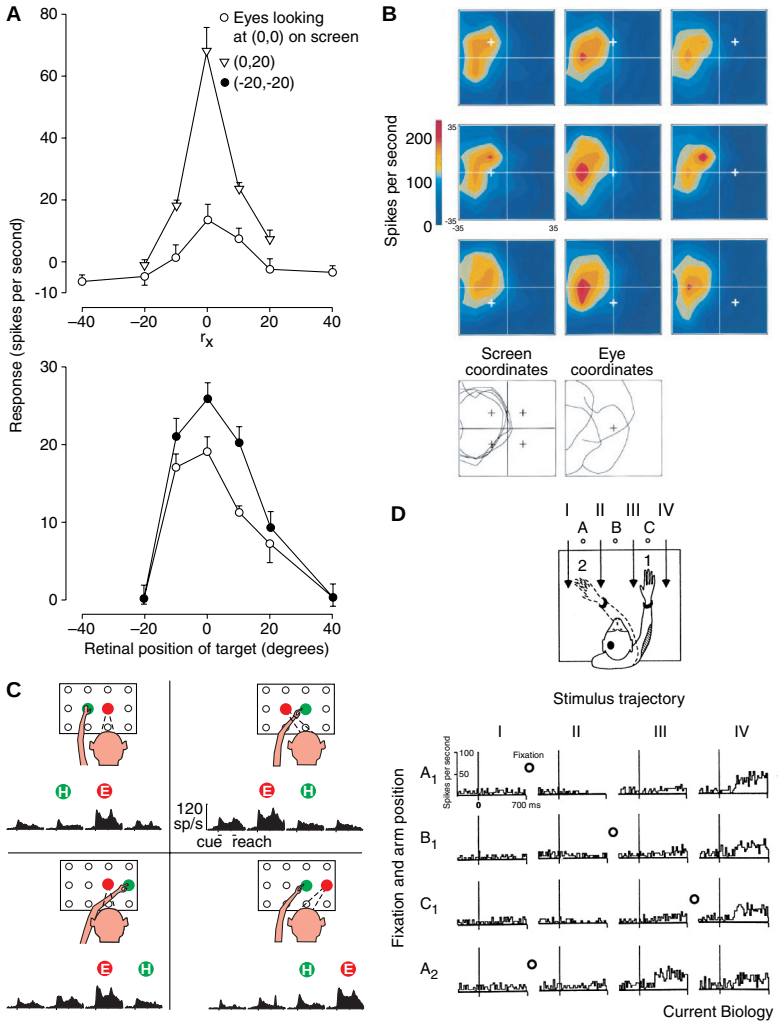

Figure 2. Some reference frames.
Panel A shows two neurons (top and bottom graphs) recorded in posterior parietal cortex. These cells have retinotopic receptive fields that are gain modulated by eye position. The two curves within each graph differ due to the different directions of gaze. Panel B shows a neuron from parietal area VIP with a head-centered receptive field. Each of the nine color plots shows the neural response in screen coordinates for nine different fixation positions, indicated by the small white cross. In the two lower plots, the contours for four of these mappings are superimposed in either screen (left) or eye (right) coordinates. They show better alignment in screen coordinates. Panel C illustrates an area MIP neuron that encodes a reach plan in retinal coordinates. In each panel, the schematic diagram shows four different configurations of the monkey's eye and initial hand position. Below the schematics are the neuron's responses for reaches to the same four targets. The E and H indicate the eye and initial hand position relative to the targets. Each plot shows the neuron's response over time as the monkey plans then performs a reach to the target at that position. The reach plan that generates the largest response is always the one directly below the eyes, regardless of where the hand begins. Panel D shows a neuron from premotor cortex that has a receptive field in arm-centered coordinates. Each row depicts neural activity over time as visual stimuli approach the monkey along four different paths. For each row, a different combination of eye or hand position is used. In the first three rows, the arm is at the same position, to the right, and the monkey fixates in three different positions. The response field does not change. However, in the last row, when the arm is moved to the left, the response field moves along with it. This neuron also had a somatosensory response on the elbow, as indicated by the shading in the schematic. (Panel A from Andersen *et al.* (1985). Science *230*, 456–458. Panel B from Duhamel *et al.* (1997). Panel C from Batista, A.P., Buneo, C.A., Snyder, L.H. and Andersen, R.A. (1999). Science *285*, 257–260. Panel D from Graziano *et al.* (1994)).

must be that additional postural information is combined to elaborate a representation from one coordinate frame to another. Important experimental work has shown some of the ways in which spatial and postural information is combined in the brain and theoretical studies have shown the computational power of merging information in this manner.

