INTRODUCTION

A central question in sensorimotor neuroscience concerns what sequence of events takes place in order to transform vision into voluntary action (Bremner & Andersen, 2014; Bruce & Goldberg, 1985; Crawford, Henriques, & Medendorp, 2011; DeCharms & Zador, 2000; Flanders, Tillery, & Soechting, 1992; Gallivan & Culham, 2015; Gnadt, Bracewell, & Andersen, 1991; Goodale, 2011; Helmbrecht, Dal Maschio, Donovan, Koutsouli, & Baier, 2018; Optican, 2005; Pouget & Snyder, 2000; Robinson, 1973; Schall, 2019; Schall & Thompson, 1999; Sparks, 1986, 2002; Westendorff, Klaes, & Gail, 2010). One of the best studied experimental models in sensorimotor neuroscience is the gaze control system, which serves to orient the fovea toward visual stimuli. A gaze shift to a visual stimulus requires the appropriate movements of the eyes (and often the head) in space and time. Therefore, sensorimotor transformation is as much of a spatial problem as it is a temporal problem (Andersen, Snyder, Li, ...
spatial models that have been proposed, and the ways these
general background and review of the SC and FEF, of the
they occur at the level of shared, distributed signals rather
than specific brain structures. First, we will provide some
general background and review of the SC and FEF, of the
spatiotemporal transformations for ordinary gaze shifts (made
directly or after a short delay toward a visual stimulus) have
only recently been demonstrated.

Macaques have proven to be useful experimental mod-
els for studying gaze control circuitry due to the anatom-
ical and functional similarities with the human system
(Kaas, 2004; Passingham, 2009). Many neurons in the
primate gaze system exhibit elevated discharge rate in
response to a visual stimulus (visual response) and/or around
the time of movement (motor/movement response; Bruce
Goldberg, 1985; Goldberg, Colby, & Duhamel, 1990;
Hikosaka & Wurtz, 1983; Mays & Sparks, 1980; Mohler
& Wurtz, 1976; Schall, 2015; Schlag-Rey & Schlag, 1984).
However, the spatial mapping between these temporal
codes is not trivial. Numerous modeling and experimen-
tal studies have attempted to address this question (e.g.
Basso & May, 2017; Cohen & Andersen, 2002; Crawford
et al., 2011; Funahashi, Takeda, & Watanabe, 2004;
Fuster, 2001; Gandhi & Katnani, 2011; Sato & Schall, 2003;
Snyder, 2000; Sparks, 2002; Sparks & Mays, 1990). As
we shall see, each of these approaches have provided im-
portant advances in understanding spatial coding for gaze
control, and each has its limitations. Most importantly,
traditional methodologies did not allow one to simultane-
ously test all spatial models, or track their progress through time.
So much of what we believe about ordinary gaze transfor-
mations relies on inferences integrated from more complex
laboratory paradigms.

The goals of this review are to (a) summarize a rela-
tively new method to identify spatiotemporal codes in the
brain, (b) describe the application of this method in two
important oculomotor structures—the frontal eye field
(FEF) and superior colliculus (SC)—during fairly ordinary
head-unrestrained gaze shifts, (c) use this as an opportunity
to directly compare the neurophysiology of these two struc-
tures, and (d) contextualize these new results with respect
to the classic oculomotor literature. The novelty of our
approach is the use of a sophisticated computational analysis
method that is able to simultaneously test between all of
the known, as well as novel, spatial models in these struc-
tures through different task events (Keith, DeSouza, Yan,
Wang, & Crawford, 2009; Sajad et al., 2015; Sajad, Sadeh,
Yan, Wang, & Crawford, 2016). As we shall see, similar
spatiotemporal transformations occur in both structures at
the level of within and between neurons, suggesting that
they occur at the level of shared, distributed signals rather
than specific brain structures. First, we will provide some
general background and review of the SC and FEF, of the
spatial models that have been proposed, and the ways these
have been tested.

2 | OVERVIEW OF SC AND FEF
ANATOMY AND ROLES IN GAZE
CONTROL

In macaques, the FEF is a cortical structure located at the
bank of the arcuate sulcus, with large pyramidal neurons in
layer 5, characteristic of cortical motor structures (Stanton,
Deng, Goldberg, & McMullen, 1989; reviewed by Schall
et al., 2017), whereas the SC is a multilayered subcorti-
cal structure located on the roof of midbrain (Mohler &
Wurtz, 1976; reviewed by May, 2006). These two struc-
tures are intimately connected (Figure 1a): the FEF sends
projections to the SC directly (Künzle, Akert, & Wurtz,
1976; Stanton, Goldberg, & Bruce, 1988a), and via the basal
ganglia (Astruc, 1971; Hikosaka & Wurtz, 1983; Stanton,
Goldberg, & Bruce, 1988b). The SC sends projections
back to the FEF via the dorsomedial thalamus (Benevento
& Fallon, 1975; Barbas & Mesulam, 1981; Goldman-
Rakic & Porrino, 1985; Lynch, Hoover, & Strick, 1994;
Figure 1a). The SC and (to a lesser extent) the FEF pro-
duct directly to the brainstem and spinal cord burst gener-
tors that innervate motoneurons for eye and head motion
(Castiglioni, Gallaway, & Coulter, 1978; Harting, 1977;
Huerta, Krubitzer, & Kaas, 1986; Isa & Sasaki, 2002;
Kawamura, Brodal, & Hoddevik, 1974; Segraves, 1992;
Stanton et al., 1988a). The causal role of the SC and
FEF in gaze shift production is well established through
various microstimulation (Bruce, Goldberg, Bushnell, &
Stanton, 1985; Klier, Wang, & Crawford, 2001; Monteon,
Constantin, Wang, Martinez-Trujillo, & Crawford, 2010;
Paré, Crommelinck, & Guitton, 1994), lesion (Schiller,
Sandell, & Maunsell, 1987), and inactivation studies
(Bollimunta, Bogadhi, & Krauzlis, 2018; Dias, Kiesau,
& Segraves, 1995; Hanes & Wurtz, 2001; Hikosaka &
Wurtz, 1985; McPeek & Keller, 2004). Both SC and FEF
also receive direct visual input from the thalamus and
visual cortex (Kaas & Huerta, 1988; Lynch et al., 1994;
Schall, Morel, King, & Bullier, 1995). The superficial
layer of the SC also receives direct visual input from the
retina (Perry & Cowey, 1984).

Both the FEF and SC can exhibit visual and motor re-
sponses (Bruce & Goldberg, 1985; Hanes & Schall, 1996;
Mohler & Wurtz, 1976; Munoz & Wurtz, 1995; Paré &
Hanes, 2003; Schiller, 1984). Neurons in these structures
are often classified according to their temporal responses
(Figure 1b): Visual neurons exhibit visual response, Motor
(or movement) neurons exhibit motor response, and
Visuomotor (or Visuomovement) neurons exhibit
both response types (Bruce & Goldberg, 1985; Wurtz &
Albano, 1980; but see Lowe & Schall, 2018). Visual and
motor responses in the FEF and SC are often spatially se-
lective for a restricted patch of space called a “response
field” (or “receptive field” for the visual response; Bruce
FEF and SC response fields are often tuned for the contralateral visual field, and SC receptive fields show anatomic topographic organization.

3 | SPATIAL MODELS FOR GAZE

As noted in the introduction, just because a neural event coincides temporally with an externally observable event (i.e. visual stimulus or saccade onset), it does not mean that one can assume which spatial variable is encoded. This is particularly true of motor-locked signals, which may (or may not) have undergone considerable processing after the initial sensory input. At the input level for gaze saccades, light from visual stimuli hit the photoreceptors on the retina. Because the retina is fixed on the eye, we can say that the retina encodes visual stimuli in an eye-centered frame where the fovea is the origin and positions can be defined by vectors projecting outwards along the spherical retina (Demb & Singer, 2015). Ultimately, the gaze system uses this to evoke patterns of muscle contractions to move the eye (rotation in head) and head (rotation on body) toward the stimulus. What remains unclear is how eye-centered stimulus representations are transformed into muscle coordinates. Despite decades of work, there is still no consensus on the sequence of spatial transformations in the gaze system. Here, we briefly review some of the alternatives that have been proposed, and ways they have been experimentally tested.

3.1 | Canonical models in gaze control

To characterize spatial processing in the brain, it is important to ask two questions: (a) what spatial parameter is encoded? and (b) what is the reference frame used to encode that parameter? (e.g. Soechting & Flanders, 1992). In the head-unrestrained gaze control system, one might expect to encode spatial parameters, such as the visual target (T; e.g. Optican, 2005; Steenrod, Phillips, & Goldberg, 2012), eye motion (E), head motion (H), or their combination: gaze motion (G; e.g. Chen, 2006; Cowie & Robinson, 1994; Freedman & Sparks, 1997; Gandhi & Katnani, 2011). Spatial parameters related to these motions might be encoded either as displacement vectors relative to initial position (dE, dH, and dG) or final positions irrespective of initial position (Crawford & Guitton, 1997; Daemi & Crawford, 2015; Kardamakis & Moschovakis, 2009). Finally, each of these parameters might be encoded relative to various egocentric frames of references, including the eye (Te, Ge, Ee, and He), the head (Th, Gh, Eh, and Hh), or the body/space (body and space frames are indissociable when body does not move) (Ts, Gs, Es, and Hs; see Figure 2a; Boussaoud & Bremmer, 1999; Colby, 1998; Crawford et al., 2011; Lappi, 2016; Soechting & Flanders, 1992). Noteworthy that in experiments conducted in complete darkness, where the surrounding objects are not visible, egocentric frames are the focus because the possibility for object-centered (i.e. allocentric) spatial representations is eliminated (but see Bharmauria, Sajad, Li, et al., 2020; Li et al., 2017). Many early conceptual models assumed that low-level representations, such as Te, must be transformed into higher level frames, such as Th, to control movement (Andersen & Zipser, 1988; Soechting, Tillery, & Flanders, 1990), but more recent neural network studies have shown that this is not necessarily the case (Blohm,
Keith, & Crawford, 2009; Pouget & Snyder, 2000; Smith & Crawford, 2005). Instead, the brain might make use of partial or intermediate reference frames, as discussed next.

3.2 Intermediate reference frames

While the canonical reference frames (above) describe the egocentric representations in gaze control, empirical data as well as computational studies have suggested evidence for reference frames that are intermediate (or hybrid) between these frames (Avillac, Deneve, Olivier, Pouget, & Duhamel, 2005; Jay & Sparks, 1984; Martinez-Trujillo, Medendorp, Wang, & Crawford, 2004; Pouget & Snyder, 2000; Stricane, Andersen, & Mazzoni, 1996). Quantitatively, intermediate reference frames are obtained from the linear combination of two canonical frames (Figure 2b). In Figure 2b, the eye frame (red) and head frame (green) and nine intermediate frames with different degrees of eye- and head-centeredness are shown. Constructing these intermediate frames of reference allows one to test nuances that are missed when one forces the data into predefined categories (e.g. Caruso, Pages, Sommer, & Groh, 2018). Recently, we have extended the concept of intermediate spatial coding to the coding of spatial parameters within the same reference frame, a key topic which we will return to below. Other coding mechanisms—such as gaze-dependent “gain fields” are likely important for implementing reference frame transformations (Andersen & Zipser, 1988; Blohm & Crawford, 2009; Salinas & Abbott, 2001; Smith & Crawford, 2005), but will not be the focus of the current review.

4 Traditional approaches to studying spatial encoding

While a spatially tuned stimulus-locked response is most likely related to stimulus location, at least in the absence of recurrent feedback, further processing means that a movement-locked response may either be related to the stimulus or the metrics of the imminent movement (Marino, Rodgers, Levy, & Munoz, 2008; Omrani, Kaufman, Hatsopoulos, & Cheney, 2017; Stanford & Sparks, 1994). Most behavioral paradigms that dissociate these locations suggest the latter: imminent movement (Everling, Dorris, Klein, & Munoz, 1999; Everling & Munoz, 2000; Funahashi, 2013; Zhang & Barash, 2000; but see Edelman & Goldberg, 2002; Frents & Van Opstal, 1997; Quessy, Quinet, & Freedman, 2010). Further, whereas most studies involve head-restrained eye motion, in natural head-unrestrained conditions, the same signal might encode eye motion, head motion, or the combination: gaze (Chen, 2006; Cullen, Galiana, & Sylvestre, 2000; Guittion, Munoz, & Galiana, 1990; Knight, 2012; Paré & Guittion, 1990; Sparks, Freedman, Chen, & Gandhi, 2001; Walton, Bechara, & Gandhi, 2007). Under such conditions, many of the models described in the previous section become impossible to disentangle. Below we will review the traditional approach to investigating spatial parameters and their respective reference frames in FEF and SC.

4.1 Differentiating spatial parameters

The simple geometry of the oculomotor system actually imposes a challenge for testing spatial parameters. Unlike the reach system (where the visual vector and hand movement vector do not align unless the hand starts moving from the location of the eyeball; e.g. Blohm & Crawford, 2007), in the saccadic system, sensory and motor parameters are highly correlated (Freedman & Sparks, 1997; Marino et al., 2008; Smith & Crawford, 2005; Snyder, 2000). One way to overcome this challenge is to study random variations between these parameters (Bremmer, Kaminiarz, Klingenhoefer, & Churan, 2016; Keith et al., 2009; Platt & Glimcher, 1998; Wimmer, Nykamp, Constantinidis, & Compte, 2014), but neurophysiology techniques that rely on averaging often wash these out. For example, the variable scatter of gaze endpoint around target in many cases averages to zero, making it impossible to know if the activity of neurons is best described by target location or the gaze endpoint position. To overcome this limitation, experimenters...
have used clever paradigms that spatially dissociate the location of visual stimulus from the gaze target. Some have used motor adaptation paradigms in which after a training period, the motor system generates a movement that is spatially distinct from that of the visual stimulus (Edelman & Goldberg, 2002; Frens & Van Opstal, 1997; Quessy...
et al., 2010; Takeichi, Kaneko, & Fuchs, 2007). Others have used experimental tasks that require a deliberate (rule-based) calculation of the gaze target to another location defined by (but different from) the visual stimulus (Everling et al., 1999; Everling & Munoz, 2000; Sato & Schall, 2003; Watanabe & Funahashi, 2007; Zhang & Barash, 2000). The most popular example of such tasks is the antisaccade task in which the subject is required to elicit an eye movement opposite to the direction of the target (Munoz & Everling, 2004). However, such transformations appear to be driven by top-down feedback, propagating “backwards” from frontal to parietal to occipital cortex (Blohm et al., 2019; Paneri & Gregoriou, 2017). These techniques are thus valuable for understanding how the brain implements rule-based, top-down transformations, but they do not trivially map onto the standard bottom-up sensorimotor transformations (Hawkins, Sayegh, Yan, Crawford, & Sergio, 2013; Jamadar, Johnson, Clough, Egan, & Fielding, 2015; Johnston, DeSouza, & Everling, 2009).

4.2 Differentiating reference frames

Classically, reference frames under head-immobilized conditions are investigated by systematically switching the initial eye orientation between several discrete positions (Figure 3a). Because the head is stationary relative to the body, the head and body/space frames remain in register. If the neural response shows systematic changes as a function of position relative to one effector but not the other, then the neuron’s response is in the reference frame fixed to that effector (Avillac et al., 2005; Caruso et al., 2018; Cohen & Andersen, 2002; Jay & Sparks, 1984; Russo & Bruce, 1994). To investigate intermediate frames of reference, some studies use the quantitative definition to explicitly test for these frames (e.g. Avillac et al., 2005; Jay & Sparks, 1984; Figure 2b). However, these techniques do not separate the head and body frames, and require repetition and averaging that are difficult to replicate under natural head-unrestrained conditions (Keith et al., 2009).

An overarching theme is that, while various ingenious methods have been used to test spatial models for vision and gaze control, they each have their own limitations, testing only parts of the question. In the following section, we describe a method that allows one to test all such models simultaneously during natural, head-unrestrained conditions.

5 A MODEL-FITTING APPROACH DEVELOPED FOR IDENTIFYING NEURONAL SPATIAL CODES

The following section describes an analytic approach that was developed to test between multiple models of spatial coding in neural activity during head-unrestrained gaze behavior. The method can be viewed as complementary to decoding approaches, where machine learning algorithms are used to derive specified information from neural data (Bremmer et al., 2016; Leavitt, Pieper, Sachs, & Martinez-Trujillo, 2017; Glaser et al., 2017; Pruszynski & Zylberberg, 2019). The latter approach tests for implicit population codes, whereas the current method tests for explicit coding, at the level of both single units and neural populations. To do this in the presence of complex and “sloppy” head-unrestrained behavior, several technical challenges had to be overcome.

5.1 Challenges and benefits of head-unrestrained gaze recordings

Head-unrestrained experiments provide the potential benefits of allowing more natural gaze behavior, testing effector coding specificity (gaze vs. eye vs. head), and separating more frames of reference (eye vs. head vs. space/body). However, they also produce major analytic challenges. One is that correlative techniques are insufficient because gaze, eye, and head motion always correlate with each other. Another is that in the range of head-unrestrained gaze motion, three-dimensional (3-D; horizontal, vertical, and torsional) measurements become important because torsional rotation of the eyes and head becomes more prominent, and linear operations on 2-D gaze/eye/head signals (only horizontal and vertical) yield large errors related to noncommutativity (Tweed, Haslwanter, Happe, & Fetter, 1999). Likewise, this requires a 3-D analysis to accurately compute positions, such as Te and Ge, which are positions in true retinal (i.e. eye-centered) coordinates (Crawford et al., 2011). A third challenge is that even for the same gaze orientation, the relative orientations of eye and head can be highly variable (DeSouza et al., 2011; Freedman & Sparks, 1997). Consequently, the traditional approach for identifying the reference frames (Figure 3a) is difficult to replicate. On the other hand, as we shall see, these same problems can be turned into advantages (Figure 3b,c).

Figure 3c illustrates the aspects of gaze behavior that we have utilized to map SC and FEF response fields in several of our recent studies (Sadeh, Sajad, Wang, Yan, & Crawford, 2015, 2018, 2020; Sajad et al., 2015, 2016). Important for addressing the spatial code is the pattern of various spatial parameters during this task. The (largely self-generated) variability in the behavior tends to separate spatial parameters. The animal’s gaze end-points form a scatter around a given target, separating T and G (Figure 3c, left panel). The animal itself uses different combinations of eye and head rotation (Figure 3c, top-right panel; including torsion, not shown) to achieve a given gaze shift, separating
different effectors. Likewise, the animal uses different combinations of initial eye and head position (Figure 3c, bottom-right panel; including torsion, not shown), which separate out different frames of reference. To increase the separation between the frames of reference, we introduced an additional variability in the initial gaze positions. Now, all that is needed is some statistical method able to account for these variations and utilize them to fit various spatial models against neural activity.

5.2  New approach to studying spatial encoding using PRESS statistics

To overcome the above challenges, Keith et al., (2009) introduced a method, which takes advantage of the property that neurons have spatially organized response fields. To identify the spatial parameter and reference frame that best describe variations in the neuron response, they exploited the natural variability in behavior described above. Figure 3b depicts the logic for this approach. Neural activity is plotted against each set of spatial parameters derived from the behavioral data. Spatial models were constructed by nonparametric fits through the distribution of data. Then, the quality of the fit for each model is quantified using Predicted Residual Error Sum of Squares (PRESS) statistics which is a form of cross-validation used in regression analysis (Keith et al., 2009). In other words, for each data point, the residual is calculated relative to a fit to all the other data points, excluding the point in question. The spatial model that yields the lowest PRESS residuals (i.e. the best-fit) is assumed to characterize the spatial parameter the neuron encodes, and models that yield significantly larger residuals (at the single neuron or population level) can be eliminated from consideration. This method can also be adapted to fitting intermediate models. For example, one can construct models based on points between and beyond the Te and Th (Figure 2b) and determine which weighting yields the lowest overall residuals (e.g. Figures 4b,c and 5b,c). As shown in these figures, this method is easiest to visualize with 2-D response fields, but in principle, it can be applied to neurons that encode any spatially variable behavior in any multidimensional coordinate system. In the following sections, we review the use of these methods to describe response fields and spatial coding, for the first time directly comparing our results from the FEF and SC.

6  VISUAL RECEPTIVE FIELDS

The current viewpoint is that the visual response in both the FEF and SC can be characterized by a salience or priority map of space (Fernandes, Stevenson, Phillips, Segraves, & Kording, 2013; Krauzlis, Lovejoy, & Zénon, 2013; Thompson & Bichot, 2005; White et al., 2017), but what spatial parameter and reference frame code does this map employ? (note that this is not the same as “retinotopy”, which is the way these signals are anatomically distributed). Most previous studies that have explicitly tested for reference frames suggest that SC and FEF visual responses encode the visual stimulus location fixed in retinal coordinates (e.g.