Neurons in the posterior parietal cortex provide a clue to one way coordinate transformations may occur. Among the parietal neurons that use a retinal reference frame, some also show a modulatory influence of the position of the eyes in the head. More concretely, these neurons have response fields that are fixed to the eyes. In addition, depending on where the gaze is directed, the response to a stimulus presented at the same location on the retina can increase or decrease (Figure 2A). This interaction is multiplicative in nature, so it is termed a *gain field*. In the nearly twenty years since the initial observation of gain fields, they have been reported in a variety of brain areas, and the modulatory influences have been attributed to a variety of postural signals, such as the position of the head on the body or with respect to gravity.

Theoretical studies have shown that a population of neurons with gain fields can support a conversion from one reference frame to another. In the original demonstration, a neural network was configured to take inputs of stimulus position in retinal coordinates along with a signal of eye position, and to combine them in a hidden layer. The network was trained to output the position of the stimulus in a head-centered reference frame. After learning, the network's hidden units developed receptive fields in a retinal reference frame that showed multiplicative modulation with eye position, just as the parietal neurons do. Therefore, gain fields like those observed in parietal neurons are sufficient to implement an eye-to-head coordinate frame transformation.

Recent developments in the theoretical studies have shown that gain fields are an efficient and flexible way to represent spatial information. A population of neurons that combines spatial and postural signals can serve as a substrate for extracting an object's

location in a wide variety of reference frames, appropriate for various uses. Depending on exactly how the population of neurons with gain fields is read out, different spatial representations can be extracted by different downstream areas. A related insight to emerge from the computational models is that it does not necessarily make sense to ascribe a particular reference frame to a brain area. Consider a population of neurons that uses a retinal reference frame and exhibits a gain modulation of eye position. As this modulation is well-modeled as a multiplication of the two signals, the terms are interchangeable: it is just as sensible to describe the neurons as encoding eye position in a head-centered coordinate frame, with a gain modulation of the retinal position of the target. When more signals are combined, it becomes even less useful to designate a particular coordinate frame for an area. The computational studies propose a useful suggestion to experimentalists: we may be better off determining which of the myriad possible spatial and postural signals modulate the neuron under study, rather than trying to establish one definitive coordinate frame employed by that cell.

In addition to gain fields, there is physiological evidence for a different mechanism of coordinate transformation. Some neurons encode space in reference frames that are intermediate between two body parts. For example, some cells in VIP show response fields that shift only partway with the eyes as gaze changes. That is, they employ a reference frame that is intermediate between head-centered and eye-centered coordinates. The presence of neurons like this is sometimes taken to indicate that a brain area containing them may actually implement a coordinate transformation. Whereas a population of neurons that use gain fields can allow coordinate transformations to occur in one step, the brain may also use a gradual, multi-step mechanism, as evidenced by neurons with partially shifted reference frames.

One conceptually straightforward mechanism for coordinate transformation, curiously, does not seem to be employed by the brain. Physiologists exploring visually guided reaching might have expected to find neurons that respond to visual stimuli in an eye-centered reference frame, but then specify the target for the hand movement in an arm-centered reference frame, just before the movement occurs. However, it appears that neurons do not individually reflect coordinate transformations in a temporal manner. Instead, for the most part, the reference frame used by a neuron does not seem to change over the time scale of a single movement.

Although much has been learned about the neural mechanisms for coordinate transformation, many important questions remain. For example, we would like to simultaneously observe two connected brain areas to see how they interact to convert information from one's reference frame into the reference frame of the other.

Reference frames for perception?

In which reference frame do we perceive the space around us? Our spatial awareness does not seem to be anchored to our bodies: as we move, we have no difficulty perceiving that objects stay still. Our perceptions seem to utilize a world-centered reference frame. However, most visual areas employ retinal reference frames. How is it that we perceive the world as stable, even as images flit across our visual areas every time our eyes move? One potential resolution to this puzzle is that we may not yet have identified the brain areas with spatial representations that can subserve perception. Another possibility is that stable spatial perception is derived from areas that do not have an explicit representation in a world-centered reference frame. Just as gain fields can allow a population of neurons to collectively encode space in a more elaborate reference frame, perhaps spatial perception emerges only from a population of neurons acting together. A third possibility is that all that will be found is a series of areas that use a coordinate frame appropriate for the task they are involved in performing — arm-centered areas for reaching, and head-centered regions for guiding food to the mouth, for example — with no centralized area tailored to support spatial perception. It may be that spatial perception, as important as it is for our experience of the world, does not require as extensive brain hardware as does a process like guiding a reach.

The study of the reference frames used throughout the brain to establish and transform representations of space will continue to be a fruitful avenue of research. The questions are well-defined, the experimental manipulations needed to answer those questions are conceptually straightforward, and most importantly, valuable insights into how the brain orchestrates perceptually guided movements will continue to emerge from these investigations.

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Further reading

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Howard Hughes Medical Institute, and Stanford University School of Medicine, Fairchild Building Room D209, Stanford, California 94305-5125, USA. Email: aaron@monkeybiz.stanford.edu