FIGURE 4  Spatial analysis of visual receptive fields in FEF and SC. (a) Raster and spike density function aligned on target onset (left) and the visual receptive field plot (right) of a representative visual response in FEF. Circles (radius: firing rate) represent data points for response field mapping. Activity was sampled from the 80–180 ms after target presentation (Figure 1b). Color-map represents the nonparametric fit to the data. (b) Triangular plots represent intermediate models constructed from three pairs of canonical models: eye (e), head (h), and body/space (s) frames based on target location (left) and gaze endpoint (right). The continua between eye and head intermediate frames (Te-Th, and Ge-Gh) are also shown in Figure 2b. Green shade indicates intermediate spatial models that are not significantly eliminated. Black square indicates the population best-fit model. (c) Similar conventions as (b) for superior colliculus. Green shades in (b) and (c) cluster around eye-centered T (Te) and G (Ge) models. The population best-fit (dark green square) was at intermediate spatial model at or close to Te for both FEF and SC. Adapted from Sajad et al., (2015) and Sadeh et al., (2015)
Bruce & Goldberg, 1985; Cassanello & Ferrera, 2007; Lee & Groh, 2012; Schiller & Stryker, 1972; Snyder, 2000; but see Caruso et al., 2018), so this is a good place to test and confirm the new method described above.

DeSouza et al. (2011) were the first to investigate the reference frame of visuomotor responses in the SC in head-unrestrained conditions using an early version of the method described above (DeSouza et al., 2011). They sampled visuomotor responses during visually guided gaze shifts and found that, overall, variations in combined SC visuomotor responses were best described by target location (and not final position of gaze) in eye-centered coordinates. However, visual responses were not clearly separated from motor responses in that experiment.

More recently, we gathered data from both the SC and FEF during an oculomotor delayed memory-guided task, which temporally separates the visual and motor responses intervened by a short memory delay (Sadeh et al., 2015; Sajad et al., 2015). We found that across the complete set of spatial models tested (see Section 2), perhaps not surprisingly, those related to the movement of the eyes (in the head) and the head (on the body) were eliminated. Indeed, the vast majority of visually responsive neurons in both FEF and SC had response fields that exhibited the highest spatial organization (and lowest residuals of fit) when they were plotted based on target position in eye-centered coordinates (Te; Figure 4a). At the population level (all neurons with visual responses), these fits were significantly better than any other model, and sometimes the preference for eye-centered coding was statistically significant even at the level of individual neurons.

However, it might be argued that by restricting our fits to canonical models, especially at the population level, one might miss either systematic or variable shifts of individual neuron coding distributions along intermediate frames, away from the canonical models. Therefore, we did a comprehensive testing of intermediate reference frames constructed based on target and gaze endpoint positions (intermediate reference frames between each pair of reference frame, eye-head, head-space, and eye-space). This analysis showed that although single FEF and SC visual neurons showed variable distributions along intermediate points between models, these distributions tended to mainly cluster around Te (Figure 4b,c). Based on these results, we concluded that the visual response in both FEF and SC encodes positions in eye-centered coordinates.

7 | MOTOR RESPONSE FIELDS

The nature of coding of the SC and FEF motor responses has been the subject of more debate than the visual response. Most visual-motor dissociation tasks suggest that the motor response in FEF and SC encodes saccade direction (e.g. Everling et al., 1999; Everling & Munoz, 2000; Moon et al., 2007; Sato & Schall, 2003), but some have shown evidence for encoding sensory stimulus location (Edelman & Goldberg, 2002; Frens & Van Opstal, 1997; Quessy et al., 2010). Also as mentioned above, it is not known how results from these studies translate to ordinary saccades in which visual-motor dissociations are absent, and the subject has to directly shift gaze toward the visual stimulus. There are also disagreements about the nature of the spatial code in FEF and SC related to eye-head gaze behavior. Most head-unrestrained studies have concluded that gaze (rather than eye or head) is the primary code (Freedman & Sparks, 1997; Guitton & Mandl, 1978; Klier et al., 2001; Knight & Fuchs, 2007; Monteon et al., 2010).
Also studies in head-restrained monkeys that recorded from neck muscle activity have drawn similar conclusions (Corneil, Olivier, & Munoz, 2002; Elsley, Nagy, Cushing, & Corneil, 2007). But some studies have shown evidence for independent eye and head movement coding in these structures (Bizzi & Schiller, 1970; Chen, 2006; Knight, 2012; Walton et al., 2007). Finally, the majority of reference frame studies suggest that an eye-centered code predominates in FEF and SC (Bruce & Goldberg, 1985; Cassanello & Ferrera, 2007; Klier et al., 2001; Russo & Bruce, 1994; Schiller & Stryker, 1972; Snyder, 2000), but yet again, there are alternative views (Caruso et al., 2018). Some of the disagreements are due to differences in experimental conditions and assumptions about the behavior or neuronal spatial code. For example, if one assumes neurons encode a certain parameter (e.g., target position in many studies) without explicitly testing this, the traditional analysis method of reference frames could yield inaccurate conclusions especially if neurons encode other spatial parameters that show systematic variations relative to the assumed parameter.

We re-examined this question by applying our model-fitting approach to motor responses that accompanied head-unrestrained gaze shifts, following the visual responses (described above) and memory delay (Sadeh et al., 2015; Sajad et al., 2015). We found that the motor response in both FEF and SC, similar to the visual response, showed a strong preference for eye-centered models. Head-centered and body/space-centered models were significantly ruled out at the population level. Importantly, spatial models based on independent eye (in head) and head (in space) position and displacement were also significantly ruled out for both FEF and SC motor responses. Overall, Ge (and very similar model dG) gave the best fits, although Te was not eliminated.

Across the tested intermediate reference frames, for both FEF and SC, similar to the visual response, target and gaze position spatial models based on high degree of eye-centeredness (but not head- and space-centeredness) were preferred (Figure 5). However, unlike the visual response, the overall best-fit model for motor response was a model closest to Ge (Figure 5b,c; or gaze displacement, dG, which is a very similar model to Ge; see Figure 5c), previously shown to be a better descriptor of SC motor output (Klier et al., 2001).

8 | VISUOMOTOR TRANSFORMATIONS

Thus far, we have described visual and motor response field fits, without considering how the former is transformed into the latter. Visuomotor transformation potentially involves multiple computational stages, each of which can contribute to inaccuracies in gaze behavior (Alikhanian, Carvalho, & Blohm, 2015; Churchland, Afshar, & Shenoy, 2006; Faisal, Selen, & Wolpert, 2008; Gnadt et al., 1991; Ma, Husain, & Bays, 2014; Spaak, Watanabe, Funahashi, & Stokes, 2017; van Beers, 2007; van Bergen, Ma, Pratte, & Jehee, 2015; White, Sparks, & Stanford, 1994; Wimmer et al., 2014). Figure 6a shows a general breakdown of these stages: (a) visual target stimulus location (T) must be integrated with task rules to work out a desired gaze target (Miller & Cohen, 2001). Although we purposefully avoided this in our studies, in certain paradigms task rules are introduced to spatially dissociate stimulus location from the desired gaze location (Munoz & Everling, 2004). (b) Sometimes the gaze target needs to be maintained in working memory for a delayed response (Curtis, Rao, & D’Esposito, 2004; Gnadt et al., 1991). (c) This representation then needs to be relayed to the motor circuitry where the gaze command is generated (Chatham & Badre, 2015; Schall, Purcell, Heitz, Logan, & Palmeri, 2011). (d) This gaze command needs to be decomposed into separate effector commands to rotate the eye in head and the head on the body (Daemi & Crawford, 2015; Gandhi & Sparks, 2007; Guittou, 1992). (e) The separate eye and head movement commands then result in muscle contraction patterns that result in repositioning the gaze (G). Figure 6b shows that the noise in spatial representations associated with each stage (represented by $E_{\text{stage}}$) can push the spatial code along the error-space from T toward G, resulting in the overall inaccuracy in gaze behavior (i.e., T-G disparity). Where along this sequence of information processing do FEF and SC visual and motor responses lie?

8.1 | Introducing T-G continuum—transformation of spatial code along the error-space

To address the question posed in the last paragraph, we created a spatial continuum between Te and Ge, analogous to the idea of intermediate frames of reference, except that Te and Ge are both in the same eye-centered frame of reference (Figure 6b). What separates these two parameters are variable inaccuracies in gaze behavior. We refer to this spatial continuum “T-G continuum” as a set of spatial models spanning the error-space. Accordingly, a change in spatial code from Te toward Ge (henceforth, we will refer to the eye-centered codes Te and Ge as T and G for simplicity) reflects the incremental accumulation of inaccuracy in spatial representations along the visuomotor pathway, realized as variable errors in gaze behavior.

Figure 6c,d show the results of this analysis for FEF and SC visual (before a memory delay) and motor responses (after a memory delay). As one can see, visual responses clustered around T and motor responses clustered around
G. Importantly, the shift from T to G was significant for both brain structures. This was also observed in plots of the motor versus visual T-G continuum fits for individual Visuomotor neurons. Note that although these data were collected in head-unrestrained conditions, these particular results would be expected to hold in head-restrained conditions, because they do not depend on separation of effectors or frames.

Based on these observations, we concluded that the FEF (Sajad et al., 2015) and SC (Sadeh et al., 2015) are involved in the spatial visual-to-motor transformations for gaze shifts. Furthermore, they show that this happens both within and
between neurons in both structures, suggesting a signal transformation that occurs at the cellular level but is distributed across brain structures.

8.2 Timing of the transformation within and between neurons in memory delay task

With the visual and motor responses in FEF and SC separated by a memory delay, does the transformation from T to G occur before, during, or after the memory delay? Furthermore, what is the differential contribution of different neuron types to this transformation? To address these questions, Sajad et al., (2016) examined the time course of the evolution of the spatial tuning along the T-G continuum (i.e. error-space) for FEF neurons by analyzing multiple time steps spanning an early visual period, the memory delay, and the motor response. We found that at the population level, the transition from T to G was characterized as monotonic and gradual through time during the entire visual-memory-motor intervals of the task (Figure 7a). A similar analysis of the SC neuronal data from Sadeh et al., 2015, done expressly for this article, revealed the same intermediate spatiotemporal transformation as the FEF (Figure 7b).

As described in more detail in the original paper (Sajad et al., 2016), further details emerged when we broke our FEF population down into four distinct subclasses. This revealed a number of fascinating details: Visual neurons encoded T, Visuomotor neurons showed an overall transition like the entire population with a visual code that was close to T but shifted toward G (Figure 7a), neurons with both delay and motor activities had a code that remained fixed between T and G, and neurons with motor-only activity showed a significant further “jump” to G at the end. Sajad et al., (2016) interpreted this latter jump as evidence for a memory-motor transformation within the FEF.

Overall, these results demonstrate that FEF and SC spatial codes evolve progressively along almost the entire T-G range during a memory delay, and that different neuron types can contribute differently to a visual-memory-motor transformation, much like a relay team (Cohecelln, Pouget, Heitz, Woodman, & Schall, 2009; Heinze, Hepp, & Martin, 2007; Lawrence, White, & Snyder, 2005; Markowitz, Curtis, & Pesaran, 2015; Merrikhi et al., 2017; Shin & Sommer, 2012; Spaak et al., 2017; Wurtz, Sommer, Paré, & Ferraina, 2001). can a similar transformation be demonstrated in simple saccades made directly to a target with no delay? To address these questions, Sadeh et al. (2020) recorded the activity of SC neurons during a direct visually guided gaze task (reactive task). As expected, gaze behavior was still inaccurate in this task albeit more accurate than the memory-guided task, likely due to a lack of memory-dependent processes vulnerable to noise (Figure 6a). This inaccuracy in behavior (i.e., disparity between T and G) allowed us to apply the T-G continuum analysis, similar to above, to show a T-to-G transition both between visually- and motor-responsive neurons and even within individual Visuomotor neurons similar to the memory-guided gaze task (Figure 8). This time, however, the transformation occurred within the short interval of the response time (i.e. ~200 ms) and followed a similar progression in all neuron types. Thus, even in the absence of a memory period, as the activity evolved from visual-to-motor temporal codes, spatial representations evolved from an accurate target representation to one that closely reflects the inaccuracy in gaze endpoint.

Overall, these studies suggest that the visuomotor transformation for gaze does not involve a discrete switch between target to gaze coding, but rather an intermediate progression that may or may not involve different neuron types, depending on timing and task details.

8.3 Rapid transformation during reactive gaze shifts

Does the T-to-G transformation described in the previous sections depend on memory-related processing? Conversely,
9 | THEORETICAL IMPLICATIONS: A NEW CONCEPTUAL MODEL FOR GAZE CONTROL

The general conclusion of our FEF and SC findings seems clear: both structures shared very similar spatiotemporal progression of signals and transformations. This suggests extensive sharing of signals between the SC and FEF, likely through their interconnections (Munoz & Schall, 2004; Sommer & Wurtz, 2000, 2001, 2004). This further supports the notion that these two structures behave as a unit in the sensorimotor transformation for gaze shifts (or saccades in head-restrained conditions), sharing both the desired transformation (designed to land gaze on target) and likely transformation-related noise, resulting in the variable gaze errors that we measured and used in our analysis. Accordingly, these two structures are largely treated as one unit in the conceptual model that follows (Figure 9).

In order to construct the conceptual model illustrated in Figure 9, we synthesized our own results with knowledge derived from the previous literature. Our conceptual model relies on the assumption that visuomotor transformations are inherently noisy (Alikhanian et al., 2015; Arieli, Sterkin, Grinvald, & Aertsen, 1996; Churchland et al., 2006; Faisal et al., 2008; Gnadt et al., 1991; van Bergen et al., 2015; Wimmer et al., 2014).

The model begins with the frontal cortex and SC receiving the true location of the visual stimulus in eye-centered (i.e., retinal) coordinates. This is based on the observation that visual response of Visual neurons in both FEF and SC was best described by the T model along the T-G continuum (Sajad et al., 2016). Having access to this accurate visual information can be achieved by direct projections from visual cortex as well as the retina (May, 2006; Perry & Cowey, 1984; Schall et al., 1995).

To guide appropriate behavior, the information about target location needs to be gated to the appropriate memory and motor circuitry to meet the requirements of the task. Such a gating mechanism can be implemented by the corticocortical and cortico-striato-thalamic loops, and subcortical circuits through the basal ganglia (Battaglia-Mayer & Caminiti, 2019; Coe et al., 2019; Krauzlis et al., 2013; Lynch & Tian, 2006; O’Reilly & Frank, 2006). These circuits can integrate various sensory information with learned associations to transfer the spotlight of attention onto relevant locations. One candidate for such a representation in FEF and SC can be the visual response of Visuomotor neurons. In our experiments, the visuospatial representation of Visuomotor neurons, at similar latency to that of T-coding Visual neurons, was slightly shifted toward G, indicating accumulation of noise. This noise can arise due to the gating that transforms visual input into a movement goal (Figure 9, the noise is labeled $E_{\text{vis}}$; Chatham & Badre, 2015; O’Reilly & Frank, 2006). Anatomically, this noise can arise from reduction in resolution due to synaptic integration in the basal ganglia circuits (Avery & Krichmar, 2015; Parthasarathy, Schall, & Graybiel, 1992; Zheng & Wilson, 2002). A leading hypothesis suggests that while this noise results in inaccurate behavior, it can offer the required flexibility to perform various cognitive transformations (Faisal et al., 2008; McDonnell & Ward, 2011). In complex tasks that involve stimulus-response incompatibility (such as the antisaccade task), this noisy gate would transform visual information into a movement goal at a location indicated by the stimulus-response mapping rule (Boettiger & D’Esposito, 2005; Dash, Yan, Wang, & Crawford, 2015; Everling & Johnston, 2013; Miller & Cohen, 2001; Munoz & Everling, 2004; Sato & Schall, 2003). In simple gaze tasks where the visual stimulus and movement goal are spatially congruent, it would simply transfer activity to the population of neurons that (roughly) represent the same patch of space (Marino et al., 2008; Spaak et al., 2017).

After the movement goal is determined, it needs to be maintained in working memory or directly routed to the motor network depending on the task requirements. It has been shown that the activity in FEF and SC during memory delay reflects the maintained representations in working memory (Funahashi, Bruce, & Goldman-Rakic, 1989; Fuster...
We observed that there was a transition in spatial representations toward G during the memory delay period in both structures. This confirms models of spatial working memory that describe the diffusion of spatial representations in a random-walk fashion due to accumulated noise in the population dynamics (Figure 9, label $\epsilon_{\text{mem}}$; Compte, Brunel, Goldman-Rakic, & Wang, 2000; Wimmer et al., 2014). Our finding that the memory responses did not exactly reach G suggests that this diffusion process does not fully account for gaze endpoint inaccuracy (Churchland et al., 2006; Faisal et al., 2008; Ma et al., 2014).

In our studies on memory-guided gaze shifts, we only found a strong preference for G code (or very similar codes) in neurons that exclusively fired during the gaze shift, suggesting noise in a memory-to-motor transformation (Figure 9, this noise is labeled $\epsilon_{\text{mem-mot}}$; Ketcham, Hodgson, Kennard, & Stelmach, 2003; Ma et al., 2014; Ploner, Rivaud-Péchoux, Gaymard, Agid, & Pierrot-Deseilligny, 1999). We propose that this transformation involves a second noisy gating of maintained movement goal from visually and memory-responsive neurons to purely motor-responsive neurons with no memory activity (M-only neurons), possibly involving striato-thalamic circuits (Brown, Bullock, & Grossberg, 2004; Chatham & Badre, 2015; Schall et al., 2011). This is in agreement with previous studies that show differential contribution of distinct subpopulations to motor preparation and their differences in anatomical and functional connections (Basso & May, 2017; Cohen et al., 2009; Doubell, Skaliora, Baron, & King, 2003; Markowitz et al., 2015; Merrikhi et al., 2017; Ninomiya, Sawamura, Inoue, & Takada, 2012; Pouget et al., 2009; Ray, Pouget, & Schall, 2009; Redgrave et al., 2010; Segraves & Goldberg, 1987; Weyand & Gafka, 1998). Once the motor network, comprised of FEFO and SC M-only neurons, is triggered to threshold levels, a gaze command is sent to downstream motor structures (Klier et al., 2001; Sparks, 2002).

One might have noticed that in the overall motor response populations, the T-G code did not quite make it all the way to G (Figures 6–8), leaving some error unaccounted for. This suggests additional noise in sensorimotor transformations downstream of the FEFO and SC, as demonstrated previously (Figure 9; this noise is labeled $\epsilon_{\text{RFT}}$; Alikhanian et al., 2015; Edelman & Goldberg, 2002; Frens & Van Opstal, 1997; Stanford & Sparks, 1994). We also found that the SC motor burst came closer to G in the memory-guided task compared to reactive gaze shifts. (Sadeh et al., 2018). The most parsimonious explanation for this result is that the unaccounted downstream noise (i.e., $\epsilon_{\text{RFT}}$) was equal in both cases, but would contribute proportionately less to the overall errors when additional memory-related noise is present.

9.1 Future directions, emerging questions, and new hypotheses

The methodologies, results, and model described in this review can lead to many more questions, such as: (a) How is...
the T-to-G transformation accomplished through the interaction of neurons within and between different layers of SC and FEF microcircuits? (Basso & May, 2017; Bastos et al., 2012; Chandrasekaran, Peixoto, Newsome, & Shenoy, 2017; Heinzle et al., 2007; Massot, Jagadisan, & Gandhi, 2019; Sajad, Godlove, & Schall, 2019; Shin & Sommer, 2012); (b) How do the spatial codes at the individual neuron and population levels change in other visuomotor behaviors, such as express saccades (latency < 100 ms), in which the temporal visual and motor responses entirely overlap (Dorris, Pare, & Munoz, 1997; Isa, 2002)?; (c) how does this methodology extend to other areas of the brain involved in gaze control (Bremmer et al., 2016; Schneider, Domínguez-Vargas, Gibson, Kagan, & Wilke, 2020)?

Further, the general applicability of the model-fitting method described here provides the opportunity to investigate other models and other behaviors, so long as there is related spatially tuned activity in the brain and variations in the behavior to distinguish the models. For example, the current review only touches on egocentric models; we have already started applying these methods to investigate the neural coding of allocentric landmarks in the gaze system (Bharmauria, Sajad, Li, et al., 2020a; Bharmauria, Sajad, Yan, Sajad, Yan, Wang, & Crawford, 2020b). We have also started using this method to differentiate gaze, head, and reach transformations in frontal cortex during coordinated eye-head-hand reaches (Arora et al., 2019; Nacher et al., 2019). There is no reason not to take this further afield, such as the analysis of activity in areas involved in spatial navigation and spatial memory, including the hippocampus and entorhinal cortex, against ego- and allocentric models during complex tasks such as natural viewing and free-moving navigation (Gulli et al., 2020; Meister & Buffalo, 2018).

Finally, since our T-G continuum (or potential analogues like a T-Hand continuum) provides a measure of neural contribution to behavioral noise, these methodologies are applicable to fitting pathological sensorimotor noise (Avery & Krichmar, 2015; Bays & Wolpert, 2007; Burns & Blohm, 2010). Errors in behavior have been commonly investigated to make inference about brain function in healthy and diseased populations. A growing trend in clinical studies is to compare systematic inaccuracies (such as amplitude gain) and (to a lesser extent) variable inaccuracies in movement in diseased populations to gain insight into the nature of their deficits (e.g., Ketcham et al., 2003; Ploner et al., 1999; Thakkar, Schall, Heckers, & Park, 2015). Our methods would allow one to trace this noise to specific neural transformations. For example, it could identify the source of noise for pathological saccades (Chan, Armstrong, Pari, Riopelle, & Munoz, 2005; Le Heron, MacAskill, & Anderson, 2005) or memory-motor transformations in Parkinson’s disease (Ketcham et al., 2003). Such tests are actually being done at this time.

10 | GENERAL CONCLUSIONS

The visuomotor transformation for gaze control has been the subject of scientific investigation for decades. While this system is celebrated as a model for understanding general sensorimotor transformations and various cognitive functions, it is extraordinarily difficult to show how its spatial codes evolve through time. Some of this is due to complexity (e.g., accounting for the many possible models in head-unrestrained behavior) and some ironically due to simplicity (i.e., due to the similarity of visual and motor vectors during ordinary saccades). But solving these technical problems has led us to a methodology with surprising power and versatility, including the ability to test simultaneously between all known models of this system, and track intermediate transformations (especially through the T-G continuum) through time.

Having applied these methods to the SC and FEF during head-unrestrained gaze shifts, with or without a memory delay, we find a similar preference for eye-centered coding in both structures, with the visual response encoding T versus the motor response encoding positions closely described by G (i.e., future gaze position). In the studies reviewed here, we have found a progressive spatiotemporal transition through intermediate T-G codes, with a memory delay, and a more rapid transition without a delay. This transformation was both local (occurring even within some neuron types) and global, appearing in parallel in these widely separated (but interconnected) brainstem and cortical structures. Importantly, this includes sharing of the neural noise that apparently both allowed us to distinguish T from G, and explains considerable behavioral errors. This does not mean that these structures do the same thing, but that the other functions they support are embedded within fundamentally similar sensorimotor “carrier waves” (Fuster, 2001; Wurtz et al., 2001). Finally, these conclusions likely generalize to other systems. For example, in the reach system, a transition from visual-to-motor coding has been observed both at the level of individual neurons, between neurons, and between areas in electrophysiological studies (Bremner & Andersen, 2014; Caminiti, Johnson, Galli, Ferraina, & Burnod, 1991; Cisek & Kalaska, 2005; Fujiwara, Lee, Ishikawa, Kakei, & Izawa, 2017; Kakei, Hoffman, & Strick, 2003; Pesaran, Nelson, & Andersen, 2006; Westendorff et al., 2010), and across lobes at the whole cortex level in neuroimaging studies (e.g., Blohm et al., 2019; Cappadocia, Monaco, Chen, Blohm, & Crawford, 2016; Gallivan & Culham, 2015). A general conclusion from this is that visuomotor transformations are not compartmentalized, but rather involve distributed signals that permeate and underlie many brain functions.

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The authors report no conflict of interest.

AUTHOR CONTRIBUTION
AS and JDC wrote the manuscript. All authors contributed to the primary research (and figures) featured in this review.

ETHICAL STATEMENT
The experiments conducted by the authors featured in this manuscript complied with the guidelines of Canadian Council on Animal Care on the use of laboratory animals and were approved by the York University Animal Care Committee.

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REFERENCES
Alikhanian, H., Carvalho, S. R. D., & Blohm, G. (2015). Quantifying effects of stochasticity in reference frame transformations on posterior distributions. *Frontiers in Computational Neuroscience*, 9, 82. https://doi.org/10.3389/fncom.2015.00082

Andersen, R. A., Snyder, L. H., Li, C. S., & Stricane, B. (1993). Coordinate transformations in the representation of spatial information. *Current Opinion in Neurobiology*, 3(2), 171–176. https://doi.org/10.1016/0959-4388(93)90206-E

Andersen, R. A., & Zipser, D. (1988). The role of the posterior parietal cortex in coordinate transformations for visual–motor integration. *Canadian Journal of Physiology and Pharmacology*, 66(4), 488–501. https://doi.org/10.1139/y88-078

Arieli, A., Sterkin, A., Grinvald, A., & Aertsen, A. D. (1996). Dynamics of ongoing activity: Explanation of the large variability in evoked cortical responses. *Science*, 273(5283), 1868–1871. https://doi.org/10.1126/science.273.5283.1868

Arora, H. K., Bharmuria, V., Yan, X., Sun, S., Wang, H., & Crawford, J. D. (2019). Eye-head-hand coordination during visually guided reaches in head-unrestrained macaques. *Journal of Neurophysiology*, 122(5), 1946–1961. https://doi.org/10.1152/jn.00072.2019

Astruc, J. (1971). Corticofugal connections of area 8 (frontal eye field) in *Macaca mulatta*. *Brain Research*, 33(2), 241–256.

Avery, M. C., & Krichmar, J. L. (2015). Improper activation of D1 and D2 receptors leads to excess noise in prefrontal cortex. *Frontiers in Computational Neuroscience*, 9, 31. https://doi.org/10.3389/fncom.2015.00031

Avillac, M., Deneve, S., Olivier, E., Pouget, A., & Duhamel, J. R. (2005). Reference frames for representing visual and tactile locations in parietal cortex. *Nature Neuroscience*, 8(7), 941. https://doi.org/10.1038/nn1480

Barbas, H., & Mesulam, M. M. (1981). Organization of afferent input to subdivisions of area 8 in the rhesus monkey. *Journal of Comparative Neurology*, 200(3), 407–431. https://doi.org/10.1002/cne.90200309

Basso, M. A., & May, P. J. (2017). Circuits for action and cognition: A view from the superior colliculus. *Annual Review of Vision Science*, 3, 197–226. https://doi.org/10.1146/annurev-vision-102016-061234

Bastos, A. M., Usrey, W. M., Adams, R. A., Mangun, G. R., Fries, P., & Friston, K. J. (2012). Canonical microcircuits for predictive coding. *Neuron*, 76(4), 695–711. https://doi.org/10.1016/j.neuron.2012.10.038

Battaglia-Mayer, A., & Caminiti, R. (2019). Corticocortical systems underlying high-order motor control. *The Journal of Neuroscience*, 39(23), 4404–4421. https://doi.org/10.1523/JNEUROSCI.2094-18.2019

Bays, P. M., & Wolpert, D. M. (2007). Computational principles of sensorimotor control that minimize uncertainty and variability. *The Journal of Physiology*, 578(2), 387–396. https://doi.org/10.1113/jphysiol.2006.120121

Benevento, L. A., & Fallon, J. H. (1975). The ascending projections of the superior colliculus in the rhesus monkey (*Macaca mulatta*). *The Journal of Comparative Neurology*, 160, 339–362. https://doi.org/10.1002/cne.90160306

Bharmuria, V., Sajad, A., Li, J., Yan, X., Wang, H., & Crawford, J. D. (2020a). Integration of eye-centered and landmark-centered codes in frontal eye field gaze responses. *Cerebral Cortex*. https://doi.org/10.1093/cercor/bhaa090

Bharmuria, V., Sajad, A., Yan, X., Wang, H., & Crawford, J. D. (2020b). Spatiotemporal coding in the macaque supplementary eye fields: Landmark influence in the target-to-gaze transformation. *bioRxiv*. https://doi.org/10.1101/2020.06.25.172031

Bizzi, E., & Schiller, P. H. (1970). Single unit activity in the frontal eye fields of unanesthetized monkeys during eye and head movement. *Experimental Brain Research*, 10(2), 151–158. https://doi.org/10.1007/BF00234728

Blohm, G., Alikhanian, H., Gaetz, W., Goltz, H. C., DeSouza, J. F., Cheyne, D. O., & Crawford, J. D. (2019). Neuromagnetic signatures of the spatiotemporal transformation for manual pointing. *NeuroImage*, 197, 306–319.

Blohm, G., & Crawford, J. D. (2007). Computations for geometrically accurate visually guided reaching in 3-D space. *Journal of Vision*, 7(5), 4. https://doi.org/10.1167/7.5.4

Blohm, G., & Crawford, J. D. (2009). Fields of gain in the brain. *Neuron*, 64(5), 598–600. https://doi.org/10.1016/j.neuron.2009.11.022

Blohm, G., Keith, G. P., & Crawford, J. D. (2009). Decoding the cortical transformations for visually guided reaching in 3D space. *Cerebral Cortex*, 19(6), 1372–1393. https://doi.org/10.1093/cercor/bhn177

Boettiger, C. A., & D’Esposito, M. (2005). Frontal networks for learning and executing arbitrary stimulus-response associations. *Journal of Neuroscience*, 25(10), 2723–2732. https://doi.org/10.1523/JNEUROSCI.3697-04.2005

Bolimunta, A., Bogadhi, A. R., & Krauzlis, R. J. (2018). Comparing frontal eye field and superior colliculus contributions to covert spatial attention. *Nature Communications*, 9(1), 3553. https://doi.org/10.1038/s41467-018-06042-2

Boussaoud, D., & Bremner, F. (1999). Gaze effects in the cerebral cortex: Reference frames for space coding and action. *Experimental Brain Research*, 128(1–2), 170–180. https://doi.org/10.1007/s002210050832

Bremner, F., Kaminiarz, A., Klingenhoefer, S., & Churan, J. (2016). Decoding target distance and saccade amplitude from population activity in the macaque lateral intraparietal area (LIP). *Frontiers in Integrative Neuroscience*, 10, 30. https://doi.org/10.3389/fnint.2016.00030

Bremmer, L. R., & Andersen, R. A. (2014). Temporal analysis of reference frames in parietal cortex area 5d during reach planning. *Journal
Caruso, V. C., Pages, D. S., Sommer, M. A., & Groh, J. M. (2018). Cappadocia, D. C., Monaco, S., Chen, Y., Blohm, G., & Crawford, J.

Chen, L. L. (2006). Head movements evoked by electrical stimulation of the frontal eye field. I. Single neurons discharging before saccades. Journal of Neurophysiology, 53(3), 603–635.

Bruce, C. J., Goldberg, M. E., Bushnell, M. C., & Stanton, G. B. (1985). Primate frontal eye fields. Human Neurobiology, 4(1), 630–635.

Bruce, C. J., & Goldberg, M. E. (1985). Primate frontal eye fields. II. Physiological and anatomical correlates of electrically evoked eye movements. Journal of Neurophysiology, 54(3), 714–734.

Burns, J. K., & Blohm, G. (2010). Multi-sensory weights depend on contextual noise in reference frame transformations. Frontiers in Human Neuroscience, 4, 221.

Caminiti, R., Johnson, P. B., Galli, C., Ferraina, S., & Burnod, Y. (1991). Making arm movements within different parts of space: The premotor and motor cortical representation of a coordinate system for reaching to visual targets. Journal of Neuroscience, 11(5), 1182–1197.

Cappadocia, D. C., Monaco, S., Chen, Y., Blohm, G., & Crawford, J. D. (2016). Temporal evolution of target representation, movement direction planning, and reach execution in occipital–parietal–frontal cortex: An fmri study. Cerebral Cortex, 27(11), 5242–5260.

Caruso, V. C., Pages, D. S., Sommer, M. A., & Groh, J. M. (2018). Beyond the labeled line: Variation in visual reference frames from intraparietal cortex to frontal eye fields and the superior colliculus. Journal of Neurophysiology, 119(4), 1411–1421.

Cassanello, C. R., & Ferrera, V. P. (2007). Computing vector differences using a gain field-like mechanism in monkey frontal eye field. The Journal of Physiology, 582(2), 647–664.

Castiglioni, A. J., Gallaway, M., & Coulter, J. D. (1978). Spinal projections from the midbrain in monkey. Journal of Comparative Neurology, 178(2), 329–345.

Chan, F., Armstrong, I. T., Pari, G., Riopelle, R. J., & Munoz, D. P. (2005). Deficits in saccadic eye-movement control in Parkinson’s disease. Neuropsychologia, 43(5), 784–796.

Chapurlat, D., & Cosnard, G. (2003). Lamina changes in decision-related neural activity in dorsal premotor cortex. Nature Communications, 8(1), 1–16.

Chatham, C. H., & Badre, D. (2015). Multiple gates on working memory. Current Opinion in Behavioral Sciences, 1, 23–31.

Chen, L. L. (2006). Head movements evoked by electrical stimulation in the frontal eye field of the monkey: Evidence for independent eye and head control. Journal of Neurophysiology, 95(6), 3528–3542.

Churchland, M. M., Afshar, A., & Shenoy, K. V. (2006). A central source of movement variability. Neuron, 52(6), 1085–1096.

Cisek, P., & Kalaska, J. F. (2005). Neural correlates of reaching decisions in dorsal premotor cortex: Specification of multiple direction choices and final selection of action. Neuron, 45(5), 801–814.

Coe, B. C., Trappenberg, T., & Munoz, D. P. (2019). Modeling saccadic action selection: Cortical and basal ganglia signals coalesce in the superior colliculus. Frontiers in Systems Neuroscience, 13.

Cohen, J. Y., Pouget, P., Heitz, R. P., Woodman, G. F., & Schall, J. D. (2009). Biophysical support for functionally distinct cell types in the frontal eye field. Journal of Neurophysiology, 101(2), 912–916.

Cohen, Y. E., & Andersen, R. A. (2002). A common reference frame for movement plans in the posterior parietal cortex. Nature Reviews Neuroscience, 3(7), 553–562.

Colby, C. L. (1998). Action-oriented spatial reference frames in cortex. Neuron, 20(1), 15–24.

Compte, A., Brunel, N., Goldman-Rakic, P. S., & Wang, X. J. (2000). Synaptic mechanisms and network dynamics underlying spatial working memory in a cortical network model. Cerebral Cortex, 10(9), 910–923.

Corneil, B. D., Olivier, E., & Munoz, D. P. (2002). Neck muscle responses to stimulation of monkey superior colliculus. I. Topography and manipulation of stimulation parameters. Journal of Neurophysiology, 88(4), 1980–1999.

Cowie, R. J., & Robinson, D. L. (1994). Subcortical contributions to head movements in macaques. I. Contrasting effects of electrical stimulation of a medial pontomedullary region and the superior colliculus. Journal of Neurophysiology, 72(6), 2648–2664.

Crawford, J. D., & Guittion, D. (1997). Visual-motor transformations required for accurate and kinematically correct saccades. Journal of Neurophysiology, 78(3), 1447–1467.

Crawford, J. D., Henriques, D. Y., & Medendorp, W. P. (2011). Three-dimensional transformations for goal-directed action. Annual Review of Neuroscience, 34, 309–331.

Cullen, K. E., Galiana, H. L., & Sylvestre, P. A. (2000). Comparing extraocular motoneuron discharges during head-restrained saccades and head-unrestrained gaze shifts. Journal of Neurophysiology, 83(1), 630–637.

Curtis, C. E., Rao, V. Y., & D’Esposito, M. (2004). Maintenance of spatial and motor codes during oculomotor delayed response tasks. Journal of Neuroscience, 24(16), 3944–3952.

Daemi, M., & Crawford, J. D. (2015). A kinematic model for 3-D head-free gaze-shifts. Frontiers in Computational Neuroscience, 9, 72.

Dash, S., Yan, X., Wang, H., & Crawford, J. D. (2015). Continuous updating of visuospatial memory in superior colliculus during slow eye movements. Current Biology, 25(3), 267–274.

DeCharms, R. C., & Zador, A. (2000). Neural representation and the cortical code. Annual Review of Neuroscience, 23(1), 613–647.

Demb, J. B., & Singer, J. H. (2015). Functional circuitry of the retina. Annual Review of Vision Science, 1, 263–289.
of Neurophysiology, 64(2), 509–531. https://doi.org/10.1152/jn.1990.64.2.509

Gulli, R. A., Duong, L. R., Corrigan, B. W., Doucet, G., Williams, S., Fusi, S., & Martinez-Trujillo, J. C. (2020). Context-dependent representations of objects and space in the primate hippocampus during virtual navigation. *Nature Neuroscience*, 23(1), 103–112. https://doi.org/10.1038/s41593-019-0548-3

Hanes, D. P., & Schall, J. D. (1996). Neuronal control of voluntary movement initiation. *Science*, 274(5286), 427–430. https://doi.org/10.1126/science.274.5286.427

Hanes, D. P., & Wurtz, R. H. (2001). Interaction of the frontal eye field and superior colliculus for saccade generation. *Journal of Neurophysiology*, 85(2), 804–815. https://doi.org/10.1152/jn.2001.85.2.804

Harting, J. K. (1977). Descending pathways from the superior colliculus: An autoradiographic analysis in the rhesus monkey (Macaca mulatta). *Journal of Comparative Neurology*, 173(3), 583–612. https://doi.org/10.1002/cne.901730311

Hawkins, K. M., Sayegh, P., Yan, X., Crawford, J. D., & Sergio, L. E. (2013). Neuronal activity in superior parietal cortex during rule-based visual-motor transformations. *Journal of Cognitive Neuroscience*, 25(3), 436–454. https://doi.org/10.1162/jocn_a_00318

Heinzel, J., Hepp, K., & Martin, K. A. (2007). A microcircuit model of the frontal eye fields. *Journal of Neuroscience*, 27(35), 9341–9353. https://doi.org/10.1523/JNEUROSCI.074-07.2007

Heitz, R. P. (2014). The speed-accuracy tradeoff: History, physiology, methodology, and behavior. *Frontiers in Neuroscience*, 8, 150. https://doi.org/10.3389/fnins.2014.00130

Helmbrcht, T. O., Dal Maschio, M., Donovan, J. C., Koutsouli, S., & Baier, H. (2018). Topography of a visuomotor transformation. *Neuron*, 100(6), 1429–1445. https://doi.org/10.1016/j.neuron.2018.10.021

Hikosaka, O., & Wurtz, R. H. (1983). Visual and oculomotor functions of monkey substantia nigra pars reticulata. III. Memory-contingent visual and saccade responses. *Journal of Neurophysiology*, 49(5), 1268–1284.

Hikosaka, O., & Wurtz, R. H. (1985). Modification of saccadic eye movements by GABA-related substances. I. Effect of muscimol and bicuculline in monkey superior colliculus. *Journal of Neurophysiology*, 53(1), 266–291.

Huerta, M. F., Krubitzer, L. A., & Kaas, J. H. (1986). Frontal eye field as defined by intracortical microstimulation in squirrel monkeys, owl monkeys, and macaque monkeys: I. Subcortical connections. *Journal of Comparative Neurology*, 253(4), 415–439. https://doi.org/10.1002/cne.902530402

Ito, T. (2002). Intrinsic processing in the mammalian superior colliculus. *Current Opinion in Neurobiology*, 12(6), 668–677. https://doi.org/10.1016/S0959-4388(02)00387-2

Ito, T., & Sasaki, S. (2002). Brainstem control of head movements during orienting; organization of the premotor circuits. *Progress in Neurobiology*, 66(4), 205–241. https://doi.org/10.1016/S0301-0082(02)00006-0

Jamadar, S. D., Johnson, B. P., Clough, M., Egan, G. F., & Fielding, J. (2015). Behavioral and neural plasticity of ocular motor control: Changes in performance and fMRI activity following antisaccade training. *Frontiers in Human Neuroscience*, 9, 653. https://doi.org/10.3389/fnhum.2015.00653

Jay, M. F., & Sparks, D. L. (1984). Auditory receptive fields in primary superior colliculus shift with changes in eye position. *Nature*, 309(5966), 345. https://doi.org/10.1038/309345a0

Johnston, K., DeSouza, J. F., & Everling, S. (2009). Monkey prefrontal cortical pyramidal and putative interneurons exhibit differential patterns of activity between prosaccade and antisaccade tasks. *Journal of Neuroscience*, 29(17), 5516–5524. https://doi.org/10.1523/JNEUROSCI.5953-08.2009

Kaas, J. H. (2004). The evolution of the visual system in primates. *The Visual Neurosciences*, 2, 1563–1572.

Kaas, J. H., & Huerta, M. F. (1988). The subcortical visual system of primates. *Comparative Primate Biology*, 4, 327–391.

Kakei, S., Hoffman, D. S., & Strick, P. L. (2003). Sensorimotor transformations in cortical motor areas. *Neuroscience Research*, 46(1), 1–10. https://doi.org/10.1016/S0168-0102(03)00031-2

Kardamakis, A. A., & Moschovakis, A. K. (2009). Optimal control of gaze shifts. *Journal of Neuroscience*, 29(24), 7723–7730. https://doi.org/10.1523/JNEUROSCI.5518-08.2009

Kawamura, K., Brodal, A., & Hoddevik, G. (1974). The projection of the superior colliculus onto the reticular formation of the brain stem an experimental anatomical study in the cat. *Experimental Brain Research*, 19(1), 1–19. https://doi.org/10.1007/BF00233392

Keith, G. P., DeSouza, J. F., Yan, X., Wang, H., & Crawford, J. D. (2009). A method for mapping response fields and determining intrinsic reference frames of single-unit activity: Applied to 3D head-unrestrained gaze shifts. *Journal of Neuroscience Methods*, 180(1), 171–184. https://doi.org/10.1016/j.jneumeth.2009.03.004

Ketcham, C. J., Hodgson, T. L., Kennard, C., & Stelmach, G. E. (2003). Memory-motor transformations are impaired in Parkinson's disease. *Experimental Brain Research*, 149(1), 30–39. https://doi.org/10.1007/s00221-002-1332-1

Klier, E. M., Wang, H., & Crawford, J. D. (2001). The superior colliculus encodes gaze commands in retinal coordinates. *Nature Neuroscience*, 4(6), 627–632. https://doi.org/10.1038/88450

Knight, T. A. (2012). Contribution of the frontal eye field to gaze shifts in the head-unrestrained rhesus monkey: Neuronal activity. *Neuroscience*, 225, 213–236. https://doi.org/10.1016/j.neuroscience.2012.08.050

Knight, T. A., & Fuchs, A. F. (2007). Contribution of the frontal eye field to gaze shifts in the head-unrestrained monkey: Effects of microstimulation. *Journal of Neurophysiology*, 97(1), 618–634. https://doi.org/10.1152/jn.00256.2006

Krauzlis, R. J., Lovejoy, L. P., & Zénon, A. (2013). Superior colliculus and visual spatial attention. *Annual Review of Neuroscience*, 36, 165–182. https://doi.org/10.1146/annurev-neuro-062012-170249

Künzel, H., Akert, K., & Wurtz, R. H. (1976). Projection of area 8 (frontal eye field) to superior colliculus in the monkey. An autoradiographic study. *Brain Research*, 117(3), 487–492.

Lappi, O. (2016). Eye movements in the wild: Oculomotor control, gaze behavior & frames of reference. *Neuroscience & Biobehavioral Reviews*, 69, 49–68.

Lawrence, B. M., White, R. L., III, & Snyder, L. H. (2005). Delay-period activity in visual, visuomovement, and movement neurons in the frontal eye field. *Journal of Neurophysiology*, 94(2), 1498–1508. https://doi.org/10.1152/jn.00214.2005

Le Heron, C. J., MacAskill, M. R., & Anderson, T. J. (2005). Memory-guided saccades in PD: Long delays can improve performance. *Experimental Brain Research*, 161, 293–298.

Leavitt, M. L., Pieper, F., Sachs, A. J., & Martinez-Trujillo, J. C. (2017). Correlated variability modifies working memory fidelity in primate prefrontal neuronal ensembles. *Proceedings of the National Academy of Sciences*, 114(12), E2494–E2503. https://doi.org/10.1073/pnas.1619949114
Lee, J., & Groh, J. M. (2012). Auditory signals evolve from hybrid-to-eye-centered coordinates in the superior principal colliculus. Journal of Neurophysiology, 108(1), 227–242. https://doi.org/10.1152/jn.00706.2011

Li, J., Sajad, A., Marino, R., Yan, X., Sun, S., Wang, H., & Crawford, J. D. (2017). Effect of allocentric landmarks on primate gaze behavior in a cue conflict task. Journal of Vision, 17(5), 20. https://doi.org/10.1167/17.5.20

Lowe, K. A., & Schall, J. D. (2018). Functional categories of visuomotor neurons in macaque frontal eye field. eNeuro, 5(5). https://doi.org/10.1523/ENEURO.0131-18.2018

Lundqvist, M., Herman, P., & Miller, E. K. (2018). Working memory: Delay activity, yes! Persistent activity? Maybe not. Journal of Neuroscience, 38(32), 7013–7019. https://doi.org/10.1523/JNEUROSCI.2485-17.2018

Lynch, J. C., Hoover, J. E., & Strick, P. L. (1994). Input to the primate frontal eye field from the substantia nigra, superior colliculus, and dentate nucleus demonstrated by transneuronal transport. Experimental Brain Research, 100, 181–186. https://doi.org/10.1007/BF00272973

Lynch, J. C., & Tian, J. R. (2006). Cortico-cortical networks and cortico-subcortical loops for the higher control of eye movements. Progress in Brain Research, 151, 461–501.

Ma, W. J., Husain, M., & Bays, P. M. (2014). Changing concepts of working memory. Nature Neuroscience, 17(3), 347. https://doi.org/10.1038/nn.3655

Marino, R. A., Rodgers, C. K., Levy, R., & Munoz, D. P. (2008). Spatial relationships of visuomotor transformations in the superior colliculus map. Journal of Neurophysiology, 100(5), 2564–2576. https://doi.org/10.1152/jn.00968.2008

Markowitz, D. A., Curtis, C. E., & Pesaran, B. (2015). Multiple component networks support working memory in prefrontal cortex. Proceedings of the National Academy of Sciences, 112(35), 11084–11089. https://doi.org/10.1073/pnas.1504172112

Martinez-Trujillo, J. C., Medendorp, W. P., Wang, H., & Crawford, J. D. (2004). Frames of reference for eye-head gaze commands in primate supplementary eye fields. Neuron, 44(6), 1057–1066. https://doi.org/10.1016/j.neuron.2004.12.004

Massot, C., Jagadisan, U. K., & Gandhi, N. J. (2019). Time-course of population activity along the dorsoventral extent of the superior colliculus during delayed saccade tasks. bioRxiv, 571307.

May, P. J. (2006). The mammalian superior colliculus: Laminar structure and connections. Progress in Brain Research, 151, 321–378.

Mays, L. E., & Sparks, D. L. (1980). Dissociation of visual and saccade-related responses in superior colliculus neurons. Journal of Neurophysiology, 43(1), 207–232. https://doi.org/10.1152/jn.1980.43.1.207

McDonnell, M. D., & Ward, L. M. (2011). The benefits of noise in neural systems: Bridging theory and experiment. Nature Reviews Neuroscience, 12(7), 415. https://doi.org/10.1038/nrn3061

McPeek, R. M., & Keller, E. L. (2004). Deficits in saccade target selection after inactivation of superior colliculus. Nature Neuroscience, 7(7), 757. https://doi.org/10.1038/nn1269

Meister, M. L., & Buffalo, E. A. (2018). Neurons in primate entorhinal cortex represent gaze position in multiple spatial reference frames. Journal of Neuroscience, 38(10), 2430–2441. https://doi.org/10.1523/JNEUROSCI.2432-17.2018

Merrihik, Y., Clark, K., Albarran, E., Parsa, M., Zirnsak, M., Moore, T., & Noudoost, B. (2017). Spatial working memory alters the efficacy of input to visual cortex. Nature Communications, 8, 15041. https://doi.org/10.1038/ncomms15041

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. Annual Review of Neuroscience, 24(1), 167–202. https://doi.org/10.1146/annurev.neuro.24.1.167

Mohler, C. W., Goldberg, M. E., & Wurtz, R. H. (1973). Visual receptive fields of frontal eye field neurons. Brain Research, 61(3), 85–93. https://doi.org/10.1016/0006-8993(73)90543-X

Mohler, C. W., & Wurtz, R. H. (1976). Organization of monkey superior colliculus: Intermediate layer cells discharging before eye movements. Journal of Neurophysiology, 39(4), 722–744. https://doi.org/10.1152/jn.1976.39.4.722

Monteon, J. A., Constantin, A. G., Wang, H., Martinez-Trujillo, J., & Crawford, J. D. (2010). Electrical stimulation of the frontal eye fields in the head-free macaque evokes kinematically normal 3D gaze shifts. Journal of Neurophysiology, 104(6), 3462–3475. https://doi.org/10.1152/jn.01032.2009

Moon, S. Y., Barton, J. J. S., Mikulski, S., Polli, F. E., Cain, M. S., Vangel, M., … Manoach, D. S. (2007). Where left becomes right: A magnetoencephalographic study of sensorimotor transformation for antisaccades. NeuroImage, 36(4), 1313–1323. https://doi.org/10.1016/j.neuroimage.2007.04.040

Munoz, D. P., & Everling, S. (2004). Look away: The anti-saccade task and the voluntary control of eye movement. Nature Reviews Neuroscience, 5(3), 218–228. https://doi.org/10.1038/nrn1345

Munoz, D. P., & Schall, J. D. (2004). Concurrent, distributed control of saccade initiation in the frontal eye field and superior colliculus. In W. C. Hall & A. Moschovakis (Eds.), The superior colliculus: New approaches for studying sensorimotor integration, (pp. 55–82). Boca Raton, FL: CRC Press.

Munoz, D. P., & Wurtz, R. H. (1995). Saccade-related activity in monkey superior colliculus. I. Characteristics of burst and buildup cells. Journal of Neurophysiology, 73(6), 2313–2333.

Nacher, V., Arora, H. K., Bharmaura, V., Yan, X., Sun, S., Wang, H., & Crawford, J. D. (2019). Rapid visuomotor transformations and multiple gain field effects in primate ventral premotor (PMv) cortex during head-unrestrained reaches. Program No. 404.15. 2019 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience.

Ninomiya, T., Sawamura, H., Inoue, K. I., & Takada, M. (2012). Segregated pathways carrying frontally derived top-down signals to visual areas MT and V4 in macaques. Journal of Neuroscience, 32(20), 6851–6858. https://doi.org/10.1523/JNEUROSCI.6295-11.2012

Omran, M., Kaufman, M. T., Hatsopoulos, N. G., & Cheney, P. D. (2017). Perspectives on classical controversies about the motor cortex. Journal of Neurophysiology, 118(3), 1828–1848. https://doi.org/10.1152/jn.00795.2016

Optican, L. M. (2005). Sensorimotor transformation for visually guided saccades. Annals of the New York Academy of Sciences, 1039(1), 132–148. https://doi.org/10.1196/annals.1325.013

O’Reilly, R. C., & Frank, M. J. (2006). Making working memory work: A computational model of learning in the prefrontal cortex and basal ganglia. Neural Computation, 18(2), 283–328. https://doi.org/10.1162/08997660677593909

Paneri, S., & Gregoriou, G. G. (2017). Top-down control of visual attention by the prefrontal cortex. Functional specialization and long-range interactions. Frontiers in Neuroscience, 11, 545.

Paré, M., Crommelinck, M., & Guittion, D. (1994). Gaze shifts evoked by stimulation of the superior colliculus in the head-free cat conform to the motor map but also depend on stimulus strength and fixation.
activity. *Experimental Brain Research*, 101(1), 123–139. https://doi.org/10.1007/BF00243222

Paré, M., & Guittton, D. (1990). Gaze-related activity of brainstem omnipause neurons during combined eye-head gaze shifts in the alert cat. *Experimental Brain Research*, 83(1), 210–214. https://doi.org/10.1007/BF00232210

Paré, M., & Hanes, D. P. (2003). Controlled movement processing: Superior colliculus activity associated with countermanded saccades. *Journal of Neuroscience*, 23(16), 6480–6489. https://doi.org/10.1523/JNEUROSCI.23-16-06480.2003

Parrhasarathy, H. B., Schall, J. D., & Graybiel, A. M. (1992). Distributed but convergent ordering of corticostriatal projections: Analysis of the frontal eye field and the supplementary eye field in the macaque monkey. *Journal of Neuroscience*, 12(11), 4468–4488. https://doi.org/10.1523/JNEUROSCI.12-11-04468.1992

Passingham, R. (2009). How good is the macaque monkey model of the human brain? *Current Opinion in Neurobiology*, 19(1), 6–11. https://doi.org/10.1016/j.conb.2009.01.002

Peel, T. R., Dash, S., Lomber, S. G., & Corneil, B. D. (2017). Frontal eye field inactivation diminishes superior colliculus activity, but delayed saccadic accumulation governs reaction time increases. *Journal of Neuroscience*, 37(48), 11715–11730. https://doi.org/10.1523/JNEUROSCI.2664-17.2017

Perry, V. H., & Covey, A. (1984). Retinal ganglion cells that project to the superior colliculus and pretectum in the macaque monkey. *Neuroscience*, 12(4), 1125–1137. https://doi.org/10.1016/0306-4522(84)90007-1

Pesaran, B., Nelson, M. J., & Andersen, R. A. (2006). Dorsal premotor neurons encode the relative position of the hand, eye, and goal during reach planning. *Neuron*, 51(1), 125–134. https://doi.org/10.1016/j.neuron.2006.05.025

Platt, M. L., & Glimcher, P. W. (1998). Response fields of intraparietal neurons quantified with multiple saccadic targets. *Experimental Brain Research*, 121(1), 65–75. https://doi.org/10.1007/s002210050438

Ploner, C. J., Rivaud-Pechoux, S., Gaymard, B. M., Agid, Y., & Pierrot-Deseilligny, C. (1999). Errors of memory-guided saccades in humans with lesions of the frontal eye field and the dorsolateral prefrontal cortex. *Journal of Neurophysiology*, 82(2), 1086–1090. https://doi.org/10.1152/jn.1999.82.2.1086

Pouget, A., & Snyder, L. H. (2000). Computational approaches to sensorimotor transformations. *Nature Neuroscience*, 3(11s), 1192. https://doi.org/10.1038/81469

Pouget, P., Stepniewska, I., Crowder, E. A., Leslie, M. W., Emeric, E. E., Nelson, M. J., & Schall, J. D. (2009). Visual and motor connectivity and the distribution of calcium-binding proteins in macaque frontal eye field: Implications for saccade target selection. *Frontiers in Neuroanatomy*, 3, 2. https://doi.org/10.3389/neuro.05.002.2009

Pruszynski, J. A., & Zylberberg, J. (2019). The language of the brain: Real-world neural population codes. *Current Opinion in Neurobiology*, 58, 30–36.

Quesy, S., Quintet, J., & Freedman, E. G. (2010). The locus of motor activity in the superior colliculus of the rhesus monkey is unaltered during saccadic adaptation. *Journal of Neuroscience*, 30(42), 14235–14244. https://doi.org/10.1523/JNEUROSCI.13111-10.2010

Ray, S., Pouget, P., & Schall, J. D. (2009). Functional distinction between visuomovement and movement neurons in macaque frontal eye field during saccade countermanding. *Journal of Neurophysiology*, 102(6), 3091–3100. https://doi.org/10.1152/jn.00270.2009

Redgrave, P., Coizet, V., Comoli, E., McHaffie, J. G., Leriche Varquez, M., Vautrelle, N., … Overton, P. G. (2010). Interactions between the midbrain superior colliculus and the basal ganglia. *Frontiers in Neuroanatomy*, 4, 132. https://doi.org/10.3389/fnana.2010.00132

Robinson, D. A. (1973). Models of the saccadic eye movement control system. *Kybernetik*, 14(2), 71–83. https://doi.org/10.1007/BF00289006

Russo, G. S., & Bruce, C. J. (1994). Frontal eye field activity preceding aurally guided saccades. *Journal of Neurophysiology*, 71(3), 1250–1253. https://doi.org/10.1152/jn.1994.71.3.1250

Sadeh, M., Sajad, A., Wang, H., Yan, X., & Crawford, J. D. (2015). Spatial transformations between superior colliculus visual and motor response fields during head-unrestrained gaze shifts. *European Journal of Neuroscience*, 42(11), 2934–2951. https://doi.org/10.1111/ejn.13093

Sadeh, M., Godlove, D. C., & Schall, J. D. (2019). Cortical microcircuitry of performance monitoring. *Nature Neuroscience*, 22(2), 265–274. https://doi.org/10.1038/s41593-018-0309-8

Sajad, A., Sadeh, M., Keith, G. P., Yan, X., Wang, H., & Crawford, J. D. (2015). Visual–motor transformations within frontal eye fields during head-unrestrained gaze shifts in the monkey. *Cerebral Cortex*, 25(10), 3932–3952. https://doi.org/10.1093/cercor/bhu279

Sajad, A., Sadeh, M., Yan, X., Wang, H., & Crawford, J. D. (2016). Transition from target to gaze coding in primate frontal eye field during memory delay and memory–motor transformation. *eNeuro*, 3(2), https://doi.org/10.1523/ENEURO.0040-16.2016

Salinas, E., & Abbott, L. F. (2001). Coordinate transformations in the visual system: How to generate gain fields and what to compute with them. In M. A. L. Nicolelis (Ed.), *Progress in brain research*., (Vol. 130, pp. 175–190). Elsevier. https://doi.org/10.1016/S0079-6123(01)0012-2

Sato, T. R., & Schall, J. D. (2003). Effects of stimulus-response compatibility on neural selection in frontal eye field. *Neuron*, 38(4), 637–648. https://doi.org/10.1016/S0896-6273(03)00237-X

Schall, J. D. (2015). Visuomotor functions in the frontal lobe. *Annual Review of Vision Science*, 1, 469–498. https://doi.org/10.1146/annurev-vision-082114-035317

Schall, J. D. (2019). Accumulators, Neurons, and Response Time. *Trends in Neurosciences*, 42(12), 848–860.. https://doi.org/10.1016/j.tins.2019.10.001

Schall, J. D., Morel, A., King, D. J., & Bullier, J. (1995). Topography of visual cortex connections with frontal eye field in macaque: Convergence and segregation of processing streams. *Journal of Neurophysiology*, 15, 4464–4487. https://doi.org/10.1523/JNEUROSCI.15-06-04464.1995

Schall, J. D., Purcell, B. A., Heitz, R. P., Logan, G. D., & Palmeri, T. J. (2011). Neural mechanisms of saccade target selection: Gated accumulator model of the visual–motor cascade. *European
Thompson, K. G., & Bichot, N. P. (2005). A visual salience map in the primate frontal eye field. Progress in Brain Research, 147, 249–262.

Tweed, D. B., Haslwanter, T. P., Happe, V., & Fetter, M. (1999). Non-commutativity in the brain. Nature, 399(6733), 261. https://doi.org/10.1038/20441

van Beers, R. J. (2007). The sources of variability in saccadic eye movements. Journal of Neuroscience, 27(33), 8757–8770. https://doi.org/10.1523/JNEUROSCI.2311-07.2007

van Bergen, R. S., Ma, W. J., Pratte, M. S., & Jehee, J. F. (2015). Sensory uncertainty decoded from visual cortex predicts behavior. Nature Neuroscience, 18(12), 1728. https://doi.org/10.1038/nn.4150

Walton, M. M., Bechara, B., & Gandhi, N. J. (2007). Role of the primate superior colliculus in the control of head movements. Journal of Neurophysiology, 98(4), 2022–2037. https://doi.org/10.1152/jn.00258.2007

Watanabe, K., & Funahashi, S. (2007). Prefrontal delay-period activity reflects the decision process of a saccade direction during a free-choice ODR task. Cerebral Cortex, 17(suppl_1), i88–i100. https://doi.org/10.1093/cercor/bhm102

Westendorff, S., Klaes, C., & Gail, A. (2010). The cortical timeline for deciding on reach motor goals. Journal of Neuroscience, 30(15), 5426–5436. https://doi.org/10.1523/JNEUROSCI.4628-09.2010

Weyand, T. G., & Gafka, A. C. (1998). Corticostriatal and corticocortical neurons in area 6 of the cat during fixation and eye movements. Visual Neuroscience, 15(1), 141–151.

White, J. M., Sparks, D. L., & Stanford, T. R. (1994). Saccades to remembered target locations: An analysis of systematic and variable errors. Vision Research, 34(1), 79–92. https://doi.org/10.1016/0042-6989(94)90259-3

Wimmer, K., Nykamp, D. Q., Constantinidis, C., & Compte, A. (2014). Bump attractor dynamics in prefrontal cortex explains behavioral precision in spatial working memory. Nature Neuroscience, 17(3), 431. https://doi.org/10.1038/nn.3645

Wurtz, R. H., & Albano, J. E. (1980). Visual-motor function of the primate superior colliculus. Annual Review of Neuroscience, 3(1), 189–226. https://doi.org/10.1146/annurev.ne.03.030180.001201

Wurtz, R. H., Sommer, M. A., Paré, M., & Ferraina, S. (2001). Signal transformations from cerebral cortex to superior colliculus for the generation of saccades. Vision Research, 41(25–26), 3399–3412. https://doi.org/10.1016/S0042-6989(01)00066-9

Zhang, M., & Barash, S. (2000). Neuronal switching of sensorimotor transformations for antisaccades. Nature, 408(6815), 971. https://doi.org/10.1038/35050097

Zheng, T., & Wilson, C. J. (2002). Corticostriatal combinatorics: The implications of corticostriatal axonal arborizations. Journal of Neurophysiology, 87(1007–1017), pmid:11826064.

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